mg of C₁₉H₁₆ClNO₄ in the portion of Capsules taken by the formula:

\[ 0.8C(A_0 / A) \]

in which \( C \) is the concentration, in \( \mu \)g per mL, of USP Indomethacin RS in the **Standard preparation**; and \( A_0 \) and \( A \) are the absorbances of the **Assay preparation** and the **Standard preparation**, respectively.

### Indomethacin Extended-Release Capsules

**Indomethacin Extended-Release Capsules**

**Packaging and storage**—Preserve in well-closed containers.

**Labeling**—The labeling indicates the **Dissolution Test** with which the product complies.

**USP Reference standards (11)**—

**USP Indomethacin RS**

**Identification**—

A: The contents of Capsules respond to the **Identification** tests under *Indomethacin Capsules*.

B: Transfer a quantity of finely powdered Capsule contents, equivalent to about 100 mg of indomethacin, to a 250-mL flask, add about 100 mL of sodium hydroxide solution (1 in 2500), shake for 5 minutes, and filter. To 1 mL of the clear filtrate add 1 mL of sodium nitrite solution (1 in 1000), mix, and allow to stand for 5 minutes. Add 0.5 mL of sulfuric acid: a golden yellow color develops.

**Dissolution (711)**—

**TEST 1**—If the product complies with this test, the labeling indicates that it meets USP **Dissolution Test 1**.

**Medium:** pH 6.2 phosphate buffer (see Buffer Solutions in the section Reagents, Indicators, and Solutions); 750 mL.

**Apparatus 1:** 75 rpm.

**Times:** 1, 2, 4, 6, 12, and 24 hours.

**Procedure**—Determine the amount of C₁₉H₁₆ClNO₄ dissolved from UV absorbances at the wavelength of maximum absorbance at about 318 nm on filtered portions of the solution under test, diluted with **Medium**, if necessary, in comparison with a Standard solution having a known concentration of USP Indomethacin RS in the same **Medium**.

**Tolerances**—The percentages of the labeled amount of C₁₉H₁₆ClNO₄ dissolved at the times specified conform to **Acceptance Table 2**.

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Amount dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>between 10% and 25%</td>
</tr>
<tr>
<td>2</td>
<td>between 20% and 40%</td>
</tr>
<tr>
<td>4</td>
<td>between 35% and 55%</td>
</tr>
<tr>
<td>6</td>
<td>between 45% and 65%</td>
</tr>
<tr>
<td>12</td>
<td>between 60% and 80%</td>
</tr>
<tr>
<td>24</td>
<td>not less than 80%</td>
</tr>
</tbody>
</table>

**TEST 2**—If the product complies with this test, the labeling indicates that it meets USP **Dissolution Test 2**.

**Medium, Apparatus, and Procedure**—Proceed as directed under **Test 1**, except to use 900 mL of **Medium**.

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Amount dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>between 15% and 40%</td>
</tr>
<tr>
<td>2</td>
<td>between 35% and 55%</td>
</tr>
<tr>
<td>4</td>
<td>between 55% and 75%</td>
</tr>
<tr>
<td>6</td>
<td>between 65% and 85%</td>
</tr>
<tr>
<td>12</td>
<td>not less than 75%</td>
</tr>
<tr>
<td>24</td>
<td>not less than 85%</td>
</tr>
</tbody>
</table>

**TEST 3**—If the product complies with this test, the labeling indicates that it meets USP **Dissolution Test 3**.

**Medium:** pH 6.8 phosphate buffer (see Buffers Solutions in the section Reagents, Indicators, and Solutions); 750 mL.

**Apparatus and Procedure**—Proceed as directed under **Test 1**.

**Times:** 1, 2, 4, 6, 12, and 24 hours.

**Tolerances**—The percentages of the labeled amount of C₁₉H₁₆ClNO₄ dissolved at the times specified conform to **Acceptance Table 2**.

