Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.6-mm × 25-cm; packing L9
Flow rate: 2.5 mL/min
Injection volume: 10 µL
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for pseudoephedrine, dextromethorphan, and doxylamine are 0.38, 0.65, and 1.0, respectively.]
Suitability requirements
Tailing factor: NMT 2.5 for the dextromethorphan, doxylamine, and pseudoephedrine peaks
Relative standard deviation: NMT 2.0% for dextromethorphan, doxylamine, and pseudoephedrine
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$) in the portion of Oral Solution taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of dextromethorphan from the *Sample solution*
r_S = peak response of dextromethorphan from the *Standard solution*
C_S = concentration of USP Dextromethorphan Hydrobromide RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of dextromethorphan hydrobromide in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of dextromethorphan hydrobromide monohydrate, 370.32
M_{r2} = molecular weight of anhydrous dextromethorphan hydrobromide, 352.32
Acceptance criteria: 90.0%–110.0% of the labeled amount of dextromethorphan hydrobromide ($C_{18}H_{25}NO \cdot HBr \cdot H_2O$)

- **DOXYLAMINE SUCCINATE**
Solution A, Mobile phase, Standard solution, Chromatographic system, and System suitability: Proceed as directed in the *Assay* for *Dextromethorphan Hydrobromide*.
Sample solution: Nominally 0.04 mg/mL of doxylamine succinate from a volume of Oral Solution in *Mobile phase* prepared as follows. Dilute a volume of Oral Solution, equivalent to about 2 mg of doxylamine succinate, in *Mobile phase*.
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$) in the portion of Oral Solution taken:

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

r_U = peak response of doxylamine from the *Sample solution*
r_S = peak response of doxylamine from the *Standard solution*
C_S = concentration of USP Doxylamine Succinate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of doxylamine succinate in the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0% of the labeled amount of doxylamine succinate ($C_{17}H_{22}N_2O \cdot C_4H_6O_4$)

- **PSEUDOEPHEDRINE HYDROCHLORIDE**
Solution A, Mobile phase, Standard solution, Chromatographic system, and System suitability: Proceed as directed in the *Assay* for *Dextromethorphan Hydrobromide*.
Sample solution: Nominally 0.2 mg/mL of pseudoephedrine hydrochloride from a volume of Oral Solution in *Mobile phase* prepared as follows. Dilute a volume of Oral Solution, equivalent to about 10 mg of pseudoephedrine hydrochloride, in *Mobile phase*.
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 Oral Solution taken:

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

r_U = peak response of pseudoephedrine from the *Sample solution*
r_S = peak response of pseudoephedrine from the *Standard solution*
C_S = concentration of USP Pseudoephedrine Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of pseudoephedrine hydrochloride in the *Sample solution* (mg/mL)
Acceptance criteria: 90.0%–110.0% of the labeled amount of pseudoephedrine hydrochloride ($C_{10}H_{15}NO \cdot HCl$)

PERFORMANCE TESTS

- **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩
For single-unit containers
Acceptance criteria: Meets the requirements
- **DELIVERABLE VOLUME** ⟨698⟩
For multiple-unit containers
Acceptance criteria: Meets the requirements

IMPURITIES

- **4-AMINOPHENOL IN ACETAMINOPHEN-CONTAINING DRUG PRODUCTS** ⟨227⟩**:** Meets the requirements

SPECIFIC TESTS

- **MICROBIAL ENUMERATION TESTS** ⟨61⟩ and **TESTS FOR SPECIFIED MICROORGANISMS** ⟨62⟩**:** The total bacterial count does not exceed 100 cfu/g, the total combined molds and yeasts count does not exceed 10 cfu/g, and it meets the requirements of the tests for absence of *Salmonella* species and *Escherichia coli*.
- **pH** ⟨791⟩**:** 4.5–6.3
- **ALCOHOL DETERMINATION** ⟨611⟩, *Method II* (if present)**:** 90.0%–110.0% of the labeled amount of alcohol (C_2H_5OH)

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨11⟩
USP Acetaminophen RS
USP Dextromethorphan Hydrobromide RS
USP Doxylamine Succinate RS
USP Pseudoephedrine Hydrochloride RS

Acetaminophen and Diphenhydramine Citrate Tablets

DEFINITION

Acetaminophen and Diphenhydramine Citrate Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and diphenhydramine citrate ($C_{17}H_{21}NO \cdot C_6H_8O_7$).

IDENTIFICATION

- **A.** The retention times of the major peaks of the *Sample solution*, obtained in the *Assay* for *Acetaminophen* and in