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# Sodium Chloride

Portions of this monograph that are national *USP* text, and are not part of the harmonized text, are marked with symbols (♦,♦) to specify this fact.

NaCl 58.44

Sodium Chloride CAS RN®: 7647-14-5.

**DEFINITION**

Sodium Chloride contains NLT 99.0% and NMT 100.5% of sodium chloride (NaCl), calculated on the dried basis.

**IDENTIFICATION**

• **A. Identification Tests—General ⟨191⟩, *Sodium*:** Meets the requirements

• **B. Chloride**

**Sample solution:** 3 mg of Sodium Chloride in 2 mL of water

**Analysis:** Acidify the *Sample solution* with diluted nitric acid, and add 0.4 mL of silver nitrate TS. Shake, and allow to stand. A curdled, white precipitate is formed. Centrifuge, wash the precipitate with three 1-mL portions of water, and discard the washings. Carry out this operation rapidly in subdued light, disregarding the fact that the supernatant may not become perfectly clear. Suspend the precipitate in 2 mL of water, and add 1.5 mL of 10 N ammonium hydroxide.

**Acceptance criteria:** The precipitate dissolves easily with the possible exception of a few large particles, which dissolve more slowly.

**ASSAY**

• **Procedure**

**Sample:** 50 mg of Sodium Chloride

**Analysis:** Dissolve the *Sample* in 50 mL of water, and titrate with 0.1 N silver nitrate VS (see *Titrimetry ⟨541⟩*), determining the endpoint potentiometrically. Each mL of 0.1 N silver nitrate is equivalent to 5.844 mg of sodium chloride (NaCl).

**Acceptance criteria:** 99.0%–100.5% on the dried basis

**IMPURITIES**

• **Aluminum** (where it is labeled as intended for use in the manufacture of peritoneal dialysis solutions, hemodialysis solutions, or hemofiltration solutions)

**Buffer:** Dissolve 50 g of ammonium acetate in 150 mL of water, adjust with glacial acetic acid to a pH of 6.0, and dilute with water to 250 mL.

**Aluminum standard solution:** To 352 mg of aluminum potassium sulfate in a 100-mL volumetric flask add a few mL of water, and swirl to dissolve. Add 20 mL of diluted sulfuric acid, dilute with water to volume, and mix. Immediately before use, transfer 1.0 mL of this solution to a 100-mL volumetric flask, and dilute with water to volume.

**Sample solution:** Dissolve 20.0 g of Sodium Chloride in 100 mL of water, and add 10 mL of *Buffer*. Extract this solution with successive portions of 20, 20, and 10 mL of a 0.5% solution of 8-hydroxyquinoline in chloroform, combining the chloroform extracts in a 50-mL volumetric flask. Dilute the combined extracts with chloroform to volume.

**Standard solution:** Prepare a mixture of 2.0 mL of *Aluminum standard solution*, 10.0 mL of *Buffer*, and 98 mL of water. Extract this mixture as described for the *Sample solution*, and dilute the combined extracts with chloroform to volume.

**Blank solution:** Prepare a mixture of 10 mL of *Buffer* and 100 mL of water. Extract this mixture as described for *Sample solution*, and dilute the combined extracts with chloroform to volume.

**Instrumental conditions**

(See *Fluorescence Spectroscopy ⟨853⟩*.)

**Mode:** Fluorescence

**Excitation wavelength:** 392 nm

**Emission wavelength:** 518 nm

**Analysis**

**Samples:** *Sample solution*, *Standard solution*, and *Blank solution*. Use the *Blank solution* to set the instrument to zero. Determine the fluorescence intensities of the *Sample solution* and *Standard solution*.

**Acceptance criteria:** The fluorescence of the *Sample solution* does not exceed that of the *Standard solution* (0.2 ppm).

***Change to read:***

• ♦▲Arsenic ⟨211⟩, *Procedures, Procedure 1*▲ (CN 1-Jun-2023) : NMT 1 ppm♦

- **Barium**

**Analysis:** To 5 mL of the solution prepared for the test for *Appearance of Solution* add 2 mL of 2 N sulfuric acid and 5 mL of water, as test solution. To another 5 mL of the solution prepared for the test for *Appearance of Solution* add 7 mL of water, as reference solution. Let stand for 2 h.

**Acceptance criteria:** Any opalescence in the test solution is not more intense than that in the reference solution.

- **Ferrocyanides**

**Sample solution:** Dissolve 2.0 g in 6 mL of water.

**Analysis:** To the *Sample solution* add 0.5 mL of a mixture of 5 mL of ferric ammonium sulfate solution (10 mg/mL in 2.5 g/L (0.05 N) of sulfuric acid) and 95 mL of ferrous sulfate solution (10 mg/mL in water).

