

flask. Add 25 milliliters of hexane and sonicate. Add 2.0 milliliters of the internal standard. Dilute to volume with methyl alcohol. Shake vigorously for 30 seconds and allow the phase to separate. Aspirate the upper hexane and cloudy layers. Dilute to volume with methyl alcohol. Centrifuge for 10 minutes at 5,700 revolutions per minute.

(iii) *System suitability requirements—*(A) *Tailing factor.* The tailing factor (*T*) is satisfactory if it is not more than 1.50 at 5 percent of peak height.

(B) *Efficiency of the column.* The efficiency of the column (*n*) is satisfactory if it is greater than 2,500 theoretical plates.

(C) *Resolution.* The resolution (*R*) between the peak for prednisolone acetate and the internal standard is satisfactory if it is not less than 2.0.

(D) *Coefficient of variation.* The coefficient of variation (*S<sub>R</sub>* in percent) of five replicate injections is satisfactory if it is not more than 2.0 percent. If the system suitability requirements have been met, then proceed as described in §436.216(b) of this chapter. Alternate chromatographic conditions are acceptable provided comparable system suitability requirements are met. However, the sample preparation described in paragraph (b)(2)(ii)(B) of this section should not be changed.

(iv) *Calculations.* Calculate the percent of prednisolone acetate as follows:

$$\text{Percent of prednisolone acetate (w/w)} = \frac{R_u \times P_s \times d \times 100}{R_s \times W_u}$$

where:

*R<sub>u</sub>*=Area of the prednisolone acetate peak in the chromatogram of the sample (at a retention time equal to that observed for the standard)/Area of internal standard peak;

*R<sub>s</sub>*=Area of the prednisolone acetate peak in the chromatogram of the prednisolone acetate working standard /Area of internal standard peak;

*P<sub>s</sub>*=Prednisolone acetate activity in the prednisolone acetate working standard solution in milligrams per milliliter;

*W<sub>u</sub>*=Weight of sample in milligrams; and

*d*=Dilution factor of the sample.

(3) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in §436.20(e)(3).

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

(5) *Metal particles.* Proceed as directed in §436.206 of this chapter.

[55 FR 2643, Jan. 26, 1990]

**§ 444.342 Neomycin sulfate ophthalmic dosage forms.**

**§ 444.342a Neomycin sulfate-ophthalmic suspension; neomycin sulfate-ophthalmic solution (the blanks being filled in with the established name(s) of the other active ingredient(s) present in accordance with paragraph (a)(1) of this section).**

(a) *Requirements for certification—*(1) *Standards of identity, strength, quality, and purity.* The drug is a suspension or a solution containing, in each milliliter, 3.5 milligrams of neomycin and the following other active ingredients in a suitable and harmless vehicle:

- (i) 15 milligrams of cortisone acetate; or
- (ii) 5 milligrams or 25 milligrams of hydrocortisone acetate; or
- (iii) 1 milligram or 2 milligrams of prednisolone; or
- (iv) 1 milligram of sodium dexamethasone phosphate; or
- (v) 5 milligrams of prednisolone phosphate.

It contains suitable and harmless buffers, dispersants, and preservatives. It is sterile. Its pH is not less than 6.0 and not more than 8.0. The neomycin sulfate used conforms to the standards prescribed by §444.42a(a)(1) (i), (vi), and (vii). 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.* It shall be labeled in accordance with the requirements of §432.5 of this chapter. Its expiration date is 12 months.

(3) *Request 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, sterility, and pH.
- (ii) Samples required:
  - (a) The neomycin sulfate used in making the batch: 10 containers, each

containing approximately 300 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 5 immediate containers.

(2) For sterility testing: 20 immediate containers collected at regular intervals throughout each filling operation.

(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*—(1) *Potency*. Proceed as directed in § 444.442a(b)(1). Its neomycin content is satisfactory if it contains not less than 90 percent and not more than 130 percent of the number of milligrams of neomycin that it is represented to contain.

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except if the steroid prevents solubilization, use 0.25 milliliter of sample in lieu of 1 milliliter and proceed as directed in paragraph (e)(2) of that section.

(3) *pH*. Proceed as directed in § 440.80a(b)(5)(ii) of this chapter, using the undiluted sample.

[39 FR 19046, May 30, 1974, as amended at 47 FR 23441, May 28, 1982; 50 FR 19919, May 13, 1985; 59 FR 8398, Feb. 22, 1994]

**§ 444.342b Neomycin sulfate-polymyxin B sulfate-gramicidin ophthalmic solution.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Neomycin sulfate-polymyxin B sulfate-gramicidin ophthalmic solution is a solution containing in each milliliter, 1.75 milligrams of neomycin, 10,000 units of polymyxin B and 0.025 milligram of gramicidin, and with one or more suitable and harmless buffers, dispersants, and preservatives in a suitable and harmless isotonic aqueous vehicle. It is sterile. Its pH is not less than 4.7 and not more than 6.0. 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. The gramicidin used con-

forms to the standards prescribed by § 448.25(a)(1)(i), (iv), (v), and (vi) 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*. It shall be labeled in accordance with the requirements of § 432.5 of this chapter. Its expiration date is 12 months.

(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 gramicidin used in making the batch for potency, residue on ignition, melting point, crystallinity, and identity.

(d) The batch for neomycin content, polymyxin content, gramicidin content, sterility, and pH.

(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 gramicidin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(d) The batch:

(1) For all tests except sterility: A minimum of 7 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation, except that if the product is sterilized after filling, a representative sample consisting of 10 immediate containers from each sterilizer load. If only 1 sterilizer load is involved, the sample shall consist of 20 immediate containers.

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