the filtrate add 5 g of anhydrous sodium sulfate, shake for 5 minutes, allow the mixture to stand for 2 hours, and filter through dry filter paper. Prepare before use.

Chloroform for Karl Fischer method See the Water Determination under the General Tests, Processes and Apparatus.

***p*-Chlorophenol** See 4-Chlorophenol.

4-Chlorophenol ClC_6H_4OH Colorless or pale red crystals or crystalline mass, having a characteristic odor. Very soluble in ethanol (95), in chloroform, in diethyl ether and in glycerin, and sparingly soluble in water.
Melting point: about 43°C.
Content: not less than 99.0%. Assay—Weigh accurately about 0.2 g of 4-chlorophenol, and dissolve in water to make 100 mL. Measure exactly 25 mL of this solution into an iodine flask, add exactly 20 mL of 0.05 mol/L bromine VS and then 5 mL of hydrochloric acid, stopper immediately, shake occasionally for 30 minutes, and allow to stand for 15 minutes. Add 5 mL of a solution of potassium iodide (1 in 5), stopper immediately, shake well, and titrate with 0.1 mol/L sodium thiosulfate VS (indicator: 1 mL of starch TS). Perform a blank determination.

Each mL of 0.05 mol/L bromine VS
= 3.2140 mg of C_6H_5ClO

Preserve in tight, light-resistant containers.

(2-Chlorophenyl)-diphenylmethanol for thin-layer chromatography $C_{19}H_{15}ClO$ To 5 g of clotrimazole add 300 mL of 0.2 mol/L hydrochloric acid TS, boil for 30 minutes, cool, and extract with 100 mL of diethyl ether. Wash the diethyl ether extract with two 10 mL portions of 0.2 mol/L hydrochloric acid TS, then with two 10-mL portions of water. Shake the diethyl ether extract with 5 g of anhydrous sodium sulfate, and filter. Evaporate the diethyl ether of the filtrate, dissolve the residue in 200 mL of methanol by warming, and filter. Warm the filtrate, and add gradually 100 mL of water by stirring. Cool in an ice bath, filter the separated crystals, and dry in a desiccator (phosphorus (V) oxide) for 24 hours. A white crystalline powder. Very soluble in dichloromethane, freely soluble in diethyl ether, soluble in methanol, and practically insoluble in water.
Melting point: 92 - 95°C
Purity Related substances—Dissolve 0.010 g of (2-chlorophenyl)-diphenylmethanol in dichloromethane to make exactly 20 mL, and perform the test with 10 μL of this solution as directed in the Purity (7) under Clotrimazole: any spot other than the principal spot does not appear.

Chloroplatinic acid See hydrogen hexachloroplatinate (IV) hexahydrate.

Chloroplatinic acid-potassium iodide TS See hydrogen hexaclhoroplatinate (IV)-potassium iodide TS.

Chloroplatinic acid TS See hydrogen hexachloroplatinate (IV) TS.

1-Chloro-2,4-dinitrobenzene $C_6H_3(NO_2)_2Cl$ [K 8478, Special class]

Chlorpheniramine maleate $C_{16}H_{19}ClN_2.C_4H_4O_4$ [Same as the namesake monograph]

Chlorpromazine hydrochloride for assay $C_{17}H_{19}ClN_2S.HCl$ [Same as the monograph Chlorpromazine Hydrochloride]

Chlorpropamide for assay $C_{10}H_{13}ClN_2O_3S$ [Same as the monograph Chlorpropamide. When dried, it contains not less than 99.0% of chlorpropamide ($C_{10}H_{13}ClN_2O_3S$).]

Cholesterol $C_{27}H_{45}OH$ [Same as the namesake monograph in Part II]

Choline chloride $[(CH_3)_3NCH_2CH_2OH]Cl$ White crystalline powder.
Melting point: 303 - 305°C (decomposition).
Water: less than 0.1%.

Chromic acid-sulfuric acid TS Saturate chromium (VI) trioxide in sulfuric acid.

Chromium trioxide See chromium (VI) trioxide.

Chromium trioxide TS See chromium (VI) trioxide TS.

