

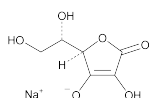
ammonium hydroxide, ammonium oxalate TS, and sodium phosphate TS: no turbidity is produced within 5 minutes.

Potassium—To a quantity of Solution, equivalent to 3.0 g of anhydrous sodium acetate, add 0.2 mL of sodium bitartrate TS: no turbidity is produced within 5 minutes.

Heavy metals, Method I (231)—Dilute a quantity of Solution, equivalent to 2.0 g of anhydrous sodium acetate, with water to 25 mL, and use glacial acetic acid instead of 1 N acetic acid for adjustment of the pH: the limit is 0.001%.

Assay—Weigh accurately about 1 g of Solution into a 250-mL conical flask, cautiously add (in a fume hood) 2.6 mL of acetic anhydride, mix, and allow to stand for 5 minutes. Add 25 mL of glacial acetic acid and 2 drops of *p*-naphtholbenzein TS, and titrate with 0.1 N perchloric acid VS. Perform a blank determination, using 0.5 mL of water, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 8.203 mg of $C_6H_7NaO_6$.

Sodium Ascorbate



$C_6H_7NaO_6$ 198.11
L-Ascorbic acid, monosodium salt;
Monosodium L-ascorbate [134-03-2].

DEFINITION

Sodium Ascorbate contains NLT 99.0% and NMT 101.0% of sodium ascorbate ($C_6H_7NaO_6$), calculated on the dried basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** (197M)
Sample: Use undried Sodium Ascorbate.
Acceptance criteria: Meets the requirements
- **B. REDUCING CAPACITY**
Sample solution: 20 mg/mL
Analysis: Add 1 mL of 0.1 N hydrochloric acid to 4 mL of the Sample solution, and add alkaline cupric tartrate TS.
Acceptance criteria: The solution reduces alkaline cupric tartrate TS slowly at room temperature, but more readily upon heating.
- **C. IDENTIFICATION TESTS—GENERAL, Sodium** (191): A 20-mg/mL solution meets the requirements.

ASSAY

- **PROCEDURE**
Sample: 400 mg of Sodium Ascorbate
Blank: 100 mL of carbon dioxide-free water and 25 mL of 2 N sulfuric acid
Titrimetric system
(See *Titrimetry* (541).)
Mode: Direct titration
Titrant: 0.1 N iodine VS
Endpoint detection: Visual
Analysis: Dissolve the Sample in a mixture of 100 mL of carbon dioxide-free water and 25 mL of 2 N sulfuric acid. Titrate immediately with the Titrant, and add 3 mL of starch TS as the endpoint is approached. Perform the Blank determination.
Calculate the percentage of sodium ascorbate ($C_6H_7NaO_6$) in the portion of Sodium Ascorbate taken:

$$\text{Result} = \{[(V_s - V_b) \times N \times F]/W\} \times 100$$

V_s = Titrant volume consumed by the Sample (mL)
 V_b = Titrant volume consumed by the Blank (mL)
 N = actual normality of the Titrant (mEq/mL)
 F = equivalency factor, 99.05 mg/mEq
 W = Sample weight (mg)

Acceptance criteria: 99.0%–101.0% on the dried basis

IMPURITIES

- **HEAVY METALS, Method II** (231): NMT 20 ppm

SPECIFIC TESTS

- **OPTICAL ROTATION, Specific Rotation** (781S)
Sample solution: 100 mg/mL in carbon dioxide-free water. Use the solution immediately after preparation.
Acceptance criteria: +103° to +108°
- **pH** (791)
Sample solution: 100-mg/mL solution
Acceptance criteria: 7.0–8.0
- **LOSS ON DRYING** (731): Dry a sample in a suitable vacuum drying tube, using phosphorus pentoxide as the desiccant, at 60° for 4 h: it loses NMT 0.25% of its weight.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.
- **USP REFERENCE STANDARDS** (11)
USP Sodium Ascorbate RS

Sodium Bicarbonate

$NaHCO_3$ 84.01
Carbonic acid monosodium salt;
Monosodium carbonate [144-55-8].

DEFINITION

Sodium Bicarbonate contains NLT 99.0% and NMT 100.5% of $NaHCO_3$, calculated on the dried basis.

