

(c) An expiration date that is 12 months after the month during which the batch was certified.

(ii) On the label of the immediate container or other labeling attached to or within the package, adequate directions under which the layman can use the drug safely and efficaciously.

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

(b) The batch for potency.

(ii) Samples required:

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

(b) The batch: A minimum of five immediate containers.

(c) In case of an initial request for certification, each other ingredient used in making the batch: One package of each containing approximately 5 grams.

(b) *Tests and methods of assay; potency.* Proceed as directed in § 444.42a(b)(1), except prepare the sample for assay as follows: Place an accurately measured representative portion into a high-speed glass blender with sufficient 0.1M potassium phosphate buffer, pH 8, to give a stock solution of convenient concentration. Blend 3 to 5 minutes. Make further dilutions with 0.1M potassium phosphate buffer, pH 8, to the proper prescribed reference concentration. Its content of neomycin 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.

[39 FR 19046, May 30, 1974, as amended at 49 FR 34351, Aug. 30, 1984]

**§ 444.542d [Reserved]**

**§ 444.542e Neomycin sulfate-polymyxin B sulfate ointment.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Neomycin sulfate-polymyxin B sulfate ointment is an ointment containing, in each gram, 3.5 milligrams of neomycin and 5,000 units of

polymyxin B with suitable and harmless emollients, dispersants, and preservatives in a suitable and harmless water-miscible base. The neomycin sulfate used conforms to the standards prescribed by § 444.42a(a)(1) (i), (vi), and (vii). The polymyxin B sulfate used conforms to the standards prescribed by § 448.30a(a)(1) (i), (vi), (vii), and (ix) of this chapter. 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) *Labeling.* Each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On the label of the immediate container and on the outside wrapper or container, if any:

(a) The batch mark.

(b) The name and quantity of each active ingredient contained in the drug.

(c) An expiration date that is 12 months after the month during which the batch was certified.

(ii) On the label of the immediate container or other labeling attached to or within the package, adequate directions under which the layman can use the drug safely and efficaciously.

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

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

(c) The batch for neomycin content and polymyxin content.

(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: A minimum of 6 immediate containers.

(d) In case of an initial request for certification, each other ingredient used in making the batch: One package

of each containing approximately 5 grams.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Neomycin content*. Proceed as directed in §444.542a(b)(1)(ii). Its content of neomycin is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of milligrams of neomycin that it is represented to contain.

(ii) *Polymyxin content*. Proceed as directed in §436.105 of this chapter, except add to each concentration of the polymyxin standards 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. 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. Remove the buffer layer and repeat the extraction procedure with each of three more 20 to 25 milliliter quantities of solution 6. Combine the extractives in a suitable volumetric flask and fill to volume with solution 6. Further dilute an aliquot with solution 6 to the reference concentration of 10 units of polymyxin B per milliliter (estimated). Its content of polymyxin is satisfactory if it is not less than 90 percent and not more than 125 percent of the number of units of polymyxin that it is represented to contain.

**§ 444.542f Neomycin sulfate-gramicidin topical ointment; neomycin sulfate-gramicidin-triamcinolone acetone ointment; neomycin sulfate-gramicidin-fludrocortisone acetate ointment.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Each gram of neomycin sulfate-gramicidin topical ointment contains 2.5 milligrams of neomycin and 0.25 milligram of gramicidin. Neomycin sulfate-gramicidin-triamcinolone acetone ointment is an ointment containing, in each gram, 2.5 milligrams of neomycin, 0.25 milligram of gramicidin, and 1.0 milligram of triamcinolone acetone. Neomycin

sulfate-gramicidin-fludrocortisone acetate ointment is an ointment containing, in each gram, 2.5 milligrams of neomycin, 0.25 milligram of gramicidin, and 1.0 milligram of fludrocortisone acetate. If it is intended for ophthalmic use, it is sterile. Their moisture content is not more than 1.0 percent. The neomycin sulfate used conforms to the standards prescribed by §444.42a(a)(1)(i), (v), (vi), and (vii), and in addition if it is used in the preparation of an ophthalmic ointment, paragraph (a)(1) of that section. The gramicidin used conforms to the standards prescribed by §448.25(a)(1)(i), (iii), (iv), (v), and (vi) of this chapter, and in addition if it is used in the preparation of an ophthalmic ointment, paragraph (a)(1) 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) *Labeling*. If it contains a steroid or it is intended for ophthalmic use, it shall be labeled in accordance with the requirements of §432.5 of this chapter, and its expiration date is 12 months. If it does not contain a steroid or it is not intended for ophthalmic use, each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On the label of the immediate container and on the outside wrapper or container, if any:

(a) The batch mark.

(b) The name and quantity of each active ingredient contained in the drug.

(c) An expiration date that is 12 months after the month during which the batch was certified.

(ii) On the label of the immediate container or other labeling attached to or within the package, adequate directions under which the layman can use the drug safely and efficaciously.

(3) *Requests for certifications; 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 neomycin sulfate used in making the batch for potency, moisture, pH, and identity.