

Guidelines for Users of Clinical Neuropathology Services

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1. Introduction

1.1 Purpose

This user manual is intended to serve as a user guide to the services available from the Clinical Neuropathology Laboratory based King's College Hospital. It is aimed for use by all staff groups involved with requesting neuropathological investigations.

1.2 ABOUT US

The Synnovis Analytics Clinical Neuropathology laboratory is a UKAS (United Kingdom Accreditation Service) accredited medical laboratory (No. 8620); accredited to ISO15189:2012 for the scope described in the UKAS Schedule of Accreditation which can be found on the UKAS web-site: <https://www.ukas.com/find-an-organisation>.

At the time of writing, certain tests and services provided by the laboratory are not covered by the UKAS scope of accreditation. Users of the Clinical Neuropathology service should refer to the UKAS schedule of accreditation on the UKAS website, for a list of currently accredited tests.

1.2.1 Neuropathology Laboratory

The Department of Clinical Neuropathology has wide-ranging connections with hospitals and scientific institutions in the UK and abroad and is one of the busiest departments of its type in the country. It has a close association with King's College London Medical School and its function as a diagnostic referral centre puts the laboratory in a unique position to provide a high-quality, wide-ranging diagnostic service and to carry out research into disease of the nervous system. It also provide clinical diagnosis for the London Brain Bank for Neurodegenerative Diseases.

The specialist diagnostic and scientific teams aim to deliver a high-quality service with cutting edge diagnostic techniques through close links with the Neuromolecular Diagnostics laboratory (multi-omics). Multidisciplinary team meetings (MDM) are held regularly, enabling close integration of clinical teams and specialist pathologists.

Areas of expertise include:

- Brain and pituitary biopsies, including intraoperative diagnosis
- Muscle and nerve biopsies
- Intra-epidermal Nerve Fibre Density analysis (IENFD)
- Epilepsy
- Neurodegenerative disease
- Autopsy and forensic neuropathology

2. CONTACT US

The Department of Clinical Neuropathology is based on the 1st floor of the Academic Neuroscience Building, Denmark Hill site and is under the control of Synnovis LLP. The 'Synnovis' brand is a relationship between the NHS, SYNLAB and pathology services in South East London.

The department is staffed between the hours of 8.30am and 5.00pm Monday to Friday. The Clinical Neuropathology satellite laboratory on the first floor of the Ruskin Wing is used to handle unfixed specimens and is staffed on an intermittent basis. The laboratory can only be accessed via security swipe cards but during core hours visitors to the department can gain access by pressing the buzzer and reporting directly to laboratory staff.

2.1 Contact address

DEPARTMENT OF CLINICAL NEUROPATHOLOGY

1st Floor, Academic Neurosciences Building,
King's College Hospital Foundation NHS Trust,
Denmark Hill,
London,
SE5 9RS

Information for Couriers – Map of KCH Denmark Hill Campus

Department of Clinical Neuropathology

1st Floor, Academic Neurosciences Building,
King's College Hospital Foundation NHS Trust,
Denmark Hill,
London,
SE5 9RS

The Department is situated within the Academic Neurosciences Centre, which is the two storey yellow brick building on stilts with a car park beneath on the west side of Denmark Hill. It is the closest point of the KCH campus to Ruskin Park and Denmark Hill train station.

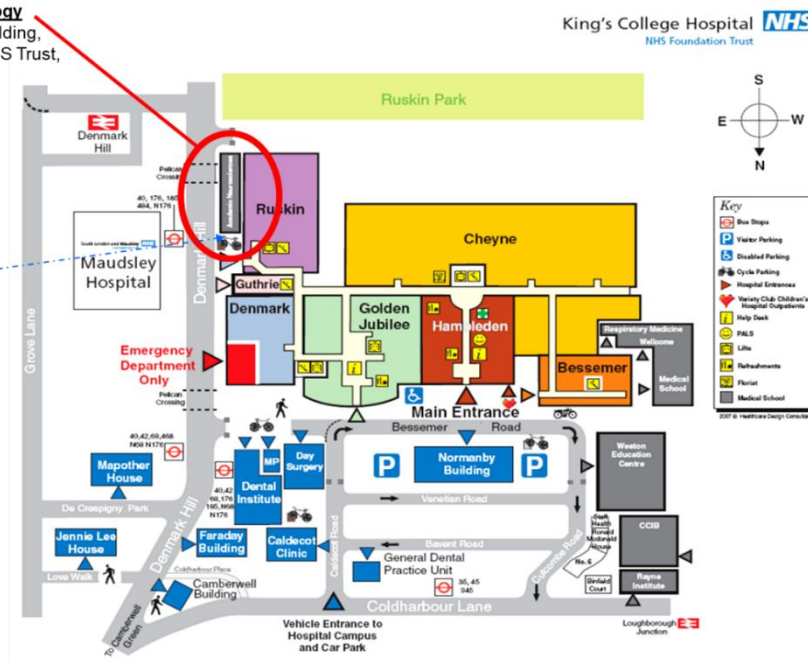
Access to the building is via a buzzer system which is outside the entrance to Ruskin Wing.

Press the button labelled Clinical Neuropathology and wait to be buzzed in.

Go up one flight of stairs, turn right and follow the signs for Clinical Neuropathology.

Use the telephone at the entrance to the department to call the laboratory (x31957) and ask to be let in.

In case of difficulties call 0203 299 1957 for assistance.



2.2 Telephone enquiries and key staff contact details

Hospital switchboard: 020 3299 9000

Name	Designation	Telephone number	Email address
Mary Davitt	Office Manager	020 3299 1955	mary.davitt@nhs.net
Michaela Small	Secretary	020 3299 1950	michaela.small1@nhs.net
Main Laboratory	Main Laboratory	020 3299 1957	kch-tr.neuropathtissuetracking@nhs.net
Prof Safa Al-Sarraj	Lab Director and Consultant Neuropathologist	020 3299 1958	safa.al-sarraj@nhs.net
Dr Andrew King	Consultant Neuropathologist	020 3299 1953	andrewking@nhs.net
Dr Istvan Bodi	Consultant Neuropathologist	020 3299 1954	istvan.bodi@nhs.net
Dr Zita Reisz	Consultant Neuropathologist	020 3299 1952	zita.reisz@nhs.net
Getnet Demissie	Operations Service Manager Tissue Sciences	020 3299 9000 Ext 33043	getnet.demissie@nhs.net
Janet Okafor	Operations Manager	020 3299 1951	Janet.Okafor@nhs.net Janet.okafor@synnovis.co.uk
Karen Boniface	Quality Manager	07999 181 198	karen.boniface@synnovis.co.uk
Nelly Ritcheva	Electron Microscopy and Neuromuscular Lead	020 3299 4556	nedialka.ritcheva@nhs.net

2.3 Hours of opening

The department is open from 08:30 – 17:00, Monday to Friday (except bank holidays).

2.4 Our of hours service

The Consultant Neuropathologists operate 24-hour cover 365 days a year on a rotational basis. The on-duty Neuropathologist carries an air-call pager out of hours and can be contacted by asking the KCH switchboard (020 3299 9000) to bleep them.

2.5 Clinical advice and interpretation

Please contact the office manager or secretary regarding reports. They will put you through to the Consultant Pathologist reporting the case if required.

2.6 Section Leads

2.6.1 Operations Service Manager Tissue Sciences

Getnet Demissie (contact details shown in section 2.2)

2.6.2 Operations Managers

Janet Okafor (contact details shown in section 2.2)

2.6.3 Quality Manager

Karen Boniface (contact details shown in section 2.2)

2.6.4 Training Officers

Currently covered by the Operations Manager (contact details shown in section 2.2)

2.6.5 Health and Safety Officer

Jaquelina Almeida (jaquelina.dos@nhs.net, 020 3299 1957)

2.6.6 Neuromuscular and Electron Microscopy Service Lead

Nelly Ritcheva (contact details shown in section 2.2)

2.7 Complaints

Complaints may be made directly to the department, via PALS or via Synnovis Customer Support. Complaints are handled according to the Synnovis Complaints Policy and Procedure located at <http://www.synnovis.co.uk/customer-service>.

2.8 Protection of patient information

All patient information is handled under the terms of the Data Protection Act 2018. All personal information received by Synnovis is dealt with according to the Synnovis Privacy, Data Protection & Cookie Policy which is available at <http://www.synnovis.co.uk/privacy-policy>.

Synnovis also has a Right of Access (Subject Access) Policy available to all staff which defines the process that the business must follow when it receives a right of access request.

3. Sample Information

3.1 Requests and labelling for surgical cases

- All Neuropathology samples are to be sent with a request generated in Epic, and the specimen pot must have the corresponding Epic label attached (for external referral cases see section 3.1.1 below)
- For specimens to be accepted by laboratory staff all details on the specimen pot must match those in Epic, including the nature of specimen.
- The sender will be contacted when samples are received without an appropriate request. Testing may be delayed until the request is corrected on **Epic. This will be logged as an incident where testing is delayed and patient** care has been compromised on to the Trust Adverse Incident reporting system (InPhase).

3.1.1 Clinical Neuropathology Request Form (for Epic Downtime and External Referrers)

- This should only be used for urgent cases when the Epic system is not available or for referrals to neuropathology from external sources. Failure to complete details on a request form or specimen pot will mean a delay in issue of a result, and result in laboratory staff contacting the sender and requesting them to attend at the laboratory and fill in/ correct the missing details (or resend if from an external source).
- The following details must be given on the request form:
 - **Patient's full name** (forename and family name)
 - **Date of Birth**
 - **Hospital number or Coroner's reference number**
 - **Sender address codes:** Consultant, hospital, destination, date and time taken
 - **Email address:** For the report to be sent to (external cases)
 - **Funding details:** indicate if NHS, private, or contract funding
 - **Clinical details:** sufficient relevant clinical details including treatment and length of episode. Note any specific neuropathology tests required.
 - **Specimen details:** Specimen type. If more than one specimen from same patient, indicate the pot number and the specific specimen site.
 - **Risk status** if applicable.

3.1.2 Specimen labels

Fill in the specimen pot details using **a ballpoint pen or permanent marker**, not a fibre-tip pen where the ink will run should a spill occur.

All details should be completed, and where more than one specimen is taken, pot numbers and specimen information should match the details on the request form. At least two forms of personal ID must match, full name, and date of birth (and/or hospital number) together with the nature of specimen. ***A discrepancy will result in a delay in processing and could impact on patient management.***

3.2 Fixatives and specimen containers

- The type of fixative and container required for a neuropathology specimens differs depending on the type of tissue and the investigations required. This is described under the individual tissue guidelines below.

- **Do not** place large specimens into small pots. This causes several problems including poor preservation, distortion and damage to the tissue when trying to remove it from the pot. If the specimen does not go into the pot under gravitational force alone, the pot is too small.
- When adding fixative (10% neutral buffered formalin) fill pots to the brim ensuring that all tissue is immersed and there are no pieces remaining uncovered on the inside of the lid or high up in the pot. Invert the pot gently to check. **Fixative must not be added to cerebrospinal fluids (CSFs), muscle and nerve biopsies. Instructions for these samples are described separately below.**

Specimen Type	Fixative	Container
Brain and pituitary biopsies (not intraoperative samples)	10% neutral buffered formalin	Standard yellow top pre-filled formalin container 60ml.
Cerebral Spinal Fluids (CSFs)	None	Sterile universal container 30ml
Intraoperative samples	None	Sterile universal container 30ml
Resections including epilepsy samples	10% neutral buffered formalin	Standard yellow top pre-filled formalin container 60ml. Larger pots available on request.
Intra-epidermal Nerve Fibre Density analysis (IENFD)	PLP Fixative which must be requested from the department at least 24 hours before it is required. See section 3.3 for more details.	Universal container 30ml provided as part of a PLP fixative kit requested from the laboratory as described.
Muscle and nerve biopsies	No fixative	See section 3.8 for more details.
Neurodegenerative disease for brain bank	Please call the Brain Bank on 0207 848 0169 for specific requirements	Please call the Brain Bank on 0207 848 0169 for specific requirements
Autopsy and forensic neuropathology	10% neutral buffered formalin. See section 3.9 for more details.	Specimen bucket provided at mortuary.

- Please note, **all** pots **must** be sent in a self-sealing clear plastic bag containing a separate compartment for any required paperwork
- Specimens should be transported through the hospital in a red specimen transport box or packaged for couriers.

3.2.1 Packaging for samples sent by couriers

- a) For fixed tissue samples, packaging must consist of three components:
 1. A primary receptacle (absorbent material)
 2. A leak proof secondary packaging
 3. An outer packaging minimum dimensions of 100mm x 100mm and marked with words "Exempt Human Specimens"

- b) Transport of formalin-fixed human tissue from known or suspected cases of CJD (or other prion diseases) is covered by United Nations number UN3373, biological substance, category B. Packaging must conform to packing instruction P650 and requires:
 1. A primary receptacle (Absorbent Material)
 2. A leak proof secondary packaging
 3. An outer packaging min dimensions of 100mm x 100mm
 4. The complete package shall be capable of passing the 1200mm drop test

The packaging must be labelled UN3373 contained within a diamond shape with minimum dimensions of 50mm by 50mm; the width of the line shall be at least 2mm and the letters at least 6mm high. The Proper shipping name " Biological Substances, Category B" must be marked adjacent to the diamond shaped mark in letters at least 6 mm high.



Biological Substances, Category B

Packages marked with the UN3373 label must always be sent by courier.

The Clinical Neuropathology satellite laboratory on the first floor of the Ruskin Wing is staffed on an intermittent basis; therefore, **do not** try to deliver any specimens without prior arrangement.

- a) Specimens for Neuropathology can be left at Neurosurgery theatre reception (ground-floor Cheyne Wing). The specimen ledger **must** be filled in. Specimens can be left out of hours. If the theatres are locked the Theatre Sister can be bleeped on 297. A member of the Clinical Neuropathology laboratory will collect, and sign for all available specimens from Neurosurgery theatre reception each day by 4pm. To arrange for urgent collection of specimens, which require immediate attention (e.g. unfixed specimens), bleep 722 or phone x31957 (see also below for CSFs, muscle and nerve biopsies).
- **All high-risk** specimens and accompanying forms (including known and suspected cases of Hepatitis, HIV, TB, and Prion disease) **must** be clearly labelled. This is Trust infection control policy and failure to do so will result in a Trust adverse incident being raised. The Neurosurgeon must contact the on-duty Neuropathologist first in cases of suspected Prion disease.
 - **Do not contaminate** the outside of the specimen pot.

3.2.2 Formalin

Specimens are normally received in **10% neutral buffered formalin** unless specifically stated in Error! Reference source not found..

Formalin is a clear fluid with a pungent toxic vapour. Samples collected in formalin should be kept at ambient room temperature (18-25°C) for optimal fixation of the tissue. Samples in formalin **should not** be stored in a fridge as this hinders fixation.

Formalin pots must be checked for leakage and expiry date and should be handled carefully using gloved hands. In the event of a formalin spillage, wipe it immediately with a De-Formalizer pad; wash the affected area with water and wash your hands.

3.2.3 Stock specimen containers

Neuropathology do not provide containers/ pots for samples. These must be provided by theatres or the referring department.

3.2.4 Hazards

Formalin is a hazardous substance and care is to be taken when in use. Beware of spills and inhaling vapour, as formaldehyde is a toxic agent that may cause mild to severe irritation of skin and mucous membranes. Wear gloves when opening a specimen pot, tighten the lid when closing, and place the labelled specimen pot into a plastic pathology specimen bag. Wash off any spills with copious amounts of water.

3.3 Special fixatives

3.3.1 Skin Biopsies (for Intra Epidermal Nerve Fibre Density- IENFD)

Skin biopsies must be sent in freshly prepared 2% PLP fixative which Container. The components are sent by neuropathology in 3 separate containers:

Container A: 15ml of 0.1M Lysine Monohydrochloride in 0.1M Phosphate Buffer.

