



PHARMASSURE

Pharmaceutical Products Proficiency Testing Scheme

Instructions for Handling Sample 1C – Other basic titration, 1F – Melting point, 2B – Trace elements, 6G, 6H, 6I – Advanced Testing, 7B – Tablet testing, 7C – Uniformity of dosage units

Round Number: 67

Version 1

Issue Date: October 2018

Receipt and Storage

On receipt of the test material, record the date and store at 2 – 8 °C and at room temperature sample 7B, 7C and 6G TLC plate only, 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

Materials supplied: 1 x 125mL solution of dipotassium hydrogen phosphate preserved with hydrochloric acid

- Take 50mL of the sample supplied and carry out a potentiometric titration (*Ph. Eur. Method 2.2.20*) using 1 M sodium hydroxide.
- Read the volume added at the 1st inflexion point (n_1 ml).
- Continue the titration to the 2nd inflexion point (total volume of 1 M sodium hydroxide required, n_2 ml).
- Assuming the percentage loss on drying was 0% (d) and the weight of dipotassium hydrogen phosphate in 50mL was 0.598g (m), calculate the purity of the dipotassium hydrogen phosphate using the formula below:

$$\frac{1742(10 - n_1)}{m(100 - d)}$$

- Report both the titre obtained, n_1 , and the purity of dipotassium hydrogen phosphate as calculated above.
- Range = titre: 4 -15mL, purity: 60 -110%

Sample 1F – Melting point

Range: 220 - 280 °C

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 h. 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 caffeine
1 x 1g of caffeine for matrix recovery/matching



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Note: Participants are advised to analyze the 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 $0.2\text{g} \pm 0.01\text{g}$ 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.

Time	Temperature
0 – 5 mins	Ramp to 130°C
5 – 10 mins	Ramp to 180°C
10 – 20 mins	Hold at 180°C
20+ mins	Cool to ambient

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 blanks, calibration standards and sample at a concentration of 2ug/L.

Sample 6G – TLC

Material supplied:

- 1 x 1g of Sample A
- 1 x 1g of Sample B
- 1 x 0.5g standard of butyl hydroxybenzoate
- 1 x 0.5g standard of propyl hydroxybenzoate
- 2 x TLC plates

Preparation of solutions:

- Test solution (a) - Dissolve 0.10g of the Sample A in acetone R and dilute to 10ml with the same solvent.
- Test solution (b) - Dilute 1ml of test solution (a) to 10ml with acetone R to produce solution Ab.
- Repeat the above steps for Sample B to produce solution Bb.
- Reference solution (RS1) - Dissolve 10mg of butyl hydroxybenzoate in acetone R and dilute to 10ml with the same solvent.
- Reference solution (RS2) - Dissolve 10mg of propyl hydroxybenzoate in acetone R and dilute to 10ml with the same solvent.

Acetone R: Propan-2-one; C₃H₆O = 58.08 (67-64-1). Analytical reagent grade of commerce.

Acetic Acid, Glacial: Analytical reagent grade of commerce.

Methanol: Methyl alcohol; CH₄O = 32.04 (67-56-1). Analytical reagent grade of commerce.



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Water. (7732-18-5) Purified Water of the British Pharmacopoeia.

Apply separately 2µl of test solutions (Ab and Bb), reference solutions (RS1 and RS2), to the plate. Develop over a path of 15cm using a mixture of glacial acetic acid R, water R, methanol R (1:30:70 V/V/V). Dry the plate at room temperature and examine in ultraviolet light at 254 nm.

Identification of Sample A and B:

The principal spot in the chromatogram obtained with test solutions (Ab and Bb) is similar in position and size to the principal spot in the chromatogram obtained with reference solution (RS1) or (RS2).

Participants should identify sample A and B and select the correct answer from the options below:

- butyl hydroxybenzoate
- propyl hydroxybenzoate
- mixture of butyl hydroxybenzoate and propyl hydroxybenzoate

Calculate and report the retention factors (R_f) for the main compound and contaminant to 2 decimal places.

Sample 6H – FLAA Range: 0.2 – 10%(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 Range: - 115 to - 135 (dried substance)

Material supplied: 1 x 1g test material

Dry the sample in an oven at 105°C for 2 hours.

