

(vi) Procedure: In 4 clean 13 × 150 mm glass-stoppered test tubes, place 1 mL each of  $S_H$ ,  $S_L$ ,  $T_H$  and  $T_L$  separately. To each tube add 0.20 mL of the thrombokinase extract: the amount of the thrombokinase extract should be controlled so that the longest coagulation time is 9 to 12 minutes. Then, to each tube add 1 mL of the sulfated whole blood, stopper each tube, mix by inverting the tubes gently, and observe each tube by gentle tilting at 15-second intervals. The coagulation time is the time required for the formation of a solid clot on the bottom of the tube which does not come down when inverting the tube. If a tube has been inverted before the coagulation is completed, stop the test, and try the test again. Repeat the complete test more than four times.

(vii) Method of calculation: Designate the logarithms of the coagulation time for each dose groups of  $S_H$ ,  $S_L$ ,  $T_H$  and  $T_L$  as  $y_1$ ,  $y_2$ ,  $y_3$  and  $y_4$ , respectively. Sum up  $y_1$ ,  $y_2$ ,  $y_3$  and  $y_4$  for each test and designate them as  $Y_1$ ,  $Y_2$ ,  $Y_3$  and  $Y_4$ , respectively.

$$\begin{aligned} & \text{Units per mg of Heparin Sodium} \\ &= \text{antilog } M \times (\text{units per mL of the high-dose} \\ & \quad \text{standard solution}) \\ & \quad \times \frac{b}{a} \end{aligned}$$

$$M = \frac{IY_a}{Y_b}$$

$$I = \log \frac{S_H}{S_L} = \log \frac{T_H}{T_L}$$

$$Y_a = -Y_1 - Y_2 + Y_3 + Y_4$$

$$Y_b = Y_1 - Y_2 + Y_3 - Y_4$$

$a$ : Mass (mg) of Heparin Sodium sample.

$b$ : Total volume (mL) of the high-dose sample solution prepared by dissolving Heparin Sodium in water.

Compute  $L$  ( $P = 0.95$ ) by using the following equation:  $L$  is not more than 0.15. If  $L$  exceeds 0.15, increase the number of the tests until  $L$  reaches 0.15 or less.

$$L = 2\sqrt{(C-1)(CM^2 + P)}$$

$$C = \frac{Y_b^2}{Y_b^2 - 4fs^2t^2}$$

$f$ : The number of the runs.

$$s^2 = \frac{\Sigma y^2 - \frac{Y}{f} - \frac{Y'}{4} + \frac{Y''}{4f}}{n}$$

$\Sigma y^2$ : The sum of the squares of each  $y_1$ ,  $y_2$ ,  $y_3$  and  $y_4$  in each test.

$$Y = Y_1^2 + Y_2^2 + Y_3^2 + Y_4^2$$

$Y'$ : The sum of the squares of the sum of  $y_1$ ,  $y_2$ ,  $y_3$  and  $y_4$  in each test, for the whole run.

$$Y'' = (Y_1 + Y_2 + Y_3 + Y_4)^2$$

$$n = 3(f-1)$$

$t^2$ : Value shown in the table in the Assay under Insulin Injection against  $n$  for which  $s^2$  is calculated.

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

## Heparin Sodium Injection

ヘパリンナトリウム注射液

Heparin Sodium Injection is an aqueous solution for injection. It contains not less than 90% and not more than 110% of the labeled heparin Units.

Label the name of organ used as the starting material of Heparin Sodium supplied for preparing Heparin Sodium Injection.

**Method of preparation** Dissolve Heparin Sodium in Isotonic Sodium Chloride Solution and prepare as directed under Injections.

**Description** Heparin Sodium Injection is a clear, colorless to light yellow liquid.

**pH** 5.5 – 8.0

**Purity (1) Barium**—Measure exactly a portion of Heparin Sodium Injection, equivalent to 3000 Units of Heparin Sodium according to the labeled Unit. Add water to make 3.0 mL and use this solution as the sample solution. To 1.0 mL of the sample solution add 3 drops of dilute sulfuric acid, and allow to stand for 10 minutes: no turbidity is produced.

(2) Protein—Proceed as directed in the Purity (4) under Heparin Sodium.

**Bacterial endotoxins** Less than 0.0030 EU/unit.

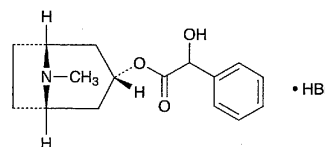
**Assay** Proceed as directed in the Assay under Heparin Sodium. However, the sample solutions indicated in (ii) are as follows.

Sample solution: Measure exactly adequate portions of Heparin Sodium Injection according to the labeled Units, dilute them with water so as to obtain two solutions containing exactly 2.00 and 1.60 Units per ml, and use them as high-dose ( $T_H$ ) and low-dose ( $T_L$ ) sample solutions, respectively.

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

## Homatropine Hydrobromide

臭化水素酸ホマトロピン



$C_{16}H_{21}NO_3 \cdot HBr$ : 356.25

(1*R*,3*r*,5*S*)-8-Methyl-8-azabicyclo[3.2.1]oct-3-yl [(*RS*)-2-hydroxy-2-phenyl]acetate monohydrobromide [51-56-9]

Homatropine Hydrobromide contains not less than 99.0% of  $C_{16}H_{21}NO_3 \cdot HBr$ , calculated on the dried basis.

**Description** Homatropine Hydrobromide occurs as white