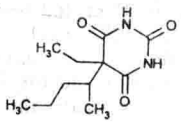
USP-NF

Pentobarbital



$C_{11}H_{18}N_2O_3$ 226.28

2,4,6(1*H*,3*H*,5*H*)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)-, (±)-.

(±)-5-Ethyl-5-(1-methylbutyl)barbituric acid [*76-74-4*].

» Pentobarbital contains not less than 98.5 percent and not more than 101.0 percent of $C_{11}H_{18}N_2O_3$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Pentobarbital RS.*

Identification—

A: *Infrared Absorption* ⟨197S⟩—

Solution: 7 in 100.

Medium: chloroform.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 1 in 62,500.

Medium: 0.1 *N* sodium hydroxide. Absorptivities at 240 nm, calculated on the dried basis, do not differ by more than 3.0%.

C: Shake about 300 mg with 5 mL of sodium hydroxide solution (1 in 125) for 2 minutes, filter, and to 1 mL of the filtrate add about 1.2 mL of silver nitrate TS: a white precipitate is formed, and it is soluble in 6 *N* ammonium hydroxide. To a second 1-mL portion of the filtrate add 3 drops of mercuric chloride TS: a white precipitate is formed, and it is soluble in 6 *N* ammonium hydroxide.

Melting range, *Class I* ⟨741⟩: between 127° and 133°.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Organic volatile impurities, *Method V* ⟨467⟩: meets the requirements.

Solvent—Use dimethyl sulfoxide as the solvent.

Isomer content—Transfer 300 ± 5 mg to a round-bottom flask equipped with a standard-taper, ground-glass joint, and add 4 mL of water. Add, dropwise, sodium hydroxide solution (4 in 10) just to dissolve the specimen (about 3 or 4 drops), then add 10 mL of alcohol. Add 300 ± 5 mg of *p*-nitrobenzyl bromide, mix, attach a condenser, and reflux for 30 minutes. Cool, filter under reduced pressure, and wash the residue with four 5-mL portions of water. Transfer the residue, as completely as possible, to a small flask, add 25 mL of alcohol, and reflux for 10 minutes: the solid dissolves completely. Cool, and filter under reduced pressure: the *p*-nitrobenzyl derivative so obtained, after being dried at 105° for 30 minutes, melts completely between 136° and 146°, when determined by the procedure for *Class Ia* (see *Melting Range or Temperature* ⟨741⟩).

Assay—

0.1 N Tetrabutylammonium hydroxide in chlorobenzene—Dilute 100 mL of 1 *N* tetrabutylammonium hydroxide VS with chlorobenzene to 1000 mL, and mix.

Standardization of 0.1 N tetrabutylammonium hydroxide in chlorobenzene—Dissolve about 180 mg, accurately weighed, of primary standard benzoic acid in about 100 mL of acetone, and titrate with *0.1 N Tetrabutylammonium hydroxide in chlorobenzene*, determining the endpoint potentiometrically, using a glass electrode and a calomel electrode containing 0.1 *N* methanolic tetrabutylammonium chloride (see *Titrimetry* ⟨541⟩). Each mL of *0.1 N Tetrabutylammonium hydroxide in chlorobenzene* is equivalent to 12.21 mg of benzoic acid.

Procedure—Transfer about 330 mg of Pentobarbital, accurately weighed, to a suitable beaker, and dissolve in 100 mL of acetone. Titrate with *0.1 N Tetrabutylammonium hydroxide in chlorobenzene*, determining the endpoint potentiometrically, using a glass electrode and a calomel electrode containing 0.1 *N* methanolic tetrabutylammonium chloride. Each mL of *0.1 N Tetrabutylammonium hydroxide in chlorobenzene* is equivalent to 22.63 mg of $C_{11}H_{18}N_2O_3$.

Pentobarbital Elixir

» Pentobarbital Elixir contains not less than 92.5 percent and not more than 107.5 percent of the labeled amount of $C_{11}H_{18}N_2O_3$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Pentobarbital RS.*

Identification—Dilute a volume of Elixir with alcohol to a concentration of about 1 mg of pentobarbital per mL. Apply 50 µL of this solution and 50 µL of a Standard solution of USP Pentobarbital RS in alcohol containing 1 mg per mL as streaks about 1 cm in length along the spotting line to a suitable thin layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the streaks to dry, and develop the chromatogram in a solvent system consisting of a mixture of isopropyl alcohol, ammonium hydroxide, chloroform, and acetone (9:4:2:2) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots by viewing the plate under short-wavelength ultraviolet light: the R_f value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

Alcohol content, *Method I* ⟨611⟩: between 16.0% and 20.0% of C_2H_5OH.

Assay—

Internal standard—*n*-Tricosane.

Internal standard solution—Dissolve an accurately weighed quantity of *n*-tricosane in chloroform, and dilute quantitatively with chloroform to obtain a solution having a known concentration of about 0.6 mg per mL.

Standard preparation—Dissolve accurately weighed quantities of USP Pentobarbital RS and *n*-tricosane in chloroform, and dilute quantitatively with chloroform to obtain a solution that contains, in each mL, known amounts of about 1 mg of USP Pentobarbital RS and about 0.4 mg of *n*-tricosane.

Assay preparation—Transfer an accurately measured volume of Elixir, equivalent to about 20 mg of pentobarbital, to a separator, add 1 mL of dilute hydrochloric acid (1 in 5), and extract with four 10-mL portions of chloroform. Filter the extracts through about 15 g of anhydrous sodium sulfate that is supported on a funnel by a small pledget of glass wool. Collect the combined filtrate in a 50-mL volumetric flask, wash the sodium sulfate with 5 mL of chloroform, dilute with chloroform to volume, and mix. Combine 4.0 mL of this solution with 1.0 mL of *Internal standard solution* in a suitable container, and reduce the volume to about 1.5 mL by evaporation, with the aid of a stream of dry nitrogen, at room temperature.

Chromatographic system and *System suitability*—Proceed as directed for *Chromatographic System* and *System Suitability* under *Barbiturate Assay* ⟨361⟩, the resolution, *R*, between pentobarbital and *n*-tricosane being not less than 2.3. [NOTE—Relative retention times are, approximately, 0.5 for *n*-tricosane and 1.0 for pentobarbital.]

Procedure—Proceed as directed for *Procedure* under *Barbiturate Assay* ⟨361⟩. Calculate the quantity, in mg, of $C_{11}H_{18}N_2O_3$ in each mL of the Elixir taken by the formula:

$$12.5(R_U)(Q_S)(C_I)/V(R_S),$$

in which V is the volume, in mL, of Elixir taken and the other terms are as defined therein.

Pentobarbital Sodium

$C_{11}H_{17}N_2NaO_3$ 248.26
2,4,6(1*H*,3*H*,5*H*)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)-, monosodium salt.
Sodium 5-ethyl-5-(1-methylbutyl)barbiturate [*57-33-0*].

» Pentobarbital Sodium contains not less than 98.5 percent and not more than 101.0 percent of $C_{11}H_{17}N_2NaO_3$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Pentobarbital RS.*

Completeness of solution—Mix 1.0 g with 10 mL of carbon dioxide–free water: after 1 minute, the solution is clear and free from undissolved solid.

Identification—

A: Recrystallize from hot alcohol the residue obtained in the *Assay*, and dry the recrystallized residue at 105° for 30 minutes: the infrared absorption spectrum of a potassium bromide dispersion of the residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Pentobarbital RS.

B: Ignite about 200 mg: the residue effervesces with acids, and responds to the tests for *Sodium* ⟨191⟩.

pH ⟨791⟩: between 9.8 and 11.0, in the solution prepared in the test for *Completeness of solution.*

Loss on drying ⟨731⟩—Dry it at 105° for 6 hours: it loses not more than 3.5% of its weight.

Heavy metals, *Method II* ⟨231⟩: 0.003%.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Isomer content—Dissolve 300 ± 5 mg in 5.0 mL of water, and dissolve 300 ± 5 mg of *p*-nitrobenzyl bromide in 10.0 mL of alcohol. Mix the two solutions, reflux for 30 minutes, cool to 25°, and filter by suction. Wash the collected solid with four 5-mL portions of water, transfer as completely as practicable to a small flask, add 25.0 mL of alcohol, and reflux for 10 minutes: the solid dissolves completely. Cool the solution to 25°, and filter by suction: the collected solid, after being dried at 105° for 30 minutes, melts completely between 136° and 146°, when determined by the procedure for *Class Ia* (see *Melting Range or Temperature* ⟨741⟩).

Assay—Dissolve about 500 mg of Pentobarbital Sodium, accurately weighed, in 15 mL of water in a separator. To the solution add 2 mL of hydrochloric acid, shake, and completely extract the liberated pentobarbital with 25-mL portions of chloroform. Test for completeness of extraction by extracting with an additional 10-mL portion of chloroform and evaporating the solvent: not more than 0.5 mg of residue remains. Filter each extract through a pledget of chloroform-washed cotton, or other suitable filter, into a tared beaker, and finally wash the separator and the filter with several small portions of chloroform. Evaporate the combined filtrate and washings on a steam bath with the aid of a current of air, add 10 mL of ether, again evaporate, dry the residue at 105° for 2 hours, cool, and weigh. The weight of the residue, multiplied by 1.097, represents the weight of $C_{11}H_{17}N_2NaO_3$.

Pentobarbital Sodium Capsules

» Pentobarbital Sodium Capsules contain not less than 92.5 percent and not more than 107.5 percent of the labeled amount of $C_{11}H_{17}N_2NaO_3$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Pentobarbital RS.*

Identification—Mix a quantity of the contents of Capsules, equivalent to about 100 mg of pentobarbital sodium, with 15 mL of water in a separator. Filter, if necessary, and saturate the solution with sodium chloride. To the solution add 2 mL of hydrochloric acid, shake, and extract the liberated pentobarbital with five 25-mL portions of chloroform. Filter each extract through a pledget of chloroform-washed cotton, or other suitable filter, into a beaker, and finally wash the separator and the filter with several small portions of chloroform. Evaporate the combined filtrate and washings on a steam bath with the aid of a current of air, add 10 mL of ether, again evaporate, recrystallize the residue from hot alcohol, and dry the recrystallized residue at 105° for 30 minutes: the residue so obtained responds to *Identification* test *A* under *Pentobarbital Sodium.*

Dissolution ⟨711⟩—

Medium: water; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

Standard preparation—Dissolve an accurately weighed quantity of USP Pentobarbital RS in freshly prepared dilute ammonium hydroxide (1 in 20) to obtain a solution having a known concentration of about 10 μg of pentobarbital per mL. The concentration of pentobarbital, multiplied by 1.097, represents the equivalent amount of pentobarbital sodium.

