Receipt and Storage

On receipt of the test material, record the date and store at 2 – 8 ºC until ready to test. The test material should be analysed in accordance with the deadlines provided.

Instructions for handling all other Basic Testing samples are provided on the sheet titled ‘Instructions for Handling Test Materials and Recording Results’

Sample 1C – Other Basic Titration  
Range: 8.5 – 9.5g/L
Material supplied: 1 x 125mL solution of sodium chloride solution

Titrate 25ml ± 0.04ml of the solution provided using 0.1M silver nitrate to an accurate end point determined by:
- Potentiometry using a calibrated pH meter (according to BP Appendix VIII, Ph Eur 2.2.20)
- Use of a suitable indicator solution (e.g. according to the equivalent USP method)

Sample 1F – Melting point  
Range: 50 - 100 ºC
Material supplied: 1 x 2g of test material

Grind the sample in a mortar and pestle to obtain fine powder. Dry the finely powdered substance in vacuo and over anhydrous silica gel R for 24 hr. Raise the temperature of the bath or melting-point apparatus to about 10°C below the melting point range and then adjust the rate of heating to about 1 °C/min. Record the temperature at which the last particle passes into the liquid phase.
Sample 2B – Trace elements

Material supplied:
- 1 x 5g of test material for trace elements determination in salicylic acid
- 1 x 1g of salicylic acid for matrix recovery/matching

**Note:** Participants are advised to analyse sample 2B by their routine techniques. The below instruction was followed during determination of trace elements for homogeneity assessment and can be used by participants who perform this analysis.

Weigh 0.2g ± 0.01g of the sample into clean Pyrex microwave digestion vessel, add 8mL of nitric acid and 0.5mL of hydrochloric acid to the sample and digest using microwave assisted heating.

<table>
<thead>
<tr>
<th>Time</th>
<th>Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 5 mins</td>
<td>Ramp to 130°C</td>
</tr>
<tr>
<td>5 – 10 mins</td>
<td>Ramp to 180°C</td>
</tr>
<tr>
<td>10 – 20 mins</td>
<td>Hold at 180°C</td>
</tr>
<tr>
<td>20+ mins</td>
<td>Cool to ambient</td>
</tr>
</tbody>
</table>

Allow the samples to cool and make to an initial volume of 50mL with deionised water of 18.2MΩ.cm resistivity, then dilute 2 fold for analysis.

In order to minimize mass-dependant matrix interferences, the internal standard of Scandium, Indium and Bismuth can be added to the blanks, calibration standards and sample at a concentration of 2ug/L.

Sample 6H – FLAA Range: 0.2 – 1%(w/w)

Material supplied: 1 x 60ml solution of sodium chloride and potassium chloride

- Dilute the sample supplied appropriately in order to bring the concentration into your routine calibration range.
- Analyse to determine the concentrations of sodium chloride and potassium chloride, using a calibrated flame photometer or equivalent (e.g. atomic absorption or atomic emission).

Report the results as %(w/v) to 2 decimal places.
Sample 6I – Polarimetry

Material supplied: 1 x 125mL test material

Analysis:
Transfer 40mL of solution into a 100mL volumetric flask, add 0.2mL of 6N ammonium hydroxide and fill to volume with DI water. Measure and report the optical rotation of this solution using DI water as the blank sample.
Calculate and report the percentage of label concentration using the formula below:

\[ \text{Result} = \frac{(100 \times A)}{(L \times \alpha)} \times \frac{1}{C_U} \times \frac{M_{r1}}{M_{r2}} \times 100 \]

where
- \( A \) = observed optical rotation (in degrees)
- \( L \) = polarimeter tube length (in decimetres)
- \( \alpha = 52.9^\circ \)
- \( C_U \) = Label Concentration (= 2g/100mL)
- \( M_{r1} \) = molecular weight of test material monohydrate (= 198.17)
- \( M_{r2} \) = molecular weight of test material anhydrous (= 180.16)

Sample 7B – Tablet testing

Material supplied: Sample A: 1 x 33 tablets for determination of weight, thickness, diameter, disintegration and resistance to crushing tests
Sample B: 1 x 15 tablets for friability test

Sample A
Note: Tablets must be tested in the following order:

