

§ 442.154b

21 CFR Ch. I (4–1–98 Edition)

F_1 = Volume of internal standard used in the sample preparation, in milliliters;
 F_2 = 0.766; The ratio of molecular weight for free-acid cefpodoxime over the molecular weight of cefpodoxime proxetil (427.46/557.61);
 F_3 = Volume of internal standard used in the standard preparation, in milliliters;
 F_4 = Average tablet weight, i.e., weight of tablets used in sample preparation divided by the number of tablets; and
 P = Purity of the cefpodoxime proxetil reference standard, expressed as a decimal.

(2) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter, except dry the sample at a temperature of 80° C and a pressure of 5 millimeters of mercury or less for 16 hours.

(3) *Dissolution test.* Proceed as directed in § 436.215 of this chapter. The quantity Q (the amount of cefpodoxime activity dissolved) is 70 percent within 30 minutes.

(4) *Identity.* Using the high-performance liquid chromatographic procedure described in paragraph (b)(1) of this section, the retention times for the peaks of the active ingredients must be within 2 percent of the retention times for the peaks of the corresponding reference standards.

[60 FR 58232, Nov. 27, 1995]

§ 442.154b Cefpodoxime proxetil granules for oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cefpodoxime proxetil granules for oral suspension is cefpodoxime proxetil and one or more suitable and harmless preservatives, sweeteners, suspending agents, buffers, and flavorings. When constituted as directed in the labeling, each milliliter contains the equivalent of either 10 or 20 milligrams cefpodoxime activity. Its cefpodoxime proxetil content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of cefpodoxime that it is represented to contain. Its loss on drying is not more than 0.5 percent. When constituted as described in the labeling, the pH of the suspension is not less than 4 and not more than

5.5. It passes the identity test. The cefpodoxime proxetil used conforms to the standards prescribed by § 442.54(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 cefpodoxime proxetil used in making the batch for potency, isomer ratio, moisture, and identity.

(B) The batch for content, loss on drying, pH, and identity.

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

(A) The cefpodoxime proxetil used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 10 intermediate containers.

(b) *Tests and methods of assay—(1) Cefpodoxime content.* Proceed as directed in § 442.54(b)(1), preparing the sample solution and calculating the cefpodoxime content as follows:

(i) *Preparation of sample solution.* Reconstitute as directed in the labeling. Immediately before sampling the suspension, shake vigorously for several seconds. Into a suitable container, accurately weigh out 6 grams of the 50 milligrams per 5 milliliters suspension, or 3 grams of the 100 milligrams per 5 milliliters suspension. Add 5 milliliters of internal standard solution and 25 milliliters of dilution solvent. Shake for 30 minutes using a horizontal platform shaker or equivalent. Centrifuge for about 10 minutes at 3,000 revolutions per minute until the particulate matter has settled. Withdraw a 1 milliliter aliquot of the supernatant and dilute with 1 milliliter of dilution solvent. The sample solutions are stable for at least 48 hours. Refrigeration is not recommended.

(ii) *Calculations.* Calculate the cefpodoxime content as follows:

$$\text{Milligrams of cefpodoxime per 5 milliliters of suspension} = (R_{sam}/R_{std}) \times (W_{std}/W_{sam}) \times (F_1/F_3) \times (F_2/F_4) \times F_5 \times P$$

where:

R_{sam} = Ratio of cefpodoxime proxetil peaks area (sum of both epimers) to the internal standard peak area in the sample preparation;

R_{std} = Ratio of cefpodoxime proxetil peaks area (sum of both epimers) to the internal standard peak area in the standard preparation;

W_{std} = Weight of cefpodoxime proxetil reference standard, in milligrams;

W_{sam} = Weight of sample, in grams;

F_1 = Volume of internal standard used in the sample; preparation, in milliliters;

F_2 = 0.766; The ratio of molecular weight for free-acid cefpodoxime over the molecular weight of cefpodoxime proxetil (427.46/557.61);

F_3 = Volume of internal standard used in the standard preparation, in milliliters;

F_4 = 0.2; Factor to convert to 5 milliliters;

F_5 = Specific gravity of suspension for milligram per 5 milliliter calculated on the air-free basis (specific gravity is determined on a sample of suspension that has been shaken gently on a platform shaker under vacuum for 2 hours); and

P = Purity of the cefpodoxime proxetil reference standard, expressed as a decimal.

(2) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter, except dry the sample at a temperature of 80° C and a pressure of 5 millimeters of mercury or less for 16 hours.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the drug constituted as directed in the labeling.

(4) *Identity.* Using the high-performance liquid chromatographic procedure described in paragraph (b)(1) of this section, the retention times for the peaks of the active ingredients must be within 2 percent of the retention times for the peaks of the corresponding reference standards.

[60 FR 58233, Nov. 27, 1995]

§ 442.180 Cefprozil oral dosage forms.

§ 442.180a Cefprozil tablets.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Cefprozil tablets are composed of cefprozil and one or more suitable and harmless diluents, binders, lubricants, colorings, and coating substances. Each tablet contains cefprozil

equivalent to either 250 milligrams or 500 milligrams of anhydrous cefprozil. The cefprozil content of the tablets is satisfactory if it is not less than 90 percent nor more than 120 percent of the number of milligrams of anhydrous cefprozil that it is represented to contain. The moisture content of the tablets is not more than 7 percent. The tablets pass the dissolution test. The tablets pass the identity tests. The cefprozil used conforms to the standards prescribed by § 442.80(a)(1) of this part.

(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 cefprozil used in making the batch for potency, E-isomer ratio, moisture, pH, crystallinity, and identity.

(B) The batch for content, moisture, dissolution, and identity.

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

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

(B) The batch: A minimum of 100 tablets.

(b) *Tests and methods of assay—(1) Cefprozil content.* Proceed as directed in § 442.80(b)(1) of this part, preparing the sample solution and calculating the cefprozil content as follows:

(i) *Preparation of sample solution.* Place one or a known number of intact tablets into a 250-milliliter volumetric flask containing about 180 milliliters of distilled water. Allow the tablet(s) to disintegrate as aided by swirling and brief ultrasonication. Dilute the contents to volume with distilled water and mix thoroughly. Transfer an aliquot of this solution to a volumetric