Container B: 5ml of 8% Paraformaldehyde in 0.1M Phosphate Buffer



Container C: 0.043g of Sodium Metaperiodate



Instructions for preparing this fixative will be sent to the requesting department.

The solution must be used (i.e. the biopsy carefully submerged) within 2 hours of making up. Upon receipt and prior to use **the kit should be stored in a refrigerator at +4°C** and may be retained under these conditions until the expiry date stated on the packaging

3.4 Unfixed tissue

Some tissues samples are sent unfixed due to clinical requirement or for rapid diagnosis. These include smears, frozen sections, muscle enzyme histochemistry and nerve biopsies. All these sample types should be pre-booked with the laboratory (see section 3.5).

These specimens must be transported immediately to the laboratory in a closed labelled container and handed to a member of laboratory staff. Any biohazard should be indicated on request and specimen pot. Any indication of infection type would be advantageous.

3.5 Specimens that should be pre-booked (24 hours' notice)

Type of specimen	How to be received	Who needs to be contacted
Rapid Frozen Section/ smear	Unfixed (dry pot) URGENT	Inform the laboratory 24 hours prior 020 3299 1957
Muscle biopsies	Unfixed (dry pot). Please do not wrap samples in saline soaked gauze	Inform the laboratory 24 hours prior 020 3299 1957
Nerve biopsies	Unfixed (dry pot)	Inform the laboratory 24 hours prior 020 3299 1957

Table 1 - specimens requiring pre-booking

3.6 Frozen sections

All frozen sections/ smears **must** be pre-booked with the department **24 hours in advance** as a Consultant Pathologist and BMS have to be made available.

To make a booking contact the Main Laboratory on 020 3299 1957 and provide:

- Patient details,
- The estimated time of frozen section,
- Theatre details,
- Contact number

If there is a delay in performing the operation contact the main laboratory and indicate the new time of the frozen section.

Samples will be collected from Neuro Theatres by laboratory staff, so please bleep the department on 722 when ready.

3.7 Cerebral Spinal Fluids (CSFs)

CSF specimens for cytology deteriorate quickly and therefore, where possible, they should be dealt with by the laboratory soon after they are taken. If there is going to be a delay they should be stored in a fridge. Bleep 722 or phone x31957 when the specimen has been left at Neurosurgery Theatre reception (ground-floor, Ruskin Wing). **Specimens will not be collected after 5pm.** Specimens can be left in the fridge in Neurosurgery theatre reception out of hours but the Neuropathology laboratory must be contacted the following morning for collection.

2-5ml of CSF is a sufficient volume to allow laboratory tests to be performed.

Samples must be labelled with a printed Epic label.

If these are not available (e.g. for referred cases) fill in the specimen pot details using a **ballpoint pen** or **permanent marker**, not a fibre-tip pen where the ink will run should a spill occur.

All details should be filled, and where more than one specimen is taken, pot numbers and specimen information should match the details on the request card. At least two forms of personal ID must match, full name, and date of birth (and/or hospital number) together with the nature of specimen. ***A discrepancy will result in a delay in processing and could impact on patient management.***

PLEASE DO NOT leave CSF (or any other specimens for neuropathology) in ward boxes. These will be taken by porters to the central Specimen Reception and this may lead to significant delays in processing that can affect the assays requested due to sample deterioration.

3.8 Neuromuscular and Nerve Samples

3.8.1 BMS assistance:

BMS assistance for muscle biopsies for KCH patients is available at request. Please contact the Main Laboratory on 020 3299 1957 to arrange this with the Neuromuscular Lead.

3.8.2 Sample preparation:

Unless specifically indicated/contra-indicated by the patient's condition, the muscle of choice to biopsy is the quadriceps or biceps and the nerve of choice is the sural. The volume of tissue required is approximately 1 cubic cm for muscle and 1-3cm in length for nerve biopsies. **Diathermy or cautery must not be used** on the tissue submitted for analysis and the sample must not be clamped or tied to a stick. Samples must be sent in a clean, dry pot, with no gauze or fixative. Samples that deviate from these recommendations pose a risk that the samples may not be of adequate quality for diagnosis.

