SPECIFIC TESTS

• **WATER DETERMINATION,** *Method I* ⟨**921**⟩
Analysis: Proceed as directed in the chapter. Maintain the mixture containing the *Test preparation* at 50°, and stir for 30 min before titrating with the *Reagent*.
Acceptance criteria
Where labeled as the dried form: 3.0%–9.0%
Where labeled as the dihydrate: 6.0%–9.0%

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers.
• **LABELING:** The label indicates whether it is the dried or the dihydrate form.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Potassium Gluconate RS

Manganese Sulfate

$MnSO_4 \cdot H_2O$ 169.02
Sulfuric acid, manganese(2+) salt (1:1) monohydrate;
Manganese(2+) sulfate (1:1) monohydrate [10034-96-5].
Anhydrous 151.00
[7785-87-7].

DEFINITION

Manganese Sulfate contains NLT 98.0% and NMT 102.0% of $MnSO_4 \cdot H_2O$.

IDENTIFICATION

• **A. IDENTIFICATION TESTS—GENERAL,** *Manganese* ⟨**191**⟩
Sample solution: 100 mg/mL
Acceptance criteria: Meets the requirements
• **B. IDENTIFICATION TESTS—GENERAL,** *Sulfate* ⟨**191**⟩
Sample solution: 100 mg/mL
Acceptance criteria: Meets the requirements

ASSAY

• **PROCEDURE**
Sample: 350 mg
Analysis: Dissolve the *Sample* in 200 mL of water. Add 10 mg of ascorbic acid. Begin the titration by adding 25 mL of 0.05 M edetate disodium VS using a suitable buret, then add 10 mL of ammonia–ammonium chloride buffer TS and 0.15 mL of eriochrome black TS. Complete the titration with 0.05 M edetate disodium VS to a blue endpoint. Each mL of 0.05 M edetate disodium is equivalent to 8.451 mg of $MnSO_4 \cdot H_2O$.
Acceptance criteria: 98.0%–102.0%

IMPURITIES

• **SUBSTANCES NOT PRECIPITATED BY AMMONIUM SULFIDE**
Sample: 2.0 g
Analysis: Dissolve the *Sample* in 90 mL of water, add 5 mL of ammonium hydroxide, warm the solution, and pass hydrogen sulfide through the solution for about 30 min. Dilute with water to 100 mL, mix, and allow the precipitate to settle. Decant the supernatant through a filter, transfer 50 mL of the clear filtrate to a tared dish, evaporate to dryness, and ignite, gently at first and finally at 800 ± 25°.
Acceptance criteria: The weight of the residue does not exceed 5 mg (NMT 0.5%).

SPECIFIC TESTS

• **LOSS ON IGNITION** ⟨**733**⟩
Analysis: Ignite a sample at 450° to constant weight: it loses 10.0%–13.0% of its weight.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers. Store at controlled room temperature.

Manganese Sulfate Injection

» Manganese Sulfate Injection is a sterile solution of Manganese Sulfate in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of manganese (Mn).

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I or Type II glass.

Labeling—Label the Injection to indicate that it is to be diluted to the appropriate strength with Sterile Water for Injection or other suitable fluid prior to administration.

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

Identification—The *Assay preparation*, prepared as directed in the *Assay*, exhibits an absorption maximum at about 279 nm when tested as directed for *Procedure* in the *Assay*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.45 USP Endotoxin Unit per µg of manganese.

pH ⟨791⟩: between 2.0 and 3.5.

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

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

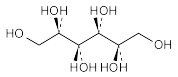
Assay—

Sodium chloride solution, Manganese stock solution, and *Standard preparations*—Prepare as directed in the *Assay* under *Manganese Chloride Injection*.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 1 mg of manganese, to a 100-mL volumetric flask, dilute with water to volume, and mix. Pipet 10 mL of this solution into a 50-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Manganese Chloride Injection*.

Mannitol



$C_6H_{14}O_6$ 182.17
D-Mannitol.
D-Mannitol [69-65-8].

» Mannitol contains not less than 96.0 percent and not more than 101.5 percent of $C_6H_{14}O_6$, calculated on the dried basis. The amounts of total sugars, other polyhydric alcohols, and any hexitol anhydrides, if detected, are not included in the requirements nor the calculated amount under *Other Impurities.*

Packaging and storage—Preserve in well-closed containers.

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

Identification, *Infrared Absorption* ⟨197K⟩.

Melting range ⟨741⟩: between 164° and 169°.

Specific rotation ⟨781S⟩: between +137° and +145°.

Test solution—Transfer about 1 g of Mannitol, accurately weighed, to a 100-mL volumetric flask, and add 40 mL of am-

monium molybdate solution (1 in 10), which previously had been filtered if necessary. Add 20 mL of 1 N sulfuric acid, dilute with water to volume, and mix.

Acidity—Dissolve 5.0 g in 50 mL of carbon dioxide-free water, add 3 drops of phenolphthalein TS, and titrate with 0.020 N sodium hydroxide to a distinct pink endpoint: not more than 0.30 mL of 0.020 N sodium hydroxide is required for neutralization.

Loss on drying ⟨731⟩**—**Dry it at 105° for 4 hours: it loses not more than 0.3% of its weight.

Chloride ⟨221⟩**—**A 2.0-g portion shows no more chloride than corresponds to 0.20 mL of 0.020 N hydrochloric acid (0.007%).

Sulfate ⟨221⟩**—**A 2.0-g portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid (0.01%).

Arsenic, *Method II* ⟨211⟩: 1 ppm.

Reducing sugars—To 5 mL of alkaline cupric citrate TS add 1 mL of a saturated solution of Mannitol (about 200 mg). Heat for 5 minutes in a boiling water bath: not more than a very slight precipitate is formed. The amount determined in this test is not included in the calculated amount under *Other Impurities.*

Assay—

Mobile phase—Use degassed water.

Resolution solution—Dissolve sorbitol and USP Mannitol RS in water to obtain a solution having concentrations of about 4.8 mg per mL of each.

Standard preparation—Dissolve an accurately weighed quantity of USP Mannitol RS in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 4.8 mg per mL.

Assay preparation—Transfer about 0.24 g of Mannitol, accurately weighed, to a 50-mL volumetric flask, dissolve in 10 mL of water, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a refractive index detector that is maintained at a constant temperature and a 4-mm × 25-cm column that contains packing L19. The column temperature is maintained at a temperature between 30° and 85° controlled within ±2° of the selected temperature, and the flow rate is about 0.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%. In a similar manner, chromatograph the *Resolution solution:* the resolution, *R,* between the sorbitol and mannitol peaks is not less than 2.0.

Procedure—Separately inject equal volumes (about 20 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_6H_{14}O_6$, in the Mannitol taken by the formula:

$$50C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Mannitol 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.

Mannitol Injection

» Mannitol Injection is a sterile solution, which may be supersaturated, of Mannitol in Water for Injection. It may require warming or autoclaving before use if crystallization has occurred. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of mannitol ($C_6H_{14}O_6$). It contains no antimicrobial agents.

Packaging and storage—Preserve in single-dose glass or plastic containers. Glass containers are preferably of Type I or Type II glass.

Labeling—The label states the total osmolar concentration in mOsmol per L. Where the contents are less than 100 mL, or where the label states that the Injection is not for direct injection but is to be diluted before use, the label alternatively may state the total osmolar concentration in mOsmol per mL. The label also states that it should be warmed before use to dissolve any crystals that may have formed.

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

Identification—

A: Evaporate a portion of Injection on a steam bath to dryness, and dry the residue at 105° for 4 hours. To 3 mL of freshly prepared solution of catechol in water (1 in 10) add 6 mL of sulfuric acid with cooling. Place 3 mL of this solution in each of two separate test tubes. To one tube add 0.3 mL of water (reagent blank) and to the other add 0.3 mL of a solution of it in water (1 in 10). Heat the tubes over an open flame for about 30 seconds: the solution in the tube containing mannitol is dark pink or wine red, and the solution in the tube containing the reagent blank is light pink.

B: The retention time for the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Specific rotation ⟨781⟩**—**Transfer an accurately measured volume of Injection, equivalent to about 1 g of mannitol as determined by the *Assay*, to a 100-mL volumetric flask: it meets the requirements of the test for *Specific rotation* under *Mannitol.*

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.04 USP Endotoxin Unit per mg of mannitol where the labeled amount of mannitol in the Injection is 10% or less, and not more than 2.5 USP Endotoxin Units per g of mannitol where the labeled amount of mannitol in the Injection is greater than 10%.

pH ⟨791⟩**:** between 4.5 and 7.0, determined potentiometrically, on a portion to which 0.30 mL of saturated potassium chloride solution has been added for each 100 mL, and which previously has been diluted with water, if necessary, to a concentration of not more than 5% of mannitol.

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

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

Assay—

Mobile phase, Resolution solution, and *Chromatographic system*—Proceed as directed in the *Assay* under *Mannitol.*

Standard preparation—Dissolve an accurately weighed quantity of USP Mannitol RS in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 5 mg per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 500 mg of mannitol, to a 100-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Mannitol.* Calculate the quantity, in mg, of mannitol ($C_6H_{14}O_6$) in each mL of the Injection taken by the formula:

$$100(C/V)(r_U / r_S)$$

in which *V* is the volume, in mL, of Injection taken; and the other terms are as defined therein.