



# PHARMASSURE

**Pharmaceutical Proficiency Testing Scheme**

## **Scheme Description**

### **LGC Standards Proficiency Testing**

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Record of issue status and modifications

ISSUE	ISSUE DATE	DETAILS	AUTHORISED BY
5	Jan 2012	Change to the robust mean description of abbreviations. Sample 2B Trial - ICP analysis included.	M. Whetton
6	Jan 2013	Added new parameters Total bacterial count; Total yeast and mould count; Enumeration and/or detection of both <i>Staphylococcus aureus</i> and <i>Escherichia coli</i> to sample 4. Additional information included for sample 1C and 2B. Change of sample name 2B ICB to 2B Trace elements. Inclusion of 2C Dissolution/Tablet testing trial sample.	T. Noblett & M. Whetton
7	Feb 2014	A new method added to sample 1F. Added new microbiological parameters: <i>Candida albicans</i> ; identification of sterility. Statement on the traceability included in appendix A. Value of SDPA for sodium chloride in sample 1C updated. Inclusion of 2D Conductivity and Particulate determination in solutions trial sample. Micro method abbreviation codes added.	T. Noblett & M. Whetton
8	Dec 2014	Range for all parameters of sample 4 reduced. Inclusion of methods to samples 1C and 2. Additional information included for sample 2. Inclusion of subcontracting information in 'Test Materials' section.	T. Noblett & M. Whetton
9	Jan 2016	Inclusion of the USP methods for chemistry samples. Additional analytes for sample 2B. Inclusion of 2E Residual solvents. Additional analytes (microbiology). Samples re-numbered: 2 changed to 6A-6J; 2C changed to 7A and B; 2D changed to 8A and B; 4 changed to 4A and B. Removed Hard copy report information.	T. Noblett & M. Whetton A. McCarthy
10	May 2016	Kinematic viscosity split by calculated / measured. Additional analytes (Hexane and Acetone) added to sample 2E.	K. Baryla
11	Jan 2017	AAS method added to sample 2B. Analytes list updated for 2E Residual solvents. Inclusion of 6K NMR and 6L XPRD samples. Additional information added to sample 7B.	K. Baryla
12	Jun 2017	Methods added to sample 1D. Temperature added to 1A and 6C samples. Ranges included for 6C sample. Inclusion of sample 7C Uniformity of dosage units. Unit changed for sample 7A.	K. Baryla
13	Jul 2018	New Micro sample 9 added for Salmonella P/A New Micro sample 10 added for microbiological quality of medicinal herbs	R. Smith
14	Dec 2018	Amended units for sample 10 to cfu/g. Updated methods section for Micro samples Website information added to page 3	A.S.Eden/R. Smith A McCarthy

Notes:

Where this document has been translated, the English version shall remain the definitive version

### **Scheme Aims and Organisation**

The primary aim of the Pharmaceutical Proficiency Testing Scheme (PHARMASSURE) is to enable laboratories performing the analysis of pharmaceutical products to monitor their performance and compare it with that of their peers. PHARMASSURE also aims to provide information to participants on technical issues and methodologies relating to testing of pharmaceutical products.

The PHARMASSURE scheme year operates from April to March. Further information about PHARMASSURE, including test material availability, round despatch dates and reporting deadlines, is available on the current PHARMASSURE application form and on the LGC website [www.lgcstandards.com](http://www.lgcstandards.com).

The PHARMASSURE scheme operates an advisory group made up of participants and industry experts. A list of advisory group members is available from LGC Standards on request. The advisory group meets twice a year and is concerned with all aspects of scheme development, operation and participant performance.

### **Test Materials**

Details of test materials available in PHARMASSURE are given in Appendix A. The test parameters are continually reviewed to ensure they meet the needs of current laboratory testing and regulatory requirements.

Test material batches are tested for homogeneity for at least one test parameter where deemed appropriate. Details of homogeneity tests performed and results are given in the PHARMASSURE Scheme Reports.

Some aspects of the scheme, such as test material production, homogeneity testing and stability assessment, can from time to time be subcontracted. When subcontracting occurs, it is placed with a competent subcontractor and LGC is responsible for this work. The planning of the scheme, the evaluation of performance and the authorisation of the final report will never be subcontracted.

### **Statistical Analysis**

Information on the statistics used in PHARMASSURE can be found in the General Protocol and in the Scheme Report. Methods for determining assigned values and the values for SDPA used for individual samples are given in Appendix A

### **Methods**

Methods are listed in PORTAL. Please select the most appropriate method from the list. If none of the methods are appropriate, then please report your method as 'Other' and record a brief description in the Comments Section in PORTAL.

