penicillinase sufficient to inactivate the cloxacillin in each tube, to use Soybean–Casein Digest Medium containing polysorbate 80 solution (1 in 200) and an amount of sterile penicillinase sufficient to inactivate the cloxacillin in each tube, and to shake the tubes once daily.

Water, *Method I* ⟨921⟩: not more than 1.0%, 20 mL of a mixture of toluene and methanol (7:3) being used in place of methanol in the titration vessel.

Assay—

0.1M Phosphate buffer, Mobile phase, Diluent, Standard preparations, and *Chromatographic system*—Proceed as directed in the *Assay* under *Cloxacillin Benzathine*.

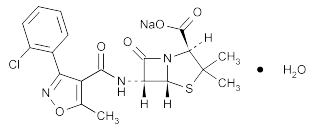
Assay preparations—In duplicate, quantitatively express the entire contents of a syringe of Cloxacillin Benzathine Intramammary Infusion into a 500-mL volumetric flask. Add about 300 mL of methanol, and stir for 45 minutes ± 1 minute. Dilute with methanol to volume, and stir for an additional 10 minutes ± 1 minute. Immediately transfer 45 mL of the resulting solution to a 50-mL polypropylene centrifuge tube, and centrifuge for 10 minutes. From the supernatant remove an aliquot, and dilute with a sufficient volume of *Diluent* to prepare a solution containing about 100 µg of cloxacillin per mL.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparations* and the *Assay preparations* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in µg, of $C_{19}H_{18}ClN_3O_5S$ in each syringe of Cloxacillin Benzathine Intramammary Infusion taken by the formula:

$$P(CD/1000)(r_U / r_S)$$

in which P is the assigned potency, in µg of cloxacillin per mg, of USP Cloxacillin Sodium RS; C is the concentration, in µg per mL, of cloxacillin sodium in the *Standard preparations; D* is the dilution factor used in preparing the *Assay preparations;* and r_U and r_S are the average peak areas of the cloxacillin peaks obtained from the *Assay preparations* and the *Standard preparations,* respectively.

Cloxacillin Sodium



$C_{19}H_{17}ClN_3NaO_5S \cdot H_2O$ 475.88

4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[[3-(2-chlorophenyl)-5-methyl-4-isoxazolyl]carbonyl]amino]-3,3-dimethyl-7-oxo-, monosodium salt, monohydrate, [2 *S*-(2α,5α,6β)]-.

Monosodium (2 *S*,5*R*,6*R*)-6-[3-(*o*-chlorophenyl)-5-methyl-4-isoxazolecarboxamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo [3.2.0]heptane-2-carboxylate monohydrate [7081-44-9].

Anhydrous 457.87 [642-78-4].

» Cloxacillin Sodium contains the equivalent of not less than 825 µg of cloxacillin ($C_{19}H_{18}ClN_3O_5S$) per mg.

Packaging and storage—Preserve in tight containers, and store at a temperature not exceeding 25 °.

Labeling—Where it is intended for use in preparing sterile dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of sterile dosage forms.

USP Reference standards ⟨11⟩—
USP Cloxacillin Sodium RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: It responds to the tests for *Sodium* ⟨191⟩.

Crystallinity ⟨695⟩: meets the requirements.

Sterility ⟨71⟩—Where the label states that Cloxacillin Sodium is sterile, it meets the requirements when tested as directed for *Direct Inoculation of the Culture Medium* under *Test for Sterility of the Product to be Examined,* except to use Fluid Thioglycollate Medium containing polysorbate 80 solution (1 in 200) and an amount of sterile penicillinase sufficient to inactivate the cloxacillin in each tube, to use Soybean–Casein Digest Medium containing polysorbate 80 solution (1 in 200) and an amount of sterile penicillinase sufficient to inactivate the cloxacillin in each tube, and to shake the tubes once daily.

pH ⟨791⟩: between 4.5 and 7.5, in a solution containing 10 mg per mL.

Water, *Method I* ⟨921⟩: between 3.0% and 5.0%.

Dimethylaniline ⟨223⟩: meets the requirement.

Assay—

Buffer—Prepare a 0.02 M solution of monobasic potassium phosphate in water, and adjust with 2 N sodium hydroxide to a pH of 6.8.

Mobile phase—Prepare a mixture of *Buffer* and acetonitrile (80:20). Make adjustments if necessar y (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Prepare a solution of USP Cloxacillin Sodium RS in *Buffer* having a known concentration of about 0.55 mg per mL.

Assay preparation—Transfer about 110 mg of Cloxacillin Sodium, accurately weighed, to a 200-mL volumetric flask, dilute with *Buffer* to volume, and mix. Stir with the aid of a magnetic stirrer for 5 minutes to dissolve.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 225-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 1.8; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in µg, of cloxacillin ($C_{19}H_{18}ClN_3O_5S$) in each mg of Cloxacillin Sodium taken by the formula:

$$200(CE / W)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Cloxacillin Sodium RS in the *Standard preparation; E* is the cloxacillin ($C_{19}H_{18}ClN_3O_5S$) equivalent, in µg per mg, of USP Cloxacillin Sodium RS; W is the weight, in mg, of Cloxacillin Sodium taken to prepare the *Assay preparation;* and r_U and r_S are the cloxacillin peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Cloxacillin Sodium Capsules

» Cloxacillin Sodium Capsules contain the equivalent of not less than 90.0 per cent and not more than 120.0 percent of the labeled amount of cloxacillin ($C_{19}H_{18}ClN_3O_5S$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Cloxacillin Sodium RS