▲Sodium Chloride

NaCl 58.44

Sodium Chloride

Sodium Chloride [*7647-14-5*].

» Sodium Chloride contains not less than 99.0 percent and not more than 100.5 percent of NaCl, calculated on the dried basis.

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.

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.

Identification—It responds to the tests for *Sodium* ⟨191⟩ and for *Chloride*.

Chloride—Dissolve about 3 mg of Sodium Chloride in 2 mL of water. Acidify 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 and 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. The precipitate dissolves easily with the possible exception of a few large particles, which dissolve more slowly.

Bacterial endotoxins ⟨85⟩—~~If intended for use in the manufacture of parenteral dosage forms, it contains not more than 5 I.U. of endotoxin per gram.~~ The level of *Bacterial endotoxins* are 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* are such that the requirement under the relevant dosage form monograph(s) in which Sodium Chloride is used can be met.

Sterility ⟨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.

Acidity or alkalinity—To 20 mL of the solution prepared for the test for *Appearance of solution,* add 0.1 mL of bromothymol blue TS: not more than 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⟩—Dry the test material at 105° for 2 hours: it loses not more than 0.5% of its weight, determined on a 1.000 g sample.

Limit of bromides—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 per mL), and mix immediately. After 2 minutes, add 0.15 mL of 0.1 N sodium thiosulfate, mix, dilute with water to 10.0 mL, and mix. The absorbance of this solution measured at 590 nm, using water as the comparison liquid, is not greater than that of a *Standard solution,* concomitantly prepared, using 5.0 mL of a solution containing

3.0 mg of potassium bromide per L and proceeding as above, starting with the addition of 2.0 mL of pH 4.7 phenol red TS (0.010%).

Limit of phosphates—~~Dilute 2 mL of the solution prepared in the test for *Appearance of solution* to 100 mL with water. Add 4 mL of sulfomolybdic acid TS, 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. Concomitantly prepare a *Standard solution* in the same manner, using a mixture of 2 mL of a freshly prepared 1 to 100 dilution of a stock solution containing 0.716 mg of monobasic potassium phosphate per mL and 98 mL of water. After 10 minutes compare the colors of 20 mL of each solution. Any color in the test solution is not more intense than that in the *Standard solution* (0.0025%, or 25 ppm).~~

Phosphate stock standard solution—Dissolve an accurately weighed quantity of monobasic potassium phosphate in water to obtain a solution with a concentration of about 0.716 mg per mL.

Phosphate standard solution—Dilute 1 mL of the S*tock standard solution* with water to 100 mL. Prepare this solution fresh.

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

Test solution—Dilute 2 mL of the solution prepared in the test for *Appearance of solution* with water to 100 mL.

Procedure—To the *Standard solution* and the *Test solution,* add 4 mL of sulfomolybdic acid TS, 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 minutes, compare the colors of 20 mL of each solution: any color in the *Test solution* is not more intense than that in the *Standard solution* (0.0025%).

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)—

Test 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.

Standard solution—[NOTE—The *Standard solution* and the *Test solution* may be modified, if necessary, to obtain solutions of suitable concentrations adaptable to the linear or working range of the instrument.] Dissolve 1.144 g of potassium chloride, previously dried at 105° for 3 hours, in water, dilute with water to 1000 mL, and mix. This solution contains the equivalent of 600 µg of potassium per mL. Dilute as required to obtain not fewer than three solutions at concentrations that span the expected value in the *Test solution*.

Procedure—Using atomic absorption spectrophotometry (see *Spectrophotometry and Light-Scattering* ⟨851⟩), measure, at least three times, the emission intensity of the *Test solution* and the *Standard solution* using an air–acetylene flame and a wavelength of 766.5 nm. Prepare a calibration curve from the mean of the readings obtained with the *Standard solution,* and determine the concentration of potassium in the *Test solution*. The limit is 0.05%.

Iodides—Moisten 5 g of Sodium Chloride by the dropwise addition of a freshly prepared mixture of 0.15 mL of sodium nitrite solution (1 in 10), 2 mL of 1 N sulfuric acid, 25 mL of iodide-free starch TS, and 25 mL of water. After 5 minutes, examine the substance in natural light. No blue color is observed.

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

Standard aluminum solution—To 352 mg of aluminum potassium sulfate in a 100-mL volumetric flask, add a few mL of water, 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, dilute with water to volume, and mix.

pH 6.0 Acetate buffer—Dissolve 50 g of ammonium acetate in 150 mL of water, adjust with glacial acetic acid to a pH of 6.0, dilute with water to 250 mL, and mix.

Test solution—Dissolve 20.0 g of Sodium Chloride in 100 mL of water, and add 10 mL of *pH 6.0 Acetate 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, and mix.

Standard solution—Prepare a mixture of 2.0 mL of *Standard aluminum solution*, 10 mL of *pH 6.0 Acetate buffer,* and 98 mL of water. Extract this mixture as described for the *Test solution*, dilute the combined extracts with chloroform to volume, and mix.

