Assay—

Buffer solution, Mobile phase, Standard preparation, System suitability preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Pilocarpine.*

Assay preparation—Select not less than 10 Ocular Systems. Cut each System into 4 pieces, transfer quantitatively to a 500-mL volumetric flask, and rinse all cutting utensils with 20 to 30 mL of methanol into the flask. Make additional rinses of the utensils with about 250 mL of *Mobile phase*, and collect all the rinses in the flasks. Allow the flasks to stand for 30 minutes, sonicate for about 15 minutes, dilute with water to volume, and mix. Transfer an aliquot of the supernatant, equivalent to 6 mg of pilocarpine to a 200-mL volumetric flask, dilute with water to volume, mix, and filter.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Pilocarpine.* Calculate the quantity, in mg, of Pilocarpine. Calculate the quantity, in mg, of Pilocarpine in each ocular system taken by the formula:

$$(208.26/271.27)(10/V)(C/N)(r_U/r_S),$$

in which 208.26 and 271.27 are the molecular weights of pilocarpine and pilocarpine nitrate, respectively, V is the volume, in mL, of the supernatant taken (see *Assay preparation*), C is the concentration, in mg per mL, of USP Pilocarpine Nitrate RS in the *Standard preparation*, N is the number of Ocular Systems taken, and r_U and r_S are the peak responses for pilocarpine obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Pilocarpine Hydrochloride

$C_{11}H_{16}N_2O_2 \cdot HCl$ 244.72

2(3*H*)-Furanone, 3-ethyldihydro-4-[(1-methyl-1*H*-imidazol-5-yl)methyl]-, monohydrochloride, (3*S*-*cis*)-.

Pilocarpine monohydrochloride [*54-71-7*].

» Pilocarpine Hydrochloride contains not less than 98.5 percent and not more than 101.0 percent of $C_{11}H_{16}N_2O_2 \cdot HCl$, calculated on the dried basis.

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

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

Identification—

A: *Infrared Absorption* ⟨197M⟩.

B: A solution (1 in 20) responds to the tests for *Chloride* ⟨191⟩.

Melting range ⟨741⟩: between 199° and 205°, but the range between beginning and end of melting does not exceed 3°.

Specific rotation ⟨781S⟩: between +88.5° and +91.5°.

Test solution: 20 mg per mL, in water.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 3.0% of its weight.

Readily carbonizable substances ⟨271⟩—Dissolve 250 mg in 5 mL of sulfuric acid TS: the solution has no more color than *Matching Fluid B.*

Ordinary impurities ⟨466⟩—

Test solution: dehydrated alcohol.

Standard solution: dehydrated alcohol.

Eluant: a mixture of hexanes, dehydrated alcohol, and ammonium hydroxide (70 : 30 : 1).

Visualization: 17.

Limits: not more than 1%.

Other alkaloids—Dissolve 200 mg in 20 mL of water, and divide the solution into two portions. To one portion add a few drops of 6 N ammonium hydroxide, and to the other add a few drops of potassium bromate TS: no turbidity is produced in either solution.

Assay—Dissolve about 500 mg of Pilocarpine Hydrochloride, accurately weighed, in a mixture of 20 mL of glacial acetic acid and 10 mL of mercuric acetate TS, warming slightly to effect solution. Cool the solution to room temperature, add 2 drops of crystal violet TS, and titrate with 0.1 N perchloric acid VS. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 24.47 mg of $C_{11}H_{16}N_2O_2 \cdot HCl$.

Pilocarpine Hydrochloride Ophthalmic Solution

» Pilocarpine Hydrochloride Ophthalmic Solution is a sterile, buffered, aqueous solution of Pilocarpine Hydrochloride. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{11}H_{16}N_2O_2 \cdot HCl$. It may contain suitable antimicrobial agents and stabilizers, and suitable additives to increase its viscosity.

Packaging and storage—Preserve in tight containers.

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

Identification—The 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.*

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 3.5 and 5.5.

Assay—

Mobile phase—Mix 300 mL of a 1 in 50 solution of ammonium hydroxide in isopropyl alcohol and 700 mL of *n*-hexane. Filter through a 0.5-µm filter before using.

Standard preparation—Using an accurately weighed quantity of USP Pilocarpine Hydrochloride RS, prepare a solution having a known concentration of about 1.6 mg per mL.

Assay preparation—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 80 mg of pilocarpine hydrochloride, to a 50-mL volumetric flask. Dilute with methanol to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm × 25-cm column that contains packing L3. The flow rate is about 2 mL per minute. Chromatograph three replicate injections of the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation 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 by means of a suitable microsyringe or sampling valve, record the chromatograms, and measure the responses for the major peaks. The retention time is about 16 minutes for pilocarpine hydrochloride. Calculate the quantity, in mg, of $C_{11}H_{16}N_2O_2 \cdot HCl$ in each mL of the Ophthalmic Solution taken by the formula:

$$50(C/V)(r_U/r_S),$$

in which C is the concentration, in mg per mL, of USP Pilocarpine Hydrochloride RS in the *Standard preparation*, V is the volume, in mL, of Ophthalmic Solution taken, and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Pilocarpine Nitrate

$C_{11}H_{16}N_2O_2 \cdot HNO_3$ 271.27

2(3*H*)-Furanone, 3-ethyldihydro-4-[(1-methyl-1*H*-imidazol-5-yl)methyl]-, (3*S*-*cis*)-, mononitrate.

Pilocarpine mononitrate [*148-72-1*].

» Pilocarpine Nitrate contains not less than 98.5 percent and not more than 101.0 percent of $C_{11}H_{16}N_2O_2 \cdot NO_3$, calculated on the dried basis.

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

USP Reference standards ⟨11⟩—*USP Pilocarpine Nitrate RS.*

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: Mix a solution (1 in 10) with an equal volume of ferrous sulfate TS, and superimpose the mixture upon 5 mL of sulfuric acid contained in a test tube: the zone of contact becomes brown.

Melting range ⟨741⟩: between 171° and 176°, with decomposition, but the range between beginning and end of melting does not exceed 3°.

Specific rotation ⟨781S⟩: between +79.5° and +82.5°.
Test solution: 20 mg per mL, in water.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 2.0% of its weight.

Readily carbonizable substances ⟨271⟩—Dissolve 100 mg in 5 mL of sulfuric acid TS: the solution has no more color than *Matching Fluid A*.

Chloride—To 5 mL of a solution (1 in 50), acidified with nitric acid, add a few drops of silver nitrate TS: no opalescence is produced immediately.

Other alkaloids—Dissolve 200 mg in 20 mL of water, and divide the solution into two portions. To one portion add a few drops of 6 N ammonium hydroxide and to the other add a few drops of potassium dichromate TS: no turbidity is produced in either solution.

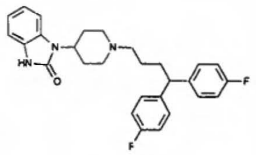
Assay—Dissolve about 600 mg of Pilocarpine Nitrate, accurately weighed, in 30 mL of glacial acetic acid, warming slightly to effect solution. Cool to room temperature, and titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 27.13 mg of $C_{11}H_{16}N_2O_2 \cdot NO_3$.

Pilocarpine Nitrate Ophthalmic Solution

» Pilocarpine Nitrate Ophthalmic Solution is a sterile, buffered, aqueous solution of Pilocarpine Nitrate. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{11}H_{16}N_2O_2 \cdot HNO_3$. It may contain suitable antimicrobial agents and stabilizers, and suitable additives to increase its viscosity.

Packaging and storage—Preserve in tight, light-resistant containers.
USP Reference standards ⟨11⟩—*USP Pilocarpine Nitrate RS.*
Identification—
A: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation* obtained as directed in the *Assay.*
B: It responds to *Identification* test *B* under *Pilocarpine Nitrate.*
Sterility ⟨71⟩: meets the requirements.
pH ⟨791⟩: between 4.0 and 5.5.
Assay—Proceed with Ophthalmic Solution as directed in the *Assay* under *Pilocarpine Hydrochloride Ophthalmic Solution*, except to read pilocarpine nitrate instead of pilocarpine hydrochloride throughout and to calculate the quantity, in mg, of $C_{11}H_{16}N_2O_2 \cdot HNO_3$ in each mL of the Ophthalmic Solution taken by the formula given therein.

Pimozide



$C_{28}H_{29}F_2N_3O$ 461.55
2*H*-Benzimidazol-2-one, 1-[1-[4,4-bis(4-fluorophenyl)butyl]-4-piperidinyl]-1,3-dihydro-.
1-[1-[4,4-Bis(*p*-fluorophenyl)butyl]-4-piperidyl]-2-benzimidazolinone [*2062-78-4*].

» Pimozide contains not less than 98.0 percent and not more than 102.0 percent of $C_{28}H_{29}F_2N_3O$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.
USP Reference standards ⟨11⟩—*USP Pimozide RS.*
Identification—
A: *Infrared Absorption* ⟨197K⟩.
B: *Ultraviolet Absorption* ⟨197U⟩—
Solution: 35 µg per mL.
Medium: 0.1 N hydrochloric acid in methanol (1 in 10).
Melting range, *Class I* ⟨741⟩: between 216° and 220°.
Loss on drying ⟨731⟩—Dry it in vacuum at 80° for 4 hours: it loses not more than 0.5% of its weight.
Residue on ignition ⟨281⟩: not more than 0.2%, a 2-g portion and a platinum crucible being used for the test.
Heavy metals, *Method II* ⟨231⟩: 0.002%.
Ordinary impurities ⟨466⟩
Test solution: chloroform.
Standard solution: chloroform.
Eluant: a mixture of cyclohexane and acetone (1 : 1).
Visualization: 1, then 17.
Limit—The total of any ordinary impurities observed does not exceed 1.0%.
Organic volatile impurities, *Method V* ⟨467⟩: meets the requirements.
Solvent—Use dimethyl sulfoxide.
Assay—Dissolve about 320 mg of Pimozide, accurately weighed, in 40 mL of glacial acetic acid. Titrate with 0.1 N perchloric acid, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 46.16 mg of $C_{28}H_{29}F_2N_3O$.

Pimozide Tablets

» Pimozide Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{28}H_{29}F_2N_3O$.

Packaging and storage—Preserve in tight, light-resistant containers.
USP Reference standards ⟨11⟩—*USP Pimozide RS.*
Identification—The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the *Standard preparation*, both relative to the internal standard obtained in the *Assay.*

Polymyxin B Sulfate and Bacitracin Zinc Topical Powder

» Polymyxin B Sulfate and Bacitracin Zinc Topical Powder contains not less than 90.0 percent and not more than 130.0 percent of the labeled amounts of polymyxin B and bacitracin.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—*USP Polymyxin B Sulfate RS. USP Bacitracin Zinc RS.*

Microbial limits—Collect aseptically in a suitable container about 1 g from not less than 5 containers, dissolve in 500 mL of *Fluid A*, filter through a membrane filter as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined* under *Sterility Tests* ⟨71⟩, except to place the filter on the surface of Soybean–Casein Digest Agar Medium in a Petri dish, incubate for 7 days at 30° to 35°, and count the number of colonies on the filter. Similarly prepare a second specimen, except to incubate at 20° to 25°. Not more than 20 colonies are observed from the two specimens. It meets also the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa* under *Microbial Limit Tests* ⟨61⟩.

Water, *Method I* ⟨921⟩: not more than 7.0%.

Assay for polymyxin B—Proceed as directed for polymyxin B under *Antibiotics—Microbial Assays* ⟨81⟩, using an accurately weighed portion of Topical Powder, equivalent to about 5000 USP Polymyxin B Units, shaken with 20 mL of water in a suitable volumetric flask. Dilute with *Buffer No. 6* to volume, and mix. Dilute an accurately measured volume of the solution so obtained quantitatively with *Buffer No. 6* to obtain a *Test Dilution* having a concentration of polymyxin B assumed to be equal to the median dose level of the Standard.

Assay for bacitracin—Proceed as directed for bacitracin under *Antibiotics—Microbial Assays* ⟨81⟩, using an accurately weighed portion of Topical Powder, equivalent to about 800 USP Bacitracin Units, added to a 100-mL volumetric flask, dilute with 0.01 N hydrochloric acid to volume, and mix. Dilute this solution quantitatively with *Buffer No. 1* to obtain a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard. In preparing each test dilution of the Standard, add additional hydrochloric acid to each to obtain the same concentration of hydrochloric acid as in the *Test Dilution*.

Polymyxin B Sulfate and Hydrocortisone Otic Solution

» Polymyxin B Sulfate and Hydrocortisone Otic Solution is a sterile solution containing not less than 90.0 percent and not more than 130.0 percent of the labeled amount of polymyxin B, and not less than 90.0 percent and not more than 110.0 percent of the labeled amount of hydrocortisone ($C_{21}H_{30}O_5$). It may contain one or more suitable buffers and preservatives.

NOTE—Where Polymyxin B Sulfate and Hydrocortisone Otic Solution is prescribed without reference to the quantity of polymyxin B or hydrocortisone contained therein, a product containing 10,000 Polymyxin B Units and 5 mg of hydrocortisone per mL shall be dispensed.

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

USP Reference standards ⟨11⟩—*USP Polymyxin B Sulfate RS. USP Hydrocortisone RS.*

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 3.0 and 5.0.

Assay for polymyxin—Proceed with Otic Solution as directed under *Antibiotics—Microbial Assays* ⟨81⟩, using an accurately measured volume of Otic Solution diluted quantitatively with *Buffer No. 6* to yield a *Test Dilution* having a concentration assumed to be equal to the median dose level of the Standard.

