

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

[44 FR 1374, Jan. 5, 1979, as amended at 44 FR 30334, May 25, 1979; 50 FR 19921, May 13, 1985]

Subpart D—Ophthalmic Dosage Forms

§ 455.310 Chloramphenicol ophthalmic dosage forms.

§ 455.310a Chloramphenicol ophthalmic solution.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Chloramphenicol ophthalmic solution contains in each milliliter 5 milligrams of chloramphenicol with or without one or more suitable and harmless preservatives, buffer substances, and surfactants, in an aqueous solution. Its potency is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of chloramphenicol that it is represented to contain. It is sterile. Its pH is not less than 3 nor more than 6; however, if the solution is buffered, its pH is not less than 7.0 nor more than 7.5. The chloramphenicol used conforms to the standards prescribed by § 455.10(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 chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

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

(ii) Samples required:

(a) The chloramphenicol used in making the batch: 10 containers, 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.

(b) *Tests and methods of assay—(1) Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the sample with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol 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.

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

[39 FR 19166, May 30, 1974, as amended at 43 FR 59057, Dec. 19, 1978; 46 FR 46313, Sept. 18, 1981; 48 FR 3961, Jan. 28, 1983; 50 FR 19921, May 13, 1985]

§ 455.310b Chloramphenicol for ophthalmic solution.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Chloramphenicol for ophthalmic solution contains 25 milligrams of chloramphenicol with one or more suitable and harmless buffer substances. When reconstituted as directed in the labeling, its potency is not less than 90 percent and not more than 130 percent of the number of milligrams of chloramphenicol that it is represented to contain. It is sterile. Its pH is not less than 7.1 and not more than 7.5. The chloramphenicol used conforms to the standards prescribed by § 455.10(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 chloramphenicol used in making the batch for potency, pH, specific rotation, melting range, absorptivity, and crystallinity.

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

(ii) Samples required:

(a) The chloramphenicol 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.

(b) *Tests and methods of assay*—(1) *Potency*. Use either of the following methods:

(i) *Microbiological turbidimetric assay*. Proceed as directed in §436.106 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Dilute an accurately measured representative aliquot of the sample with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an

aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(ii) *Spectrophotometric assay*. Reconstitute the sample as directed in the labeling and dilute a 1.0-milliliter aliquot in sufficient distilled water to obtain a solution containing 20 micrograms of chloramphenicol per milliliter. Dissolve an accurately weighed portion of the working standard in sufficient distilled water to obtain a solution containing 20 micrograms per milliliter. Using a suitable spectrophotometer and distilled water as the blank, determine the absorbance of the sample and standard solutions at 278 nanometers. Calculate the potency of the sample as follows:

$$\text{Milligrams of chloramphenicol per milliliter} = \frac{\text{Absorbance of sample} \times \text{labeled potency per milliliter in milligrams}}{\text{Absorbance of standard}}$$

(2) *Sterility*. Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

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

[49 FR 6093, Feb. 17, 1984, as amended at 50 FR 19921, May 13, 1985]

§455.310c Chloramphenicol ointment (chloramphenicol cream).

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Chloramphenicol ointment is chloramphenicol in a suitable and harmless ointment base, with or without suitable and harmless buffer substances, dispersing and suspending agents. It may contain cortisone or a suitable derivative of cortisone. If such base is water-miscible, it shall contain a suitable and harmless preservative. Its potency is not less than 1.0 milligram per gram. If it is intended for ophthalmic use, it is sterile. The chloramphenicol used conforms to the requirements of §455.10a(a)(1), except

paragraphs (a)(1) (ii), (iii), and (v) of that section. The chloramphenicol used in making the chloramphenicol ophthalmic ointment conforms to the requirements of §455.10a(a)(1), except paragraphs (a)(1) (iii) and (v) of that section. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging*. Unless it is packaged in a single dose container, chloramphenicol ointment shall be packaged in collapsible tubes, which shall be well-closed containers as defined by the U.S.P., and shall not be larger than the 1/8-ounce size if such ointment is represented for ophthalmic use, and in no case larger than the 2-ounce size, except that if it is labeled solely for hospital use it may be packaged in immediate containers of glass which meet the test for tight containers as defined by the U.S.P. The composition of the immediate container and closure shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in