Chromium (VI) trioxide CrO_3 [K 8434: 1980, Special class]

Chromium (VI) trioxide TS Dissolve 3 g of chromium (VI) trioxide in water to make 100 mL.

Chromotropic acid See disodium chromotropate dihydrate.

Chromotropic acid TS Dissolve 0.05 g of disodium chromotropate dihydrate in the solution prepared by cautiously adding 68 mL of sulfuric acid to 30 mL of water, cooling, then adding water to make 100 mL. Preserve in light-resistant containers.

Chromotropic acid TS, concentrated Suspend 0.5 g of disodium chromotropate dihydrate in 50 mL of sulfuric acid, centrifuge, and use the supernatant liquid. Prepare before use.

Cinchonidine $C_{19}H_{22}N_2O$ White crystals or crystalline powder. Soluble in ethanol (95), in methanol and in chloroform, sparingly soluble in diethyl ether, and practically insoluble in water. A solution of cinchonidine in ethanol (95) (1 in 100) is levorotatory.
Melting point: about 207°C
Content: not less than 98.0%. Assay—Weigh accurately about 0.3 g of cinchonidine, dissolve in 20 mL of acetic acid (100), add 80 mL of acetic anhydride, and titrate with 0.1 mol/L perchloric acid VS (indicator: 3 drops of crystal violet). Perform a blank determination in the same manner.

Each mL of 0.1 mol/L perchloric acid VS
= 14.720 mg of $C_{19}H_{22}N_2O$

Cinchonine $C_{19}H_{22}N_2O$ [K 8571: 1979, Special class]

Cineol for assay $C_{10}H_{18}O$ Clear and colorless liquid, having a characteristic aroma.
Refractive index n_D^{20}: 1.457 - 1.459
Specific gravity d_{20}^{20}: 0.920 - 0.930
Purity (1) Related substances (i)—Dissolve 0.2 g of cineol for assay in 10 mL of hexane and use this solution as the sample solution. Perform the test with the sample solution as directed under the Thin-layer Chromatography. Spot 5 μL of the sample solution on a plate of silica gel for thin-layer chromatography, develop the plate with a mixture of hexane and ethyl acetate (9:1) to a distance of about 10

cm, and air-dry. Spray evenly 4-methoxybenzaldehyde-sulfuric acid TS, and heat at 105°C for 5 minutes: any spot other than the principal spot does not appear.

(2) Related substances (ii)—Dissolve cineol for assay in 25 mL of hexane and use this solution as the sample solution. Perform the test with 2 μL of the sample solution as directed under the Gas Chromatography according to the following conditions. Measure each peak area by the automatic integration method and calculate the amount of cineol by the area percentage method: it is not less than 99.0%.

Operating conditions

Proceed the operating conditions in the Assay under Eucalyptus Oil except detection sensitivity and time span of measurement.

Detection sensitivity: Measure 1 mL of the sample solution and add hexane to make 100 mL. Adjust the detection sensitivity so that the peak height of cineol obtained from 2 μL of this solution is 40% to 60% of the full scale.

Time span of measurement: About 3 times as long as the retention time of cineol after the solvent peak.

Cinobufagin for component determination $C_{26}H_{34}O_6.nH_2O$ White crystalline odorless powder.

Absorbance $E^{1\%}_{1\,cm}$ (295 nm): 125 – 127 (0.01 g, methanol, 250 mL). Use the sample dried in a desiccator (silica gel) for 24 hours for the test.

Purity Related substances—Proceed with 0.040 g of cinobufagin for component determination as directed in the Purity under bufalin for component determination.

Content: not less than 98.0%. Content determination—Weigh accurately about 0.01 g of cinobufagin for component determination, previously dried in a desiccator (silica gel) for 24 hours, dissolve in methanol to make exactly 10 mL, and use this solution as the sample solution. Perform the test with 20 μL of the sample solution as directed under the Liquid Chromatography according to the following conditions. Measure each peak area by the automatic integration method and calculate the amount of cinobufagin by the area percentage method.

Operating conditions

Detector: Ultraviolet absorption photometer (wavelength: 295 nm).

Column: A stainless steel column 4 to 6 mm in inside diameter and 15 to 30 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5 to 10 μm in particle diameter).

