of phenylephrine bitartrate ($C_9H_{13}NO_2 \cdot C_4H_6O_6$) in each mL of the Aerosol taken by the formula:

$$(317.30 / 203.67)(0.01Cd / W)(A_U / A_S)$$

in which 317.30 and 203.67 are the molecular weights of phenylephrine bitartrate and phenylephrine hydrochloride, respectively; *C* is the concentration, in µg per mL, of USP Phenylephrine Hydrochloride RS in the *Phenylephrine hydrochloride standard preparation*; *d* is the density, in g per mL, of Aerosol taken; *W* is the weight, in g, of the sample taken; and A_U and A_S are the absorbances of the solutions from the *Assay preparation* and the *Phenylephrine hydrochloride standard preparation*, respectively.

Isoproterenol Sulfate

$(C_{11}H_{17}NO_3)_2 \cdot H_2SO_4 \cdot 2H_2O$ 556.62
1,2-Benzenediol, 4-[1-hydroxy-2-[(1-methylethyl)amino]ethyl]-, sulfate (2:1) (salt), dihydrate.
3,4-Dihydroxy-α-[(isopropylamino)methyl]benzyl alcohol sulfate (2:1) (salt) dihydrate [6700-39-6].
Anhydrous 520.60 [299-95-6].

» Isoproterenol Sulfate contains not less than 97.0 percent and not more than 103.0 percent of $(C_{11}H_{17}NO_3)_2 \cdot H_2SO_4$, calculated on the anhydrous basis.

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

USP Reference standards ⟨11⟩—
USP Isoproterenol Hydrochloride RS

Identification—

A: *Ultraviolet Absorption* ⟨197U⟩—
Solution: 50 µg per mL.
Medium: 0.1 N hydrochloric acid.

B: To a solution of 10 mg in 5 mL of water add 1 drop of ferric chloride TS: an intense green color is produced, and it becomes olive-green on standing.

C: To a solution of 10 mg in 1 mL of water add 1 drop of phosphotungstic acid TS: a white precipitate is formed immediately and it becomes brown on standing (*distinction from epinephrine, which forms no precipitate*).

D: Dilute 1.0 mL of a solution (1 in 1000) with water to 10 mL, add 0.1 mL of dilute hydrochloric acid (1 in 120), then add 1.0 mL of 0.10 N iodine. Allow to stand for 5 minutes, and add 2.0 mL of 0.10 N sodium thiosulfate: a salmon pink color is produced (*distinction from norepinephrine, which, at the same pH, about 3, produces no color or at most only a slight pink color*).

E: It responds to the tests for *Sulfate* ⟨191⟩.

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

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

Chloride ⟨221⟩—A 0.10-g portion shows no more chloride than corresponds to 0.20 mL of 0.020 N hydrochloric acid (0.14%).

Limit of isoproterenone—It meets the requirements of the test for *Isoproterenone* under *Isoproterenol Hydrochloride.*

Assay—

Standard preparation—Prepare as directed in the *Assay* under *Isoproterenol Hydrochloride.*

Assay preparation—Transfer about 125 mg of Isoproterenol Sulfate, accurately weighed, to a 25-mL volumetric flask, dissolve in sodium bisulfite solution (3 in 1000), dilute with sodium bisulfite solution to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with 0.17 N acetic acid to volume, and mix.

Chromatographic system—Proceed as directed for *Procedure* in the *Assay* under *Isoproterenol Hydrochloride.* Calculate the quantity, in mg, of $(C_{11}H_{17}NO_3)_2 \cdot H_2SO_4$ in the portion of Isoproterenol Sulfate taken by the formula:

$$(260.30 / 247.72)(0.5C)(h_U / h_S)$$

in which 260.30 is one-half of the molecular weight of anhydrous isoproterenol sulfate, 247.72 is the molecular weight of isoproterenol hydrochloride; and *C*, h_U, and h_S are as defined therein.

Isoproterenol Sulfate Inhalation Aerosol

» Isoproterenol Sulfate Inhalation Aerosol is a suspension of microfine Isoproterenol Sulfate in fluorochlorohydrocarbon propellants in a pressurized container. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of isoproterenol sulfate $[(C_{11}H_{17}NO_3)_2 \cdot H_2SO_4]$.

Packaging and storage—Preserve in small, nonreactive, light-resistant aerosol containers equipped with metered-dose valves and provided with oral inhalation actuators.

USP Reference standards ⟨11⟩—
USP Isoproterenol Hydrochloride RS

Identification—

A: Place 10 mL of water in a small beaker, and deliver 10 sprays from the Aerosol under the surface of the water, actuating the valve by pressing the tip against the bottom of the beaker. Filter, and to 5 mL of the filtrate add 1 drop of dilute hydrochloric acid (1 in 120). Add 0.50 mL of 0.10 N iodine, allow to stand for 5 minutes, and add 1.0 mL of 0.10 N sodium thiosulfate: a red-brown color is produced.

B: A portion of the filtrate obtained in *Identification* test *A* responds to the tests for *Sulfate* ⟨191⟩.

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩—It meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa.*

Dose uniformity over the entire contents: meets the requirements for *Metered-Dose Inhalers* under *Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers* ⟨601⟩.

PROCEDURE FOR DOSE UNIFORMITY—

Ferro-citrate solution and *Buffer solution*—Prepare as directed under *Epinephrine Assay* ⟨391⟩.

Standard preparation—Dissolve an accurately weighed quantity of USP Isoproterenol Hydrochloride RS in a freshly prepared sodium bisulfite solution (1 in 500), and dilute quantitatively and stepwise with the same sodium bisulfite solution as necessary to obtain a solution having a known concentration of about 4 µg per mL.

Test preparation—Discharge the minimum recommended dose into the sampling apparatus and detach the inhaler as directed. Rinse the apparatus (filter and interior) with four 5.0-mL portions of a freshly prepared sodium bisulfite solution (1 in 500), and transfer the resulting solutions quantitatively to a 50-mL centrifuge tube. Add 10 mL of chloroform, insert the stopper, shake vigorously for 1 minute, and centrifuge for 5 minutes. Use the clear supernatant as directed in the *Procedure.*

Procedure—Into three separate flasks transfer the *Test preparation*, 20.0 mL of the *Standard preparation*, and