

standards prescribed by § 446.67. The polymyxin B sulfate used conforms to the standards prescribed by § 448.30(a)(1) of this chapter.

(2) *Labeling.* 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.

(c) An expiration date that is 12 months after the month during which the batch was certified, unless the use of a longer expiration period has been approved in accordance with the provisions of § 432.5(a)(3) of this chapter.

(ii) On the label of the immediate container or other labeling attached to or within the package, adequate directions for lay use of the drug.

(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 content, and loss on drying.

(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 high-speed glass blender jar with sufficient 0.1N hydrochloric acid to ob-

tain a stock solution of convenient concentration containing not less than 150 micrograms of oxytetracycline hydrochloride per milliliter (estimated). Blend for 3 to 5 minutes. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.24 microgram of oxytetracycline per milliliter (estimated).

(ii) *Polymyxin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Accurately weigh 1 gram of the powder and place into a 50-milliliter centrifuge tube. Add 15 milliliters of acetone and 1 drop of concentrated hydrochloric acid and stir well. Add 20 milliliters of acetone and centrifuge for 10 minutes at 3,000 revolutions per minute. Decant the supernatant liquid and repeat the acetone-acid extraction once more. Dissolve and dilute the residue with sufficient 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) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

[43 FR 11173, Mar. 17, 1978, as amended at 50 FR 19920, May 13, 1985]

§ 446.581 Tetracycline hydrochloride dermatologic dosage forms.

§§ 446.581a–446.581b [Reserved]

§ 446.581c Tetracycline hydrochloride for topical solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Tetracycline hydrochloride for topical solution is a dry mixture of tetracycline hydrochloride, 4-epitetracycline hydrochloride, and sodium bisulfite packaged in combination with a suitable and harmless aqueous vehicle. When reconstituted as directed in the labeling, each milliliter contains 2.2 milligrams of tetracycline hydrochloride. The tetracycline hydrochloride content of the reconstituted solution is satisfactory if it contains not less than 90 percent and not more