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

Mobile phase: A mixture of water and acetonitrile (1:1).

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

Selection of column: Dissolve 0.01 g each of bufalin for component determination, cinobufagin for component determination and resibufogenin for component determination in methanol to make 200 mL. Proceed with 20 μL of this solution under the above operating conditions. Use a column giving elution of bufalin, cinobufagin and resibufogenin in this order, and clearly dividing each peak.

Detection sensitivity: Pipet 1 mL of the sample solution, add methanol to make exactly 100 mL, and use this solution as the standard solution (1). Pipet 1 mL of the standard solution (1), add methanol to make exactly 20 mL, and use this solution as the standard solution (2). Adjust the detection sensitivity so that the peak area of cinobufagin obtained from 20 μL of the standard solution (2) can be measured by the automatic integration method, and the peak height of cinobufagin from 20 μL of the standard solution (1) is about 20% of the full scale.

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

Citric acid See citric acid monohydrate.

Citric acid-acetic acid TS To 1 g of citric acid monohydrate add 90 mL of acetic anhydride and 10 mL of acetic acid (100), and dissolve under shaking.

Citric acid-acetic anhydride TS To 1 g of citric acid monohydrate add 50 mL of acetic anhydride, and dissolve by heating. Prepare before use.

Citric acid monohydrate $C_6H_8O_7.H_2O$ [K 8283, or same as the namesake monograph]

0.01 mol/L Citric acid TS Dissolve 2.1 g of citric acid monohydrate in water to make 1000 mL.

1 mol/L Citric acid TS for buffer solution Dissolve 210.14 g of citric acid monohydrate in water to make 1000 mL.

Clotrimazole $C_{22}H_{17}ClN_2$ [Same as the namesake monograph]

Cloxazolam $C_{17}H_{14}Cl_2N_2O_2$ [Same as the namesake monograph]

Cobalt (II) chloride-ethanol TS Dissolve 0.5 g of cobalt (II) chloride hexahydrate, previously dried at 105°C for 2 hours, in ethanol (99.5) to make 100 mL.

Cobalt (II) chloride TS Dissolve 2 g of cobalt (II) chloride hexahydrate in 1 mL of hydrochloric acid and water to make 100 mL (0.08 mol/L).

Cobalt (II) chloride hexahydrate $CoCl_2.6H_2O$ [K 8129, Special class]

Cobalt (II) nitrate hexahydrate $Co(NO_3)_2.6H_2O$ [K 8552, Special class]

Cobaltous chloride See cobalt (II) chloride hexahydrate.

Cobaltous nitrate See cobalt (II) nitrate hexahydrate.

Codeine phosphate for assay $C_{18}H_{21}NO_3.H_3PO_4.½H_2O$ [Same as the monograph Codeine Phosphate. It contains not less than 99.0% of codeine phosphate ($C_{18}H_{21}NO_3.H_3PO_4$), calculated on the anhydrous basis.]

Collodion Clear, colorless, viscous liquid, having a diethyl ether-like odor.

pH: 5.0–8.0

Stir 5 g of collodion while warming, add 10 mL of water gradually, and dry at 110°C after evaporating to dryness: mass of the residue is 0.250–0.275 g.

Concentrated chromotropic acid TS See chromotropic acid, concentrated.

Concentrated diazobenzenesulfonic acid TS See diazobenzenesulfonic acid TS, concentrated.

Congo red $C_{32}H_{22}N_6Na_2O_6S_2$ [K 8352, Special class]

Congo red paper Immerse filter paper in congo red TS, and air-dry.

Congo red TS Dissolve 0.5 g of congo red in 100 mL of a mixture of ethanol (95) and water (1:9).

Coomassie brilliant blue R-250 $C_{45}H_{44}N_3NaO_7S_2$ Deep blue-purple powder. Odorless.
Content: not less than 50%.

Copper Cu [K 8660, Special class]

Copper (II) acetate monohydrate $Cu(CH_3COO)_2.H_2O$ [K 8370, Special class]

Copper (II) acetate TS, strong Dissolve 13.3 g of copper (II) acetate monohydrate in a mixture of 195 mL of water and 5 mL of acetic acid.

