In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Chemical Medicines Monographs 5 Expert Committee has revised the Potassium Chloride Extended-Release Tablets monograph. The purpose for the revision is to add *Dissolution Test 2* to accommodate FDA-approved drug products with different tolerances than the existing dissolution test. *Labeling* information has been incorporated to support the inclusion of *Dissolution Test 2*.

The Potassium Chloride Extended-Release Tablets Revision Bulletin supersedes the currently official monograph.

Should you have any questions, please contact Ren-Hwa Yeh, Ph.D., Senior Scientific Liaison (301-998-6818 or rhy@usp.org).
Potassium Chloride Extended-Release Tablets

**DEFINITION**
Potassium Chloride Extended-Release Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of potassium chloride (KCl).

**IDENTIFICATION**
- **A. IDENTIFICATION TESTS—GENERAL** (191), Chemical Identification Tests, Potassium
- **B. IDENTIFICATION TESTS—GENERAL** (191), Chemical Identification Tests, Chloride

**ASSAY**

- **METHOD (See Atomic Absorption Spectroscopy (852).)**

**Instrumental conditions**
- Model: Atomic absorption spectrophotometry
- Analytical wavelength: Potassium emission line at 766.5 nm
- Lamp: Potassium hollow-cathode
- Flame: Air–acetylene
- Blank: Water

**Analysis**
- **Samples:** Standard solutions, Sample solution 1 or Sample solution 2, and Blank
- Plot the absorbances of the Standard solutions versus the concentration of potassium, in µg/mL, and draw the straight line best fitting the three plotted points. From the graph, determine the concentration of potassium in the Sample solution (µg/mL).
- Calculate the percentage of the labeled amount of potassium chloride (KCl) in each Tablet taken:

\[
\text{Result} = \left( \frac{C}{C_0} \right) \times \left( \frac{M_c}{A_c} \right) \times 100
\]

- C = concentration of potassium in the Sample solution as determined in this test (µg/mL)
- C₀ = nominal concentration of potassium chloride in the Sample solution (µg/mL)
- Mc = molecular weight of potassium chloride, 74.55
- Ac = atomic weight of potassium, 39.10

**Acceptance criteria:** 90.0%–110.0%

**PERFORMANCE TESTS**

**Change to read:**

- **Dissolution (711)**
- **Test 1** (88 1-Sep-1988)

<table>
<thead>
<tr>
<th>Medium</th>
<th>900 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparatus 2</td>
<td>50 rpm</td>
</tr>
<tr>
<td>Time</td>
<td>2 h</td>
</tr>
</tbody>
</table>

**Standard stock solution:** 19.07 µg/mL of potassium chloride, previously dried at 105° for 2 h, in water. This solution contains 10 µg/mL of potassium chloride.

**Standard preparation 1**
- Transfer 10.0, 15.0, and 20.0 mL, respectively, of the Standard solution to a 100-mL volumetric flask, and dilute with water to volume.

**Sample preparation 1**
- Nominally 0.06 mg/mL of potassium chloride prepared as follows. Place NLT 20 Tablets in a suitable container with 400 mL of water, heat to boiling, and boil for 20 min. Allow to cool, transfer the solution to a 1000-mL volumetric flask, and dilute with water to volume. Filter and discard the first 20 mL of the filtrate. Transfer a measured volume of the subsequent filtrate, equivalent to 60 mg of potassium chloride, to a 1000-mL volumetric flask, and dilute with water to volume.

**Sample preparation 2** (for formulations containing crystals coated with hydrophilic polymers)

**Sample stock solution 2:** Nominally 0.06 mg/mL of potassium chloride prepared as follows. Place NLT 20 Tablets in a 2000-mL volumetric flask. Add 1200 mL of a mixture of acetonitrile and water (1:1), and shake by mechanical means, or stir using a magnetic bar for 90 min. Dilute the mixture of acetonitrile and water (1:1) to volume. Allow to stand for 90 min. Pass through a filter of 0.2-µm pore size. Transfer a measured volume of the filtrate, and quantitatively dilute with water to obtain a solution with a concentration of 0.06 mg/mL.

**Sample solution 2:** Nominally 3 µg/mL of potassium chloride prepared as follows. Transfer an appropriate amount of the powder, equivalent to about 5–6 Tablets, to a suitable volumetric flask, add 10% of the final flask volume of acetone, and sonicate for 45 min with intermittent shaking. Add 80% of the final flask volume of water and sonicate for 45 min with intermittent shaking. Cool to room temperature and dilute with water to volume. Centrifuge a portion of the solution at 5000 rpm for 10 min. Transfer an appropriate amount of the supernatant to a 100-mL volumetric flask, add 2.0 mL of sodium chloride solution (1 in 5) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

**Performance tests**

- **Change to read:**

<table>
<thead>
<tr>
<th>Medium</th>
<th>900 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparatus 2</td>
<td>50 rpm</td>
</tr>
<tr>
<td>Time</td>
<td>2 h</td>
</tr>
</tbody>
</table>

**Standard stock solution:** 19.07 µg/mL of potassium chloride, previously dried at 105° for 2 h, in water. This solution contains 10 µg/mL of potassium chloride.

**Sample preparation**
- Sample solution 1: Nominally 0.06 mg/mL of potassium chloride prepared as follows. Place NLT 20 Tablets in a suitable container with 400 mL of water, heat to boiling, and boil for 20 min. Allow to cool, transfer the solution to a 1000-mL volumetric flask, and dilute with water to volume. Filter and discard the first 20 mL of the filtrate. Transfer a measured volume of the subsequent filtrate, equivalent to 60 mg of potassium chloride, to a 1000-mL volumetric flask, and dilute with water to volume.

**Sample preparation 2** (for formulations containing crystals coated with hydrophilic polymers)

**Sample stock solution 2:** Nominally 0.06 mg/mL of potassium chloride prepared as follows. Place NLT 20 Tablets in a 2000-mL volumetric flask. Add 1200 mL of a mixture of acetonitrile and water (1:1), and shake by mechanical means, or stir using a magnetic bar for 90 min. Dilute the mixture of acetonitrile and water (1:1) to volume. Allow to stand for 90 min. Pass through a filter of 0.2-µm pore size. Transfer a measured volume of the filtrate, and quantitatively dilute with water to obtain a solution with a concentration of 0.06 mg/mL.

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**Acceptance criteria:** 90.0%–110.0%
**2 Potassium**

- **Sample stock solution**: Filter the solution under test, and dilute with Medium to obtain a solution containing nominally 60 µg/mL of potassium chloride.
- **Sample solution**: Transfer 5.0 mL of the Sample stock solution to a 100-mL volumetric flask. Add 2.0 mL of sodium chloride solution (1 in 5) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

**Instrumental conditions**
(See Atomic Absorption Spectroscopy (852).)

**Mode**: Atomic absorption spectrophotometry

**Analytical wavelength**: Potassium emission line at 766.3 nm

**Lamp**: Potassium hollow-cathode

**Flame**: Air–acetylene

**Blank**: Water

**Analysis**

**Samples**: Standard solutions, Sample solution, and Blank

Plot the absorbances of the Standard solutions versus the concentration of potassium, in µg/mL, and draw the straight line best fitting the three plotted points. From the graph, determine the concentration of potassium in the Sample solution (µg/mL).

