solve the residue in hexane, evaporate with the aid of a current of warm air, and dry the residue in vacuum over silica gel for 24 hours: the crystalline precipitate so obtained responds to *Identification* test *A* under *Lidocaine*.

Assay—Transfer an accurately measured volume of Oral Topical Solution, equivalent to about 150 mg of lidocaine, to a 125-mL conical flask, and protect from atmospheric moisture with a stopper fitted with a tube containing silica gel. Add 20 mL of glacial acetic acid and 2 drops of crystal violet TS. Titrate immediately with 0.1 N perchloric acid VS to a blue endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 23.43 mg of $C_{14}H_{22}N_2O$.

Lidocaine Hydrochloride

$C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$ 288.81
Acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)-, monohydrochloride, monohydrate;
2-(Diethylamino)-2′,6′-acetoxylidide monohydrochloride monohydrate [6108-05-0].
Anhydrous 270.80
[73-78-9].

DEFINITION
Lidocaine Hydrochloride contains NLT 97.5% and NMT 102.5% of $C_{14}H_{22}N_2O \cdot HCl$, calculated on the anhydrous basis.

IDENTIFICATION
- **A. Infrared Absorption** ⟨197K⟩
  Standard: Prepare as directed in ⟨197K⟩, using USP Lidocaine RS.
  Sample: Dissolve 300 mg in 5–10 mL of water in a separator, add 4 mL of 6 N ammonium hydroxide, and extract with four 15-mL portions of chloroform. Combine the chloroform extracts, evaporate with the aid of a current of warm air, and dry the residue in vacuum over silica gel for 24 h.
  Acceptance criteria: Meets the requirements
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.
- **C. Identification Tests—General,** *Chloride* ⟨**191**⟩**:** Meets the requirements

ASSAY
- **Procedure**
  Solution A: Water and glacial acetic acid (930:50). Adjust with 1 N sodium hydroxide to a pH of 3.40.
  Mobile phase: Acetonitrile and *Solution A* (1:4), so that the retention time of lidocaine is 4–6 min
  Standard solution: Dissolve 85 mg of USP Lidocaine RS, with warming if necessary, in 0.5 mL of 1 N hydrochloric acid in a 50-mL volumetric flask. Dilute with *Mobile phase* to volume (1.7 mg/mL of lidocaine).
  System suitability stock solution: 220 µg/mL of methylparaben in *Mobile phase*
  System suitability solution: Mix 2 mL of *System suitability stock solution* and 20 mL of *Standard solution*.
  Sample solution: 2 mg/mL of Lidocaine Hydrochloride in *Mobile phase*
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: 3.9-mm × 30-cm; packing L1
  Flow rate: 1.5 mL/min
  Injection size: 20 µL
  System suitability
  Samples: *Standard solution* and *System suitability solution*
  Suitability requirements
  Resolution: NLT 3.0 between lidocaine and methylparaben, *System suitability solution*
  Relative standard deviation: NMT 1.5%, *Standard solution*
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of $C_{14}H_{22}N_2O \cdot HCl$ in the portion of Lidocaine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Lidocaine RS in the *Standard solution* (mg/mL)
C_U = concentration of Lidocaine Hydrochloride in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of lidocaine hydrochloride, 270.80
M_{r2} = molecular weight of lidocaine, 234.34

Acceptance criteria: 97.5%–102.5% on the anhydrous basis

IMPURITIES
Inorganic Impurities
- **Residue on Ignition** ⟨**281**⟩**:** NMT 0.1%
- **Chloride and Sulfate,** *Sulfate* ⟨**221**⟩**:** Dissolve 100 mg in 10 mL of water, and add 1 mL of 3 N hydrochloric acid. Mix, and add 1 mL of barium chloride TS. The turbidity does not exceed that produced by 0.10 mL of 0.020 N sulfuric acid (NMT 0.1%).
- **Heavy Metals,** *Method I* ⟨**231**⟩**:** 20 ppm

SPECIFIC TESTS
- **Melting Range or Temperature** ⟨**741**⟩**:** 74°–79°
  [Note—The preliminary drying treatment is omitted.]
- **Water Determination,** *Method I* ⟨**921**⟩**:** 5.0%–7.0%
- **Sterility Tests** ⟨**71**⟩**:** Where the label states that Lidocaine Hydrochloride is sterile, it meets the requirements.
- **Bacterial Endotoxins Test** ⟨**85**⟩**:** Where the label states that Lidocaine Hydrochloride is sterile or must be subjected to further processing during the preparation of injectable dosage forms, it contains NMT 1.1 USP Endotoxin Units/mg of lidocaine hydrochloride.

ADDITIONAL REQUIREMENTS
- **Packaging and Storage:** Preserve in well-closed containers. Store at room temperature.
- **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 Lidocaine RS

Lidocaine Hydrochloride Injection

» Lidocaine Hydrochloride Injection is a sterile solution of Lidocaine Hydrochloride in Water for Injection, or a sterile solution prepared from Lidocaine with the aid of Hydrochloric Acid in Water for Injection. It contains not less than 95.0 percent and not more than 105.0 percent of the

labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$).