Procedure—Determine the amount of $C_{11}H_{17}N_2NaO_3$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 240 nm of filtered portions of the solution under test, suitably diluted with freshly prepared dilute ammonium hydroxide (1 in 20), in comparison with the *Standard preparation.*

Tolerances—Not less than 75% (*Q*) of the labeled amount of $C_{11}H_{17}N_2NaO_3$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Procedure for content uniformity—Transfer the contents of 1 Capsule to a 250-mL volumetric flask, with the aid of about 5 mL of alcohol. Add 10 mL of freshly prepared dilute ammonium hydroxide (1 in 200), and without delay dilute with the same solution to volume. Mix, filter if necessary, and discard the first 20 mL of the filtrate. Dilute a portion of the clear solution with dilute ammonium hydroxide (1 in 200) to obtain a solution having a concentration of about 10 μg of pentobarbital sodium per mL. Dissolve a suitable quantity of USP Pentobarbital RS in dilute ammonium hydroxide (1 in 200) to obtain a Standard solution having a known concentration of about 10 μg per mL. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 240 nm, with a suitable spectrophotometer, using dilute ammonium hydroxide (1 in 200) as the blank. Calculate the quantity, in mg, of $C_{11}H_{17}N_2NaO_3$ in the Capsule taken by the formula:

$$1.097(T/C_U)C_S(A_U/A_S),$$

in which T is the labeled quantity, in mg, of pentobarbital sodium in the Capsule, C_U is the concentration, in μg per mL, of pentobarbital sodium in the solution from the Capsule contents, on the basis of the labeled quantity per Capsule and the extent of dilution, C_S is the concentration, in μg per mL, of USP Pentobarbital RS in the Standard solution, and A_U and A_S are the absorbances of the solution from the Capsule contents and the Standard solution, respectively.

Assay—

Internal standard—*n*-Tricosane.

Internal standard solution—Dissolve an accurately weighed quantity of *n*-tricosane in chloroform, and dilute quantitatively with chloroform to obtain a solution having a known concentration of about 0.4 mg per mL.

Standard preparation—Dissolve accurately weighed quantities of USP Pentobarbital RS and *n*-tricosane in chloroform, and dilute quantitatively with chloroform to obtain a solution that contains, in each mL, known amounts of about 0.9 mg of USP Pentobarbital RS and about 0.4 mg of *n*-tricosane.

Assay preparation—Weigh not less than 20 Capsules, and transfer the contents as completely as possible to a suitable container. Remove any residual powder from the empty capsules with the aid of a current of air, and weigh the capsule shells, determining the weight of the contents by difference. Mix the contents of the Capsules, transfer an accurately weighed portion of the powder, equivalent to about 50 mg of pentobarbital sodium, to a separator. Add 15 mL of water and 1 mL of hydrochloric

acid, and extract with five 25-mL portions of chloroform. Filter the extracts through about 15 g of anhydrous sodium sulfate that is supported on a funnel by a small pledget of glass wool. Collect the combined filtrate in a 100-mL volumetric flask, wash the sodium sulfate with 15 mL of chloroform, collecting the washing with the filtrate, dilute with chloroform to volume, and mix. Combine 2.0 mL of this solution with 1.0 mL of *Internal standard solution* in a suitable container, and reduce the volume to about 1 mL by evaporation, with the aid of a stream of dry nitrogen, at room temperature.

Chromatographic system and *System suitability*—Proceed as directed for *Chromatographic System* and *System Suitability* under *Barbiturate Assay* ⟨361⟩, the resolution, R, between pentobarbital and *n*-tricosane being not less than 2.3. [NOTE—Relative retention times are, approximately, 0.5 for *n*-tricosane barbital and 1.0 for pentobarbital.]

Procedure—Proceed as directed for *Procedure* under *Barbiturate Assay* ⟨361⟩. Calculate the quantity, in mg, of $C_{11}H_{17}N_2NaO_3$ in the portion of Capsules taken by the formula:

$$(248.26/226.28)(50)(R_U)(Q_S)(C_i/(R_S),$$

in which 248.26 and 226.28 are the molecular weights of pentobarbital sodium and pentobarbital, respectively.

Pentobarbital Sodium Injection

» Pentobarbital Sodium Injection is a sterile solution of Pentobarbital Sodium in a suitable solvent. Pentobarbital may be substituted for the equivalent amount of Pentobarbital Sodium, for adjustment of the pH. The Injection contains the equivalent of not less than 92.0 percent and not more than 108.0 percent of the labeled amount of $C_{11}H_{17}N_2NaO_3$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass. The Injection may be packaged in 50-mL containers.

Labeling—The label indicates that the Injection is not to be used if it contains a precipitate.

USP Reference standards ⟨11⟩—*USP Pentobarbital RS. USP Endotoxin RS.*

Identification—The residue obtained in the *Assay* responds to *Identification* test *A* under *Pentobarbital Sodium*.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.8 USP Endotoxin Unit per mg of pentobarbital sodium.

pH ⟨791⟩: between 9.0 and 10.5.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—Pipet a volume of Injection, equivalent to about 500 mg of pentobarbital sodium, into a separator, and dilute with water to about 15 mL. Proceed as directed in the *Assay* under *Pentobarbital Sodium*, beginning with "To the solution add 2 mL of hydrochloric acid."

Peppermint—*see* Peppermint NF

Peppermint Oil—*see* Peppermint Oil NF

Peppermint Spirit

» Peppermint Spirit contains, in each 100 mL, not less than 9.0 mL and not more than 11.0 mL of peppermint oil.

Peppermint Oil	100 mL
Peppermint, in coarse powder	10 g
Alcohol, a sufficient quantity, to make	1000 mL

Macerate the peppermint leaves, freed as much as possible from stems and coarsely powdered, for 1 hour in 500 mL of purified water, and then strongly express them. Add the moist, macerated leaves to 900 mL of alcohol, and allow the mixture to stand for 6 hours with frequent agitation. Filter, and to the filtrate add the oil and add alcohol to make the product measure 1000 mL.

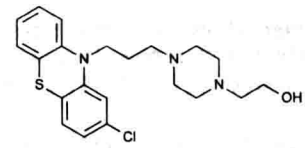
Packaging and storage—Preserve in tight containers, protected from light.

Alcohol content, *Method II* ⟨611⟩: between 79.0% and 85.0% of C_2H_5OH.

Assay—Transfer 5.0 mL of Spirit to a Babcock bottle, graduated to 8%, add 1.0 mL of kerosene, and mix. Add saturated calcium chloride solution, acidified with hydrochloric acid, almost to fill the bulb of the bottle. Rotate the bottle vigorously to ensure mixing, and then add a sufficient quantity of the calcium chloride solution to bring the separated oil into the neck of the bottle. Centrifuge at about 1500 rpm for 5 minutes, and read the volume of oil in the stem. Subtract five divisions for the kerosene added, and multiply the remaining number of divisions by 4.2 to obtain the volume, in mL, of peppermint oil in 100 mL of the Spirit.

Peppermint Water—*see* Peppermint Water NF

Perphenazine



$C_{21}H_{26}ClN_3OS$ 403.98

1-Piperazineethanol, 4-[3-(2-chloro-10*H*-phenothiazin-10-yl)propyl]-.

4-[3-(2-Chlorophenothiazin-10-yl)propyl]-1-piperazineethanol [*58-39-9*].

» Perphenazine contains not less than 98.0 percent and not more than 102.0 percent of $C_{21}H_{26}ClN_3OS$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—*USP Perphenazine RS. USP Perphenazine Sulfoxide RS.*

Clarity and color of solution—Dissolve 500 mg in 25 mL of methanol: the solution is clear and not more than light yellow.

NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

Identification—
A: *Infrared Absorption* ⟨197M⟩.
B: *Ultraviolet Absorption* ⟨197U⟩—
Solution: 1 in 100,000.
Medium: methanol. Absorptivities at 257 nm, calculated on the dried basis, do not differ by more than 2.5%.

Melting range, *Class I* ⟨741⟩: between 94° and 100°.

Loss on drying ⟨731⟩—Dry it in vacuum at 65° for 3 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Ordinary impurities ⟨466⟩—
Test solution: a mixture of acetone and methanol (3:1).
Standard solution: solutions of USP Perphenazine Sulfoxide RS in a mixture of acetone and methanol (3:1) except that the solution having a concentration of 0.01 mg per mL is replaced with a solution having a concentration of 0.02 mg per mL.
Eluant: a mixture of acetone and ammonium hydroxide (95:5).
Visualization: 1.

Organic volatile impurities, *Method V* ⟨467⟩: meets the requirements.
Solvent—Use dimethyl sulfoxide as the solvent.

Assay—Dissolve about 400 mg of Perphenazine, previously dried and accurately weighed, in 50 mL of glacial acetic acid, warming slightly to effect solution. Cool to room temperature, add 10 mL of acetic anhydride, and allow to stand for 5 minutes. Add 1 drop of crystal violet TS, and titrate with 0.1 *N* perchloric acid VS to a green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 *N* perchloric acid is equivalent to 20.20 mg of $C_{21}H_{26}ClN_3OS$.

Perphenazine Injection

» Perphenazine Injection is a sterile solution of Perphenazine in Water for Injection, prepared with the aid of Citric Acid. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{26}ClN_3OS$, as the citrate.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light.

USP Reference standards ⟨11⟩—*USP Perphenazine RS. USP Endotoxin RS.*

NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

Identification—Dilute 1 mL with methanol to 5 mL. Apply 5 µL each of this solution and a solution of USP Perphenazine RS in methanol containing 1 mg per mL to a suitable thin-layer chromatographic plate, coated with a 0.25-mm layer of chromatographic silica gel. Develop the chromatogram in a solvent system consisting of a mixture of acetone and ammonium hydroxide (200:1) until the solvent front has moved about 15 cm. Air-dry the plate, and spray lightly with a solution of iodoplatinic acid prepared by dissolving 100 mg of chloroplatinic acid in 1 mL of 1 *N* hydrochloric acid, adding 25 mL of potassium iodide solution (4 in 100), diluting with water to 100 mL, and adding 0.50 mL of formic acid: the R_f value of the principal spot obtained from the Injection corresponds to that obtained from the Standard solution.

Bacterial endotoxins ⟨85⟩—It contains not more than 35.7 USP Endotoxin Units per mg of perphenazine.

pH ⟨791⟩: between 4.2 and 5.6.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—
Acid-alcohol solution—Transfer 10 mL of hydrochloric acid to a 1000-mL flask containing 500 mL of alcohol and 300 mL of water. Dilute with water to volume.
Palladium chloride solution—Dissolve 100 mg of palladium chloride in a mixture of 1 mL of hydrochloric acid and 50 mL of water in a 100-mL volumetric flask, heating on a steam bath to effect solution. Cool, dilute with water to volume, and mix. Store in an amber bottle and use within 30 days. On the day of use, transfer 50 mL to a 500-mL volumetric flask, add 4 mL of hydrochloric acid and 4.1 g of anhydrous sodium acetate, dilute with water to volume, and mix.
Standard preparation—Dissolve an accurately weighed quantity of USP Perphenazine RS in *Acid-alcohol solution* to obtain a solution having a known concentration of about 150 µg per mL.
Assay preparation—Dilute 3.0 mL of Injection with *Acid-alcohol solution* to 100 mL in a volumetric flask.
Procedure—Mix 10.0 mL each of the *Assay preparation* and the *Standard preparation* with 15.0 mL of *Palladium chloride solution*, filter, if necessary, and concomitantly determine the absorbances of these solutions, against a reagent blank, in 1-cm cells at the wavelength of maximum absorbance at about 480 nm, with a suitable spectrophotometer. Calculate the quantity, in mg, of $C_{21}H_{26}ClN_3OS$ in the volume of Injection taken by the formula:

$$0.1C(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Perphenazine RS in the *Standard preparation*, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Perphenazine Oral Solution

» Perphenazine Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{26}ClN_3OS$.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩—*USP Perphenazine RS. USP Perphenazine Sulfoxide RS.*

NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

Identification—It responds to the *Identification* test under *Perphenazine Injection.*

Limit of perphenazine sulfoxide—
Mobile phase and *Chromatographic system*—Proceed as directed in the *Assay*.
Standard preparation—Using an accurately weighed quantity of USP Perphenazine Sulfoxide RS, prepare a solution in methanol having a known concentration of about 10 µg per mL.
Test preparation—Using a "to contain" pipet, transfer an accurately measured volume of the Oral Solution, equivalent to 20 mg of perphenazine to a 100-mL volumetric flask. Rinse the pipet with methanol, collecting the methanol in the volumetric flask. Dilute with methanol to volume, and mix.
Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Test preparation* into the chromatograph, and record the chromatograms. The *Test preparation* may exhibit a minor peak whose retention time corresponds to the peak exhibited by the *Standard preparation;* the peak response of the minor peak from the *Test preparation* is not greater than the peak response of the *Standard preparation* corresponding to not more than 5.0% of perphenazine sulfoxide.

