ed under the Ultraviolet-visible Spectrophotometry, and compare the spectrum with the Reference Spectrum: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectrum of Pethidine Hydrochloride, previously dried, as directed in the potassium bromide disk 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.

(3) A solution of Pethidine Hydrochloride (1 in 50) responds to the Qualitative Tests (2) for chloride.

Melting point 187 - 189°C

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

(2) Sulfate—Perform the test with 0.20 g of Pethidine Hydrochloride. Prepare the control solution with 1.0 mL of 0.005 mol/L sulfuric acid VS (not more than 0.240%).

(3) Related substances—Dissolve 0.05 g of Pethidine Hydrochloride in 20 mL of the mobile phase, and use this solution as the sample solution. Pipet 1 mL of the sample solution, add the mobile phase to make exactly 100 mL, and use this solution as the standard solution. Perform the test with 20 μL each of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions. Determine each peak area obtained from both solutions by the automatic integration method: the total area of the peaks other than that of pethidine from the sample solution is not larger than the peak area of perthidine from the standard solution.

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 257 nm).

Column: A stainless steel column about 4 mm in inside diameter and about 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (about 5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 2.0 g of sodium lauryl sulfate in 1000 mL of diluted phosphoric acid (1 in 1000), adjust the pH to 3.0 with sodium hydroxide TS, and to 550 mL of this solution add 450 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of pethidine is about 7 minutes.

Selection of column: To 2 mL each of the sample solution and a solution of isoamyl parahydroxybenzoate in the mobile phase (1 in 50,000) add the mobile phase to make 10 mL. Proceed with 20 μL of this solution under the above operating conditions, and calculate the resolution. Use a column giving elution of pethidine and isoamyl parahydroxybenzoate in this order with the resolution between these peaks being not less than 2.0.

Detection sensitivity: Adjust the detection sensitivity so that the peak height of pethidine from 20 μL of the standard solution is between 7 mm and 14 mm.

Time span of measurement: About 2 times as long as the retention time of pethidine after the solvent peak.

Loss on drying Not more than 0.5% (1 g, 105°C, 3 hours).

Residue on ignition Not more than 0.1% (0.5 g).

Assay Weigh accurately about 0.5 g of Pethidine Hydrochloride, previously dried, dissolve in 50 mL of a mixture of acetic anhydride and acetic acid (100) (7:3), 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
= 28.380 mg of $C_{15}H_{21}NO_2.HCl$

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

Pethidine Hydrochloride Injection

Operidine Injection

塩酸ペチジン注射液

Pethidine Hydrochloride Injection is an aqueous solution for injection. It contains not less than 95% and not more than 105% of the labeled amount of pethidine hydrochloride ($C_{15}H_{21}NO_2.HCl$: 283.79).

Method of preparation Prepare as directed under Injections, with Pethidine Hydrochloride.

Description Pethidine Hydrochloride Injection is a clear, colorless liquid.

It is affected by light.

pH 4.0 - 6.0

Identification Take a volume of Pethidine Hydrochloride Injection equivalent to 0.1 g of Pethidine Hydrochloride according to the labeled amount, and add water to make 200 mL. Determine the absorption spectrum of this solution as directed under the Ultraviolet-visible Spectrophotometry: it exhibits maxima between 250 nm and 254 nm, between 255 nm and 259 nm, and between 261 nm and 265 nm.

Assay Measure exactly a volume of Pethidine Hydrochloride Injection, equivalent to about 0.1 g of pethidine hydrochloride ($C_{15}H_{21}NO_2.HCl$) according to the labeled amount, add exactly 10 mL of the internal standard solution, and add the mobile phase to make 50 mL. To 5 mL of this solution add the mobile phase to make 20 mL, and use this solution as the sample solution. Separately, weigh accurately about 0.1 g of pethidine hydrochloride for assay, previously dried at 105°C for 3 hours, add exactly 10 mL of the internal standard solution, and add the mobile phase to make 50 mL. To 5 mL of this solution add the mobile phase to make 20 mL, and use this solution as the standard solution. Perform the test with 20 μL of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the ratios, Q_T and Q_S, of the peak area of pethidine to that of the internal standard.

Amount (mg) of pethidine hydrochloride ($C_{15}H_{21}NO_2.HCl$)
= amount (mg) of pethidine hydrochloride for assay
$\times \frac{Q_T}{Q_S}$

Internal standard solution—A solution of isoamyl para-

hydroxybenzoate in the mobile phase (1 in 12,500).

Operating conditions—

Detector: An ultraviolet absorption photometer (wavelength: 257 nm).

Column: A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 μm in particle diameter).

Column temperature: A constant temperature of about 40°C.

Mobile phase: Dissolve 2.0 g of sodium lauryl sulfate in 1000 mL of diluted phosphoric acid (1 in 1000), adjust the pH to 3.0 with sodium hydroxide TS, and to 550 mL of this solution add 450 mL of acetonitrile.

