moved three-fourths the length of the plate. Remove the plate from the chamber, mark the solvent front, and allow the solvent to evaporate in warm circulating air. Spray with *Spray reagent*, followed by sodium carbonate solution (1 in 10).

Acceptance criteria: The R_F value of the principal spot from the *Sample solution* corresponds to that of *Standard solution A*. Any spot from the *Sample solution* is not larger or more intense than the spot with the same R_F value from *Standard solution B*, corresponding to NMT 4.0% norepinephrine.

SPECIFIC TESTS

- **Optical Rotation,** *Specific Rotation* ⟨781S⟩: −50.0° to −54.0°

  Sample solution: 20 mg/mL, in 0.6 N hydrochloric acid
- **Loss on Drying** ⟨731⟩: Dry it in a vacuum over silica gel for 18 h: it loses NMT 2.0% of its weight.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers.
- **USP Reference Standards** ⟨11⟩

  USP Epinephrine Bitartrate RS

  USP Norepinephrine Bitartrate RS

Epinephrine Inhalation Aerosol

» Epinephrine Inhalation Aerosol is a solution of Epinephrine in propellants and Alcohol prepared with the aid of mineral acid in a pressurized container. It contains not less than 90.0 percent and not more than 115.0 percent of the labeled amount of epinephrine ($C_9H_{13}NO_3$).

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 Epinephrine Bitartrate RS

Identification—Place 10 mL of water in a small beaker, and deliver 2 sprays from the Inhalation Aerosol under the surface of the water, actuating the valve by pressing the tip against the bottom of the beaker. To 5 mL of the solution add 1 drop of dilute sulfuric acid (1 in 200), add 0.5 mL of 0.1 N iodine, allow to stand for 5 minutes, and add 1 mL of 0.1 N sodium thiosulfate: a red-brown color is produced.

Delivered 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 Epinephrine Bitartrate 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 18 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 20.0 mL of water to provide the blank. To each flask add 100 µL of *Ferro-citrate solution* and 1.0 mL of *Buffer solution*, and mix. Concomitantly determine the absorbances with a suitable spectrophotometer, in 5-cm cells, of the solutions from the *Test preparation* and the *Standard preparation*, at the wavelength of maximum absorbance at about 530 nm, against the blank. Calculate the quantity, in µg, of $C_9H_{13}NO_3$ contained in the minimum dose taken by the formula:

$$(183.20 / 333.29)(20CN)(A_U / A_S)$$

in which C is the concentration, in µg per mL, of USP Epinephrine Bitartrate RS in the *Standard preparation*; N is the number of sprays discharged to obtain the minimum recommended dose; 183.20 and 333.29 are the molecular weights of epinephrine and epinephrine bitartrate, respectively; and A_U and A_S are the absorbances of the solutions from the *Test preparation* and the *Standard preparation*, respectively.

Assay—Weigh the Inhalation Aerosol, chill to a temperature below −30°, remove the valve by suitable means, and allow the Inhalation Aerosol to warm slowly to room temperature to expel the more volatile propellant fractions. Transfer the residues in the aerosol container and valve to a 125-mL separator with the aid of six 5-mL portions of dilute sulfuric acid (1 in 1000), and extract the solution with three 25-mL portions of chloroform. Proceed as directed in the *Assay* under *Epinephrine Nasal Solution*, beginning with "Rinse the stopper and mouth of the separator," but use 10.0 mL instead of 5.0 mL of chloroform in the determination of the specific rotation. Dry the empty aerosol container and valve, weigh them, and determine the net weight of the Inhalation Aerosol. Calculate the quantity, in mg, of $C_9H_{13}NO_3$ in the Inhalation Aerosol taken by the formula:

$$(183.20 / 309.32)(W)(0.5 + 0.5R / 93)$$

in which 183.20 and 309.32 are the molecular weights of epinephrine and triacetylepinephrine, respectively, and W is the weight, in mg, and R is the specific rotation (in degrees, without regard to the sign), of the isolated triacetylepinephrine.

Epinephrine Injection

» Epinephrine Injection is a sterile solution of Epinephrine in Water for Injection prepared with the aid of Hydrochloric Acid or other suitable buffers. It contains not less than 90.0 percent and not more than 115.0 percent of the labeled amount of epinephrine ($C_9H_{13}NO_3$).

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

Labeling—The label indicates that the Injection is not to be used if its color is pinkish or darker than slightly yellow or if it contains a precipitate.

Change to read:

USP Reference standards ⟨11⟩—
• (CN 1-May-2018)
USP Epinephrine Bitartrate RS