Assay—[NOTE—Conduct this procedure with a minimum exposure to light.]
Mobile phase—Prepare a suitably degassed mixture of methanol and 0.005 *M* ammonium acetate (4:1). Prior to mixing,

adjust the 0.005 *M* ammonium acetate with glacial acetic acid if necessary to a pH of 5.25 ± 0.05. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Transfer about 40 mg of amitriptyline hydrochloride to a 100-mL volumetric flask, add methanol to volume, and mix.

Standard preparation—Transfer about 20 mg of USP Perphenazine RS, accurately weighed, to a 50-mL volumetric flask, add methanol to volume, and mix. Transfer 2.0 mL of this solution to a 100-mL volumetric flask, add 10.0 mL of *Internal standard solution*, dilute with methanol to volume, and mix to obtain a solution having a known concentration of about 8 μg of USP Perphenazine RS per mL.

Assay preparation—Using a "to contain" pipet, transfer an accurately measured volume of Oral Solution, equivalent to about 16 mg of perphenazine to a 200-mL volumetric flask. Rinse the pipet with methanol, collecting the methanol in the volumetric flask. Dilute with methanol to volume, and mix. Pipet 10 mL of this solution into a 100-mL volumetric flask, add 10.0 mL of *Internal standard solution*, dilute with methanol to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L10. The flow rate is about 3.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the tailing factor for the analyte peak is not more than 3.0, the resolution, *R*, between the analyte and internal standard peaks is not less than 3.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 1.6 for amitriptyline and 1.0 for perphenazine. Calculate the quantity, in mg, of $C_{21}H_{26}ClN_3OS$ in each mL of Oral Solution taken by the formula:

$$(2C/V)(R_U/R_S),$$

in which C is the concentration, in μg per mL, of USP Perphenazine RS in the *Standard preparation*, V is the volume, in mL, of Oral Solution taken for the *Assay preparation*, and R_U and R_S are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Perphenazine Syrup

» Perphenazine Syrup contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{26}ClN_3OS$.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩—*USP Perphenazine RS.*

NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

Identification—Add 10 mL of water to a volume of Syrup, equivalent to about 4 mg of perphenazine, render alkaline by dropwise addition of sodium hydroxide to a pH of 11 to 12, and extract with four 5-mL portions of chloroform, combining the extracts through a bed of anhydrous sodium sulfate in a funnel into a beaker. Evaporate the extracts on a steam bath nearly to dryness, and dissolve the residue in 4 mL of methanol: the solution so obtained responds to the *Identification* test under *Perphenazine Injection.*

Assay—

Acid-alcohol solution and *Palladium chloride solution*—Prepare as directed in the *Assay* under *Perphenazine Injection.*

Standard preparation—Dissolve an accurately weighed quantity of USP Perphenazine RS in *Acid-alcohol solution* to obtain a solution having a known concentration of about 160 μg per mL.

Assay preparation—Transfer an accurately measured volume of Syrup, equivalent to about 6 mg of perphenazine, to a 25-mL volumetric flask, dilute with water to volume, and mix. Transfer 10 mL to a 125-mL separator, add 25 mL of water, adjust with ammonium hydroxide to a pH of 10 to 11, and extract with four 20-mL portions of chloroform, filtering the extracts through anhydrous sodium sulfate. Evaporate the combined extracts on a steam bath with the aid of a stream of nitrogen to about 5 mL. Complete the evaporation without application of heat, and dissolve the residue in 15.0 mL of *Acid-alcohol solution*, filtering if necessary.

Procedure—Mix 10.0 mL each of the *Assay preparation* and the *Standard preparation* with 15.0 mL of *Palladium chloride solution*, filter if necessary, and concomitantly determine the absorbances of these solutions, against a reagent blank, in 1-cm cells at the wavelength of maximum absorbance at about 480 nm, with a suitable spectrophotometer. Calculate the quantity, in mg, of $C_{21}H_{26}ClN_3OS$ in each mL of the Syrup taken by the formula:

$$0.0375(C/V)(A_U/A_S),$$

in which C is the concentration, in μg per mL, of USP Perphenazine RS in the *Standard preparation*, V is the volume, in mL, of Syrup taken, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Perphenazine Tablets

» Perphenazine Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{21}H_{26}ClN_3OS$.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—*USP Perphenazine RS.*

NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

Identification—Shake a portion of finely powdered Tablets, equivalent to about 5 mg of perphenazine, with about 10 mL of chloroform, filter, evaporate the filtrate on a steam bath nearly to dryness, and dissolve the residue in 5 mL of methanol: the solution so obtained responds to the *Identification* test under *Perphenazine Injection.*

Dissolution ⟨711⟩—

Medium: 0.1 *N* hydrochloric acid; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{21}H_{26}ClN_3OS$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 257 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Perphenazine RS in the same medium.

Tolerances—Not less than 75% (Q) of the labeled amount of $C_{21}H_{26}ClN_3OS$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Acid-alcohol solution and *Palladium chloride solution*—Prepare as directed in the *Assay* under *Perphenazine Injection.*

Standard preparation—Prepare as directed in the *Assay* under *Perphenazine Syrup.*

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer a portion of the powder, equivalent to about 4 mg of perphenazine, to a glass-stoppered conical flask, pipet into the flask 25 mL of *Acid-alcohol solution*, shake by me-

chanical means for 30 minutes, and centrifuge a portion of the mixture. The clear supernatant fluid is the *Assay preparation.*

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Perphenazine Injection.* Calculate the quantity, in mg, of $C_{21}H_{26}ClN_3OS$ in the portion of Tablets taken by the formula:

$$0.025C(A_U/A_S),$$

in which C is the concentration, in μg per mL, of USP Perphenazine RS in the *Standard preparation*, and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Standard preparation*, respectively.

Perphenazine and Amitriptyline Hydrochloride Tablets

» Perphenazine and Amitriptyline Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of perphenazine ($C_{21}H_{26}ClN_3OS$) and amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—*USP Perphenazine RS. USP Amitriptyline Hydrochloride RS.*

NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.

Identification—Transfer a portion of powdered Tablets, equivalent to about 40 mg of perphenazine, to a 100-mL volumetric flask containing about 50 mL of alcohol. Agitate for 20 minutes, add alcohol to volume, mix, and filter or centrifuge. Separately prepare two Standard solutions containing 0.4 mg per mL of USP Perphenazine RS and USP Amitriptyline Hydrochloride RS, respectively, in alcohol. Separately apply 5 μL of the test solution and 5 μL of each Standard solution to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Develop the chromatogram using a solvent system consisting of a mixture of cyclohexane, ethyl acetate, and diethylamine (85:25:5) until the solvent front has moved about 15 cm. Remove the plate from the developing chamber, air-dry for 20 minutes, and examine the plate under short-wavelength ultraviolet light: the R_f values of the principal spots obtained from the test solution correspond to those obtained from the Standard solutions.

Dissolution ⟨711⟩—

Medium: 0.1 *N* hydrochloric acid; 900 mL.

Apparatus 2: 50 rpm.

Time: 60 minutes.

Procedure—[NOTE—Due to potential decrease in the recovery of perphenazine when multiple injections are made from a vial, no more than two withdrawals should be made from any single vial.] Determine the amounts of perphenazine and amitriptyline hydrochloride in solution in filtered portions of the solution under test, in comparison with a Standard solution having known concentrations of USP Perphenazine RS and USP Amitriptyline Hydrochloride RS in the same medium, as directed for *Procedure* in the *Assay.*

Tolerances—Not less than 75% (Q) of the labeled amounts of perphenazine ($C_{21}H_{26}ClN_3OS$) and amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements for *Content uniformity* with respect to perphenazine and to amitriptyline hydrochloride.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, methanol, and methanesulfonic acid (490:310:200:2). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Perphenazine RS in methanol, and dilute quantitatively with methanol to obtain a solution having a known concentration of about 0.8 mg per mL (*Solution P*). Transfer $4J$ mg of USP Amitriptyline Hydrochloride RS to a 50-mL volumetric flask, J being the ratio of the labeled amount, in mg, of amitriptyline hydrochloride to the labeled amount, in mg, of perphenazine per Tablet. Add 5.0 mL of *Solution P* and 20 mL of 0.2 *N* acetic acid, shake, and sonicate to dissolve the Reference Standards. Dilute with methanol to volume, and mix. Pipet 25 mL of this solution into a 100-mL volumetric flask, dilute with a mixture of methanol and 0.04 *N* acetic acid (3:2) to volume, and mix to obtain a *Standard preparation* having known concentrations of about 20 μg of USP Perphenazine RS per mL and about $20J$ μg of USP Amitriptyline Hydrochloride RS per mL.

Assay preparation—Transfer 10 Tablets to a 250-mL volumetric flask, add 100 mL of 0.2 *N* acetic acid, and shake the mixture until the Tablets have disintegrated. Add methanol to volume, mix, and filter. Dilute an accurately measured volume (V_F mL) of the clear filtrate quantitatively with a mixture of methanol and 0.04 *N* acetic acid (3:2) to obtain a solution (V_A mL) containing about 20 μg of perphenazine per mL, and filter through a membrane filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1 mL per minute, and is adjusted until the relative retention times for perphenazine and amitriptyline are about 1 and 1.5, respectively. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the relative standard deviation is not more than 2.0% for replicate injections, and the resolution, R, between perphenazine and amitriptyline is not less than 4.

Procedure—Separately inject equal volumes (about 20 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of perphenazine ($C_{21}H_{26}ClN_3OS$) in each Tablet taken by the formula:

$$0.25(C/10)(V_A/V_F)(r_U/r_S),$$

in which C is the concentration, in μg per mL, of USP Perphenazine RS in the *Standard preparation*, V_A is the volume, in mL, of the *Assay preparation*, V_F is the volume, in mL, of the filtrate taken for the *Assay preparation*, and r_U and r_S are the responses of the perphenazine peaks obtained from the *Assay preparation* and the *Standard preparation*, respectively. Calculate the quantity, in mg, of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) taken by the same formula, reading amitriptyline hydrochloride instead of perphenazine.

Pertechnetate, Tc 99m Injection, Sodium—*see under "technetium"*

Pertussis Immune Globulin

» Pertussis Immune Globulin conforms to the regulations of the FDA concerning biologics (see *Biologics* ⟨1041⟩). It is a sterile, non-pyrogenic solution of globulins derived from the blood plasma of adult human donors who have been immunized with pertussis vaccine such that each 1.25 mL contains not less than the amount of immune globulin to be equivalent to 25 mL of human hyperimmune serum. It may contain 0.3 *M* glycine as a stabilizing agent, and it contains a suitable preservative.

