Acetaminophen Oral Suspension

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Posting Date: 27–Jul–2018
Official Date: 01–Aug–2018
Expert Committee: Chemical Medicines Monographs 6
Reason for Revision: Compliance

In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 6 Expert Committee has revised the Acetaminophen Oral Suspension monograph. The purpose for the revision is to postpone the implementation of the Assay and the test for Organic Impurities and the omission of the test for 4-Aminophenol in Acetaminophen-Containing Drug Products.

The Acetaminophen Oral Suspension Revision Bulletin supersedes the revision of the Acetaminophen Oral Suspension monograph, which was published in the First Supplement to USP 41–NF 36 and is scheduled to become official on 1–Aug–2018.

Should you have any questions, please contact Clydewyn M. Anthony, Ph.D., Senior Scientific Liaison (301-816-8139 or cma@usp.org).
Acetaminophen Oral Suspension

**DEFINITION**
Acetaminophen Oral Suspension is a suspension of Acetaminophen Oral Suspension

**IDENTIFICATION**

- **A. INFRARED ABSORPTION (197K)**
  
  **Sample:** Transfer a volume of Oral Suspension, equivalent to 240 mg of acetaminophen, to a separator. Add 50 mL of ethyl acetate, and shake. Filter the ethyl acetate extract through a funnel containing glass wool and 10 g of anhydrous sodium sulfate. Collect the filtrate in a beaker, and evaporate on a steam bath to dryness. Dry the residue under vacuum over silica gel.

  **Acceptance criteria:** The crystals so obtained meet the requirements.

**ASSAY**

**Add the following:**

- **B.** The retention time of the acetaminophen peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay.

**Procedure**

- **Solution A:** Acetonitrile, trifluoroacetic acid, and water (14: 0.1: 86)
- **Solution B:** Acetonitrile, trifluoroacetic acid, and water (90: 0.1: 10)

**Mobile phase:** See Table 1.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Solution A (%)</th>
<th>Solution B (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>4.0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>5.0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>6.0</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>10.0</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

**Chromatographic system**

(See Chromatography (621), System Suitability.)

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm x 15-cm; 3.5-µm packing L11

Flow rate: 1 mL/min

Injection volume: 30 µL

**System suitability**

Sample: Standard solution

Suitability requirements

- Column efficiency: NLT 1000 theoretical plates
- Tailing factor: NMT 2.0
- Relative standard deviation: NMT 2.0%

**Analysis**

Samples: Standard solution and Sample solution

Calculate the percentage of the labeled amount of acetaminophen (C₈H₉NO₂) in the portion of Oral Suspension taken:

\[ \text{Result} = \left( \frac{r_f}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100 \]

\[ r_f = \text{peak response from the Sample solution} \]

\[ r_S = \text{peak response of acetaminophen from the Standard solution} \]

\[ C_S = \text{concentration of USP Acetaminophen RS in the Standard solution (mg/mL)} \]

\[ C_U = \text{nominal concentration of acetaminophen in the Sample solution (mg/mL)} \]

Acceptance criteria: 90.0%–110.0% (RB 1-Aug-2018)

**Diluent:** Methanol, phosphoric acid, and water (50: 0.1: 50)

**Standard stock solution:** 1.6 mg/mL of USP Acetaminophen RS in Diluent

**Standard solution:** 0.064 mg/mL of USP Acetaminophen RS in Solution A, from Standard stock solution

**Sample stock solution:** Nominally 0.064 mg/mL of acetaminophen prepared as follows. Transfer a quantity equivalent to about 160 mg of acetaminophen from a volume of Oral Suspension, previously well shaken, to a 100-mL volumetric flask. Add 60 mL of Diluent, and shake by mechanical means for 30 min. Dilute with Diluent to volume. Mix well. Allow the sample to settle, or centrifuge.

**Sample solution:** Nominally 0.064 mg/mL of acetaminophen in Solution A, from Sample stock solution

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Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **Unimority of Dosage Units (905)**
  - For single-unit containers: Meets the requirements
  - **Deliverable Volume (698)**
  - For multiple-unit containers: Meets the requirements

IMPURITIES

Delete the following:

**4-Aminophenol in Acetaminophen-Containing Drug Products (227):** Meets the requirements (Postponed on 1-Aug-2018)

Add the following:

**Organic Impurities**

Solution A: 0.2% trifluoroacetic acid in water
Solution B: 0.2% trifluoroacetic acid in water
Mobile phase: See Table 2.

![Table 2](image)

**Column temperature:** 40°C
**Flow rate:** 0.5 mL/min
**Injection volume:** 2.5 µL

**System suitability**

- **Samples:** Sensitivity solution and Standard solution
  - **NOTE—**See Table 3 for relative retention times.

**Suitability requirements**

- **Tailing factor:** NMT 2.0 for acetaminophen and 4-aminophenol, Standard solution
- **Relative standard deviation:** NMT 5.0% for acetaminophen and 4-aminophenol, Standard solution
- **Signal-to-noise ratio:** NLT 10 for acetaminophen and 4-aminophenol, Sensitivity solution

**Analysis**

**Samples:** Standard solution and Sample solution

Calculate the percentage of 4-aminophenol in the portion of Oral Suspension taken:

\[
\text{Result} = \left( \frac{r_4}{r_0} \right) \times \left( \frac{C_4}{C_0} \right) \times 100
\]

Calculate the percentage of acetaminophen dimer or any unspecified impurity in the portion of Oral Suspension taken:

\[
\text{Result} = \left( \frac{r_d}{r_0} \right) \times \left( \frac{C_d}{C_0} \right) \times 100
\]

**Acceptance criteria:** See Table 3. The reporting threshold is 0.05% for any impurities.

![Table 3](image)

**Specific Tests**

- **pH (791):** 4.0–6.9
ADDITIONAL REQUIREMENTS

• Packaging and Storage: Preserve in tight containers, and store at controlled room temperature.

• USP Reference Standards (11)
  USP Acetaminophen RS
  USP 4-Aminophenol RS