LGC Standards

Excellence through measurement

TDM

THERAPEUTIC DRUGS MONITORING PROFICIENCY TESTING SCHEME

Scheme Description

LGC Standards
Proficiency Testing
1 Chamberhall Business Park
Chamberhall Green
Bury
Lancashire
BL9 0AP
United Kingdom

Telephone: +44 (0) 161 762 2500
Fax: +44 (0) 161 762 2501
Email: tdm@lgcpt.com
Website: www.lgcpt.com

UKAS PROFICIENCY TESTING 0001

Issue: 6

Issue date: December 2013

Record of issue status and modifications

ISSUE	ISSUE DATE	DETAILS	AUTHORISED BY
1	Oct 2011	Version 1 issued.	K. Morgan
2	Jan 2012	Units of psychoactives amended to µg/L. Spelling of Netilmicin amended (AT04).	K. Morgan
3	Sept 2012	UKAS logo added. Update to number of levels of TD1,2 and 3 per month. Updates to concentration ranges of PS4, PS5 and introduction of additional samples.SA1, SA2, PS26, PS27, PS28 and PS29.	K. Morgan
4	August 2013	Additional AE3, AE4 and NC samples added. TD1 Carbamazepine+CBZ epoxide clarified.	K Morgan
5	October 2013	Restructure of TD1, TD2, TD3, Methotrexate and Clobazam/Norclobazam. Updates to concentration ranges covered on analytes in scheme.	K Morgan
6	December 2013	Clarification of traceability of Assigned Values, Clarification of Units for Methotrexate	K Morgan

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

Scheme Aims and Organisation

The primary aim of the Therapeutic Drugs Monitoring proficiency testing scheme (TDM) is to enable laboratories performing the analysis of therapeutic drugs to monitor their performance and compare it with that of their peers. The TDM scheme also aims to provide information to participants on technical issues and methodologies relating to Therapeutic Drug Monitoring.

The TDM scheme year operates from January to December. Further information about TDM, including test material availability, round despatch dates and reporting deadlines, are available on the current TDM application form.

The operation of all schemes is supported by an Advisory Group consisting of members of the professional bodies, scheme participants, and others experienced in the field of therapeutic drug monitoring. The scheme reports on the performance of U.K. participants to the National Quality Assurance Advisory Panels for Chemical Pathology and for Medical Microbiology.

Test Materials

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

Samples are prepared using pre-screened human serum and newborn calf serum (for the majority of the psychoactive drug samples).

The human serum is pooled and is obtained from donors who have verbally declared themselves drug free. The serum has been sterile-filtered, tested and found negative for:

- HEP B antigen
- HEP C antigen
- Combo HIV 1 and 2
- Syphilis
- Alanine transferase

Certificates of Analysis of the serum are retained at LGC.

The newborn calf serum of New Zealand origin is collected from calves less than 14 days old. The serum has been sterile-filtered. Certificates of Analysis of the serum are retained at LGC.

Note: All test materials provided are intended for use as proficiency testing materials only and are not to be used for any other purposes.

Statistical Analysis

Information on the statistics used in TDM 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.

Results and Reports

TDM 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.

TDM 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.

Hard-copy reports are available for an additional charge; these are sent to participants by post within 15 working days of the results deadline.

APPENDIX A - Description of abbreviations used

Assigned Value (AV)

The assigned value may be derived in the following ways:

- From the robust mean (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 as illustrated 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 (Formulation). 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 mesasurement 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. Wherever possible, the SDPA is based on a concentration dependent model derived from historic data. Otherwise the SDPA is based upon the RobustSD.

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.