Assay for hydrocortisone—

Mobile phase—Prepare a suitable solution of about 500 volumes of methanol, 500 volumes of water, and 1 volume of glacial acetic acid such that the retention time of hydrocortisone is between 6 and 10 minutes.

Standard preparation—Dissolve a suitable quantity of USP Hydrocortisone RS, accurately weighed, in a mixture of methanol and water (1 : 1) to obtain a solution having a known concentration of about 0.15 mg per mL.

Assay preparation—Transfer an accurately measured volume of Otic Solution, equivalent to about 15 mg of hydrocortisone, to a 100-mL volumetric flask, dilute with a mixture of methanol and water (1 : 1) to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph five replicate injections of the *Standard preparation*, and record the peak responses as directed for *Procedure*: the relative standard deviation 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 by means of a suitable microsyringe or sampling valve, adjusting the specimen size and other operating parameters such that the peak obtained from the *Standard preparation* is about 0.6 full scale. Record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{21}H_{30}O_5$ in each mL of the Otic Solution taken by the formula:

$$(100C/V)(H_U/H_S),$$

in which C is the concentration, in mg per mL, of USP Hydrocortisone RS in the *Standard preparation*, V is the volume, in mL, of the portion of Otic Solution taken, and H_U and H_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Polymyxin B Sulfate and Trimethoprim Ophthalmic Solution

» Polymyxin B Sulfate and Trimethoprim Ophthalmic Solution is a sterile, isotonic, aqueous solution of Polymyxin B Sulfate and Trimethoprim Sulfate or of Polymyxin B Sulfate and Trimethoprim that has been solubilized with Sulfuric Acid. It contains not less than 90.0 percent and not more than 130.0 percent of the labeled amount of polymyxin B and the equivalent of not less than 90.0 percent and not more than 110.0 percent of the labeled amount of trimethoprim ($C_{14}H_{18}N_4O_3$). It contains one or more preservatives.

Packaging and storage—Preserve in tight, light-resistant containers and store at controlled room temperature.

Labeling—Label it to indicate that it is to be stored at 15° to 25°, protected from light.

USP Reference standards ⟨11⟩—*USP Polymyxin B Sulfate RS. USP Trimethoprim RS.*

Identification—

A: It meets the requirements for polymyxin B under *Thin-Layer Chromatographic Identification Test* ⟨201BNP⟩.

B: The retention time of the trimethoprim peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay for trimethoprim*.

Sterility ⟨71⟩—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined.*

pH ⟨791⟩: between 4.0 and 6.2.

Assay for polymyxin B—Proceed as directed for polymyxin B under *Antibiotics—Microbial Assays* ⟨81⟩, using an accurately measured volume of Ophthalmic Solution, diluted quantitatively and stepwise with *Buffer No. 6*, to obtain a *Test Dilution* having a concentration of polymyxin B assumed to be equal to the median dose level of the Standard.

Assay for trimethoprim—

Diluent—Prepare a mixture of 0.01 N hydrochloric acid and acetonitrile (870 : 130).

Mobile phase—Dissolve 1.65 g of ethanesulfonic acid in 1000 mL of a mixture of water and acetonitrile (870 : 130). Adjust with 10 N sodium hydroxide or 0.1 N hydrochloric acid to a pH of 3.5. Pass this solution through a filter having a 0.5-µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Trimethoprim RS in *Diluent* to obtain a solution having a known concentration of about 0.04 mg per mL.

Assay preparation—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 1 mg of trimethoprim, to a 25-mL volumetric flask, dilute with *Diluent* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 30-cm column that contains packing L11. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 1.5, when calculated at 10% height of the peak; 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 trimethoprim ($C_{14}H_{18}N_4O_3$) in each mL of the Ophthalmic Solution taken by the formula:

$$25(C/V)(r_U/r_S),$$

in which C is the concentration, in mg per mL, of USP Trimethoprim RS in the *Standard preparation;* V is the volume, in mL, of Ophthalmic Solution taken to prepare the *Assay preparation;* and r_U and r_S are the trimethoprim peak area responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Polyvinyl Alcohol

$(C_2H_4O)_n$

Ethenol, homopolymer.

Vinyl alcohol polymer [*9002-89-5*].

» Polyvinyl Alcohol is a water-soluble synthetic resin, represented by the formula:

$$(C_2H_4O)_n,$$

in which the average value of n lies between 500 and 5000. It is prepared by 85 percent to 89 percent hydrolysis of polyvinyl acetate. The apparent viscosity, in centipoises, at 20°, of a solution containing 4 g of Polyvinyl Alcohol in each 100 g is not less than 85.0 percent and not more than 115.0 percent of that stated on the label.

Packaging and storage—Preserve in well-closed containers.

Viscosity—After determining the *Loss on drying*, weigh a quantity of undried Polyvinyl Alcohol, equivalent to 6.00 g on the dried basis. Over a period of seconds, transfer the test specimen with continuous slow stirring to about 140 mL of water contained in a suitable tared flask. When the specimen is well-wetted, increase the rate of stirring, avoiding mixing in excess air. Heat the mixture to 90°, and maintain the temperature at 90° for about 5 minutes. Discontinue heating, and continue stirring for 1 hour. Add water to make the mixture weigh 150 g. Resume stirring to obtain a homogenous solution. Filter the solution through a tared 100-mesh screen into a 250-mL conical flask, cool to about 15°, mix, and proceed as directed under *Viscosity* ⟨911⟩.

pH ⟨791⟩: between 5.0 and 8.0, in a solution (1 in 25).

Loss on drying ⟨731⟩—Dry it at 110° to constant weight: it loses not more than 5.0% of its weight.

Residue on ignition ⟨281⟩: not more than 2.0%.

Water-insoluble substances—Wash the tared 100-mesh screen used in the test for *Viscosity* with two 25-mL portions of water, and dry at 110° for 1 hour: not more than 6.4 mg of water-insoluble substances is found (0.1%).

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

Degree of hydrolysis—

Procedure—Transfer about 1 g of Polyvinyl Alcohol, previously dried at 110° to constant weight and accurately weighed, to a wide-mouth, 250-mL conical flask fitted by means of a suitable glass joint to a reflux condenser. Add 35 mL of dilute methanol (3 in 5), and mix gently to assure complete wetting of the solid. Add 3 drops of phenolphthalein TS, and add 0.2 N hydrochloric acid or 0.2 N sodium hydroxide, if necessary, to neutralize. Add 25.0 mL of 0.2 N sodium hydroxide VS, and reflux gently on a hot plate for 1 hour. Wash the condenser with 10 mL of water, collecting the washings in the flask, cool, and titrate with 0.2 N hydrochloric acid VS. Concomitantly perform a blank determination in the same manner, using the same quantity of 0.2 N sodium hydroxide VS.

Calculation of saponification value—Calculate the saponification value by the formula:

$$[(B - A)N56.11]/W,$$

in which B and A are the volumes, in mL, of 0.2 N hydrochloric acid VS consumed in the titration of the blank and the test preparation, respectively, N is the exact normality of the hydrochloric acid solution, W is the weight, in g, of the portion of Polyvinyl Alcohol taken, and 56.11 is the molecular weight of potassium hydroxide.

Calculation of degree of hydrolysis—Calculate the degree of hydrolysis, expressed as percentage of hydrolysis of polyvinyl acetate, by the formula:

$$100 - [7.84S/(100 - 0.075S)],$$

in which S is the saponification value of the Polyvinyl Alcohol taken: between 85% and 89% is found.

Sulfurated Potash

Thiosulfuric acid, dipotassium salt, mixture with potassium sulfide (K_2S_x).

Dipotassium thiosulfate mixture with potassium sulfide (K_2S_x) [*39365-88-3*].

» Sulfurated Potash is a mixture composed chiefly of potassium polysulfides and potassium thiosulfate. It contains not less than 12.8 percent of sulfur (S) in combination as sulfide.

Packaging and storage—Preserve in tight containers. Containers from which it is to be taken for immediate use in compounding prescriptions contain not more than 120 g.

Identification—

A: To a 1 in 10 solution add an excess of 6 N acetic acid: hydrogen sulfide is evolved, and sulfur is precipitated.

Standard preparation—Dissolve a suitable, accurately weighed quantity of USP Prednisolone RS in methylene chloride, and dilute quantitatively and stepwise with methylene chloride to obtain a solution having a known concentration of about 16 µg per mL. Pipet 10 mL of the solution into a glass-stoppered, 100-mL cylinder, and add 1.0 mL of *Alkaline phosphatase solution* and 1.0 mL of water. Allow to stand, with occasional gentle inversion, for 2 hours.

Assay preparation—Dissolve about 100 mg of Prednisolone Sodium Phosphate, accurately weighed, in water that has been saturated with methylene chloride, to make 50.0 mL, and mix. Pipet 10 mL of this solution into a 125-mL separator, and shake with two 25-mL portions of water-washed methylene chloride, discarding the methylene chloride layers.

Procedure—Pipet 1 mL of the *Assay preparation* into a glass-stoppered, 100-mL cylinder, add 1.0 mL of *Alkaline phosphatase solution* and about 50 mL of methylene chloride, insert the stopper, and allow to stand, with occasional gentle inversion (about once every 15 minutes), for 2 hours. Add methylene chloride to volume, mix, and allow to stand until the methylene chloride layer is clear (about 20 minutes). Concomitantly and without delay, determine the absorbances of the methylene chloride solution obtained from the *Assay preparation* and the *Standard preparation* at 241 nm, with a suitable spectrophotometer, using methylene chloride as the blank. Calculate the quantity, in mg, of $C_{21}H_{27}Na_2O_8P$ in the portion of Prednisolone Sodium Phosphate taken by the formula:

$$1.344[5C(A_U/A_S)],$$

in which 1.344 is the ratio of the molecular weight of prednisolone sodium phosphate to that of prednisolone, C is the concentration, in µg per mL, of USP Prednisolone RS in the *Standard preparation*, and A_U and A_S are the absorbances of the solution from the *Assay preparation* and the *Standard preparation*, respectively.

Prednisolone Sodium Phosphate Injection

» Prednisolone Sodium Phosphate Injection is a sterile solution of Prednisolone Sodium Phosphate in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of prednisolone phosphate ($C_{21}H_{29}O_8P$), present as the disodium salt.

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 Prednisolone RS. USP Endotoxin RS.*

Identification—

A: Dissolve 65 mg of phenylhydrazine hydrochloride in 100 mL of dilute sulfuric acid (3 in 5), add 5 mL of isopropyl alcohol, and mix. Heat 5 mL of this solution with 1 mL of *Assay preparation* (obtained as directed in the *Assay*) at 70° for 2 hours: a yellow color develops.

B: It responds to *Identification* test *A* under *Prednisolone Sodium Phosphate.*

Bacterial endotoxins ⟨85⟩—It contains not more than 5.0 USP Endotoxin Units per mg of prednisolone phosphate.

pH ⟨791⟩: between 7.0 and 8.0.

Particulate matter ⟨788⟩: meets the requirements under small-volume injections.

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

Assay—

pH 9 buffer with magnesium—Prepare as directed in the *Assay* under *Prednisolone Sodium Phosphate.*

Alkaline phosphatase solution—Prepare as directed in the *Assay* under *Prednisolone Sodium Phosphate.*

Standard preparation—Prepare as directed in the *Assay* under *Prednisolone Sodium Phosphate.*

Assay preparation—Pipet a volume of Injection, equivalent to about 100 mg of prednisolone phosphate, into a separator containing 10 mL of water. Wash the solution with two 10-mL portions of methylene chloride, and discard the washings. Transfer the aqueous layer to a 50-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Prednisolone Sodium Phosphate.* Calculate the quantity, in mg, of $C_{21}H_{29}O_8P$ in each mL of the Injection taken by the formula:

$$6.11(C/V)(A_U/A_S),$$

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

Prednisolone Sodium Phosphate Ophthalmic Solution

» Prednisolone Sodium Phosphate Ophthalmic Solution is a sterile solution of Prednisolone Sodium Phosphate in a buffered, aqueous medium. It contains not less than 90.0 percent and not more than 115.0 percent of the labeled amount of prednisolone phosphate ($C_{21}H_{29}O_8P$), present as the disodium salt.

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

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

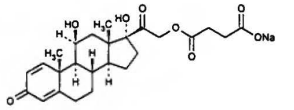
Identification—It responds to *Identification* test *A* under *Prednisolone Sodium Phosphate* and to *Identification* test *A* under *Prednisolone Sodium Phosphate Injection.*

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 6.2 and 8.2.

Assay—Proceed with Ophthalmic Solution as directed in the *Assay* under *Prednisolone Sodium Phosphate Injection.*

Prednisolone Sodium Succinate for Injection



$C_{25}H_{31}NaO_8$ 482.50

Pregna-1,4-diene-3,20-dione, 21-(3-carboxy-1-oxopropoxy)-11,17-dihydroxy-, monosodium salt, (11β)-.

11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione 21-(sodium succinate) [*1715-33-9*].

» Prednisolone Sodium Succinate for Injection is sterile prednisolone sodium succinate prepared from Prednisolone Hemisuccinate with the aid of Sodium Hydroxide or Sodium Carbonate. It contains the equivalent of not less than 90.0 percent and not more than 110.0 percent of the labeled amount of prednisolone ($C_{21}H_{28}O_5$). It contains suitable buffers.