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Amount dissolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>between 15% and 40%</td>
</tr>
<tr>
<td>2</td>
<td>between 35% and 55%</td>
</tr>
<tr>
<td>4</td>
<td>between 55% and 75%</td>
</tr>
<tr>
<td>6</td>
<td>between 65% and 85%</td>
</tr>
<tr>
<td>12</td>
<td>not less than 75%</td>
</tr>
<tr>
<td>24</td>
<td>not less than 85%</td>
</tr>
</tbody>
</table>

**Uniformity of dosage units (905):** meet the requirements.

**Procedure for content uniformity**—Transfer the contents of 1 Capsule to a 200-mL volumetric flask, and add 100 mL of a mixture of equal volumes of methanol and pH 7.5 phosphate buffer, prepared by dissolving 17.42 g of dibasic potassium phosphate in about 800 mL of water, adjusting with phosphoric acid to a pH of 7.5, and diluting with water to 1000 mL. Sondicate until the contents are dispersed, dilute with the methanol and pH 7.5 phosphate buffer mixture (1:1) to volume, mix, and centrifuge. Dilute a portion of the clear solution quantitatively, and stepwise if necessary, with the methanol and pH 7.5 phosphate buffer mixture (1:1) to obtain a solution containing about 25 \( \mu \)g of indomethacin per mL. Concomitantly determine the absorbances of this solution and a standard solution of USP Indomethacin RS, in the methanol and pH 7.5 phosphate buffer mixture (1:1) having a known concentration of about 25 \( \mu \)g per mL, in 1-cm cells at the wavelength of maximum absorbance at about 318 nm, with a suitable spectrophotometer, using the methanol and pH 7.5 phosphate buffer mixture as the blank. Calculate the quantity, in mg, of C₁₉H₁₆ClNO₄ in the Capsule taken by the formula:

\[ \frac{(TC / D)(A_0 / A)}{C} \]

in which \( T \) is the labeled quantity, in mg, of indomethacin in the Capsule; \( C \) is the concentration, in \( \mu \)g per mL, of USP Indomethacin RS in the Standard solution; \( D \) is the concentration, in \( \mu \)g per mL, of indomethacin in the test solution, based upon the labeled quantity per Capsule and the extent of dilution; and \( A_0 \) and \( A \) are the absorbances of the solution from the Capsule contents and the Standard solution, respectively.

**Assay and limit of 4-chlorobenzoic acid**—

**Mobile phase**—Prepare a suitable mixture of methanol, water, and phosphoric acid (600:400:0.8), and pass through a membrane filter having a 0.5-\( \mu \)m or finer porosity. Make adjustments if necessary (see **System Suitability** under Chromatography 〈621〉).

**Diluted phosphoric acid**—Dilute 10 mL of phosphoric acid with water to make 1000 mL of solution.
Standard indomethacin preparation—Transfer about 40 mg of USP Indomethacin RS, accurately weighed, to a 50-mL volumetric flask, and dissolve in 30 mL of acetonitrile. Dilute with Diluted phosphoric acid to volume, and mix.

Standard 4-chlorobenzoic acid preparation—Dissolve a suitable quantity of 4-chlorobenzoic acid, accurately weighed, in acetonitrile to obtain a solution having a concentration of about 0.18 mg per mL. Transfer 1.0 mL of this solution to a 50-mL volumetric flask, dilute with Diluted phosphoric acid to volume, and mix. This solution contains about 3.6 µg of 4-chlorobenzoic acid per mL.

Assay preparation—Weigh and finely powder the contents of not fewer than 20 Capsules. Transfer an accurately weighed portion of the powder, equivalent to about 75 mg of indomethacin, to a 100-mL volumetric flask, add 40 mL of Diluted phosphoric acid, and shake for 1 hour. Sonicate for 15 minutes, add 40 mL of acetonitrile, mix, sonicate for 15 minutes, dilute with acetonitrile to volume, and mix. Centrifuge a portion of this solution, and pass the supernatant through a filter having a 0.5-µm or finer porosity. Use the filtrate as the Assay preparation.

Chromatographic system (see Chromatography (621))—The liquid chromatograph is equipped with a 240-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the Standard indomethacin preparation, and record the peak responses as directed for Procedure: the column efficiency determined from the indomethacin peak is not less than 1000 theoretical plates; the capacity factor, \( k' \), for the indomethacin peak is not less than 4.0; the tailing factor for the indomethacin peak is not more than 2.0; and the relative standard deviation for replicate injections is not more than 2.0%. Chromatograph the Standard 4-chlorobenzoic acid preparation, and record the peak responses as directed for Procedure: the capacity factor, \( k' \), for the 4-chlorobenzoic acid peak is not less than 0.9.