CDM
Concentration Dependent Model

Therapeutic Drugs

Sample TD1 **Anti-epileptic drugs mixture**
Participants will receive: 3 x 5ml samples of lyophilised human serum (A, B, and C)

Analyte	Method	Range	AV	SDPA	Units	DP
Carbamazepine	All	0 to 40	RMean	Fixed from CDM	mg/L	2
CBZ-epoxide	All	0 to 30	RMean	Fixed from CDM	mg/L	2
Carbamazepine + CBZ-epoxide	All	0 to 70	RMean	Fixed from CDM	mg/L	2
Clonazepam	All	0 to 100	RMean	Fixed from CDM	µg/L	2
Lamotrigine	All	0 to 25	RMean	Fixed from CDM	mg/L	2
Phenytoin	All	0 to 40	RMean	Fixed from CDM	mg/L	2
Ethosuximide	All	0 to 190	RMean	Fixed from CDM	mg/L	2
Phenobarbitone	All	0 to 60	RMean	Fixed from CDM	mg/L	2
Primidone	All	0 to 40	RMean	Fixed from CDM	mg/L	2
Valproate	All	0 to 200	RMean	Fixed from CDM	mg/L	2
Caffeine	All	0 to 150	RMean	Fixed from CDM	mg/L	2
Digoxin	All	0 to 5	RMean	Fixed from CDM	µg/L	2
Lithium	All	0 to 4	RMean	Fixed from CDM	mmol/L	2
Theophylline	All	0 to 55	RMean	Fixed from CDM	mg/L	2
Methotrexate	All	0 to 10	RMean	Fixed from CDM	µmol/L	2
TD-Amikacin	All	0 to 60	RMean	Fixed from RSD	mg/L	2
TD-Gentamicin	All	0 to 16	RMean	Fixed from CDM	mg/L	2
TD-Tobramycin	All	0 to 15	RMean	Fixed from RSD	mg/L	2
TD-Vancomycin	All	0 to 47	RMean	Fixed from CDM	mg/L	2

Sample CN1 **Clobazam and Norclobazam**
Participants will receive: 2 x 2ml samples of lyophilised human serum (A and B)

Analyte	Method	Range	AV	SDPA	Units	DP
Clobazam	All	0 to 1000	RMean	Fixed from CDM	µg/L	2
Norclobazam	All	0 to 6000	RMean	Fixed from CDM	µg/L	2

Other Therapeutic Drugs

Sample AE1 **Anti-epileptic drugs mixture**
Participants will receive: 1 x 4ml sample of lyophilised human serum

Analyte	Method	Range	AV	SDPA	Units	DP
OH-oxcarbazepine	All	0 to 45	RMean	Fixed from CDM	mg/L	2
Gabapentin	All	0 to 35	RMean	Fixed from CDM	mg/L	2
Tiagabine	All	0 to 300	RMean	Fixed from CDM	µg/L	2
Levetiracetam	All	0 to 125	RMean	Fixed from CDM	mg/L	2
Pregabalin	All	0 to 25	RMean	Fixed from CDM	mg/L	2

Sample AE2 **Anti-epileptic drugs mixture**
Participants will receive: 1 x 4ml sample of lyophilised human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Topiramate	All	0 to 45	RMean	Fixed from CDM	mg/L	2
Vigabatrin	All	0 to 65	RMean	Fixed from CDM	mg/L	2
Felbamate	All	0 to 155	RMean	Fixed from CDM	mg/L	2
Zonisamide	All	0 to 55	RMean	Fixed from CDM	mg/L	2
Rufinamide	All	0 to 105	RMean	Fixed from CDM	mg/L	2
Lacosamide	All	0 to 30	RMean	Fixed from CDM	mg/L	2

Sample AE3* **Retigabine**
Participants will receive: 1 x 2ml lyophilised human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Retigabine (Ezogabine)	All	0-100	RMean	RobustSD	mg/L	2

Sample AE4* **Perampanel**
Participants will receive: 1 x 2ml lyophilised human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Perampanel	All	0-1000	RMean	RobustSD	µg/L	2

*not currently included in LGC Standards' UKAS Scope of Accreditation

Sample CRD **Cardiac mixture**

Participants will receive: 1 x 2ml lyophilised human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Amiodarone	All	0 to 4000	RMean	Fixed from CDM	µg/L	2
Desethylamiodarone	All	0 to 4000	RMean	Fixed from CDM	µg/L	2
Flecainide	All	0 to 1500	RMean	Fixed from CDM	µg/L	2

Drugs used for the Treatment of substance related disorders

Sample SA01 **Buprenorphine and Norbuprenorphine**

Participants will receive: 2 x 2ml lyophilised human serum (A and B)