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

USP Reference standards ⟨11⟩—*USP Prednisolone Hemisuccinate RS. USP Endotoxin RS.*

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

between the least resolved peaks is not less than 1.2; and the relative standard deviation for replicate injections of the *Standard solution* is not more than 6.0% for each component or, if the *Assay* is performed concomitantly, the relative standard deviation for the propantheline bromide peak in the replicate injections of the *Standard solution* is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of xanthanoic acid, xanthone, and propantheline bromide related compound A greater than or equal to 0.1% in the portion of Tablets taken by the formula:

$$100C/C_X(r_U/r_S),$$

in which C is the concentration, in µg, of xanthanoic acid, xanthone, or propantheline bromide related compound A per mL of the *Standard solution;* C_X is the theoretical concentration, in µg per mL, of Propantheline Bromide in the *Test solution;* and r_U and r_S are the related compound peak responses obtained from the *Test solution* and the *Standard solution*, respectively: not more than 4.0% of propantheline bromide related compound A and 1.0% each of xanthone and xanthanoic acid are found.

Assay—

pH 3.5 buffer solution and *Mobile phase*—Prepare as directed for *Related compounds* under *Propantheline Bromide*.

Standard preparation—Dissolve an accurately weighed quantity of USP Propantheline Bromide RS in *Mobile phase* to obtain a solution having a known concentration of about 0.3 mg per mL.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to 15 mg of propantheline bromide, to a 50-mL volumetric flask, dissolve in *Mobile phase*, dilute with *Mobile phase* to volume, mix. and filter.

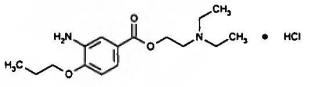
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 25-cm column that contains packing L7. The flow rate is about 2.0 mL per minute. Chromatograph the *Standard preparation,* and record peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the quantity, in mg, of $C_{23}H_{30}BrNO_3$ 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 Propantheline Bromide RS in the *Standard preparation;* and r_U and r_S are the peak responses due to Propantheline Bromide obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Proparacaine Hydrochloride



$C_{16}H_{26}N_2O_3 \cdot HCl$ 330.85

Benzoic acid, 3-amino-4-propoxy-, 2-(diethylamino)ethyl ester, monohydrochloride.

2-(Diethylamino)ethyl 3-amino-4-propoxybenzoate monohydrochloride [*5875-06-9*].

» Proparacaine Hydrochloride contains not less than 97.0 percent and not more than 103.0 percent of $C_{16}H_{26}N_2O_3 \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

USP Reference standard ⟨11⟩—*USP Proparacaine Hydrochloride RS.*

Identification—

A: It meets the requirements under *Identification—Organic Nitrogenous Bases* ⟨181⟩.

B: Dissolve 50 mg, accurately weighed, in water to make 250 mL, and mix. Pipet 10 mL of this solution into a 100-mL volumetric flask, add 2 mL of 10 percent, pH 6.0 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*), and water to volume, and mix: the UV absorption spectrum of the solution exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Proparacaine Hydrochloride RS, concomitantly measured, and the respective absorptivities, calculated on the dried basis, at the wavelength of maximum absorbance at about 310 nm do not differ by more than 3.0%.

C: A solution (1 in 50) responds to the tests for *Chloride* ⟨191⟩, the procedure for alkaloidal hydrochlorides being used.

Melting range ⟨741⟩: between 178° and 185°, but the range between beginning and end of melting does not exceed 2°.

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: it loses not more than 0.5% of its weight.

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

Ordinary impurities ⟨466⟩—

Test solution: methanol.

Standard solution: methanol.

Eluant: a mixture of butyl alcohol, water, and glacial acetic acid (5 : 3 : 1).

Visualization: 1; 17.

Assay—Place 250 mg of Proparacaine Hydrochloride, accurately weighed, in a 250-mL conical flask, add 80 mL of a 1 in 20 solution of acetic anhydride in glacial acetic acid, and heat on a steam bath for 10 minutes. Cool to room temperature, add 10 mL of mercuric acetate TS and 1 or 2 drops of crystal violet TS, and titrate with 0.1 N perchloric acid VS to a blue-green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 33.09 mg of $C_{16}H_{26}N_2O_3 \cdot HCl$.

Proparacaine Hydrochloride Ophthalmic Solution

» Proparacaine Hydrochloride Ophthalmic Solution is a sterile, aqueous solution of Proparacaine Hydrochloride. It contains not less than 95.0 percent and not more than 110.0 percent of the labeled amount of $C_{16}H_{26}N_2O_3 \cdot HCl$.

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

Labeling—Label it to indicate that it is to be stored in a refrigerator after the container is opened.

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

Identification—To 1 mL of Ophthalmic Solution in a test tube add 1 mL of dilute hydrochloric acid (1 in 100), mix, and cool in an ice bath for 2 minutes. Add 2 drops of sodium nitrite solution (1 in 10), shake, and cool again for 2 minutes. Add 1 mL of a solution prepared by dissolving 200 mg of 2-naphthol in 10 mL of 1 N sodium hydroxide: a scarlet-red precipitate is formed. Add 5 mL of acetone: the precipitate does not dissolve.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 3.5 and 6.0.

Assay—

pH 7.5 buffer—Dissolve 6.8 g of monobasic potassium phosphate in 1000 mL of water, add 5 mL of triethylamine, and adjust with potassium hydroxide to a pH of 7.5. Filter through a filter having a porosity of 0.5 µm or finer, and degas.

Mobile phase—Prepare a mixture of *pH 7.5 buffer* and acetonitrile (60 : 40). Make adjustments if necessary (see *System Suitability* in *Chromatography* ⟨621⟩).

Standard preparation—Transfer about 25 mg of USP Proparacaine Hydrochloride RS, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Transfer 5.0 mL of this stock solution to a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. [NOTE—Use this solution within 6 hours.]

Assay preparation—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 10 mg of proparacaine hydrochloride, to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. [NOTE—Use this solution within 6 hours.]

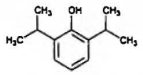
Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 270-nm detector and a 4-mm × 15-cm column that contains 5-µm spherical packing L10. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 1.5, the column efficiency is not less than 3000 theoretical plates, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—[NOTE—Use peak areas where peak responses are indicated.] 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 $C_{16}H_{26}N_2O_3 \cdot HCl$ in each mL of the Ophthalmic Solution taken by the formula:

$$100(C/V)(r_U/r_S),$$

in which C is the concentration, in mg per mL, of USP Proparacaine Hydrochloride RS in the *Standard preparation*, V is the volume, in mL, of Ophthalmic Solution taken, and r_U and r_S are the proparacaine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Propofol



$C_{12}H_{18}O$ 178.27

Phenol, 2,6-bis(1-methylethyl)-.

2,6-Diisopropylphenol [*2078-54-8*].

Propofol contains not less than 98.0 percent and not more than 102.0 percent of $C_{12}H_{18}O$.

Packaging and storage— Preserve in tight, light-resistant containers under an atmosphere of inert gas. Store at 25°, excursions permitted between 15° and 30°.

Labeling—The labeling indicates the *Related compounds* test with which the article complies.

USP Reference standards ⟨11⟩—*USP Propofol RS. USP Propofol Related Compound A RS. USP Propofol Related Compound B RS. USP Propofol Resolution RS. USP Propofol for System Suitability RS.*

Identification, *Infrared Absorption* ⟨197F⟩.

Refractive index ⟨831⟩: between 1.5125 and 1.5145 at 20°.

Related compounds—[NOTE—On the basis of knowledge of the manufacturing process, either (1) *Related compounds Test 1* is performed in conjunction with the *Limit of propofol related compound A, Limit of propofol related compound B Test 1,* and *Assay Test 1* procedures; or (2) *Related compounds Test 2* is performed in conjunction with the *Limit of propofol related compound B Test 2* and the *Assay Test 2* procedures.]

TEST 1—

Resolution solution—Dissolve an accurately weighed quantity of USP Propofol Resolution RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to obtain a solution having a concentration of about 100 mg per mL.

Standard solution—Dissolve an accurately weighed quantity of USP Propofol RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to obtain a solution having a concentration of about 0.1 mg per mL.

Test solution— Transfer about 1000 mg of Propofol, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with methanol to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—Proceed as directed under *Assay Test 1,* except to chromatograph the *Standard solution* six times and chromatograph the *Resolution solution:* the relative retention time is about 0.18 for 2,6-diisopropylphenyl isopropylether, 1.0 for propofol, and about 1.1 for 2-isopropyl-6-*n*-propylphenol; the resolution, R, between propofol and 2-isopropyl-6-*n*-propylphenol is not less than 2. Chromatograph the *Standard solution* six times, and record the peak responses as directed for *Procedure:* the column efficiency determined from the propofol peak is not less than 5000 theoretical plates; and the relative standard deviation for replicate injections is not more than 3.5%.

Procedure—Separately inject equal volumes (about 1.0 µL) of the *Resolution solution,* the *Standard solution,* and the *Test solution* into the chromatograph, record the chromatograms, and measure all the peak responses. Calculate the percentage of each impurity in the portion of Propofol taken by the formula:

$$0.1(r_i/r_S),$$

in which r_i is the peak response for each impurity obtained from the *Test solution;* and r_S is the peak response for propofol obtained from the *Standard solution:* not more than 0.1% of 2,6-diisopropylphenyl isopropylether is found; not more than 0.1% of each other individual impurity is found; and not more than 0.3% of total impurities is found.

TEST 2—

Mobile phase—Prepare as directed in *Assay Test 2.*

System suitability solution 1—Transfer 5 µL of USP Propofol RS and 15 µL of USP Propofol Related Compound B RS to a 50-mL volumetric flask, dissolve in and dilute with hexane to volume, and mix.

System suitability solution 2—Dissolve 1 mL of USP Propofol for System Suitability RS with hexane to make 10 mL.

Test solution—Transfer about 1000 mg of Propofol, accurately weighed, to a 10-mL volumetric flask, dissolve in and dilute with hexane to volume, and mix.

Reference solution—Dilute 1 mL of the *Test solution* with hexane to 100 mL, and mix. Dilute 1 mL of this solution with hexane to 10 mL, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—Proceed as directed in *Assay Test 2.* Chromatograph *System suitability solution 1* and *System suitability solution 2,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.8 for propofol related compound B from *System suitability solution 1,* 0.5 for 2-(1-methylethoxy)-1,3-bis(1-methylethylbenzene), 1.0 for propofol, and 5.0 for propofol related compound A from *System suitability solution 2;* the resolution, R, between propofol related compound B and propofol is at least 4.0.

Procedure—Separately inject a volume (about 10 µL) of the *Test solution* and the *Reference solution* into the chromatograph, record the chromatogram, and measure all peak responses. Calculate the percentage of each impurity in the portion of Propofol taken by the formula:

$$0.1(r_i/r_S)(1/F),$$

in which r_i is the peak response for each impurity obtained from the *Test solution;* r_S is the peak response for propofol obtained from the *Reference solution;* and F is the response factor. F is 0.2 for 2,6-diisopropylphenylisopropyl ether and 4.0 for propofol related compound A: not more than 0.2% of 2-(1-methylethoxy)-1,3-bis(1-methylethylbenzene) is found; not more than 0.2% of 2,6-diisopropylphenylisopropyl ether is found; not more than 0.01% of propofol related compound A is found; not more than 0.05% of each other individual impurity is found; and not more than 0.3% of total impurities is found.

Limit of propofol related compound A—[NOTE—This test is to be performed in conjunction with *Related compounds Test 1.*]

Mobile phase—Prepare a filtered and degassed mixture of acetonitrile, water, and methanol (50 : 40 : 10).

Standard solution—Prepare a solution in methanol containing 20 µg per mL of USP Propofol Related Compound A RS.

Bacterial endotoxins ⟨85⟩—It contains not more than 555.0 USP Endotoxin Units per mg of scopolamine hydrobromide.

pH ⟨791⟩: between 3.5 and 6.5.

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

Assay—

Buffer pH 9.0 Buffer—Dissolve 34.8 g of dibasic potassium phosphate in 1000 mL of water, and adjust with 3 N hydrochloric acid or 1 N sodium hydroxide, as necessary, to a pH of 9.0, determined electrometrically, and mix.

Internal standard solution—Transfer about 25 mg of homatropine hydrobromide to a 50-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Prepare fresh daily.

Standard stock solution—Transfer about 10 mg of USP Scopolamine Hydrobromide RS, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Prepare fresh daily.

Standard preparation—Pipet 10 mL of the *Standard stock solution* into a separator, add 2.0 mL of *Internal standard solution* and 5.0 mL of *Buffer pH 9.0 Buffer*, and carefully adjust the solution with 1 N sodium hydroxide to a pH of 9.0, avoiding any excess. Immediately extract with two 10-mL portions of methylene chloride, filter the methylene chloride extracts through 1 g of anhydrous sodium sulfate supported by a small cotton plug in a funnel into a 50-mL beaker, and evaporate under nitrogen to approximately 2.0 mL.

Assay solution—Transfer an accurately measured volume of Injection, equivalent to about 10 mg of scopolamine hydrobromide, to a 100-mL volumetric flask. Dilute with water to volume, and mix.

Assay preparation—Pipet 10 mL of the *Assay solution* into a separator, and proceed as directed for *Standard preparation*, beginning with "add 2.0 mL of *Internal standard solution*."

