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Federal Register
Vol. 53, No. 79
Monday, April 25, 1988

NUCLEAR REGULATORY COMMISSION

10 CFR Part 51

Revision of Telephone Numbers for Environmental Inquiries

AGENCY: Nuclear Regulatory Commission.

ACTION: Final rule.

SUMMARY: The Nuclear Regulatory Commission (NRC) is amending its regulations pertaining to environmental matters to indicate the revision of five telephone numbers that enable prospective applicants or petitioners to consult with members of the NRC's staff. These amendments are required because of the assignment of new telephone numbers in conjunction with the recent consolidation of approximately one-half of the NRC's headquarters staff to its new location in Rockville, Maryland. These amendments are being made to inform NRC licensees and members of the public of the new telephone numbers.

EFFECTIVE DATE: April 25, 1988.

FOR FURTHER INFORMATION CONTACT: Donnie H. Grimsley, Director, Division of Rules and Records, Office of Administration and Resources Management, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: 301–492–7211.

SUPPLEMENTARY INFORMATION: On March 28, 1988, the Office of the Executive Director for Operations and portions of the Office of Governmental and Public Affairs (GPA)—the Director of GPA and the Public Affairs staff—relocated at the agency's new office building in Rockville, Maryland. A notice to that effect was published in the **Federal Register** on March 31, 1988 (53 FR 10449). These amendments reflect the assignment of new telephone numbers to certain relocated agency personnel.

Because these amendments deal solely with the organization and relocation of agency personnel, the notice and comment provisions of the Administrative Procedure Act do not apply under 5 U.S.C. 553(b)(A). These amendments are effective upon publication in the the **Federal Register.** Good cause exists to dispense with the usual 30-day delay in the effective date, because these amendments are of a minor and administrative nature.

Environmental Impact: Categorical Exclusion

The NRC has determined that this final rule is the type of action described in categorical exclusion 10 CFR 51.22(c)(2). Therefore, neither an environmental impact statement nor an environmental assessment has been prepared for this final rule.

Paperwork Reduction Act Statement

This final rule contains no information collection requirements and therefore is not subject to the requirements of the Paperwork Reduction Act of 1980 (44 U.S.C. 3501 *et seq.*).

List of Subjects in 10 CFR Part 51

Administrative practice and procedure, Environmental impact statement, Nuclear materials, Nuclear power plants and reactors, Reporting and recordkeeping requirements.

For the reasons set out in the preamble and under the authority of the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974, as amended, and 5 U.S.C. 553, the NRC is adopting the following amendments to 10 CFR Part 51.

PART 51—LICENSING AND REGULATORY POLICY AND PROCEDURES FOR ENVIRONMENTAL PROTECTION

1. The authority citation for Part 51 continues to read as follows:

Authority: Sec. 161, 68 Stat. 948, as amended (42 U.S.C. 2201); sec. 201, 88 Stat. 1242, as amended (42 U.S.C. 5841).

2. In § 51.40, paragraph (c) is revised to read as follows:

§ 51.40 Consultation with NRC staff.

* * * * *

(c) Questions concerning environmental matters should be addressed to the following NRC staff offices as appropriate:

(1) *Utilization facilities:* Director, Office of Nuclear Reactor Regulation, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–1270.

(2) *Production facilities:* Director, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–3352.

(3) *Materials licenses:* Director, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–3352.

(4) *Rulemaking:* Director, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–3700.

(5) *General Environmental Matters:* Executive Director for Operations, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–1700.

3. Section 51.121 is revised to read as follows:

§ 51.121 Status of NEPA actions.

Individuals or organizations desiring information on the NRC's NEPA process or on the status of specific NEPA actions should address inquiries to:

(a) *Utilization facilities:* Director, Office of Nuclear Reactor Regulation, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone (301) 492–1270.

(b) *Production facilities:* Director, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–3352.

(c) *Materials licenses:* Director, Office of Nuclear Material Safety and Safeguards, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–3352.

(d) *Rulemaking:* Director, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–3700.

(e) *General Environmental Matters:* Executive Director for Operations, U.S. Nuclear Regulatory Commission, Washington, DC 20555, Telephone: (301) 492–1700.

Dated at Rockville, Maryland, this 13th day of April 1988.

For the Nuclear Regulatory Commission.
Victor Stello, Jr.,
Executive Director for Operations.
[FR Doc. 88-8985 Filed 4-22-88; 8:45 am]
BILLING CODE 7590-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 430, 436, and 442

[Docket No. 88N-0047]

Antibiotic Drugs; Cefmenoxime Hydrochloride for Injection

AGENCY: Food and Drug Administration.
ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the antibiotic drug regulations to provide for the inclusion of accepted standards for a new antibiotic drug, cefmenoxime hydrochloride for injection. The manufacturer has supplied sufficient data and information to establish its safety and efficacy.

DATES: Effective April 25, 1988; comments, notice of participation, and request for hearing by May 25, 1988; data, information, and analyses to justify a hearing by June 24, 1988.

ADDRESS: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Peter A. Dionne, Center for Drug Evaluation and Research (HFN-815), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4290.

SUPPLEMENTARY INFORMATION: FDA has evaluated data submitted in accordance with regulations promulgated under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357), as amended, with respect to a request for approval of a new antibiotic drug, cefmenoxime hydrochloride for injection. The agency has concluded that the data supplied by the manufacturer concerning this antibiotic drug are adequate to establish its safety and efficacy when used as directed in the labeling and that the regulations should be amended in 21 CFR Parts 430, 436, and 442 to provide for the inclusion of accepted standards for the product.

Environmental Impact

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Submitting Comments and Filing Objections

This final rule announces standards that FDA has accepted in a request for approval of an antibiotic drug. Because this final rule is not controversial and because when effective it provides notice of accepted standards, notice and comment procedure and delayed effective date are found to be unnecessary and not in the public interest. This final rule, therefore, is effective April 25, 1988. However, interested persons may, on or before May 25, 1988, submit written comments to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Any person who will be adversely affected by this final rule may file objections to it and request a hearing. Reasonable grounds for the hearing must be shown. Any person who decides to seek a hearing must file: (1) On or before May 25, 1988, a written notice of participation and request for hearing, and (2) on or before June 24, 1988, the data, information, and analyses on which the person relies to justify a hearing, as specified in 21 CFR 314.300. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for hearing that no genuine and substantial issue of fact precludes the action taken by this order, or if a request for hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who request(s) the hearing, making findings and conclusions and denying a hearing. All submissions must be filed in three copies, identified with the docket number appearing in the heading of this order and filed with the Dockets Management Branch.

The procedures and requirements governing this order, a notice of participation and request for hearing, a submission of data, information, and analyses to justify a hearing, other comments, and grant or denial of a hearing are contained in 21 CFR 314.300.

All submissions under this order, except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects

21 CFR Part 430

Administrative practice and procedure, Antibiotics.

21 CFR Part 436

Antibiotics.

21 CFR Part 442

Antibiotics.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, Parts 430, 436, and 442 are amended as follows:

PART 430—ANTIBIOTIC DRUGS; GENERAL

1. The authority citation for 21 CFR Part 430 continues to read as follows:

Authority: Secs. 507, 701(a), 59 Stat. 463 as amended, 52 Stat. 1055 (21 U.S.C. 357, 371(a)); 21 CFR 5.10.

2. Section 430.4 is amended by adding new paragraph (a)(58) to read as follows:

§ 430.4 Definitions of antibiotic substances.

(a) * * *

(58) *Cefmenoxime.* Cefmenoxime is 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-3-[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-, [6*R*-[6-α,7-β(Z)]]-.

3. Section 430.5 is amended by adding new paragraphs (a)(92) and (b)(94) to read as follows:

§ 430.5 Definitions of master and working standards.

(a) * * *

(92) *Cefmenoxime.* The term "cefmenoxime master standard" means a specific lot of cefmenoxime that is designated by the Commissioner as the standard of comparison in determining the potency of the cefmenoxime working standard.

(b) * * *

(94) *Cefmenoxime.* The term "cefmenoxime working standard" means a specific lot of a homogeneous preparation of cefmenoxime

4. Section 430.6 is amended by adding new paragraph (b)(94) to read as follows:

§ 430.6 Definitions of the terms "unit" and "microgram" as applied to antibiotic substances.

* * * * *

(b) * * *

(94) *Cefmenoxime.* The term "microgram" applied to cefmenoxime means the cefmenoxime activity (potency) contained in 1.0482 micrograms of the cefmenoxime master standard.

PART 436—TESTS AND METHODS OF ASSAY OF ANTIBIOTIC AND ANTIBIOTIC-CONTAINING DRUGS

5. The authority citation for 21 CFR Part 436 continues to read as follows:

Authority: Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357); 21 CFR 5.10.

6. Section 436.20 is amended by adding new paragraph (d)(10) to read as follows:

§ 436.20 Sterility test methods and procedures.

* * * * *

(d) * * *

(10) *Diluting fluid J.* Sterilize 2.0 grams of anhydrous sodium carbonate by dry-heating at 180° C for 2 hours. Dissolve in 100 milliliters of diluting fluid A just prior to use.

* * * * *

7. Section 436.31 is amended by adding new paragraph (b)(16) to read as follows:

§ 436.31 Equipment and diluents for use in biological testing.

* * * * *

(b) * * *

(16) Diluent 16 (0.13*M* sterile pyrogen-free sodium carbonate solution). Dissolve 14.0 grams of anhydrous pyrogen-free sodium carbonate (prepared as described in paragraph (a)(5) of this section) in 1,000 milliliters pyrogen-free, distilled water. Sterilize in an autoclave at 121 °C for 20 minutes.

8. Section 436.32 is amended by adding a new paragraph (j) to read as follows:

§ 436.32 Pyrogen test.

* * * * *

(j) *Method 10.* Proceed as directed in paragraph (a) of this section, except dilute the sample with sodium carbonate solution (diluent 16).

9. Part 436 is amended by adding new §§ 436.363 and 436.364 to Subpart F to read as follows:

§ 436.363 High-performance liquid chromatographic assay for cefmenoxime.

(a) *Apparatus.* A suitable high-performance liquid chromatograph equipped with:

(1) A suitable detection system specified in the monograph for the drug being tested;

(2) A suitable recording device of at least 18-centimeter deflection;

(3) A suitable chromatographic data managing system; and

(4) An analytical column, 3 to 30 centimeters long, packed with a material as defined in the monograph for the drug being tested; and if specified in that monograph, the inlet of this column may be connected to a guard column, 3 to 5 centimeters in length, packed with the same material of 30 to 60 micrometers particle size.

(b) *Procedure.* Perform the assay and calculate the drug content using the temperature, instrumental conditions, and calculations specified in the monograph for the drug being tested with a flow rate not to exceed 2.0 milliliters per minute. Use a detector sensitivity setting that gives a peak height for the working standard that is at least 50 percent of scale with typical chart speed of not less than 2.5 millimeters per minute. Use the apparatus described in paragraph (a) of this section; and the reagents and working standard and sample solutions described in the monograph for the drug being tested. Equilibrate and condition the column by passage of 10 to 15 void volumes of mobile phase followed by 5 replicate injections of the same volume (between 10 and 20 microliters) of the working standard solution. Allow an operating time sufficiently long to obtain satisfactory separation and elution of the expected components after each injection. Record the peak responses and calculate the prescribed system suitability requirements described for the system suitability test in paragraph (c) of this section.

(c) *System suitability test.* Using the apparatus and procedure described in this section, test the chromatographic system for assay as follows:

(1) *Tailing factor.* Calculate the tailing factor (T), from distances measured along the horizontal line at 5 percent of the peak height above the baseline, as follows:

$$T = \frac{W_{0.05}}{2f}$$

where:

$W_{0.05}$ = Width of peak at 5 percent height; and

f = Horizontal distance from point of ascent to a point coincident with maximum peak height.

(2) *Efficiency of the column.* Calculate the number of theoretical plates (n) of the column as follows:

$$n = 5.545\left[\frac{t_R}{w_h}\right]^2$$

where:

n = Efficiency, as number of theoretical plates for column;

t_R = Retention time of solute; and

w_h = Peak width at half-height.

(3) *Resolution.* Calculate the resolution (R) as follows:

$$R = \frac{2(t_{Rj} - t_{Ri})}{w_i + w_j}$$

where:

t_{Rj} = Retention time of a solute eluting after i (t_{Rj} is larger than t_{Ri});

t_{Ri} = Retention time of any solute;

w_i = Width of peak at baseline of any solute; and

w_j = Width of peak at baseline of any solute eluting after i.

(4) *Coefficient of variation (Relative standard deviation).* Calculate the coefficient of variation (S_R) in percent) as follows:

$$S_R = \frac{100}{\bar{X}}\left[\frac{\sum_{i=1}^{N}(X_i - \bar{X})^2}{N-1}\right]^{\frac{1}{2}}$$

where:

X is the mean of N individual measurements of X_i. If the complete operating system meets the system suitability requirements of the monograph for the drug being tested, proceed as described in paragraph (b) of this section, using the sample solution in lieu of the working standard solution.

§ 436.364 Atomic absorption test for sodium carbonate content of cefmenoxime hydrochloride for injection.

(a) *Apparatus.* A suitable atomic absorbance spectrophotometer equipped with:

(1) A suitable sodium hollow-cathode discharge lamp;

(2) An oxidizing air-acetylene flame;

(3) A nebulizer-burner system;
(4) An optical dispersing device capable of isolating a resonance line of sodium from other wavelengths produced by the emission source; and
(5) A suitable radiation detector.
(b) *Reagents.* Ionization buffer: Dissolve 19.07 grams of potassium chloride in distilled water and dilute to 1,000 milliliters.
(c) *Preparation of reference standard and sample solutions*—(1) *Reference standard solution.* Accurately weigh approximately 140 milligrams of sodium chloride which has been previously dired for 40 to 50 minutes at a temperature of 500 to 650 °C. Dissolve and dilute with sufficient distilled water to obtain a stock solution containing 5.5 micrograms of sodium per milliliter. Mix 10 milliliters of the stock solution with 10 milliliters of ionization buffer and dilute the mixture with distilled water to obtain a solution containing 0.55 microgram of sodium per milliliter.
(2) *Sample solution.* Dilute the sample solution used in § 442.222(b)(1)(ii)(B)(*1*) of this chapter, with sufficient distilled water to obtain a stock solution containing 5.5 micrograms of sodium per milliliter (estimated). Mix 10 milliliters of the stock solution with 10 milliliters of ionization buffer and dilute the mixture with distilled water to obtain a solution containing 0.55 microgram of sodium per milliliter (estimated).
(3) *Procedure.* Determine the atomic absorbance of the reference standard and sample solutions at a wavelength of 589 nanometers, using the atomic absorbance spectrophotometer and a reagent blank prepared by diluting 10 milliliters of ionization buffer to 100 milliliters with distilled water.
(d) *Calculations.* Calculate the percent sodium carbonate as follows:

$$\text{Percent sodium carbonate} = \frac{A_u \times P_s \times 100 \times 0.9068 \times d}{A_s \times C_u}$$

where:
A_u = Absorbance of sodium in the sample solution;
A_s = Absorbance of sodium in the reference standard solution;
P_s = Milligrams of sodium chloride per milliliter of the reference standard solution;
C_u = Milligrams of sample per milliliter of sample solution; and
d = Dilution factor of the sample.

PART 442—CEPHA ANTIBIOTIC DRUGS

10. The authority citation for 21 CFR Part 442 continues to read as follows:

Authority: Sec. 507, 59 Stat. 463 as amended (21 U.S.C. 357); 21 CFR 5.10.

