Determine the end-point potentiometrically using a glass calomel combination electrode. Each milliliter of 0.1*N* sulfuric acid is equivalent to 8.401 milligrams of sodium bicarbonate.

(8) *Identity*. Using a 0.0025-percent solution of the sample in water and a suitable spectrophotometer, record the ultraviolet absorption spectrum from 220 to 310 nanometers. The spectrum compares qualitatively to that of the working standard similarly tested.

[40 FR 5355, Feb. 5, 1975, as amended at 46 FR 38503, July 28, 1981; 48 FR 51293, Nov. 8, 1983; 49 FR 5097, Feb. 10, 1984; 50 FR 19919, May 13, 1985]

§ 442.229 Sterile cephapirin sodium.

The requirements for certification and the tests and methods of assay for sterile cephapirin sodium packaged for dispensing are described in § 442.29a.

§ 442.240 Cephradine injectable dosage forms.

§ 442.240a Cephradine for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Cephradine for injection is a dry mixture of cephradine and one or more suitable and harmless solubilizing and buffering agents. Its potency is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of cephradine that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 5.0 percent. Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 8.0 and not more than 9.6. The cephradine used conforms to the standards prescribed by § 442.40a(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 sterile cephradine used in making the batch for potency, moisture, pH, cephalexin content, identity, and crystallinity.

(*b*) The batch for potency, sterility, pyrogens, loss on drying, and pH.

(ii) Samples required:

(*a*) The cephradine 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 assay*—(1) *Potency*. Use either of the following methods; however, the results obtained from the microbiological agar diffusion 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: Reconstitute the sample as directed in the labeling for intramuscular use. 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. Further dilute an aliquot of this solution with solution 1 to the reference concentration of 10.0 micrograms of cephradine per milliliter (estimated).

(ii) *Hydroxylamine colorimetric assay*. Proceed as directed in § 442.40(b)(1)(ii), preparing the sample as follows: Reconstitute the sample as directed in the labeling for intramuscular use. 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. Further dilute an aliquot of this solution with distilled water to 1 milligram of cephradine per milliliter (estimated)

(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 80 milligrams of cephradine per milliliter.

(4) [Reserved]

(5) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

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

[40 FR 51626, Nov. 6, 1975. Redesignated at 43 FR 14646, Apr. 7, 1978; 50 FR 19919, May 13, 1985]

§ 442.240b Sterile cephradine.

The requirements for certification and the tests and methods of assay for sterile cephradine packaged for dispensing are described in § 442.40a.

[43 FR 14646, Apr. 7, 1978]

§ 442.250 Ceforanide for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Ceforanide for injection is a dry mixture of ceforanide and *L*-lysine. Each milligram of ceforanide for injection contains not less than 900 micrograms and not more than 1,050 micrograms of ceforanide when corrected for *L*-lysine content. Its ceforanide content is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of ceforanide that it is represented to contain. It is sterile. It is nonpyrogenic. Its moisture content is not more than 3.0 percent. When reconstituted as directed in the labeling, its pH is not less than 5.5 and not more than 8.5. The ceforanide used conforms to the standards prescribed by § 442.50a(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 sterile ceforanide used in making the batch for ceforanide content, moisture, pH, and identity.

(*b*) The batch for ceforanide content, sterility, pyrogens, moisture, and pH.

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

(*a*) The ceforanide 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 assay*—(1) *Ceforanide content.* Determine both micrograms of ceforanide per milligram of sample and milligrams of ceforanide per container. Proceed as directed in § 436.348 of this chapter, preparing the sample solution and calculating the ceforanide content as follows:

(i) *Preparation of sample solution.* Use separate containers for preparation of each sample solution as described in paragraph (b)(1)(i) (*a*) and (*b*) of this section.

(*a*) *Micrograms of ceforanide per milligram.* Prepare a solution containing 1.0 milligrams per milliliter in mobile phase. Inject each sample within 5 minutes after dissolution.

(*b*) *Milligrams of ceforanide per container.* Reconstitute the sample with distilled water as directed in the labeling. 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 ceforanide content in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute with mobile phase to obtain a stock solution containing 10.0 milligrams per milliliter (estimated). Immediately dilute an aliquot of the stock solution with mobile phase to a concentration of 1.0 milligrams of ceforanide per milliliter (estimated). Inject within 5 minutes, after preparation.

(ii) *Calculations*—(*a*) *Micrograms of ceforanide per milligram.* Calculate the micrograms of ceforanide per milligram of sample as follows:

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

where:

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

A_s=Area of the ceforanide peak in the chromatogram of the ceforanide working