

to make 5 mL, and perform the test with this solution using Apparatus B (not more than 2 ppm).

**Loss on drying** Not more than 0.5% (1 g, 105°C, 2 hours).

**Assay** Weigh accurately about 0.3 g of Sodium Salicylate, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 16.010 mg of  $C_7H_5NaO_3$

**Containers and storage** Containers—Tight containers.  
Storage—Light-resistant.

## Sodium Thiosulfate

チオ硫酸ナトリウム

$Na_2S_2O_3 \cdot 5H_2O$ : 248.18

Sodium Thiosulfate, when dried, contains not less than 99.0% of  $Na_2S_2O_3$  (mol. wt.: 158.11).

**Description** Sodium Thiosulfate occurs as colorless crystals or crystalline powder. It is odorless.

It is very soluble in water, and very slightly soluble in ethanol (95), and practically insoluble in diethyl ether.

It effloresces in dry air, and is deliquescent in moist air.

**Identification** A solution of Sodium Thiosulfate (1 in 10) responds to the Qualitative Tests for sodium salt and for thiosulfate.

**pH** Dissolve 1.0 g of Sodium Thiosulfate in 10 mL of water: the pH of the solution is between 6.0 and 8.0.

**Purity (1)** Clarity and color of solution—Dissolve 1.0 g of Sodium Thiosulfate in 10 mL of water: the solution is clear and colorless.

(2) Heavy metals—Dissolve 1.0 g of Sodium Thiosulfate in 10 mL of water, add slowly 5 mL of dilute hydrochloric acid, and evaporate on a water bath to dryness. Add 15 mL of water to the residue, boil gently for 2 minutes, and filter. Heat the filtrate to boil, and add bromine TS to the hot filtrate to produce a clear solution and provide a slight excess of bromine. Boil the solution to expel the bromine. Cool, add 1 drop of phenolphthalein TS, and add dropwise sodium hydroxide TS until a slight red color is produced. Add 2 mL of dilute acetic acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 2.0 mL of Standard Lead Solution add 2 mL of dilute acetic acid and water to make 50 mL (not more than 20 ppm).

(3) Calcium—Dissolve 1.0 g of Sodium Thiosulfate in 10 mL of water, add 2 mL of ammonium oxalate TS, and allow to stand for 4 minutes: no turbidity is produced.

(4) Arsenic—To 0.40 g of Sodium Thiosulfate add 3 mL of nitric acid and 5 mL of water, evaporate on a water bath to dryness, and perform the test with the residue. Prepare the test solution according to Method 2, and perform the test using Apparatus B (not more than 5 ppm).

**Loss on drying** 32.0 – 37.0% (1 g, dry first over silica gel for 2 hours in vacuum, and then dry at 105°C for 3 hours).

**Assay** Weigh accurately about 0.4 g of Sodium Thiosulfate, previously dried, dissolve in 30 mL of water, and titrate with 0.05 mol/L iodine VS (indicator: 1 mL of starch TS).

Each mL of 0.05 mol/L iodine VS  
= 15.811 mg of  $Na_2S_2O_3$

**Containers and storage** Containers—Tight containers.

## Sodium Thiosulfate Injection

チオ硫酸ナトリウム注射液

Sodium Thiosulfate Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of sodium thiosulfate ( $Na_2S_2O_3 \cdot 5H_2O$ : 248.18).

**Method of preparation** Prepare as directed under Injections, with Sodium Thiosulfate.

**Description** Sodium Thiosulfate Injection is a clear, colorless liquid.

**Identification** Sodium Thiosulfate Injection responds to the Qualitative Tests for sodium salt and for thiosulfate.

**Pyrogen** Perform the test with Sodium Thiosulfate Injection stored in a container in a volume exceeding 10 mL: it meets the requirements of the Pyrogen Test.

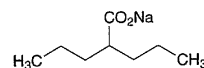
**Assay** Measure exactly a volume of Sodium Thiosulfate Injection, equivalent to about 0.5 g of sodium thiosulfate ( $Na_2S_2O_3 \cdot 5H_2O$ ), add water to make 30 mL, and titrate with 0.05 mol/L iodine VS (indicator: 1 mL of starch TS).

Each mL of 0.05 mol/L iodine VS  
= 24.819 mg of  $Na_2S_2O_3 \cdot 5H_2O$

**Containers and storage** Containers—Hermetic containers.

## Sodium Valproate

バルプロ酸ナトリウム



$C_8H_{15}NaO_2$ : 166.19  
Monosodium 2-propylpentanoate [1069-66-5]

Sodium Valproate, when dried, contains not less than 98.5% of  $C_8H_{15}NaO_2$ .

**Description** Sodium Valproate occurs as a white, crystalline powder. It has a characteristic odor and a slightly bitter taste.

It is very soluble in water, freely soluble in formic acid, in ethanol (95), in ethanol (99.5) and in acetic acid (100), and

practically insoluble in chloroform and in diethyl ether.

It is hygroscopic.

**Identification (1)** To 1 mL of a solution of Sodium Valproate in ethanol (99.5) (1 in 200) add 4 mL of hydroxylamine perchlorate-dehydrated ethanol TS and 1 mL of *N,N'*-dicyclohexylcarbodiimide-dehydrated ethanol TS, shake well, and allow to stand in lukewarm water for 20 minutes. After cooling, add 1 mL of iron (III) perchlorate-dehydrated ethanol TS, and shake: a purple color develops.

