

is not more than 2.0 percent. If the system suitability parameters have been met, then proceed as described in §436.216(b) of this chapter.

(iv) *Calculations.* Calculate the milligrams of trimethoprim per milliliter of sample as follows:

$$\begin{array}{l} \text{Milligrams of} \\ \text{trimethoprim} \\ \text{per milliliter} \end{array} = \frac{A_u \times W_s \times 0.8555}{A_s \times 40}$$

where:

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

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

W_s =Weight of the trimethoprim working standard in milligrams; and

0.855=Gravimetric conversion factor trimethoprim hemisulfate to trimethoprim.

(3) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

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

[54 FR 38376, Sept. 18, 1989, as amended at 59 FR 8399, Feb. 22, 1994]

Subpart E—Otic Dosage Forms

§ 448.421 Colistin sulfate-neomycin sulfate-thonzonium bromide-hydrocortisone acetate otic suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Colistin sulfate-neomycin sulfate-thonzonium bromide-hydrocortisone acetate otic suspension is a suspension containing colistin sulfate, neomycin sulfate, thonzonium bromide, and hydrocortisone acetate, and one or more preservatives, dispersing agents, and buffer substances. Each milliliter contains 3.0 milligrams of colistin, 3.3 milligrams of neomycin, 0.5 milligram of thonzonium bromide, and 10 milligrams of hydrocortisone acetate. Its content of colistin is satisfactory if it is not less than 90 percent and not more than 135 percent of the number of milligrams of colistin per milliliter that it is represented to contain. Its content of neomycin is satisfactory

if it is not less than 90 percent and not more than 125 percent of the number of milligrams of neomycin per milliliter that it is represented to contain. It is sterile. Its pH is not less than 4.8 and not more than 5.2. The colistin sulfate used conforms to the standards prescribed therefor by §448.21(a)(1). The neomycin sulfate used conforms to the standards prescribed in §444.42a(a)(1) (i), (v), (vi), and (vii) 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 colistin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(b) The neomycin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(c) The batch for colistin content, neomycin content, sterility, and pH.

(ii) Samples required:

(a) The colistin sulfate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The neomycin sulfate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(c) The batch:

(1) For all tests except sterility: A minimum of six 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—(i) Colistin content.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Thoroughly mix the sample and transfer an accurately measured representative portion of the sample into a 100-milliliter volumetric flask. Fill the flask to mark with 10 percent potassium phosphate buffer, pH 6.0 (solution 6). Further dilute with solution 6 to the reference concentration of 1.0 microgram of colistin per milliliter (estimated).

(ii) *Neomycin content.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows:

Thoroughly mix the sample and transfer an accurately measured representative portion into a 100-milliliter volumetric flask. Fill the flask to mark with 0.1M potassium phosphate buffer, pH 8.0 (solution 3). Further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except transfer 0.25 milliliter of sample in lieu of 1 milliliter.

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

[39 FR 19115, May 30, 1974, as amended at 50 FR 19920, May 13, 1985]

§ 448.430 Polymyxin B sulfate-hydrocortisone otic solution.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Polymyxin B sulfate-hydrocortisone otic solution contains in each milliliter 10,000 units of polymyxin B and 5 milligrams of hydrocortisone in a suitable and harmless vehicle. Its polymyxin B sulfate content is satisfactory if it contains not less than 90 percent and not more than 130 percent of the number of units of polymyxin B that it is represented to contain. It is sterile. Its pH is not less than 3.0 and not more than 5.0. The polymyxin B sulfate used conforms to the standards prescribed by § 448.30(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 the following:

(i) Results of tests and assays on—

(a) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, and identity; and

(b) The batch for potency, sterility, and pH.

(ii) Samples required:

(a) The polymyxin B sulfate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 5 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.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the sample (usually 1.0 milliliter) with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 6 to the reference concentration of 10 units of polymyxin B 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, except if the steroid prevents solubilization, use 0.25 milliliter of the sample in lieu of 1 milliliter and proceed as directed in paragraph (e)(2) of that section.

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

[44 FR 5880, Jan. 30, 1979, as amended at 50 FR 1504, Jan. 11, 1985; 50 FR 19920, May 13, 1985]

Subpart F—Dermatologic Dosage Forms

§ 448.510 Bacitracin dermatologic dosage forms.

§ 448.510a Bacitracin ointment.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Bacitracin ointment is composed of 500 units of bacitracin per gram in a suitable ointment base. It may contain a suitable local anesthetic. Its potency is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of units of bacitracin that it is represented to contain. Its moisture content is not more than 0.5 percent. The bacitracin used conforms to the standards described by § 448.10(a)(1).

(2) *Labeling.* (i) On the label of the immediate container and on the outside wrapper or container, if any:

(a) The batch mark.