TDM-SOP-SER-002

User's Guide to Therapeutic Drug Monitoring Unit

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1. USEFUL NAMES AND TELEPHONE NUMBERS

Chalfont Centre switchboard number	01494 601300
Head of Unit/Clinical Scientist: Dr. P. Kampanis	01494 601467
R&D Manager: Mr. A. Giram	01494 601427
Biomedical Scientist: Ms. Q. Munir	01494 601423
Biomedical Scientist: Ms. S. Masoumzadeh	01494 601423
Biomedical Scientist: Ms. H. Jones	01424 601424
Patient results and enquiries	01494 601423
Quality & Administration Manager: Ms. S Allen-Phillips	01494 601468
TDM Unit Administrator: Ms C Dance	01494 601434
Phlebotomy Services: Ms A Ivey	01494 601345
Phlebotomy Services: Ms K Browne	01494 601345
Business Manager Medical Services: Mr. T Brighton	01494 601448

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2. GENERAL INFORMATION

The Unit provides a drug monitoring assay service for anti-seizure medications and a pharmacokinetic consultation service as an aid to individualisation of patient drug therapy. The Unit will undertake the detailed pharmacokinetic investigation of individual patients with unusual clinical response to drugs during therapy or following overdose.

The Unit is located in the Queen Elizabeth Medical Centre of the Chalfont Centre for Epilepsy.

2.1 Assay Service

The assay service is routinely available Monday to Friday between the hours of 09:00 and 17:00. For urgent assay requests (please contact Unit in advance), blood samples will be prioritised and reported on as soon as possible. Non urgent assay request will be reported within 3 working days of receiving the samples, excluding weekends or bank holidays.

The Unit is accredited by United Kingdom Accreditation Service (UKAS) in accordance with the International Standard ISO 15189:2022- Medical Laboratories: Requirements for Quality and Competence (Laboratory No. 8353).

2.2 On-Call Service

The Unit does not provide an on-call service. Urgent anti-seizure medication (carbamazepine, phenytoin, phenobarbital and valproic acid only) analysis is usually available through local hospital's Department of Clinical Biochemistry.

2.3 Requesting

An anti-seizure medication assay request form (TDM-FRM-SER-006) is available to be downloaded from the Epilepsy Society website: https://www.epilepsysociety.org.uk/ (from following TDM sub-section https://epilepsysociety.org.uk/what-we-do/medical-services/therapeutic-drug-monitoring/therapeutic-drug-monitoring-tdm/using-tdm-service).
The Form needs to be completed appropriately and clearly so as to enable efficient processing of assay request.

Also, for patients seen at the Epilepsy Society or UCLH Trust requests for assays may be made using the EPIC (electronic health record) system.

2.4 Minimum Data Set for Patient Identification

It is important that certain minimum criteria for sample identification and Request Form details are met.

Sample and request form information must be compatible. The following table indicates the essential data required on samples and request forms and outlines other desirable information, which ideally should also be included.

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ESSENTIAL	DESIRABLE
Sample: □ Patient's full name □ Date of birth □ Sample date	□ Unique hospital number □ Time specimen taken
Request Form: □ Patient's full name □ Date of birth □ Date and time sample collected □ Patient's Consultant or GP □ Destination for report	□ Unique hospital number □ Clinical information □ Patient's NHS Number □ Patient's sex □ Clinician's bleep number or contact telephone/mobile phone number □ Drug dose and time and date of last dose

2.5 Specimens and Sampling Time

An appropriate specimen is a prime necessity for effective monitoring. This requires that the patient is at steady state on the present dose of the drug, except when suspected toxicity is being investigated, when waiting to attain steady state is clearly contraindicated. Steady state concentrations can be expected to be achieved when five half-lives have elapsed, unless loading doses are employed when they are attained more rapidly.

Urgent specimens can be accepted only with prior verbal or written notification / agreement with TDM Unit members of staff.

It is the clinician's duty to ensure that laboratory staff are informed of known and suspect high-risk specimens.

2.6 Patient Consent

All samples referred to the TDM Laboratory for analysis are considered to have been collected with the consent of the patient. It is the responsibility of the referring laboratory or institution to ensure that consent has been obtained from the patient for the tests requested.

By presenting themselves to TDM Unit phlebotomists and agreeing to be sampled, patients are understood to have given implicit consent for their sampling and testing.

2.6 Sample Transportation to the TDM Laboratory

Samples transported between the referral laboratory and TDM Unit must be done in accordance with Transport regulations and samples can be transported at ambient temperatures. Specimen transport boxes or envelopes which bear Biological Substance Category B warning label and conform UN 3373 standard should be used by referring laboratory to send samples to Epilepsy Society's TDM Unit.

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The location of the TDM Unit is following:

TDM Unit
Epilepsy Society
Chesham Lane
Chalfont St Peter
Buckinghamshire, SL9 0RJ

2.7 Time Limits for Requesting Additional Drug Analysis

Subject to adequate sample quantity, additional drug analysis can be requested up to one month after original date of sample collection.

To request additional add-on tests a request should be made by email to TDM_Unit@epilpsysociety.org.uk or by telephone to 01494 601423.

2.8 Reference Ranges

This is the range associated with optimal efficacy and minimal toxicity for the majority of patients. It is important to recognise that some patients will require concentrations (levels) outside of the quoted reference range for optimal clinical response.

Please note that reference ranges are based on trough (pre-dose) samples in adult human subjects. Additional interpretation of results will remain the responsibility of the clinician.