The time and temperature of incubation does not need to be reported.

### **Results and Reports**

PHARMASSURE results are returned through our electronic reporting software, PORTAL, full instructions for which are provided by email. However, participants may request result submission forms on which to report and return results if they are unable to report through electronic means. This will incur an additional charge.

PHARMASSURE reports will be available on the website within 10 working days of round closure. Participants will be emailed a link to the report when it is available.

## APPENDIX A - Description of abbreviations used

### Assigned Value (AV)

The assigned value may be derived in the following ways:

- From the robust mean (median) of participant results (RMean). This is the median of participant results after the removal of test results that are inappropriate for statistical evaluation, e.g. miscalculations, transpositions and other gross errors. Generally, the assigned value will be set using results from all methods, unless the measurement is considered method-dependant, in which case the assigned value will be set by method and indicated in the report tables.  
For some analytes, where there is a recognised reference method for that type of measurement, this may be used as the assigned value for a particular analyte i.e. it would be applied to results obtained by any method.

*Traceability: Assigned values which are derived from the participant results, or a sub-set of the results are not traceable to an international measurement standard. The uncertainty of assigned values derived in this way is estimated from the participant results, according to ISO 13528.*

- From a formulation value (Form). This denotes the use of an assigned value derived from sample preparation details, where known and exact quantities of analyte have been used to prepare the sample.

*Traceability: Assigned values calculated from the formulation of the test sample are traceable, via an unbroken metrological traceability chain, to an international measurement standard. The measurement uncertainty of the assigned value is calculated using the contributions from each calibration in the traceability chain.*

- From a qualitative formulation (Qual Form). This applies to qualitative tests where the assigned value is simply based on the presence/absence of the analyte in the test material.

*Traceability: Assigned values calculated from the qualitative formulation of the test sample are traceable to a certified reference standard or a microbiological reference strain.*

- From expert labs (Expert). The assigned value for the analyte is provided by an 'expert' laboratory.

*Traceability: Assigned values provided by an 'expert' laboratory may be traceable to an international measurement standard, according to the laboratory and the method used. The uncertainty of measurement for an assigned value produced in this way will be provided by the laboratory undertaking the analysis. Details of traceability and the associated uncertainty will be provided in the report for the scheme/round.*

### Range

This indicates the concentration range at which the analyte may be present in the test material.

### SDPA

SDPA represents the 'standard deviation for proficiency assessment' which is used to assess participant performance for the measurement of each analyte. This may be a fixed value (as stated), a percentage (%) of the assigned value or based on the robust standard deviation of the participant measurement results, either across all methods or by method depending on whether the measurement made is method dependent (see assigned value).

**Units**

This indicates the units used for the assessment of data. These are the units in which participants should report their results. For some analytes in some schemes participants may have a choice of which units to report their results, however, the units stipulated in this scheme description are the default units to which any results reported using allowable alternative results will be converted to.

**DP**

This indicates the number of decimal places to which participants should report their measurement results.

**Chemistry samples**  
**Chemical Testing**

**Sample 1**                      **Basic Chemical Testing**

**Sample 1A**                      **pH**  
**Supplied as:**                1 x 60mL buffer solution

Analyte	Method	AV	Range	SDPA	Units	DP
pH (20°C)	Ph. Eur. 2.2.3 USP 791	RMean	4-10	0.05	-	2

**Sample 1B**                      **Acid/Base Titration**  
**Supplied as:**                1 x 60mL acid solution

Analyte	Method	AV	Range	SDPA	Units	DP
Acid/base titration	Phenolphthalein endpoint Potentiometric endpoint	Formulation	15-25	0.15	mL	2

**Sample 1C**                      **Other Basic Titration**  
**Supplied as:**                1 x 60mL or 125mL solution (sample format dependant on test type)

Analyte	Method	AV	Range	SDPA	Units	DP
Titre	Various	Formulation	All	0.15	mL	2
		RMean				
Sodium bicarbonate	Various	Formulation	All	0.10	%(w/v)	2
Magnesium	Mordant black endpoint Other endpoint	Formulation	All	1% of AV	mg/L	0
Dipotassium hydrogen phosphate	Ph. Eur. 2.2.20 USP 541	RMean	All	2% of AV	%	2
Sodium chloride	Ph. Eur. 2.2.20 USP 541 Mohr Volhard	Formulation	All	1% of AV	g/L	2

Samples for this test will vary by round.