Calculate the percentage of the labeled amount of potassium chloride (KCl) dissolved:

\[
\text{Result} = \left[ \frac{C \times D \times (V/L)}{M_r} \right] \times \frac{A_i}{A_i} \times 100
\]

- **C** = concentration of potassium in the Sample solution as determined in this test (µg/mL)
- **D** = dilution factor of the Sample solution
- **V** = volume of Medium, 900 mL
- **L** = labeled amount of potassium chloride (µg/Tablet)
- **M_r** = molecular weight of potassium chloride, 74.55
- **A_i** = atomic weight of potassium, 39.10

**Tolerances**: NMT 35% (Q) of the labeled amount of potassium chloride (KCl) is dissolved in 2 h. The requirements are met if the quantities dissolved from the Tablets tested conform to Table 1 instead of the table shown in Dissolution (711).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number Tested</th>
<th>Acceptance Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>S_1</td>
<td>6</td>
<td>Each unit is within the range Q ± 30%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S_2</td>
<td>6</td>
<td>Average of 12 units (S_1 + S_2) is within the range between Q – 30% and Q + 35%, and no unit is outside the range Q ± 40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S_3</td>
<td>12</td>
<td>Average of 24 units (S_1 + S_2 + S_3) is within the range between Q – 30% and Q + 35%, and NMT 2 units are outside the range Q ± 40%</td>
</tr>
</tbody>
</table>

**Test 2**: If the product complies with this procedure, the labeling indicates that it meets USP Dissolution Test 2.

**Standard stock solution and Standard solutions**: Prepare as directed in Test 1.

**Medium**: Water, 900 mL

**Apparatus 2**: 50 rpm

**Times**: 1, 2, 4, and 8 h

**Sample stock solution**: Transfer 4.0 mL of the solution under test into either a 50-mL volumetric flask (for 750-mg Tablet) or a 100-mL volumetric flask (for 1500-mg Tablet), dilute with water to volume, and filter.

**Sample solution**: Transfer 4.0 mL of the Sample stock solution to a 100-mL volumetric flask. Add 2.0 mL of sodium chloride solution (1 in 5) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

**Blank solution**: To a 100-mL volumetric flask, add 2.0 mL of sodium chloride solution (1 in 5) and 1.0 mL of hydrochloric acid, and dilute with water to volume.

**Instrumental conditions**: Proceed as directed in Test 1, except do not use the Blank.

**System suitability**

**Samples**: Standard solutions

**Suitability requirements**

- **Linearity**: Correlation coefficient NLT 0.99
- **Relative standard deviation**: NMT 5.0% from 5 replicate analyses of the 1.5-µg/mL Standard solution

**Analysis**

**Samples**: 1.5-µg/mL Standard solution, Sample solution, and Blank solution

Calculate the percentage of the labeled amount of potassium chloride (KCl) dissolved:

\[
\text{Result} = \left[ \frac{(A_i/A_m) \times C_i \times D \times (V/L)}{(M_r/A_m)} \right] \times 100
\]

- **A_i** = absorbance of potassium in the Sample solution
- **A_m** = absorbance of potassium in the Standard solution
- **C_i** = concentration of potassium in the Standard solution (µg/mL)
- **D** = dilution factor of the Sample solution
- **V** = volume of Medium, 900 mL
- **L** = labeled amount of potassium chloride (µg/Tablet)
- **M_r** = molecular weight of potassium chloride, 74.55
- **A_m** = atomic weight of potassium, 39.10

**Tolerances**: See Table 2.

<table>
<thead>
<tr>
<th>Time Point (h)</th>
<th>Amount Dissolved (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>750 mg/Tablet</td>
</tr>
<tr>
<td>1</td>
<td>10–30</td>
</tr>
<tr>
<td>2</td>
<td>30–50</td>
</tr>
<tr>
<td>3</td>
<td>60–80</td>
</tr>
<tr>
<td>4</td>
<td>NLT 80</td>
</tr>
</tbody>
</table>

The percentages of the labeled amount of potassium chloride (KCl), dissolved at the times specified, conform to Dissolution (711), Acceptance Table 2.

- **Uniformity of Dosage Units** (905); Meet the requirements

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage**: Preserve in tight containers, and store at a temperature not exceeding 30°.

**Change to read:**

- **Labeling**: The label states with which Sample preparation the product complies only if Sample preparation 1 is not used. *When more than one Dissolution test is given, the labeling states the Dissolution test used only if Test 1 is not used.*