Blank solution—Prepare a mixture of 10 mL of *pH 6.0 Acetate buffer* and 100 mL of water. Extract this mixture as described for the *Test solution*, dilute the combined extracts with chloroform to volume, and mix.

Procedure—Determine the fluorescence intensities of the *Test solution* and the *Standard solution* in a fluorometer set at an excitation wavelength of 392 nm and an emission wavelength of 518 nm, using the *Blank solution* to set the instrument to zero. The fluorescence of the *Test solution* does not exceed that of the *Standard solution* (0.2 µg per g).

Magnesium and alkaline-earth metals—To 200 mL of water add 0.1 g of hydroxylamine hydrochloride, 10 mL of pH 10.0 ammonia–ammonium chloride buffer (prepared by dissolving 5.4 g of ammonium chloride in 20 mL of water, adding 20 mL of ammonium hydroxide and diluting to 100 mL), 1 mL of 0.1 M zinc sulfate, and about 0.2 g of eriochrome black T trituration. Heat to about 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. The volume of 0.01 M edetate disodium consumed in the second titration does not exceed 2.5 mL (0.01%, calculated as Ca).

Arsenic, *Method I* ⟨211⟩: 1 µg per g.

Iron—

Test 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⟩) 1 to 10 with water. This solution contains the equivalent of 1 µg of iron per mL. Combine 4 mL of this solution and 6 mL of water.

Procedure—To each of the solutions, add 2 mL of a 200 g per L 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. After 5 minutes, any pink color in the *Test solution* is not more intense than that from the *Standard solution*. The limit is 2 µg per g.

Barium—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. To another 5 mL of the solution prepared for the test for *Appearance of solution,* add 7 mL of water. The solutions are equally clear after standing for 2 hours.

Ferrocyanides—Dissolve 2.0 g in 6 mL of water. Add 0.5 mL of a mixture of 5 mL of ferric ammonium sulfate solution (1 g in 100 mL of 0.1 N sulfuric acid) and 95 mL of ferrous sulfate solution (1 in 100): no blue color develops in 10 minutes.

Sulfate—

Standard sulfate 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, dilute with 30% alcohol to volume, and mix. This solution contains 10 µg of sulfate per mL.

Standard sulfate 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, dilute with water to volume, and mix. This solution contains 10 µg of sulfate per mL.

Sodium chloride solution—Dissolve 2.5 g of Sodium Chloride in 50 mL of water.

Procedure—To 1.5 mL of *Standard sulfate solution A* add 1 mL of a barium chloride solution (1 in 4), shake, and allow to stand for 1 minute. To 2.5 mL of the resulting suspension, add 15 mL of the Sodium Chloride solution and 0.5 mL of 5 N acetic acid, and mix (*Test solution*). Prepare the *Standard solution* in the same manner, except use 15 mL of *Standard sulfate solution B* instead of the Sodium Chloride solution: any turbidity produced in the *Test solution* after 5 minutes standing is not greater than that produced in the *Standard solution* (0.020%).

Nitrites—To 10 mL of the solution prepared in the test for *Appearance of solution,* add 10 mL of water, and measure the absorbance of the solution in a 1-cm cell at 354 nm. The absorbance is not greater than 0.01.

Heavy metals, *Method I* ⟨231⟩: 5 ppm.

Assay—Dissolve 50 mg of Sodium Chloride, accurately weighed, in water and make 50 mL. Titrate with 0.1 N silver nitrate VS, determining the endpoint potentiometrically (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N silver nitrate is equivalent to 5.844 mg of NaCl.▲*USP28*

MONOGRAPHS (NF)

BRIEFING

Benzyl Alcohol, *NF 22* page 2830 and page 879 of *PF* 28(3) [May–July 2002]. The European Pharmacopoeia is the coordinating pharmacopeia for the international harmonization of the compendial standards for *Benzyl Alcohol*, as part of the process of international harmonization of monographs and general analytical methods of the European, Japanese, and United States pharmacopeias. The following draft monograph represents the **ADOPTION STAGE 6** draft, which has been accepted by the members of the Pharmacopeial Discussion Group.

Pharmacopeial Discussion Group Sign-Off Document

Attributes	EP	JP	USP
Definition	+	+	+
Identification	+	+	+
Appearance of solution	+	+	+
Refractive index	+	+	+
Acidity	+	+	+
Benzaldehyde and other related substances	+	+	+
Peroxide value	+	+	+
Residue on evaporation	+	+	+
Assay	+	+	+

Legend: + will adopt and implement; – will not stipulate.
Nonharmonized attributes: Characters, Labeling, Storage.
Reagents and reference materials: Each pharmacopeia will adapt the text to take account of local reference substances and spectra and reagent specifications.

Proposed changes to the current *NF* monograph include the following: