

(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 doxycycline 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 doxycycline hyclate used in making the batch for potency, moisture, pH, doxycycline content, identity, and crystallinity.

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

(ii) Samples required:

(a) The doxycycline hyclate used in making the batch: 10 packages, each containing approximately 300 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. Transfer a 10-milliliter aliquot to a 100-milliliter volumetric flask and dilute to volume with 0.1N hydrochloric acid. Further dilute an aliquot of this solution with 0.1M potassium phosphate buffer, pH 4.5 (solution 4), to the reference concentration of 0.1 microgram of doxycycline per milliliter.

(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 §436.201 of this chapter.

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

§ 460.55 Lincomycin hydrochloride monohydrate diagnostic sensitivity powder.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Lincomycin hydrochloride monohydrate diagnostic sensitivity powder is lincomycin hydrochloride monohydrate powder packaged in vials and intended for use in clinical laboratories for determining in vitro the sensitivity of microorganisms to lincomycin. Each vial contains 20 milligrams of lincomycin. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of lincomycin that it is represented to contain. It is sterile. Its moisture content is not more than 7 percent. It gives a positive identity test for lincomycin hydrochloride monohydrate. The lincomycin hydrochloride monohydrate used conforms to the standards prescribed by §453.30(a)(1) (i), (iii), (iv), (v), and (ix) of this chapter.

(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 broth medium when preparing a stock solution for use in making serial 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 statements "Not for therapeutic use" and "For laboratory diagnosis only".

(b) The statement "Sterile."

(c) The batch mark.

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

(e) The statements "Store in a refrigerator" and "Reconstituted solutions should be refrigerated."

(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 lincomycin hydrochloride monohydrate used in making the batch for potency, moisture, pH, crystallinity, and specific rotation.

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

(ii) Samples required:

(a) The lincomycin hydrochloride monohydrate 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 §436.105 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Dilute an aliquot with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 2.0 micrograms of lincomycin 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) *Moisture.* Proceed as directed in §436.201 of this chapter.

(4) *Identity.* In a 100-milliliter beaker, dissolve sufficient sample to yield a concentration of at least 80 milligrams per milliliter, using no more than 2.0 milliliters of water. Add acetone until precipitation begins and then add an additional 20 milliliters of acetone. Filter the solution through filter paper and wash with two 10-milliliter portions of acetone. Expose the residue at room temperature until it is dry enough to be reduced to moderately fine particles. Dry the material for 4 hours in a 60° C. vacuum oven. After drying the material, care must be taken to avoid extended exposure to the atmosphere. The infrared spectrum of a mineral oil dispersion of the residue thus obtained exhibits maxima at the same wavelengths as that of the

lincomycin working standards, similarly treated.

§ 460.58 Methacycline hydrochloride diagnostic sensitivity powder.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Methacycline hydrochloride diagnostic sensitivity powder is the crystalline methacycline hydrochloride, 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 methacycline. Each vial contains methacycline hydrochloride equivalent to 20 milligrams of methacycline. 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 4.0 percent. When reconstituted as directed in the labeling, its pH is not less than 2.0 and not more than 3.5. The methacycline hydrochloride used conforms to the standards prescribed by §446.50(a)(1) (i), (iii), (v), and (vi) of this chapter.

(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) 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.”

(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: