LESLIE BRENT LABORATORY
ICHNT Renal & Transplant Centre
Imperial College Healthcare NHS Trust
London, W12 0HS

LESLIE BRENT LABORATORY USER GUIDE

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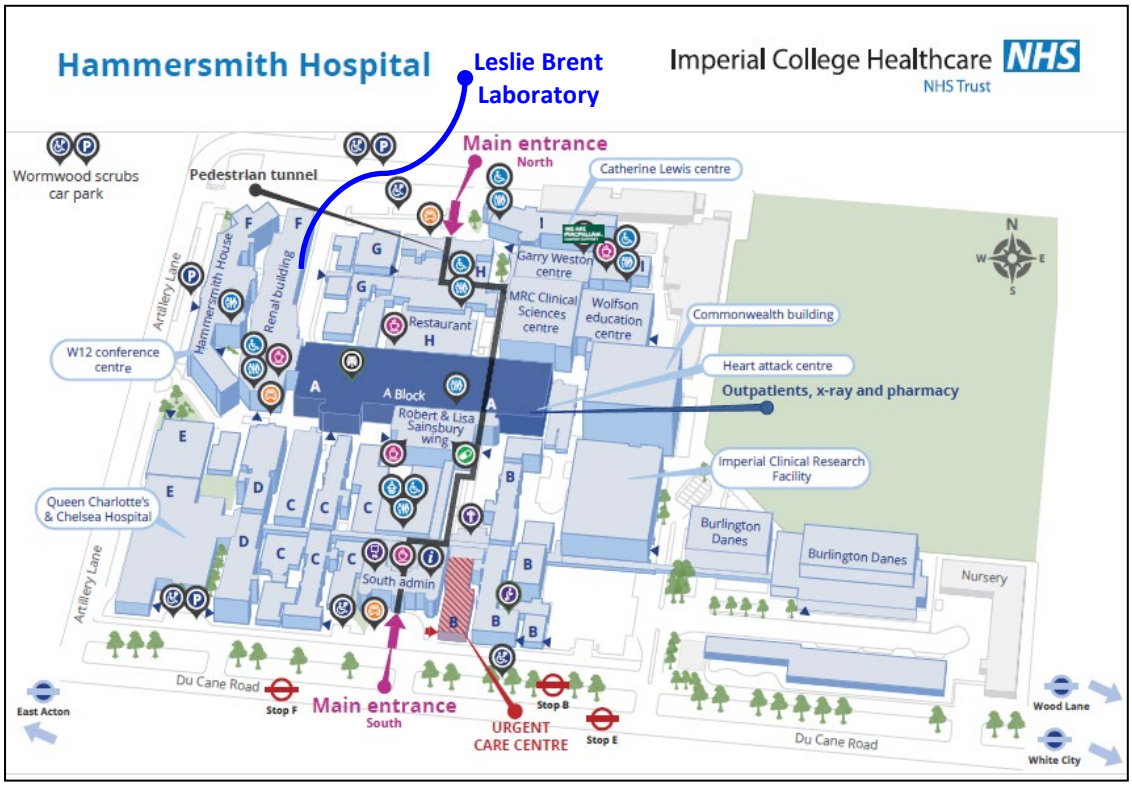
1. INTRODUCTION

The Leslie Brent Laboratory is part of the Department of Renal and Transplant Medicine within the Division of Medicine and Integrated Care (MIC) and part of Imperial College Healthcare NHS Trust (ICHNT). The laboratory provides a Therapeutic Drug Monitoring Service (TDM) for prescribed immunosuppressive/immunomodulatory drugs in adult and paediatric patients. Selective and sensitive detection is via liquid chromatography with tandem mass-spectrophotometric detection (LC-TMS) where service provision currently includes the following; Tacrolimus, Ciclosporin, Mycophenolic Acid (MPA), Sirolimus, five anti-fungal drugs; 5-flucytosine, Itraconazole, Hydroxy-itraconazole, Posaconazole, and Voriconazole and the immuno-modulatory compound Hydroxychloroquine (HCQ).

2. LOCATION

The Leslie Brent Laboratory is situated on the ground floor of the Renal building (F block) at Hammersmith Hospital, Du Cane Road, London.



3. CONTACT DETAILS FOR RESULTS, ADVICE & SUPPORT

Address: Leslie Brent Laboratory
Ground Floor
West London Renal & Transplant Centre
Imperial College Healthcare NHS Trust
Hammersmith Hospital
Du Cane Round
W12 0HS

Dr. Tom Cairns Laboratory Director 07958468693 (Mobile)

Dr. Janet Lee	Laboratory Manager	020 331 36639
Results/Enquiries		020 331 36637/36642
E-mail		imperial.leslie.brentlab@nhs.net

4. COMPLAINTS OR CONCERNS

Should the need arise to lodge a complaint related to the Leslie Brent Laboratory, please contact the Laboratory Manager via telephone on 020 331 36639 or via email imperial.leslie.brentlab@nhs.net. Alternatively contact PALS via telephone 020 331 30088, Monday to Friday, 09:30-17.00 or via email imperial.pals@nhs.net. All concerns / complaints will be promptly responded to in line with Trust and Leslie Brent Laboratory policies and procedures.

5. CONFIDENTIALITY AND THE PROTECTION OF PERSONAL INFORMATION

Imperial College Healthcare NHS Trust is committed to delivering a first class confidential service ensuring that all patient information is processed fairly, lawfully and transparently. Confidential information about patients can only be used for healthcare and relevant business purposes. All Trust staff follow the Trust Information Security Policy. The Trust has also issued Confidentiality Guidance for staff which is available via the Trust Intranet. In addition to this, all Health and Care Professions Council (HCPC) registered staff follow the HCPC confidentiality guidance for registrants.

6. LABORATORY OPENING TIMES (OUT OF HOURS, BANK HOLIDAYS)

Normal opening hours are 09:00 to 17:00, Monday to Friday.
Only one day during each Bank holiday weekend is covered.
There is **no** routine provision for an on-call/out-of-hours service.

This information is available on the Leslie Brent Laboratory (intranet) or from Internet-Leslie Brent Laboratory

7. TESTS PROVIDED

Hospitals within the Trusts' network should request tests via Cerner using the specific drug name and bring them to the Leslie Brent Laboratory, Hammersmith Hospital. Alternatively, samples can be taken to any of the NWL Pathology Specimen Receptions areas across the sites, who will forward them.

For requests from departments outside of the Trust's network, samples can be sent directly to the address given in Section 3 and in accordance with test and transport requirements given in Sections 10 & 11. For turnaround times refer to Section 13.

The tests below are performed on the following days:

- Ciclosporin whole blood levels (Monday to Friday)
- Tacrolimus whole blood levels (Monday to Friday)
- Mycophenolic Acid (MPA) plasma levels (2 times per week)
- Sirolimus whole blood levels (1 – 2 times per week depending on demand)

- Anti-fungal drug plasma levels (Voriconazole, Itraconazole/Hydroxyitraconazole, Posaconazole and 5-Flucytosine) – (Tuesday and Friday's only)*****
- Hydroxychloroquine – (Every 2 weeks)

*****To ensure results are reported on Tuesday and Friday, samples should ideally arrive by 4:30pm the previous day or by 10am on the day. Where there is a request for either Hydroxyitraconazole (the main metabolite with pharmacological activity) or Itraconazole, both results will be reported – Refer to Section 13 for Trust therapeutic ranges.

Please indicate if the patient is on Atazanavir if taking Itraconazole, is on Ritonavir if taking Hydroxyitraconazole, and is on Metformin, Vigabatrin or Emtricitabin if taking 5-Flucytosine.

8. SAMPLE REQUIRED (PER TEST)

For the immunosuppressant drugs a single blood sample is taken just before the subsequent dose (trough level) and at a constant interval; **12h** for Tacrolimus (Prograf/Adoport), Ciclosporin and Mycophenolate; **24h** for Tacrolimus (Advagraf) and Sirolimus from the time of the previous dose. Section 13 lists the sample tube type for each test whilst below gives the minimum volume of blood required to perform each test.

- Ciclosporin / Tacrolimus / Sirolimus: EDTA-anti-coagulated whole blood (0.5ml to 2ml)
- Mycophenolic Acid (MPA): EDTA-anti-coagulated whole blood bottle "Purple Top" (0.5ml to 2ml, preferred 1ml).
- For anti-fungal drug monitoring a pre-dose trough level should always be taken within 1 hour prior to the time that the dose is due. 5-Flucytosine also requires a 1 hour POST dose level
- Voriconazole / Posaconazole / Itraconazole / Hydoxyitraconazole / 5-Flucytosine: red plain top blood bottle (plain clotted, not serum separator tubes [SST]) or EDTA-anti-coagulated whole blood bottle "Purple Top" (0.5 to 2ml)
- **Other types of blood collection tubes are not suitable and cannot be used**

  Refer to Trust guideline 'Anti-fungal Guidelines For Adults, Paediatrics and Neonates' from ICHNT intranet
- Hydroxychloroquine (HCQ): EDTA-anti-coagulated whole blood (0.5ml - 2ml)

(**N.B**. Fluoride-oxalate anti-coagulated samples CANNOT be used for any assay)

9. REQUESTS FOR TDM TESTING

Each request accepted by the laboratory for examination of the tests given above is considered an agreement to provide services as described in the introduction.
The Leslie Brent Laboratory is responsible for the provision of the requested investigation and will only perform analysis on samples that are in keeping with acceptance and rejection criteria given below. Instructions for sample collection are available on the Leslie Brent Laboratory website:

- OPD Instructions Sample Collection for Therapeutic Drug Monitoring (**IS018**)
- Inpatient Instructions Sample Collection for Therapeutic Drug Monitoring (**IS019**)

The laboratory performs examinations that have been assessed and UKAS accredited to Standard ISO15189:2022, the current Schedule of Accreditation can be found on the UKAS website (www.ukas.com) under customer number 9280, Imperial College Healthcare NHS Trust, Leslie Brent Laboratory.

The laboratory may also perform examinations that are non UKAS accredited and will be reported with a statement to the effect of "This is a newly implemented test and is awaiting UKAS assessment" for new methods. Reporting of results on such tests will have followed a period of R&D and agreement, and with the intention of adding the examination as an "Extension to Scope" with UKAS. There may be other situations where the platform may change, an additional matrix has been added, or the test is not accredited. Under these circumstances the following statements will be attached to the report:

"Due to a recent change in analytical platform, this test is not currently UKAS accredited".
"The laboratory is not UKAS accredited for this test on this sample type".
"The laboratory is not UKAS accredited for this test"

All local requests (ICHNT) should be made via Cerner. In the event of Cerner Downtime, requests can be made using the Leslie Brent Laboratory Form, which is available on the Trust Intranet.

For requests for tests external to the Trusts' network of hospitals, a local request form is sufficient but should state contact details of requesting department including email address.

Requests for Tacrolimus Profiles should be discussed with the laboratory before collecting and sending samples. Samples should be brought to the laboratory and have the appropriate request form. Samples should be taken as per the instructions on Request Form & Instructions (IS011) form, which is available on the Leslie Brent Laboratory webpage on the Trust Intranet.

It is imperative that the correct patient is selected on the local electronic ordering system to ensure that the correct result is being issued on the correct patient. If an error is made, contact the Leslie Brent Laboratory on 0203 313 6637 as soon as possible.

It is the responsibility of the requesting doctor completing the request form or sample label to ensure that sufficient information is provided and that all information is correct, even if these duties are delegated. The onus is not on the laboratory to make assumptions about the origins or nature of specimens or the accuracy of any given details. If the information given is inadequate to process the request then delays may occur or the request may be rejected/returned to the sender. Every effort will be made to ensure that specimens are processed correctly and that vital specimens are not discarded, but if the integrity of the information provided or the source of a specimen cannot be fully established the sample will have to be discarded.

