

(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 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, pH, loss on drying, 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 sample 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 fill 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, pre-

paring the sample for assay as follows: Weigh accurately 0.5 to 1.0 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 washings 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 11171, Mar. 17, 1978, as amended at 50 FR 19920, May 13, 1985]

Subpart F—Dermatologic Dosage Forms

§ 446.510 Chlortetracycline hydrochloride ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality and purity.* Chlortetracycline hydrochloride ointment contains chlortetracycline hydrochloride and one or more suitable and harmless preservatives in a suitable and harmless ointment base. Each gram contains 30 milligrams of chlortetracycline hydrochloride. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of chlortetracycline hydrochloride that it is represented to contain. Its moisture content is not more than 0.5 percent. The chlortetracycline hydrochloride used conforms to the standards prescribed by § 446.10(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 complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

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

(b) The batch for potency and moisture.

(ii) Samples required:

(a) The chlortetracycline hydrochloride used in making the batch: 10 packages, each containing approximately 60 milligrams.

(b) The batch: A minimum of five immediate containers:

(b) *Tests and methods of assay*—(1) *Potency.* 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 sample and ether until homogeneous. Add 20 to 25 milliliters of 0.01*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 0.01*N* hydrochloric acid. Combine the extractives in a suitable volumetric flask and dilute to volume with 0.01*N* hydrochloric acid. Further dilute an aliquot with sterile distilled water to the reference concentration of 0.06 microgram of chlortetracycline hydrochloride 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]

§ 446.542 Meclocycline sulfosalicylate cream.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Meclocycline sulfosalicylate cream contains meclocycline sulfosalicylate in a suitable and harmless cream base. Each gram contains meclocycline sulfosalicylate equivalent to 10 milligrams of meclocycline. Its potency is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of meclocycline that it is represented to contain. The meclocycline sulfosalicylate used conforms to the standards prescribed by §446.42(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 meclocycline sulfosalicylate used in making the batch for potency, moisture, pH, and crystallinity.

(b) The batch for potency.

(ii) Samples required:

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

(b) The batch: A minimum of five immediate containers.

(b) *Tests and methods of assay; potency.* Use either of the following methods; however, the results obtained from the high-pressure liquid chromatography method shall be conclusive.

(1) *Microbiological turbidimetric assay.* 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 containing sufficient 0.01*N* methanolic hydrochloric acid (solution 13) to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 0.06 microgram of meclocycline per milliliter (estimated).

(2) *High-pressure liquid chromatography.* Proceed as directed in