

or more suitable preservatives and anesthetic agents, and with or without one or more suitable solubilizers and stabilizers. Its potency is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of tetracycline hydrochloride that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 5 percent. Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 2.0 and not more than 3.0. Its 4-epianhydrotetracycline content is not more than 3.0 percent. The tetracycline phosphate complex conforms to the standards prescribed by § 446.82(a)(1), and it contains no depressor substance.

(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 tetracycline phosphate complex used in making the batch for potency, moisture, pH, depressor substances, absorptivity, 4-epianhydrotetracycline content, identity, and crystallinity.

(b) The batch for potency, sterility, pyrogens, loss on drying, pH, and 4-epianhydrotetracycline content.

(ii) Samples required:

(a) The tetracycline phosphate complex used in making the batch: 10 packages, each containing approximately 300 milligrams, and one package containing approximately 1 gram.

(b) The batch: A minimum of 10 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency.* Reconstitute the sample as directed in the labeling. Then, using a suitable hypodermic needle and syringe, remove all 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 sample thus obtained with sufficient 0.1N hydrochloric acid to obtain a stock solution of convenient concentration containing not less

than 150 micrograms of tetracycline hydrochloride per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride 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 use 50 milligrams in lieu of 300 milligrams of sample.

(3) *Pyrogens.* Proceed as directed in § 436.32(b) of this chapter, using a solution containing 5.0 milligrams of tetracycline hydrochloride per milliliter.

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

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(6) *Depressor substances in the tetracycline phosphate complex used in making the batch.* Proceed as directed in § 436.35 of this chapter. Prepare the test solution by dissolving 40 milligrams of sample in 2.0 milliliters of 0.1N hydrochloric acid and diluting with sterile distilled water (diluent 3) to the prescribed concentration.

(7) *4-Epianhydrotetracycline.* Proceed as directed in § 436.309 of this chapter.

[43 FR 11168, Mar. 17, 1978, as amended at 46 FR 60568, Dec. 11, 1981; 50 FR 19920, May 13, 1985]

### Subpart D—Ophthalmic Dosage Forms

#### § 446.310 Chlortetracycline hydrochloride ophthalmic ointment.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Chlortetracycline hydrochloride ophthalmic ointment contains chlortetracycline hydrochloride in a suitable and harmless ointment base. Each gram contains 10 milligrams of chlortetracycline hydrochloride. Its potency is satisfactory if it contains 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. It is sterile. Its moisture content is not more than 0.5 percent. It passes

the test for metal particles. The chlortetracycline hydrochloride used conforms to the standards prescribed by § 446.10a(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 chlortetracycline hydrochloride used in making the batch for potency, loss on drying, pH, crystallinity, and identity.

(b) The batch for potency, sterility, moisture, and metal particles.

(ii) Samples required:

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

(b) The batch:

(1) For all tests except sterility: A minimum of 15 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 § 436.106 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) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(3) of that section.

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

(4) *Metal particles.* Proceed as directed in § 436.206 of this chapter.

[43 FR 11169, Mar. 17, 1978, as amended at 50 FR 19920, May 13, 1985]

**§ 446.367 Oxytetracycline hydrochloride ophthalmic dosage forms.**

**§ 446.367c Oxytetracycline hydrochloride-hydrocortisone acetate ophthalmic suspension.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Oxytetracycline hydrochloride-hydrocortisone acetate ophthalmic suspension is oxytetracycline hydrochloride and hydrocortisone acetate in a suitable and harmless oil base containing aluminum tristearate. Each milliliter contains oxytetracycline hydrochloride equivalent to 5 milligrams of oxytetracycline and 15 milligrams of hydrocortisone acetate. Its potency is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of oxytetracycline that it is represented to contain. It is sterile. Its moisture content is not more than 1 percent. The oxytetracycline hydrochloride used conforms to the standards prescribed by § 446.67a (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 oxytetracycline hydrochloride used in making the batch for potency, loss on drying, pH, absorptivity, crystallinity, and identity.

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

(ii) Samples required:

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

(b) The batch:

(1) For all tests except sterility: A minimum of five immediate containers.

(2) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.