Space is available on the request forms for the following information which the referrers should provide:

- **The patient's Forename, Surname and Date of Birth**
- **The patient's Hospital number or NHS number (if available) and their gender**
- **The test required**
- **The most recent drug dose (in mg) and the time and date of that dose**
- **The time and date of the blood sample taken for testing**

- **The legible Name of the requesting healthcare professional and a contact number**
- **The clear address to which the report of the result should be sent**
- **Any other pertinent information e.g., co-medication; liver dysfunction; infection risk**

Samples must have

- **The patient's Forename and Surname**
- **Date of Birth**
- **The patient's Hospital Number or NHS number**
- **And very importantly the sample date**

Leslie Brent Laboratory Sample Acceptance and Rejection Criteria

Acceptance/Rejection Criteria	***Action***
Unlabelled Sample/Mismatched Sample	Sample will be discarded
Wrong sample container: e.g., clotted sample for Ciclosporin, Tacrolimus or Sirolimus Fluoride/Oxalate for MPA, Gel containers for Anti-Fungal Drugs Not enough sample	Clinic/Ward/Clinic/Requestor will be informed. Can another sample be taken? Is there another suitable sample available? If yes arrange for collection. **IF NOT:** The test will be cancelled and a comment added such as "No appropriate sample received: please send [*insert type of sample required*]"
Unlabelled request form (sample is labelled appropriately)	If sufficient information is provided on sample this will transcribed onto the form.
Mismatched information on sample and/or form, e.g., misspelling of name, differences in DoB or Hospital number	The sender will be contacted to confirm details are correct if Cerner or other databases are not helpful
Leaking sample: Minor leak Major leak	 If minor leak from ***non*** high-risk sample, an attempt to clean it will be made If sample is known to be ***high-risk*** the sample will be discarded Clinician/Ward/Clinic or sender if sent by Courier will be informed If significant leak which contaminates other samples and obscures patient information – the samples will be discarded Clinician/Ward/Clinic or sender if sent by Courier will be informed
Mismatched information on sample and form, e.g., miss-spelling of name, differences in DoB or Hospital number	• The sender will be contacted the sender to confirm details if Cerner or other databases are not helpful
No test indicated on request form or sample	• Clinician/Ward/Clinic will be contacted for advice

Requests for additional tests must be made directly to the laboratory by the requesting clinician or a senior Clinical Nurse Specialist, within 24 hours of receipt of the original sample and request form.

10. STABILITY

If samples are not transported immediately, they should be stored refrigerated and as stated in Table 1. Primary samples for MPA and Aanti-Fungals should not be frozen. Ideally,

plasma for MPA and Anti-Fungals should be separated from blood before dispatch to the laboratory if the sample will not reach us within 24hrs.

Test	Storage and Acceptance Conditions
Tacrolimus	- Samples stored at room temperature for 4 days - Samples stored in the fridge for 2 weeks - Samples stored frozen
Ciclosporin (CSA)	- Samples stored at room temperature for 4 days - Samples stored in the fridge for 2 weeks - Samples stored frozen
Hydroxychloroquine	- Samples stored in the fridge for 1month - Samples stored frozen
Mycophenolic Acid (MPA)	- Whole blood sample stored in the fridge and not haemolysed (~1 week) - Plasma or serum stored in the fridge for 1 week - Plasma or serum stored frozen
Sirolimus	- Samples stored in the fridge overnight - Samples stored frozen for 2 weeks
Anti-Fungals	- Whole blood or clotted samples stored between 2-8ºC and not haemolysed (~1 week) - Plasma or serum stored in the fridge up to 7 days - Plasma or serum stored frozen

Table 1: Sample Storage Conditions

11. TRANSPORT OF SAMPLES

Samples from departments external to the Trust should be packaged in accordance with UN Packaging Instructions PI650. This requires that the primary sample container must be leak proof and be wrapped in sufficient absorbent material to absorb any spillage. The primary container and absorbent material must be placed in a single bag with the request form in the pouch. The outer rigid box should have a printed label stating that the content is Category B Biological Substance and is assigned to UN3373. Please contact the Leslie Brent Laboratory, on 0203 313 6637 for further advice and information.

12. REPORTS, CLINICAL SUPPORT, ADVICE & GUIDANCE

Depending on the frequency of analysis – Refer to Section 7, results are usually reported within 24 hours of receipt, this is particularly the case for Ciclosporin and Tacrolimus. Results will be reported as follows:

- Electronically via Cerner or ICE
- Proton (Renal Medicine only)
- By email (preferably sent to NHS.NET but can be sent encrypted to other emails)
- By phone (020 331 36637) but are divulged only to an official healthcare representative of the patient. Please have your / patient identifiers ready
- As printed results - (issued by first class mail to referrers by request only)

It is preferable to send results for requests received from outside of the Trust's network of hospitals by email. Reports will be sent as a PDF copy of the result and sent either to NHS.NET email addresses or sent encrypted to other email addresses. There is no facility to send a Faxed report.