Chromatographic system (see *Chromatography* ⟨621⟩)—The gas chromatograph contains a 2-mm × 1.8-m glass column packed with 3% liquid phase G3 on support S1AB. The carrier gas is nitrogen, flowing at a rate of 25 mL per minute. The column temperature is maintained at 225°. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the resolution factor, *R*, between homatropine and scopolamine is not less than 5; the tailing factor 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 1 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak areas. Calculate the ratio, A_U, of the area of the scopolamine hydrobromide peak to the area of the internal standard peak in the chromatogram from the *Assay preparation*, and similarly calculate the ratio, A_S, in the chromatogram from the *Standard preparation*. Calculate the quantity, in mg, of scopolamine hydrobromide ($C_{17}H_{21}NO_4 \cdot HBr \cdot 3H_2O$) in the volume of Injection taken by the formula:

$$1.141W(A_U/A_S),$$

in which 1.141 is the ratio of the molecular weight of scopolamine hydrobromide trihydrate to that of anhydrous scopolamine hydrobromide; W is the weight, in mg, of USP Scopolamine Hydrobromide RS in the *Standard preparation;* and A_U and A_S are as calculated above.

Scopolamine Hydrobromide Ophthalmic Ointment

» Scopolamine Hydrobromide Ophthalmic Ointment is Scopolamine Hydrobromide in a suitable ophthalmic ointment base. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ($C_{17}H_{21}NO_4$) · HBr · $3H_2O$. It is sterile.

Packaging and storage—Preserve in collapsible ophthalmic ointment tubes.

USP Reference standards ⟨11⟩—*USP Scopolamine Hydrobromide RS.*

Identification—

A: Transfer a portion of Ophthalmic Ointment, equivalent to about 50 mg of scopolamine hydrobromide, to a suitable separator, and dissolve in 25 mL of ether. Add 25 mL of 0.01 N hydrochloric acid, shake vigorously, allow the layers to separate, and discard the organic phase. Proceed as directed under *Identification—Organic Nitrogenous Bases* ⟨181⟩, beginning with "In a second separator dissolve 50 mg."

B: Transfer about 5 g of Ophthalmic Ointment to a separator, dissolve in 50 mL of ether, and extract with 20 mL of water: the extracted solution so obtained responds to the tests for *Bromide* ⟨191⟩.

Sterility ⟨71⟩: meets the requirements.

Metal particles—It meets the requirements of the test for *Metal Particles in Ophthalmic Ointments* ⟨751⟩.

Assay—Proceed with Ophthalmic Ointment as directed in the *Assay* under *Scopolamine Hydrobromide Injection*, but to prepare the *Assay solution*, weigh accurately a portion of Ophthalmic Ointment equivalent to about 10 mg of scopolamine hydrobromide into a separator containing 50 mL of ether, shake to dissolve, extract with three 25-mL portions of 0.2 N sulfuric acid, collect the acid extracts in a 100-mL volumetric flask, dilute with 0.2 N sulfuric acid to volume, and mix. Calculate the quantity, in mg, of $C_{17}H_{21}NO_4 \cdot HBr \cdot 3H_2O$ in the portion of Ophthalmic Ointment taken by the formula given therein.

Scopolamine Hydrobromide Ophthalmic Solution

» Scopolamine Hydrobromide Ophthalmic Solution is a sterile, buffered, aqueous solution of Scopolamine Hydrobromide. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{17}H_{21}NO_4 \cdot HBr \cdot 3H_2O$. It may contain suitable antimicrobial agents and stabilizers, and may contain suitable additives for the purpose of increasing its viscosity.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Scopolamine Hydrobromide RS.*

Identification—

A: A volume of Ophthalmic Solution, equivalent to about 3 mg of scopolamine hydrobromide, responds to *Identification* test *A* under *Scopolamine Hydrobromide Injection.*

B: Add to the Ophthalmic Solution silver nitrate TS: a yellowish white precipitate, insoluble in nitric acid but slightly soluble in 6 N ammonium hydroxide, is formed.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 4.0 and 6.0.

Assay—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 10 mg of scopolamine hydrobromide, to a 100-mL volumetric flask, dilute with water to volume, and mix. Using this as the *Assay solution*, proceed as directed in the *Assay* under *Scopolamine Hydrobromide Injection.* Calculate the quantity, in mg, of $C_{17}H_{21}NO_4 \cdot HBr \cdot 3H_2O$ in the volume of Ophthalmic Solution taken by the formula given therein.

Scopolamine Hydrobromide Tablets

» Scopolamine Hydrobromide Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{17}H_{21}NO_4 \cdot HBr \cdot 3H_2O$.

Silver Nitrate Ophthalmic Solution

» Silver Nitrate Ophthalmic Solution is a solution of Silver Nitrate in a water medium. It contains not less than 0.95 percent and not more than 1.05 percent of $AgNO_3$. The solution may be buffered by the addition of Sodium Acetate.

Packaging and storage—Preserve it protected from light, in inert, collapsible capsules or in other suitable single-dose containers.

Clarity and color of solution—It is clear and colorless.

Identification—It responds to the tests for *Silver* ⟨191⟩ and for *Nitrate* ⟨191⟩.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 4.5 and 6.0.

Assay—Place 5 mL of Ophthalmic Solution, accurately measured, in a conical flask, dilute with 20 mL of water, add 1 mL of nitric acid and 1 mL of ferric ammonium sulfate TS, and titrate with 0.02 N ammonium thiocyanate VS. Each mL of 0.02 N ammonium thiocyanate is equivalent to 3.397 mg of $AgNO_3$.

Toughened Silver Nitrate

» Toughened Silver Nitrate contains not less than 94.5 percent of $AgNO_3$, the remainder consisting of silver chloride (AgCl).

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

Identification—

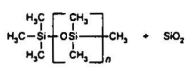
A: A solution (1 in 50) responds to the tests for *Silver* ⟨191⟩.

B: Mix a solution (1 in 10) in a test tube with 1 drop of diphenylamine TS, then carefully superimpose it upon sulfuric acid: a deep blue color appears at the zone of contact.

Copper—A solution (1 in 10) shows no trace of blue coloration when treated with an excess of 6 N ammonium hydroxide.

Assay—Add about 700 mg of Toughened Silver Nitrate, accurately weighed, to 50 mL of water, and when the silver nitrate has dissolved, filter the solution. Thoroughly wash the filter and sediment with water, add 2 mL of nitric acid and 2 mL of ferric ammonium sulfate TS to the combined filtrate and washings, and titrate with 0.1 N ammonium thiocyanate VS. Each mL of 0.1 N ammonium thiocyanate is equivalent to 16.99 mg of $AgNO_3$.

Simethicone



Simethicone.
α-(Trimethylsilyl)-ω-methylpoly[oxy(dimethylsilylene)], mixture with silicon dioxide [*8050-81-5*].

» Simethicone is a mixture of fully methylated linear siloxane polymers containing repeating units of the formula $[-(CH_3)_2SiO-]_n$, stabilized with trimethylsiloxy end-blocking units of the formula $[(CH_3)_3SiO-]$, and silicon dioxide. It contains not less than 90.5 percent and not more than 99.0 percent of polydimethylsiloxane ($[-(CH_3)_2SiO-]_n$), and not less than 4.0 percent and not more than 7.0 percent of silicon dioxide.

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—*USP Polydimethylsiloxane RS*. *USP Simethicone RS*.

Identification, *Infrared Absorption* ⟨197S⟩—

Test solution—Prepare as directed for *Assay preparation* in the *Assay*.

Standard solution—Prepare as directed for *Standard preparation* in the *Assay*.

Cell size: 0.5 mm.

Defoaming activity—

Foaming solution—Dissolve 1 g of octoxynol 9 in 100 mL of water.

Test preparation—Transfer 200 mg of Simethicone to a 60-mL bottle, add 50 mL of tertiary butyl alcohol, cap the bottle, and shake vigorously. [NOTE—Warm slightly, if necessary, to effect solution.]

Procedure—[NOTE—For each test, employ a clean, unused, 25-mL glass jar.] Add, dropwise, 500 µL of the *Test preparation* to a clean, unused, cylindrical 250-mL glass jar, fitted with a 50-mm cap, containing 100 mL of the *Foaming solution*. Cap the jar, and clamp it in an upright position on a wrist-action shaker. Employing a radius of 13.3 ± 0.4 cm (measured from center of shaft to center of bottle), shake for 10 seconds through an arc of 10 degrees at a frequency of 300 ± 30 strokes per minute. Record the time required for the foam to collapse. The time, in seconds, for foam collapse is determined as the instant the first portion of foam-free liquid surface appears, measured from the end of the shaking period. The defoaming activity time does not exceed 15 seconds.

Loss on heating—Heat about 15 g, accurately weighed, in an open, tared vessel having a diameter of 5.5 ± 0.5 cm and a wall height of 2.5 ± 1.0 cm at 200° in a circulating air oven for 4 hours, and allow to come to room temperature in a desiccator before weighing: it loses not more than 18.0% of its weight.

Heavy metals—Mix 1.0 g of Simethicone with 10 mL of chloroform and dilute with the same solvent to 20 mL. Add 1.0 mL of a freshly prepared 0.002% solution of dithizone in chloroform, 0.5 mL of water, and 0.5 mL of a mixture of 1 volume of ammonia TS and 9 volumes of a 0.2% solution of hydroxylamine hydrochloride. Concomitantly prepare a Standard solution as follows: to 20 mL of chloroform add 1.0 mL of a freshly prepared 0.002% solution of dithizone in chloroform, 0.5 mL of *Standard Lead Solution* (see *Heavy Metals* ⟨231⟩) (containing 10 µg of lead per mL) and 0.5 mL of a mixture of 1 volume of ammonia TS and 9 volumes of a 0.2% solution of hydroxylamine hydrochloride. Immediately shake both solutions vigorously for 1 minute. Any red color in the test solution is not more intense than that in the Standard solution (5 µg per g).

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

Content of silicon dioxide—Transfer 3.00 g of Simethicone to a screw-capped bottle, add 10.0 mL of *n*-hexane, cap, and mix by shaking *(Test solution)*. Prepare a *Standard solution* by similarly treating a 3.00-g portion of USP Simethicone RS. Prepare a *Dimethicone preparation* by similarly treating a 3.00-g portion of dimethicone having a viscosity of 500 centistokes. Using an IR spectrophotometer and 0.1-mm cells, determine the absorbance spectra of well-mixed portions of the *Test solution*, the *Standard solution*, and the *Dimethicone preparation* between 7 and 9 µm using *n*-hexane as the blank. Determine the absorbances of the *Test solution*, the *Standard solution*, and the *Dimethicone preparation* at the wavelength of minimum absorbance at about 8.2 µm observed in the spectrum obtained from the *Dimethicone preparation*. Calcu

USP Reference standards ⟨11⟩—*USP Endotoxin RS. USP Methylparaben RS. USP Propylparaben RS.*

Antimicrobial agent(s)—It meets the requirements under *Antimicrobial Preservatives—Effectiveness* ⟨51⟩, and meets the labeled claim for content of the antimicrobial agent(s) as determined by the method set forth under *Antimicrobial Agents—Content* ⟨341⟩, except to use the following procedure when methylparaben and propylparaben are used as the antimicrobial agents.

Mobile phase—Prepare a filtered and degassed mixture of methanol and water (70:30). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve accurately weighed quantities of USP Methylparaben RS and USP Propylparaben RS in methanol, and dilute quantitatively, and stepwise if necessary, with methanol to obtain a solution having known concentrations of about 1.2 and 0.12 mg per mL, respectively. Pipet 5 mL of this solution into a 50-mL volumetric flask, add by pipet 30 mL of methanol, dilute with water to volume, and mix.

Test preparation—Pipet 1 mL of Injection into a 10-mL volumetric flask, add by pipet 7 mL of methanol, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation* as directed for *Procedure:* the capacity factor, k', is 0.52 for methylparaben and 1.05 for propylparaben, with a minimum separation factor (α) of about 2.0.

Procedure—Separately inject equal volumes (about 12 µL) of the *Standard preparation* and the *Test preparation* into the chromatograph by means of a suitable microsyringe or sampling valve, adjusting the specimen size and other operating parameters such that the peak obtained with the *Standard preparation* is about 0.7 full scale. Record the chromatograms, and measure the height of the peaks, at identical retention times, obtained with the *Test preparation* and the *Standard preparation*, and calculate the concentration in mg per mL, in the portion of methylparaben or propylparaben taken by the formula:

$$C(H_U/H_S),$$

in which C is the concentration, in mg per mL, of USP Methylparaben RS or USP Propylparaben RS in the *Standard preparation;* and H_U and H_S are the peak heights obtained from the *Test preparation* and the *Standard preparation*, respectively.

Bacterial endotoxins ⟨85⟩—It contains not more than 1.0 USP Endotoxin Unit per mL.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

Other requirements—It responds to the *Identification* test and meets the requirements for *pH*, *Iron*, *Heavy metals*, and *Assay* under *Sodium Chloride Injection.* It meets also the requirements under *Injections* ⟨1⟩.

Sodium Chloride Irrigation

» Sodium Chloride Irrigation is Sodium Chloride Injection that has been suitably packaged, and it contains no antimicrobial agents. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of NaCl.

Packaging and storage—Preserve in single-dose glass or plastic containers. Glass containers are preferably of Type I or Type II glass. The container may be designed to empty rapidly and may contain a volume of more than 1 liter.

Labeling—The designation "not for injection" appears prominently on the label.

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

Identification—It responds to the tests for *Sodium* ⟨191⟩ and for *Chloride* ⟨191⟩.

Bacterial endotoxins ⟨85⟩—It contains not more than 0.5 USP Endotoxin Unit per mL.

Sterility ⟨71⟩: meets the requirements.

Other requirements—It meets the requirements for *pH*, *Iron*, *Heavy metals*, and *Assay* under *Sodium Chloride Injection.*

Sodium Chloride Ophthalmic Ointment

» Sodium Chloride Ophthalmic Ointment is Sodium Chloride in a suitable ophthalmic ointment base. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of NaCl. It is sterile.

