Medium—Proceed as directed for *Test 2*.
Apparatus 2: 50 rpm.
Times: 1, 4, and 8 hours.
Procedure—Proceed as directed for *Procedure* in *Test 1*.
Tolerances—Proceed as directed for *Tolerances* in *Test 2*.
FOR 250 MG TABLETS—

Time (hours)	Amount dissolved
1	between 30% and 60%
4	between 60% and 90%
8	not less than 80%

FOR 500 MG TABLETS—

Time (hours)	Amount dissolved
1	between 30% and 50%
4	between 60% and 80%
8	not less than 85%

FOR 750 MG TABLETS—

Time (hours)	Amount dissolved
1	between 30% and 50%
4	between 60% and 80%
8	not less than 80%

TEST 8—If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 8*.
Medium— Proceed as directed for *Method B* under *Delayed-Release Dosage Forms*.
ACID STAGE: 0.1 N hydrochloric acid; 900 mL for 1 hour.
BUFFER STAGE: 0.05 M phosphate buffer, pH 7.5; 900 mL (see *Buffer Solutions* under *Reagents, Indicators, and Solutions*) for not less than 8 hours.
Apparatus 2: 50 rpm, with sinkers.
Times: 1, 4, 6, and 8 hours.
Procedure—Proceed as directed for *Procedure* in *Test 1*.
Tolerances—Proceed as directed for *Tolerances* in *Test 2*.

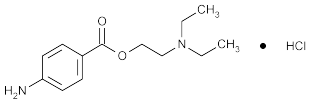
Time (hours)	Amount dissolved
1	between 33% and 50%
4	between 70% and 85%
6	not less than 80%
8	not less than 85%

Uniformity of dosage units ⟨905⟩: meet the requirements.
Assay—
Mobile phase—Prepare a suitable mixture of water, methanol, and triethylamine (140:60:1), adjust with phosphoric acid to a pH of 7.5, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).
Standard preparation—Dissolve an accurately weighed quantity of USP Procainamide Hydrochloride RS in *Mobile phase* to obtain a solution having a known concentration of about 0.5 mg per mL (*Stock standard solution*). Quantitatively dilute an accurately measured volume of this solution with *Mobile phase* to obtain a solution having a known concentration of about 0.05 mg per mL (*Standard preparation*).
Assay preparation—Transfer not fewer than 10 Tablets, accurately counted, to a 1000-mL volumetric flask, and add 100 mL of a mixture of methanol and methylene chloride (1:1). Place the flask in a 40° sonicator bath, and sonicate, with occasional shaking, until the Tablets have disintegrated completely. Add about 700 mL of methanol, and sonicate for 10 minutes, with occasional shaking. Allow to cool, dilute with methanol to volume, and mix. Filter a portion of this solution, discarding the first 10 mL of the filtrate. Quantitatively dilute an accurately measured volume of the filtrate with *Mobile phase* to obtain a solution having a concentration of about 0.5 mg of procainamide hydrochloride per mL. Use a portion of this stock solution for the *Identification* test. Quantitatively dilute another accurately measured volume of the stock solution with *Mobile phase* to obtain a solution having a concentration of about 0.05 mg per mL (*Assay preparation*).
Resolution solution—Prepare a solution of *p*-aminobenzoic acid in *Mobile phase* containing 0.1 mg per mL. Pipet 10 mL of this solution and 10 mL of the *Stock standard* into a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.
Chromatographic system (see *Chromatography*)—The liquid chromatograph is equipped with a 280-nm detector and a 3.9-mm × 30-cm column that contains 10-µm packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Resolution solution:* the resolution, *R,* is not less than 2.0. Chromatograph replicate injections of the *Standard preparation:* the relative standard deviation 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. The relative retention times are about 0.5 for *p*-aminobenzoic acid and 1.0 for procainamide. Calculate the quantity, in mg, of procainamide hydrochloride ($C_{13}H_{21}N_3O \cdot HCl$) per Tablet taken by the formula:

$$(L / D)(C)(r_U / r_S)$$

in which *L* is the labeled quantity, in mg, of procainamide hydrochloride in each Tablet; *D* is the concentration, in mg per mL, of procainamide hydrochloride in the *Assay preparation,* based on the number of Tablets taken, the labeled quantity per Tablet, and the extent of dilution; *C* is the concentration, in mg per mL, of USP Procainamide Hydrochloride RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Procaine Hydrochloride



$C_{13}H_{20}N_2O_2.HCl$ 272.78
Benzoic acid, 4-amino-, 2-(diethylamino)ethyl ester, monohydrochloride.
2-(Diethylamino)ethyl *p*-aminobenzoate monohydrochloride [51-05-8].

» Procaine Hydrochloride contains not less than 99.0 percent and not more than 101.0 percent of $C_{13}H_{20}N_2O_2 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.
Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

USP Reference standards ⟨11⟩**—**
USP Endotoxin RS
USP Procaine Hydrochloride RS
Identification—
A: *Infrared Absorption* ⟨197K⟩.
B: Dissolve 10 mg in 1 mL of water, add 1 drop each of hydrochloric acid and sodium nitrite solution (1 in 10), then add 1 mL of a solution prepared by dissolving 0.2 g of 2-

naphthol in 10 mL of sodium hydroxide solution (1 in 10), and shake: a scarlet-red precipitate is formed.

C: It responds to the tests for *Chloride* ⟨191⟩.