(2) To 5 mL of a solution of Sodium Valproate (1 in 20) add 1 mL of a solution of cobalt (II) nitrate hexahydrate (1 in 20), and warm on a water bath: a purple precipitate is formed.

(3) Dissolve 0.5 g of Sodium Valproate in 5 mL of water, add 5 mL of chloroform and 1 mL of 2 mol/L hydrochloric acid TS, and shake vigorously for 1 minute. After allowing to stand, separate the chloroform layer, dehydrate the chloroform with anhydrous sodium sulfate, then filter, and evaporate the filtrate to dryness. Determine the infrared absorption spectrum of the residue as directed in the liquid film method under the Infrared Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wave numbers.

(4) A solution of Sodium Valproate (1 in 10) responds to the Qualitative Tests for sodium salt.

**pH** Dissolve 1.0 g of Sodium Valproate in 20 mL of water: the pH of this solution is between 7.0 and 8.5.

**Purity (1)** Clarity and color of solution—Dissolve 1.0 g of Sodium Valproate in 10 mL of water: the solution is clear and colorless.

(2) Chloride—Dissolve 0.5 g of Sodium Valproate in 25 mL of ethanol (95), and add 6 mL of dilute nitric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.70 mL of 0.01 mol/L hydrochloric acid VS add 25 mL of ethanol (95), 6 mL of dilute nitric acid and water to make 50 mL (not more than 0.050%).

(3) Sulfate—Dissolve 0.5 g of Sodium Valproate in 25 mL of ethanol (95), and add 1 mL of dilute hydrochloric acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 0.50 mL of 0.005 mol/L sulfuric acid VS add 25 mL of ethanol (95), 1 mL of dilute hydrochloric acid and water to make 50 mL (not more than 0.048%).

(4) Heavy metals—Dissolve 2.0 g of Sodium Valproate in 44 mL of water, shake with 6 mL of dilute hydrochloric acid, allow to stand for 5 minutes, and filter. Discard the first 5 mL of the filtrate, neutralize the subsequent 25 mL with ammonia TS, and add 2 mL of dilute acetic acid and water to make 50 mL. Perform the test using this solution as the test solution. Prepare the control solution as follows: to 2.0 mL of Standard Lead Solution add 2 mL of dilute acetic acid and water to make 50 mL (not more than 20 ppm).

(5) Arsenic—Dissolve 2.0 g of Sodium Valproate in 10 mL of water, shake with 10 mL of dilute hydrochloric acid, allow to stand for 5 minutes, and filter. Discard the first 5 mL of the filtrate, and perform the test with the subsequent 10 mL using Apparatus B (not more than 2 ppm).

(6) Related substances—Dissolve 0.10 g of Sodium Valproate in 10 mL of a mixture of formic acid and chloroform (1:1), and use this solution as the sample solution. Pipet 1

mL of the sample solution, add a mixture of formic acid and chloroform (1:1) to make exactly 200 mL, and use this solution as the standard solution. Perform the test with 2  $\mu$ L each of the sample solution and the standard solution as directed under the Gas Chromatography according to the following conditions. Determine each peak area of both solutions by the automatic integration method: the total area of all peaks other than the area of the valproic acid from the sample solution is not larger than the peak area of the valproic acid from the standard solution.

**Operating conditions—**

Detector: A hydrogen flame-ionization detector.

Column: A glass column about 3 mm in inside diameter and about 2 m in length, packed with siliceous earth for gas chromatography (150 to 180  $\mu$ m in particle diameter) coated with diethylene glycol adipate ester for gas chromatography and phosphoric acid at the ratios of 5% and 1%, respectively.

Column temperature: A constant temperature of about 145°C.

Carrier gas: Nitrogen

Flow rate: Adjust the flow rate so that the retention time of valproic acid is between 6 and 10 minutes.

Selection of column: Mix 1 mL of the sample solution and 4 mL of a solution of *n*-valerianic acid in a mixture of formic acid and chloroform (1:1) (1 in 1000). Proceed with 2  $\mu$ L of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of *n*-valerianic acid and valproic acid in this order with the resolution between these peaks being not less than 3.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of valproic acid obtained from 2  $\mu$ L of the standard solution is between 4 mm and 10 mm.

Time span of measurement: About twice as long as the retention time of valproic acid after the solvent peak.

**Loss on drying** Not more than 1.0% (1 g, 105°C, 3 hours).

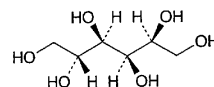
**Assay** Weigh accurately about 0.2 g of Sodium Valproate, previously dried, dissolve in 80 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS (potentiometric titration). Perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS  
= 16.620 mg of C<sub>8</sub>H<sub>15</sub>NaO<sub>2</sub>

**Containers and storage** Containers—Tight containers.

## D-Sorbitol

D-ソルビトール



C<sub>6</sub>H<sub>14</sub>O<sub>6</sub>: 182.17  
D-Glucitol [50-70-4]

D-Sorbitol, when dried, contains not less than 97.0% of C<sub>6</sub>H<sub>14</sub>O<sub>6</sub>.