**Acceptance criteria:** No blue color develops in 10 min.

- **Iodides**

**Sample:** 5 g of Sodium Chloride

**Analysis:** Moisten the *Sample* by the dropwise addition of a freshly prepared mixture of 0.15 mL of sodium nitrite solution (100 mg/mL), 2 mL of 1 N sulfuric acid, 25 mL of iodide-free starch TS, and 25 mL of water. After 5 min, examine the substance in natural light.

**Acceptance criteria:** No blue color is observed.

***Change to read:***

- **Iron**

**Sample solution:** Use a 10-mL portion of the solution prepared for the test for *Appearance of Solution*.

**Standard solution:** Immediately before use, dilute *Standard Iron Solution* (see ▲*Iron ⟨241⟩, Procedures, Procedure 1*▲ (CN 1-Jun-2023) ) 1 to 10 with water. This solution contains the equivalent of 1 µg/mL of iron. Combine 4 mL of this solution and 6 mL of water.

**Analysis:** To each of the solutions add 2 mL of a 200-mg/mL solution of citric acid and 0.1 mL of thioglycolic acid. Mix, make alkaline with stronger ammonia water, and dilute with water to 20 mL.

**Acceptance criteria:** After 5 min, any pink color in the *Sample solution* is not more intense than that from the *Standard solution* (NMT 2 ppm).

- **Limit of Bromides**

[Note—Prepare the *Sample solution* and the *Standard solution* concomitantly.]

**Standard solution:** To 5.0 mL of a solution containing 3 µg/mL of potassium bromide add 2.0 mL of pH 4.7 phenol red TS and 1.0 mL of chloramine T solution (0.1 mg/mL), and mix immediately. After 2 min, add 0.15 mL of 0.1 N sodium thiosulfate, mix, and dilute with water to 10.0 mL.

**Sample solution:** To 0.5 mL of the solution prepared for the test for *Appearance of Solution* add 4.0 mL of water, 2.0 mL of pH 4.7 phenol red TS, and 1.0 mL of chloramine T solution (0.1 mg/mL), and mix immediately. After 2 min, add 0.15 mL of 0.1 N sodium thiosulfate, mix, and dilute with water to 10.0 mL.

**Instrumental conditions**

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

**Mode:** UV-Vis

**Analytical wavelength:** 590 nm

**Comparison liquid:** Water

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

**Acceptance criteria:** The absorbance of the *Sample solution* is not greater than that of the *Standard solution* (NMT 100 ppm).

- **Limit of Phosphates**

**Sulfomolybdic acid solution:** Dissolve with heating 2.5 g of ammonium molybdate in 20 mL of water. Dilute 28 mL of sulfuric acid in 50 mL of water, then cool. Mix the two solutions, and dilute with water to 100 mL.

**Phosphate standard stock solution:** 0.716 mg/mL of monobasic potassium phosphate in water

**Phosphate standard solution:** 7.16 µg/mL from *Phosphate standard stock solution* in water. [Note—Prepare this solution fresh.]

**Standard solution:** Dilute 2 mL of the *Phosphate standard solution* with water to 100 mL.

**Sample solution:** Dilute 2 mL of the solution prepared in the test for *Appearance of Solution* with water to 100 mL.

**Analysis:** To the *Standard solution* and the *Sample solution* add 4 mL of *Sulfomolybdic acid solution*, and add 0.1 mL of a mixture of 1 mL of stronger acid stannous chloride TS and 10 mL of 2 N hydrochloric acid. After 10 min, compare the colors of 20 mL of each solution.

**Acceptance criteria:** Any color in the *Sample solution* is not more intense than that in the *Standard solution* (NMT 25 ppm).

- **Limit of Potassium** (where it is labeled as intended for use in the manufacture of injectable dosage forms, peritoneal dialysis solutions, hemodialysis solutions, or hemofiltration solutions)

[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.]

**Standard solutions:** Dissolve 1.144 g of potassium chloride, previously dried at 105° for 3 h, in water. Dilute with water to 1000 mL, and mix. This solution contains the equivalent of 600 µg/mL of potassium. Dilute as required to obtain NLT 3 solutions at concentrations that span the expected value in the *Sample solution*.

**Sample solution:** Transfer 1.00 g of Sodium Chloride to a 100-mL volumetric flask. Add water and swirl to dissolve, dilute with water to volume, and mix.

**Instrumental conditions**

(See *Atomic Absorption Spectroscopy ⟨852⟩*.)

**Mode:** Atomic emission spectroscopy

**Analytical wavelength:** 766.5 nm

**Flame:** Air–acetylene

**Analysis**

**Samples:** *Standard solutions* and *Sample solution*

Measure, at least three times, the emission intensity of the *Sample solution* and the *Standard solutions*. Prepare a calibration curve from the mean of the readings obtained with the *Standard solutions,* and determine the concentration of potassium in the *Sample solution*.

**Acceptance criteria:** NMT 500 ppm

- **Magnesium and Alkaline-Earth Metals**

**Buffer:** Prepare pH 10.0 ammonia–ammonium chloride buffer by dissolving 5.4 g of ammonium chloride in 20 mL of water, adding 20 mL of ammonium hydroxide, and diluting with water to 100 mL.

