

(3) *Labeling.* Each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On its outside wrapper or container and on the immediate container.

(a) The statements "Not for therapeutic use" and "For laboratory diagnosis only".

(b) The statement "Sterile".

(c) The batch mark.

(d) The number of milligrams of colistin base activity in each immediate container.

(e) The statements "Stock solutions are stable for 14 days when refrigerated. For periods of storage up to 6 months, they should be frozen".

(f) Its expiration date which is 12 months, except that the date may be used that is 18, 24, 30, 36, 42, 48, 54, or 60 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that such drug as prepared by him is stable for such period of time. If the manufacturer or repacker of the drug has been exempted from the certification requirements, such date shall be the number of months after the month during which the batch was last assayed and released by the manufacturer or repacker.

(ii) On the circular or other labeling within or attached to the package, adequate information for use of the drug in the clinical laboratory.

(4) *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 sodium colistimethate used in making the batch for potency, moisture, pH, and identity.

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

(ii) Samples required:

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

(b) The batch:

(1) For all tests except sterility: A minimum of 30 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 §448.20a(b)(1) of this chapter, except prepare the sample for assay as follows: Reconstitute as directed in the labeling and further dilute with 10 percent potassium phosphate buffer, pH 6.0, to the proper prescribed reference concentration. Its potency is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of colistin base activity 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.

(3) *Moisture.* Proceed as directed in §440.80a(b)(5)(i) of this chapter.

(4) *pH.* Proceed as directed in §440.80a(b)(5)(ii) of this chapter, using the drug reconstituted as directed in the labeling.

(5) *Identity.* Proceed as directed in §448.20a(b)(7) of this chapter.

**§460.42 Dihydrostreptomycin sulfate diagnostic sensitivity powder.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Dihydrostreptomycin sulfate sensitivity powder is crystalline dihydrostreptomycin sulfate, with or without one or more suitable buffers and diluents, packaged in vials and intended for use in clinical laboratories for determining in vitro the sensitivity of microorganisms to dihydrostreptomycin. Each vial contains dihydrostreptomycin sulfate equivalent to 20 milligrams of dihydrostreptomycin. The potency of each immediate container is satisfactory if it contains not less than 90 percent and not more than 115 percent of its labeled content. It is sterile. Its loss on drying is not more than 5.0 percent. When reconstituted as directed in the labeling, its pH is not less than 4.5 and not more than 7.0. The dihydrostreptomycin sulfate used conforms to the standards prescribed by §444.10a(a)(1) of this chapter, except the standards for sterility, pyrogens, and depressor substances. 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) *Packaging.* The immediate container shall be of colorless, transparent glass and it shall be a tight container as defined by the U.S.P. It shall be so sealed that the contents cannot be used without destroying such seal. It shall be of appropriate size to permit the addition of 20 milliliters of sterile diluent when preparing a stock solution for use in making further dilutions for microbial susceptibility testing.

(3) *Labeling.* In addition to the requirements of § 432.5(a)(3) of this chapter, each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On its outside wrapper or container and on the immediate container:

(a) The statement "For laboratory diagnostic use only".

(b) The statement "Sterile".

(c) The batch mark.

(d) The number of milligrams of dihydrostreptomycin in each immediate container.

(ii) On the circular or other labeling within or attached to the package, adequate information for use of the drug in the clinical laboratory.

(4) *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 dihydrostreptomycin sulfate used in making the batch for potency, moisture, pH, streptomycin content, and crystallinity.

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

(ii) Samples required:

(a) The dihydrostreptomycin 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 20 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: Reconstitute as directed in the labeling. Dilute an aliquot with sterile distilled water to the prescribed reference concentration.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Loss on drying.* Proceed as directed in § 436.200(b) of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using the drug reconstituted as directed in the labeling.

[39 FR 19181, May 30, 1974, as amended at 46 FR 60569, Dec. 11, 1981; 50 FR 19921, May 13, 1985]

**§ 460.47 Doxycycline hyclate diagnostic sensitivity powder.**

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Doxycycline hyclate diagnostic sensitivity powder is crystalline doxycycline hyclate, with or without one or more suitable buffers and diluents, packaged in vials and intended for use in clinical laboratories for determining in vitro the sensitivity of microorganisms to doxycycline. Each vial contains doxycycline hyclate equivalent to 20 milligrams of doxycycline. The potency of each immediate container is satisfactory if it contains not less than 90 percent and not more than 115 percent of its labeled content. It is sterile. Its moisture content is not more than 4 percent. When reconstituted as directed in the labeling, its pH is not less than 2.0 and not more than 3.5. The doxycycline hyclate used conforms to the standards prescribed by § 446.20(a)(1) (i), (iii), (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) *Packaging.* The immediate container shall be of colorless, transparent glass and it shall be a tight container as defined by the U.S.P. It shall be so sealed that the contents cannot be used without destroying such seal. It shall be of appropriate size to permit the addition of 20 milliliters of sterile diluent when preparing a stock solution for use in making further dilutions for microbial susceptibility testing.

(3) *Labeling.* In addition to the requirements of § 432.5(a)(3) of this chapter, each package shall bear on its label or labeling, as hereinafter indicated, the following: