

lyophilized powder, its moisture content is not more than 2.0 percent.

(iii) The pH of an aqueous solution containing 250 milligrams per milliliter is not less than 4.5 and not more than 6.5.

(iv) It passes the identity test if the retention times of the sample and working standard agree within  $\pm 3.0$  percent.

(v) It is crystalline, except if it is the lyophilized powder.

(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 cefoperazone content, moisture, pH, identity, and crystallinity (if it is not the lyophilized powder).

(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) *Cefoperazone content.* Proceed as directed in § 436.338 of this chapter.

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

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 250 milligrams per milliliter.

(4) *Identity.* From the high-performance liquid chromatograms of the sample and the cefoperazone working standard determined as directed in paragraph (b)(1) of this section, calculate the adjusted retention times of the cefoperazone in the sample and standard solutions as follows:

Adjusted retention time of cefoperazone =  $t - t_0$   
where:

$t$  = Retention time measured from point of injection into the chromatograph until the maximum of the cefoperazone sample or working standard peak appears on the chromatogram; and

$t_0$  = Retention time measured from point of injection into the chromatograph until the maximum of nonretarded solute appears in the chromatogram.

The sample and the cefoperazone working standard should have corresponding

adjusted cefoperazone retention times within  $\pm 3.0$  percent.

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

[51 FR 36688, Oct. 15, 1986, as amended at 55 FR 11583, Mar. 29, 1990]

#### § 442.12a Sterile cefoperazone sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile cefoperazone sodium is the sodium salt of (6*R*, 7*R*)-7-[(*R*)-2-(4-ethyl-2,3-dioxo-1-piperazinecarboxamido)-2-(*p*-hydroxyphenyl)acetamido]-3-[[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate. It is a white to off-white crystalline powder or it may be a lyophilized powder. It is so purified and dried that:

(i) If the cefoperazone sodium is not packaged for dispensing, its cefoperazone content is not less than 870 micrograms and not more than 1,015 micrograms of cefoperazone per milligram on an anhydrous basis. If the cefoperazone sodium is packaged for dispensing, its cefoperazone content is not less than 870 micrograms and not more than 1,015 micrograms of cefoperazone per milligram on an anhydrous basis and also, each container contains not less than 90 percent and not more than 120 percent of the number of milligrams of cefoperazone that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) Its moisture content is not more than 5.0 percent, except if it is the lyophilized powder, its moisture content is not more than 2.0 percent.

(v) Its pH in an aqueous solution containing 250 milligrams per milliliter is not less than 4.5 and not more than 6.5.

(vi) It passes the identity test if the retention times of the sample and working standard agree within  $\pm 3$  percent.

(vii) It is crystalline, except if it is the lyophilized powder, it is not 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 cefoperazone content, sterility, pyrogens, moisture, pH, identity, and crystallinity (if it is not the lyophilized powder).

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

(a) If the batch is packaged for re-packaging or for manufacturing use:

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

(2) For sterility testing: 20 packages, each containing equal portions of approximately 300 milligrams.

(b) If the batch is packaged for dispensing:

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

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

(b) *Tests and methods of assay*—(1) *Cefoperazone content.* Proceed as directed in §436.338 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 10 milligrams of cefoperazone 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 250 milligrams per milliliter.

(6) *Identity.* From the high-pressure liquid chromatograms of the sample and the cefoperazone working standard determined as directed in paragraph (b)(1) of this section, calculate the adjusted retention times of the cefoperazone in the sample and standard solutions as follows:

Retention time of cefoperazone =  $t_s - t_r$

where:

$t_s$  = Retention time of working standard measured from point of injection into the chromatograph until the peak maximum appears on the chromatogram; and

$t_r$  = Retention time of sample measured from point of injection into the chromatograph until the peak maximum appears on the chromatogram.

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

[48 FR 790, Jan. 7, 1983; 43 FR 7439, Feb. 22, 1983; 48 FR 28250, June 21, 1983, as amended at 55 FR 11583, Mar. 29, 1990]

**§ 442.13 Cefotaxime sodium.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefotaxime sodium is the sodium salt of 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-7-[[2-amino-4-thiazolyl] (methoxyimino)acetyl]amino]-8-oxo-[6R-[6 alpha, 7 beta(Z)]]-. It is so purified and dried that:

(i) Its potency is not less than 855 micrograms and not more than 1,002 micrograms of cefotaxime per milligram on an anhydrous basis.

(ii) Its moisture content is not more than 6.0 percent.

(iii) Its pH in an aqueous solution is not less than 4.5 and not more than 6.5.

(iv) It gives a positive 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, moisture, pH, and identity.

(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) *Potency.* Use either of the following methods; however, the results obtained from the hydroxylamine colorimetric 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: Dissolve an accurately weighed sample in sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution