Constituted solution—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* ⟨1⟩.

Identification—To 50 mg contained in a small test tube add 10 mL of ascorbic acid solution (1 in 50), and mix. Add 1 mL of dilute hydrochloric acid (1 in 10), mix, and add dropwise, while mixing, 1 to 2 mL of 1 N sodium hydroxide: a transient blue color is produced.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.05 USP Endotoxin Unit per µg of sodium nitroprusside.

Water, *Method I* ⟨921⟩: not more than 15.0%.

Other requirements—It responds to the *Identification* test *A* under *Sodium Nitroprusside*. It meets also the requirements for *Sterility Tests* ⟨71⟩, *Uniformity of Dosage Units* ⟨905⟩, and *Labeling* under *Injections* ⟨1⟩.

Assay—

pH 7.1 buffer—Dissolve 1.36 g of monobasic potassium phosphate and 5.2 mL of a 1 in 4 solution of tetrabutylammonium hydroxide in methanol in water to make 1000 mL, and adjust with phosphoric acid or with the tetrabutylammonium hydroxide solution to a pH of 7.1.

Mobile phase—Prepare a suitable filtered mixture of *pH 7.1 buffer* and acetonitrile (about 70:30).

NOTE—Use low-actinic glassware throughout the following sections.

Standard preparation—Dissolve an accurately weighed quantity of USP Sodium Nitroprusside RS, in *Mobile phase* to obtain a solution having a known concentration of about 0.05 mg per mL.

Assay preparation 1 (where the label states only the total contents of the container)—Transfer the contents of 1 container of Sodium Nitroprusside for Injection to a 100-mL volumetric flask with the aid of *Mobile phase*, dilute with *Mobile phase* to volume, and mix. Dilute an accurately measured volume of this solution quantitatively with *Mobile phase* to obtain a solution containing about 0.05 mg of $Na_2[Fe(CN)_5NO] \cdot 2H_2O$ per mL.

Assay preparation 2 (where the label states the quantity of $Na_2[Fe(CN_5)NO] \cdot 2H_2O$ in a given volume of constituted solution)—Constitute Sodium Nitroprusside for Injection as directed in the labeling. Dilute an accurately measured volume of the constituted solution thus obtained quantitatively and stepwise with *Mobile phase* to obtain a solution containing about 0.05 mg of $Na_2[Fe(CN)_5NO] \cdot 2H_2O$ per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 210-nm detector and a 3.9-mm × 30-cm column that contains 10-µm packing L11. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the tailing factor for the analyte peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 1.5%.

Procedure—Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $Na_2[Fe(CN)_5NO] \cdot 2H_2O$ in the container or in the portion of constituted solution taken by the formula:

$$L(C / D)(r_U / r_S)$$

in which L is the labeled quantity, in mg of $Na_2[Fe(CN)_5NO] \cdot 2H_2O$ in the container, or in the volume of constituted solution taken; C is the concentration, in mg per mL, of USP Sodium Nitroprusside RS in the *Standard preparation; D* is the concentration, in mg of $Na_2[Fe(CN)_5NO] \cdot 2H_2O$ per mL, of *Assay preparation 1* or of *Assay preparation 2*, on the basis of the labeled quantity in the container, or in the volume of constituted solution taken, respectively, and the extent of dilution; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Dibasic Sodium Phosphate

$Na_2HPO_4 \cdot 12H_2O$	358.14
$Na_2HPO_4 \cdot 7H_2O$	268.07
$Na_2HPO_4 \cdot 2H_2O$	177.99
$Na_2HPO_4 \cdot H_2O$	159.94
Na_2HPO_4	141.96

Phosphoric acid, disodium salt, dodecahydrate;
Disodium hydrogen phosphate, dodecahydrate [10039-32-4].
Phosphoric acid, disodium salt, heptahydrate;
Disodium hydrogen phosphate heptahydrate [7782-85-6].
Phosphoric acid, disodium salt, dihydrate;
Disodium hydrogen phosphate, dihydrate [10028-24-7].
Phosphoric acid, sodium salt, monohydrate;
Disodium hydrogen phosphate, monohydrate [118830-14-1].
Phosphoric acid, disodium salt, hydrate;
Disodium hydrogen phosphate hydrate [10140-65-5].
Anhydrous [7558-79-4].

DEFINITION

Dibasic Sodium Phosphate is dried or contains one, two, seven, or twelve molecules of water of hydration. It contains NLT 98.0% and NMT 100.5% of Na_2HPO_4, calculated on the dried basis.

IDENTIFICATION

- **A. Identification Tests—General,** *Sodium* ⟨**191**⟩
  Sample solution: Equivalent to 1 part of Na_2HPO_4 in 30
  Acceptance criteria: The solution meets the requirements.
- **B. Identification Tests—General,** *Phosphate* ⟨**191**⟩
  Sample solution: Equivalent to 1 part of Na_2HPO_4 in 30
  Acceptance criteria: The solution meets the requirements.

ASSAY

- **Procedure**
  Sample: Equivalent to 2.5 g of Na_2HPO_4
  Sample solution: Transfer the *Sample* to a 250-mL beaker. Add 50 mL of water and 40.0 mL of 1 N hydrochloric acid, and stir until dissolved.
  Blank: Transfer 40.0 mL of 1 N hydrochloric acid to a 250-mL beaker. Add 50 mL of water.
  Analysis: Titrate the *Blank* with 1 N sodium hydroxide VS, and record the volume of 1 N sodium hydroxide VS consumed. Titrate the excess acid in the *Sample solution* potentiometrically with 1 N sodium hydroxide VS to the inflection point at about pH 4, and record the buret reading. Subtract this buret reading from that of the *Blank*, and designate the volume of 1 N sodium hydroxide VS resulting from this subtraction as *A*. Continue the titration with 1 N sodium hydroxide VS to the inflection point at about pH 8.8, record the buret reading, and calculate the volume (*B*) of 1 N sodium hydroxide required in the titration between the two inflection points (pH 4–8.8). Where *A* is equal to or less than *B*, each mL of the volume *A* of 1 N sodium hydroxide is equivalent to 142.0 mg of Na_2HPO_4. Where *A* is greater than *B*, each mL of the volume (*2B – A*) of 1 N sodium hydroxide is equivalent to 142.0 mg of Na_2HPO_4.
  Acceptance criteria: 98.0%–100.5% on the dried basis

IMPURITIES

- **Insoluble Substances**
  Sample solution: Equivalent to 5.0 g of Na_2HPO_4 in 100 mL of hot water
  Analysis: Filter through a tared filtering crucible, wash the insoluble residue with hot water, and dry at 105° for 2 h.
  Acceptance criteria: NMT 20 mg (NMT 0.4%)
- **Chloride and Sulfate,** *Chloride* ⟨**221**⟩
  Sample: Equivalent to 0.5 g of Na_2HPO_4
  Acceptance criteria: Shows no more chloride than corresponds to 0.42 mL of 0.020 N hydrochloric acid (NMT 0.06%)

- **CHLORIDE AND SULFATE,** *Sulfate* ⟨**221**⟩
  Sample: Equivalent to 0.1 g of Na_2HPO_4
  Acceptance criteria: Shows no more sulfate than corresponds to 0.2 mL of 0.020 N sulfuric acid (NMT 0.2%)
- **ARSENIC,** *Method I* ⟨**211**⟩
  Test preparation: Equivalent to 187.5 mg of Na_2HPO_4 in 35 mL of water
  Acceptance criteria: NMT 16 ppm
- **HEAVY METALS** ⟨**231**⟩
  Sample stock solution: Dissolve the equivalent to 2.1 g of Na_2HPO_4 in enough water to make 50 mL.
  Analysis: Transfer 12 mL of the *Sample stock solution* to a 50-mL color-comparison tube (*Test Preparation*). Transfer 11 mL of the *Sample stock solution* to a second color-comparison tube containing 1.0 mL of *Standard Lead Solution* (*Monitor Preparation*). Transfer 1.0 mL of *Standard Lead Solution* and 11 mL of water to a third color-comparison tube (*Standard Preparation*). Proceed as directed for *Procedure,* omitting the dilution to 50 mL.
  Acceptance criteria: NMT 20 ppm

SPECIFIC TESTS

- **LOSS ON DRYING** ⟨**731**⟩**:** Dry a sample at 130° to constant weight.
  Acceptance criteria: See *Table 1*.

Table 1

Hydrate Form	Acceptance Criteria
Dried	NMT 5.0%
Monohydrate	10.3%–12.0%
Dihydrate	18.5%–21.5%
Heptahydrate	43.0%–50.0%
Dodecahydrate	55.0%–64.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **LABELING:** Label it to indicate whether it is dried or is the monohydrate, the dihydrate, the heptahydrate, or the dodecahydrate.

Monobasic Sodium Phosphate

$NaH_2PO_4 \cdot xH_2O$
(anhydrous) 119.98
Phosphoric acid, monosodium salt, monohydrate.
Monosodium phosphate monohydrate 137.99 [10049-21-5]
.
Phosphoric acid, monosodium salt, dihydrate.
Monosodium phosphate dihydrate 156.01 [13472-35-0].
Anhydrous [7558-80-7].

» Monobasic Sodium Phosphate contains one or two molecules of water of hydration, or is anhydrous. It contains not less than 98.0 percent and not more than 103.0 percent of NaH_2PO_4, calculated on the anhydrous basis.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate whether it is anhydrous or is the monohydrate or the dihydrate.

Identification—A solution (1 in 20) responds to the tests for *Sodium* ⟨191⟩ and for *Phosphate* ⟨191⟩.

pH ⟨791⟩**:** between 4.1 and 4.5, in a solution containing the equivalent of 1.0 g of $NaH_2PO_4 \cdot H_2O$ in 20 mL of water.

Water, *Method I* ⟨921⟩**:** less than 2.0% (anhydrous form); between 10.0% and 15.0% (monohydrate); between 18.0% and 26.5% (dihydrate). For the monohydrate, the sample may be ground to a fine powder in an atmosphere of temperature and relative humidity known not to influence the results, prior to performing the test.

Insoluble substances—Dissolve a portion equivalent to 10.0 g of $NaH_2PO_4 \cdot H_2O$ in 100 mL of hot water, filter through a tared filtering crucible, wash the insoluble residue with hot water, and dry at 105° for 2 hours: the weight of the residue so obtained does not exceed 20 mg (0.2%).

Chloride ⟨221⟩**—**A portion equivalent to 1.0 g of $NaH_2PO_4 \cdot H_2O$ shows no more chloride than corresponds to 0.20 mL of 0.020 N hydrochloric acid (0.014%).

Sulfate ⟨221⟩**—**A portion equivalent to 0.20 g of $NaH_2PO_4 \cdot H_2O$ shows no more sulfate than corresponds to 0.30 mL of 0.020 N sulfuric acid (0.15%).

Aluminum, calcium, and related elements—A solution containing the equivalent of 1.0 g of $NaH_2PO_4 \cdot H_2O$ in 10 mL of water does not become turbid when rendered slightly alkaline to litmus paper with 6 N ammonium hydroxide.

Arsenic, *Method I* ⟨211⟩**—**Dissolve a portion equivalent to 0.375 g of $NaH_2PO_4 \cdot H_2O$ in 35 mL of water: the limit is 8 ppm.

Heavy metals ⟨231⟩**—**Dissolve a portion equivalent to 1.0 g of $NaH_2PO_4 \cdot H_2O$ in 20 mL of water, and add 1 mL of 3 N hydrochloric acid and water to make 25 mL: the limit is 0.002%.

Assay—Dissolve about 2.5 g of Monobasic Sodium Phosphate, accurately weighed, in 10 mL of cold water, add 20 mL of a cold, saturated solution of sodium chloride, then add phenolphthalein TS, and titrate with 1 N sodium hydroxide VS, keeping the temperature of the solution between 10° and 15° during the entire titration. Perform a blank determination, and make any necessary correction. Each mL of 1 N sodium hydroxide is equivalent to 120.0 mg of NaH_2PO_4.

Sodium Phosphates Injection

» Sodium Phosphates Injection is a sterile solution of Monobasic Sodium Phosphate and Dibasic Sodium Phosphate in Water for Injection. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amounts of monobasic sodium phosphate ($NaH_2PO_4 \cdot H_2O$) and dibasic sodium phosphate ($Na_2HPO_4 \cdot 7H_2O$). It contains no bacteriostat or other preservative.

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

Labeling—The label states the sodium content in terms of milliequivalents in a given volume, and states also the phosphorus content in terms of millimoles in a given volume. Label the Injection to indicate that it is to be diluted to appropriate strength with water or other suitable fluid prior to administration and that once opened any unused portion is to be discarded. The label states also 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 *Phosphate* ⟨191⟩.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 1.10 USP Endotoxin Units per mg of sodium phosphates.

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