

micrograms of cefamandole per milligram on an anhydrous basis.

- (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 containing 100 milligrams per milliliter is not less than 3.5 and not more than 7.0.
- (vii) It passes the identity test.

(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 potency, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples required:

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

(b) For sterility testing: 20 packages, each containing equal portions of approximately 250 milligrams.

(b) *Tests and methods of assay—(1) Potency.* Use any of the following methods; however, the results obtained from the hydroxylamine colorimetric assay shall be conclusive.

(i) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except use the cefamandole working standard.

(ii) *Polarographic assay.* Proceed as directed in § 436.324 of this chapter.

(iii) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to obtain a concentration of 1 milligram of cefamandole per milliliter (estimated). Hydrolyze this solution in a 37° C constant temperature water bath for 60 minutes. Further dilute a portion of the hydrolyzed solution with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 2.0 micrograms of cefamandole per milliliter (estimated).

(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 cefamandole 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 § 436.211 of this chapter, using the mineral oil mull prepared as described in paragraph (b)(2) of that section.

[47 FR 32708, June 1, 1982, as amended at 50 FR 19919, May 13, 1985]

§ 442.9a Sterile cefamandole sodium.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Sterile cefamandole sodium is 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[(hydroxyphenylacetyl)amino]-3-[[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-, monosodium salt [6R-[6 α , 7 β (R*)]]-. It is so purified and dried that:

(i) Its cefamandole content is not less than 860 micrograms and not more than 1,000 micrograms of cefamandole per milligram on an anhydrous basis.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 3.0 percent.

(vi) Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 3.5 and not more than 7.0.

(vii) It passes the identity test.

(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 cefamandole content, sterility, pyrogens, moisture, pH, and identity.

(ii) Samples required:

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

(b) For sterility testing: 20 packages, each containing equal portions of approximately 250 milligrams.

(b) *Tests and methods of assay*—(1) *Cefamandole content*. Proceed as directed in § 436.324 of this chapter.

(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 cefamandole 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 § 436.211 of this chapter, using the mineral oil mull prepared as described in paragraph (b)(2) of that section.

[47 FR 20756, May 14, 1982, as amended at 50 FR 19919, May 13, 1985]

§ 442.10 Cefazolin.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Cefazolin is 3-[[5-methyl-1,3,4-thiadiazol-2-yl)-thio]methyl]-7-[2-(1H-tetrazol-1-yl) acetamido]-3-cephem-4-carboxylic acid. It is so purified and dried that:

(i) Its cefazolin content is not less than 950 micrograms and not more than 1,030 micrograms of cefazolin per milligram calculated on an anhydrous basis.

(ii) Its moisture content is not more than 2 percent.

(iii) Its heavy metals content is not more than 20 parts per million.

(iv) It gives a positive identity test for cefazolin.

(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 cefazolin content, moisture, heavy metals, and identity.

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

Research: Nine packages, each containing approximately 500 milligrams, and one package containing approximately 5 grams.

(b) *Tests and methods of assay*—(1) *Cefazolin content*. Proceed as directed in § 436.342 of this chapter.

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

(3) *Heavy metals*. Proceed as directed in § 436.208 of this chapter.

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

[48 FR 33479, July 22, 1983, as amended at 55 FR 11582, Mar. 29, 1990]

§ 442.11a Sterile cefazolin sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Sterile cefazolin sodium is the sodium salt of 3-[[5-methyl-1,3,4-thiadiazol-2-yl)-thio]methyl]-7-[2-(1H-tetrazol-1-yl)acetamido]-3-cephem-4-carboxylic acid. It is so purified and dried that:

(i) Its potency is not less than 850 micrograms and not more than 1050 micrograms of cefazolin per milligram calculated on an anhydrous basis. If it is packaged for dispensing, its cefazolin content is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of cefazolin that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 6 percent.

(vi) Its pH in an aqueous solution containing 100 milligrams of cefazolin per milliliter is not less than 4.5 and not more than 6.0.

(vii) The specific rotation in a 0.1M sodium bicarbonate solution containing 50 milligrams of cefazolin per milliliter at 25° C. is $-17^{\circ} \pm 7^{\circ}$ calculated on an anhydrous basis.

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

(2) *Labeling*. It shall be labeled in accordance with the requirements of § 432.5 of this chapter.