Due to the amount of work that needs to be carried out on receipt **specimens will not be accepted after 4.00pm.**

3.8.3 Specimen labels

Attach a printed Epic label onto the pot.

If these are not available (e.g. for referred cases) fill in the specimen pot details using a **ballpoint pen** or **permanent marker**, not a fibre-tip pen where the ink will run should a spill occur.

All details should be filled, and where more than one specimen is taken, pot numbers and specimen information should match the details on the request card. At least two forms of personal ID must match, full name, and date of birth (and/or hospital number) together with the nature of specimen. ***A discrepancy will result in a delay in processing and could impact on patient management.***

3.9 Autopsies

Hospital post-mortems will be performed when required. Please call the departmental office on 0203 299 1950/5 and a pathologist will be assigned to the case. Reports will comprise 3 parts; autopsy report, macroscopic description report and full microscopy report if applicable. The department expects that appropriate consent be obtained for retention of any tissues (including the brain) for research, teaching and training, in addition to the diagnosis. It is at the pathologist's discretion whether he/she proceeds with the autopsy taking into account the level of consent available.

The department can also perform neurologically related autopsy examinations (including the diagnosis of Creutzfeldt-Jakob disease) and forensic neuropathology, particularly for head injury. Our services are offered to HM Coroners and forensic pathologists in the South East and Midlands. Please contact the department on 0203 299 1950/5 if you wish to utilise these services and to obtain information on how to send these samples.

Appropriate consent must be obtained to meet all legal requirements before any investigations can be carried out (to reach a diagnosis) and for any retention of tissues (including the brain) for research, teaching and training.

3.10 Referral Cases

Note – this refers to cases with slides and blocks that are to be sent to the department for second opinion and/or further testing.

These cases should be addressed to:

DEPARTMENT OF CLINICAL NEUROPATHOLOGY

1st Floor, Academic Neurosciences Building,

King's College Hospital Foundation NHS Trust,

Denmark Hill,

London,

SE5 9RS

It is recommended that material is sent using special/recorded delivery or a courier service for tracking/audit purposes.

3.11 Neuropathology Turnaround Times

The times given below are for an “average” case. Cases that are difficult to diagnose will inevitably take longer as more tests will be required to be carried out.

Specimen type	Number of working days	Target of % within turn-round time
CSF cytology	2	95
Brain biopsies (surgical)	5 (2 if no special stains required)	95
Pituitary biopsies	4	95
Epilepsy Surgery	15	95
Muscle biopsies	10 (main report)	95
Nerve biopsies	5 (paraffin)	95
	20 (semi-thin resin)	90
Skin biopsies (IENFD test)	20 (Biopsies are batch processed in groups of 5-6)	90
Bone biopsies	Depends on how long it takes to decalcify specimen (usually within 5 once decalcified).	90
Other biopsies	5 (2 if no special stains required)	80
Electron microscopy	30 (from when request issued)	90
Autopsy general report	5	90
Autopsy macro report	30	90
Autopsy histology (Micro)	60	90

3.12 Retention of formalin fixed specimens

Formalin fixed surgical specimens are only retained in the laboratory for four weeks following verification of the report, unless otherwise requested by the clinician at the time of the original request for Neuropathology, or by the reporting Consultant Pathologist. In both cases, a reason must be specified for retention of the tissue beyond the four weeks post-authorisation of report.

3.13 Notes

Results are available on Epic for those with access. For referred cases to the department, an email address is required for the report to be sent to. The department is closed at the weekend and consequently results on specimens received on Friday will only be available by Monday or Tuesday at the earliest. Specimens from bone will require decalcification prior to processing and this will extend the report time. Time for decalcification to take place is specific to each individual sample.

3.14 Specimen deliveries to the laboratory

Fixed specimens are to be received in the Neuropathology laboratory no later than 4.30pm. Fresh samples must be received before 4pm.

3.15 Patient Preparation/Consent:

Consent must be gained before any procedure can commence. This is the responsibility of the patient's clinician/consultant to complete.

The patient will also need to consent to their medical/clinical history being disclosed for their onward care.