§ 436.329 of this chapter, except, prepare the working standard and sample solution and calculate the meclocycline content as follows:

(i) *Preparation of standard solution.* Accurately weigh an amount of working standard equivalent to approximately 25 milligrams of meclocycline into a 50-milliliter volumetric flask. Dissolve and dilute to volume with methanol and mix. Transfer exactly 2.0 milliliters of this solution to a 100-milliliter volumetric flask, dilute to volume with mobile phase, and mix.

(ii) *Preparation of sample solution.* Accurately weigh approximately 0.4 to 0.7 gram of sample into a 50-milliliter glass-stoppered centrifuge tube. Add 20 milliliters of methanol and 20 milliliters of 0.025*N* sulfuric acid. Disperse the sample thoroughly by a combination of ultrasonic/vortexing and shaking by hand. Shake for 15 minutes on a wrist action shaker. Quantitatively transfer the contents of the centrifuge tube into a 50-milliliter volumetric flask. Rinse the centrifuge tube with two 5-milliliter portions of methanol and add to the flask. Dilute to volume with methanol and mix. Transfer a portion of the content of the volumetric flask into an appropriate-sized centrifuge tube. Centrifuge for 5 minutes at 2,000 revolutions per minute. Transfer 5.0 milliliters of this solution into a 50-milliliter volumetric flask and dilute to volume with mobile phase and mix. Filter this solution through a 0.5 micrometer filter. Inject the filtrate onto the column as described in § 436.329(e) of this chapter.

(iii) *Calculations.* Calculate the meclocycline content as follows:

$$\text{Meclocycline content of cream in percent} = \frac{A \times 2 \times \text{milligrams of working standard} \times \text{Potency of working standard in micrograms per milligram}}{B \times 100 \times \text{milligrams of sample}}$$

where:

A=Area or peak height of the sample peak (at a retention time equal to that observed for the standard);

B=Area or peak height of the standard peak.

[46 FR 3837, Jan. 16, 1981; 46 FR 21361, Apr. 10, 1981, as amended at 47 FR 22515, May 25, 1982; 50 FR 1504, Jan. 11, 1985]

§ 446.567 Oxytetracycline hydrochloride dermatologic dosage forms.

§ 446.567a [Reserved]

§ 446.567b Oxytetracycline hydrochloride-polymyxin B sulfate topical ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Oxytetracycline hydrochloride-polymyxin B sulfate topical ointment is oxytetracycline hydrochloride and polymyxin B sulfate in a suitable and harmless ointment base. Each gram contains oxytetracycline hydrochloride equivalent to 30 milligrams of oxytetracycline and polymyxin B sulfate equivalent to 10,000 units of polymyxin B. Its oxytetracycline content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of oxytetracycline that it is represented to contain. Its polymyxin B sulfate content is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of units of polymyxin B that it is represented to contain. Its moisture content is not more than 1 percent. The oxytetracycline hydrochloride used conforms to the standards prescribed by § 446.67(a)(1). The polymyxin B sulfate conforms to the standards prescribed by § 448.30(a)(1).

(2) *Labeling.* In addition to the labeling requirements prescribed by § 432.5(a)(3) of this chapter, each package shall bear on its label or labeling as hereinafter indicated, the following:

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

(*a*) The batch mark.

(*b*) The name and quantity of each active ingredient contained in the drug.

(ii) On the label of the immediate container or other labeling attached to or within the package: Adequate directions under which the layman can use the drug safely and efficaciously.

(3) *Requests for certification; samples.* In addition to the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The oxytetracycline hydrochloride used in making the batch for potency, loss on drying, pH, absorptivity, identity, and crystallinity.

(*b*) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, residue on ignition, and identity.

(*c*) The batch for oxytetracycline content, polymyxin B content, and moisture.

(ii) Samples required:

(*a*) The oxytetracycline hydrochloride used in making the batch: 10 packages, each containing approximately 300 milligrams.

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

(*c*) The batch: A minimum of six immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Oxytetracycline content.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of peroxide-free ether. Shake the ointment and ether until homogeneous. Add 20 to 25 milliliters of 0.1*N* hydrochloric acid and shake well. Allow the layers to separate. Remove the acid layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of 0.1*N* hydrochloric acid. Combine the acid extractives in a suitable volumetric flask and dilute to volume with 0.1*N* hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of oxytetracycline per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of oxytetracycline per milliliter (estimated).

(ii) *Polymyxin B content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Weigh accurately 0.5 to 1 gram of the ointment and place into a 15-milliliter centrifuge tube. Add 10 milliliters of peroxide-free ether. Stir until contents are homogeneous and centrifuge for 10 minutes at 3,000 revolutions per minute. Decant the supernatant ether. Repeat washing and centrifugation steps once more. Add 10 milliliters of acetone, stir until contents are homogeneous, and centrifuge for 10 minutes at 3,000 revolutions per minute. Decant the supernatant acetone. Repeat acetone wash and centrifugation once more. Continue acetone washing until the yellow color in the residue disappears. Add 3 to 4 drops of polysorbate 80 to the residue and mix well. Gently wash the residue into a 100-milliliter volumetric flask with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated).

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

[43 FR 11172, Mar. 17, 1978, as amended at 50 FR 19920, May 13, 1985]

§ 446.567c Oxytetracycline hydrochloride-polymyxin B sulfate topical powder.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Oxytetracycline hydrochloride-polymyxin B sulfate topical powder is oxytetracycline hydrochloride and polymyxin B sulfate with a suitable filler. Each gram contains 30 milligrams of oxytetracycline and 10,000 units of polymyxin B. Its oxytetracycline content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of oxytetracycline that it is represented to contain. Its polymyxin B content is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of units of polymyxin B that it is represented to contain. The loss on drying is not more than 2.0 percent. The oxytetracycline hydrochloride used conforms to the