

reconstituted as directed in the labeling.

[42 FR 59871, Nov. 22, 1977, as amended at 43 FR 9799, Mar. 10, 1978; 45 FR 22922, Apr. 4, 1980; 50 FR 19918, 19919, May 13, 1985]

§ 440.280c Penicillin G potassium injection.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Penicillin G potassium injection is a frozen, aqueous, iso-osmotic solution of penicillin G potassium which may contain one or more suitable and harmless buffer substances and a tonicity adjusting agent. Each milliliter contains penicillin G potassium equivalent to 20,000, 40,000, or 60,000 units of penicillin G. Its penicillin G content 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. It is sterile. It is nonpyrogenic. Its pH is not less than 5.5 and not more than 8.0. The penicillin G potassium used conforms to the standards prescribed by § 440.80(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter. In addition, this drug shall be labeled "penicillin G potassium injection".

(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 penicillin G potassium used in making the batch for potency, loss on drying, pH, penicillin G content, and crystallinity.

(B) The batch for penicillin G content, sterility, pyrogens, and pH.

(ii) Samples, if required by the Center for Drug Evaluation and Research:

(A) The penicillin G potassium used in making the batch: 10 packages, each containing approximately 300 milligrams.

(B) The batch:

(1) For all tests except sterility: A minimum of 10 immediate containers.

(2) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay.* Thaw the sample as directed in the labeling.

The sample solution used for testing must be at room temperature.

(1) *Penicillin G content.* Proceed as directed in § 440.280b(b)(1) of this chapter, except use the thawed solution.

(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(a) of this chapter, except inject a sufficient volume of the undiluted solution to deliver 20,000 units of penicillin G per kilogram.

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

[55 FR 38675, Sept. 20, 1990]

§ 440.281 Pencillin G sodium injectable dosage forms.

§ 440.281a Sterile penicillin G sodium.

The requirements for certification and the tests and methods of assay for sterile penicillin G sodium packaged for dispensing are described in § 440.81a.

[42 FR 59872, Nov. 22, 1977]

§ 440.281b Penicillin G sodium for injection.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Penicillin G sodium for injection 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. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of units of penicillin G that it is represented to contain. It is sterile. It is nonpyrogenic. Its loss on drying is not more than 1.5 percent. Its pH is not less than 6.0 and not more than 7.5. The penicillin G sodium, buffered, used conforms to the standards prescribed by § 440.1081a(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 penicillin G sodium, buffered, used in making the batch for potency, loss on drying, pH, penicillin G content, crystallinity, and heat stability.

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

(ii) Samples required:

(a) The penicillin G sodium, buffered, used in making the batch: 10 packages, each containing approximately 60 milligrams.

(b) The batch:

(1) For all tests except sterility: A minimum of 10 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*—(i) *Sample preparation.* Reconstitute as directed in the labeling. Then using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or, if the labeling specifies the amount of potency in a given volume of the resultant preparation, remove an accurately measured representative portion from each container. Dilute with 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 meth-

od 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 §436.202 of this chapter, using an aqueous solution containing 60 milligrams per milliliter.

[42 FR 59872, 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]

§ 440.283 Sterile piperacillin sodium.

The requirements for certification and the tests and methods of assay for sterile piperacillin sodium packaged for dispensing are described in §440.83a [47 FR 15770, Apr. 13, 1982]

§ 440.290 Ticarcillin disodium injectable dosage forms.

§ 440.290a Sterile ticarcillin disodium.

The requirements for certification and the tests and methods of assay for sterile ticarcillin disodium packaged for dispensing are described in §440.90a.

[43 FR 9800, Mar. 10, 1978. Redesignated at 50 FR 33518, Aug. 20, 1985]

§ 440.290b Sterile ticarcillin disodium and clavulanate potassium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Ticarcillin disodium and clavulanate potassium is a dry mixture of ticarcillin disodium and clavulanate potassium, in which the ratio of ticarcillin to clavulanic acid is 15:1 or 30:1. Its ticarcillin potency is not less than 755 micrograms of ticarcillin per milligram on an anhydrous basis if the ratio is 30:1 and 733 micrograms of ticarcillin per milligram on an anhydrous basis if the ratio is 15:1. Its ticarcillin disodium content is satisfactory if it contains not less than 90 percent and not more than 115 percent of the number of milligrams of ticarcillin that it is represented to contain. Its clavulanate potassium content is satisfactory if it contains not less than 85 percent and not more than 120 percent of the number of milligrams of