Melting range ⟨741⟩: between 153° and 158°.

Bacterial endotoxins ⟨85⟩—Where the label states that Procaine Hydrochloride is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains not more than 0.6 USP Endotoxin Unit per mg of procaine hydrochloride.

Sterility ⟨71⟩—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.

Acidity—To a solution of 1.0 g in 25 mL of water add 1 drop of methyl red TS, and titrate with 0.020 N sodium hydroxide: not more than 0.50 mL is required for neutralization.

Loss on drying ⟨731⟩—Dry it over silica gel for 18 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.15%.

Heavy metals ⟨231⟩: 0.002%.

Chromatographic purity—

Solvent—Prepare a mixture of methanol and trichloroethane (7:3).

Standard preparations—Prepare a solution of USP Procaine Hydrochloride RS in *Solvent* containing 1.6 mg per mL. Dilute quantitatively with *Solvent* to obtain Standard preparations having the following compositions:

Standard preparation	Dilution	Concentration (mg RS per mL)	Percentage (%, for comparison with test specimen)
A	2.5 in 10	0.4	0.5
B	2.0 in 10	0.32	0.4
C	1.0 in 10	0.16	0.2
D	0.5 in 10	0.08	0.1

Test preparation—Transfer 1.6 g of Procaine Hydrochloride, accurately weighed, to a suitable capped container, add 20 mL of *Solvent*, close the container, and sonicate for 2 minutes. Use this solution as the *Test preparation*.

Procedure—Apply separately 10 µL of the *Test preparation* and 10 µL of each *Standard preparation* to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture, prewashed with methanol and allowed to dry. Use a double-trough chromatographic chamber. Fill one trough with ammonium hydroxide, and allow the chamber to equilibrate for 1 hour. Position the plate in the other trough, and develop the chromatogram in a solvent system consisting of a mixture of methylene chloride and methanol (95:6) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Examine the plate under short-wavelength UV light. Compare the intensities of any secondary spots observed in the chromatogram of the *Test preparation* with those of the principal spots in the chromatograms of the *Standard preparations:* no secondary spot is more intense than the principal spot obtained from *Standard* (0.5%), and the sum of the intensities of all secondary spots obtained from the *Test preparation* does not exceed 1.0%.

Assay—Transfer about 0.5 g of Procaine Hydrochloride, accurately weighed, to a beaker, add 100 mL of cold water, 5 mL of hydrochloric acid, and 100 mg of potassium bromide, and stir until dissolved. Proceed as directed under *Nitrite Titration* ⟨451⟩, beginning with "cool to about 15°." Perform a blank determination, and make any necessary correction. Each mL of 0.1 M sodium nitrite is equivalent to 27.28 mg of $C_{13}H_{20}N_2O_2$.HCl.

Procaine Hydrochloride Injection

» Procaine Hydrochloride Injection is a sterile solution of Procaine Hydrochloride in Water for Injection. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_{13}H_{20}N_2O_2 \cdot HCl$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I or Type II glass. The Injection may be packaged in 100-mL multiple-dose containers.

USP Reference standards ⟨11⟩—
USP Endotoxin RS
USP Procaine Hydrochloride RS

Identification—Evaporate a portion of Injection, equivalent to about 20 mg of procaine hydrochloride, on a steam bath just to dryness, and dry over silica gel for 18 hours: the residue responds to *Identification* tests *A* and *B* under *Procaine Hydrochloride.*

Bacterial endotoxins ⟨85⟩—It contains not more than 0.6 USP Endotoxin Unit per mg of procaine hydrochloride.

pH ⟨791⟩: between 3.0 and 5.5.

Particulate matter ⟨788⟩: meets the requirements under Small-volume injections.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Standard preparation—Transfer to a 125-mL separator about 50 mg, accurately weighed, of USP Procaine Hydrochloride RS, and dilute with water to 20 mL.

Assay preparation—Transfer to a 125-mL separator an accurately measured volume of Injection, equivalent to about 50 mg of procaine hydrochloride, and dilute with water to 20 mL.

Procedure—To the *Standard preparation* and also to the *Assay preparation* add 5 mL of 6 N ammonium hydroxide, then treat each as follows. Extract with five 25-mL portions of chloroform, and filter the combined extracts through about 1 g of anhydrous sodium sulfate supported on a pledget of glass wool. Receive the filtrate in a 200-mL volumetric flask, add chloroform to volume, and mix. Transfer 3.0 mL of this solution to a 100-mL volumetric flask, add chloroform to volume, and mix. Concomitantly determine the absorbances of both solutions at the wavelength of maximum absorbance at about 280 nm, with a suitable spectrophotometer, using chloroform as the blank. Calculate the quantity, in mg, of $C_{13}H_{20}N_2O_2 \cdot HCl$ in each mL of the Injection taken by the formula:

$$(W / V)(A_U / A_S)$$

in which W is the weight, in mg, of USP Procaine Hydrochloride RS used, V is the volume, in mL, of Injection taken, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Procaine Hydrochloride and Epinephrine Injection

» Procaine Hydrochloride and Epinephrine Injection is a sterile solution of Procaine Hydrochloride and Epinephrine Hydrochloride in Water for Injection. The content of epinephrine does not exceed 0.002 percent (1 in 50,000). It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of procaine hydrochloride ($C_{13}H_{20}N_2O_2 \cdot HCl$), and not less than