2.9 Reports

Reports are generated, upon completion and validation of drug assay, throughout the day. Most organisations are notified of Patient Report / result once authorised by a suitably trained laboratory team member, via an automated email sent from SLIMS (Smart Laboratory Information Management System). These organisations are able to access SLIMS, review results and download the Patient Report. However, a few organisations require reports to be printed and posted by first class post.

Results for UCLH patients will be accessible through EPIC (electronic health record system) system.

2.10 Clinical Advice and Interpretation

Clinical advice and interpretation is available from the Head of Unit during working hours.

2.11 Target Turnaround Times

Our target turnaround time for all anti-seizure medications is 3 working days after receiving the samples, excluding weekends or bank holidays.

2.12 Communication, Complaints and Compliments

The following routes can be used for communication, complaints and compliments about TDM service: 1) using direct phone numbers to individuals outlined in section 1 or 2) by emailing TDM_Unit@epilepsysociety.org.uk.

3. DRUG ASSAYS

We are the only Unit in the UK that provides a routine anti-seizure medications therapeutic drug monitoring service for the analysis of 24 anti-seizure medications (and 4 pharmacologically active metabolites) that are licensed for clinical use in the UK.

3.1 Specimen Type

5 mL of blood collected into a plain glass tube or lithium heparin tube to provide serum or plasma respectively is usually sufficient for most assays or assay groups.

For patients who have difficulty getting to a phlebotomist or local clinic to be bled, a saliva sample may be provided as an alternative. Please contact the TDM Unit (01494 601423) for further information.

All tests are available for blood and saliva. All anti-seizure medication assays are available as total plasma/serum concentrations or as free non-protein-bound concentrations.

3.2 Reason for Request

In order to aid interpretation of results and to identify additional test requirement, it is helpful if the reason for the assay request is indicated. This can be readily indicated by entering the information in the reasons for assay section on the Request Form. This information is also useful for audit purposes.

3.3 Ideal Sampling Time

The ideal sampling time is immediately before the next oral dose and this should be adhered to whenever possible. Drug concentrations (levels) measured at these times provide more meaningful information. Samples not taken at the "ideal time" can be interpreted if the exact time of drug dose and actual sample time are known. Please clearly indicate this information on ALL Request Forms. During suspected toxicity, sampling should be undertaken at time when adverse events are presenting.

3.4 Time to Steady-state

This is the earliest time a drug concentration (level) should be measured either following initiation of therapy or a change of dosage (unless therapeutic failure or toxicity is suspected). During suspected toxicity, sampling should be undertaken at time when adverse events are presenting.

PLEASE NOTE THAT ALL OF THE GUIDELINES THAT FOLLOW RELATE TO ADULTS

4. ANTI-SEIZURE MEDICATIONS

Anti-seizure Medications	Time to Steady-state	Reference Range (mg/L)
Brivaracetam	1 to 2 days	0.2 to 2.0
Carbamazepine	2 to 4 days[1]	4 to12
Carbamazepine-epoxide (metabolite)	7 days[1]	up to 2.3
Clobazam	7 to 10 days	0.03 to 0.3 (30 to 300µg/L)
Desmethyl clobazam (metabolite)	7 to 10 days	0.3 to 3.0 (300 to 3000µg/L)
Clonazepam	3 to 10 days	0.02 to 0.07 (20 to 70µg/L)
Eslicarbazepine acetate (reported as eslicarbazepine or 10-hydroxycarbazepine, metabolite)	3 to 4 days	3 to 35
Ethosuximide	8 to 12 days	40 to 100
Felbamate	3 to 5 days	30 to 60
Gabapentin	1 to 2 days	2 to 20
Lacosamide	2 to 3 days	10 to 20
Lamotrigine	3 to 8 days	3 to 15
Levetiracetam	1 to 2 days	12 to 46
Oxcarbazepine (reported as 10-hydroxycarbazepine, metabolite)	2 to 3 days	3 to 35
Perampanel	10 to 19 days	0.2 to 1.0 (200 to 1000µg/L)
Phenobarbital	15 to 30 days	10 to 40
Phenytoin	6 to 21 days	10 to 20
Pregabalin	1 to 2 days	2 to 8
Primidone	2 to 5 days	5 to10
Rufinamide	1to 2 days	30 to 40
Stiripentol	1 to 3 days	4 to 22
Tiagabine	1 to 2 days	0.02 to 0.2 20 to 200µg/L)
Topiramate	4 to7 days	5 to 20
Valproic Acid	2 to4 days	50 to100
Vigabatrin	1 to2 days	2 to 36
Zonisamide	9 to12 days	10 to 40

[1] If carbamazepine is being introduced for the first time, steady-state is only achieved after 20 days of treatment due to autoinduction.

- Carbamazepine, gabapentin, lacosamide, levetiracetam, pregabalin, rufinamide, tiagabine, valproic acid and vigabatrin exhibit significant diurnal variation, sampling time in relation to dose is critical.
- During therapy with primidone, monitoring of only the active metabolite phenobarbital is recommended in most circumstances.
- During therapy with oxcarbazepine, monitoring of only the active metabolite 10-hydroxycarbazepine is recommended.

Not UKAS accredited:

Anti-seizure Medications	Time to Steady-state	Reference Range (mg/L)
Cenobamate	14 days	5 to 35
Fenfluramine	4 days	*
Norfenfluramine	5 days	*

*Reference range for fenfluramine as anorectic 50 to 200 ng/mL, reference range for seizure control not yet established.

All tests are available for blood (plasma or serum) and saliva. All antiepileptic drug assays are available as total plasma/serum concentrations or as free non-protein-bound concentrations. Please note that reference ranges are based on trough (pre-dose) samples in adult human subjects. Additional interpretation of results will remain the responsibility of the clinician.