minutes should be not less than 80%.

Dissolution rate (%) with respect to the labeled amount of propylthiouracil ($C_7H_{10}N_2OS$)

$$= W_S \times \frac{A_T}{A_S} \times \frac{1}{C} \times 90$$

W_S: Amount (mg) of propylthiouracil for assay.
C: Labeled amount (mg) of propylthiouracil ($C_7H_{10}N_2OS$) in 1 tablet.

Assay Weigh accurately and powder not less than 20 Propylthiouracil Tablets. Weigh accurately a portion of the powder, equivalent to about 0.3 g of propylthiouracil ($C_7H_{10}N_2OS$), transfer to a Soxhlet extractor, and extract with 100 mL of acetone for 4 hours. Evaporate the acetone extract by warming on a water bath to dryness. To the residue add 30 mL of water, and proceed as directed in the Assay under Propylthiouracil.

Each mL of 0.1 mol/L sodium hydroxide VS
= 8.512 mg of $C_7H_{10}N_2OS$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Protamine Sulfate

硫酸プロタミン

Protamine Sulfate is the sulfate of protamine prepared from the mature spermary of fish belonging to the family *Salmonidae* and others.

Description Protamine Sulfate occurs as a white to light grayish yellow powder.

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

The pH of a solution of Protamine Sulfate (1 in 100) is between 4.0 and 7.0.

Identification (1) Dissolve 1 mg of Protamine Sulfate in 2 mL of water, add 5 drops of a solution prepared by dissolving 0.1 g of 1-naphthol in 100 mL of diluted ethanol (99.5) (7 in 10) and 5 drops of sodium hypochlorite TS, then add sodium hydroxide TS until the solution becomes alkaline: a vivid red color develops.

(2) Dissolve 5 mg of Protamine Sulfate in 1 mL of water by warming, add 1 drop of a solution of sodium hydroxide (1 in 10) and 2 drops of copper (II) sulfate TS: a red-purple color develops.

(3) An aqueous solution of Protamine Sulfate (1 in 20) responds to the Qualitative Tests for sulfate.

Purity (1) Clarity and color of solution—Dissolve 0.10 g of Protamine Sulfate in 10 mL of water: the solution is clear and colorless.

(2) Nitrogen—Weigh accurately about 0.01 g of Protamine Sulfate, previously dried at 105°C to constant mass, and perform the test as directed under the Nitrogen Determination: not more than 0.255 mg of nitrogen (N: 14.01) is found for each mg of Protamine Sulfate.

Potency as antiheparin (i) Sample solution—Dissolve 20.0 mg of Protamine Sulfate in isotonic sodium chloride solution to make exactly 20 mL.

(ii) Heparin sodium standard solution—Dissolve 10.0 mg of Heparin Sodium Reference Standard in isotonic sodium chloride solution to make a standard solution containing exactly 0.7 mg per ml.

(iii) Sulfated whole blood—Place 250 mL of fresh bovine blood in a wide-mouthed stoppered polyethylene bottle containing 50 mL of a solution of sodium sulfate decahydrate (9 in 50), and store between 1°C and 4°C. Remove any clotted substance before use.

(iv) Thrombokinase extract—To 1.5 g of acetone-dried cattle brain add 60 mL of water, extract at 50°C for 10 to 15 minutes, and centrifuge for 2 minutes at 1500 revolutions per minute. To the supernatant add cresol to make 0.3% as a preservative, and store between 1°C and 4°C. The potency of this solution will be maintained for several days.

(v) Procedure—To one of 10 clean, glass-stoppered test tubes, 13 mm in inside diameter and 150 mm in length, transfer 1.30 mL of isotonic sodium chloride solution and 0.20 mL of thrombokinase extract, then add exactly 1 mL of sulfated whole blood, stopper the tube, mix the contents by inverting once, and note the time on a stop watch. When the solid clot which is formed at the bottom of the tube does not fall on inverting the tube, designate this time as the control clotting time. Adjust appropriately the volume of thrombokinase extract so that the control clotting time is between 2 and 3 minutes. To the nine remaining tubes add 0.50 mL of the sample solution and the same volume of thrombokinase extract as was used in the previous measurement of the control clotting time, pipet into the tubes 0.43 mL, 0.45 mL, 0.47 mL, 0.49 mL, 0.50 mL, 0.51 mL, 0.53 mL, 0.55 mL and 0.57 mL of the heparin sodium standard solution, respectively, and make the volume in each tube up to 1.50 mL by adding isotonic sodium chloride solution. Add finally 1.0 mL of sulfated whole blood, stopper, mix the contents by inverting once, and determine the clotting times with a stop watch. The estimated ratio, v/V, is between 0.85 and 1.15, where v is the volume of the heparin sodium standard solution and V is the volume of the sample solution in that tube in which the clotting time is most nearly the same as the control clotting time.

Containers and storage Containers—Tight containers.

Protamine Sulfate Injection

硫酸プロタミン注射液

Protamine Sulfate Injection is an aqueous solution for injection.

The amount of Protamine Sulfate should be labeled.

Method of preparation Prepare as directed under Injections, with Protamine Sulfate.

Description Protamine Sulfate Injection is a colorless liquid. It is odorless or has the odor of preservatives.

Identification (1) Dilute a volume of Protamine Sulfate Injection, equivalent to 1 mg of Protamine Sulfate according to the labeled amount, with water to make 2 mL, and

proceed as directed in the Identification (1) under Protamine Sulfate.