IDENTIFICATION

- **A. IDENTIFICATION TESTS—GENERAL, Sodium** (191): Meets the requirements
- **B. IDENTIFICATION TESTS—GENERAL, Bicarbonate** (191): Meets the requirements

ASSAY

- **PROCEDURE**
Sample: 3 g
Analysis: Mix the Sample with 100 mL of water, add methyl red TS, and titrate with 1 N hydrochloric acid VS. Add the acid slowly, with constant stirring, until the solution becomes faintly pink. Heat the solution to boiling, cool, and continue the titration until the faint pink color no longer fades after boiling. Each mL of 1 N hydrochloric acid is equivalent to 84.01 mg of sodium bicarbonate.
Acceptance criteria: 99.0%–100.5% on the dried basis

IMPURITIES

- **INSOLUBLE SUBSTANCES**
Sample solution: Dissolve 1 g in 20 mL of water.
Acceptance criteria: The resulting solution is complete and clear.
- **CARBONATE** (where it is labeled as intended for use in hemodialysis)
Apparatus: The apparatus (see *Figure 1*) consists of a 50-mL flask with a side arm connected to a source of carbon dioxide humidified by bubbling through a saturated solution of sodium bicarbonate. The flask is equipped with a top-mounted stopper fitted with an exit tube. The exit tube is connected via a T-tube to a system vent and a leveling buret and reservoir.

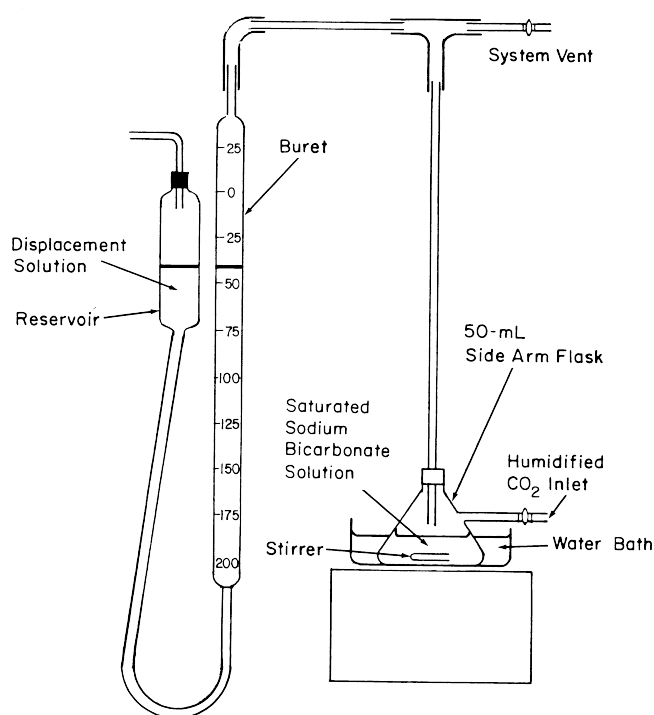


Figure 1. Carbonate apparatus.

Reagents

Saturated sodium bicarbonate solution: Mix 20 g of sodium bicarbonate in 100 mL of water, and allow any undissolved crystals to settle. Use the clear supernatant.

Displacement solution: Dissolve 100 g of sodium chloride in 350 mL water, and add 1 g of sodium bicarbonate and 1 mL of methyl orange TS. After the sodium bicarbonate has dissolved, add 6 N sulfuric acid until the solution turns pink. Use this solution to fill the reservoir of the apparatus.

