

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

(3) *Pyrogens*. Proceed as directed in § 436.32(a) of this chapter, except inject a sufficient volume of the undiluted solution to deliver 100 milligrams of ticarcillin per kilogram.

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

(5) *Identity*. The high-performance liquid chromatogram of the sample determined as directed in paragraph (b)(1) of this section compares qualitatively to that of the ticarcillin and clavulanic acid working standard.

[55 FR 5840, Feb. 20, 1990]

Subparts D–J [Reserved]

Subpart K—Bulk Drug Formulations for Repacking or for Manufacturing Use

§ 440.1080a Sterile penicillin G potassium buffered.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Penicillin G potassium, buffered, is a dry mixture of penicillin G potassium and the buffer sodium citrate in a quantity not less than 4.0 percent and not more than 5.0 percent by weight of its total solids. It may contain citric acid in a quantity not more than 0.15 percent of its total solids in place of a corresponding amount of sodium citrate. The sodium citrate and citric acid used in making the batch must conform to all U.S.P. specifications. It is so purified and dried that:

(i) Its potency is not less than 1,355 units and not more than 1,595 units per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

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

(vi) Its pH is not less than 6.0 and not more than 8.5.

(vii) Its penicillin G content is not less than 76.3 percent and not more than 89.8 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, loss on drying, 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*—(i) *Sample preparation*. Dissolve an accurately weighed sample in sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration.

(ii) *Assay procedures*. Assay for potency by any of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(a) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, diluting an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(b) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(c) *Hydroxylamine colorimetric assay*. Proceed as directed in § 436.205 of this chapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(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 20,000 units of penicillin G per milliliter.

(4) [Reserved]

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

(6) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 60 milligrams 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 59872, Nov. 22, 1977, as amended at 45 FR 22922, Apr. 4, 1980; 50 FR 19918, 19919, May 13, 1985]

§ 440.1081a Sterile penicillin G sodium, buffered.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Penicillin G sodium, buffered, is a dry mixture of penicillin G sodium and the buffer sodium citrate in a quantity not less than 4.0 percent and not more than 5.0 percent by weight of its total solids. It may contain citric acid in a quantity not more than 0.15 percent of its total solids in place of a corresponding amount of sodium citrate. The sodium citrate and citric acid used in making the batch must conform to all U.S.P. specifications. It is so purified and dried that:

(i) Its potency is not less than 1,420 units and not more than 1,667 units per milligram.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

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

(vi) Its pH is not less than 6.0 and not more than 7.5.

(vii) Its penicillin G content is not less than 80 percent and not more than 93.8 percent.

(viii) It is crystalline.

(ix) It passes the test for heat stability if it does not show a loss of more than 10 percent of its original potency.

(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, loss on drying, pH, penicillin G content, crystallinity, and heat stability.

(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*—(i) *Sample preparation*. Dissolve an accurately weighed sample in sufficient 1.0 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration.

(ii) *Assay procedures*. Assay for potency by any of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(a) *Microbiological agar diffusion assay*. Proceed as directed in § 436.105 of this chapter, diluting an aliquot of the stock solution with solution 1 to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(b) *Iodometric assay*. Proceed as directed in § 436.204 of this chapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(c) *Hydroxylamine colorimetric assay*. Proceed as directed in § 436.205 of this chapter, diluting an aliquot of the stock solution with solution 1 to the prescribed concentration.

(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 20,000 units of penicillin G per milliliter.

(4) [Reserved]

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

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

(9) *Heat stability*. Proceed as directed in § 436.214 of this chapter.

[42 FR 59873, Nov. 22, 1977; 43 FR 2393, Jan. 17, 1978, as amended at 45 FR 22922, Apr. 4, 1980; 50 FR 19918, 19919, May 13, 1985]