levothyroxine sodium; and 900 mL for Tablets labeled to contain 200 or 300 µg of levothyroxine sodium
Apparatus 2: 75 rpm
Time: 45 min
Determine the amount of $C_{15}H_{10}I_4NNaO_4$ dissolved by using the following method.
Mobile phase: Acetonitrile, water, and phosphoric acid, (500:700:2)
Standard stock solution: Transfer about 100 mg of USP Levothyroxine RS to a 100-mL volumetric flask. Add 80 mL of alcohol and 1 mL of 1 N hydrochloric acid, sonicate for 2 min, dilute with alcohol to volume, and mix.
Standard solution: Dilute the *Standard stock solution* with a mixture of alcohol and water (1:1) to obtain a solution having a concentration of 0.01 mg/mL of levothyroxine. Dilute the resulting solution with *Medium* to obtain a final concentration similar to that expected in the *Sample solution*.
Sample solution: Sample per *Dissolution* ⟨711⟩. Centrifuge the solution under analysis.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 225 nm
Column: 4.0-mm × 12.5-cm; packing L7
Flow rate: 1.5 mL/min
Injection size: 500 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 1.5
Relative standard deviation: NMT 4.0% of levothyroxine
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the amount of $C_{15}H_{10}I_4NNaO_4$ dissolved.
Tolerances: NLT 80% (Q) of the labeled amount of $C_{15}H_{10}I_4NNaO_4$ is dissolved.

- **UNIFORMITY OF DOSAGE UNITS ⟨905⟩:** Meet the requirements

IMPURITIES
Organic Impurities

- **PROCEDURE: LIMIT OF LIOTHYRONINE SODIUM**

[NOTE—Use *Sample solution 2* for Tablets labeled to meet the requirements of *Dissolution Test 3*. For all other products, use the *Sample solution*.]
Mobile phase, Standard solution, Sample solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Analysis: Calculate the percentage of $C_{15}H_{11}I_3NNaO_4$ in the portion of Tablets taken:

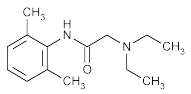
$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of liothyronine from the *Sample solution*
r_S = peak response of liothyronine from the *Standard solution*
C_S = concentration of USP Liothyronine RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of levothyroxine sodium in the *Sample solution* (µg/mL)
M_{r1} = molecular weight of liothyronine sodium, 672.96
M_{r2} = molecular weight of liothyronine, 650.98
Acceptance criteria: NMT 2.0% of liothyronine

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP REFERENCE STANDARDS ⟨11⟩**
USP Levothyroxine RS
USP Liothyronine RS

Lidocaine



$C_{14}H_{22}N_2O$ 234.34
Acetamide, 2-(diethylamino)-*N*-(2,6-dimethylphenyl)-; 2-(Diethylamino)-2′,6′-acetoxylidide [137-58-6].

DEFINITION
Lidocaine contains NLT 97.5% and NMT 102.5% of $C_{14}H_{22}N_2O$.

IDENTIFICATION

- **A. INFRARED ABSORPTION ⟨197K⟩:** Previously dried in vacuum over silica gel for 24 h
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

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.
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: Dissolve 85 mg of Lidocaine, 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.
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 $C_{14}H_{22}N_2O$ in the portion of Lidocaine taken:

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

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 in the *Sample solution* (mg/mL)

Acceptance criteria: 97.5%–102.5%

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%
- **CHLORIDE AND SULFATE,** *Chloride* ⟨**221**⟩**:** Dissolve 1.0 g in a mixture of 3 mL of 2 N nitric acid and 12 mL of water, and add 1 mL of silver nitrate TS: the turbidity does not exceed that produced by 50 µL of 0.020 N hydrochloric acid (0.0035%).
- **CHLORIDE AND SULFATE,** *Sulfate* ⟨**221**⟩**:** Dissolve 100 mg in a mixture of 1 mL of 2 N nitric acid and 10 mL of water. Filter if necessary, 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**⟩
  Test preparation: 1.0 g
  Analysis: Dissolve the *Test preparation* in a mixture of 2 mL of 3 N hydrochloric acid and 10 mL of water. Evaporate on a steam bath to dryness, and dissolve the residue in 25 mL of water.
  Acceptance criteria: 20 ppm