**Analysis:** To 200 mL of water add 0.1 g of hydroxylamine hydrochloride, 10 mL of *Buffer*, 1 mL of 0.1 M zinc sulfate, and 0.15 g of eriochrome black T trituration. Heat to 40°. Titrate this solution with 0.01 M edetate disodium VS until the violet color changes to deep blue. To this solution add 10.0 g of Sodium Chloride dissolved in 100 mL of water. If the color changes to violet, titrate the solution with 0.01 M edetate disodium VS to a deep blue endpoint.

**Acceptance criteria:** The volume of 0.01 M edetate disodium consumed in the second titration does not exceed 2.5 mL (NMT 100 ppm, calculated as Ca).

- **Nitrites**

**Sample solution:** To 10 mL of the solution prepared in the test for *Appearance of Solution* add 10 mL of water.

**Instrumental conditions**

(See *Ultraviolet-Visible Spectroscopy ⟨857⟩*.)

**Mode:** UV-Vis

**Analytical wavelength:** 354 nm

**Cell:** 1 cm

**Analysis**

**Sample:** *Sample solution*

**Acceptance criteria:** Absorbance is NMT 0.01.

- **Sulfate**

[Note—All solutions used for this test must be prepared with distilled water.]

**Sulfate standard solution A:** To 181 mg of potassium sulfate in a 100-mL volumetric flask add a few mL of 30% alcohol. Swirl to dissolve, dilute with 30% alcohol to volume, and mix. Immediately before use, transfer 10.0 mL of this solution to a 1000-mL volumetric flask, and dilute with 30% alcohol to volume (10 µg/mL of sulfate).

**Sulfate standard solution B:** To 181 mg of potassium sulfate in a 100-mL volumetric flask add a few mL of water. Swirl to dissolve, dilute with water to volume, and mix. Immediately before use, transfer 10.0 mL of this solution to a 1000-mL volumetric flask, and dilute with water to volume (10 µg/mL of sulfate).

**Sodium chloride solution:** 50 mg/mL of Sodium Chloride in water

**Barium chloride solution:** 250 mg/mL of barium chloride in water

**Standard solution:** To 1.5 mL of *Sulfate standard solution A* add 1 mL of *Barium chloride solution*. Shake, and allow to stand for 1 min. To 2.5 mL of the resulting suspension add 15 mL of *Sulfate standard solution B* and 0.5 mL of 5 N acetic acid, and mix.

**Sample solution:** To 1.5 mL of *Sulfate standard solution A* add 1 mL of *Barium chloride solution*. Shake, and allow to stand for 1 min. To 2.5 mL of the resulting suspension add 15 mL of *Sodium chloride solution* and 0.5 mL of 5 N acetic acid, and mix.

**Acceptance criteria:** Any opalescence produced in the *Sample solution* after 5 min standing is NMT that produced in the *Standard solution* (200 ppm).

## SPECIFIC TESTS

- **Appearance of Solution:** Dissolve 20.0 g of Sodium Chloride in carbon dioxide-free water, and dilute with the same solvent to 100.0 mL. This solution is clear and colorless.

- **Acidity or Alkalinity**

**Analysis:** To 20 mL of the solution prepared for the test for *Appearance of Solution* add 0.1 mL of bromothymol blue TS.

**Acceptance criteria:** NMT 0.5 mL of 0.01 N hydrochloric acid or 0.01 N sodium hydroxide is required to change the color of this solution.

- **Loss on Drying ⟨731⟩**

**Sample:** 1.000 g

**Analysis:** Dry the *Sample* in an oven at 105° for 2 h.

**Acceptance criteria:** NMT 0.5%

- **Bacterial Endotoxins Test ⟨85⟩:** The level of bacterial endotoxins is such that the requirement under the relevant dosage form monograph(s) in which Sodium Chloride is used can be met. Where the label states that Sodium Chloride must be subjected to further processing during the preparation of injectable dosage forms, the level of bacterial endotoxins is such that the requirement under the relevant dosage form monograph(s) in which Sodium Chloride is used can be met.

• **Sterility Tests ⟨71⟩:** Where the label states that Sodium Chloride is sterile, it meets the requirements for *Sterility* under the relevant dosage form monograph(s) in which Sodium Chloride is used.

**ADDITIONAL REQUIREMENTS**

• **Packaging and Storage:** Preserve in well-closed containers.

• **Labeling:** Where Sodium Chloride is intended for use in the manufacture of injectable dosage forms, peritoneal dialysis solutions, hemodialysis solutions, or hemofiltration solutions, it is so labeled. Where Sodium Chloride must be subjected to further processing during the preparation of injectable dosage forms to ensure acceptable levels of bacterial endotoxins, it is so labeled. Where Sodium Chloride is sterile, it is so labeled.

**Auxiliary Information** - Please check for your question in the FAQs before contacting USP.

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**Chromatographic Database Information:** Chromatographic Database

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