Packaging and storage—Preserve at a temperature between 2° and 8°.

Expiration date—The expiration date is not later than 3 years after date of issue from manufacturer's cold storage (5°, 3 years).

Labeling—Label it to state that it is not intended for intravenous injection.

Pertussis Vaccine

» Pertussis Vaccine conforms to the regulations of the FDA concerning biologics (620.1 to 620.7) (see *Biologics* ⟨1041⟩). It is a sterile bacterial fraction or suspension of killed pertussis bacilli (*Bordetella pertussis*) of a strain or strains selected for high antigenic efficiency. It has a potency determined by the specific mouse potency test based on the U.S. Standard Pertussis Vaccine, and a pertussis challenge of 12 protective units per total immunizing dose, and, in the case of whole bacterial vaccine, such dose contains not more than 60 opacity units. It meets the requirements of the specific mouse toxicity test. It contains a preservative.

Packaging and storage—Preserve at a temperature between 2° and 8°.

Expiration date—The expiration date is not later than 18 months after date of issue from manufacturer's cold storage (5°, 1 year).

Labeling—Label it to state that it is to be well shaken before use and that it is not to be frozen.

Pertussis Vaccine, Diphtheria and Tetanus Toxoids and—*see* Diphtheria and Tetanus Toxoids and Pertussis Vaccine

Pertussis Vaccine Adsorbed

» Pertussis Vaccine Adsorbed conforms to the regulations of the FDA concerning biologics (620.1 to 620.7) (see *Biologics* ⟨1041⟩). It is a sterile bacterial fraction or suspension, in a suitable diluent, of killed pertussis bacilli (*Bordetella pertussis*) of a strain or strains selected for high antigenic efficiency precipitated or adsorbed by the addition of aluminum hydroxide or aluminum phosphate, and re-suspended. It has a potency determined by the specific mouse potency test based on the U.S. Standard Pertussis Vaccine, and a pertussis challenge of 12 protective units per total immunizing dose, and, in the case of whole bacterial vaccine, such dose contains not more than 48 opacity units. It meets the requirements of the specific mouse toxicity test. It contains a preservative.

Packaging and storage—Preserve at a temperature between 2° and 8°, and avoid freezing.

Expiration date—The expiration date is not later than 18 months after date of issue from manufacturer's cold storage (5°, 1 year).

Labeling—Label it to state that it is to be well shaken before use and that it is not to be frozen.

Pertussis Vaccine Adsorbed, Diphtheria and Tetanus Toxoids and—*see* Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed

Petrolatum

» Petrolatum is a purified mixture of semisolid hydrocarbons obtained from petroleum. It may contain a suitable stabilizer.

Packaging and storage—Preserve in well-closed containers.

Labeling—Label it to indicate the name and proportion of any added stabilizer.

Color—Melt about 10 g on a steam bath, and pour about 5 mL of the liquid into a clear-glass 15- × 150-mm test tube, keeping the petrolatum melted. The petrolatum is not darker than a solution made by mixing 3.8 mL of ferric chloride CS and 1.2 mL of cobaltous chloride CS in a similar tube, the comparison of the two being made in reflected light against a white background, the petrolatum tube being held directly against the background at such an angle that there is no fluorescence.

Specific gravity ⟨841⟩: between 0.815 and 0.880 at 60°.

Melting range, *Class III* ⟨741⟩: between 38° and 60°.

Consistency—

Apparatus—Determine the consistency of Petrolatum by means of a penetrometer fitted with a polished cone-shaped metal plunger weighing 150 g, having a detachable steel tip of the following dimensions: the tip of the cone has an angle of 30°, the point being truncated to a diameter of 0.381 ± 0.025 mm, the base of the tip is 8.38 ± 0.05 mm in diameter, and the length of the tip is 14.94 ± 0.05 mm. The remaining portion of the cone has an angle of 90°, is about 28 mm in height, and has a maximum diameter at the base of about 65 mm. The containers for the test are flat-bottom metal cylinders that are 100 ± 6 mm in diameter and not less than 65 mm in height. They are constructed of at least 1.6-mm (16-gauge) metal, and are provided with well-fitting, water-tight covers.

Procedure—Place the required number of containers in an oven, and bring them and a quantity of Petrolatum to a temperature of 82 ± 2.5°, pour the Petrolatum into one or more of the containers, filling to within 6 mm of the rim. Cool to 25 ± 2.5° over a period of not less than 16 hours, protected from drafts. Two hours before the test, place the containers in a water bath at 25 ± 0.5°. If the room temperature is below 23.5° or above 26.5°, adjust the temperature of the cone to 25 ± 0.5° by placing it in the water bath.

Without disturbing the surface of the substance under test, place the container on the penetrometer table, and lower the cone until the tip just touches the top surface of the test substance at a spot 25 mm to 38 mm from the edge of the container. Adjust the zero setting and quickly release the plunger, then hold it free for 5 seconds. Secure the plunger, and read the total penetration from the scale. Make three or more trials, each so spaced that there is no overlapping of the areas of penetration. Where the penetration exceeds 20 mm, use a separate container of the test substance for each trial. Read the penetration to the nearest 0.1 mm. Calculate the average of the three or more readings, and conduct further trials to a total of 10 if the individual results differ from the average by more than ±3%: the final average of the trials is not less than 10.0 mm and not more than 30.0 mm, indicating a consistency value between 100 and 300.

Acidity—If the addition of phenolphthalein TS in the test for *Alkalinity* produces no pink color, add 0.1 mL of methyl orange TS: no red or pink color is produced.

Alkalinity—Introduce 35 g into a suitable beaker, add 100 mL of boiling water, cover, and place on a stirring hot-plate maintained at the boiling point of water. After 5 minutes, allow the phases to separate. Draw off the separated water into a casserole, wash the petrolatum further with two 50-mL portions of boiling water, and add the washings to the casserole. To the pooled washings add 1 drop of phenolphthalein TS, and boil: the solution does not acquire a pink color.

Residue on ignition ⟨281⟩—Heat 2 g in an open porcelain or platinum dish over a Bunsen flame: it volatilizes without emitting an acrid odor and on ignition yields not more than 0.1% of residue.

Organic acids—Weigh 20.0 g, add 100 mL of a 1 in 2 mixture of neutralized alcohol and water, agitate thoroughly, and heat to boiling. Add 1 mL of phenolphthalein TS, and titrate rapidly with 0.1 *N* sodium hydroxide VS, with vigorous agitation to the production of a sharp pink endpoint, noting the color change in the alcohol-water layer: not more than 400 µL of 0.100 *N* sodium hydroxide is required.

Fixed oils, fats, and rosin—Digest 10 g with 50 mL of 5 *N* sodium hydroxide at 100° for 30 minutes. Separate the water layer, and acidify it with 5 *N* sulfuric acid: no oily or solid matter separates.

Petrolatum Gauze—*see* Gauze, Petrolatum

Hydrophilic Petrolatum

» Prepare Hydrophilic Petrolatum as follows:

Cholesterol	30 g
Stearyl Alcohol	30 g
White Wax	80 g
White Petrolatum	860 g
To make	1000 g

Melt the Stearyl Alcohol and White Wax together on a steam bath, then add the Cholesterol, and stir until completely dissolved. Add the White Petrolatum, and mix. Remove from the bath, and stir until the mixture congeals.

White Petrolatum

» White Petrolatum is a purified mixture of semisolid hydrocarbons obtained from petroleum, and wholly or nearly decolorized. It may contain a suitable stabilizer.

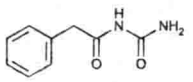
Color—Melt about 10 g on a steam bath, and pour 5 mL of the liquid into a clear-glass, 16- × 150-mm bacteriological test tube: the warm, melted liquid is not darker than a solution made by mixing 1.6 mL of ferric chloride CS and 3.4 mL of water in a similar tube, the comparison of the two being made in reflected light against a white background, the tubes being held directly against the background at such an angle that there is no fluorescence.

Residue on ignition ⟨281⟩—Heat 2 g in an open porcelain or platinum dish over a flame: it volatilizes without emitting an acrid odor and on ignition yields not more than 0.05% of residue.

Other requirements—It meets the requirements for *Packaging and storage*, *Labeling*, *Specific gravity*, *Melting range*, *Consistency*, *Alkalinity*, *Acidity*, *Organic acids*, and *Fixed oils, fats, and rosin* under *Petrolatum*.

Pharmaceutical Glaze—*see* Glaze, Pharmaceutical NF

Phenacemide



$C_9H_{10}N_2O_2$ 178.19
Benzeneacetamide, *N*-(aminocarbonyl)-.
(Phenylacetyl)urea [*63-98-9*].

» Phenacemide contains not less than 98.0 percent and not more than 100.5 percent of $C_9H_{10}N_2O_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phenacemide RS*.

Identification—
A: *Infrared Absorption* ⟨197K⟩.
B: *Ultraviolet Absorption* ⟨197U⟩—
Solution: 3 in 10,000.
Medium: methanol. Absorptivities at 257 nm, calculated on the dried basis, do not differ by more than 3.0%.

Loss on drying ⟨731⟩—Dry it at 105° for 4 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Ordinary impurities ⟨466⟩—
Test solution: 5 mg of phenacemide per mL in methanol.
Standard solutions: 0.01, 0.025, 0.05, and 0.1 mg per mL in methanol.
Application volume: 10 µL.
Eluant: a mixture of toluene, ethyl acetate, and formic acid (50:45:5), in a nonequilibrated chamber.
Visualization: Expose the plate to chlorine gas for about 2 minutes in a closed chamber, and air-dry for about 15 minutes under a well-ventilated hood, followed by *Visualization* technique 18.

Organic volatile impurities, *Method V* ⟨467⟩: meets the requirements, except that the limit for 1,4-dioxane is 1000 ppm.
Solvent—Use dimethyl sulfoxide as the solvent.

Assay—Transfer about 400 mg of Phenacemide, accurately weighed, to a round-bottom flask, add 50 mL of water and 8 mL of sulfuric acid, attach a condenser, and reflux gently for 1 hour. Cool, transfer the contents of the flask to a separator, rinse the condenser and flask with three 15-mL portions of chloroform, and add the rinsings to the separator. Shake, allow the layers to separate, and transfer the chloroform layer to a flask. Extract the aqueous layer with five 30-mL portions of chloroform after previously rinsing the condenser and flask with each portion, and add the chloroform extracts to the main extract. Filter the chloroform solution, rinse the filter with a few mL of hot chloroform, add the rinsing to the filtrate, and evaporate without heating, with the aid of a current of air, to dryness. Dissolve the residue in 25 mL of dehydrated alcohol, add phenolphthalein TS, and titrate with 0.1 *N* sodium hydroxide VS. Perform a blank determination, and make any necessary correction. Each mL of 0.1 *N* sodium hydroxide is equivalent to 17.82 mg of $C_9H_{10}N_2O_2$.

Phenacemide Tablets

» Phenacemide Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_9H_{10}N_2O_2$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—*USP Phenacemide RS.*

Identification—Transfer a quantity of powdered Tablets, equivalent to about 300 mg of phenacemide, to a separator, add 50 mL of water, and extract with five 20-mL portions of chloroform. Filter the chloroform extracts, evaporate on a steam bath with the aid of a gentle current of air to dryness, and dry at 105° for 2 hours: the residue so obtained responds to *Identification* test *A* under *Phenacemide.*

Dissolution ⟨711⟩—

Medium: 0.1 *N* hydrochloric acid; 900 mL.

Apparatus 2: 100 rpm.

Time: 60 minutes.

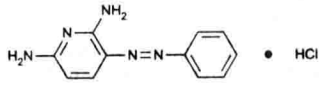
Procedure—Determine the amount of $C_9H_{10}N_2O_2$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 257 nm of filtered portions of the solution under test, suitably diluted with 0.1 *N* hydrochloric acid, in comparison with a Standard solution having a known concentration of USP Phenacemide RS in the same medium.

Tolerances—Not less than 35% (*Q*) of the labeled amount of $C_9H_{10}N_2O_2$ is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—Weigh and finely powder not less than 20 Tablets. Using an accurately weighed portion of the powder, equivalent to about 400 mg of phenacemide, proceed as directed in the *Assay* under *Phenacemide.*

Phenazopyridine Hydrochloride



$C_{11}H_{11}N_5 \cdot HCl$ 249.70

2,6-Pyridinediamine, 3-(phenylazo)-, monohydrochloride.

2,6-Diamino-3-(phenylazo)pyridine monohydrochloride [*136-40-3*].

» Phenazopyridine Hydrochloride contains not less than 99.0 percent and not more than 101.0 percent of $C_{11}H_{11}N_5 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phenazopyridine Hydrochloride RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 1 in 200,000.

Medium: sulfuric acid in alcohol (1 in 360).

C: Prepare a solution of it in alcohol containing about 0.2 mg per mL. Transfer 10 mL of this solution to a glass-stoppered, 100-mL graduated cylinder, add chloroform to volume, and mix. Apply 10 µL of the solution so obtained to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel. Apply to the same plate 10 µL of a Standard solution of USP Phenazopyridine Hydrochloride RS in the same medium having a known concentration of about 0.02 mg per mL. Develop the chromatogram in a solvent system consisting of a mixture of chloroform, ethyl acetate, and methanol (85:10:5) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber and allow it to dry. Locate the spots by spraying the plate lightly with 2 *N* hydrochloric acid: the R_f of the principal spot in the chromatogram of the test solution corresponds to that obtained from the Standard solution.

Loss on drying ⟨731⟩—Dry it at 105° for 4 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Water-insoluble substances—Dissolve about 2 g, accurately weighed, in 200 mL of water, heat to boiling, then heat in a covered container on a steam bath for 1 hour. Filter through a tared, fine-porosity, sintered-glass crucible, wash thoroughly with water, and dry at 105° to constant weight: the weight of the residue does not exceed 0.1% of the weight of Phenazopyridine Hydrochloride taken.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Ordinary impurities ⟨466⟩—

Test solution—Prepare a solution of it in alcohol having a concentration of 2.0 mg per mL.

Standard solutions—Prepare solutions of USP Phenazopyridine Hydrochloride RS in alcohol containing 0.04, 0.02, and 0.01 mg per mL, respectively.

Eluant: a mixture of chloroform, ethyl acetate, and methanol (85:10:5).

Visualization—Spray the plate with 5 *N* hydrochloric acid.

Assay—Transfer about 100 mg of Phenazopyridine Hydrochloride, accurately weighed, to a 200-mL volumetric flask. Add about 100 mL of a mixture of sulfuric acid and alcohol (1 in 360), heat gently on a steam bath for 10 minutes, shake by mechanical means to dissolve, cool to room temperature, dilute with the alcoholic sulfuric acid to volume, and mix. Transfer 10.0 mL of this solution to a 100-mL volumetric flask, dilute with the alcoholic sulfuric acid to volume, and mix. Transfer 5.0 mL of the resulting solution to a 50-mL volumetric flask, dilute with the alcoholic sulfuric acid to volume, and mix. Concomitantly determine the absorbances of this solution and a Standard solution of USP Phenazopyridine Hydrochloride RS in the same medium having a known concentration of about 5 µg per mL, in 1-cm cells at the wavelength of maximum absorbance at about 390 nm, with a suitable spectrophotometer, using dilute alcoholic sulfuric acid (1 in 360) as the blank. Calculate the quantity, in mg, of $C_{11}H_{11}N_5 \cdot HCl$ in the Phenazopyridine Hydrochloride taken by the formula:

$$20C(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Phenazopyridine Hydrochloride RS in the Standard solution, and A_U and A_S are the absorbances of the solution of Phenazopyridine Hydrochloride and the Standard solution, respectively.

Phenazopyridine Hydrochloride Tablets

» Phenazopyridine Hydrochloride Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_{11}H_{11}N_5 \cdot HCl$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phenazopyridine Hydrochloride RS.*

Identification—Transfer a quantity of finely ground Tablets, equivalent to about 50 mg of phenazopyridine hydrochloride, to a 125-mL separator, add 50 mL of water, 1 mL of 1 *N* hydrochloric acid, and 5 mL of a saturated sodium chloride solution, and shake to dissolve. Extract with two 25-mL portions of chloroform, and discard the chloroform. Add 5 mL of 1 *N* sodium hydroxide to the aqueous solution, and extract with one 50-mL portion of chloroform. Transfer the chloroform layer to a second 125-mL separator, and wash with one 50-mL portion of 0.1 *N* sodium hydroxide. Filter the chloroform layer through a pledget of cotton previously washed with chloroform. Add 5 drops of hydrochloric acid to the filtrate, and evaporate under a current of air on a steam bath to dryness. Add 5 mL of alcohol, and

evaporate. Dry the residue at 105° for 4 hours: the infrared absorption spectrum of a potassium bromide dispersion of the dried residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Phenazopyridine Hydrochloride RS.

Dissolution ⟨711⟩—
Medium: water; 900 mL.
Apparatus 2: 50 rpm.
Time: 45 minutes.
Procedure—Determine the amount of $C_{11}H_{11}N_5 \cdot HCl$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 412 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium* in comparison with a Standard solution having a known concentration of USP Phenazopyridine Hydrochloride RS in the same medium.
Tolerances—Not less than 75% (*Q*) of the labeled amount of $C_{11}H_{11}N_5 \cdot HCl$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

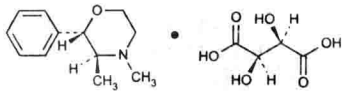
Assay—
Phosphate buffer—Dissolve 2.64 g of dibasic ammonium phosphate in about 900 mL of water. Adjust with phosphoric acid to a pH of 3.0, dilute with water to 1000 mL, and mix.
Mobile phase—Prepare a mixture of *Phosphate buffer* and methanol (50:50). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).
Standard preparation—Transfer about 50 mg of USP Phenazopyridine Hydrochloride RS, accurately weighed, to a 100-mL volumetric flask. Add 50 mL of methanol, and swirl to dissolve. Dilute with *Phosphate buffer* to volume, mix, and filter through a filter having a 0.5 μm or finer porosity.
Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of phenazopyridine hydrochloride, to a 200-mL volumetric flask. Add 100 mL of methanol, and sonicate for 10 minutes. Add about 75 mL of *Phosphate buffer*, and sonicate for an additional 10 minutes, with occasional mixing. Dilute with *Phosphate buffer* to volume, and mix. Filter this solution through a filter having a 0.5 μm or finer porosity.
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the responses as directed under *Procedure:* the column efficiency is not less than 1400 theoretical plates, the tailing factor for the analyte peak is not more than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%.
Procedure—Separately inject equal volumes (about 10 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{11}H_{11}N_5 \cdot HCl$ in the portion of Tablets taken by the formula:

$$200C(r_U/r_S),$$

in which C is the concentration, in mg per mL, of USP Phenazopyridine Hydrochloride RS in the *Standard preparation*, and r_U and r_S are the phenazopyridine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Phenazopyridine Hydrochlorides and Sulfamethizole Capsules, Oxytetracycline and—*see* Oxytetracycline and Phenazopyridine Hydrochlorides and Sulfamethizole Capsules

Phendimetrazine Tartrate



$C_{12}H_{17}NO \cdot C_4H_6O_6$ 341.36
Morpholine, 3,4-dimethyl-2-phenyl-, (2*S*-*trans*)-, [*R*-(*R**,*R**)]-2,3-dihydroxybutanedioate (1:1).
(2*S*,3*S*)-3,4-Dimethyl-2-phenylmorpholine L-(+)-tartrate (1:1) [*50-58-8*].

» Phendimetrazine Tartrate contains not less than 98.0 percent and not more than 102.0 percent of $C_{12}H_{17}NO \cdot C_4H_6O_6$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phendimetrazine Tartrate RS.*

Identification—
A: *Infrared Absorption* ⟨197K⟩.
B: *Ultraviolet Absorption* ⟨197U⟩—
Solution: 1 in 1000.
Medium: methanol.
C: It responds to the test for *Tartrate* ⟨191⟩.

Melting range ⟨741⟩: between 182° and 188°, with decomposition, but the range between beginning and end of melting does not exceed 3°.

Specific rotation ⟨781S⟩: between +32° and +36°.
Test solution: 10 mg per mL, in water.

pH ⟨791⟩: between 3.0 and 4.0, in a solution (1 in 40).

Loss on drying ⟨731⟩—Dry it to constant weight at 105°: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Chloride ⟨221⟩—A 1.0-g portion shows no more chloride than corresponds to 0.50 mL of 0.020 *N* hydrochloric acid (0.035%).

Sulfate ⟨221⟩—A 1.0-g portion shows no more sulfate than corresponds to 0.10 mL of 0.020 *N* sulfuric acid (0.01%).

Heavy metals ⟨231⟩: 0.001%.

Chromatographic purity—Dissolve 500 mg in water, dilute with water to 5.0 mL, and mix. Apply 10 μL of this preparation and 10 μL of an aqueous solution of USP Phendimetrazine Tartrate RS containing about 100 mg per mL to the starting line to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Develop the chromatogram in a suitable chamber with a solvent system consisting of a mixture of acetone, methanol, and ammonium hydroxide (50:50:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, air-dry, view under short-wavelength ultraviolet light, and observe the location of the spots. Expose the plate to iodine vapors in a closed chamber: yellow spots appear at the same locations as the spots observed under ultraviolet light, and the R_f value of the spot obtained from the test preparation corresponds to that obtained from the Standard solution, and no other spot is obtained.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

L-*erythro* isomer—Dissolve 3.0 g of Phendimetrazine Tartrate in 25 mL of sodium hydroxide solution (1 in 20) in a suitable separator. Add 25 mL of sodium hydroxide solution (1 in 2), swirl, and allow the phendimetrazine base to separate. Discard the lower, alkaline layer, and collect the upper layer, centrifuging, if necessary, to obtain a clear liquid. Inject 1.0 μL of this liquid into a suitable gas chromatograph equipped with a flame-ionization detector, a 100:1 specimen splitter, and a 25-m × 0.25-mm capillary column, the inside wall of which is coated with a 0.4-μm film of liquid phase G1. The temperatures of the injection port, column, and detector block are 250°, 140°, and 280°, respectively. The carrier gas is helium. Preferably using an electronic integrator, determine the areas of all peaks in the chromatogram. The retention times are about 8.5 minutes for the D-

threo isomer and 9 minutes for the L-*erythro* isomer. Calculate the percentage of L-*erythro* isomer in the test specimen taken by the formula:

$$100(r_U/r_S),$$

in which r_U is the peak area response of the L-*erythro* isomer peak and r_S is the sum of the areas of the L-*erythro* isomer peak and the D-*threo* isomer peak: the limit is 0.1%.