Flow rate: Adjust the flow rate so that the retention time of pethidine is about 7 minutes.

System suitability—

System performance: When the procedure is run with 20 μL of the standard solution under the above operating conditions, pethidine and the internal standard are eluted in this order with the resolution between these peaks being not less than 2.0.

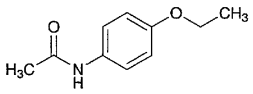
System repeatability: When the test is repeated 6 times with 20 μL of the standard solution under the above operating conditions, the relative standard deviation of the ratios of the peak area of pethidine to that of the internal standard is not more than 1.0%.

Containers and storage Containers—Hermetic containers, and colored containers may be used.

Storage—Light-resistant.

Phenacetin

フェナセチン



$C_{10}H_{13}NO_2$: 179.22

N-(4-Ethoxyphenyl)acetamide [*62-44-2*]

Phenacetin, when dried, contains not less than 98.0% of $C_{10}H_{13}NO_2$.

Description Phenacetin occurs as white crystals or crystalline powder.

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

Its saturated solution is neutral.

Identification Boil 0.1 g of Phenacetin with 1 mL of hydrochloric acid for 1 minute, dilute with 10 mL of water, cool, and filter. Add 1 drop of potassium dichromate TS to the filtrate: a red color develops gradually.

Melting point 134 - 137°C

Purity **(1)** Acetanilide—Boil 0.5 g of Phenacetin with 10 mL of water for 1 minute, cool, filter, and add bromine TS dropwise to the filtrate, agitating after each addition until the color of the solution remains permanently: no turbidity is produced.

(2) *p*-Chloroacetanilide—To 1.5 g of Phenacetin add 0.05 g of Raney nickel catalyst, 2 mL of sodium hydroxide TS, 5 mL of ethanol (95) and 10 mL of water, and boil for 10 minutes under a reflux condenser. Cool, filter, and wash the residue with a small quantity of water. Combine the washings with the filtrate, add 10 mL f dilute nitric acid and water to make 50 mL, and use this solution as the sample solution. Take 0.05 g of Raney nickel catalyst, 2 mL of sodium hydroxide TS, 5 mL of ethanol (95) and 10 mL of water, and boil for 10 minutes under a reflux condenser. Cool, filter, and wash the residue with a small quantity of water. Combine the washings with the filtrate, add 10 mL of dilute nitric acid and 1.0 mL of 0.01 mol/L hydrochloric acid VS and water to make 50 mL, and use this solution as the control solution. To each solution add 1 mL of silver nitrate TS, mix, and allow to stand for 5 minutes: the sample solution has no more turbidity than the control solution.

(3) *p*-Phenetidine—Boil 0.30 of Phenacetin with 1 mL of ethanol (95), 1 drop of iodine TS and 3 mL of water: no red color develops or, if any color develops, the solution has no more color than the following control solution.

Control solution: Weigh accurately 0.2613 g of phenacetin, add 30 mL of dilute hydrochloric acid, and boil for 1 hour under a reflux condenser. Cool, and add 25 mL of a solution of sodium hydroxide (1 in 5), transfer to a separator, and extract with three 30-mL portions of chloroform. Filter the combined chloroform extract, wash the filter paper with five 2-mL portions of chloroform, combine the washings with the filtrate, and add chloroform to make exactly 100 mL. Pipet 3 mL of the solution, and add ethanol (95) to make exactly 100 mL. Pipet 1 mL of the solution, add 1 drop of iodine TS and 3 mL of water, and boil.

(4) Readily carbonizable substances—Take 0.5 g of Phenacetin, and perform the test: the solution has no more color than Matching Fluid T.

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

Residue on ignition Not more than 0.05% (1 g).

Assay Weigh accurately about 0.3 g of Phenacetin, previously dried, add 30 mL of dilute hydrochloric acid, and boil for 1 hour under a reflux condenser. Cool, add 25 mL of a solution of sodium hydroxide (1 in 5), and transfer to a separator. Extract with three 30-mL portions of chloroform, filter each extract through the same pledget of cotton successively, and wash the cotton with five 2-mL portions of chloroform. Combine the washings with the filtrate, and titrate with 0.1 mol/L perchloric acid VS (indicator: 2 drops of crystal violet TS). To 30 mL of dilute hydrochloric acid add 25 mL of a solution of sodium hydroxide (1 in 5). Proceed with the solution as directed for the sample, add 15 mL of acetic acid (100) to a solution prepared by combining the chloroform extract with the washings, perform a blank determination, and make any necessary correction.

Each mL of 0.1 mol/L perchloric acid VS
= 17.922 mg of $C_{10}H_{13}NO_2$

Containers and storage Containers—Well-closed containers.