Analysis: Add 25 mL of *Saturated sodium bicarbonate solution* to the 50-mL flask, and flush the system by allowing humidified carbon dioxide to enter through the side arm. Close the carbon dioxide inlet and the system vent, and stir the *Saturated sodium bicarbonate solution* until no further carbon dioxide absorption is noted from successive buret readings. Maintain atmospheric pressure in the apparatus by adjusting the *Displacement solution* to the same level in both the reservoir and the buret, noting the buret reading. Open the system vent, and reintroduce humidified carbon dioxide through the side arm of the flask. Close the carbon dioxide inlet and the system vent, and stir the *Saturated sodium bicarbonate solution* vigorously until no further carbon dioxide absorption is noted. Repeat the carbon dioxide absorption procedure starting with "Open the system vent" until NMT a 0.2-mL change in buret reading is noted. Discontinue stirring, reintroduce humidified carbon dioxide through the side arm of the flask, remove the top-mounted stopper from the flask briefly, and promptly add 10 g of Sodium Bicarbonate to the flask. Replace the stopper, continue the flow of humidified carbon dioxide for about 30 s, and then close the carbon dioxide inlet and the system vent. Stir the solution in the flask vigorously until carbon dioxide absorption ceases, noting the volume absorbed from the buret reading. Restore atmospheric pressure in the apparatus by leveling the *Displacement solution* in the reservoir and the buret, and discontinue stirring. Open the system vent, and flush humidified carbon dioxide through

the system. Close the carbon dioxide inlet and the system vent, and stir the solution in the flask vigorously until carbon dioxide absorption ceases.

Determine the total volume, V , in mL, of carbon dioxide absorbed after the addition of the specimen to the flask, and calculate the percentage of carbonate in the portion of specimen tested:

$$\text{Result} = 273V \times (6001P) / [22400 \times (273 + T) \times (760W)]$$

V = total volume of carbon dioxide absorbed (mL)

P = ambient atmospheric pressure (mm of mercury)

T = ambient temperature

W = weight of Sodium Bicarbonate taken (g)

[NOTE—Maintain a constant temperature during the measurement of the volume of carbon dioxide absorbed.]

Acceptance criteria: NMT 0.23%

- **NORMAL CARBONATE**

Sample: 1 g

Analysis: Dissolve the *Sample* in 20 mL of water with very gentle swirling at a temperature not exceeding 15°. Add 2.0 mL of 0.10 N hydrochloric acid and 2 drops of phenolphthalein TS.

Acceptance criteria: The solution does not assume more than a faint pink color immediately.

- **CHLORIDE AND SULFATE, Chloride <221>**

Sample: 0.35 g

Acceptance criteria: No more chloride than corresponds to 1.48 mL of 0.0010 N hydrochloric acid (NMT 0.015%).

- **LIMIT OF SULFUR COMPOUNDS**

Sample: 2.0 g

Sample solution: Dissolve the *Sample* in 20 mL of water, and evaporate to 5 mL by boiling. Add 1 mL of bromine TS, evaporate to dryness, and cool. Dissolve the residue in 10 mL of 3 N hydrochloric acid, evaporate to dryness, and cool. Dissolve the residue in 5 mL of 3 N hydrochloric acid, evaporate to dryness, and cool. Dissolve the residue in 10 mL of water, and adjust with 3 N hydrochloric acid or 6 N ammonium hydroxide to a pH of 2. If necessary to obtain a clear solution, filter the solution, washing the filter with two 2-mL portions of water. Dilute with water to 20 mL.

Standard solution: To 0.30 mL of 0.020 N sulfuric acid add 1 mL of 0.06 N hydrochloric acid, and dilute with water to 20 mL.

Analysis: Add 1 mL of barium chloride TS to each of the *Sample solution* and the *Standard solution*. Mix, and allow to stand for 30 min.

Acceptance criteria: Any turbidity produced in the *Sample solution* is not more intense than that produced in the *Standard solution* (NMT 0.015%).

- **ALUMINUM <206>** (where it is labeled as intended for use in hemodialysis)

Test preparation: Transfer 1.0 g to a 100-mL plastic volumetric flask. Carefully add 4 mL of nitric acid. Sonicate for 30 min, and dilute with water to volume.

Acceptance criteria: NMT 2 µg/g

- **ARSENIC, Method 1 <211>**

Test preparation: Dissolve 1.5 g in 20 mL of 7 N sulfuric acid and add 35 mL of water.

Analysis: Proceed as directed in the chapter, omitting the addition of 20 mL of 7 N sulfuric acid.

Acceptance criteria: NMT 2 ppm

- **CALCIUM** (where it is labeled as intended for use in hemodialysis)

[NOTE—The *Standard solutions* and the *Sample solution* may be modified, if necessary, to obtain solutions of suitable concentrations, adaptable to the linear or working range of the instrument.]