Copper (II) chloride-acetone TS Dissolve 0.3 g of copper (II) chloride dihydrate in acetone to make 10 mL.

Copper (II) chloride dihydrate $CuCl_2.2H_2O$ [K 8145, Special class]

Copper (II) disodium ethylenediamine tetraacetate tetrahydrate $C_{10}H_{12}CuN_2Na_2O_8.4H_2O$ A blue powder.
pH: 7.0 - 9.0
Purity Clarity and color of solution—Add 0.10 g of copper (II) disodium ethylenediamine tetraacetate tetrahydrate to 10 mL of freshly boiled and cooled water: the solution is blue in color and clear.
Content: not less than 98.0%. Assay—Weigh accurately about 0.45 g of coppor (II) disodium ethylenediamine tetraacetate tetrahydrate, and add water to make exactly 100 mL. Pipet 10 mL of this solution, adjust the pH of the mixture to about 1.5 by adding 100 mL of water and dilute nitric acid, then add 5 mL of a solution of 1,10-phenanthroline monohydrate in methanol (1 in 20), and titrate with 0.01 mol/L bismuth nitrate VS until the color of the solution changes from yellow to red (indicator: 2 drops of xylenol orange TS).

Each mL of 0.01 mol/L bismuth nitrate VS
= 4.698 mg of $C_{10}H_{12}CuN_2Na_2O_8.4H_2O$

Copper (II) hydroxide $Cu(OH)_2$ Light blue powder. Practically insoluble in water.
Content: not less than 95.0% as $Cu(OH)_2$. Assay—Weigh accurately about 0.6 g of Copper (II) hydroxide, dissolve in 3 mL of hydrochloric acid and water to make exactly 500 mL. Pipet 25 mL of this solution, add 75 mL of water, 10 mL of a solution of ammonium chloride (3 in 50), 3 mL of diluted ammonia solution (28) (1 in 10) and 0.05 g of murexide-sodium chloride indicator, and titrate with 0.01 mol/L disodium dihydrogen ethylenediamine tetraacetate VS until the color of the liquid is changed from yellow-green to red-purple.

Each mL of 0.01 mol/L disodium dihydrogen
ethylenediamine tetraacetate VS
= 0.9756 mg of $Cu(OH)_2$

Copper (II) sulfate (anhydrous) $CuSO_4$ [K 8984, First class]

Copper (II) sulfate pentahydrate $CuSO_4.5H_2O$ [K 8983, Special class]

Copper (II) sulfate-pyridine TS Dissolve 4 g of copper (II) sulfate pentahydrate in 90 mL of water, then add 30 mL of pyridine. Prepare before use.

Copper (II) sulfate solution, alkaline Dissolve 150 g of potassium bicarbonate, 101.4 g of potassium carbonate and 6.93 g of copper (II) sulfate pentahydrate in water to make 1000 mL.

Copper (II) sulfate TS Dissolve 12.5 g of copper (II) sulfate pentahydrate in water to make 100 mL (0.5 mol/L).

Copper (standard reagent) Cu [K 8005, Standard reagent for quantitative analysis]

Corn oil [Same as the namesake monograph in Part II]

Cortisone acetate $C_{23}H_{30}O_6$ [Same as the namesake monograph]

Cottonseed oil A refined, nonvolatile fatty oil obtained from the seed of plants of *Gossypium hirsutum* Linné (*Gossypium*) or of other similar species. A pale yellow, odorless, oily liquid. Miscible with diethyl ether, and with hexane. Slightly soluble in ethanol (95).
Refractive index n_D^{20}: 1.472 - 1.474
Specific gravity d_{25}^{25}: 0.915 - 0.921
Acid value: not more than 0.5.
Saponification value: 190 - 198
Iodine value: 103 - 116

Cresol $CH_3C_6H_4(OH)$ [Same as the namesake monograph in Part II]

***m*-Cresol** $CH_3C_6H_4(OH)$ [K 8305, Special class]

Cresol red $C_{21}H_{18}O_5S$ [K 8308, Special class]

Cresol red TS Dissolve 0.1 g of cresol red in 100 mL of ethanol (95), and filter if necessary.