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**Sample 1D**  
**Supplied as:** Density  
 1 x 60mL oil sample

Analyte	Method	AV	Range	SDPA	Units	DP
Density	Density meter Pycnometer	RMean	All	0.002	g/cm <sup>3</sup>	3

**Sample 1E**  
**Supplied as:** Refractive Index  
 1 x 60mL sugar solution

Analyte	Method	AV	Range	SDPA	Units	DP
Refractive Index	Ph. Eur. 2.2.6 USP 831	Formulation	All	0.0010	-	4

**Sample 1F**  
**Supplied as:** Melting Point  
 1 x 2g sample

Analyte	Method	AV	Range	SDPA	Units	DP
Melting Point	Ph. Eur. 2.2.14 Ph. Eur. 2.2.60 USP 741	RMean	All	1.0	°C	1

**Sample 2A**  
**Supplied as:** HPLC Analysis  
 1 x sample and reference standard for analysis by HPLC (Sample format will vary from round to round)

Analyte	Method	AV	Range	SDPA	Units	DP
TBC*	Ph. Eur. 2.2.29 USP 621	RMean	All	2.5% of AV	TBC*	2

\*Information regarding the format of the sample will be provided on the preparation instructions for each round. Samples will be formulated in such a way that the analysis will be applicable to the majority of laboratories performing HPLC analysis.

**Sample 2B\*\***  
**Supplied as:** Trace elements  
 1 x 5g sample for the determination of trace element impurities  
 1 x 1g of matrix

Analyte	Method	AV	Range	SDPA	Units	DP
Arsenic	ICP-MS ICP-OES AAS	RMean	0.1-1.5	Robust SD	µg/g	2
Cadmium		RMean	0.1-0.5	Robust SD	µg/g	2
Lead		RMean	0.1-1.0	Robust SD	µg/g	2
Mercury		RMean	0.1-1.5	Robust SD	µg/g	2

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Analyte	Method	AV	Range	SDPA	Units	DP
Chromium		RMean	0.1 - 25	Robust SD	µg/g	2
Copper		RMean	0.1 - 130	Robust SD	µg/g	2
Zinc		RMean	0.1 - 1300	Robust SD	µg/g	2

\*\*Test material currently not included in LGC's UKAS Scope of Accreditation.

**Sample 2E\*\*\***

**Residual solvents**

**Supplied as:**

1 x 2g sample for the determination of residual solvents  
1 x 1ml spiking solution

Analyte	Method	AV	Range	SDPA	Units	DP
Benzene	Ph. Eur. 2.4.24	RMean	0 - 2	Robust SD	µg/g	2
Carbon tetrachloride	Ph. Eur. 2.2.28	RMean	0 - 4	Robust SD	µg/g	2
1,2-Dichloroethane	USP 467	RMean	0 - 5	Robust SD	µg/g	2
1,1- Dichloroethene	GC-FID	RMean	0 - 8	Robust SD	µg/g	2
1,1,1-Trichloroethane	GC-MS	RMean	0 - 1500	Robust SD	µg/g	0
Chloroform	GC-ECD	RMean	0 - 60	Robust SD	µg/g	1
Hexane	GC-PID	RMean	0 - 290	Robust SD	µg/g	0
Methanol	GC-TCD	RMean	0 - 3000	Robust SD	µg/g	0
Toluene		RMean	0 - 890	Robust SD	µg/g	0
Acetone		RMean	0 - 5000	Robust SD	µg/g	0
Ethanol		RMean	0 - 5000	Robust SD	µg/g	0

\*\*\*Analytes, assigned values, ranges and SDPAs are subject to alterations. Test material currently not included in LGC's UKAS Scope of Accreditation.

**Advanced Chemical Testing**

**Sample 6A**

**Gas Chromatography (GC)**

**Supplied as:**

Sample and reference standard (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
GC	Ph. Eur. 2.2.28 USP 621	Formulation or RMean	All	Robust SD	See instruction sheet	

**Sample 6B**

**UV**

**Supplied as:**

1 x sample (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
UV	Ph. Eur. 2.2.25	RMean	All	Robust SD	See instruction sheet	



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**Sample 6C**

**Viscosity**

**Supplied as:**

1 x 250ml solution sample

Technique	Method	AV	Range	SDPA	Units	DP
Dynamic viscosity (20°C)	Ph. Eur. 2.2.9 Ph. Eur. 2.2.10 USP 911 USP 912	RMean	10-300	Robust SD	mPa·s	0
Kinematic viscosity - measured (20°C)	Ph. Eur. 2.2.9 USP 911	RMean	10-300	Robust SD	mm <sup>2</sup> /s	0
Kinematic viscosity - calculated from dynamic viscosity (20°C)	Ph. Eur. 2.2.9 Ph. Eur. 2.2.10 USP 911 USP 912	RMean	10-300	Robust SD	mm <sup>2</sup> /s	0