Weight (20) → Thickness (5) → Diameter (5) → Disintegration (max. 24) → Resistance to crushing (min. 5)

Uniformity of Weight (Ph. Eur. method 2.9.5)

- Weigh individually 20 units taken at random and determine the average mass.
- Acceptable criteria: not more than 2 of the individual masses deviate from the average mass by more than 5% deviation and none deviates by more than twice that percentage.
- Results should be reported as ‘pass’; indicating that the tablets set meet the acceptable criteria; or ‘fail’; indicating that the tablets set does not meet the acceptable criteria. Additionally record the individual weight for each capsule and average mass into provided spreadsheet 7B Tablet testing R71.
Thickness of tablets
- Randomly select 5 tablets and measure the thickness of each tablet by using your routine method and equipment.
- Report the result as the mean value of the thickness measured, all expressed in mm. Additionally record the individual thickness value for each tablet into provided spreadsheet 7B Tablet testing R71.

Diameter of tablets
- Randomly select 5 tablets and measure the diameter of each tablet by using your routine method and equipment.
- Report the result as the mean value of the diameter measured, all expressed in mm. Additionally record the individual diameter value for each tablet into provided spreadsheet 7B Tablet testing R71.
Instructions for Handling Sample 1C – Other basic titration, 1F – Melting point, 2B – Trace Elements, 6H – FLAA, 6I – Polarimetry, 7B – Tablet Testing, 7C – Uniformity of Dosage

Disintegration (Ph. Eur. method 2.9.1)

This test is provided to determine whether tablets or capsules disintegrate within the prescribed time when placed in a liquid medium under the experimental conditions presented below.

- The apparatus consists of a basket-rack assembly, a 1 litre, low-form beaker, 149 ± 11 mm in height and having an inside diameter of 106 ± 9 mm for the immersion fluid, a thermostatic arrangement for heating the fluid between 35 °C and 39 °C, and a device for raising and lowering the basket in the immersion fluid at a constant frequency rate between 29 and 32 cycles per minute, through a distance of 55 ± 2 mm. The volume of the fluid in the vessel is such that at the highest point of the upward stroke the wire mesh remains at least 15 mm below the surface of the fluid, and descends to not less than 25 mm from the bottom of the vessel on the downward stroke. At no time should the top of the basket-rack assembly become submerged. The time required for the upward stroke is equal to the time required for the downward stroke, and the change in stroke direction is a smooth transition, rather than an abrupt reversal of motion. The basket-rack assembly moves vertically along its axis. There is no appreciable horizontal motion or movement of the axis from the vertical.

- Place 1 dosage unit in each of the 6 tubes of the basket and add a disc to each tube. Operate the apparatus using 0.1 M hydrochloric acid, maintained at 37 ± 2 °C, as the immersion fluid. Operate the apparatus for 30 min, then lift the basket from the fluid and observe the dosage units. If tablets fail to comply because of adherence to the discs, the results are invalid. Repeat the test on a further 6 tablets omitting the discs.

- At the end of the specified time, lift the basket from the fluid and observe the dosage units: all of the dosage units have disintegrated completely. If 1 or 2 dosage units fail to disintegrate, repeat the test on 12 additional dosage units.

- Acceptable criteria: not less than 16 of the 18 dosage units tested have disintegrated.

- Results should be reported as ‘Pass’; indicating that the tablets set meets the acceptable criteria; or ‘Fail’; indicating that the tablets set does not meet the acceptable criteria. Additionally, record the number of dosage units tested and number of dosage units that disintegrated during this test, into provided spreadsheet 7B Tablet testing R71.

Resistance to crushing of tablets (Ph. Eur. method 2.9.8)

This test is intended to determine, under defined conditions, the resistance to crushing of tablets, measured by the force needed to disrupt them by crushing.

- The apparatus consists of 2 jaws facing each other, one of which moves towards the other. The flat surfaces of the jaws are perpendicular to the direction of movement. The crushing surfaces of the jaws are flat and larger than the zone of contact with the tablet. The apparatus is calibrated using a system with a precision of 1 newton.
Instructions for Handling Sample 1C – Other basic titration, 1F – Melting point, 2B – Trace Elements, 6H – FLAA, 6l – Polarimetry, 7B – Tablet Testing, 7C – Uniformity of Dosage

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- Place the tablet between the jaws, taking into account, where applicable, the shape, the break-mark and the inscription; for each measurement orient the tablet in the same way with respect to the direction of application of the force. Carry out the measurement on minimum 5 tablets, taking care that all fragments of tablets have been removed before each subsequent determination. This procedure does not apply when fully automated equipment is used.