SPECIFIC TESTS

- **MELTING RANGE OR TEMPERATURE** ⟨**741**⟩**:** *66°–69°*

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Lidocaine RS

Lidocaine Topical Aerosol

» Lidocaine Topical Aerosol is a solution of Lidocaine in a suitable flavored vehicle with suitable propellants in a pressurized container equipped with a metering valve. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{14}H_{22}N_2O$, and it delivers not less than 85.0 percent and not more than 115.0 percent of the labeled amount of $C_{14}H_{22}N_2O$ per actuation.

Packaging and storage—Preserve in nonreactive aerosol containers equipped with metered-dose valves.

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

Identification—

A: To about 5 mL of Aerosol spray, collected in a separator, add about 10 mL of water and 3 mL of dilute hydrochloric acid (1 in 2), wash with two 15-mL portions of chloroform, and discard the chloroform washings. Render the solution in the separator alkaline with 5 to 6 mL of ammonium hydroxide, and extract with three 20-mL portions of chloroform, filtering the chloroform extracts through a pledget of cotton previously moistened with chloroform. Evaporate the combined chloroform extracts with the aid of gentle heat to dryness, and dry the residue in vacuum over silica gel for 24 hours: a potassium bromide dispersion of the lidocaine so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Lidocaine RS.

B: To about 2 mL of Aerosol spray, collected in a test tube, add 10 to 15 drops of cobaltous chloride TS, and shake for about 2 minutes: a bright green color develops, and a fine precipitate is formed (lidocaine).

C: To about 2 mL of Aerosol spray, collected in a test tube, add 5 mL of water, 1 mL of 2 N nitric acid, and 3 mL of mercuric nitrate TS: a light yellow color develops (lidocaine).

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Other requirements—It meets the requirements for *Total Number of Discharges per Container* and *Delivered Dose Uniformity* for *Topical Aerosols* under *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩.

Assay—Accurately weigh 1 Aerosol container and actuator. Transfer a counted number of not less than 10 doses to a 125-mL conical flask by carefully discharging the doses in a manner such as to avoid loss of material, and take precautions to protect the specimen from absorption of atmospheric moisture. Accurately weigh the container and actuator to obtain the specimen weight. To the specimen add 20 mL of chloroform, mix, and add 10 mL of dioxane and 2 drops of crystal violet TS. Titrate with 0.1 N perchloric acid in dioxane 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 Ointment

» Lidocaine Ointment is Lidocaine in a suitable hydrophilic ointment base. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of lidocaine ($C_{14}H_{22}N_2O$).

Packaging and storage—Preserve in tight containers.

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

Identification—Stir a quantity of Ointment, equivalent to about 300 mg of lidocaine, with 20 mL of water, transfer to a separator, and extract with two 30-mL portions of solvent hexane. Wash the combined hexane extracts with 10 mL of water, 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*.

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

Minimum fill ⟨755⟩: meets the requirements.

Assay—Proceed with Ointment as directed in the *Assay* under *Lidocaine Hydrochloride Jelly*. Each mL of 0.01 N sulfuric acid is equivalent to 2.343 mg of $C_{14}H_{22}N_2O$.

Lidocaine Oral Topical Solution

» Lidocaine Oral Topical Solution contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of lidocaine ($C_{14}H_{22}N_2O$). It contains a suitable flavor.

Packaging and storage—Preserve in tight containers.

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

Identification—Transfer a quantity of Oral Topical Solution, equivalent to about 250 mg of lidocaine, to a separator with 20 mL of water, and extract with 20 mL of chloroform. Wash the chloroform extract with 20 mL of water, and evaporate the chloroform extract with the aid of a current of warm air. Dis-