

(a) The neomycin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(b) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, and identity.

(c) The batch for neomycin content, polymyxin B content, sterility, and pH.

(i) Samples required:

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

(b) The polymyxin B sulfate used in making the batch: 10 packages each containing approximately 300 milligrams.

(c) The batch:

(1) For all tests except sterility: A minimum of 6 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*—(i) *Neomycin content*. Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Place an accurately measured representative portion of the sample into an appropriate-sized volumetric flask with sufficient 0.1 M potassium phosphate buffer, pH 8.0 (solution 3), to obtain a stock solution of convenient concentration. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(ii) *Polymyxin B content*. Proceed as directed in §436.105 of this chapter, except add to each concentration of the polymyxin B standard response line a quantity of neomycin to yield the same concentration of neomycin as that present when the sample is diluted to contain 10 units of polymyxin B per milliliter. Prepare the sample for assay as follows: Place an accurately measured representative portion of the sample into an appropriate-sized volumetric flask with sufficient 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to obtain a stock solution of convenient concentration. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B 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 0.25 milliliter in lieu of 1.0 milliliter.

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

[47 FR 23441, May 28, 1982; 47 FR 25320, June 11, 1982, as amended at 50 FR 19919, May 13, 1985; 55 FR 14969, Apr. 20, 1990; 59 FR 8399, Feb. 22, 1994]

**§ 444.342k Neomycin sulfate-polymyxin B sulfate-dexamethasone ophthalmic ointment.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Neomycin sulfate-polymyxin B sulfate-dexamethasone ophthalmic ointment contains in each gram neomycin sulfate equivalent to 3.5 milligrams of neomycin, polymyxin B sulfate equivalent to 10,000 units of polymyxin B and 1.0 milligram of dexamethasone with suitable preservatives in a suitable and harmless ointment base. Its neomycin sulfate content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of neomycin that it is represented to contain. Its polymyxin B sulfate content is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of milligrams of polymyxin B 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 neomycin sulfate used conforms to the standards prescribed by §444.42(a)(1). The polymyxin B sulfate used conforms to the standards prescribed by §448.30(a)(1) of this chapter.

(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 neomycin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(b) The polymyxin B sulfate used in making the batch for potency, loss on drying, pH, and identity.

(c) The batch for neomycin content, polymyxin B content, moisture, and metal particles.

(ii) Samples required:

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

(b) The polymyxin B sulfate used in making the batch: 10 packages, each containing approximately 300 milligrams.

(c) The batch:

(1) For all tests except sterility: A minimum of 16 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*—(i) *Neomycin content*. Proceed as directed in § 436.105 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 0.1 M potassium phosphate buffer, pH 8.0 (solution 3), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 3. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 3. Remove an aliquot and further dilute with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(ii) *Polymyxin B content*. Proceed as directed in § 436.105 of this chapter, except add to each concentration of the polymyxin B standard response line a quantity of neomycin to yield the same concentration of neomycin as that present when the sample is diluted to contain 10 units of polymyxin B per milliliter. Prepare 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 10 percent potassium phosphate buffer, pH 6.0 (solution 6), and shake well. Allow the layers to sepa-

rate. Remove the buffer layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of solution 6. Combine the buffer extractives in a suitable volumetric flask and dilute to volume with solution 6. Remove an aliquot and further dilute with solution 6 to the reference concentration of 10 units of polymyxin B 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.

[47 FR 23442, May 28, 1982; 47 FR 25320, June 11, 1982, as amended at 50 FR 19919, May 13, 1985; 55 FR 14969, Apr. 20, 1990]

#### § 444.380 Tobramycin ophthalmic dosage forms.

##### § 444.380a Tobramycin ophthalmic solution.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Tobramycin ophthalmic solution contains in each milliliter 3.0 milligrams of tobramycin in a suitable and harmless aqueous vehicle. It contains suitable and harmless buffers, dispersants, preservatives, and tonicity agents. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of tobramycin that it is represented to contain. It is sterile. Its pH is not less than 7.0 and not more than 8.0. The tobramycin used conforms to the standards prescribed by § 444.80(a)(1), except heavy metals.

(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 tobramycin used in making the batch for potency, moisture, pH, identity, and residue on ignition.

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

(ii) Samples required: