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USP 40
NF 35

Volume 1

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2017

USP 40

THE UNITED STATES PHARMACOPEIA

NF 35

THE NATIONAL FORMULARY

Volume 1

*By authority of the United States Pharmacopeial Convention
Prepared by the Council of Experts and its Expert Committees*

Official from May 1, 2017

The designation on the cover of this publication, "USP NF 2017," is for ease of identification only. The publication contains two separate compendia: *The United States Pharmacopeia*, Fortieth Revision, and *The National Formulary*, Thirty-Fifth Edition.

THE UNITED STATES PHARMACOPEIAL CONVENTION
12601 Twinbrook Parkway, Rockville, MD 20852

SIX-MONTH IMPLEMENTATION GUIDELINE

The *United States Pharmacopeia–National Formulary* and its supplements become official **six months** after being released to the public. The *USP–NF*, which is released on November 1 of each year, becomes official on May 1 of the following year. This six-month implementation timing gives users more time to bring their methods and procedures into compliance with new and revised *USP–NF* requirements.

The table below describes the official dates of the *USP–NF* and its supplements. The 2016 *USP 39–NF 34*, and its supplements, *Interim Revision Announcements (IRAs)* and *Revision Bulletins* to that edition, will be official until May 1, 2017, at which time the *USP 40–NF 35* becomes official.

Publication	Release Date	Official Date	Official Until
<i>USP 40–NF 35</i>	November 1, 2016	May 1, 2017	May 1, 2018 (except as superseded by supplements, <i>IRAs</i> , and <i>Revision Bulletins</i>)
<i>First Supplement to the USP 40–NF 35</i>	February 1, 2017	August 1, 2017	May 1, 2018 (except as superseded by <i>Second Supplement</i> , <i>IRAs</i> , and <i>Revision Bulletins</i>)
<i>Second Supplement to the USP 40–NF 35</i>	June 1, 2017	December 1, 2017	May 1, 2018 (except as superseded by <i>IRAs</i> and <i>Revision Bulletins</i>)
<i>USP 41–NF 36</i>	November 1, 2017	May 1, 2018	May 1, 2019 (except as superseded by supplements, <i>IRAs</i> , and <i>Revision Bulletins</i>)

The table below gives the details of the *IRAs* that will apply to *USP 40–NF 35*.

IRA	PF Posting Date	Comment Due Date	IRA Posting Date	IRA Official Date
42(1)	January 4, 2017	March 31, 2017	May 27, 2017	July 1, 2017
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42(5)	September 1, 2017	November 30, 2017	January 27, 2018	March 1, 2018
42(6)	November 1, 2017	January 31, 2018	March 31, 2018	May 1, 2018

Revision Bulletins published on the USP website become official on the date specified in the *Revision Bulletin*.

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Peppermint Oil: Colorless or pale yellow liquid, having a strong, penetrating, characteristic odor and a pungent taste, followed by a sensation of cold when air is drawn into the mouth. *NF category:* Flavors and fragrance.

Peppermint Spirit: A clear, colorless liquid with a peppermint fragrance. Freely soluble in methanol and in diethyl ether; soluble in water. *NF category:* Flavors and fragrance.

Peppermint Water: *NF category:* Vehicle (flavored and/or sweetened).

Perflubron: Clear, colorless, practically odorless liquid.

Pergolide Mesylate: White to off-white powder. Sparingly soluble in methanol; slightly soluble in water, in dehydrated alcohol, and in chloroform; very slightly soluble in acetone; practically insoluble in ether.

Add the following:

▲Perindopril Erbumine: White or off-white, crystalline powder; freely soluble in water and in alcohol; sparingly soluble in methylene chloride. ▲*USP40*

Perphenazine: White to creamy white, odorless powder. Freely soluble in alcohol and in chloroform; soluble in acetone; practically insoluble in water.

Pertussis Immune Globulin: Transparent or slightly opalescent liquid, practically colorless, free from turbidity or particles, and practically odorless. May develop a slight, granular deposit during storage. Is standardized for agglutinating activity with the U.S. Standard Antipertussis Serum.

Petrolatum: Unctuous yellowish to light amber mass, having not more than a slight fluorescence even after being melted. Is transparent in thin layers. Is free or practically free from odor and taste. Freely soluble in benzene, in carbon disulfide, in chloroform, and in turpentine oil; soluble in ether, in solvent hexane, and in most fixed and volatile oils; practically insoluble in cold and hot alcohol and in cold dehydrated alcohol; insoluble in water. *NF category:* Ointment base; emollient.

Hydrophilic Petrolatum: *NF category:* Ointment base.

White Petrolatum: White or faintly yellowish, unctuous mass, transparent in thin layers even after cooling to 0°. Freely soluble in benzene, in carbon disulfide, and in chloroform; soluble in ether, in solvent hexane, and in most fixed and volatile oils; slightly soluble in cold or hot alcohol, and in cold dehydrated alcohol; insoluble in water. *NF category:* Ointment base.

Phenazopyridine Hydrochloride: Light or dark red to dark violet, crystalline powder. Is odorless, or has a slight odor. Melts at about 235°, with decomposition. Slightly soluble in water, in alcohol, and in chloroform.

Phendimetrazine Tartrate: White, odorless, crystalline powder. Freely soluble in water; sparingly soluble in warm alcohol; insoluble in chloroform, in acetone, in ether, and in benzene. Phendimetrazine base is extracted by organic solvents from alkaline solution.

Phenelzine Sulfate: White to yellowish white powder, having a characteristic odor. Freely soluble in water; practically insoluble in alcohol, in chloroform, and in ether.

Pheniramine Maleate: White, crystalline powder having a faint amine-like odor. Soluble in water and in alcohol.

Phenmetrazine Hydrochloride: White to off-white, crystalline powder. Very soluble in water; freely soluble in alcohol and in chloroform.

Phenobarbital: White, odorless, glistening, small crystals, or white, crystalline powder, which may exhibit polymorphism. Is stable in air. Its saturated solution has a pH of about 5. Soluble in alcohol, in ether, and in solutions of fixed alkali hydroxides and carbonates; sparingly soluble in chloroform; very slightly soluble in water.

Phenobarbital Sodium: Flaky crystals, or white, crystalline granules, or white powder. Is odorless, has a bitter

taste, and is hygroscopic. Its solutions are alkaline to phenolphthalein TS, and decompose on standing. Very soluble in water; soluble in alcohol; practically insoluble in ether and in chloroform.

Phenol: Colorless to light pink, interlaced or separate, needle-shaped crystals, or white to light pink, crystalline mass. Has a characteristic odor. Is liquefied by warming and by the addition of 10% of water. Boils at about 182°, and its vapor is flammable. Gradually darkens on exposure to light and air. Very soluble in alcohol, in glycerin, in chloroform, in ether, and in fixed and volatile oils; soluble in water; sparingly soluble in mineral oil. *NF category:* Antimicrobial preservative.

Liquefied Phenol: Colorless to pink liquid, which may develop a red tint upon exposure to air or light. Has a characteristic, somewhat aromatic odor. It whitens and cauterizes the skin and mucous membranes. Specific gravity is about 1.065. Miscible with alcohol, with ether, and with glycerin. A mixture of equal volumes of Liquefied Phenol and glycerin is miscible with water.

Camphorated Phenol Topical Gel: Clear, colorless, oily gel.

Phenolsulfonphthalein: A bright-red to dark-red, crystalline powder. Slightly soluble in alcohol; very slightly soluble in water.

Phenoxyethanol: A colorless, slightly viscous liquid. Slightly soluble in water, in peanut oil, and in olive oil. Miscible with acetone, with alcohol, and with glycerol. *NF category:* Antimicrobial preservative.

Phensuximide: White to off-white, crystalline powder. Is odorless, or has not more than a slight odor. Very soluble in chloroform; soluble in alcohol; slightly soluble in water.

Phentermine Hydrochloride: White, odorless, hygroscopic, crystalline powder. Soluble in water and in the lower alcohols; slightly soluble in chloroform; insoluble in ether.

Phentolamine Mesylate: White or off-white, odorless, crystalline powder. Its solutions are acid to litmus, having a pH of about 5, and slowly deteriorate. Melts at about 178°. Freely soluble in water and in alcohol; slightly soluble in chloroform.

Phenylalanine: White, odorless crystals, having a slightly bitter taste. Sparingly soluble in water; very slightly soluble in methanol, in alcohol, and in dilute mineral acids.

Phenylbenzimidazole Sulfonic Acid: White to ivory-colored, odorless powder. Soluble in alcohol; practically insoluble in oily solvents and in water. Its salts are freely soluble in water.

Phenylbutazone: White to off-white, odorless, crystalline powder. Freely soluble in acetone and in ether; soluble in alcohol; very slightly soluble in water.

Phenylephrine Bitartrate: White or almost white powder or colorless crystals. Freely soluble in water.

Phenylephrine Hydrochloride: White or practically white, odorless crystals, having a bitter taste. Freely soluble in water and in alcohol.

Phenylephrine Hydrochloride Nasal Solution: Clear, colorless or slightly yellow, odorless liquid. Is neutral or acid to litmus.

Phenylephrine Hydrochloride Ophthalmic Solution: Clear, colorless or slightly yellow liquid, depending on the concentration.

Phenylethyl Alcohol: Colorless liquid, having a rose-like odor and a sharp, burning taste. Very soluble in alcohol, in fixed oils, in glycerin, and in propylene glycol; sparingly soluble in water; slightly soluble in mineral oil. *NF category:* Antimicrobial preservative.

Phenylmercuric Acetate: White to creamy white, crystalline powder, or small white prisms or leaflets. Is odorless. Soluble in alcohol and in acetone; slightly soluble in water. *NF category:* Antimicrobial preservative.

tion (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 *Diluent*, collecting the aqueous extracts in a 100-mL volumetric flask, and dilute with *Diluent* to volume.

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum at about 256 nm

Cell: 1 cm

Blank: 0.5 N hydrochloric acid

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of phenmetrazine hydrochloride ($C_{11}H_{15}NO \cdot HCl$) in the portion of Tablets taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

- A_U = absorbance of the *Sample solution*
 A_S = absorbance of the *Standard solution*
 C_S = concentration of USP Phenmetrazine Hydrochloride RS in the *Standard solution* (mg/mL)
 C_U = nominal concentration of phenmetrazine hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 93.0%–107.0%

PERFORMANCE TESTS

• DISSOLUTION (711)

Medium: Water; 900 mL

Apparatus 2: 50 rpm

Time: 45 min

Standard solution: USP Phenmetrazine Hydrochloride RS in *Medium*

Sample solution: A filtered portion of the solution under test, suitably diluted with *Medium*, if necessary, to a concentration similar to that of the *Standard solution* in the same *Medium*

Instrumental conditions

Mode: UV

Analytical wavelength: Maximum at about 256 nm

Analysis: Determine the percentage of the labeled amount of phenmetrazine hydrochloride ($C_{11}H_{15}NO \cdot HCl$) dissolved.

Tolerances: NLT 75% (Q) of the labeled amount of phenmetrazine hydrochloride ($C_{11}H_{15}NO \cdot HCl$) is dissolved.

• UNIFORMITY OF DOSAGE UNITS (905):

Meet the requirements

ADDITIONAL REQUIREMENTS

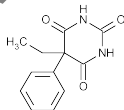
• PACKAGING AND STORAGE:

Preserve in tight containers.

• USP REFERENCE STANDARDS (11)

USP Phenmetrazine Hydrochloride RS

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 IR 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 USP 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%.

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 for *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 Oral Solution

» Phenobarbital Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of phenobarbital ($C_{12}H_{12}N_2O_3$).

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

USP Reference standards (11)—
USP Phenobarbital RS

Identification—

A: Place 10 mL of Oral Solution 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 meets the requirements for *Identification* test A under *Phenobarbital*.

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

Alcohol Determination, 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*.

Diluent—Prepare a mixture of methanol and *pH 4.5 Buffer solution* (2:1).

Internal standard solution—Dissolve a sufficient quantity of caffeine in *Diluent* to obtain a solution having a concentration of about 1.7 mg per mL.

Standard preparation—Transfer about 33 mg of USP Phenobarbital RS, accurately weighed, to a 25-mL volumetric flask containing 2.0 mL of *Internal standard solution*. Dilute with *Diluent* to volume, and mix.

Assay preparation—Transfer a quantity of Oral Solution, equivalent to about 33 mg of phenobarbital, to a 25-mL volumetric flask containing 2.0 mL of *Internal standard solution*. Dilute with *Diluent* to volume, and mix.

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

$$W(R_U / R_S)$$

in which the terms are as defined therein.

Phenobarbital Compounded Oral Suspension

DEFINITION

Phenobarbital Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amount of phenobarbital ($C_{12}H_{12}N_2O_3$).

Prepare Phenobarbital Compounded Oral Suspension 10 mg/mL as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* (795)).

Phenobarbital tablets ^a equivalent to	1.2 g of phenobarbital
Vehicle: a 1:1 mixture of Ora-Sweet ^b (regular or sugar-free) and Ora-Plus, ^b a sufficient quantity to make	120 mL

^a Phenobarbital 60-mg tablets, Excellium Pharmaceutical, Inc., Fairfield, NJ.

^b Paddock Laboratories, Minneapolis, MN.

Calculate the required quantity of each ingredient for the total amount to be prepared. Place the required number of *Phenobarbital tablets* in a suitable mortar, and comminute to a fine powder with a pestle. Add the *Vehicle* in small portions, and triturate to make a smooth paste. Add increasing volumes of the *Vehicle* to make a phenobarbital liquid that is pourable. Transfer the contents of the mortar, stepwise and quantitatively, to a calibrated bottle. Add enough of the *Vehicle* to bring to final volume, and mix well.

ASSAY

• PROCEDURE

Mobile phase: Acetonitrile and water (30:70). Adjust with dilute sulfuric acid to a pH of 3.0.

Standard stock solution: 0.4 mg/mL of USP Phenobarbital RS in *Mobile phase*

Standard solution: 20 µg/mL of phenobarbital prepared from *Standard stock solution* and *Mobile phase*

Sample solution: Shake thoroughly by hand each bottle of Oral Suspension. Prepare 20 µg/mL of phenobarbital from Oral Suspension and *Mobile phase*, and centrifuge.

Chromatographic system

(See *Chromatography* (621), *System Suitability*.)

Mode: LC

Detector: UV 235 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 60°

Flow rate: 1.0 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

[NOTE—The retention time for phenobarbital is about 6.8 min.]

Suitability requirements

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of phenobarbital ($C_{12}H_{12}N_2O_3$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Phenobarbital RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of phenobarbital in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

• **PH** (791): 3.8–4.8

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Package in tight, light-resistant containers. Store at controlled room temperature.

• **BEYOND-USE DATE:** NMT 115 days after the date on which it was compounded, when stored at controlled room temperature

• **LABELING:** Label it to indicate that it is to be well shaken before use, and to state the *Beyond-Use Date*.

- **USP REFERENCE STANDARDS** <11>
USP Phenobarbital RS

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 UV absorbances at the wavelength of maximum absorbance at about 240 nm on 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.

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 fewer 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 having a 0.5- μ m 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 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.

Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

USP Reference standards <11>—

USP Endotoxin RS

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 IR 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 relative retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, 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.

Delete the following:

• **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%. • (Official 1-Jan-2018)

Other requirements—Where the label states that Phenobarbital Sodium is sterile, it meets the requirements for *Sterility Tests* <71> and for *Bacterial endotoxins* under *Phenobarbital Sodium for Injection*. Where the label states that Phenobarbital Sodium must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements for *Bacterial endotoxins* under *Phenobarbital Sodium for Injection*.

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. Pass through a membrane filter having a 0.5- μ m 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 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 Endotoxin RS

USP Phenobarbital 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 IR 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 Test (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 and Implanted Drug Products* (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.

Phenobarbital Sodium for Injection

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

Change to read:

Packaging and storage—Preserve as described in *Packaging and Storage Requirements* (659), *Injection Packaging*, *Packaging for constitution* (CN 1-May-2017).

USP Reference standards (11)—

USP Endotoxin RS

USP Phenobarbital RS

Constituted solution—At the time of use, it meets the requirements for *Injections and Implanted Drug Products* (1), *Specific Tests*, *Completeness and clarity of solutions*.

Bacterial Endotoxins Test (85)—It contains not more than 0.8 USP Endotoxin Unit per mg of phenobarbital sodium.

Change to read:

Other requirements—It conforms to the Definition, responds to the *Identification* tests, and meets the requirements for *Completeness of solution*, *pH*, *Loss on drying*, *•* (Official 1-Jan-2018) and *Assay* under *Phenobarbital Sodium*. It meets also the requirements for *Sterility Tests* (71), *Uniformity of Dosage Units* (905), and *Labeling* (7), *Labels and Labeling for Injectable Products*.

Phenol



C_6H_6O
Phenol [108-95-2].

94.11

DEFINITION

Phenol contains NLT 99.0% and NMT 100.5% of phenol (C_6H_6O), calculated on the anhydrous basis. It may contain a suitable stabilizer.

IDENTIFICATION

[CAUTION]—Avoid contact with skin because serious burns may result.]