

(b) *Tests and methods of assay*—(1) *Potency*. Assay for potency by any of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Microbiological agar diffusion assay*. Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 unit of penicillin V per milliliter (estimated).

(ii) *Iodometric assay*. Proceed as directed in §436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay*. Proceed as directed in §436.205 of this chapter.

(2) [Reserved]

(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 an aqueous solution containing 30 milligrams per milliliter.

(5) *Penicillin V content*. Dissolve and dilute approximately 20 milligrams of the sample, accurately weighed to 100 milliliters with 0.1*N* sodium hydroxide solution. Treat a portion of the penicillin V working standard in the same manner. Using a suitable spectrophotometer equipped with a quartz cell and 0.1*N* sodium hydroxide solution as the blank, determine the absorbance of the peak at 275 nanometers. Calculate the percent penicillin V as follows:

$$\text{Percent penicillin V} = \frac{\text{Absorbance of sample} \times \text{Weight in milligrams of standard} \times \text{Percent penicillin V in standard}}{\text{Absorbance of standard} \times \text{Weight in milligrams of sample}}$$

(6) *Crystallinity*. Proceed as directed in §436.203(a) of this chapter.

[42 FR 59859, Nov. 22, 1977, as amended at 50 FR 19918, 19919, May 13, 1985]

§440.74a Sterile penicillin G procaine.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Penicillin G procaine is 3,3 - dimethyl - 7 - oxo - 6 - (2 - phenylacetamido) - 4 - thia - 1 - azabicyclo [3.2.0]heptane-2-carboxylic acid 2-(diethylamino) ethyl *p*-aminobenzoate compound (1:1). It is so purified and dried that:

(i) Its potency is not less than 900 units and not more than 1,050 units per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not less than 2.8 percent and not more than 4.2 percent.

(vi) Its pH in a saturated aqueous solution (about 300 milligrams per milliliter) is not less than 5.0 and not more than 7.5.

(vii) Its penicillin G content is not less than 51.0 percent and not more than 59.6 percent.

(viii) It is crystalline.

(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 the batch for potency, sterility, pyrogens, moisture, pH, penicillin G content, and crystallinity.

(ii) Samples required:

(a) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(b) For sterility testing: 20 packages, each containing approximately 600 milligrams.

(b) *Tests and methods of assay*—(1) *Potency*. Use any of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed sample in sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in §436.204 of this chapter.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed §436.205 of this chapter.

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except add sufficient penicillinase to diluting fluid A and swirl the flask to completely solubilize the sample before filtration. If the product contains lecithin, use diluting fluid D in lieu of A.

(3) *Pyrogens.* Proceed as directed in §436.32(h) of this chapter, using a solution containing 2,000 units of penicillin G per milliliter.

(4) [Reserved]

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

(6) *pH.* Proceed as directed in §436.202 of this chapter, using a saturated solution prepared by suspending 300 milligrams of sample per milliliter.

(7) *Penicillin G content.* Proceed as directed in §436.316 of this chapter.

(8) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[42 FR 59860, Nov. 22, 1977, as amended at 45 FR 16472, Mar. 14, 1980; 45 FR 22921, Apr. 4, 1980; 50 FR 19918, 19919, May 13, 1985]

§ 440.80 Penicillin G potassium.

(a) *Requirements for certification—(1) Standards of identity, strength, quality and purity.* Penicillin G potassium is potassium 3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate. It is so purified and dried that:

(i) Its potency is not less than 1,440 units and not more than 1,680 units per milligram.

(ii) Its loss on drying is not more than 1.5 percent.

(iii) The pH of an aqueous solution containing 60 milligrams per milliliter is not less than 5.0 and not more than 7.5.

(iv) Its penicillin G content is not less than 80.8 percent and not more than 94.3 percent.

(v) It is crystalline.

(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 test and assays on the batch for potency, loss on drying, pH, penicillin G content, and crystallinity.

(ii) Samples, if required by the Center for Drug Evaluation and Research: 10 packages, each containing approximately 300 milligrams.

(b) *Test and methods of assay—(1) Potency.* Proceed as directed in §440.80a(b)(1).

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

(3) *pH.* Proceed as directed in §436.202 of this chapter, using an aqueous solution containing 60 milligrams per milliliter.

(4) *Penicillin G content.* Proceed as directed in §436.316 of this chapter.

(5) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

[55 FR 38674, Sept. 20, 1990]

§ 440.80a Sterile penicillin G potassium.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Penicillin G potassium is potassium 3,3-dimethyl-7-oxo-6-(2-phenylacetamido)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate. It is so purified and dried that:

(i) Its potency is not less than 1,440 units and not more than 1,680 units per milligram. If it is packaged for dispensing, its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of units of penicillin G that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]