Analyte	Method	Range	AV	SDPA	Units	DP
Buprenorphine	All	0 to 15 µg/L	RMean	RobustSD	µg/L	2
Norbuprenorphine	All	0 to 15 µg/L	RMean	RobustSD	µg/L	2

Sample SA02 **Methadone and EDDP**

Participants will receive: 2 x 2ml lyophilised human serum (A and B)

Analyte	Method	Range	AV	SDPA	Units	DP
Methadone	All	0 to 750 µg/L	RMean	RobustSD	µg/L	2
EDDP	All	0 to 750 µg/L	RMean	RobustSD	µg/L	2

Psychoactive Drugs

Sample PS01 **Amitriptyline and Nortriptyline**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Amitriptyline	All	0 to 500	RMean	Fixed from CDM	µg/L	2
Nortriptyline	All	0 to 500	RMean	Fixed from CDM	µg/L	2

Sample PS02 **Imipramine and Desipramine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Imipramine	All	0 to 500	RMean	Fixed from CDM	µg/L	2
Desipramine	All	0 to 500	RMean	Fixed from CDM	µg/L	2

Sample PS03 **Clomipramine and Norclomipramine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Clomipramine	All	0 to 550	RMean	Fixed from CDM	µg/L	2
Norclomipramine	All	0 to 550	RMean	Fixed from CDM	µg/L	2

Sample PS04 **Clozapine and Norclozapine**

Participants will receive: 1 x 5ml lyophilised human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Clozapine	All	0 to 2500	RMean	Fixed from CDM	µg/L	2
Norclozapine	All	0 to 2500	RMean	Fixed from CDM	µg/L	2

Sample PS05 **Doxepin and Nordoxepin**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Doxepin	All	0 to 450	RMean	Fixed from CDM	µg/L	2
Nordoxepin	All	0 to 450	RMean	Fixed from CDM	µg/L	2

Sample PS06 **Fluoxetine and Norfluoxetine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Fluoxetine	All	0 to 600	RMean	Fixed from CDM	µg/L	2
Norfluoxetine	All	0 to 600	RMean	Fixed from CDM	µg/L	2

Sample PS07 **Fluphenazine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Fluphenazine	All	0 to 25	RMean	Fixed from CDM	µg/L	2

Sample PS08 **Sertraline and Norsertraline**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Sertraline	All	0 to 300	RMean	Fixed from CDM	µg/L	2
Norsertraline	All	0 to 350	RMean	Fixed from CDM	µg/L	2

Sample PS09 **Trimipramine and Nortrimipramine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Trimipramine	All	0 to 600	RMean	Fixed from CDM	µg/L	2
Nortrimipramine	All	0 to 500	RMean	Fixed from CDM	µg/L	2

Sample PS10 **Risperidone and HO-risperidone**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Risperidone	All	0 to 140	RMean	Fixed from CDM	µg/L	2
HO-risperidone	All	0 to 350	RMean	Fixed from CDM	µg/L	2

Sample PS11 **Mirtazapine and Normirtazapine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Mirtazapine	All	0 to 160	RMean	Fixed from CDM	µg/L	2
Normirtazapine	All	0 to 100	RMean	Fixed from CDM	µg/L	2

Sample PS12 **Maprotiline and Normaprotiline**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Maprotiline	All	0 to 450	RMean	Fixed from CDM	µg/L	2
Normaprotiline	All	0 to 300	RMean	Fixed from CDM	µg/L	2

Sample PS13 **Thioridazine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Thioridazine	All	0 to 2000	RMean	Fixed from CDM	µg/L	2

Sample PS14 **Haloperidol**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Haloperidol	All	0 to 70	RMean	Fixed from CDM	µg/L	2

Sample PS15 **Olanzapine**

Participants will receive: 1 x 5ml lyophilised human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Olanzapine	All	0 to 150	RMean	Fixed from CDM	µg/L	2

Sample PS16 **Perphenazine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Perphenazine	All	0 to 25	RMean	Fixed from CDM	µg/L	2

Sample PS17 **Quetiapine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Quetiapine	All	0 to 1000	RMean	Fixed from CDM	µg/L	2
Norquetiapine (N-desalkylquetiapine)	All	0 to 500	RSD	Fixed from CDM	µg/L	2