Packaging and storage—Preserve in collapsible ophthalmic ointment tubes.

Identification—Transfer a quantity of Ophthalmic Ointment, equivalent to about 200 mg of sodium chloride, to a separator containing about 25 mL of ether, and extract with 5 mL of water: the aqueous extract so obtained responds to the tests for *Sodium* ⟨191⟩, and for *Chloride* ⟨191⟩.

Sterility ⟨71⟩: meets the requirements.

Minimum fill ⟨755⟩: meets the requirements.

Metal particles ⟨751⟩: meets the requirements.

Assay—Transfer an accurately weighed quantity of Ophthalmic Ointment, equivalent to about 100 mg of sodium chloride, to a separator containing about 50 mL of ether, and extract with four 20-mL portions of water. Combine the aqueous extracts in a conical flask, evaporate to a volume of about 10 mL, and add 10 mL of glacial acetic acid, 75 mL of methanol, and 0.5 mL of eosin Y TS. Titrate, with shaking, with 0.1 N silver nitrate VS to a pink endpoint. Each mL of 0.1 N silver nitrate is equivalent to 5.844 mg of NaCl.

Sodium Chloride Inhalation Solution

» Sodium Chloride Inhalation Solution is a sterile solution of Sodium Chloride in water purified by distillation or by reverse osmosis and rendered sterile. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of NaCl. It contains no antimicrobial agents or other added substances.

Packaging and storage—Preserve in single-dose containers.

Identification—It responds to the test for *Sodium* ⟨191⟩ and for *Chloride* ⟨191⟩.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 4.5 and 7.0.

Assay—Pipet a volume of Inhalation Solution, equivalent to about 90 mg of sodium chloride, into a conical flask, and add 10 mL of glacial acetic acid, 75 mL of methanol, and 0.5 mL of eosin Y TS. Titrate, with shaking, with 0.1 N silver nitrate VS to a pink endpoint. Each mL of 0.1 N silver nitrate is equivalent to 5.844 mg of NaCl.

Sodium Chloride Ophthalmic Solution

» Sodium Chloride Ophthalmic Solution is a sterile solution of Sodium Chloride. It contains not less than 90.0 percent and not more than 110.0 percent of the

labeled amount of sodium chloride. It may contain suitable antimicrobial and stabilizing agents. It contains a buffer.

Packaging and storage—Preserve in tight containers.

Identification—Heat a portion of Ophthalmic Solution to boiling, and filter while hot. After cooling, the filtrate responds to the tests for *Sodium* ⟨191⟩ and for *Chloride* ⟨191⟩.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 6.0 and 8.0.

Assay—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 90 mg of sodium chloride, to a conical flask, and add 10 mL of glacial acetic acid, 75 mL of methanol, and 0.5 mL of eosin Y TS. Titrate, with shaking, with 0.1 N silver nitrate VS to a pink endpoint. Each mL of 0.1 N silver nitrate is equivalent to 5.844 mg of NaCl.

Sodium Chloride Tablets

» Sodium Chloride Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of NaCl.

Packaging and storage—Preserve in well-closed containers.

Identification—A filtered extract of Tablets responds to the tests for *Sodium* ⟨191⟩ and for *Chloride* ⟨191⟩.

Disintegration ⟨701⟩: 30 minutes.

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

Iodide or bromide—Digest 2.0 g of powdered Tablets with 25 mL of warm alcohol for 3 hours, cool, and filter. Evaporate the filtrate to dryness, dissolve the residue in 5 mL of water, filter if necessary, and add 1 mL of chloroform. Cautiously introduce, dropwise, with constant agitation, 5 drops of dilute chlorine TS (1 in 3): the chloroform does not acquire a violet, yellow, or orange color.

Barium—Digest 4.0 g of powdered Tablets with 20 mL of water, filter, and divide the solution into two equal portions. To one portion add 2 mL of 2 N sulfuric acid and to the other add 2 mL of water: the solutions are equally clear after standing for 2 hours.

Calcium and magnesium—Digest 1 g of powdered Tablets with 50 mL of water, and filter. Add 4 mL of 6 N ammonium hydroxide to the filtrate, and divide the mixture into two equal portions. Treat one portion with 1 mL of ammonium oxalate TS and the other portion with 1 mL of dibasic sodium phosphate TS: neither mixture becomes turbid within 5 minutes.

Assay—Dissolve a counted number of not less than 20 Tablets in about 100 mL of water, filter into a 500-mL volumetric flask, and wash the original container and the filter with 100 mL of water in divided portions, adding the washings to the original filtrate. Dilute with water to volume. Pipet a volume of the solution, equivalent to about 90 mg of sodium chloride, to a conical flask, and add 10 mL of glacial acetic acid, 75 mL of methanol, and 0.5 mL of eosin Y TS. Titrate, with shaking, with 0.1 N silver nitrate VS to a pink endpoint. Each mL of 0.1 N silver nitrate is equivalent to 5.844 mg of NaCl.

Sodium Chloride Tablets for Solution

» Sodium Chloride Tablets for Solution are composed of Sodium Chloride in compressed form, containing no added substance. Sodium Chloride Tablets for Solution contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of NaCl.

Other requirements—The Sodium Chloride Tablets for Solution respond to the *Identification* test and meet the requirements for *Packaging and storage*, *Iodide or bromide*, *Barium*, *Calcium and magnesium*, *Disintegration*, *Uniformity of dosage units*, and *Assay* under *Sodium Chloride Tablets*.

Sodium Chloride and Dextrose Tablets

» Sodium Chloride and Dextrose Tablets contain not less than 92.5 percent and not more than 107.5 percent of the labeled amount of sodium chloride (NaCl) and of dextrose ($C_6H_{12}O_6 \cdot H_2O$).

Packaging and storage—Preserve in well-closed containers.

Identification—

A: A filtered solution of Tablets responds to the flame test for *Sodium* ⟨191⟩ and to the test for *Chloride* ⟨191⟩.

B: Add a few drops of the filtered solution tablets to 5 mL of hot alkaline cupric tartrate TS: a copious red precipitate of cuprous oxide is formed.

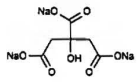
Disintegration ⟨701⟩: 30 minutes.

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

Assay for sodium chloride—Transfer 20.0 mL of the solution prepared for the *Assay for dextrose* to a 100-mL volumetric flask, dilute with water to volume, mix, and proceed as directed in the *Assay* under *Sodium Chloride Tablets*, beginning with "Pipet a volume of the solution."

Assay for dextrose—Dissolve not less than 10 Tablets, containing from 2 to 5 g of dextrose, in about 75 mL of water in a 100-mL volumetric flask, add several drops of 6 N ammonium hydroxide, dilute with water to volume, and mix. After 30 minutes, filter through a dry filter, and determine the angular rotation in a 200-mm tube at 25°, retaining the excess of the solution for the *Assay for sodium chloride*. The observed rotation in degrees, multiplied by 1.042, represents the weight, in g, of $C_6H_{12}O_6 \cdot H_2O$ in the specimen taken.

Sodium Citrate



$C_6H_5Na_3O_7$ (anhydrous) 258.07
1,2,3-Propanetricarboxylic acid, 2-hydroxy-, trisodium salt.
Trisodium citrate (anhydrous) [*68-04-2*].
Trisodium citrate dihydrate 294.10 [*6132-04-3*].

» Sodium Citrate is anhydrous or contains two molecules of water of hydration. It contains not less than 99.0 percent and not more than 100.5 percent of $C_6H_5Na_3O_7$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers.

Labeling—Label it to indicate whether it is anhydrous or hydrous.

Identification—

A: A solution (1 in 20) responds to the tests for *Sodium* ⟨191⟩ and for *Citrate* ⟨191⟩.

B: Upon ignition, it yields an alkaline residue which effervesces when treated with 3 N hydrochloric acid.

Alkalinity—A solution of 1.0 g in 20 mL of water is alkaline to litmus paper, but after the addition of 0.20 mL of 0.10 N sulfuric acid no pink color is produced by 1 drop of phenolphthalein TS.

Water, *Method III* ⟨921⟩—Dry it at 180° for 18 hours: the anhydrous form loses not more than 1.0%, and the hydrous form between 10.0 and 13.0%, of its weight.

Assay preparation—Transfer about 50 mg of Suprofen, accurately weighed, to a 50-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 5.0 mL of this solution to a 25-mL volumetric flask, dilute with *Buffer solution* to volume, and mix. Transfer 2.0 mL of this solution to a 25-mL volumetric flask, dilute with *Buffer solution* to volume, and mix.

Chromatographic system—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-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 column efficiency determined from the analyte peak is not less than 500 theoretical plates, the tailing factor for the peak is not more than 2.0, and the relative standard deviation for replicate injections is not more than 2%.

Procedure—[NOTE—Use peak areas where peak responses are indicated.] 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 $C_{14}H_{12}O_3S$ in the portion of Suprofen taken by the formula:

$$3125C(r_U/r_S),$$

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

Suprofen Ophthalmic Solution

» Suprofen Ophthalmic Solution is a sterile, buffered, aqueous solution of Suprofen adjusted to a suitable tonicity. It contains a suitable antimicrobial preservative. It contains not less than 90.0 percent and not more than 115.0 percent of the labeled amount of $C_{14}H_{12}O_3S$.

Packaging and storage—Preserve in tight containers.

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

Identification—The 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.*

Sterility ⟨71⟩: meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined.*

pH ⟨791⟩: between 6.5 and 8.0.

Assay—

Buffer solution, Mobile phase, Standard preparation, and *Chromatographic system*—Proceed as directed in the *Assay* under *Suprofen.*

Assay preparation—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 20 mg of suprofen, to a 100-mL volumetric flask. Dilute with *Buffer solution* to volume, and mix. Transfer 2.0 mL of this solution to a 25-mL volumetric flask, dilute with *Buffer solution* to volume, and mix.

Procedure—Proceed as directed in the *Assay* under *Suprofen.* Calculate the quantity, in mg, of $C_{14}H_{12}O_3S$ in each mL of the Ophthalmic Solution taken by the formula:

$$1250(C/V)(r_U/r_S),$$

in which C is the concentration, in mg per mL, of USP Suprofen RS in the *Standard preparation,* V is the volume, in mL, of Ophthalmic Solution taken, and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Absorbable Surgical Suture

» Absorbable Surgical Suture is a sterile, flexible strand prepared from collagen derived from healthy mammals, or from a synthetic polymer. Suture prepared from synthetic polymer may be in either monofilament or multifilament form. It is capable of being absorbed by living mammalian tissue, but may be treated to modify its resistance to absorption. Its diameter and tensile strength correspond to the size designation indicated on the label, within the limits prescribed herein. It may be modified with respect to body or texture. It may be impregnated or treated with a suitable coating, softening, or antimicrobial agent. It may be colored by a color additive approved by the FDA. The collagen suture is designated as either *Plain Suture* or *Chromic Suture.* Both types consist of processed strands of collagen, but *Chromic Suture* is processed by physical or chemical means so as to provide greater resistance to absorption in living mammalian tissue.

Packaging and storage—Preserve dry or in fluid, in containers (packets) so designed that sterility is maintained until the container is opened. A number of such containers may be placed in a box.

Labeling—The label of each individual container (packet) of Suture indicates the size, length, type of Suture, kind of needle (if a needle is included), number of sutures (if multiple), lot number, and name of the manufacturer or distributor. If removable needles are used, the labeling so indicates. Suture size is designated by the metric size (gauge number) and the corresponding USP size. The label of the box indicates also the address of the manufacturer, packer, or distributor, and the composition of any packaging fluids used.

NOTE—If the Suture is packaged with a fluid, make the required measurements for the first four of the following tests within 2 minutes after removing it from the fluid.

Length—Determine the length of Suture without stretching: the length of each strand is not less than 95.0% of the length stated on the label.

Diameter—Determine the diameter of 10 strands of Suture as directed under *Sutures—Diameter* ⟨861⟩.

Collagen suture—The average diameter, and not fewer than 20, of the 30 measurements on the 10-strand sample are within the limits on average diameter prescribed in *Table 1* for the respective size. None of the individual measurements is less than the midpoint of the range for the next smaller size or more than the midpoint of the range for the next larger size.

Synthetic suture—The average diameter of the strands being measured is within the tolerances prescribed in *Table 2* for the respective size. None of the observed measurements is less than the midpoint of the range for the next smaller size or more than the midpoint of the range for the next larger size.

Tensile strength—Determine the tensile strength on not fewer than 10 strands of Suture as directed for *Surgical Sutures* under *Tensile Strength* ⟨881⟩.

Collagen suture—The tensile strength, determined as the minimum strength for each individual strand tested, and calculated as the average strength from any one lot, is as set forth in *Table 1.* If not more than one strand fails to meet the limit on individual strands, repeat the test with not fewer than 20 additional strands: the requirements of the test are met if none of the additional strands fall below the limit on individual strands, and if the average strength of the strands tested does not fall below the stated limit in *Table 1.*

Synthetic suture—The minimum tensile strength of each size of synthetic suture, calculated as the average strength from any one lot, is as set forth in *Table 2.*

Needle attachment—Suture on which eyeless needles are swaged meets the requirements under *Sutures—Needle Attachment* ⟨871⟩.

Sterility ⟨71⟩: meets the requirements.

Extractable color (if Suture is dyed)—Prepare the *Matching Solution* that corresponds to the extractable color of the Suture

pH ⟨791⟩: between 5.0 and 6.0, in a solution (1 in 100).

Water, *Method I* ⟨921⟩: not more than 2.0%.