Potassium chloride solution: 10 mg/mL of potassium chloride in 0.36 N hydrochloric acid

Standard solutions: Transfer 249.7 mg of calcium carbonate, previously dried at 300° for 3 h and cooled in a desiccator for 2 h, to a 100-mL volumetric flask. Dissolve in 6 mL of 6 N hydrochloric acid, add 1 g of potassium chloride, and dilute with water to volume. Transfer 10.0 mL of this solution to a second 100-mL volumetric flask, and dilute with *Potassium chloride solution* to volume. This solution contains 100 µg/mL of calcium. Transfer 2.0, 3.0, 4.0, and 5.0 mL portions of this solution to separate 100-mL volumetric flasks (each containing 6 mL of 6 N hydrochloric acid), and dilute with *Potassium chloride solution* to volume. These *Standard solutions* contain 2.0-, 3.0-, 4.0-, and 5.0-µg/mL of calcium, respectively.

Sample solution: Transfer 3.0 g to a 100-mL volumetric flask. Add 6 mL of 6 N hydrochloric acid and 1 g of potassium chloride, and dilute with water to volume.

Blank: *Potassium chloride solution*

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* (851).)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Calcium emission line at 422.7 nm

Lamp: Calcium hollow-cathode

Flame: Nitrous oxide-acetylene

Analysis

Samples: *Standard solutions* and *Sample solution*
Plot the absorbances of the *Standard solutions* versus their contents of calcium, in µg/mL, by drawing a straight line best fitting the four plotted points. From the graph so obtained determine the concentration, C , in µg/mL, of calcium in the *Sample solution*.
Calculate the percentage of calcium in the portion of Sodium Bicarbonate taken:

$$\text{Result} = (C/C_U) \times 100$$

C = concentration of calcium in the *Sample solution* (µg/mL)

C_U = concentration of Sodium Bicarbonate in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 0.01%

- **MAGNESIUM** (where it is labeled as intended for use in hemodialysis)

[NOTE—The *Standard solutions* and the *Sample solution* may be modified, if necessary, to obtain solutions of suitable concentrations, adaptable to the linear or working range of the instrument.]

Potassium chloride solution, Sample solution, and Blank: Proceed as directed in the test for *Calcium*.

Standard solutions: To 1.000 g of magnesium in a 250-mL beaker containing 20 mL of water, carefully add 20 mL of hydrochloric acid, warming if necessary to complete the reaction. Transfer this solution to a 1000-mL volumetric flask containing 10 g of potassium chloride, and dilute with water to volume. Transfer 10.0 mL of this solution to a 100-mL volumetric flask containing 1 g of potassium chloride, and dilute with water to volume. Transfer 10.0 mL of this solution to a second 100-mL volumetric flask, and dilute with *Potassium chloride solution* to volume. This solution contains 10.0 µg/mL of magnesium. Transfer 2.0-, 3.0-, 4.0-, and 5.0-mL portions of this solution to separate 100-mL volumetric flasks (each containing 6 mL of 6 N hydrochloric acid), and dilute with *Potassium chloride solution* to volume. These *Standard solutions* contain 0.2, 0.3, 0.4, and 0.5 µg/mL of magnesium, respectively.

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* (851).)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Magnesium emission line at 285.2 nm

Lamp: Magnesium hollow-cathode

Flame: Reducing air-acetylene

Analysis

Samples: *Standard solutions* and *Sample solution*
Plot the absorbances of the *Standard solutions* versus their contents of magnesium, in µg/mL, by drawing a straight line best fitting the four plotted points. From the graph so obtained determine the concentration, C , in µg/mL, of magnesium in the *Sample solution*.
Calculate the percentage of magnesium in the portion of Sodium Bicarbonate taken:

$$\text{Result} = (C/C_U) \times 100$$

C = concentration of magnesium in the *Sample solution* (µg/mL)

C_U = concentration of Sodium Bicarbonate in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 0.004%

- **COPPER** (where it is labeled as intended for use in hemodialysis)

[NOTE—The *Standard solution* and the *Sample solution* may be modified, if necessary, to obtain solutions of suitable concentrations, adaptable to the linear or working range of the instrument.]