- Report the result as the mean value of the forces measured, all expressed in newtons. Indicate the type of apparatus and, where applicable, the orientation of the tablets into comments section in Portal. Additionally record the individual force value for each tablet into provided spreadsheet 7B Tablet testing R71.

Sample B
Friability (Ph. Eur. method 2.9.7)

- For tablets with a unit mass equal to or less than 650 mg, take a sample of whole tablets corresponding as near as possible to 6.5 g. For tablets with a unit mass of more than 650 mg, take a sample of 10 whole tablets. The tablets are carefully dedusted prior to testing. Accurately weigh the tablet sample (weight 1), and place the tablets in the drum. Rotate the drum 100 times, and remove the tablets. Remove any loose dust from the tablets as before, and accurately weigh (weight 2).

- If obviously cracked, cleaved, or broken tablets are present in the tablet sample after tumbling, the sample fails the test.

- Acceptable criteria: a maximum loss of mass not greater than 1.0%.

- Results should be reported as 'Pass'; indicating that the tablets set meets the acceptable criteria; or 'Fail'; indicating that the tablets set does not meet the acceptable criteria. Additionally, record the weight 1 and weight 2 into provided spreadsheet 7B Tablet testing R71.

Note: The spreadsheet must be returned via email to Rachel.Connolly@LGCGroup.com by the reporting deadline. Please include your Lab ID in the file name.
**Sample 7C – Uniformity of dosage units**

**Material supplied:**
- Sample A: 1 x 10 capsules for determination of uniformity of dosage units
- Reference Standard: 1 x 100mg Paracetamol (Acetaminophen) reference standard (purity 100 %)

**Method:**

**Standard Preparation:**

Stock standard - Weigh out an amount of Paracetamol reference standard and dissolve in DI water to a final concentration of 100 ug/mL.

Working standards – Dilute the stock standard in DI water to create four working standards from 2.5 to 20 ug/mL.

Calibrate the spectrophotometer using these four working standards at a wavelength of 243 nm and using a 1cm quartz cell, with DI water as the blank measurement.

**Test Preparation:**

Fill a 250ml volumetric flask or lidded bottle with 250ml warm DI water and add one capsule. Put into a water bath at 40°C for at least 30 minutes, swirling occasionally until the capsule completely dissolves. Once dissolved, invert the container 10 times to thoroughly mix the solution, dilute the liquid by a factor of 200 with DI water and measure the absorbance of the solution at 243 nm using a 1cm quartz cell.

Record the absorbance of each solution and calculate the concentration of Paracetamol in each solution. The provided spreadsheet 7C Uniformity of dosage R71 may be used to aid calculation of the concentrations if participants do not feel comfortable doing it themselves. Please record the final concentrations of the dissolved capsules into the provided spreadsheet 7C Uniformity of dosage R71.

Determine if the batch are uniform in dosage (with at most a relative standard deviation of 5%). The result should be reported as “Pass”; indicating that the batch of capsules are uniform and pass the criteria, or “Fail”; indicating that the batch of capsules are not uniform and do not pass the criteria.

**Note:** The spreadsheet must be returned via email to Rachel.Connolly@LGCGroup.com by the reporting deadline. Please include your Lab ID in the file name.
Instructions for Handling Sample 1C – Other basic titration, 1F – Melting point, 2B – Trace Elements, 6H – FLAA, 6I – Polarimetry, 7B – Tablet Testing, 7C – Uniformity of Dosage

Round Number: 71  
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Issue Date: November 2019

- All results should be submitted using PORTAL
- Please go to https://portal.proficiencytestingschemes.com/
- Login using your Lab ID, username and password.
- A PORTAL user guide can be downloaded from the help section.

If you need any help at all please do not hesitate to contact our support team using the details below or your local LGC representative.

Tel: +44(0)161 762 2500  
Email: pharmassure@LGCGroup.com