Residue on ignition—Weigh accurately about 500 mg, transfer to a beaker, and dissolve in 10 mL of methanol. Filter through paper previously washed with methanol, collecting the filtrate in an ignited and tared crucible and washing the beaker and the filter paper with 25 mL to 30 mL of methanol. Evaporate with the aid of heat and a current of air to dryness, and proceed as directed under *Residue on Ignition* ⟨281⟩, beginning with "Heat, gently at first." Not more than 0.1% of residue is found.

Chromatographic purity—Dissolve an accurately weighed quantity of Tetracaine Hydrochloride for Injection in water to obtain a test solution containing 50 mg per mL, and proceed as directed in the test for *Chromatographic purity* under *Tetracaine*, beginning with "Prepare a Standard solution."

Other requirements—It meets the requirements for *Sterility Tests* ⟨71⟩ and *Labeling* under *Injections* ⟨1⟩.

Assay—

Standard preparation—Prepare as directed in the *Assay* under *Tetracaine Hydrochloride in Dextrose Injection.*

Assay preparation—Transfer to a tared 20-mL beaker the contents of a sufficient number of containers of Tetracaine Hydrochloride for Injection to yield about 100 mg of tetracaine hydrochloride. Weigh immediately, and transfer with the aid of water to a 500-mL volumetric flask. Add water to volume, and mix. Transfer 5.0 mL to a 100-mL volumetric flask, add 5 mL of dilute hydrochloric acid (1 in 200) and 10 mL of *Buffer No. 6*, 10 percent, pH 6.0 (see *Phosphate Buffers* ⟨81⟩), then add water to volume, and mix.

Procedure—Concomitantly determine the absorbances of the *Assay preparation* and the *Standard preparation* at the wavelength of maximum absorbance at about 310 nm, with a suitable spectrophotometer, using water as the blank. Calculate the quantity, in mg, of $C_{15}H_{24}N_2O_2 \cdot HCl$ in the portion of Tetracaine Hydrochloride for Injection taken by the formula:

$$10C(A_U / A_S),$$

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

Tetracaine Hydrochloride Ophthalmic Solution

» Tetracaine Hydrochloride Ophthalmic Solution is a sterile, aqueous solution of Tetracaine Hydrochloride. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{15}H_{24}N_2O_2 \cdot HCl$. It may contain suitable antimicrobial and thickening agents.

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

Labeling—Label it to indicate that the Ophthalmic Solution is not to be used if it contains crystals, or if it is cloudy or discolored.

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

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩

Solutions: solutions of the Ophthalmic Solution employed for measurement of absorbance in the *Assay.*

B: It responds to the tests for *Chloride* ⟨191⟩.

pH ⟨791⟩: between 3.7 and 6.0.

Assay—

Mobile phase—Prepare 0.01 M of dibasic ammonium phosphate in water, and adjust with phosphoric acid to a pH of 3.0. Prepare a filtered and degassed mixture of this solution and acetonitrile (70:30). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Tetracaine Hydrochloride RS in water to obtain a solution having a known concentration of about 0.1 mg per mL.

Assay preparation—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 10 mg of tetracaine hydrochloride, to a 100-mL volumetric flask, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 25-cm column containing packing L10. The flow rate is about 2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the column efficiency is not less than 500 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 $C_{15}H_{24}N_2O_2 \cdot HCl$ in each mL of the Ophthalmic Solution taken by the formula:

$$100(C / V)(r_U / r_S),$$

in which C is the concentration, in mg per mL, of USP Tetracaine Hydrochloride RS in the *Standard preparation; V* is the volume, in mL, of Ophthalmic Solution taken; and r_U and r_S are the tetracaine peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Tetracaine Hydrochloride Topical Solution

» Tetracaine Hydrochloride Topical Solution is an aqueous solution of Tetracaine Hydrochloride. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_{15}H_{24}N_2O_2 \cdot HCl$. It contains a suitable antimicrobial agent.

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

Labeling—Label it to indicate that the Topical Solution is not to be used if it contains crystals, or if it is cloudy or discolored.

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

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩

Solutions: solutions of the Topical Solution employed for measurement of absorbance in the *Assay.*

B: It responds to the tests for *Chloride* ⟨191⟩.

pH ⟨791⟩: between 4.5 and 6.0.

Assay—

Standard preparation—Prepare as directed in the *Assay* under *Tetracaine Hydrochloride in Dextrose Injection.*

Assay preparation—Using an accurately measured volume of Topical Solution, prepare as directed in the *Assay* under *Tetracaine Hydrochloride in Dextrose Injection.*

Procedure—Proceed as directed for *Procedure* in the *Assay* under *Tetracaine Hydrochloride in Dextrose Injection.* Calculate the quantity, in mg, of $C_{15}H_{24}N_2O_2 \cdot HCl$ in the volume of Topical Solution taken by the formula:

$$C(A_U / A_S),$$

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

Microbial limits ⟨61⟩—It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

pH ⟨791⟩: between 5.3 and 6.5.

Assay—

Oxidized nitroprusside reagent—Dissolve 1.0 g of sodium nitroferricyanide in water to make 10.0 mL (*Solution A*). Dissolve 1.0 g of potassium ferricyanide in water to make 10.0 mL (*Solution B*). Transfer 1.0 mL each of *Solution A* and *Solution B* to a 100-mL volumetric flask, add 1 mL of sodium hydroxide solution (1 in 10), and allow to stand until the solution changes to a light yellow color (about 20 to 30 minutes). Dilute with water to volume, and mix. Store in a refrigerator or keep in an ice bath, and use within 4 hours.

Standard preparation—Dissolve a suitable quantity of USP Tetrahydrozoline Hydrochloride RS, accurately weighed, in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 100 µg per mL.

Assay preparation—Transfer an accurately measured volume of Nasal Solution, equivalent to about 10 mg of tetrahydrozoline hydrochloride, to a 100-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Transfer 5.0 mL each of the *Standard preparation* and the *Assay preparation* to separate glass-stoppered test tubes. Pipet 5 mL of water into a third tube to provide a blank. To each tube add 4.0 mL of *Oxidized nitroprusside reagent*, mix, and allow to stand at 30° for 15 minutes. Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 570 nm, with a suitable spectrophotometer, using the blank to set the instrument. Calculate the quantity, in mg, of $C_{13}H_{16}N_2 \cdot HCl$ in each mL of the Nasal Solution taken by the formula:

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

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

Tetrahydrozoline Hydrochloride Ophthalmic Solution

» Tetrahydrozoline Hydrochloride Ophthalmic Solution is a sterile, isotonic solution of Tetrahydrozoline Hydrochloride in water. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{13}H_{16}N_2 \cdot HCl$.

Packaging and storage—Preserve in tight containers.

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

Identification—The UV absorption spectrum of the Ophthalmic Solution, diluted with dilute hydrochloric acid (1 in 100) to a concentration of about 1 in 4000, exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Tetrahydrozoline Hydrochloride RS, concomitantly measured.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 5.8 and 6.5.

Assay—

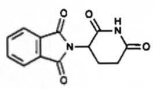
Standard preparation—Dissolve a suitable quantity of USP Tetrahydrozoline Hydrochloride RS, accurately weighed, in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 500 µg per mL.

Procedure—Transfer 2.0 mL of *Standard preparation* to a 50-mL volumetric flask. Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 1 mg of tetrahydrozoline hydrochloride, to a second 50-mL flask, and transfer 2 mL of water to a third 50-mL volumetric flask to provide a blank. To each flask add 1 mL of bromophenol blue sodium salt solution (1 in 1000), dilute each flask with potassium biphthalate solution (1 in 100) to volume, and mix. Allow to stand for 20 minutes, and filter each mixture through a suitable filter paper (Whatman No. 42 or the equivalent) that does not absorb the dye, discarding the first 15 mL of the filtrate. Transfer 20.0 mL of the subsequent filtrate to separate 125-mL separators, and extract each solution with four 20-mL portions of chloroform, filtering each extract through a pledget of glass wool into a 100-mL volumetric flask. Dilute the combined extracts from each solution with chloroform to volume, and mix. Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 415 nm, with a suitable spectrophotometer, using the blank to set the instrument. Calculate the quantity, in µg, of $C_{13}H_{16}N_2 \cdot HCl$ in each mL of the Ophthalmic Solution taken by the formula:

$$2(C/V)(A_U/A_S),$$

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

Thalidomide



$C_{13}H_{10}N_2O_4$ 258.23

1*H*-Isoindole-1,3(2*H*)-dione, 2-(2,6-dioxo-3-piperidinyl)-, (±)-.

(±)-*N*-(2,6-Dioxo-3-piperidyl)phthalimide.

α-(*N*-Phthalimido)glutarimide [*50-35-1*].

» Thalidomide contains not less than 98.0 percent and not more than 101.5 percent of $C_{13}H_{10}N_2O_4$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight containers, protected from light, at controlled room temperature.

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

Identification, *Infrared Absorption* ⟨197K⟩.

Microbial limits ⟨61⟩: meets the requirements.

Water, *Method Ic* ⟨921⟩: not more than 0.5%.
Solvent: anhydrous dimethyl sulfoxide.

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

Chromatographic purity—

Solution A—Prepare a filtered and degassed mixture of water, acetonitrile, and phosphoric acid (95 : 5 : 0.1).

Solution B—Prepare a filtered and degassed mixture of water, acetonitrile, and phosphoric acid (85 : 15 : 0.1).

Diluent—Prepare a mixture of water, acetonitrile, and phosphoric acid (50 : 50 : 0.1).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Phthalic acid stock solution—Transfer about 100 mg of phthalic acid to a 100-mL volumetric flask, dissolve in a mixture of acetonitrile and water (80 : 5), and dilute with acetonitrile to volume. Mix, and dilute quantitatively, and stepwise if necessary, with acetonitrile to obtain a solution having a concentration of about 0.1 mg per mL.

Standard stock solution—Dissolve, with the aid of sonication, an accurately weighed quantity of USP Thalidomide RS in acetonitrile to obtain a solution having a known concentration of about 1 mg per mL.

Standard solution—Pipet 2.0 mL of the *Standard stock solution* and 2.0 mL of the *Phthalic acid stock solution* into a 100-mL volumetric flask, dilute with *Diluent* to volume, and mix. Pipet 10.0 mL of this solution into a 100-mL volumetric flask, add 10.0 mL of phosphoric acid solution (1 in 100), dilute with water to volume, and mix to obtain a solution having a known concentration of about 0.0002 mg of phthalic acid per mL.

stepwise with methanol to obtain Standard solutions having the following compositions:

Standard solution	Concentration (µg RS per mL)	Percentage (%, for comparison with test specimen)
A	200	0.4
B	100	0.2
C	50	0.1

Separately apply 10-µL portions of the solutions to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of chloroform, methanol, and ammonium hydroxide (80 : 20 : 1) 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. Expose the plate to iodine vapors for 2 hours, and locate the spots on the plate by examination under short-wavelength UV light. Compare the intensities of any secondary spots observed in the chromatogram of the test solution, excluding the origin spot due to the maleate anion, with those of the principal spots in the chromatograms of the Standard solutions: no secondary spot is more intense than the principal spot obtained from Standard solution A (0.4%), and the sum of the intensities of all secondary spots, excluding any having intensities less than the principal spot obtained from Standard solution C, does not exceed 1.0%.

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

Assay—Dissolve about 800 mg of Timolol Maleate, accurately weighed, in about 90 mL of glacial acetic acid, and titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically, using a platinum electrode and a sleeve-type calomel electrode containing 0.1 N lithium perchlorate in acetic anhydride (see *Titrimetry* ⟨541⟩). Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 43.25 mg of $C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$.

Timolol Maleate Ophthalmic Solution

» Timolol Maleate Ophthalmic Solution is a sterile, aqueous solution of Timolol Maleate. It contains an amount of $C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$ equivalent to not less than 90.0 percent and not more than 110.0 percent of the labeled amount of timolol ($C_{13}H_{24}N_4O_3S$).

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

USP Reference standards ⟨11⟩—*USP Timolol Maleate RS.*

Identification—Dilute a suitable quantity of Ophthalmic Solution with water to obtain a solution having a concentration of about 20 µg of timolol per mL: the UV absorption spectrum of the solution so obtained exhibits maxima and minima at the same wavelengths as that of a similar preparation of USP Timolol Maleate RS, concomitantly measured.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 6.5 and 7.5.

Assay—

pH 2.8 phosphate buffer—Dissolve 11.1 g of monobasic sodium phosphate in 1000 mL of water, adjust with phosphoric acid to a pH of 2.8 ± 0.05, filter, and degas.

Diluent—Prepare a mixture of acetonitrile and *pH 2.8 phosphate buffer* (2 : 1).

Mobile phase—Prepare a mixture of *pH 2.8 phosphate buffer* and methanol (65 : 35). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩). [NOTE—Minimize the time the Reference Standard, the Ophthalmic Solution, the standard stock solution, the *Standard preparation,* and the *Assay preparation* are exposed to direct light.]

Standard preparation—Transfer about 34 mg of USP Timolol Maleate RS, accurately weighed, to a 25-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Transfer 5.0 mL of this stock solution to a 50-mL volumetric flask, add 15 mL of *Diluent*, dilute with water to volume, and mix.

Assay preparation—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 5 mg of timolol, to a 50-mL volumetric flask, add 15 mL of *Diluent*, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 295-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L1. The column temperature is maintained at 40°, and the flow rate is about 1.2 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the tailing factor is not more than 2.0, the column efficiency is not less than 3600 theoretical plates, 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 peak area responses for the major peaks. Calculate the quantity, in mg, of timolol ($C_{13}H_{24}N_4O_3S$) in each mL of Ophthalmic Solution taken by the formula:

$$(316.43 / 432.49)(50C / V)(r_U / r_S),$$

in which 316.43 and 432.49 are the molecular weights of timolol and timolol maleate, respectively, C is the concentration, in mg per mL, of USP Timolol Maleate RS in the *Standard preparation*, V is the volume, in mL, of Ophthalmic Solution taken, and r_U and r_S are the peak area responses of the timolol peaks obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Timolol Maleate Tablets

» Timolol Maleate Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$.

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—*USP Timolol Maleate RS.*

Identification—Transfer a portion of powdered Tablets, equivalent to about 30 mg of timolol maleate, to a 50-mL volumetric flask, add about 2 mL of 0.1 N hydrochloric acid, and shake gently. Add about 30 mL of methanol, agitate for 20 minutes, add methanol to volume, mix, and centrifuge. Similarly prepare a Standard solution containing 0.6 mg of USP Timolol Maleate RS per mL. Separately apply 10 µL of the test solution and 10 µL of the 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 chloroform, methanol, and ammonium hydroxide (80 : 20 : 1) until the solvent front has moved about three-fourths of the length of the plate. Air-dry, and examine under short-wavelength UV light: the R_f values of the principal spots obtained from the test solution correspond to those obtained from the Standard solution.

Dissolution, *Procedure for a Pooled Sample* ⟨711⟩—

Medium: 0.1 N hydrochloric acid; 500 mL.

Apparatus 1: 100 rpm.

Time: 20 minutes.

Procedure—Determine the amount of timolol maleate in solution in filtered portions of the solution under test, in comparison with a Standard solution having a known concentration of USP Timolol Maleate RS in the same medium, employing the procedure set forth in the *Assay*, making any necessary modifications.

Tolerances—Not less than 80% (*Q*) of the labeled amount of timolol maleate ($C_{13}H_{24}N_4O_3S \cdot C_4H_4O_4$) is dissolved in 20 minutes.

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

Assay—

pH 2.8 phosphate buffer—Transfer 22.08 g of monobasic sodium phosphate to a 2-liter volumetric flask, dilute with water to volume, adjust with phosphoric acid to a pH of 2.8 ± 0.05, and filter.

acid to a pH of 6.0. Dilute with water to obtain a solution having a known concentration of about 1.1 mg per mL.

System suitability solution 1—Dilute the *System suitability stock solution* quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration of about 0.22 mg per mL.

System suitability solution 2—Heat a portion of the *System suitability stock solution* in a suitable sealed glass container at 100° for 8 to 9 hours. Cool to room temperature, and dilute with water to obtain a solution having a known concentration of about 0.22 mg per mL.

Standard solution—Prepare a solution of about 55 mg of USP Tobramycin RS, accurately weighed, in a 50-mL volumetric flask. Dissolve in water, add 1.0 mL of 1.0 N sulfuric acid, dilute with water to volume, and mix. Dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a concentration of 1.10 µg of tobramycin per mL.

Test solution—Transfer an accurately measured volume of Inhalation Solution, equivalent to about 240 mg of tobramycin, to a 50-mL volumetric flask, dilute with water to volume, and mix. Dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a concentration of 192 µg of tobramycin per mL.

Derivatization procedure—[NOTE—Heat all solutions at the same temperature and for the same duration as indicated. Move all flasks to and from the 60° constant-temperature bath at the same time.] To separate 50-mL flasks transfer 15.0 mL of *System suitability solution 1*, 15.0 mL of *System suitability solution 2*, 15.0 mL of *Standard solution*, 15.0 mL of *Test solution*, and 15.0 mL of *Blank solution*. To each flask, add 10 mL of *2,4-Dinitrofluorobenzene reagent* and 10 mL of *Tris(hydroxymethyl)aminomethane reagent*, shake, and insert the stopper. Place the flasks in a constant-temperature bath at 60 ± 2°, and heat for 50 ± 5 minutes. Remove the flasks from the bath, and allow to stand for 10 minutes. Add acetonitrile to about 2 mL below the 50-mL mark, allow to cool to room temperature, dilute with acetonitrile to volume, and mix. Allow the solutions to stand for 16 hours. The solutions thus obtained are *Derivatized system suitability solution 1*, *Derivatized system suitability solution 2*, the *Derivatized standard solution*, the *Derivatized test solution*, and the *Derivatized blank solution*.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 365-nm detector and a 4.6-mm × 25-cm column that contains packing L11. The flow rate is about 1.2 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	79	21	equilibration
0–14	79→66	21→34	linear gradient
14–25	66→30	34→70	linear gradient
25–35	30	70	isocratic
35–40	30→20	70→80	linear gradient
40–50	20→5	80→95	linear gradient

Chromatograph *Derivatized system suitability solution 2*, and record the peak responses as directed for *Procedure:* the capacity factor, k', determined from tobramycin is not less than 15.5. Chromatograph *Derivatized system suitability solution 1*, and use the chromatogram to locate the degradation peaks from comparison to *Derivatized system suitability solution 2* (deoxystreptamine kanosaminide and nebramine will increase in response in *Derivatized system suitability solution 2* when viewed at a 0–10 mAbs unit or 0–5 mV unit full scale). Record the peak responses as directed for *Procedure:* the relative retention times are about 0.36 for an impurity, 0.66 for deoxystreptamine kanosaminide, 0.94 for nebramine, 0.96 for kanamycin B, and 1.00 for tobramycin. The resolution, R, between the nebramine and kanamycin peaks is not less than 1.0. The relative standard deviation for replicate injections of the *Derivatized standard solution* is not more than 2.0%.

Procedure—Separately inject equal volumes (about 45 µL) of *Derivatized system suitability solution 1*, *Derivatized system suitability solution 2*, the *Derivatized standard solution*, the *Derivatized test solution*, and the *Derivatized blank solution*, record the chromatograms, and measure the peak responses, disregarding any peak corresponding to those obtained from the *Derivatized blank solution*, and subtracting the quantities of any such peaks found at the relative retention times of 0.36, 0.66, and 0.94 from those found in the *Derivatized test solution*. For unknown peak determinations, disregard any peaks found in the chromatogram of the *Derivatized test solution* that correspond to those in the chromatogram of *Derivatized system suitability solution 1*. Calculate the percentage of each impurity in relation to the tobramycin content of the Inhalation Solution taken by the formula:

$$(110/192)(r_i/r_s),$$

in which r_i is the peak area of any impurity obtained from the *Derivatized test solution;* and r_s is the peak area for tobramycin obtained from the *Derivatized standard solution:* not more than 0.25% of the impurity noted at a relative retention time of 0.36 is found; not more than 0.3% of deoxystreptamine kanosaminide is found; not more than 0.4% of nebramine is found; not more than 0.1% of any unknown impurity is found; not more than 0.2% of total unknown impurities is found; and not more than 1.0% of total impurities is found.

Content of sodium chloride—Pipet 25 mL of Inhalation Solution into a suitable container. Add between 70 and 100 mL of water. Add 10 mL of an acidic gelatin solution, prepared by dissolving 2 g of gelatin and 50 mL of nitric acid in 1000 mL of water. Titrate potentiometrically with 0.1 N silver nitrate VS using a suitable silver electrode: not less than 90.0% and not more than 110.0% of the labeled amount of sodium chloride is found.

Other requirements—It meets the requirements for the *Identification* tests under *Tobramycin*.

Assay—

Mobile phase, *2,4-Dinitrofluorobenzene reagent*, *Tris(hydroxymethyl)aminomethane reagent*, *Standard preparation*, *Derivatization procedure*, *Resolution solution*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Tobramycin*.

Assay preparation—Transfer an accurately measured volume of Inhalation Solution to a suitable volumetric flask, and quantitatively dilute with water to obtain a solution having a concentration of about 192 µg of tobramycin per mL.

Procedure—Proceed as directed in the *Assay* under *Tobramycin*. Calculate the quantity, in mg, of tobramycin ($C_{18}H_{37}N_5O_9$) in each mL of Inhalation Solution taken by the formula:

$$(CE)(L/D)(r_U/r_S),$$

in which C, E, r_U, and r_S are as defined therein; L is the labeled quantity, in mg, of tobramycin per mL in the Inhalation Solution taken; and D is the concentration, in µg per mL, of tobramycin in the *Assay preparation*.

Tobramycin Ophthalmic Solution

» Tobramycin Ophthalmic Solution contains the equivalent of not less than 90.0 percent and not more than 120.0 percent of the labeled amount of tobramycin ($C_{18}H_{37}N_5O_9$). It may contain one or more suitable buffers, dispersants, preservatives, and tonicity agents.

Packaging and storage—Preserve in tight containers, and avoid exposure to excessive heat.

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

Identification—

A: Prepare a Standard solution of USP Tobramycin RS containing 3 mg per mL. Separately apply 6 µL of Ophthalmic Solution, 6 µL of the Standard solution, and 6 µL of a mixture consisting of equal volumes of the two solutions to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Proceed as directed for *Identification* test *A* under *Tobramycin*, beginning with "Place the plate in a suitable chromatographic chamber." The specified results are obtained.

B: The retention time of the major peak for tobramycin in the chromatogram of the *Derivatized assay preparation* corresponds to that in the chromatogram of the *Derivatized standard preparation*, as obtained in the *Assay*.

Sterility ⟨71⟩—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.

pH ⟨791⟩: between 7.0 and 8.0.

Assay—

Mobile phase, *2,4-Dinitrofluorobenzene reagent*, *Tris(hydroxymethyl)aminomethane reagent*, and *Resolution solution*—Prepare as directed in the *Assay* under *Tobramycin*.

Standard preparation—Transfer about 33 mg of USP Tobramycin RS, accurately weighed, to a 50-mL volumetric flask, add 20 mL of water and 1 mL of 1 N sulfuric acid, and swirl to dissolve. Dilute with water to volume, and mix. Transfer 10.0 mL of this solution to a second 50-mL volumetric flask, dilute with water to volume, and mix. This solution contains about 0.132 mg of USP Tobramycin RS per mL.

Assay preparation—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 6 mg of tobramycin, to a 50-mL volumetric flask, dilute with water to volume, and mix.

Derivatization procedure—Proceed as directed in the *Assay* under *Tobramycin*, except to use 5.0 mL each of the *Standard preparation* and the *Assay preparation*, instead of 4.0 mL of each.

Chromatographic system—Proceed as directed in the *Assay* under *Tobramycin*, except to use a 4-mm × 15-cm column and to maintain the column temperature at 40°.

Procedure—Proceed as directed in the *Assay* under *Tobramycin*. Calculate the quantity, in mg, of tobramycin ($C_{18}H_{37}N_5O_9$) in each mL of the Ophthalmic Solution taken by the formula:

$$0.05(CE/V)(r_U/r_S),$$

in which V is the volume, in mL, of Ophthalmic Solution taken to prepare the *Assay preparation;* and the other terms are as defined therein.

Tobramycin and Dexamethasone Ophthalmic Ointment

» Tobramycin and Dexamethasone Ophthalmic Ointment contains not less than 90.0 percent and not more than 120.0 percent of the labeled amount of tobramycin ($C_{18}H_{37}N_5O_9$), and not less than 90.0 percent and not more than 110.0 percent of the labeled amount of dexamethasone ($C_{22}H_{29}FO_5$).

Packaging and storage—Preserve in collapsible ophthalmic ointment tubes.

USP Reference standards ⟨11⟩—*USP Dexamethasone RS*. *USP Tobramycin RS*.

Identification—

A: To 1 g of Ophthalmic Ointment in a test tube add 2 mL of chloroform, and shake to dissolve. Add 0.5 mL of sodium sulfate solution (1 in 10), shake vigorously, and centrifuge: the clear supernatant aqueous liquid meets the requirements for *Identification* test *A* under *Tobramycin*. [NOTE—If, after centrifuging, an oily film remains on top of the supernatant aqueous liquid, transfer the supernatant aqueous liquid to a second test tube, and wash it with 2 mL of chloroform.]

B: The retention time of the major peak for dexamethasone in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay for dexamethasone*.

Sterility ⟨71⟩—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*.

Minimum fill ⟨755⟩: meets the requirements.

Water, *Method I* ⟨921⟩: not more than 1.0%, 20 mL of a mixture of toluene and methanol (7 : 3) being used in place of methanol in the titration vessel.

Metal particles ⟨751⟩: meets the requirements.

Assay for tobramycin—

Mobile phase, *2,4-Dinitrofluorobenzene reagent*, *Tris(hydroxymethyl)aminomethane reagent*, *Standard preparation*, *Resolution solution*, and *Chromatographic system*—Proceed as directed in the *Assay* under *Tobramycin*.

Assay preparation—Transfer an accurately weighed portion of Ophthalmic Ointment, equivalent to about 4.5 mg of tobramycin, to a separator, add 50 mL of ether, and extract with four 20- to 25-mL portions of water. Combine the water extracts in a 100-mL volumetric flask, dilute with water to volume, and mix.

Derivatization procedure—Proceed as directed in the *Assay* under *Tobramycin*, except to use 15.0 mL of *Assay preparation* instead of 4.0 mL.

Procedure—Proceed as directed in the *Assay* under *Tobramycin*. Calculate the quantity of tobramycin ($C_{18}H_{37}N_5O_9$), in mg, in the portion of Ophthalmic Ointment taken by the formula:

$$(4/150)(CE)(r_U/r_S),$$

in which the terms are as defined therein.

Assay for dexamethasone—

Diluent—Prepare a mixture of methanol and water (750 : 250).