Crystalline trypsin for ulinastatin assay A proteolytic enzyme prepared from bovine pancreas. White to light yellow crystalline powder. Odorless. Sparingly soluble in water, and dissolves in 0.001 mol/L hydrochloric acid TS.
Content: not less than 3200 trypsin Units per mg. Assay—(i) Sample solution: Weigh accurately about 0.02 g of crystalline trypsin for ulinastatin assay, and dissolve in 0.001 mol/L hydrochloric acid TS so that each mL of the solution contains about 3000 trypsin Units. Dilute this solution with 0.001 mol/L hydrochloric acid TS so that each mL of the solution contains about 40 trypsin Units, and use this solution as the sample solution. (ii) Diluent: Dissolve 4.54 g of potassium dihydrogen phosphate in water to make exactly 500 mL (Solution I). Dissolve 4.73 g of anhydrous disodium hydrogen phosphate in water to make exactly 500 mL (Solution II). To 80 mL of Solution II add a suitable amount of Solution I to adjust to pH 7.6. (iii) Substrate solution: Dissolve 0.0857 g of *N*-α-benzoyl-L-arginine ethyl ester hydrochloride in water to make exactly 100 mL, and use this solution as the substrate stock solution. Pipet 10 mL of the stock solution, add the diluent to make exactly 100 mL, and use this solution as the substrate solution. The absorbance of the substrate solution determined at 253 nm as directed under the Ultraviolet-visible Spectrophotometry using water as the blank is between 0.575 and 0.585. If the absorbance of the substrate solution is not in this range, adjust with the diluent or the substrate stock solution. (iv) Procedure: Pipet 3 mL of the substrate solution, previously warmed at 25 ± 0.1°C, into a 1-cm quartz cell, add exactly 0.2 mL of the sample solution, and start the determination of the absor-

bance change at 253 nm for 5 minutes at 25 ± 0.1°C using a solution prepared by adding exactly 0.2 mL of 0.001 mol/L hydrochloric acid TS to exactly 3 mL of the substrate solution as the blank. Determine the difference of the absorbance change per minute, A, when the difference has been constant for at least 3 minutes. (v) Calculation: Trypsin Units per mg is obtained by use of the following equation. One trypsin Unit is an amount of the enzyme which gives 0.003 change in absorbance per minute under the conditions described above.

$$\text{Trypsin Units per mg} = \frac{A}{0.003 \times W}$$

W: Amount (mg) of the substance to be assayed in 0.2 mL of the sample solution

Storage—Preserve in a cold place.

Crystallized trypsin To trypsin obtained from bovine pancreas gland add an appropriate amount of trichloroacetic acid to precipitate the trypsin, and recrystallize in ethanol (95). White to yellowish white crystals or powder. It is odorless. Freely soluble in water and in sodium tetraborate-calcium chloride buffer solution, pH 8.0.

Content: not less than 45 FIP Units of trypsin per mg. Assay—(i) Sample solution: Weigh accurately an appropriate amount of crystallized trypsin according to the labeled Units, dissolve in 0.001 mol/L hydrochloric acid TS to prepare a solution containing 50 FIP Units per mL, and use this solution as the sample solution. Prepare before use, and preserve in ice. (ii) Apparatus: Use a glass bottle as a reaction reservoir 20 mm in inside diameter and 50 mm in height, equipped with a rubber stopper for attachment to a glass/silver-silver chloride electrode for pH determination, nitrogen-induction tube and an exhaust port. Fix the reaction reservoir in a thermostat, and keep the temperature at 25 ± 0.1°C by means of a precise thermoregulator. (iii) Procedure: Pipet 1.0 mL of *N*-α-benzoyl-L-arginine ethyl ester TS, transfer to the reaction reservoir, and add 9.0 mL of sodium tetraborate-calcium chloride buffer solution, pH 8.0. Allow to stand in the thermostat for 10 minutes to make the temperature of the contents reach to 25 ± 0.1°C, adjust the pH of the solution to 8.00 by adding dropwise 0.1 mol/L sodium hydroxide VS while stirring and passing a current of nitrogen, add exactly 0.05 mL of the sample solution previously allowed to stand at 25 ± 0.1°C, then immediately add dropwise 0.1 mol/L sodium hydroxide VS by a 50 μL-micropipet (minimum graduation of 1 μL) while stirring to keep the reaction solution at pH 8.00, and read the amount of 0.1 mol/L sodium hydroxide VS consumed and the reaction time when the pH reached 8.00. Continue this procedure up to 8 minutes. Separately, transfer 10 mL of sodium tetraborate-calcium chloride buffer solution, pH 8.0, and perform a blank determination in the same manner. (iv) Calculation: Plot the amount of consumption (μL) of 0.1 mol/L sodium hydroxide VS against the reaction time (minutes), select linear reaction times, t_1 and t_2, designate the corresponding consumption amount of 0.1 mol/L sodium hydroxide VS as v_1 and v_2, respectively, and designate μmol of sodium hydroxide consumed per minute as M (FIP Unit).

