Analysis
Samples: *Standard solution* and *Sample solution*
Calculate individually the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$) in the portion of Tablets taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio of acetaminophen or aspirin to benzoic acid from the *Sample solution*
R_S = peak response ratio of acetaminophen or aspirin to benzoic acid from the *Standard solution*
C_S = concentration of USP Acetaminophen RS or USP Aspirin RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of acetaminophen or aspirin in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0% of the labeled amount of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$)

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩
Procedure for a pooled sample
Medium: Water; 900 mL
Apparatus 2: 50 rpm
Time: 45 min
Solution A, Mobile phase, and Chromatographic system (except for *Injection volume*): Proceed as directed in the *Assay*.
Injection volume: 20 µL
Internal standard solution: 1 mg/mL of benzoic acid in methanol
Standard stock solution A: 70 µg/mL of USP Salicylic Acid RS in *Solution A*
Standard solution A: Combine 4.0 mL of *Standard stock solution A* and 1.0 mL of *Internal standard solution*.
Standard stock solution B: 360 µg/mL each of USP Acetaminophen RS and USP Aspirin RS in *Solution A*
Standard solution B: Combine 4.0 mL of *Standard stock solution B* and 1.0 mL of *Internal standard solution*.
Sample stock solution: Filtered portions of sample suitably diluted with *Medium* to a concentration that is similar to that of *Standard stock solution A* or *Standard stock solution B*
Sample solution: Combine 4.0 mL of the *Sample stock solution* and 1.0 mL of *Internal standard solution*.
Analysis
Samples: *Standard solution A*, *Standard solution B*, and *Sample solution*
[NOTE—The relative retention times for acetaminophen, salicylic acid, aspirin, and benzoic acid are about 0.3, 0.4, 0.6, and 1.0, respectively.]
Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) dissolved:

$$\text{Result} = (R_U/R_S) \times (C/W) \times 90$$

R_U = relative peak response ratio of acetaminophen to the internal standard from the *Sample solution*
R_S = relative peak response ratio of acetaminophen to the internal standard from *Standard solution B*
C = concentration of USP Acetaminophen RS in *Standard solution B* (µg/mL)
W = labeled amount of acetaminophen (mg)

Calculate the percentage of the labeled amount of aspirin ($C_9H_8O_4$) dissolved:

$$\text{Result} = \{[90C_1 \times (R_{U1}/R_{S1})] + [90C_2 \times (R_{U2}/R_{S2}) \times 1.3044]\}/W$$

C_1 = concentration of USP Aspirin RS in *Standard solution B* (µg/mL)
R_{U1} = relative peak response ratio of aspirin to the internal standard from the *Sample solution*
R_{S1} = relative peak response ratio of aspirin to the internal standard from *Standard solution B*
C_2 = concentration of USP Salicylic Acid RS in *Standard solution A* (µg/mL)
R_{U2} = relative peak response ratio of salicylic acid to the internal standard from the *Sample solution*
R_{S2} = relative peak response ratio of salicylic acid to the internal standard from *Standard solution A*
W = labeled amount of aspirin (mg)

Tolerances: NLT 75% (Q) of the labeled amount of acetaminophen ($C_8H_9NO_2$) and aspirin ($C_9H_8O_4$) is dissolved.

• **Uniformity of Dosage Units** ⟨905⟩, *Content Uniformity*: Meet the requirements with respect to acetaminophen and to aspirin

IMPURITIES

• **Limit of Salicylic Acid**
Solution A, Mobile phase, Internal standard solution, Sample solution, Chromatographic system, and System suitability: Proceed as directed in the *Assay*.
Standard stock solution: 1.0 mg/mL of USP Salicylic Acid RS in *Solution A*
Standard solutions: Transfer 1.0-, 5.0-, and 10.0-mL portions of *Standard stock solution* to separate 100-mL volumetric flasks. Add 10.0 mL of *Internal standard solution* to each flask, and dilute with *Solution A* to volume.
Analysis
Samples: *Sample solution* and *Standard solutions*
Plot the ratios of the peak responses for salicylic acid and benzoic acid for each of the *Standard solutions* versus concentrations, in mg/mL, of salicylic acid, and draw the straight line best fitting the three plotted points. From the graph so obtained, and from the ratio of the peak responses for salicylic acid and benzoic acid from the *Sample solution* as obtained in the *Assay*, determine the concentration, in mg/mL, of salicylic acid ($C_7H_6O_3$) in the *Sample solution*.
Calculate the percentage of salicylic acid in relation to the concentration of aspirin in the *Sample solution*, as obtained in the *Assay*.
Acceptance criteria: NMT 3.0%

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

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
• **USP Reference Standards** ⟨11⟩
USP Acetaminophen RS
USP Aspirin RS
USP Salicylic Acid RS

Acetaminophen, Aspirin, and Caffeine Tablets

DEFINITION

Acetaminophen, Aspirin, and Caffeine Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of acet-