

Therapeutic Drug Monitoring Unit

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1. USEFUL NAMES AND TELEPHONE NUMBERS

Chalfont Centre switchboard number:	01494 601300
Head of Unit/Consultant Clinical Scientist: Dr K. Kipper	1355
Consultant Clinical Scientist (part-time): Dr E. P. Spencer	1424
Clinical Scientist: Mr A. W. James	1424
Clinical Scientist: Mr F. P. Quinlivan	1424
Biomedical Scientist: Ms Q. Munir	1424
Main Laboratory	1424
Patient results and enquiries	1423
Quality & Administration Manager: Mrs Kate Choinkowska	1490
Administrator: Ms Pam Kamal	1490
Phlebotomy Services: Mrs Julie Dick	1345
Phlebotomy Services: Ms Leah Edwin	1345
Medical Director: Professor Ley Sander	1343

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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 0900 and 1700. 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 15189:2012- 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 Epilepsy Society or UCLH Trust requests for assays are 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: <ul style="list-style-type: none"> <input type="checkbox"/> Patient's full name <input type="checkbox"/> Date of birth <input type="checkbox"/> Sample date 	<ul style="list-style-type: none"> <input type="checkbox"/> Unique hospital number <input type="checkbox"/> Time specimen taken
Request Form: <ul style="list-style-type: none"> <input type="checkbox"/> Patient's full name <input type="checkbox"/> Date of birth <input type="checkbox"/> Date and time sample collected <input type="checkbox"/> Patient's Consultant or GP <input type="checkbox"/> Destination for report 	<ul style="list-style-type: none"> <input type="checkbox"/> Unique hospital number <input type="checkbox"/> Clinical information <input type="checkbox"/> Patient's NHS Number <input type="checkbox"/> Patient's sex <input type="checkbox"/> Clinician's bleep number or contact telephone/mobile phone number

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 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 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.

The location of the TDM Unit is following:

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

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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.

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 printed, upon completion and validation of drug assay, throughout the day.

Results for UCLH patients will be accessible through EPIC (electronic health record system) system. Some outside organisations request that Patient Reports be emailed. This facility is available and proceeds automatically in an encrypted manner upon authorisation of the report by a HCPC registered Clinical or Biomedical Scientist. All other reports are printed and posted by first class post.

2.10 Clinical Advice and Interpretation

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

2.11 Target turnaround times

Our target turnaround time for all anti-seizure medications is 3 working days of 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.

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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 26 anti-seizure medications (and 5 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 Dr Karin Kipper, Head of Unit (01494 601355) 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

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4. ANTI-SEIZURE MEDICATIONS

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

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	5-35
Fenfluramine	4 days	*
Norfenfluramine	5 days	*

*Reference range for fenfluramine as anorectic 50-200 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.

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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.

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