$$M\ (\mu\text{mol NaOH/min}) = \frac{v_2 - v_1}{t_2 - t_1} \times \frac{1}{10} \times f$$

f: Factor of 0.1 mol/L sodium hydroxide VS

FIP Units per mg of crystallized trypsin to be tested

$$= \frac{(M_1 - M_0) \times T}{L \times W}$$

M_1: μmol of sodium hydroxide consumed in 1 minute when the sample solution is used

M_0: μmol of sodium hydroxide consumed in 1 minute when the solution for blank determination is used

W: Amount (mg) of crystallized trypsin sampled

L: Amount (mL) of the sample solution put in the reaction reservoir

T: Total volume (mL) of the sample solution prepared by dissolving in 0.001 mol/L hydrochloric acid TS

One FIP Unit is an amount of enzyme which decomposes 1 μmol of *N*-α-benzoyl-L-arginine ethyl ester per minute under the conditions described in the Assay.

Storage—Preserve in a cold place.

Crystal violet $C_{25}H_{30}CN_3.9H_2O$ [K 8294, Special class]

Crystal violet TS Dissolve 0.1 g of crystal violet 10 mL of acetic acid (100).

Cu-PAN Prepare by mixing 1 g of 1-(2-pyridylazo)-2-naphthol (free acid) with 11.1 g of coppor (II) disodium ethylenediamine tetraacetate tetrahydrate.

A grayish orange-yellow, grayish red-brown or light grayish purple powder.

Absorbance—Dissolve 0.50 g of Cu-PAN in diluted 1,4-dioxane (1 in 2) to make exactly 50 mL. Pipet 1 mL of this solution, add methanol to make exactly 100 mL. Read the absorbance of this solution at 470 nm as directed under the Ultraviolet-visible Spectrophotometry, using water as the blank solution: the absorbance is not less than 0.48.

Purity Clarity and color of solution—Dissolve 0.50 g of Cu-PAN in 50 mL of diluted 1,4-dioxane (1 in 2): the solution is clear and yellow-brown.

Cu-PAN TS Dissolve 1 g of Cu-PAN in 100 mL of diluted 1,4-dioxane (1 in 2).

Cupferron $C_6H_9N_3O_2$ [K 8289, Special class]

Cupferron TS Dissolve 6 g of cupferron in water to make 100 mL. Prepare before use.

Cupric acetate See copper (II) acetate monohydrate.

Cupric acetate TS, strong See copper (II) acetate monohydrate TS, strong.

Cupric carbonate See cupric carbonate monohydrate.

Cupric carbonate monohydrate $CuCO_3.Cu(OH)_2.H_2O$ A blue to blue-green powder. It is insoluble in water, and dissolves foamingly in dilute acid. It dissolves in ammonia TS and shows a deep blue color.

Purity (1) Chloride: not more than 0.036%.

(2) Sulfate: not more than 0.120%.

(3) Iron—Dissolve 5.0 g of cupric carbonate monohydrate in excess ammonia TS and filter. Wash the residue with ammonia TS, dissolve in dilute hydrochloric acid, add excess ammonia TS and filter. Wash the residue with ammonia TS, and dry to constant mass: the residue is not more than 10 mg.

Cupric chloride See copper (II) chloride dihydrate.

Cupric chloride-acetone TS See copper (II) chloride-acetone TS.