

identity test. The ceftazidime pentahydrate conforms to the standards prescribed by § 442.16(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 ceftazidime pentahydrate used in making the batch for potency, loss on drying, pH, crystallinity, identity, and high molecular weight polymer content.

(B) The batch for ceftazidime content, sterility, pyrogens, pH, and identity.

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

(A) The ceftazidime pentahydrate used in making the batch: 10 packages, each containing 500 milligrams.

(B) The batch:

(1) For all tests except sterility: A minimum of 10 immediate containers.

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

(b) *Tests and methods of assay.* Thaw the sample as directed in the labeling. The sample solution used for testing must be at room temperature.

(1) *Ceftazidime content.* Proceed as directed in § 442.216(b)(1), except prepare the sample solution and calculate the ceftazidime content as follows:

(i) *Preparation of sample solution.* Remove an accurately measured representative portion from each container immediately after thawing and reaching room temperature and dilute with mobile phase to obtain a solution containing 100 micrograms of ceftazidime per milliliter (estimated). Prepare the sample solution just prior to its introduction into the chromatograph.

(ii) *Calculation.* Calculate the milligrams of ceftazidime per milliliter of sample as follows:

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

where:

A_u =Area of the ceftazidime peak in the chro-

matogram of the sample (at a retention time equal to that observed for the standard);

A_s =Area of the ceftazidime peak in the chromatogram of the ceftazidime working standard;

P_s =Ceftazidime activity in the ceftazidime 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, except inject a sufficient volume of the diluted solution to deliver 80 milligrams of ceftazidime per kilogram.

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

(5) *Identify.* The high performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the ceftazidime working standard.

[54 FR 40652, Oct. 3, 1989]

§ 442.217 Ceftizoxime injectable dosage forms.

§ 442.217a Sterile ceftizoxime sodium.

The requirements for certification and the tests and methods of assay for sterile ceftizoxime sodium packaged for dispensing are described in § 442.17a.

[48 FR 46272, Oct. 12, 1983. Redesignated at 49 FR 49286, Dec. 19, 1984]

§ 442.217b Ceftizoxime sodium injection.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Ceftizoxime sodium injection is a frozen aqueous solution of ceftizoxime sodium with one or more suitable and harmless buffer substances in an isoosmotic diluent. Each milliliter contains ceftizoxime sodium equivalent to either 20 milligrams or 40 milligrams of ceftizoxime per milliliter. Ceftizoxime content is satisfactory if it is not less than 90 percent and not more than 115 percent of the represented number of milligrams of ceftizoxime. It is sterile. It is nonpyrogenic. Its pH is not less than

5.5 and not more than 8.0. It passes the identity test. The ceftizoxime sodium used conforms to the standards prescribed by § 442.17(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 ceftizoxime sodium used in making the batch for ceftizoxime content, moisture, pH, identity, and crystallinity.

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

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

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

(b) The batch:

(1) For all tests except sterility: A minimum of 10 immediate containers.

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

(b) *Tests and methods of assays.* Thaw the sample as directed in the labeling. The sample solution used for testing must be at room temperature.

(1) *Ceftizoxime content.* Proceed as directed in § 436.345 of this chapter, except prepare the sample solution and calculate the ceftizoxime content as follows:

(i) *Sample solution.* Using a suitable hypodermic needle and syringe, transfer an accurately measured representative portion from each container, equivalent to 40 milligrams of ceftizoxime, to a 100-milliliter volumetric flask. Dilute to volume with pH 7.0 buffer solution and mix. Transfer 10.0 milliliters of this solution to a 200-milliliter volumetric flask, add 5.0 milliliters of internal standard solution, dilute to volume with pH 7.0 buffer solution, and mix.

(ii) *Calculations.* Calculate the milligrams of ceftizoxime per milliliter of sample as follows:

$$\text{Milligrams of ceftizoxime per milliliter} = \frac{R_u \times P_s \times d}{R_s \times 1,000}$$

where:

R_u =Area of the ceftizoxime peak in the chromatogram of the sample (at a retention time equal to that observed for the standard)/Area of the internal standard peak;

R_s =Area of the ceftizoxime peak in the chromatogram of the ceftizoxime working standard/Area of the internal standard peak;

P_s =Ceftizoxime activity in the ceftizoxime 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(a) of this chapter, except inject a sufficient volume of the undiluted solution to deliver 50 milligrams of ceftizoxime per kilogram.

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

(5) *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 ceftizoxime working standard.

[49 FR 49286, Dec. 19, 1984; 50 FR 253, Jan. 3, 1985, as amended at 55 FR 11583, Mar. 29, 1990]

§ 442.218 Cefuroxime injectable dosage forms.

§ 442.218a Sterile cefuroxime sodium.

The requirements for certification and the tests and methods of assay for sterile cefuroxime sodium packaged for dispensing are described in § 442.18a.

[48 FR 38461, Aug. 24, 1983. Redesignated at 54 FR 40654, Oct. 3, 1989]

§ 442.218b Cefuroxime sodium injection.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cefuroxime sodium injection is a frozen, aqueous, iso-osmotic solution of cefuroxime sodium which may contain one or more suitable and harmless buffer substances and a tonicity adjusting agent. Each milliliter