**Sample 6D**

**Loss on Drying (LOD)**

**Supplied as:**

1 x sample (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
Loss on drying (LOD)	Ph. Eur. 2.2.32 USP 731	RMean	All	0.1	%(w/w)	2

**Sample 6E**

**FTIR**

**Supplied as:**

Sample and reference standard (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
IR/FTIR	Ph. Eur. 2.2.24 USP 197	Qualitative Pharmaceutical Analysis				

**Sample 6F**

**Karl Fischer**

**Supplied as:**

1 x sample (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
Moisture by Karl Fischer	Ph. Eur. 2.5.12 USP 921	RMean	All	Robust SD	%(w/w)	2

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**Sample 6G**  
**Supplied as:**

**TLC**  
Sample, reference standard and TLC plates (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
TLC	Ph. Eur. 2.2.27 USP 621	Qualitative Pharmaceutical Analysis				

**Sample 6H**  
**Supplied as:**

**FLAA**  
1 x 60ml solution sample

Technique	Method	AV	Range	SDPA	Units	DP
Flame spectroscopy	Ph. Eur. 2.2.22 Ph. Eur. 2.2.23 Ph. Eur. 2.2.57 USP 232 USP 233	Formulation	All	Robust SD	%(w/v)	2

**Sample 6I**  
**Supplied as:**

**Polarimetry**  
1 x sample (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
Polarimetry	Ph. Eur. 2.2.7 USP 781	RMean	All	Robust SD	°	2

**Sample 6J**  
**Supplied as:**

**Advanced Titration**  
1 x sample (Format depends upon type of test material)

Technique	Method	AV	Range	SDPA	Units	DP
Advanced titration (potentiometric, non-aqueous)	Various	RMean	All	Robust SD	See instruction sheet	

**Sample 6K\*\*\*\***  
**Supplied as:**

**Nuclear Magnetic Resonance (NMR) Spectrometry**  
1 x 1g sample

Technique	Method	AV	Range	SDPA	Units	DP
Qualitative	Ph. Eur. 2.2.33	Qualitative Pharmaceutical Analysis				
Quantitative	USP 761	RMean	All	Robust SD	%	2

\*\*\*\*This sample is a trial sample. Test material currently not included in LGC's UKAS Scope of Accreditation.

**Sample 6L\*\*\*\*****X-ray Powder Diffraction (XRPD)****Supplied as:**

1 x 1g sample

Technique	Method	AV	Range	SDPA	Units	DP
Qualitative phase	Ph. Eur. 2.9.33	Qualitative Pharmaceutical Analysis				
Quantitative phase	USP 941	RMean	All	Robust SD	%	2

\*\*\*\*This sample is a trial sample. Test material currently not included in LGC's UKAS Scope of Accreditation.

**Sample 7A\*\*****Dissolution testing****Supplied as:**

1 x sample for dissolution testing and reference standard

Analyte	Method	AV	Range	SDPA	Units	DP
Dissolution	Ph. Eur. 2.9.3 USP 711	RMean	All	Robust SD	%	2

\*\*Test material currently not included in LGC's UKAS Scope of Accreditation.

**Sample 7B\*\*****Tablet testing****Supplied as:**

1 x sample for tablet testing

Analyte	Method	AV	Range	SDPA	Units	DP
Diameter	Various	RMean	All	Robust SD	mm	2
Disintegration	Ph. Eur. 2.9.1 USP 701	Qual Form	All	N/A	N/A	N/A
Friability	Ph. Eur. 2.9.7 USP 1216	Qual Form	All	N/A	N/A	N/A
Resistance to crushing	Ph. Eur. 2.9.8 USP 1217	RMean	All	Robust SD	N	2
Thickness	Various	RMean	All	Robust SD	mm	2
Uniformity of weight	Ph. Eur. 2.9.5	Qual Form	All	N/A	N/A	N/A

\*\*Test material currently not included in LGC's UKAS Scope of Accreditation.

**Sample 7C\*\*****Uniformity of dosage units****Supplied as:**

1 x 10 dosage units\* and reference standard

Analyte	Method	AV	Range	SDPA	Units	DP
Uniformity of dosage units	Ph. Eur. 2.9.40 USP 905	RMean	All	Robust SD	%	2

\* One of the following: tablets, capsules, powders or suspensions.

