

remove an accurately measured representative portion from each container. Dilute this portion with sufficient distilled water to give a stock solution of convenient concentration. If the preparation is packaged in a prefilled syringe, eject the entire contents of the syringe and dilute with distilled water to obtain a stock solution of convenient concentration. Further dilute the stock solution to the reference concentration of 2.5 micrograms of tobramycin 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) *Pyrogens*. Proceed as directed in §436.32(a) of this chapter, using a solution containing 10 milligrams of tobramycin per milliliter.

(4) [Reserved]

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

[40 FR 57798, Dec. 12, 1975, as amended at 50 FR 19919, May 13, 1985]

**§ 444.281 Sterile tobramycin sulfate.**

The requirements for certification and the tests and methods of assay for sterile tobramycin sulfate packaged for dispensing are described in §444.81a.

[44 FR 26072, May 4, 1979]

**Subpart D—Ophthalmic Dosage Forms**

**§ 444.320 Gentamicin sulfate ophthalmic dosage forms.**

**§ 444.320a Gentamicin sulfate ophthalmic solution.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Gentamicin sulfate ophthalmic solution contains in each milliliter the equivalent of 3.0 milligrams of gentamicin and suitable buffers and preservatives. Its potency is satisfactory if it is not less than 90 and not more than 135 percent of the number of milligrams of gentamicin it is represented to contain. It is sterile. Its pH is not less than 6.5 nor more than 7.5. The gentamicin sulfate conforms to the standards prescribed by §444.20(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 gentamicin sulfate used in making the batch for potency, loss on drying, pH, specific rotation, content of gentamicins C<sub>1</sub>, C<sub>1a</sub>, and C<sub>2</sub>, and identity.

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

(ii) Samples required:

(a) The gentamicin sulfate used in making the batch: 10 packages, each containing not less than 500 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 §436.105 of this chapter, preparing the sample for assay as follows: Dilute an accurately measured representative portion of the product with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 0.1 microgram of gentamicin 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 sample.

[39 FR 19046, May 30, 1974, as amended at 50 FR 19919, May 13, 1985]

**§ 444.320b Gentamicin sulfate ophthalmic ointment.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Gentamicin sulfate ointment contains in each gram the equivalent of 3.0 milligrams of gentamicin with suitable preservatives in a white petrolatum base. Its potency is satisfactory if it is not less than 90 percent and not more than 135 percent of the number of milligrams of gentamicin

that it is represented to contain. It is sterile. Its moisture content is not more than 1.0 percent. It passes the test for particulate contamination. The gentamicin sulfate used conforms to the standards prescribed therefor by § 444.20a(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 gentamicin sulfate used in making the batch for potency, loss on drying, pH, specific rotation, content of gentamicins C<sub>1</sub>, C<sub>1a</sub>, and C<sub>2</sub>, and identity.

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

(ii) Samples required:

(a) The gentamicin sulfate used in making the batch: 10 packages, each containing not less than 500 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 § 436.105 of this chapter, except prepare the sample as follows: Place an accurately weighed representative portion of the ointment into a separatory funnel containing 50 milliliters of peroxide-free ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of 0.1M potassium phosphate buffer, pH 8.0 (solution 3), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction with new portions of solution 3. Repeat any additional times necessary to insure complete extraction of the antibiotic. Combine the extractives and adjust to an appropriate volume to give a stock solution of convenient concentration. Further dilute with solution 3 to the reference concentration of 0.1 microgram of gentamicin per milliliter (estimated).

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the meth-

od described in paragraph (e)(3) of that section.

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

(4) *Particulate contamination.* Proceed as directed in § 436.206 of this chapter.

[39 FR 19046, May 30, 1974, as amended at 50 FR 19919, May 13, 1985]

**§ 444.320c Gentamicin sulfate-prednisolone acetate ophthalmic suspension.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Gentamicin sulfate-prednisolone acetate ophthalmic suspension is an aqueous suspension containing in each milliliter gentamicin sulfate equivalent to 3.0 milligrams of gentamicin and 10.0 milligrams of prednisolone acetate. It contains suitable and harmless chelating agents, tonicity agents, buffers, and preservatives. Its gentamicin content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of gentamicin that it is represented to contain. Its prednisolone acetate content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of prednisolone acetate that it is represented to contain. Its pH is not less than 5.4 and not more than 6.6. It is sterile. The gentamicin sulfate used conforms to the standards prescribed by § 444.20(a)(1). The prednisolone acetate used conforms to the standards prescribed by the USP XXI.

(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 gentamicin sulfate used in making the batch for potency, loss on drying, pH, specific rotation, content of gentamicin C<sub>1</sub>, C<sub>1a</sub>, C<sub>2</sub>, and identify.

(B) The prednisolone acetate used in making the batch for all USP XXI specifications.

(C) The batch for gentamicin content, prednisolone acetate content, sterility, and pH.