ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨11⟩
  USP Acetaminophen RS
  USP Diphenhydramine Citrate RS

Acetaminophen, Diphenhydramine Hydrochloride, and Pseudoephedrine Hydrochloride Tablets

DEFINITION

Acetaminophen, Diphenhydramine Hydrochloride, and Pseudoephedrine Hydrochloride Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$), diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$), and pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$).

IDENTIFICATION

- **A.** The retention time of the acetaminophen peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Acetaminophen*.
- **B.** The retention time of the diphenhydramine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Diphenhydramine Hydrochloride*.
- **C.** The retention time of the pseudoephedrine peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay* for *Pseudoephedrine Hydrochloride*.

ASSAY

- **ACETAMINOPHEN**

Solution A: Transfer 6.8 g of monobasic potassium phosphate to a 1000-mL volumetric flask, and add water to dissolve. Add 2.0 mL of triethylamine, and dilute with water to volume. Adjust with phosphoric acid to a pH of 4.0.
Diluent: Acetonitrile and *Solution A* (11:89)
Mobile phase: Acetonitrile and *Solution A* (6:94)
Standard solution: 25 µg/mL of USP Acetaminophen RS, 12.5 µg/mL of USP Diphenhydramine Hydrochloride RS, and 30 µg/mL of USP Pseudoephedrine Hydrochloride RS in *Diluent*
Sample stock solution: Nominally 5 mg/mL of acetaminophen in *Diluent* prepared as follows. Transfer an amount nominally equivalent to 500 mg of acetaminophen from NLT 20 finely powdered Tablets to a 100-mL volumetric flask, add 75 mL of *Diluent*, shake, and sonicate for 15 min. Dilute with *Diluent* to volume.
Sample solution: Nominally 25 µg/mL of acetaminophen from the *Sample stock solution* in *Diluent*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 15-cm; packing L10
Flow rate: 2 mL/min
Injection volume: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Tailing factor: NMT 2.0 for the acetaminophen, diphenhydramine, and pseudoephedrine peaks
Relative standard deviation: NMT 2.0% determined from the acetaminophen, diphenhydramine hydrochloride, and pseudoephedrine hydrochloride responses for replicate injections
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Tablets taken:

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

r_U = peak response of acetaminophen from the *Sample solution*
r_S = peak response of acetaminophen from the *Standard solution*
C_S = concentration of USP Acetaminophen RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of acetaminophen in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$)

- **DIPHENHYDRAMINE HYDROCHLORIDE**

Solution A, Diluent, Mobile phase, Standard solution, Chromatographic system, and System suitability: Proceed as directed in the *Assay* for *Acetaminophen*.
Sample stock solution: Nominally 0.125 mg/mL of diphenhydramine hydrochloride in *Diluent* prepared as follows. Transfer an amount nominally equivalent to 12.5 mg of diphenhydramine hydrochloride from a portion of finely powdered Tablets (NLT 20) to a 100-mL volumetric flask, add 75 mL of *Diluent*, and sonicate for 15 min. Dilute with *Diluent* to volume.
Sample solution: Nominally 12.5 µg/mL of diphenhydramine hydrochloride from the *Sample stock solution* in *Diluent*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of diphenhydramine from the *Sample solution*
r_S = peak response of diphenhydramine from the *Standard solution*
C_S = concentration of USP Diphenhydramine Hydrochloride RS in the *Standard solution* (µg/mL)
C_U = nominal concentration of diphenhydramine hydrochloride in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amount of diphenhydramine hydrochloride ($C_{17}H_{21}NO \cdot HCl$)

- **PSEUDOEPHEDRINE HYDROCHLORIDE**

Solution A, Diluent, Mobile phase, Standard solution, Chromatographic system, and System suitability: Proceed as directed in the *Assay* for *Acetaminophen*.
Sample stock solution: Nominally 0.3 mg/mL of pseudoephedrine hydrochloride in *Diluent* prepared as follows. Transfer an amount nominally equivalent to 30 mg of pseudoephedrine hydrochloride from a portion of finely powdered Tablets (NLT 20) to a 100-mL volumetric flask, add 75 mL of *Diluent*, and sonicate for 15 min. Dilute with *Diluent* to volume.
Sample solution: Nominally 30 µg/mL of pseudoephedrine hydrochloride from the *Sample stock solution* in *Diluent*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$) in the portion of Tablets taken:

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

r_U = peak response of pseudoephedrine from the *Sample solution*