

containing oxytetracycline hydrochloride with or without one or more suitable and harmless buffers, preservatives, diluents, binders, and lubricants. They may contain glucosamine hydrochloride. Each capsule contains 50 milligrams, 100 milligrams, 125 milligrams, or 250 milligrams of oxytetracycline. Its potency 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. The loss on drying is not more than 5.0 percent. It passes the dissolution test. The oxytetracycline hydrochloride used conforms to the standards prescribed by § 446.67(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 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 batch for potency, loss on drying, and dissolution.

(ii) Samples required:

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

(b) The batch: A minimum of 30 capsules.

(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 a representative number of capsules into a high-speed glass blender jar containing sufficient 0.1N hydrochloric acid to give a stock solution of convenient concentration containing not less than 150 micrograms of oxytetracycline 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).

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

(3) *Dissolution.* Proceed as directed in § 436.215 of this chapter, except in lieu

of paragraph (a) of that section, a distance of  $4.5 \pm 0.5$  centimeters should be maintained between the lower edge of the stirring blade and the lowest inner surface of the vessel during the test. The quantity  $Q$  (the amount of oxytetracycline dissolved) is 60 percent within 30 minutes and 85 percent within 60 minutes.

[43 FR 11164, Mar. 17, 1978, as amended at 44 FR 48189, Aug. 17, 1979; 47 FR 32938, July 30, 1982; 48 FR 51293, Nov. 3, 1983; 49 FR 37058, Sept. 21, 1984; 50 FR 19920, May 13, 1985]

#### § 446.180 Tetracycline oral dosage forms.

#### §§ 446.180a—446.180b [Reserved]

#### § 446.180c Tetracycline oral suspension.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Tetracycline oral suspension is composed of tetracycline with or without one or more suitable and harmless buffer substances, suspending and stabilizing agents, and preservatives, suspended in a suitable and harmless vehicle. Each milliliter contains tetracycline equivalent to 25 milligrams of tetracycline hydrochloride. Its potency is satisfactory if it contains the equivalent of not less than 90 percent and not more than 125 percent of the number of milligrams of tetracycline hydrochloride that it is represented to contain. Its pH is not less than 3.5 and not more than 6.0. Its 4-epianhydrotetracycline content is not more than 5.0 percent. The tetracycline used conforms to the standards prescribed by § 446.80(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 tetracycline used in making the batch for potency, moisture, pH, absorptivity, 4-epianhydrotetracycline content, crystallinity, and identity.

(b) The batch for potency, pH, and 4-epianhydrotetracycline content.

(ii) Samples required:

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

(b) The batch: A minimum of 5 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: Transfer an accurately measured representative portion of the well-shaken suspension to an appropriate-sized volumetric flask and dilute to volume with 0.1*N* hydrochloric acid to give a stock solution of convenient concentration containing not less than 150 micrograms of tetracycline hydrochloride per milliliter (estimated). Mix well. Remove an aliquot of the stock solution and further dilute with sterile distilled water to the reference concentration of 0.24 microgram of tetracycline hydrochloride per milliliter (estimated).

(2) *pH*. Proceed as directed in § 436.202 of this chapter, using the undiluted suspension.

(3) *4-Epianhydrotetracycline*. Proceed as directed in § 436.309(b) of this chapter.

[43 FR 11164, Mar. 17, 1978; 43 FR 34456, Aug. 4, 1978, as amended at 45 FR 16472, 16476, Mar. 14, 1980; 50 FR 19920, May 13, 1985]

**§ 446.181 Tetracycline hydrochloride oral dosage forms.**

**§§ 446.181a–446.181c [Reserved]**

**§ 446.181d Tetracycline hydrochloride tablets.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Tetracycline hydrochloride tablets contain tetracycline hydrochloride with or without one or more buffer substances, preservatives, diluents, binders, lubricants, colorings, and flavorings. Each tablet contains 250 milligrams or 500 milligrams of tetracycline 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 tetracycline hydrochloride that it is represented to contain. Its loss on drying is not more than 3.0 percent. It passes the dissolution test. Its 4-epianhydrotetracycline content is not more than 3.0 percent. The tetracycline

hydrochloride used conforms to the standards prescribed by § 446.81(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 tetracycline hydrochloride used in making the batch for potency, loss on drying, pH, absorptivity, 4-epianhydrotetracycline content, crystallinity, and identity.

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

(ii) Samples required:

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

(b) The batch: A minimum of 36 tablets.

(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 a representative number of tablets into a high-speed glass blender jar containing sufficient 0.1*N* hydrochloric acid to obtain a stock solution of convenient concentration containing not less than 150 micrograms of tetracycline 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 tetracycline hydrochloride per milliliter (estimated).

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

(3) *Dissolution*. Proceed as directed in § 436.215 of this chapter, except in lieu of paragraph (a) of that section, a distance of 4.5±0.5 centimeters should be maintained between the lower edge of the stirring blade and the lowest inner surface of the vessel during the test. The quantity *Q* (the amount of tetracycline hydrochloride dissolved) is 60 percent within 30 minutes and 85 percent within 60 minutes.