Analysis:

Dissolve 50.00 mg in 0.05 M sodium hydroxide free from carbonate and dilute to 10.0ml with the same alkaline solution (if a larger volume is required make up to the same concentration 5mg/ml). Measure the optical rotation within 30 min of dissolution.

Sodium hydroxide: Analytical reagent grade of commerce containing not less than 97% of total alkali calculated as NaOH and not more than 2.0% of Na₂CO₃.



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Reporting:

Report the result as the optical rotation for solution and the calculated specific optical rotation using the equation below:

$$[\alpha]_D^{20} = \frac{1000\alpha}{l \cdot c}$$

where:

α = angle of rotation in degrees read at 20±0.5°C

l = length in decimetres of the polarimeter tube

c = concentration of the solution in g/l


Report the exact weight of test material taken for testing in mg to 2 decimal places.

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) 

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 R67.



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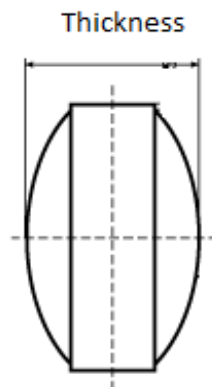
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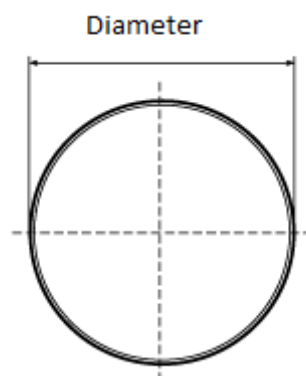
Thickness of tablets

- 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 R63.



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 R63.





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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 $35\text{ }^{\circ}\text{C}$ and $39\text{ }^{\circ}\text{C}$, 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 the 0.1 M hydrochloric acid, maintained at $37 \pm 2\text{ }^{\circ}\text{C}$, 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 R67.

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



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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.

- 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 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 R67.

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 R67.

Note: The spreadsheet must be returned via email to fiona.bury@LGCGroup.com by the reporting deadline.



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Sample 7C – Uniformity of dosage units

Material supplied: Sample A: 1 x 13 tablets for determination of uniformity of dosage units
Reference Standard: 1 x 100mg Pantoprazole Sodium RS (purity 94.38%)

Method:

Standard Preparation:

Dissolve approximately 43mg of Pantoprazole Sodium reference standard, accurately weighed, in 100ml 0.1N Sodium Hydroxide, dilute 5.0ml to 100ml with 0.1N Sodium Hydroxide.

Test Preparation:

Perform on 10 individual tablets; put one tablet into 100ml volumetric flask, add 80.0ml of 0.1N Sodium hydroxide and sonicate for 30 minutes. Complete the volume to the mark with 0.1N NaOH, mix well, then centrifuge at approximately 4000rpm for 15 minutes and dilute 5.0ml to 100ml with 0.1N Sodium Hydroxide.

Procedure:

Measure the absorbance of the test preparation and standard preparation at wavelength max at approximately 295nm (1cm quartz cell) using 0.1M NaOH as blank.

Calculate the percentage Pantoprazole (label claim) as follows:

$$\text{Pantoprazole (\%LC)} = \frac{A_t \times S_w \times P \times 383.4}{A_s \times LC (1 \text{ tablet}) \times 405.4}$$

Where:

A_t = Absorbance due to test preparation
 A_s = Absorbance due to standard preparation
 S_w = Weight of standard (mg)
 P = Potency of standard (94.38%)
 LC = Label claim (40mg Pantoprazole per tablet)
383.4 = Molecular weight of Pantoprazole
405.4 = Molecular weight of Pantoprazole Sodium



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Report the result as the mean value of the percentage Pantoprazole (label claim), and the relative standard deviation (RSD) to 2 decimal places in Portal. Additionally record the individual values for each tablet into provided spreadsheet 7C Uniformity of dosage units R67.

$$RSD = \frac{100s}{\bar{x}}$$

Where:

s = sample standard deviation

\bar{x} = mean of the values obtained from the units tested (%LC)

Note: The spreadsheet must be returned via email to fiona.bury@LGCGroup.com by the reporting deadline.

- All results should be submitted using PORTAL
- Please go to <https://www.lgcpt.com/portal>
- 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