(2) Dilute a volume of Protamine Sulfate Injection, equivalent to 5 mg of Protamine Sulfate according to the labeled amount, with water to make 1 mL, and proceed as directed in the Identification (2) under Protamine Sulfate.

(3) Protamine Sulfate Injection responds to the Qualitative Tests for sulfate.

pH 5.0 - 7.0

Purity Nitrogen—Transfer an exactly measured volume of Protamine Sulfate Injection, equivalent to about 0.010 g of Protamine Sulfate according to the labeled amount, to a Kjeldahl flask, and evaporate on a water bath with the aid of a current of air to dryness. Perform the test as directed under the Nitrogen Determination: 0.225 to 0.255 mg of nitrogen (N: 14.01) is found for each mg of the labeled amount of Protamine Sulfate.

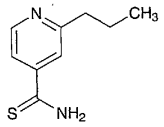
Potency as antiheparin Proceed as directed in the Potency as antiheparin under Protamine Sulfate, but use the following sample solution.

Sample solution: Dilute an exactly measured volume of Protamine Sulfate Injection, equivalent to 20.0 mg of Protamine Sulfate according to the labeled amount, with isotonic sodium chloride solution to make exactly 20 mL.

Containers and storage Containers—Hermetic containers.

Prothionamide

プロチオナミド



$C_9H_{12}N_2S$: 180.27
2-Propylpyridine-4-carbothioamide [*14222-60-7*]

Prothionamide, when dried, contains not less than 98.0% of $C_9H_{12}N_2S$.

Description Prothionamide occurs as yellow crystals or crystalline powder. It has a slight, characteristic odor.

It is freely soluble in methanol and in acetic acid (100), soluble in ethanol (95), slightly soluble in diethyl ether, and practically insoluble in water.

It dissolves in dilute hydrochloric acid and in dilute sulfuric acid.

Identification **(1)** Mix 0.05 g of Prothionamide with 0.1 g of 1-chloro-2,4-dinitrobenzene, transfer about 0.01 g of this mixture to a test tube, and heat for several seconds over a small flame until the mixture is fused. Cool, and add 3 mL of potassium hydroxide-ethanol TS: a red to orange-red color develops.

(2) Place 0.5 g of Prothionamide in a 100-mL beaker, and dissolve in 20 mL of sodium hydroxide TS by heating while shaking occasionally: the gas evolved turns a moistened red litmus paper to blue. Boil gently, and evaporate the solution to 3 to 5 mL. After cooling, add gradually 20 mL of acetic acid (100), and heat on a water bath: the gas evolved darkens moistened lead (II) acetate paper. Evaporate the solution on a water bath to 3 to 5 mL with the aid of a current of air, cool, add 10 mL of water, and mix well. Filter the crystals by suction, recrystallize from water immediately, and dry in a desiccator (in vacuum, silica gel) for 6 hours: the crystals melt between 198°C and 203°C (with decomposition).

Melting point 142 - 145°C

Purity **(1)** Clarity and color of solution—Dissolve 0.5 g of Prothionamide in 20 mL of ethanol (95): the solution is clear, and shows a yellow color.

(2) Acid—Dissolve 3.0 g of Prothionamide in 20 mL of methanol with warming. Add 100 mL of water to the solution, cool in an ice water bath with agitation, and remove any precipitate by filtration. Allow 80 mL of the filtrate to cool to room temperature, and add 0.8 mL of cresol red TS and 0.20 mL of 0.1 mol/L sodium hydroxide VS: a red color develops.

(3) Heavy metals—Proceed with 1.0 g of Prothionamide according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 20 ppm).

(4) Arsenic—Prepare the test solution with 0.6 g of Prothionamide according to Method 3, and perform the test using Apparatus B. To the test solution add 10 mL of a solution of magnesium nitrate hexahydrate in ethanol (95) (1 in 50), then add 1.5 mL of strong hydrogen peroxide, and ignite to burn (not more than 3.3 ppm).

Loss on drying Not more than 0.5% (1 g, 80°C, 3 hours).

Residue on ignition Not more than 0.10% (1 g).

Assay Weigh accurately about 0.3 g of Prothionamide, previously dried, dissolve in 50 mL of acetic acid (100), and titrate with 0.1 mol/L perchloric acid VS until the color of the solution changes from orange-red to dark orange-brown (indicator: 2 mL of *p*-naphtholbenzein TS). Perform a blank determination.

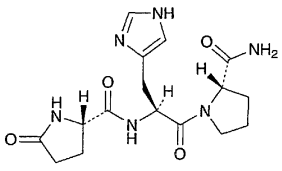
Each mL of 0.1 mol/L perchloric acid VS
= 18.027 mg of $C_9H_{12}N_2S$

Containers and storage Containers—Well-closed containers.

Storage—Light-resistant.

Protirelin

プロチレリン



$C_{16}H_{22}N_6O_4$: 362.38
5-Oxo-L-prolyl-L-histidyl-L-prolinamide [*24305-27-9*]

Protirelin contains not less than 98.5% of $C_{16}H_{22}N_6O_4$, calculated on the dehydrated basis.

Description Protirelin occurs as a white powder.

It is freely soluble in water, in methanol, in ethanol (95) and in acetic acid (100).