11. Part 442 is amended by adding new §§ 442.22a to Subpart A and 442.222 to Subpart C to read as follows:

§ 442.22a Sterile cefmenoxime hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefmenoxime hydrochloride is 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-3-[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-, hydrochloride (2:1), [6*R*-[6α,7β(*Z*)]]-. It is so purified and dried that:
(i) Its cefmenoxime content is not less than 869 and not more than 1,015 micrograms of cefmenoxime per milligram on an anhydrous basis.
(ii) It is sterile.
(iii) It is nonpyrogenic.
(iv) Its moisture content is not more than 1.5 percent.
(v) It passes the identity test.
(vi) It is 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 cefmenoxime content, sterility, pyrogens, moisture, identity, and crystallinity.
(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:
(A) For all tests except sterility: 10 packages, each containing approximately 500 milligrams.
(B) For sterility testing: 1 package containing approximately 6 grams of a composite sample.
(b) *Tests and methods of assay*—(1) *Cefmenoxime content.* Proceed as directed in § 436.363 of this chapter, using ambient temperature, an ultraviolet detection system operating at a wavelength of 254 nanometers, a column packed with microparticulate (3 to 10 micrometers in diameter) reversed phase packing material such as octadecyl hydrocarbon bonded silicas, a flow rate not to exceed 2.0 milliliters per minute, and a known injection volume between 10 and 20 microliters. Reagents, working standard and sample solutions, system suitability requirements, and calculations are as follows:
(i) *Reagents*—(A) *0.1M Phosphate buffer solution, pH 6.8.* Dissolve 6.4 grams of monobasic potassium phosphate and 18.9 grams of dibasic sodium phosphate in 750 milliliters of water. Adjust the pH to 6.8 with 1*N* sodium hydroxide and dilute to 1,000 milliliters.
(B) *Internal standard solution.* Dissolve and dilute 0.15 gram of phthalimide in methanol to 100 milliliters.
(C) *Mobile phase.* Mix water:acetonitrile:glacial acetic acid (50:10:1). Filter through a suitable filter capable of removing particulate matter to 0.5 micron in diameter. Degas the mobile phase just prior to its introduction into the chromatograph.
(ii) *Preparation of working standard and sample solutions*—(A) *Working standard solution.* Dissolve approximately 50 milligrams of the cefmenoxime working standard, accurately weighed, in 10 milliliters of 0.1*M* phosphate buffer solution, pH 6.8 and dilute to 50 milliliters with mobile phase. Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase to obtain a solution containing 80 micrograms of cefmenoxime per milliliter.
(B) *Sample solution.* Dissolve approximately 50 milligrams of cefmenoxime sample, accurately weighed, in 10 milliliters of 0.1*M* phosphate buffer solution, pH 6.8. Dilute to 50 milliliters with mobile phase. Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase.
(iii) *System suitability requirements*—(A) *Tailing factor.* The tailing factor (*T*) for the cefmenoxime peak is satisfactory if it is not more than 1.6 at 5 percent of peak height.
(B) *Efficiency of the column.* The efficiency of the column (*n*) is satisfactory if it is greater than 1,200 theoretical plates for the cefmenoxime peak.
(C) *Resolution.* The resolution (*R*) between the peak for cefmenoxime and phthalimide is satisfactory if it is not less than 2.3.
(D) *Coefficient of variation.* The coefficiednt of variation (S_R in percent) of 5 replicate injections is satisfactory if it is not more than 2.0 percent. If the system suitability requirements have been met, then proceed as described in § 436.363(b) of this chapter.
(iv) *Calculations.* Calculate the micrograms of cefmenoxime per milligram of sample as follows:

$$\text{Micrograms of cefmenoxime per milligram} = \frac{R_u \times P_s \times 100}{R_s \times C_u \times (100-m)}$$

where:

R_u = Area of cefmenoxime peak in the chromatogram of the sample/Area of internal standard peak;

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

P_s = Cefmenoxime activity in the cefmenoxime working standard solution in micrograms per milliliter;

C_u = Milligrams of sample per milliliter of sample solution; and

m = Percent moisture content 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, except in lieu of diluting fluid A use diluting fluid H.

(3) *Pyrogens.* Proceed as directed in § 436.32(i) of this chapter, using a solution containing 60 milligrams per milliliter.

(4) *Moisture.* Proceed as directed in § 436.201 of this chapter, using the sample preparation described in paragraph (d)(4) of that section and the titration procedure described in paragraph (e)(3) of that section, except:

(i) In lieu of 3 milliliters of anhydrous methanol solution, inject 20 milliliters of a formamide:methanol solution (2:1) into the container and shake to dissolve the contents (prior to use in preparation of the formamide:methanol solution, dry 500 grams of formamide over 20 grams of anhydrous sodium for 24 hours);

(ii) Rinse the syringe, needle, and immediate container with two separate 5-milliliter portions of anhydrous methanol, in lieu of one 3-milliliter portion of anhydrous methanol; and

(iii) In § 436.201(e)(3) of this chapter, add a sufficient volume of the formamide:methanol solution (2:1) to cover the electrodes in the dry titrating vessel, in lieu of 20 milliliters of solvent A before starting the titration.

(5) *Identity.* Using a 0.0025-percent solution of the sample in 0.1*M* phosphate buffer, pH 6.8 and a suitable spectrophotometer, record the ultraviolet absorption spectrum from 220 to 310 nanometers. The spectrum compares qualitatively to that of the cefmenoxime working standard similarly tested.

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

§ 442.222 Cefmenoxime hydrochloride for injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Cefmenoxime hydrochloride for injection is a dry mixture of cefmenoxime hydrochloride and sodium carbonate. Each milligram of cefmenoxime hydrochloride for injection contains not less than 869 and not more than 1,015 micrograms of cefmenoxime on an anhydrous and sodium carbonate-free basis. Its cefmenoxime content is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of cefmenoxime that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 1.5 percent. Its pH in an aqueous solution containing 100 milligrams per milliliter is not less than 6.4 and not more than 7.9. The cefmenoxime hydrochloride used conforms to the standards prescribed by § 442.22a(a)(1) of this chapter.

(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 cefmenoxime hydrochloride used in making the batch for cefmenoxime content, moisture, identity, and crystallinity.

(B) The batch for cefmenoxime content, sterility, pyrogens, loss on drying, pH, and sodium carbonate content.

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

(A) The cefmenoxime hydrochloride 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) *Cefmenoxime content.* Proceed as directed in § 436.363 of this chapter, using ambient temperature, an ultraviolet detection system operating at a wavelength of 254 nanometers, a column packed with microparticulate (3 to 10 micrometers in diameter) reversed phase packing material such as octadecyl hydrocarbon bonded silicas, a flow rate not to exceed 2.0 milliliters per minute, and a known injection volume between 10 and 20 microliters. Reagents, working standard and sample solutions, system suitability requirements, and calculations are as follows:

(i) *Reagents*—(A) *0.1M Phosphate buffer solution, pH 6.8.* Dissolve 6.4 grams of monobasic potassium phosphate and 18.9 grams of dibasic sodium phosphate in 750 milliliters of water. Adjust the pH to 6.8 with 1*N* sodium hydroxide and dilute to 1,000 milliliters.

(B) *Internal standard solution.* Dissolve and dilute 0.15 gram of phthalimide in methanol to 100 milliliters.

(C) *Mobile phase.* Mix water:acetonitrile:glacial acetic acid (50:10:1). Filter through a suitable filter capable of removing particulate matter to 0.5 micron in diameter. Degas the mobile phase just prior to its introduction into the chromatograph.

(ii) *Preparation of working standard and sample solutions*—(A) *Working standard solution.* Dissolve approximately 50 milligrams of the cefmenoxime working standard, accurately weighed, in 10 milliliters of 0.1*M* phosphate buffer solution, pH 6.8 and dilute to 50 milliliters with mobile phase. Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase to obtain a solution containing 80 micrograms of cefmenoxime per milliliter.

(B) *Sample solutions.* Determine both micrograms of cefmenoxime per milligram of the sample and milligrams of cefmenoxime per container. Use separate containers for preparation of each sample solution as described in paragraphs (b)(1)(ii)(B) (*1*) and (*2*) of this section.

(*1*) *Micrograms of cefmenoxime per milligram.* Dissolve the accurately weighed dry contents of a sample with sufficient distilled water to obtain a solution containing 1 milligram of cefmenoxime per milliliter (estimated). Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase to obtain a solution containing 80 micrograms of cefmenoxime per milliliter (estimated).

(*2*) *Milligrams of cefmenoxime per container.* Reconstitute the sample as directed in the labeling. Then, 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. Dilute the solution thus obtained with sufficient distilled water to obtain a solution containing 1 milligram of cefmenoxime per milliliter (estimated). Transfer 4.0 milliliters of this solution to a 50-milliliter volumetric flask, add 20 milliliters of internal standard solution and dilute to volume with mobile phase to obtain a solution containing 80 micrograms of cefmenoxime per milliliter (estimated).

(iii) *System suitability requirements*—(A) *Tailing factor.* The tailing factor (T) for the cefmenoxime peak is satisfactory if it is not more than 1.6 at 5 percent of peak height.

(B) *Efficiency of the column.* The efficiency of the column (n) is satisfactory if it is greater than 1,200 theoretical plates for the cefmenoxime peak.

(C) *Resolution.* The resolution (R) between the peak for cefmenoxime and phthalimide is satisfactory if it is not less than 2.3.

(D) *Coefficient of variation.* The coefficient of variation (S_R in percent) of 5 replicate injections is satisfactory if it is not more than 2.0 percent. If the system suitability requirements have been met, then proceed as described in § 436.363(b) of this chapter.