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass. Injection may be packaged in 50-mL multiple-dose containers.

Labeling—Injections that are of such concentration that they are not intended for direct injection into tissues are labeled to indicate that they are to be diluted prior to administration.

USP Reference standards ⟨11⟩—
USP Endotoxin RS
USP Lidocaine RS

Identification—Place in a separator a volume of Injection equivalent to about 300 mg of lidocaine hydrochloride, and extract with four 15-mL portions of chloroform, discarding the chloroform extracts. Add 2 mL of 2 N sodium hydroxide to the aqueous solution remaining in the separator, and extract with four 15-mL portions of chloroform. Combine the chloroform extracts, and evaporate with the aid of a current of warm air to dryness. Dissolve the crystals so obtained in solvent hexane, evaporate with the aid of warm air, and dry the residue in vacuum over silica gel for 24 hours: the residue so obtained responds to *Identification* test *A* under *Lidocaine*.

Bacterial endotoxins ⟨85⟩—It contains not more than 1.1 USP Endotoxin Units per mg of lidocaine hydrochloride.

pH ⟨791⟩: between 5.0 and 7.0.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

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

Assay—Proceed with Injection as directed in the *Assay for lidocaine hydrochloride* under *Lidocaine Hydrochloride and Epinephrine Injection*.

Lidocaine Hydrochloride Jelly

» Lidocaine Hydrochloride Jelly is Lidocaine Hydrochloride in a suitable, water-soluble, sterile, viscous base. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Lidocaine RS

Identification—Place in a separator containing 10 to 15 mL of water a quantity of Jelly, equivalent to about 300 mg of lidocaine hydrochloride, mix to assure thorough dilution of the Jelly, add 4 mL of 6 N ammonium hydroxide, and extract with four 15-mL portions of chloroform. Combine the chloroform extracts, and evaporate with the aid of a current of warm air to dryness. Redissolve the crystals in solvent hexane, evaporate with the aid of warm air, and dry the residue in vacuum over silica gel for 24 hours: the lidocaine so obtained responds to *Identification* test *A* under *Lidocaine.*

Sterility ⟨71⟩: meets the requirements.

Minimum fill ⟨755⟩: meets the requirements.

pH ⟨791⟩: between 6.0 and 7.0.

Assay—Accurately weigh into a separator containing 10 to 15 mL of water a quantity of Jelly, equivalent to 20 to 30 mg of lidocaine hydrochloride, mix to assure thorough dilution of the Jelly, add 1 mL of 6 N ammonium hydroxide, and extract by shaking with four 20-mL portions of chloroform. Combine the chloroform extracts, and evaporate with the aid of a current of warm air, adding 25.0 mL of 0.01 N sulfuric acid VS just before the last trace of chloroform is expelled. Complete the evaporation of the chloroform, and titrate the excess acid with 0.01 N sodium hydroxide VS, determining the endpoint potentiometrically (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.01 N sulfuric acid is equivalent to 2.708 mg of $C_{14}H_{22}N_2O \cdot HCl$.

Lidocaine Hydrochloride Oral Topical Solution

» Lidocaine Hydrochloride Oral Topical Solution contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$). It contains a suitable flavor and/or sweetening agent.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Lidocaine RS

Identification—Place in a separator a volume of Oral Topical Solution, equivalent to about 300 mg of lidocaine hydrochloride, and extract with four 15-mL portions of chloroform, discarding the chloroform extracts. Add 2 mL of 2 N sodium hydroxide to the aqueous solution remaining in the separator, and extract with four 15-mL portions of chloroform. Combine the chloroform extracts, and evaporate with the aid of a current of warm air to dryness. Dissolve the crystals so obtained in solvent hexane, evaporate with the aid of warm air, and dry the residue in vacuum over silica gel for 24 hours: the residue so obtained responds to *Identification* test *A* under *Lidocaine*.

pH ⟨791⟩: between 5.0 and 7.0.

Assay—

Mobile phase, Standard preparation, and *Resolution preparation*—Prepare as directed in the *Assay for lidocaine hydrochloride* under *Lidocaine and Epinephrine Injection*.

Assay preparation—Transfer an accurately measured volume of Oral Topical Solution, equivalent to about 100 mg of lidocaine hydrochloride, to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay for lidocaine hydrochloride* under *Lidocaine and Epinephrine Injection*. Calculate the quantity, in mg, of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$) in each mL of the Oral Topical Solution taken by the formula:

$$(270.80 / 234.34)(50)(C / V)(r_U / r_S)$$

in which V is the volume, in mL, of Oral Topical Solution taken; and the other terms are as defined therein.

Lidocaine Hydrochloride Topical Solution

» Lidocaine Hydrochloride Topical Solution contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of lidocaine hydrochloride ($C_{14}H_{22}N_2O \cdot HCl$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Lidocaine RS