



# PHARMASSURE

**Pharmaceutical Proficiency Testing Scheme**

## **Scheme Description**

### **LGC Standards Proficiency Testing**

1 Chamberhall Business Park  
Chamberhall Green  
Bury, BL9 0AP  
UK.

Telephone: +44 (0) 161 762 2500  
Fax: +44 (0) 161 762 2501  
Email: [pharmassure@lgcgroup.com](mailto:pharmassure@lgcgroup.com)  
Website: [www.lgcstandards.com](http://www.lgcstandards.com)



# PHARMASSURE Scheme Description

## Record of issue status and modifications

ISSUE	ISSUE DATE	DETAILS	AUTHORISED BY
1	Feb 2008	Removed scheme year from title page. Updated details of levels and analytes.	M.Whetton
2	Jan 2009	Inclusion of Level 4 – sterility testing. Samples renamed as Level 1 – basic chemical testing, Level 2 – advanced chemical testing, Level 3 – Basic microbiological testing and Level 4 – sterility testing. Inclusion of 'Other basic titrations' in Level 1. Appendix A updated for various parameters	M.Whetton
3	Jan 2010	Appendix restructured. 'Levels' altered to 'Samples'.	M.Whetton
4	Jan 2011	Change of address details. Removed details regarding outliers in Appendix A. Included details of advisors and collaborators. Amended sample 4 units from cfu/100ml to cfu/ml. Inclusion of HPLC sample	T.Noblett
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

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, are available on the current PHARMASSURE application form.

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 Appendix A and 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.

Abbreviations for microbiological method codes can be found in Appendix A. 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.

**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	Ph. Eur. 2.2.3	RMean	4-10	0.05	-	2
	USP 791					

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

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

**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	Formulation	All	1% of AV	mg/L	0
	Other endpoint					
Dipotassium hydrogen phosphate	Ph. Eur. 2.2.20	RMean	All	2% of AV	%	2
	USP 541					
Sodium chloride	Ph. Eur. 2.2.20	Formulation	All	1% of AV	g/L	2
	USP 541					
	Mohr					
	Volhard					

Samples for this test will vary by round.

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

Analyte	Method	AV	Range	SDPA	Units	DP
Density	Various	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	Formulation	All	0.0010	-	4
	USP 831					

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

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

**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	RMean	All	2.5% of AV	TBC*	2
	USP 621					

\*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
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\*\*\*****Supplied as:****Residual solvents**

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	Formulation or RMean	All	Robust SD	See instruction sheet	
	USP 621					

**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	

**Sample 6C****Viscosity****Supplied as:**

1 x 250ml solution sample

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

**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	RMean	All	0.1	%(w/w)	2
	USP 731					

# PHARMASSURE Scheme Description

**Sample 6E**  
**Supplied as:**

**FTIR**  
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	Qualitative Pharmaceutical Analysis				
	USP 197					

**Sample 6F**  
**Supplied as:**

**Karl Fischer**  
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	RMean	All	Robust SD	%(w/w)	2
	USP 921					

**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	Qualitative Pharmaceutical Analysis				
	USP 621					

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

**FLAA**  
1 x 60ml solution sample

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

**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	RMean	All	Robust SD	°	2
	USP 781					

**Sample 6J****Advanced Titration****Supplied as:**

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\*\*\*\*****Nuclear Magnetic Resonance (NMR) Spectrometry****Supplied as:**

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.

Further details, for example, analytes and methods, will be published on the preparation instructions supplied with the samples.

**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	RMean	All	Robust SD	%(w/w)	2
	USP 711					

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

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

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	Qual Form	All	N/A	N/A	N/A
	USP 701					
Friability	Ph. Eur. 2.9.7	Qual Form	All	N/A	N/A	N/A
	USP 1216					
Resistance to crushing	Ph. Eur. 2.9.8	RMean	All	Robust SD	N	2
	USP 1217					
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 8A\*\*****Supplied as:****Conductivity in solutions**

1 x 125ml sample for conductivity in solutions

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

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

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

1 x sample for particulate determination in solutions

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

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

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

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	Biochemical Microscopy Serology Selective agar Molecular	Qual Form	<500	N/A	N/A	N/A
Low-level enumeration	MEMF PCA MEMF TSA	RMean	<500	0.35	cfu/100ml	0

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

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	PCA TSA MEMF TSA	RMean	<5,000	0.35	cfu/ml	0
Total bacterial count	PCA TSA MEMF TSA	RMean	<5,000	0.35	cfu/ml	0
Detection and/or enumeration of <i>Staphylococcus aureus</i>	BP + RPF BP Petrifilm	RMean	<1,000	0.35	cfu/ml	0
Detection and/or enumeration of <i>Escherichia coli</i>	TBX COLI ID Petrifilm MPN Chromagenic agar	RMean	<1,000	0.35	cfu/ml	0
Detection and/or enumeration of bile-tolerant gram-negative bacteria	VRBGA Petrifilm MPN	RMean	<1,000	0.35	cfu/ml	0

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

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

Detection of <i>Pseudomonas aeruginosa</i>	CF agar CN agar	Qual Form	<1000	N/A	cfu/ml	N/A
Detection and/or enumeration of <i>Candida albicans</i>	OGYE RB SD Petrifilm	RMean	<1,000	0.35	cfu/ml	0
Total yeast and mould count and/or enumeration of yeast, enumeration of mould	OGYE RB SD Petrifilm	RMean	<2,000	0.35	cfu/ml	0

**Sample 5****Supplied as:****Sterility and identification**

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	Broth/agar MEMF SteriTest	Qual Form	<100	N/A	cfu/vial	N/A
Identification of microorganism	Biochemical Microscopy Serology Selective agar Molecular	Qual Form	<100	N/A	cfu/vial	N/A

**ABBREVIATIONS FOR MICROBIOLOGICAL METHOD CODES**

BP = Baird parker agar

BP + RPF = Baird parker agar with rabbit plasma

MPN = Most probable number

MEMF = Membrane filtration

VRBGA = Violet red bile glucose agar

OGYE = Oxytetracycline-Glucose Yeast Extract agar

PCA = Plate count agar

RB = Rose Bengal agar

SD = Sabouraud dextrose agar

TSA = Tryptone soya agar

All analytes will also have 'OTHER' as a method choice in case your method is not listed