Procedure—Separately inject equal volumes (about 20 µL) of the Standard indomethacin preparation, the Standard 4-chlorobenzoic acid preparation, and the Assay preparation into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, \( C_1 \), in mg, of indomethacin in the portion of Capsules taken by the formula:

\[
100(C_1 / r_0 / r_1)
\]

in which \( C_1 \) is the concentration, in mg per mL, of USP Indomethacin RS in the Standard indomethacin preparation, and \( r_0 \) and \( r_1 \) are the indomethacin peak responses obtained from the Assay preparation and the Standard indomethacin preparation, respectively. Calculate the per centage of 4-chlorobenzoic acid (\( C_1 H_7CIO_3 \)) in the portion of Capsules taken by the formula:

\[
10(C_4 / C_3)(r_0 / r_1)
\]

in which \( C_4 \) is the concentration, in µg per mL, of 4-chlorobenzoic acid in the Standard 4-chlorobenzoic acid preparation; \( C_3 \) is the quantity, in mg, of indomethacin (\( C_{19}H_{16}ClNO_4 \)) in the portion of Capsule contents taken, determined as directed herein; and \( r_0 \) and \( r_1 \) are the 4-chlorobenzoic acid peak responses obtained from the Assay preparation and the Standard 4-chlorobenzoic acid preparation, respectively: not more than 0.44% is found.

**Indomethacin Topical Gel**

» Indomethacin Topical Gel contains not less than 0.90 g and not more than 1.10 g of Indomethacin in 100 mL of gel. Prepare Indomethacin Topical Gel as follows:

**Indomethacin** ................. 1.0 g

**Carbomer 941** ................ 2.0 g

**Purified Water** ................ 10 mL

**Alcohol (95% ethyl alcohol)**, a sufficient quantity to make ........... 100 mL

Transfer the Indomethacin to a suitable beaker, and dissolve it in 55 mL of Alcohol. Transfer this solution to a glass mortar, and slowly add the Carbomer 941 so that it is thoroughly distributed. Press out any white lumps until a smooth gel is formed. Slowly add the Purified Water with mixing. Add a sufficient quantity of Alcohol to obtain a final volume of 100 mL, and mix. Transfer the Gel to a wide-mouth container or ointment jar.

**Packaging and storage**—Preserve in tight, light-resistant, wide-mouth containers or ointment jars. Store at controlled room temperature.

**Labeling**—Label it to state that it is for topical, external use only, that it should be used only as directed, and that the container should be kept tightly closed.

**Beyond-use date**—Thirty days after the day on which it was compounded.

**Indomethacin Suppositories**

» Indomethacin Suppositories contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of \( C_{19}H_{16}ClNO_4 \).

**Packaging and storage**—Preserve in well-closed containers, at controlled room temperature.

**USP Reference standards (11)**—USP Indomethacin RS

**Identification**

Standard preparation—Prepare a solution, containing about 125 µg of USP Indomethacin RS per mL, by first dissolving the Reference Standard in a volume of methanol that is one one-hundredth of the volume of the solution to be prepared, then adding ether to volume, and mixing.

Test preparation—Use the ether extract contained in the 200-mL volumetric flask obtained as directed under Assay preparation in the Assay.

Procedure—Separately apply 10 µL of each of the Test preparation and the Standard preparation to a thin-layer chromatographic plate (see Chromatography (621)) coated with a 0.25-mm layer of chromatographic silica gel mixture. Develop the chromatogram in a solvent system consisting of a mixture of chloroform and glacial acetic acid (19:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, air-dr y, and examine under short-wavelength UV light: the Rf value of the principal spot in the chromatogram of the Test preparation corresponds to that obtained from the Standard preparation.

**Dissolution (711)**

**Medium**: 0.1 M, pH 7.2 phosphate buffer (see Buffer Solutions in the section Reagents, Indicators, and Solutions); 900 mL

**Apparatus 2**: 50 rpm.

**Time**: 60 minutes.

Procedure—Determine the amount of \( C_{19}H_{16}ClNO_4 \) dissolved from UV absorbances at the wavelength of maximum absorbance at about 320 nm of filtered portions of the solution under