(iv) *Calculations*—(A) *Micrograms per milligram.* Calculate the micrograms of cefmenoxime per milligram as follows:

$$\text{Micrograms of cefmenoxime per milligram} = \frac{R_u \times P_s \times 100 \times d}{R_s \times C_u(100\text{-L-S})}$$

where:

R_u = Area of the cefmenoxime peak in the chromatogram of the sample/Area of internal standard peak;

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

P_s = Cefmenoxime activity in the cefmenoxime working standard solution in micrograms per milliliter;

C_u = Milligrams of sample per milliliter of sample solution;

d = Dilution factor of the sample;

L = Percent loss on drying (determined as directed in paragraph (b)(4) of this section); and

S = Percent sodium carbonate (determined as directed in paragraph (b)(6) of this section).

(B) *Milligrams of cefmenoxime per vial.* Calculate the cefmenoxime content of the vial as follows:

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

where:

R_u = Area of the cefmenoxime peak in the chromatogram of the sample/Area of internal standard peak;

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

P_s = Cefmenoxime activity in the cefmenoxime 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, using a solution containing 60 milligrams of cefmenoxime per milliliter.

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

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 100 milligrams per milliliter.

(6) *Sodium carbonate content.* Proceed as directed in § 436.364 of this chapter.

Dated: April 15, 1988.

Daniel L. Michels,

Director, Office of Compliance, Center for Drug Evaluation and Research.

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DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

Office of the Assistant Secretary for Housing—Federal Housing Commissioner

24 CFR Parts 200, 203, 204, 213, 220, 221, 222, 226, 227, 235, 237, and 240

[Docket No. R-88-1357; FR-2382]

Mortgage Insurance for the Allegeny Reservation of the Seneca Nation of Indians; Correction

AGENCY: Office of the Assistant Secretary for Housing—Federal Housing Commissioner, HUD.

ACTION: Interim rule; correction.

SUMMARY: On December 21, 1987 (52 FR 48197) the Department published an interim rule entitled "Mortgage Insurance for the Allegeny Reservation of the Seneca Nation of Indians" (Seneca rule). The effective date of the rule was delayed in accordance with the legislative review requirements of section 7(o)(3) of the Department of Housing and Urban Development Act (42 U.S.C. 3535(o)(3)). By Notice published on March 28, 1988 (53 FR 9869), the Department announced the effective date for the interim rule as March 28, 1988. This document makes corrections in the text of the interim rule that are necessary to reflect the fact that another HUD rule, published before the Seneca rule but not yet announced for effect, contains amendments to, or adds, some of the same sections that were amended in the December 21, 1987 Seneca rule. The delay in announcing the effectiveness of the other HUD rule requires technical adjustments in the content of the Seneca rule. These corrections will not change the effective date of the Seneca rule, nor will they affect the operations of the insurance program outlined in that rule.

EFFECTIVE DATE: April 25, 1988.

FOR FURTHER INFORMATION CONTACT: Donald B. Alexander, Chief Attorney, Home Mortgage Insurance Division, Office of the General Counsel, Department of Housing and Urban Development, Room 9258, 451 Seventh Street SW., Washington, DC 20410, telephone (202) 755-7070. (This is not a toll-free number.)

SUPPLEMENTARY INFORMATION: The Department published a final rule entitled "Temporary Mortgage Assistance Payments" on March 5, 1987 to implement a new program authorized by section 341 of the Housing and Community Development Act of 1980. Section 341 amended section 230 of the National Housing Act—the provision of the Act setting out the forms of mortgage foreclosure relief available under HUD's single family insuring authorities. While the March 5, 1987 rule (TMAP rule) was published as a final rule, its effective date has been postponed. Accordingly, a conflict has developed in the content of the later-published Seneca rule, because that rule contains amendments to certain HUD regulations that were earlier amended by, or added by, the TMAP rule. The purpose of this document is to correct the Seneca rule to permit it to be a freestanding rule setting out all necessary features of the new mortgage insurance program authorized under section 203(q) of the National Housing Act, pending the effectiveness of the TMAP rule.

Accordingly, the rule published on December 21, 1987 (52 FR 48197) (FR Doc. 87-29092) is corrected as follows:

§§ 203.640, 203.645 and 203.654 [Corrected]

1. Amendments of §§ 203.640, 203.645 and 203.654 (items 12, 13 and 14 of the published rule, 52 FR 48202-48203) are withdrawn.

§ 203.350 [Corrected]

2. In § 203.350 (item 8), the amendatory language is corrected to read: "Section 203.350 is amended by reserving paragraph (c) and adding new paragraph (d) to read as follows:".

§ 203.355 [Amended]

3. In § 203.355, the reference in the last line of the introductory text to "203 658" is revised to read "203.660".