Diluent: Dilute 40 mL of nitric acid with water to 1000 mL.

Standard solution: 10.0 µg/mL of copper, prepared as follows. Transfer 1.000 g of copper to a 1000-mL volumetric flask. Dissolve in 20 mL of nitric acid, and dilute with 0.2 N nitric acid to volume. Transfer 10.0 mL of this solution to a second 1000-mL volumetric flask, and dilute with 0.2 N nitric acid to volume. Store in a polyethylene bottle.

Sample solution: Transfer 5.0 g of Sodium Bicarbonate to a 100-mL plastic volumetric flask, and carefully add 4 mL of nitric acid. Sonicate for 30 min, and dilute with water to volume.

Spiked sample solution: To 10.0 mL of the *Sample solution* add 20 µL of *Standard solution*. This solution contains 0.02 µg/mL of added copper.

Blank: *Diluent*

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* (851).)

Mode: Atomic absorption spectrophotometry

Analytical wavelength: Copper emission line at 324.7 nm

Lamp: Copper hollow-cathode

Flame: Flameless electrically heated furnace

Analysis

Samples: *Sample solution* and *Spiked sample solution*
Plot the absorbances of the *Sample solution* and the *Spiked sample solution* versus their contents of added copper, in µg/mL. Draw a line connecting the two points, and extrapolate the line until it intercepts the concentration axis. From the intercept, determine the concentration, C , in µg/mL, of copper in the *Sample solution*.

Calculate the percentage of copper in the portion of Sodium Bicarbonate taken:

$$\text{Result} = (C/C_U) \times 100$$

C = concentration of copper in the *Sample solution* (µg/mL)

C_U = concentration of Sodium Bicarbonate in the *Sample solution* (µg/mL)

Acceptance criteria: NMT 1 ppm

- **IRON** (241) (where it is labeled as intended for use in hemodialysis)

Sample solution: Place 2.0 g of Sodium Bicarbonate in a beaker, and neutralize with hydrochloric acid, noting the volume of acid consumed. Transfer this solution to a 25-mL volumetric flask with the aid of water.

Standard solution: Transfer 1.0 mL of *Standard Iron Solution* to a 25-mL volumetric flask. Add the same volume of hydrochloric acid as used to prepare the *Sample solution*.

Blank: Use the same volume of hydrochloric acid in a 25-mL volumetric flask as used to prepare the *Sample solution*.

Instrumental conditions

(See *Spectrophotometry and Light-Scattering* <851>.)

Mode: UV-Vis

Analytical wavelength: 480 nm

Analysis

Samples: *Sample solution*, *Standard solution*, and *Blank*
To each of the flasks containing the *Standard solution*, the *Sample solution*, and the *Blank* add 50 mg of ammonium peroxydisulfate crystals and 2 mL of *Ammonium Thiocyanate Solution*. Dilute with water to volume. Concomitantly determine the absorbances of the solutions from the *Standard solution* and the *Sample solution*.

Acceptance criteria: The absorbance of the *Sample solution* is NMT that of the *Standard solution* (NMT 5 ppm).

• **HEAVY METALS, Method I** <231>

Test preparation: Mix 4.0 g with 5 mL of water and 19 mL of 3 N hydrochloric acid, heat to boiling, and maintain that temperature for 1 min. Add 1 drop of phenolphthalein TS, then add sufficient 6 N ammonium hydroxide, dropwise, to give the solution a faint pink color. Cool, and dilute with water to 25 mL.

Acceptance criteria: NMT 5 ppm

• **LIMIT OF AMMONIA**

Sodium hypochlorite solution: Use a commercially available solution that contains 4.0%–6.0% of sodium hypochlorite.

Oxidizing solution: Alkaline sodium citrate TS and *Sodium hypochlorite solution* (4:1). [NOTE—Prepare on the day of use.]

Diluted sodium nitroferricyanide solution: Sodium nitroferricyanide TS and water (1:10)

Sample solution: 25 mg/mL in water

Analysis: [NOTE—Carefully follow the order of addition stated below.] To 4.0 mL of the *Sample solution* add 0.4 mL of phenol TS, 0.4 mL of *Diluted sodium nitroferricyanide solution*, and 1.0 mL of *Oxidizing solution*. Dilute with water to 10 mL, and allow to stand for 1 h.