Sample PS18 **Citalopram and Norcitalopram**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Citalopram	All	0 to 350	RMean	Fixed from CDM	µg/L	2
Norcitalopram	All	0 to 90	RMean	Fixed from CDM	µg/L	2

Sample PS19 **Dothiepin and Northiaden**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Dosulepin (Dothiepin)	All	0 to 260	RMean	Fixed from CDM	µg/L	2
Northiaden	All	0 to 260	RMean	Fixed from CDM	µg/L	2

Sample PS20 **Venlafaxine and Norvenlafaxine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Venlafaxine	All	0 to 450	RMean	Fixed from CDM	µg/L	2
Norvenlafaxine	All	0 to 550	RMean	Fixed from CDM	µg/L	2

Sample PS21 **Paroxetine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Paroxetine	All	0 to 525	RMean	Fixed from CDM	µg/L	2

Sample PS22 **Fluvoxamine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Fluvoxamine	All	0 to 1000	RMean	Fixed from CDM	µg/L	2

Sample PS23 **Zuclopenthixol**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Zuclopenthixol (zuclopentixol)	All	0 to 125	RMean	Fixed from CDM	µg/L	2

Sample PS24 **Amisulpride**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Amisulpride	All	0 to 650	RMean	Fixed from CDM	µg/L	2

Sample PS25 **Aripiprazole and Dehydroaripiprazole**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Aripiprazole	All	0 to 1000	RMean	Fixed from CDM	µg/L	2
Dehydroaripiprazole	All	0 to 500	RMean	Fixed from CDM	µg/L	2

Sample PS26 **Ziprasidone**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Ziprasidone	All	0 to 500	RMean	RobustSD	µg/L	2

Sample PS27 **Duloxetine**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Duloxetine	All	0 to 400	RMean	RobustSD	µg/L	2

Sample PS28 **Escitalopram**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Escitalopram	All	0 to 350	RMean	RobustSD	µg/L	2

Sample PS29 **Trazodone**

Participants will receive: 1 x 5ml lyophilised newborn calf serum

Analyte	Method	Range	AV	SDPA	Units	DP
Trazodone	All	0 to 1500	RMean	RobustSD	µg/L	2

Smoking Related Drugs

Sample NC01* **Nicotine and Cotinine in Urine**

Participants will receive: 2 x 5 ml human urine lyophilised issued quarterly (A and B)

Analyte	Method	Range	AV	SDPA	Units	DP
Nicotine	All	0 to 5	RMean	RobustSD	mg/L	3
Cotinine	All	0 to 3	RMean	RobustSD	mg/L	3

*not currently included in LGC Standards' UKAS Scope of Accreditation

Antibiotic Drugs

Sample AT01 **Gentamicin and Vancomycin**

Participants will receive: 1 x 1ml human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Gentamicin	All	TBC	RMean	Fixed from CDM	mg/L	2
Vancomycin	All	TBC	RMean	Fixed from CDM	mg/L	2

Sample AT02 **Tobramycin**

Participants will receive: 1 x 1ml human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Tobramycin	All	TBC	RMean	Fixed from CDM	mg/L	2

Sample AT03 **Amikacin**

Participants will receive: 1 x 1ml human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Amikacin	All	TBC	RMean	Fixed from CDM	mg/L	2

Sample AT04 **Netilmicin**

Participants will receive: 1 x 1ml human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Netilmicin	All	TBC	RMean	Fixed from CDM	mg/L	2

Sample AT05 **Chloramphenicol**

Participants will receive: 1 x 1ml human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Chloramphenicol	All	TBC	RMean	Fixed from CDM	mg/L	2

Sample AT06 **Flucytosine**

Participants will receive: 1 x 1ml human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Flucytosine	All	TBC	RMean	Fixed from CDM	mg/L	2

Sample AT07 **Teicoplanin**

Participants will receive: 1 x 1ml human serum

Analyte	Method	Range	AV	SDPA	Units	DP
Teicoplanin	All	TBC	RMean	Fixed from CDM	mg/L	2