

(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*. Use either 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: 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, remove an accurately measured representative portion from each container. Dissolve the sample thus obtained in 50 to 100 milliliters of absolute methyl alcohol and add sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Immediately 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, preparing the sample as follows: 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, remove an accurately measured representative portion from each container. Dissolve and dilute the sample thus obtained with 1 percent potassium phosphate buffer, pH 6.0 (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, except add sufficient penicillinase to diluting fluid A and swirl the flask to completely solubilize the procaine penicillin before filtration. If the product contains lecithin, use diluting fluid D in lieu of diluting fluid A. If the product contains sodium carboxymethylcellulose, add sufficient sterile carboxymethylcellulase to di-

luting fluid A or D to completely solubilize the sodium carboxymethylcellulose before filtration. If the preparation contains homogenizers or suspending agents that prevent solubilization, proceed as directed in paragraph (e)(2) of that section, except use medium B in lieu of medium 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) *pH*. Proceed as directed in §436.202 of this chapter, using the undiluted drug.

[42 FR 59870, 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]

§ 440.274c Sterile penicillin G procaine for suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Sterile penicillin G procaine for suspension is a dry mixture of penicillin G procaine and one or more suitable suspending or dispersing agents, buffer substances, and preservatives. 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. It is sterile. It is nonpyrogenic. Its moisture content is not less than 2.8 and not more than 4.2 percent. When reconstituted as directed in the labeling, its pH is not less than 5.0 and not more than 7.5. The penicillin G procaine used conforms to the standards prescribed by §440.74a(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 procaine used in making the batch for potency, moisture, pH, penicillin G content, and crystallinity.

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

(ii) Samples required:

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

(b) The batch:

(1) If the batch is packaged for repackaging:

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

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

(2) If the batch is packaged for dispensing:

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

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

(b) *Tests and methods of assay*—(1) *Potency*. Use either 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: If it is packaged for repackaging, dissolve an accurately weighed sample, equivalent to one dose, in 50 to 100 milliliters of absolute methyl alcohol and add sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. If it is packaged for dispensing, 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. Dissolve the sample thus obtained in 50 to 100 milliliters of absolute methyl alcohol and add sufficient 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to give a stock solution of convenient concentration. Immediately 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, pre-

paring the sample as follows: If it is packaged for repackaging, dissolve and dilute an accurately weighed sample, equivalent to one dose, with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the prescribed concentration. If it is packaged for dispensing, 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, remove an accurately measured representative portion from each container. Dissolve and dilute the sample thus obtained with 1 percent potassium phosphate buffer, pH 6.0 (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, except add sufficient penicillinase to diluting fluid A and swirl the flask to completely solubilize the procaine penicillin before filtration. If the product contains lecithin, use diluting fluid D in lieu of diluting fluid A. If the product contains sodium carboxymethylcellulose, add sufficient sterile carboxymethylcellulase to diluting fluid A or D to completely solubilize the sodium carboxymethylcellulose before filtration. If the preparation contains homogenizers or suspending agents that prevent solubilization, proceed as directed in paragraph (e)(2) of that section, except use medium B in lieu of medium 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 the suspension obtained when reconstituted as directed in the labeling.

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