

(ii) Samples required:

(a) The paromomycin sulfate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Remove an appropriate aliquot of the sirup and transfer to an appropriate-sized volumetric flask. Dilute to volume with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), and mix well. Further dilute with solution 3 to the reference concentration of 1.0 microgram of paromomycin per milliliter (estimated).

(2) *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]

### Subpart C—Injectable Dosage Forms

#### § 444.206 Amikacin sulfate injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Amikacin sulfate injection is an aqueous solution of amikacin with suitable and harmless buffer substances and preservatives. Each milliliter contains amikacin sulfate equivalent to either 50 milligrams or 250 milligrams of amikacin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of amikacin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 3.5 and not more than 5.5. The amikacin used conforms to the standards prescribed by §444.6(a)(1) or, if amikacin sulfate is used, to the standards prescribed by §444.7(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 amikacin used in making the batch for potency, moisture, pH, identity, residue on ignition, specific rotation, and crystallinity.

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

(i) Samples required:

(a) The amikacin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 12 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: Place an accurately measured representative portion of the sample into an appropriate-sized volumetric flask and dilute to volume with sterile distilled water to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with sterile distilled water to the reference concentration of 10.0 micrograms of amikacin 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(b) of this chapter, using a solution containing 25 milligrams of amikacin per milliliter.

(4) [Reserved]

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

[41 FR 49483, Nov. 9, 1976, as amended at 50 FR 19919, May 13, 1985; 55 FR 38677, Sept. 20, 1990]

#### § 444.220 Gentamicin sulfate injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Gentamicin sulfate injection is an aqueous solution of gentamicin sulfate with or without one or more suitable buffers, sequestering agents, tonicity agents, or preservatives. Each milliliter contains gentamicin sulfate equivalent to either 0.4, 0.6, 0.7, 0.8, 0.9, 1.0, 1.2, 1.6, 2.0, 2.4, 10.0, or 40 milligrams of gentamicin. Its potency is satisfactory if it contains

not less than 90 percent nor more than 125 percent of the number of milligrams of gentamicin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 3.0 nor more than 5.5. The gentamicin sulfate used 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 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  $C_1$ ,  $C_{1a}$ ,  $C_2$ , and identity.

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

(ii) Samples required:

(a) The gentamicin sulfate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 40 containers if each milliliter contains the equivalent of 2.0 milligrams or 10.0 milligrams of gentamicin; a minimum of 12 containers if each milliliter contains the equivalent of 40.0 milligrams of gentamicin; or, a minimum of 10 containers if each milliliter contains the equivalent of 1.0 milligram of gentamicin.

(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: Using 0.1M potassium phosphate buffer, pH 8.0 (solution 3), dilute an accurately measured representative portion of the product 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) [Reserved]

(4) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, except inject

a sufficient volume of the undiluted solution to deliver 10 milligrams of gentamicin per kilogram, but not to exceed 10 milliliters per kilogram.

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

[39 FR 19046, May 30, 1974, as amended at 46 FR 2994, Jan. 13, 1981; 46 FR 16683, Mar. 13, 1981; 46 FR 31009, June 12, 1981; 47 FR 56490, Dec. 17, 1982; 48 FR 44775, Sept. 30, 1983; 49 FR 49287, Dec. 19, 1984; 50 FR 10754, Mar. 18, 1985; 50 FR 19919, May 13, 1985]

#### § 444.230 Kanamycin sulfate injection.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Kanamycin sulfate injection is an aqueous solution of kanamycin sulfate with suitable and harmless buffer substances and preservatives. It contains either 75 milligrams of kanamycin per 2.0 milliliters, or 250 milligrams of kanamycin per milliliter, or 1.0 gram of kanamycin per 3.0 milliliters. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of milligrams of kanamycin that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 3.5 and not more than 5.0. The kanamycin sulfate used conforms to the standards prescribed by § 444.30a(a)(1)(i), (v), (vii), (viii), (ix), and (x).

(2) *Labeling.* In addition to the requirements prescribed by § 432.5 of this chapter, the labeling of each package shall bear a warning to the effect that older patients and patients receiving a total dose of more than 20 grams of the drug should be carefully observed for signs of eighth-nerve damage. In patients with impaired kidney function or with prerenal azotemia, the risk of severe ototoxic reaction that may result in permanent deafness is sharply increased.

(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 kanamycin sulfate used in making the batch for potency, residue on ignition, loss on drying, identity, crystallinity, and kanamycin B content.