Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Capsules 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* (mg/mL)
C_U = nominal concentration of acetaminophen in the *Sample solution* (mg/mL)

Calculate the percentage of the labeled amount of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$) in the portion of Capsules taken:

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

r_U = peak response of codeine from the *Sample solution*
r_S = peak response of codeine from the *Standard solution*
C_S = concentration of USP Codeine Phosphate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of codeine phosphate in the *Sample solution* (mg/mL)
M_{r1} = molecular weight of codeine phosphate, 406.37
M_{r2} = molecular weight of anhydrous codeine phosphate, 397.37

Acceptance criteria
Acetaminophen: 90.0%–110.0%
Codeine phosphate: 90.0%–110.0%

PERFORMANCE TESTS
• **Dissolution** ⟨711⟩
Medium: 0.01 N hydrochloric acid; 900 mL
Apparatus 2: 50 rpm
Time: 30 min
Analysis: Determine the labeled amount of acetaminophen ($C_8H_9NO_2$) and codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$) dissolved by using the method set forth in the *Assay*, except use 0.01 N hydrochloric acid to prepare the *Codeine phosphate standard stock solution*, and make any other necessary volumetric adjustments.
Tolerances: NLT 75% (*Q*) of the labeled amount of acetaminophen ($C_8H_9NO_2$) and codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$) is dissolved.
• **Uniformity of Dosage Units** ⟨905⟩
Procedure for content uniformity
Solution A, Mobile phase, Codeine phosphate standard stock solution, Standard solution, Chromatographic system, and System suitability: Proceed as directed in the *Assay*.
Sample stock solution: Transfer the contents of 1 Capsule to a 100-mL volumetric flask. Add 75 mL of *Mobile phase*, and sonicate for 10 min. Dilute with *Mobile phase* to volume.
Sample solution: Dilute 5.0 mL of the *Sample stock solution* with *Mobile phase* to 50 mL, and pass a portion through a suitable filter of 1-µm pore size.
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the quantity, in mg, of acetaminophen ($C_8H_9NO_2$) in the Capsule taken:

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

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* (mg/mL)
F = dilution volume, 1000 mL

Calculate the quantity, in mg, of the labeled amount of codeine phosphate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$) in the Capsule taken:

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

r_U = peak response of codeine from the *Sample solution*
r_S = peak response of codeine from the *Standard solution*
C_S = concentration of USP Codeine Phosphate RS in the *Standard solution* (mg/mL)
M_{r1} = molecular weight of codeine phosphate, 406.37
M_{r2} = molecular weight of anhydrous codeine phosphate, 397.37
F = dilution volume, 1000 mL

Acceptance criteria: Meet the requirements

IMPURITIES
• **4-Aminophenol in Acetaminophen-Containing Drug Products** ⟨227⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS
• **Packaging and Storage:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
• **USP Reference Standards** ⟨11⟩
USP Acetaminophen RS
USP Codeine Phosphate RS

Acetaminophen and Codeine Phosphate Oral Solution

DEFINITION
Acetaminophen and Codeine Phosphate Oral Solution contains NLT 90.0% and NMT 110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and codeine phosphate hemihydrate ($C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$).

IDENTIFICATION
• **A.** The retention times of the major peaks of the *Sample solutions* correspond to those of the *Standard solutions*, as obtained in the *Assays* for *Acetaminophen* and *Codeine Phosphate*.
• **B. Thin-Layer Chromatography**
Standard solution: 12 mg/mL each of USP Acetaminophen RS and USP Codeine Phosphate RS in methanol
Sample solution: Transfer a volume of Oral Solution, equivalent to 12 mg of codeine phosphate, to a separator. Add 1 mL of ammonium hydroxide and 5 mL of methylene chloride. Shake for 1 min, and allow the layers to separate. Use the clear lower layer.
Developing solvent system: Methanol and ammonium hydroxide (49:1)
Chromatographic system
(See *Chromatography* ⟨621⟩, *Thin-Layer Chromatography*.)
Mode: TLC
Adsorbent: 0.25-mm layer of chromatographic silica gel mixture
Application volume: 10 µL
Analysis
Samples: *Standard solution* and *Sample solution*
Develop the chromatogram in the *Developing solvent system* until the solvent front has moved three-fourths of the length of the plate. Locate the spots on the plate by examination under short-wavelength UV light.