the label. Manufacturers must demonstrate a correlation between the assay and a validated and approved growth-promotion based bioassay. [NOTE—One mg of anhydrous Somatropin is equivalent to 3.0 USP Somatropin Units.]

Packaging and storage—Preserve in tight containers, and store between 2° and 8°.

Labeling—The labeling states that the material is of recombinant DNA origin.

USP Reference standards ⟨11⟩**—**
USP Endotoxin RS
USP Somatropin RS

Identification—It meets the requirements for *Identification* test *A* under *Somatropin*.

Bioidentity—[NOTE—If the bulk material used to prepare Somatropin for Injection was tested and meets the requirements, it is not necessary to perform this test.] It meets the requirements for *Bioidentity* under *Somatropin*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 20 USP Endotoxin Units per mg of somatropin.

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

Chromatographic purity—Proceed as directed for the *Chromatographic purity* test under *Somatropin:* not more than 12% of total impurities is found.

Limit of high molecular weight proteins—Proceed as directed in the test for *Limit of high molecular weight proteins* under *Somatropin,* except to use the *Assay preparation* as the *Test solution:* not more than 6% of high molecular weight proteins is found.

Assay—

Phosphate buffer, Mobile phase, Diluent, Resolution solution, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Somatropin*.

Assay preparation—Dissolve the contents of a suitable number of containers in *Diluent* to obtain a concentration of 1 mg of somatropin per mL.

Procedure—Proceed as directed under *Somatropin.* Calculate the quantity of somatropin, in mg of somatropin per container, by the formula:

$$C(V/N)(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Somatropin RS in the *Standard preparation; V* is the total volume of the *Assay preparation; N* is the number of containers used to obtain the *Assay preparation;* and r_U and r_S are the peak responses of the monomer in the *Assay preparation* and the *Standard preparation,* respectively.

Sorbitol Solution

DEFINITION

Sorbitol Solution is an aqueous solution containing NLT 64.0% of D-sorbitol ($C_6H_{14}O_6$). The amounts of total sugars, other polyhydric alcohols, and any hexitol anhydrides, if detected, are not included in the requirements or in the calculated amount under *General Notices, 5.60.10. Other Impurities in USP and NF Articles*.

IDENTIFICATION

- **A. PROCEDURE**

Sample solution: Dissolve 1.4 g of Sorbitol Solution in 75 mL of water.

Analysis: Transfer 3 mL of the *Sample solution* to a 15-cm test tube. Add 3 mL of freshly prepared catechol solution (1 in 10), and mix. Add 6 mL of sulfuric acid, mix again, and gently heat the tube in a flame for 30 s.

Acceptance criteria: A deep pink or wine-red color appears.

- **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. LIMIT OF DIETHYLENE GLYCOL AND ETHYLENE GLYCOL**

Diluent: Acetone and water (96:4)

Standard solution: 0.08 mg/mL of USP Diethylene Glycol RS and 0.08 mg/mL of USP Ethylene Glycol RS in *Diluent*

Sample solution: Transfer 2.0 g of Sorbitol Solution to a 25-mL volumetric flask. Add 1.0 mL of *Diluent* to the flask, and mix on a vortex mixer for 3 min. Add the remaining *Diluent* to the flask to volume in three equal portions. Mix on a vortex mixer for about 3 min after each addition of *Diluent*. Pass a portion of the supernatant layer obtained through a 0.45-µm nylon filter. Discard the first 2 mL of the filtrate, and collect the rest of the filtrate for analysis. [NOTE—Acetone is used to precipitate sorbitol.]

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: GC
Detector: Flame ionization
Column: 0.32-mm × 15-m fused-silica capillary column; 0.25-µm layer of phase G46
Temperature
Detector: 300°
Injector port: 240°
Column: See the temperature program table below.

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
70	—	70	2
70	50	300	5

Carrier gas: Helium
Flow rate: 3.0 mL/min
Injection size: 1.0 µL
Injection type: Split injection. The split ratio is about 10:1. [NOTE—A split liner, deactivated with glass wool, is used.]

System suitability
Sample: *Standard solution*
[NOTE—Diethylene glycol elutes after ethylene glycol in the chromatogram.]
Suitability requirements
Resolution: NLT 30 between ethylene glycol and diethylene glycol

Analysis
Samples: *Standard solution* and *Sample solution*
Based on the *Standard solution*, identify the peaks of ethylene glycol and diethylene glycol. Compare peak areas of ethylene glycol and diethylene glycol in the *Standard solution* and the *Sample solution.*

Acceptance criteria
Diethylene glycol: The peak area of diethylene glycol in the *Sample solution* is NMT the peak area of diethylene glycol in the *Standard solution*, corresponding to NMT 0.10% of diethylene glycol in Sorbitol Solution.
Ethylene glycol: The peak area of ethylene glycol in the *Sample solution* is NMT the peak area of ethylene glycol in the *Standard solution*, corresponding to NMT 0.10% of ethylene glycol in Sorbitol Solution.

ASSAY

- **PROCEDURE**

Mobile phase: Water
System suitability solution: 4.8 mg/g of mannitol and 4.8 mg/g of USP Sorbitol RS in water

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Standard solution: 4.8 mg/g of USP Sorbitol RS in water
Sample solution: 6.0 mg/g of Sorbitol Solution in water
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: Refractive index
Column: 7.8-mm × 10-cm; packing L34
Temperature
Detector: 35°
Column: 50 ± 2°
Flow rate: 0.7 mL/min
Injection size: 10 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for mannitol and sorbitol are 0.6 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 2.0 between sorbitol and mannitol, *System suitability solution*
Relative standard deviation: NMT 2.0% for sorbitol, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of $C_6H_{14}O_6$ in the Sorbitol Solution 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 Sorbitol RS in the *Standard solution* (mg/g)
C_U = nominal concentration of Sorbitol Solution in the *Sample solution* (mg/g)
Acceptance criteria: NLT 64.0%

IMPURITIES

Inorganic Impurities

- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%, calculated on the anhydrous basis, determined on a 2-g portion
- **LIMIT OF NICKEL**

Solution A: A saturated ammonium pyrrolidine dithiocarbamate solution (containing 10 mg/mL of ammonium pyrrolidine dithiocarbamate)
Sample solution: Dissolve and dilute 20.0 g of Sorbitol Solution to 100 mL with diluted acetic acid. Add 2.0 mL of *Solution A* and 10.0 mL of methyl isobutyl ketone, and shake for 30 s. Protect from bright light. Allow the two layers to separate, and use the methyl isobutyl ketone layer.
Standard solutions: Prepared as directed for *Sample solution*, except to prepare three solutions by adding 0.5, 1.0, and 1.5 mL of nickel standard solution TS.
Blank solution: Prepare as directed for *Sample solution*, except to omit the use of the Sorbitol Solution.
Spectrometric conditions
(See *Spectrophotometry and Light-Scattering* ⟨851⟩.)
Mode: Atomic absorption spectrophotometry
Analytical wavelength: 232.0 nm (maximum absorbance)
Lamp: Nickel hollow-cathode
Flame: Air–acetylene
Analysis
Samples: *Standard solutions, Sample solution,* and *Blank solution*
Set the instrument to zero using the *Blank solution.* Concomitantly determine the absorbances of the *Standard solutions* and the *Sample solution* at least three times each. Record the average of the steady readings for each of these solutions. Between each measurement, aspirate the *Blank solution*, and ascertain that the reading returns to zero. Plot the absorbances of the *Standard solutions* and the *Sample solution* versus the added quantity of nickel. Extrapolate the line joining the points on the graph until it meets the concentration axis. The distance between this point and the intersection of the axes represents the concentration of nickel in the *Sample solution*.
Acceptance criteria: NMT 1 ppm, calculated on the anhydrous basis

Organic Impurities

- **PROCEDURE: REDUCING SUGARS**

Sample: Equivalent to 3.3 g of sorbitol on the anhydrous basis from Sorbitol Solution
Analysis: To the *Sample*, add 3 mL of water, 20.0 mL of cupric citrate TS, and a few glass beads. Heat so that boiling begins after 4 min, and maintain boiling for 3 min. Cool rapidly, and add 40 mL of diluted acetic acid, 60 mL of water, and 20.0 mL of 0.05 N iodine VS. With continuous shaking, add 25 mL of a mixture of 6 mL of hydrochloric acid and 94 mL of water. When the precipitate has dissolved, titrate the excess of iodine with 0.05 N sodium thiosulfate VS using 2 mL of starch TS, added toward the end of the titration, as an indicator.
Acceptance criteria: NLT 12.8 mL of 0.05 N sodium thiosulfate VS is required, corresponding to NMT 0.3% of reducing sugars, on the anhydrous basis, as glucose.
[NOTE—The amount determined in this test is not included in the calculated amount under *General Notices, 5.60.10. Other Impurities in USP and NF Articles*.]

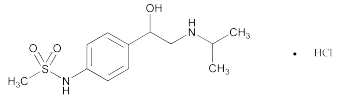
SPECIFIC TESTS

- **pH ⟨791⟩:** 5.0–7.5, in a 14% (w/w) solution of Sorbitol Solution in carbon dioxide-free water
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** 28.5%–31.5%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. No storage requirements specified.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Diethylene Glycol RS
USP Ethylene Glycol RS
USP Sorbitol RS

Sotalol Hydrochloride



$C_{12}H_{20}N_2O_3S \cdot HCl$ 308.83
Methanesulfonamide, *N*-[4-[1-hydroxy-2-[(1-methylethyl)amino]ethyl]phenyl]-, monohydrochloride.
4′-[1-Hydroxy-2-(isopropylamino)ethyl]methanesulfonanilide monohydrochloride [959-24-0].

» Sotalol Hydrochloride contains not less than 98.5 percent and not more than 101.5 percent of $C_{12}H_{20}N_2O_3S \cdot HCl$.

Packaging and storage—Preserve in well-closed containers. Store at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Sotalol Hydrochloride RS
USP Sotalol Related Compound A RS
N[(4-[[(1-Methylethyl)amino]acetyl]phenyl] methanesulfonamide monohydrochloride.
$C_{12}H_{18}N_2O_3S \cdot HCl$ 306.81
USP Sotalol Related Compound B RS
N-(4-Formylphenyl)methanesulfonamide.
$C_8H_9NO_3S$ 199.23
USP Sotalol Related Compound C RS
N-[4-[2-[(1-Methylethyl)amino]ethyl]phenyl] methanesulfonamide monohydrochloride.
$C_{12}H_{20}N_2O_2S \cdot HCl$ 292.83

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