\*\*Test material currently not included in LGC's UKAS Scope of Accreditation.

**Sample 8A\*\*****Conductivity in solutions****Supplied as:**

1 x 125ml sample for conductivity in solutions

Analyte	Method	AV	Range	SDPA	Units	DP
Low level conductivity	Ph. Eur. 2.2.38 USP 1644	RMean	1 - 50	Robust SD	µS/cm	2

\*\*Test material currently not included in LGC's UKAS Scope of Accreditation.

**Sample 8B\*\*****Particulate determination in solutions****Supplied as:**

1 x sample for particulate determination in solutions

Analyte	Method	AV	Range	SDPA	Units	DP
Particulate determination	Ph. Eur. 2.9.19 Ph. Eur. 2.9.20 USP 788	RMean	All	Robust SD	-	0

\*\*Test material currently not included in LGC's UKAS Scope of Accreditation.

Further details for Advanced Chemical Testing, for example analytes and reporting format, will be published on the preparation instructions supplied with the samples.

**Microbiological samples****Sample 3****Low-level Enumeration and Identification (intended for membrane filtration)****Supplied as:**

1 x 10ml glass sealed vial containing a single culture of lyophilised microorganism. Final sample volume 1mL (for identification only) or 100mL (identification & enumeration).

Analyte	Method	AV	Range	SDPA	Units	DP
Identification of microorganism	All	Qual Form	<500	N/A	N/A	N/A
Low-level enumeration	All	RMean	<500	0.35	cfu/100ml	0

**Sample 4A****Enumeration of TAMC and indicator organisms****Supplied as:**

1 x 10ml glass sealed vial containing a mixed culture of lyophilised microorganism(s). Final sample volume 100mL (neat).

Analyte	Method	AV	Range	SDPA	Units	DP
Total aerobic microbial count	All	RMean	<5,000	0.35	cfu/ml	0
Total bacterial count	All	RMean	<5,000	0.35	cfu/ml	0
Detection and/or enumeration of <i>Staphylococcus aureus</i>	All	RMean	<1,000	0.35	cfu/ml	0
Detection and/or enumeration of <i>Escherichia coli</i>	All	RMean	<1,000	0.35	cfu/ml	0
Detection and/or enumeration of bile-tolerant gram-negative bacteria	All	RMean	<1,000	0.35	cfu/ml	0

**Sample 4B****Enumeration of yeast, mould and *Pseudomonas*****Supplied as:**

1 x 10ml glass sealed vial containing a mixed culture of lyophilised microorganism(s). Final sample volume 100mL (neat).

Analyte	Method	AV	Range	SDPA	Units	DP
Detection of <i>Pseudomonas aeruginosa</i>	All	Qual Form	<1000	N/A	cfu/ml	N/A
Detection and/or enumeration of <i>Candida albicans</i>	All	RMean	<1,000	0.35	cfu/ml	0
Total yeast and mould count and/or enumeration of yeast, enumeration of mould	All	RMean	<2,000	0.35	cfu/ml	0

**Sample 5**

**Sterility and identification**

**Supplied as:**

5 x 5ml glass sealed vials which may or may not contain microorganisms at low levels (final sample volume up to 100mL)

Analyte	Method	AV	Range	SDPA	Units	DP
Sterility	All	Qual Form	<100	N/A	cfu/vial	N/A
Identification of microorganism	All	Qual Form	<100	N/A	cfu/vial	N/A

**Sample 9**

***Salmonella* presence/absence**

**Supplied as:**

1 x 10mL glass sealed vial which may or may not contain the target organism. Final sample volume 10ml (neat).

Analyte	Method	AV	Range	SDPA	Units	DP
Detection of <i>Salmonella</i> spp	All	Qual Form	<100	N/A	Detected/not detected in 1ml	N/A

**Sample 10**

**Microbiological testing of medicinal herbs**

**Supplied as:**

1 x 10ml glass sealed vial & 10g medicinal herb matrix

Analyte	Method	AV	Range	SDPA	Units	DP
Total aerobic microbial count	All	RMean	<5,000	0.35	cfu/g	0
Detection and/or enumeration of <i>Staphylococcus aureus</i>	All	RMean	<1,000	0.35	cfu/g	0
Detection and/or enumeration of coliforms	All	RMean	<1,000	0.35	cfu/g	0
Detection and/or enumeration of yeast and/or mould	All	RMean	<1,000	0.35	cfu/g	0