

§ 446.10

21 CFR Ch. I (4–1–98 Edition)

- 446.160b Minocycline hydrochloride capsules.
- 446.160c Minocycline hydrochloride oral suspension.
- 446.165 Oxytetracycline oral dosage forms.
- 446.165a Oxytetracycline tablets.
- 446.165b–446.165c [Reserved]
- 446.165d Oxytetracycline for oral suspension.
- 446.166 Oxytetracycline calcium oral suspension.
- 446.167 Oxytetracycline hydrochloride capsules.
- 446.180 Tetracycline oral dosage forms.
- 446.180a–446.180b [Reserved]
- 446.180c Tetracycline oral suspension.
- 446.181 Tetracycline hydrochloride oral dosage forms.
- 446.181a–446.181c [Reserved]
- 446.181d Tetracycline hydrochloride tablets.
- 446.181e Tetracycline hydrochloride capsules.
- 446.182 Tetracycline phosphate complex capsules.

**Subpart C—Injectable Dosage Forms**

- 446.220 Doxycycline hyclate for injection.
- 446.260 Sterile minocycline hydrochloride.
- 446.265 Oxytetracycline injection.
- 446.267 Oxytetracycline hydrochloride for injection.
- 446.275 Rolitetracycline injectable dosage forms.
- 446.275a Rolitetracycline for intravenous use.
- 446.275b Rolitetracycline for intramuscular use.
- 446.276 Rolitetracycline nitrate injectable dosage forms.
- 446.276a Rolitetracycline nitrate for intravenous use.
- 446.276b Rolitetracycline nitrate for intramuscular use.
- 446.281 Tetracycline hydrochloride injectable dosage forms.
- 446.281a Sterile tetracycline hydrochloride.
- 446.281c Tetracycline hydrochloride for intramuscular use.
- 446.281d Tetracycline hydrochloride for intravenous use.
- 446.282 Tetracycline phosphate complex for injection.

**Subpart D—Ophthalmic Dosage Forms**

- 446.310 Chlortetracycline hydrochloride ophthalmic ointment.
- 446.367 Oxytetracycline hydrochloride ophthalmic dosage forms.
- 446.367c Oxytetracycline hydrochloride-hydrocortisone acetate ophthalmic suspension.
- 446.367e Oxytetracycline hydrochloride-polymyxin B sulfate ophthalmic ointment.
- 446.381 Tetracycline hydrochloride ophthal-

- mic dosage forms.
- 446.381a Tetracycline hydrochloride ophthalmic ointment.
- 446.381b Tetracycline hydrochloride ophthalmic suspension.

**Subpart E—Otic Dosage Forms**

- 446.467 Oxytetracycline hydrochloride-polymyxin B sulfate otic ointment.

**Subpart F—Dermatologic Dosage Forms**

- 446.510 Chlortetracycline hydrochloride ointment.
- 446.542 Meclocycline sulfosalicylate cream.
- 446.567 Oxytetracycline hydrochloride dermatologic dosage forms.
- 446.567a [Reserved]
- 446.567b Oxytetracycline hydrochloride-polymyxin B sulfate topical ointment.
- 446.567c Oxytetracycline hydrochloride-polymyxin B sulfate topical powder.
- 446.581 Tetracycline hydrochloride dermatologic dosage forms.
- 446.581a–446.581b [Reserved]
- 446.581c Tetracycline hydrochloride for topical solution.
- 446.581d Tetracycline hydrochloride ointment.

**Subpart G—Vaginal Dosage Forms**

- 446.667 Oxytetracycline hydrochloride-polymyxin B sulfate vaginal tablets.

**Subpart H—Rectal Dosage Forms  
[Reserved]**

**Subpart I [Reserved]**

**Subpart J—Certain Other Dosage Forms  
[Reserved]**

AUTHORITY: 21 U.S.C. 357.

SOURCE: 39 FR 19076, May 30, 1974, unless otherwise noted.

**Subpart A—Bulk Drugs**

**§ 446.10 Chlortetracycline hydrochloride.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Chlortetracycline hydrochloride is [4S - (4 $\alpha$ ,4 $\alpha$ ,5 $\alpha$ ,6 $\beta$ , 12 $\alpha$ ) - 7 - chloro - 4 - (dimethylamino) - 1,4,4a,5,5a,6,11,12a - octahydro - 3,6,10,12,12a - pentahydroxy - 6 - methyl - 1,11 - dioxo - 2 - naphthacenicarboxamidemonohydrochloride. Chlortetracycline is produced by the growth of *Streptomyces*

*aureofaciens*. It is a yellow powder. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms per milligram.

(ii) [Reserved]

(iii) Its loss on drying is not more than 2.0 percent.

(iv) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 2.3 and not more than 3.3.

(v) It is crystalline.

(vi) It meets the identity test for chlortetracycline.

(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 the batch for potency, loss on drying, pH, crystallinity, and identity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.01*N* hydrochloric acid to obtain a concentration of 1,000 micrograms of chlortetracycline hydrochloride per milliliter (estimated). Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 0.06 microgram of chlortetracycline hydrochloride per milliliter (estimated).

(2) [Reserved]

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

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

(5) *Crystallinity*. Proceed as directed in § 436.203(a) of this chapter.

(6) *Identity*. To 1 milligram of sample, add 2.0 milliliters of concentrated sulfuric acid. In the presence of chlortetracycline, a deep blue color is produced that becomes dark green.

[43 FR 11154, Mar. 17, 1978; 43 FR 34456, Aug. 4, 1978, as amended at 50 FR 19920, May 13, 1985]

#### § 446.10a Sterile chlortetracycline hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Chlortetracycline hydrochloride is [4S - (4 $\alpha$ ,4 $\alpha$ ,5 $\alpha$ ,6 $\beta$ ,12 $\alpha$ ) - 7 - chloro - 4 - (dimethylamino) - 1,4,4a,5,5a,6,11,12a - octahydro - 3,6,10,12,12a - pentahydroxy - 6 - methyl - 1,11 - dioxo - 2 - naphthacene]carboxamide

monohydrochloride. Chlortetracycline is produced by the growth of *Streptomyces aureofaciens*. It is a yellow powder. It is so purified and dried that:

(i) Its potency is not less than 900 micrograms per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) It contains no depressor substances.

(vi) Its loss on drying is not more than 2.0 percent.

(vii) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 2.3 and not more than 3.3.

(viii) It is crystalline.

(ix) It meets the identity test for chlortetracycline.

(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 the batch for potency, sterility, pyrogens, depressor substances, loss on drying, pH, crystallinity, and identity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(b) For sterility testing: 20 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 0.01*N* hydrochloric acid to obtain a concentration of 1,000 micrograms of chlortetracycline hydrochloride per milliliter (estimated). Further dilute an aliquot of the stock solution with