Mobile phase—Prepare a suitable mixture of methanol and water (55 : 45), pass through a suitable filter having a 1-µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Dexamethasone RS in *Diluent* to obtain a stock solution having a known concentration of about 0.2 mg per mL. Transfer 15.0 mL of this stock solution to a separator containing about 50 mL of *n*-hexane, and shake. Allow the layers to separate, and drain the lower phase into a 50-mL volumetric flask. Repeat the extraction with two 15-mL portions of *Diluent*, combining the lower phase from each extraction in the same 50-mL volumetric flask. Dilute with *Diluent* to volume, and mix. This solution contains about 0.06 mg of USP Dexamethasone RS per mL.

Resolution solution—Prepare a stock solution of chlorobutanol and USP Dexamethasone RS in *Diluent* containing about 1 mg of anhydrous chlorobutanol and 0.2 mg of USP Dexamethasone RS per mL. Proceed as directed for *Standard preparation* beginning with "Transfer 15.0 mL of this stock solution to a separator." The solution so obtained contains about 0.3 mg of anhydrous chlorobutanol and 0.06 mg of USP Dexamethasone RS per mL.

Assay preparation—Transfer an accurately weighed quantity of Ophthalmic Ointment, equivalent to about 3 mg of dexamethasone, to a separator containing about 50 mL of *n*-hexane, and shake. Add 15 mL of *Diluent*, and shake. Allow the layers to separate, and drain the lower phase into a 50-mL volumetric flask. Repeat the extraction with two 15-mL portions of *Diluent*, combining the lower phase from each extraction in the same 50-mL volumetric flask. Dilute with *Diluent* to volume, mix, and centrifuge. Use the clear solution.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 206-nm detector and an 8.0-mm × 10-cm column that contains packing L1. The flow rate is about 3 mL per minute. Chromatograph the *Resolution solution*, and measure the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for chlorobutanol and 1.0 for dexamethasone; and the resolution, R, between chlorobutanol and dexamethasone is not less than 1.8. Chromatograph the *Standard preparation*, and measure the peak responses as directed for *Procedure:* the tailing factor is not more than 2; the column efficiency is not less than 350 theoretical plates; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 100 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 dexamethasone ($C_{22}H_{29}FO_5$) in the portion of Ophthalmic Ointment taken by the formula:

$$50C(r_U/r_S),$$

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

pH ⟨791⟩: between 10.0 and 11.5, in a solution prepared as directed in the labeling.

Water, *Method I* ⟨921⟩—Add 5 mL of glacial acetic acid prior to the titration: the content is not more than 1.0%.

Particulate matter ⟨788⟩: meets the requirements for small-volume injections.

Potassium chloride content—

Standard solutions—Prepare five standard solutions (*1*, *2*, *3*, *4*, and *5*) each containing 0.60 mEq of sodium (35 mg of sodium chloride) per liter, and to the solutions add, respectively, 0-, 2-, 4-, 6-, and 8-mg supplements of potassium, in the form of the chloride, per liter. If necessary, because of changes in the sensitivity of the photometer, vary the levels of concentration of the potassium, keeping the ratios between solutions approximately as given.

Standard graph—Set a suitable flame photometer for maximum emittance at a wavelength of 766 nm to 767 nm. (The exact wavelength setting will vary slightly with the instrument.) Adjust the instrument to zero emittance with solution *1*. Then adjust the instrument to 100% emittance with solution *5*. Read the percentage emittance of solutions *2*, *3*, and *4*. Plot the observed emittance of solutions *2*, *3*, *4*, and *5* as the ordinate and the concentration, in µg per mL, of potassium as the abscissa on arithmetic coordinate paper.

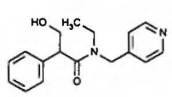
Procedure—Dissolve the entire contents of 1 container of Tromethamine for Injection in sufficient water, and dilute quantitatively and stepwise with water to obtain a solution containing about 4 µg of potassium per mL, or a quantity corresponding to the concentration of the *Standard solutions*. Adjust the instrument to zero emittance with solution *1* and to 100% emittance with solution *5*. Read the percentage emittance of the test solution. By reference to the *Standard graph*, determine the concentration, in µg per mL, of potassium in the test solution, apply the dilution factor, and calculate the quantity, in mg, of potassium in the container of Tromethamine for Injection. Each mg of potassium is equivalent to 1.907 mg of potassium chloride (KCl).

Sodium chloride content—Proceed as directed under *Potassium chloride content*, with the following modifications: (1) Prepare the *Standard solutions* to contain 0, 2, 4, 6, and 8 mg of sodium, in the form of the chloride, per 1000 mL, without added potassium; (2) prepare the *Standard graph* with the flame photometer set at 588 nm to 589 nm; and (3) under *Procedure* read "sodium" for "potassium" throughout. Each mg of sodium is equivalent to 2.542 mg of sodium chloride (NaCl).

Other requirements—It meets the requirements for *Sterility Tests* ⟨71⟩, *Uniformity of Dosage Units* ⟨905⟩, and *Labeling* under *Injections* ⟨1⟩.

Assay for tromethamine—Dissolve the entire contents of 1 container of Tromethamine for Injection in sufficient water, diluting with water to an accurately measured volume to obtain a solution containing about 36 mg of tromethamine per mL. Transfer to a beaker an accurately measured volume of the solution, equivalent to about 180 mg of tromethamine, dilute with water to about 100 mL, add bromocresol purple TS, and titrate with 0.1 N hydrochloric acid VS to a yellow endpoint. Each mL of 0.1 N hydrochloric acid is equivalent to 12.11 mg of $C_4H_{11}NO_3$.

Tropicamide



$C_{17}H_{20}N_2O_2$ 284.35

Benzeneacetamide, *N*-ethyl-α-(hydroxymethyl)-*N*-(4-pyridinylmethyl)-, (±)-.

(±)-*N*-Ethyl-2-phenyl-*N*-(4-pyridylmethyl)hydracrylamide [*1508-75-4*].

» Tropicamide contains not less than 99.0 percent and not more than 101.0 percent of $C_{17}H_{20}N_2O_2$, calculated on the dried basis.

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

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

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 25 µg per mL.

Medium: 3 N hydrochloric acid.

Melting range, *Class I* ⟨741⟩: between 96° and 100°.

Loss on drying ⟨731⟩—Dry about 500 mg, accurately weighed, in vacuum over phosphorus pentoxide at 80° for 4 hours: it loses not more than 0.5% of its weight.

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

Assay—Dissolve about 750 mg of Tropicamide, accurately weighed, in 80 mL of glacial acetic acid, add 4 drops of crystal violet TS, and titrate with 0.1 N perchloric acid VS to a blue-green endpoint. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 28.44 mg of $C_{17}H_{20}N_2O_2$.

Tropicamide Ophthalmic Solution

» Tropicamide Ophthalmic Solution is a sterile, aqueous solution of Tropicamide. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $C_{17}H_{20}N_2O_2$. It contains a suitable antimicrobial agent, and may contain suitable substances to increase its viscosity.

Packaging and storage—Preserve in tight containers, and avoid freezing.

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

Identification—

A: Extract 10 mL of it with 25 mL of chloroform, filter the chloroform extract through dry, folded filter paper, and evaporate the filtrate to dryness: the residue so obtained responds to *Identification* test *A* under *Tropicamide*.

B: The UV absorption spectrum of the solution employed for measurement of absorbance in the *Assay* exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Tropicamide RS, concomitantly measured.

Sterility ⟨71⟩: meets the requirements.

pH ⟨791⟩: between 4.0 and 5.8.

Assay—Transfer an accurately measured volume of Ophthalmic Solution, equivalent to about 30 mg of tropicamide, to a 100-mL volumetric flask, add water to volume, and mix. Transfer 10.0 mL of this solution to a separator, add 2 mL of sodium carbonate solution (1 in 10), extract with four 20-mL portions of chloroform, and combine the extracts in a second separator. Wash the combined extracts with a 25-mL portion of pH 6.5 phosphate buffer (see *Buffer Solutions* in the section *Reagents, Indicators, and Solutions*), and transfer to another separator. Wash the aqueous layer with 10 mL of chloroform, and add it to the extracts. Extract the chloroform solution with four 20-mL portions of dilute sulfuric acid (1 in 6), combine the acid extracts in a 100-mL volumetric flask, and add the dilute acid to volume. Dissolve an accurately weighed quantity of USP Tropicamide RS in dilute sulfuric acid (1 in 6), and dilute quantitatively and stepwise with the same solvent to obtain a Standard solution having a known concentration of about 30 µg per mL. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 253 nm, with a suitable spectrophotometer, using dilute sulfuric acid (1 in 6) as the blank. Calculate the quantity, in mg, of $C_{17}H_{20}N_2O_2$ in each mL of the Ophthalmic Solution taken by the formula:

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

in which C is the concentration, in µg per mL, of USP Tropicamide RS in the Standard solution, V is the volume, in mL, of Ophthalmic Solution taken, and A_U and A_S are the absorbances of the solution from the Ophthalmic Solution and the Standard solution, respectively.

Zinc Sulfate Ophthalmic Solution

» Zinc Sulfate Ophthalmic Solution is a sterile solution of Zinc Sulfate in Water rendered isotonic by the addition of suitable salts. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of $ZnSO_4$.

Packaging and storage—Preserve in tight containers.

Identification—It responds to the tests for *Zinc* ⟨191⟩ and for *Sulfate* ⟨191⟩.

Sterility ⟨71⟩: meets the requirements..

pH ⟨791⟩: between 5.8 and 6.2; or, if it contains sodium citrate, between 7.2 and 7.8.

Assay—Pipet into a beaker a volume of Ophthalmic Solution, equivalent to about 25 mg of zinc sulfate. Add 1 mL of glacial acetic acid, and adjust by the dropwise addition of 6 N ammonium hydroxide to a pH of between 5.0 and 5.5. Add 1 drop of copper ethylenediaminetetraacetate solution [prepared by mixing 1 mL of cupric sulfate solution (1 in 40) and 1 mL of 0.1 M edetate disodium] and 3 drops of a 1 in 1000 solution of 1-(2-pyridylazo)-2-naphthol in anhydrous methanol, and titrate with 0.01 M edetate disodium VS. Each mL of 0.01 M edetate disodium is equivalent to 1.614 mg of $ZnSO_4$.

Add the following:

▲Zinc Sulfide Topical Suspension

(Monograph under this new title—to become official July 1, 2007)
(Current monograph title is White Lotion)

» Prepare Zinc Sulfide Topical Suspension as follows:

Zinc Sulfate	40 g
Sulfurated Potash	40 g
Purified Water, a sufficient quantity to make	1000 mL

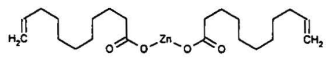
Dissolve the Zinc Sulfate and the Sulfurated Potash separately, each in 450 mL of Purified Water, and filter each solution. Add the sulfurated potash solution slowly to the zinc sulfate solution with constant stirring. Then add the required amount of Purified Water, and mix.

NOTE—Prepare the Topical Suspension fresh, and shake it thoroughly before dispensing.

Packaging and storage—Dispense in tight containers.▲USP28

(Official July 1, 2007)

Zinc Undecylenate



$C_{22}H_{38}O_4Zn$ 431.92
10-Undecenoic acid, zinc(2+) salt.
Zinc 10-undecenoate [*557-08-4*].

» Zinc Undecylenate contains not less than 98.0 percent and not more than 102.0 percent of $C_{22}H_{38}O_4Zn$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Identification—

A: Acidify about 5 g with 25 mL of 2 N sulfuric acid, add 20 mL of water, and extract in a separator with two 25-mL portions of ether. Evaporate the ether solution until the odor of ether no longer is perceptible. Add potassium permanganate TS dropwise to a 1-mL portion of this residue: the permanganate color is discharged.

B: A 3-mL portion of the residue of undecylenic acid obtained in *Identification* test *A* responds to *Identification* test *B* under *Undecylenic Acid.*

C: Dissolve about 100 mg in a mixture of 10 mL of water and 1 mL of ammonium hydroxide, and add a few drops of sodium sulfide TS: a white, flocculent precipitate of zinc sulfide is formed.

Loss on drying ⟨731⟩—Dry it at 105° for 2 hours: it loses not more than 1.25% of its weight.

Alkalies and alkaline earths—Boil 1.50 g with a mixture of 50 mL of water and 10 mL of hydrochloric acid, filter while hot, and wash the separated acid with about 50 mL of hot water. Render the combined filtrate and washings alkaline with 6 N ammonium hydroxide, add ammonium sulfide TS to precipitate the zinc completely, dilute with water to 200 mL, mix, and filter. To 100 mL of the clear filtrate add 0.5 mL of sulfuric acid, evaporate to dryness, and ignite over a low flame to constant weight: the weight of the residue does not exceed 7.5 mg (1.0%).

Assay—Boil 50.0 mL of 0.1 N sulfuric acid VS with about 1 g of Zinc Undecylenate, accurately weighed, for 10 minutes, or until the undecylenic acid layer is clear, adding water, as necessary, to maintain the original volume. Cool, and transfer the mixture, with the aid of water, to a 500-mL separator. Dilute with water to about 250 mL, and extract with two 100-mL portions of solvent hexane. Wash the combined extracts with water until the last washing is neutral to litmus, add the washings to the original water layer, and evaporate on a steam bath to about 100 mL. Cool, add 3 drops of methyl orange TS, and titrate the excess sulfuric acid with 0.1 N sodium hydroxide VS. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.1 N sulfuric acid is equivalent to 21.60 mg of $C_{22}H_{38}O_4Zn$.