The values for immunosuppressant drugs are *guidelines only* based on LC-TMS methodology and on target levels in use within the Imperial College Renal & Transplant Centre. Laboratory staff are unable to offer clinical advice in relation to drug dose changes.

There are no therapeutic ranges established by this laboratory for these drugs that are applicable to non-renal patients. For clinical interpretation of results contact the patients' senior specialist as this is not provided by the laboratory.

For antifungal drugs, refer to the Trust's '**Anti-fungal Guidelines For Adults, Paediatrics and Neonates'** guidelines found on the Trust Intranet.

13. DETAILS OF TESTS PROVIDED

Drug	Sample Type	Container	Turnaround Time (From Receipt)*	Therapeutic Ranges¥ (NB: Concentration refer to trough samples)	Additional Requirements
Ciclosporin (CSA)	Whole blood	3.5mL EDTA (purple top)	24hrs	100 - 200µg/L	Trough level sample collected 12hr post dose
Tacrolimus	Whole blood	3.5mL EDTA (purple top)	24hrs	5 - 12µg/L	Trough levels for slow release formulations (e.g. Advagraf) is 24hr post dose, otherwise 12hr post dose (twice daily formulation)
Sirolimus	Whole blood	3.5mL EDTA (purple top)	4 days	4 - 20µg/L	Trough level sample collected 24hr post dose
Mycophenolic Acid (MPA)	Plasma	3.5mL EDTA (purple top)	4days	1.2 – 2.4mg/L	Trough level sample collected 12hr post dose
5-Flucytosine	Serum	6mL plain (Red top)	4days	N/A For 5-Flucytosine therapeutic ranges, please discuss this with a specialist infection team	Samples collected in Gold or Rust top SST tubes will **not** be accepted.
Itraconazole	Serum	6mL plain (Red top)	4days	For range see result for Hydroxy-itraconazole	Samples collected in Gold or Rust top SST tubes will **not** be accepted.
Hydroxy-itraconazole	Serum	6mL plain (Red top)	4days	Prophylaxis: 0.5 -4.0mg/L^ Therapy: 1.0 – 4.0mg/L^	Samples collected in Gold or Rust top SST tubes will **not** be accepted.
Posaconazole	Serum	6mL plain (Red top)	4days	Prophylaxis: 0.7-1.5mg/L^ Therapy: 1.0- 3.75-mg/L^	Samples collected in Gold or Rust top SST tubes will **not** be accepted.
Voriconazole	Serum	6mL plain (Red top)	4days	Prophylaxis Trough > or = to 1mg/L ^ Therapy Trough: >1.0 – 2.0mg/L^ Higher target trough level (i.e. > or = 2 mg/L) should be used in complex diseases (e.g. CNS infection, extensive or bulky infection, multifocal or disseminating infection). Dosage adjustments	Samples collected in Gold or Rust top SST tubes will **not** be accepted.

				to keep trough levels < or = 5mg/L help minimise drug related toxicity^	
Hydroxychloroquine (HCQ)	Whole blood	3.5mL EDTA (purple top)	14 days	Therapeutic range: >0.60mg/L# There is no defined upper limit of a therapeutic range. The lower limit has been described (0.60mg/L#) below which was considered to be therapeutically inadequate.	Trough level sample collected preferably 12hr post dose

¥ Numerous variables determine the target drug levels e.g. graft or disease type, time after transplant, co-medication, drug formulation, and clinical and graft function which should be taken into consideration when interpreting results.

^ Reference: ICHNT guidelines for anti-fungal drugs “Anti-fungal Guidelines For Adults, Paediatrics and Neonates”. If levels are outside of this range please see Anti-Fungal Guideline on the intranet or discuss with an infection specialist

Cunha C, et al. Hydroxychloroquine blood concentration in lupus nephritis: a determinant of disease outcome? *Nephrol Dial Transplant (2017) 1–7*

*This is the time of receipt of the sample within the Leslie Brent Laboratory. Working days only.