Assay—Transfer to a beaker about 500 mg of Phendimetrazine Tartrate, accurately weighed, and dissolve in 50 mL of glacial acetic acid. Add 1 drop of crystal violet TS, and titrate with 0.1 *N* perchloric acid VS to a green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 *N* perchloric acid is equivalent to 34.14 mg of $C_{12}H_{17}NO \cdot C_4H_6O_6$.

Phendimetrazine Tartrate Capsules

» Phendimetrazine Tartrate Capsules contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_{12}H_{17}NO \cdot C_4H_6O_6$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phendimetrazine Tartrate RS.*

Identification—

A: Shake a quantity of Capsule contents, equivalent to about 300 mg of phendimetrazine tartrate, with about 50 mL of water, filter, and transfer the filtrate to a 200-mL separator. Add 3 mL of 12.5 *N* sodium hydroxide, and extract with two 50-mL portions of chloroform. Extract the combined chloroform extracts in a 250-mL separator with two 15-mL portions of 0.5 *N* hydrochloric acid, and evaporate the combined aqueous extracts on a steam bath to dryness. Dissolve the residue in 5 mL of acetone, and add 50 mL of anhydrous ether to the solution. On standing, phendimetrazine hydrochloride crystallizes out. Filter the precipitate, wash with anhydrous ether, and dry at 105°: the crystals so obtained melt between 189° and 193°, but the range between beginning and end of melting does not exceed 2°.

B: A portion of Capsule contents responds to the test for *Tartrate* ⟨191⟩.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Mobile phase—Dissolve 1.1 g of sodium 1-heptanesulfonate in 575 mL of water, add 400 mL of methanol, 25 mL of dilute acetic acid (1 in 100), and mix. Adjust with glacial acetic acid to a pH of 3.0 ± 0.1, if necessary. Filter through a 0.45-μm membrane filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of water, methanol, and dilute acetic acid (14 in 100) (57.5:40:2.5).

Internal standard solution—Prepare a solution of salicylamide in *Diluent* having a concentration of about 0.1 mg per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Phendimetrazine Tartrate RS in *Internal standard solution*, and dilute quantitatively with *Internal standard solution* to obtain a solution having a known concentration of about 0.7 mg of USP Phendimetrazine Tartrate RS per mL.

Assay preparation—Remove, as completely as possible, the contents of not less than 20 Capsules, and weigh accurately. Mix the combined contents, and transfer an accurately weighed quantity of the powder, equivalent to about 35 mg of phendimetrazine tartrate, to a 50-mL volumetric flask, add 25 mL of *Internal standard solution*, and sonicate for about 15 minutes. Cool the solution to room temperature, dilute with *Internal standard solution* to volume, mix, and filter through a 0.45-μm membrane filter.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 256-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the resolution, *R*, between the analyte and internal standard peaks is not less than 3.0, and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 20 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.5 for salicylamide and 1.0 for phendimetrazine tartrate. Calculate the quantity, in mg, of $C_{12}H_{17}NO \cdot C_4H_6O_6$ in the portion of Capsules taken by the formula:

$$50C(R_U/R_S),$$

in which C is the concentration, in mg per mL, of USP Phendimetrazine Tartrate RS in the *Standard preparation*, and R_U and R_S are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Phendimetrazine Tartrate Tablets

» Phendimetrazine Tartrate Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{12}H_{17}NO \cdot C_4H_6O_6$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—*USP Phendimetrazine Tartrate RS.*

Identification—A quantity of finely powdered Tablets, equivalent to about 300 mg of phendimetrazine tartrate, responds to the *Identification* tests under *Phendimetrazine Tartrate Capsules.*

Dissolution ⟨711⟩—

Medium: water; 900 mL.

Apparatus 1: 100 rpm.

Time: 45 minutes.

pH 7.5 phosphate buffer—Prepare a solution of 0.025 *M* monobasic potassium phosphate, and adjust to a pH of 7.5 by the addition of 1 *N* potassium hydroxide.

Mobile phase—Prepare a suitable degassed and filtered mixture of acetonitrile and *pH 7.5 phosphate buffer* (65:35).

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 210-nm detector and a 4-mm × 15-cm column that contains packing L15. The flow rate is about 1.0 mL per minute. Chromatograph three replicate injections of the Standard solution, and record the peak responses as directed under *Procedure:* the relative standard deviation is not more than 3.0%.

Procedure—Separately inject equal volumes (about 50 μL) of the Standard solution and a filtered aliquot of the solution under test into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of $C_{12}H_{17}NO \cdot C_4H_6O_6$ dissolved in comparison with a Standard solution of USP Phendimetrazine Tartrate RS, similarly prepared and chromatographed.

Tolerances—Not less than 60% (*Q*) of the labeled amount of $C_{12}H_{17}NO \cdot C_4H_6O_6$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Mobile phase, Diluent, Internal standard solution, Standard preparation, and *Chromatographic system*—Prepare as directed in the *Assay* under *Phendimetrazine Tartrate Capsules.*

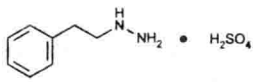
Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 35 mg of phendimetrazine tartrate, to a 50-mL volumetric flask, add 25 mL of *Internal standard solution*, and sonicate for about 15 minutes. Cool the solution to room temperature, dilute with *Internal standard solution* to volume, mix, and filter through a 0.45-μm membrane filter.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Phendimetrazine Tartrate Capsules.* Calculate the quantity, in mg, of $C_{12}H_{17}NO \cdot C_4H_6O_6$ in the portion of Tablets taken by the formula:

$$50C(R_U/R_S),$$

in which C is the concentration, in mg per mL, of USP Phendimetrazine Tartrate RS in the *Standard preparation*, and R_U and R_S are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Phenelzine Sulfate



$C_8H_{12}N_2 \cdot H_2SO_4$ 234.28
Hydrazine, (2-phenylethyl)-, sulfate (1:1).
Phenethylhydrazine sulfate (1:1) [*156-51-4*].

» Phenelzine Sulfate contains not less than 97.0 percent and not more than 100.5 percent of $C_8H_{12}N_2 \cdot H_2SO_4$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers, protected from heat and light.

USP Reference standards ⟨11⟩—*USP Phenelzine Sulfate RS.*

Identification—
A: *Infrared Absorption* ⟨197K⟩.
B: Dissolve 100 mg in 5 mL of water, render the solution alkaline with 1 *N* sodium hydroxide, and add 1 mL of alkaline cupric tartrate TS: a red to yellow-red precipitate is formed.
C: A solution (1 in 10) responds to the tests for *Sulfate* ⟨191⟩.

Melting range ⟨741⟩: between 164° and 168°.

pH ⟨791⟩: between 1.4 and 1.9, in a solution (1 in 100).

Loss on drying ⟨731⟩—Dry it at a pressure not exceeding 5 mm of mercury over silica gel at 80° for 2 hours: it loses not more than 1.0% of its weight.

Heavy metals, *Method I* ⟨231⟩: 0.002%.

Ordinary impurities ⟨466⟩—
Test solution: a mixture of methanol and water (1:1).
Standard solution: a mixture of methanol and water (1:1).
Eluant: acetone.
Visualization: 1.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—Dissolve about 235 mg of Phenelzine Sulfate, accurately weighed, in 50 mL of water in a glass-stoppered flask. Dissolve 1.5 g of sodium bicarbonate in the solution, add 50.0 mL of 0.1 *N* iodine VS, insert the stopper, and allow to stand for 90 minutes. Cautiously add 20 mL of 3 *N* hydrochloric acid, and titrate the excess iodine with 0.1 *N* sodium thiosulfate VS, adding 3 mL of starch TS as the endpoint is approached. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.1 *N* iodine is equivalent to 5.857 mg of $C_8H_{12}N_2 \cdot H_2SO_4$.

Phenelzine Sulfate Tablets

» Phenelzine Sulfate Tablets contain an amount of phenelzine sulfate ($C_8H_{12}N_2 \cdot H_2SO_4$) equivalent to not less than 95.0 percent and not more than 105.0 percent of the labeled amount of phenelzine ($C_8H_{12}N_2$).

Packaging and storage—Preserve in tight containers, protected from heat and light.

USP Reference standards ⟨11⟩—*USP Phenelzine Sulfate RS.*

Identification—Extract a portion of powdered Tablets, equivalent to about 30 mg of phenelzine, with 10 mL of water, and filter: the filtrate responds to *Identification* tests *B* and *C* under *Phenelzine Sulfate.*

Disintegration ⟨701⟩: 1 hour.

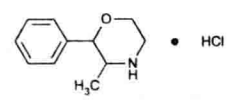
Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—
Mobile phase—Dissolve 6.9 g of monobasic sodium phosphate and 4.4 g of sodium 1-heptanesulfonate into 800 mL of water, and adjust with phosphoric acid to a pH of 2.5. Add 200 mL of acetonitrile, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).
Standard preparation—Dissolve an accurately weighed quantity of USP Phenelzine Sulfate RS in *Mobile phase*, and dilute quantitatively with *Mobile phase* to obtain a solution having a known concentration of about 258 μg per mL equivalent to about 150 μg of phenelzine per mL.
Assay preparation—Weigh and finely powder not less than 20 Tablets. [NOTE—The ground Tablets are hygroscopic and should be used immediately.] Transfer an accurately weighed portion of the powder, equivalent to about 15.0 mg of phenelzine, to a 100-mL volumetric flask, add about 75 mL of *Mobile phase*, and place in an ultrasonic bath for 1 minute. Shake the mixture for 5 minutes, dilute with *Mobile phase* to volume, mix, and filter.
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 209-nm detector and 4.6-mm × 10-cm column that contains packing L1. The flow rate is about 1 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the tailing factor is not more than 3.5, and the relative standard deviation for replicate injections is not more than 2.0%.
Procedure—Separately inject equal volumes (about 20 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_8H_{12}N_2$ in the portion of Tablets taken by the formula:

$$(136.20/234.27)(0.1C)(r_U/r_S),$$

in which 136.20 and 234.27 are the molecular weights of phenelzine and phenelzine sulfate, respectively, C is the concentration, in μg per mL, of USP Phenelzine Sulfate RS in the *Standard preparation*, and r_U and r_S are the phenelzine peak responses from the *Assay preparation* and the *Standard preparation*, respectively.

Phenmetrazine Hydrochloride



$C_{11}H_{15}NO \cdot HCl$ 213.71
Morpholine, 3-methyl-2-phenyl-, hydrochloride.
3-Methyl-2-phenylmorpholine hydrochloride
[*1707-14-8*].

» Phenmetrazine Hydrochloride, dried at 105° for 2 hours, contains not less than 98.0 percent and not more than 102.0 percent of $C_{11}H_{15}NO \cdot HCl$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phenmetrazine Hydrochloride RS.*

Identification—
A: *Infrared Absorption* ⟨197S⟩—
Solution: 1 in 20.
Medium: chloroform.
B: *Ultraviolet Absorption* ⟨197U⟩—
Solution: 1 in 2000.
Medium: 0.5 *N* hydrochloric acid.

Melting range, *Class Ia* ⟨741⟩: between 172° and 182°, but the range between beginning and end of melting does not exceed 3°.

pH ⟨791⟩: between 4.5 and 5.5, in a solution (1 in 40).

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Sulfate ⟨221⟩—A 2.0-g portion shows no more sulfate than corresponds to 0.20 mL of 0.020 *N* sulfuric acid (0.01%).

Chloride content—Transfer about 350 mg, previously dried and accurately weighed, to a 250-mL beaker. Add about 125 mL of water and 10 drops of sulfuric acid, and stir for 15 minutes with a magnetic stirrer. Titrate the solution potentiometrically with 0.1 *N* silver nitrate VS, using a silver–mercurous sulfate electrode system with a saturated salt bridge of potassium sulfate. Each mL of 0.1 *N* silver nitrate is equivalent to 3.545 mg of Cl: the content is between 16.3% and 17.0%.

Heavy metals, *Method II* ⟨231⟩: 0.001%.

Ordinary impurities ⟨466⟩—
Test solution: methanol.
Standard solution: methanol.
Eluant: a mixture of chloroform, absolute alcohol, and ammonium hydroxide (80:20:1).
Visualization: 1.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—Transfer to a 200-mL volumetric flask about 100 mg of Phenmetrazine Hydrochloride, previously dried and accurately weighed. Dissolve in 0.5 *N* hydrochloric acid, dilute with 0.5 *N* hydrochloric acid to volume, and mix to obtain the *Assay preparation.* Concomitantly determine the absorbances of the *Assay preparation* and of a Standard solution of USP Phenmetrazine Hydrochloride RS, in the same medium having a known concentration of about 500 µg per mL, in 1-cm cells, at the wavelength of maximum absorbance at about 256 nm, with a suitable spectrophotometer, using 0.5 *N* hydrochloric acid as the blank. Calculate the quantity, in mg, of $C_{11}H_{15}NO \cdot HCl$ in the Phenmetrazine Hydrochloride taken by the formula:

$$0.2C(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Phenmetrazine Hydrochloride RS in the Standard solution, and A_U and A_S are the absorbances from the *Assay preparation* and the Standard solution, respectively.

Phenmetrazine Hydrochloride Tablets

» Phenmetrazine Hydrochloride Tablets contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of $C_{11}H_{15}NO \cdot HCl$.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phenmetrazine Hydrochloride RS.*

Identification—Dissolve 5 Tablets in 40 mL of water in a 250-mL separator. Add 3 mL of sodium hydroxide solution (1 in 2), and extract with two 50-mL portions of chloroform. Extract the combined chloroform extracts in a 250-mL separator with two 15-mL portions of 0.5 *N* hydrochloric acid, and evaporate the combined aqueous extracts on a steam bath to dryness. Dissolve the residue in 5 mL of acetone, and add 50 mL of anhydrous ether to the solution. On standing, phenmetrazine hydrochloride will crystallize out. Filter the precipitate, wash with anhydrous ether, and dry at 105°: the crystals so obtained melt within a range of 3° between 172° and 182° (see *Melting Range or Temperature* ⟨741⟩).

Dissolution ⟨711⟩—
Medium: water; 900 mL.
Apparatus 2: 50 rpm.
Time: 45 minutes.

Procedure—Determine the amount of $C_{11}H_{15}NO \cdot HCl$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 256 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium,* if necessary, in comparison with a Standard solution having a known concentration of USP Phenmetrazine Hydrochloride RS in the same medium.

Tolerances—Not less than 75% (*Q*) of the labeled amount of $C_{11}H_{15}NO \cdot HCl$ is dissolved in 45 minutes.

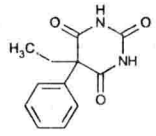
Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 250 mg of phenmetrazine hydrochloride, to a 250-mL volumetric flask, add about 125 mL of 0.5 *N* hydrochloric acid, shake by mechanical means for 1 hour, dilute with 0.5 *N* hydrochloric acid to volume, and mix. Transfer 50.0 mL of the solution to a 250-mL separator, add 5 mL of sodium hydroxide solution (1 in 2), and extract with four 50-mL portions of chloroform, collecting the chloroform extracts in a second 250-mL separator. Extract the combined chloroform extracts with six 15-mL portions of 0.5 *N* hydrochloric acid, collecting the aqueous extracts in a 100-mL volumetric flask, and dilute with 0.5 *N* hydrochloric acid to volume to obtain the *Assay preparation.* Concomitantly determine the absorbances of the *Assay preparation* and of a Standard solution of USP Phenmetrazine Hydrochloride RS in the same medium, having a known concentration of about 500 µg per mL, in 1-cm cells, at the wavelength of maximum absorbance at about 256 nm, with a suitable spectrophotometer, using 0.5 *N* hydrochloric acid as the blank. Calculate the quantity, in mg, of $C_{11}H_{15}NO \cdot HCl$ in the portion of Tablets taken by the formula:

$$0.5C(A_U/A_S),$$

in which C is the concentration, in µg per mL, of USP Phenmetrazine Hydrochloride RS in the Standard solution, and A_U and A_S are the absorbances from the *Assay preparation* and the Standard solution, respectively.

Phenobarbital



$C_{12}H_{12}N_2O_3$ 232.24
2,4,6(1*H*,3*H*,5*H*)-Pyrimidinetrione, 5-ethyl-5-phenyl-.
5-Ethyl-5-phenylbarbituric acid [*50-06-6*].

» Phenobarbital contains not less than 98.0 percent and not more than 101.0 percent of $C_{12}H_{12}N_2O_3$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—*USP Phenobarbital RS.*

Identification—
A: The infrared absorption spectrum of a potassium bromide dispersion of it exhibits maxima only at the same wavelengths as that of a similar preparation of USP Phenobarbital RS. If a difference appears, dissolve portions of both the test specimen and the Reference Standard in a suitable solvent, evaporate the solutions to dryness, and repeat the test on the residues.
B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation,* both relative to the internal standard, as obtained in the *Assay.*

Melting range ⟨741⟩: between 174° and 178°, but the range between beginning and end of melting does not exceed 2°.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.15%.

Organic volatile impurities, *Method V* ⟨467⟩: meets the requirements.

Solvent—Use dimethyl sulfoxide as the solvent.

Assay—

pH 4.5 buffer solution—Dissolve about 6.6 g of sodium acetate trihydrate and 3.0 mL of glacial acetic acid in 1000 mL of water, and adjust, if necessary, with glacial acetic acid to a pH of 4.5 ± 0.1.

Mobile phase—Prepare a filtered and degassed mixture of *pH 4.5 buffer solution* and methanol (3:2), making adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Dissolve a sufficient quantity of caffeine in a mixture of methanol and *pH 4.5 buffer solution* (1:1) to obtain a solution having a concentration of about 125 µg per mL.

Standard preparation—Dissolve about 20 mg of USP Phenobarbital RS, accurately weighed, in 15.0 mL of *Internal standard solution.* Sonicate if necessary.

Assay preparation—Transfer about 20 mg of Phenobarbital, accurately weighed, to a conical flask, add 15.0 mL of *Internal standard solution*, mix, and sonicate for 15 minutes. Filter through a membrane filter (0.5 µm or finer porosity) before use.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 25-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure:* the resolution, R, between the analyte and the internal standard peaks is not less than 1.2, the tailing factor for the analyte and the internal standard peaks is not greater than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. The relative retention times are about 0.6 for caffeine and 1.0 for phenobarbital. Calculate the quantity, in mg, of $C_{12}H_{12}N_2O_3$ in the portion of Phenobarbital taken by the formula:

$$W(R_U/R_S),$$

in which W is the weight, in mg, of USP Phenobarbital RS taken for the *Standard preparation*, and R_U and R_S are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Phenobarbital Capsules, Ephedrine Sulfate and—*see* Ephedrine Sulfate and Phenobarbital Capsules

Phenobarbital Elixir

» Phenobarbital Elixir contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{12}H_{12}N_2O_3$.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩—*USP Phenobarbital RS.*

Identification—

A: Place 10 mL of Elixir in a separator containing 20 mL of water, add 5 mL of 1 *N* sodium hydroxide, and extract with two 10-mL portions of chloroform, discarding the chloroform extracts. Add 5 mL of 3 *N* hydrochloric acid, and extract with two 25-mL portions of chloroform, filtering the extracts through paper into a beaker. Remove the chloroform by evaporation on a steam bath, and dry the residue at 105° for 2 hours: the residue so obtained responds to *Identification* test *A* under *Phenobarbital.*

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation*, both relative to the internal standard, as obtained in the *Assay.*

Alcohol content, *Method II* ⟨611⟩: between 12.0% and 15.0% of C_2H_5OH.

Assay—

pH 4.5 buffer solution, *Mobile phase*, and *Chromatographic system*—Prepare as directed in the *Assay* under *Phenobarbital.*

Internal standard solution—Dissolve a sufficient quantity of caffeine in a solvent mixture of dichloromethane and methanol (4:1) to obtain a solution having a concentration of about 1 mg per mL.

Standard preparation—Dissolve about 40 mg of USP Phenobarbital RS, accurately weighed, in 4.0 mL of *Internal standard solution*, and evaporate the solvent with the aid of a stream of nitrogen. Dissolve the residue in 20 mL of methanol, add 10 mL of *pH 4.5 buffer solution*, and mix.

Assay preparation—Pipet a quantity of Elixir, equivalent to about 20 mg of phenobarbital, into a separator. Add 1 mL of hydrochloric acid, and extract with three 10-mL portions of dichloromethane. Filter the extracts through a funnel containing about 15 mg of anhydrous sodium sulfate supported on a small pledget of glass wool. Collect the extracts in a 50-mL volumetric flask containing 2.0 mL of *Internal standard solution*, dilute with dichloromethane to volume, and evaporate about 5 mL of the extract with the aid of a stream of nitrogen. Dissolve the residue in 1 mL of methanol, add 0.5 mL of *pH 4.5 buffer solution*, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Phenobarbital.* Calculate the quantity, in mg, of $C_{12}H_{12}N_2O_3$ in each mL of the Elixir taken by the formula:

$$0.5(W/V)(R_U/R_S),$$

in which V is the volume, in mL, of Elixir taken, and the other terms are as defined therein.

Phenobarbital Tablets

» Phenobarbital Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{12}H_{12}N_2O_3$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—*USP Phenobarbital RS.*

Identification—

A: Triturate a quantity of finely powdered Tablets, equivalent to about 60 mg of phenobarbital, with 50 mL of chloroform, and filter. Evaporate the clear filtrate to dryness, and dry at 105° for 2 hours: the residue so obtained responds to *Identification* test *A* under *Phenobarbital.*

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation*, both relative to the internal standard, as obtained in the *Assay.*

Dissolution ⟨711⟩—

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{12}H_{12}N_2O_3$ dissolved from ultraviolet absorbances at the wavelength of maximum absorbance at about 240 nm of filtered portions of the solution under test, suitably diluted with pH 9.6 alkaline borate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*), in comparison with a Standard solution having a known concentration of USP Phenobarbital RS in the same medium.

Tolerances—Not less than 75% (Q) of the labeled amount of $C_{12}H_{12}N_2O_3$ is dissolved in 45 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Procedure for content uniformity—Transfer 1 finely powdered Tablet to a 200-mL volumetric flask with the aid of, first, 10 mL of alcohol, and then about 150 mL of pH 9.6 alkaline borate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*). Shake the mixture vigorously, dilute with pH 9.6 alkaline borate buffer to volume, mix, and filter. Dilute the filtrate quantitatively with a 1 in 20 solution of alcohol in pH 9.6 alkaline borate buffer to obtain a test solution having a concentration of about 10 µg per mL. Concomitantly determine the absorbances of this solution and of a Standard solution of USP Phenobarbital RS in the same medium, having a known concentration of about 10 µg per mL, in 1-cm cells at the wavelength of maximum absorbance at about 240 nm, with a suitable spectrophotometer, using a 1 in 20 solution of alcohol in pH 9.6 alkaline borate buffer as the blank. Calculate the quantity, in mg, of $C_{12}H_{12}N_2O_3$ in the Tablet taken by the formula:

$$(TC/D)(A_U/A_S),$$

in which T is the labeled quantity, in mg, of phenobarbital in the Tablet, C is the concentration, in µg per mL, of USP Phenobarbital RS in the Standard solution, D is the concentration, in µg per mL, of phenobarbital in the test solution, on the basis of the labeled quantity per Tablet and the extent of dilution, and A_U and A_S are the absorbances of the test solution and the Standard solution, respectively.

Assay—

pH 4.5 buffer solution, Mobile phase, Internal standard solution, Standard preparation, and *Chromatographic system*—Prepare as directed in the *Assay* under *Phenobarbital.*

Assay preparation—Weigh and finely powder not less than 20 Tablets. Weigh accurately a portion of the powder, equivalent to about 20 mg of phenobarbital, add 15.0 mL of *Internal standard solution,* mix, and sonicate for 15 minutes. Filter through a membrane filter (0.5 µm or finer porosity) before use.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Phenobarbital.* Calculate the quantity, in mg, of $C_{12}H_{12}N_2O_3$ in the portion of Tablets taken by the formula:

$$(W)(R_U/R_S),$$

in which the terms are as defined therein.

Phenobarbital Tablets, Theophylline, Ephedrine Hydrochloride, and—*see* Theophylline, Ephedrine Hydrochloride, and Phenobarbital Tablets

Phenobarbital Sodium

$C_{12}H_{11}N_2NaO_3$ 254.22

2,4,6(1*H*,3*H*,5*H*)-Pyrimidinetrione, 5-ethyl-5-phenyl-, monosodium salt.

Sodium 5-ethyl-5-phenylbarbiturate [*57-30-7*].

» Phenobarbital Sodium contains not less than 98.5 percent and not more than 101.0 percent of $C_{12}H_{11}N_2NaO_3$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Phenobarbital RS.*

Completeness of solution—Mix 1.0 g with 10 mL of carbon dioxide–free water: after 1 minute, the solution is clear and free from undissolved solid.

Identification—

A: Dissolve about 50 mg of Phenobarbital Sodium in 15 mL of water in a separator, add 2 mL of hydrochloric acid, shake, and extract the liberated phenobarbital with four 25-mL portions of chloroform. Filter the combined extracts through a pledget of cotton or other suitable filter into a beaker, and wash the separator and the filter with several small portions of chloroform. Evaporate a 50-mL portion of the chloroform solution of phenobarbital on a steam bath with the aid of a current of air. Add 10 mL of ether, again evaporate, and dry the residue at 105° for 2 hours: the infrared absorption spectrum of a potassium bromide dispersion of the residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Phenobarbital RS.

B: Ignite about 200 mg: the residue effervesces with acids, and responds to the tests for *Sodium* ⟨191⟩.

C: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation,* both relative to the internal standard, as obtained in the *Assay.*

pH ⟨791⟩: between 9.2 and 10.2, in the solution prepared in the test for *Completeness of solution.*

Loss on drying ⟨731⟩—Dry it at 150° for 4 hours: it loses not more than 7.0% of its weight.

Heavy metals ⟨231⟩—Dissolve 2.0 g in 52 mL of water. Add slowly, with vigorous stirring, 8 mL of 1 *N* hydrochloric acid, and filter, discarding the first 5 mL of the filtrate. Dilute 20 mL of the subsequent filtrate with water to 25 mL: the limit is 0.003%.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—

pH 4.5 buffer solution, Mobile phase, Internal standard solution, Standard preparation, and *Chromatographic system*—Prepare as directed in the *Assay* under *Phenobarbital.*

Assay preparation—Transfer about 22 mg of Phenobarbital Sodium, accurately weighed, to a conical flask, add 15.0 mL of *Internal standard solution,* mix, and sonicate for 15 minutes. Filter through a membrane filter (0.5 µm or finer porosity) before use.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Phenobarbital.* Calculate the quantity, in mg, of $C_{12}H_{11}N_2NaO_3$ in the portion of Phenobarbital Sodium taken by the formula:

$$(254.22/232.24)(W)(R_U/R_S),$$

in which 254.22 and 232.24 are the molecular weights of phenobarbital sodium and phenobarbital, respectively, and the other terms are as defined therein.

Phenobarbital Sodium Injection

» Phenobarbital Sodium Injection is a sterile solution of Phenobarbital Sodium in a suitable solvent. Phenobarbital may be substituted for the equivalent amount of Phenobarbital Sodium, for adjustment of the pH. The Injection contains the equivalent of not less than 90.0 percent and not more than 105.0 percent of the labeled amount of $C_{12}H_{11}N_2NaO_3$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass.

Labeling—The label indicates that the Injection is not to be used if it contains a precipitate.

USP Reference standards ⟨11⟩—*USP Phenobarbital RS. USP Endotoxin RS.*

Identification—

A: Transfer to a separator a volume of Injection, equivalent to about 50 mg of phenobarbital sodium, add 15 mL of water, add 2 mL of hydrochloric acid, shake, and extract the liberated phenobarbital with four 25-mL portions of chloroform. Filter the combined extracts through a pledget of cotton or other suitable filter into a beaker, and wash the separator and the filter with several small portions of chloroform. Evaporate a 50-mL portion of the chloroform solution of phenobarbital on a steam bath with

the aid of a current of air. Add 10 mL of ether, again evaporate, and dry the residue at 105° for 2 hours: the infrared absorption spectrum of a potassium bromide dispersion of the residue so obtained exhibits maxima only at the same wavelengths as that of a similar preparation of USP Phenobarbital RS.

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that of the *Standard preparation*, both relative to the internal standard, as obtained in the *Assay*.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.3 USP Endotoxin Unit per mg of phenobarbital sodium.

pH ⟨791⟩: between 9.2 and 10.2.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

pH 4.5 buffer solution, *Mobile phase*, *Internal standard solution*, and *Chromatographic system*—Prepare as directed in the *Assay* under *Phenobarbital*.

Standard preparation—Transfer about 15 mg of USP Phenobarbital RS, accurately weighed, to a 50-mL volumetric flask, add 25 mL of *Mobile phase*, and sonicate if necessary to dissolve. Add 15.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, and mix to obtain a solution having a known concentration of about 0.3 mg of USP Phenobarbital RS per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 65 mg of phenobarbital sodium, to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Transfer 25.0 mL of this solution to a 50-mL volumetric flask, add 15.0 mL of *Internal standard solution*, dilute with *Mobile phase* to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Phenobarbital*. Calculate the quantity, in mg, of $C_{12}H_{11}N_2NaO_3$ in each mL of the Injection taken by the formula:

$$(254.22/232.24)(4W/V)(R_U/R_S),$$

in which 254.22 and 232.24 are the molecular weights of phenobarbital sodium and phenobarbital, respectively, V is the volume, in mL, of Injection taken, and the other terms are as defined therein.

Sterile Phenobarbital Sodium

» Sterile Phenobarbital Sodium is Phenobarbital Sodium suitable for parenteral use.

Packaging and storage—Preserve in *Containers for Sterile Solids* as described under *Injections* ⟨1⟩.

USP Reference standards ⟨11⟩—*USP Phenobarbital RS*. *USP Endotoxin RS*.

Constituted solution—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* ⟨1⟩.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.8 USP Endotoxin Unit per mg of phenobarbital sodium.

Other requirements—It conforms to the Definition, responds to the *Identification* tests, and meets the requirements for *Completeness of solution*, *pH*, *Loss on drying*, *Heavy metals*, and *Assay* under *Phenobarbital Sodium*. It meets also the requirements for *Sterility Tests* ⟨71⟩, *Uniformity of Dosage Units* ⟨905⟩, and *Labeling* under *Injections* ⟨1⟩.

Phenol

C_6H_6O 94.11
Phenol.
Phenol [*108-95-2*].

» Phenol contains not less than 99.0 percent and not more than 100.5 percent of C_6H_6O, calculated on the anhydrous basis. It may contain a suitable stabilizer.

Caution—Avoid contact with skin, since serious burns may result.

Packaging and storage—Preserve in tight, light-resistant containers.

Labeling—Label it to indicate the name and amount of any substance added as a stabilizer.

Clarity of solution and reaction—A solution (1 in 15) is clear, and is neutral or acid to litmus paper.

Identification—

A: To a solution add bromine TS: a white precipitate is formed, and it dissolves at first but becomes permanent as more of the reagent is added.

B: To 10 mL of a solution (1 in 100) add 1 drop of ferric chloride TS: a violet color is produced.

Congealing temperature ⟨651⟩: not lower than 39°.

Water, *Method I* ⟨921⟩: not more than 0.5%.

Limit of nonvolatile residue—Heat about 5 g, accurately weighed, in a tared porcelain dish on a steam bath until it has evaporated, and dry the residue at 105° for 1 hour: not more than 0.05% of residue remains.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.

Assay—Place about 2 g of Phenol, accurately weighed, in a 1000-mL volumetric flask, dilute with water to volume, and mix. Pipet 20 mL of the solution into an iodine flask, add 30.0 mL of 0.1 *N* bromine VS, then add 5 mL of hydrochloric acid, and immediately insert the stopper. Shake the flask repeatedly during 30 minutes, allow it to stand for 15 minutes, add quickly 5 mL of potassium iodide solution (1 in 5), taking precautions against the escape of bromine vapor, and at once insert the stopper in the flask. Shake thoroughly, remove the stopper, and rinse it and the neck of the flask with a small quantity of water, so that the washing flows into the flask. Add 1 mL of chloroform, shake the mixture, and titrate the liberated iodine with 0.1 *N* sodium thiosulfate VS, adding 3 mL of starch TS as the endpoint is approached. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.1 *N* bromine is equivalent to 1.569 mg of C_6H_6O.

Liquefied Phenol

» Liquefied Phenol is Phenol maintained in a liquid condition by the presence of about 10 percent of water. It contains not less than 89.0 percent by weight of C_6H_6O. It may contain a suitable stabilizer.

Caution—Avoid contact with skin, since serious burns may result.

NOTE—When phenol is to be mixed with a fixed oil, mineral oil, or white petrolatum, use crystalline Phenol, not Liquefied Phenol.

Packaging and storage—Preserve in tight, light-resistant containers.

Labeling—Label it to indicate the name and amount of any substance added as a stabilizer.

Distilling range, *Method I* ⟨721⟩: not higher than 182.5°, an air-cooled condenser being used.

Organic volatile impurities, *Method I* ⟨467⟩: meets the requirements.