Acceptance criteria: No blue color develops.

• **LIMIT OF ORGANICS** (where it is labeled as intended for use in hemodialysis)

Silver sulfate solution: 11 g/L of silver sulfate in sulfuric acid

Indicator solution: 14.85 mg/mL of 1,10-phenanthroline and 6.95 mg/mL of ferrous sulfate in water

Standard solution: Transfer 850.3 mg of potassium biphthalate, previously crushed lightly and dried at 120° for 2 h, to a 1000-mL volumetric flask. Dilute with water to volume. Transfer 6.0 mL of this solution to a 100-mL volumetric flask, and dilute with water to volume. It contains the equivalent of 0.06 mg/mL of organic equivalents. Transfer 40.0 mL of this solution to a 500-mL reflux flask.

Sample solution: Transfer 20 g of Sodium Bicarbonate to a 500-mL reflux flask. Add 20 mL of water, and swirl. Cautiously add 20 mL of sulfuric acid, and swirl.

[**CAUTION**—Perform this operation under a hood.]

Blank: Add 40 mL of water to a 500-mL reflux flask.

Analysis

Samples: *Standard solution*, *Sample solution*, and *Blank*
Concomitantly treat the *Samples* as follows: to each flask add 1 g of mercuric sulfate and about 5 glass beads. Cool the flask in an ice bath, and add 5 mL of *Silver sulfate solution*. While gently swirling the flask in the ice bath, add 25.0 mL of 0.025 N potassium dichromate VS and, slowly, 70 mL of *Silver sulfate solution*. Fit a cold water condenser on the reflux flask, and reflux for 2 h. Allow the contents of the flask to cool for 10 min, and

wash the condenser with 50 mL of water, collecting the washings in the flask. Add water to the flask to obtain a volume of about 350 mL. Add 3 drops of *Indicator solution*, and titrate at room temperature with 0.07 N ferrous ammonium sulfate VS until the solution changes from greenish blue to reddish brown.

To verify the suitability of the system, calculate the amount, in mg, of organic equivalents in the *Standard solution*:

$$\text{Result} = (V_B - V_S) \times 8N$$

V_B = volume of 0.07 N ferrous ammonium sulfate VS consumed by the *Blank* (mL)

V_S = volume of 0.07 N ferrous ammonium sulfate VS consumed by the *Standard solution* (mL)

N = normality of the ferrous ammonium sulfate VS

Suitability criteria: 2.328–2.424 mg

Calculate the amount, in mg, of organic equivalents in the portion of Sodium Bicarbonate taken:

$$\text{Result} = (V_B - V_U) \times 8N$$

V_B = volume of 0.07 N ferrous ammonium sulfate VS consumed by the *Blank* (mL)

V_U = volume of 0.07 N ferrous ammonium sulfate VS consumed by the *Sample solution* (mL)

N = normality of the ferrous ammonium sulfate VS

Acceptance criteria: NMT 0.01%

SPECIFIC TESTS

• **LOSS ON DRYING** <731>: Dry 4 g over silica gel for 4 h: it loses NMT 0.25% of its weight.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in well-closed containers.

• **LABELING:** Where Sodium Bicarbonate is intended for use in hemodialysis, it is so labeled.

Sodium Bicarbonate Injection

» Sodium Bicarbonate Injection is a sterile solution of Sodium Bicarbonate in Water for Injection, the pH of which may be adjusted by means of added Carbon Dioxide. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of NaHCO_3 .
NOTE—Do not use the Injection if it contains a precipitate.

Packaging and storage—Preserve in single-dose glass or plastic containers. Glass containers are preferably of Type I glass. Store at controlled room temperature.

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.

USP Reference standards <11>—

USP Endotoxin RS

Identification—It responds to the tests for *Sodium* <191> and for *Bicarbonate* <191>.

Bacterial endotoxins <85>—It contains not more than 5.0 USP Endotoxin Units per mEq.

pH <791>: between 7.0 and 8.5.

Particulate matter <788>: meets the requirements under small-volume injections.