University College London Hospitals
NHS Foundation Trust

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Neuroimmunology & CSF Laboratory User Handbook

NICL-UH-001

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This document together with the Policy and Procedure documents to which it refers describes and defines the Quality Management System of the Neuroimmunology & CSF Laboratory (NICL). It has been compiled to meet the requirements of the Clinical Pathology Accreditation (UK) Ltd. (CPA), ISO 15189:2012 (E) and other appropriate national and international standards.

Review date	Reviewed by	Changes
July 2014	**VCW**	**Requirements for patient consent added And HIV cognitive panel added to test list**
March 2015	**MDC**	**Added lactate, NfH, edited asialotransferrin storage, anti-recoverin TaT**

Document cross-index

The following documents should also be consulted in the context contained herein:

NICL-QMD-001_NICL_Quality manual

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STAFF STRUCTURE

Neuroimmunology & CSF Laboratory	**Queen Square Division**
Clinical Lead	
Dr MPT Lunn MBBS PhD FRCP	Consultant Neurologist
Laboratory Manager	
Dr VC Worthington BSc PhD CSci	Consultant Clinical Scientist
Administration	
Mrs JE Johnson	Office Manager
Analytical	
Position Vacant	Principal Clinical Scientist
Dr AJ Church BSc PhD	Senior Biomedical Scientist
Dr MD Chapman BSc MSc PhD	Senior Biomedical Scientist
Ms D Grant BSc MA MSc	Biomedical Scientist
Ms NJ Lakdawala BSc MSc	Biomedical Scientist
Mr MKL Chou BSc	Biomedical Scientist
Ms R Monero BSc MSc	Medical Technical Officer
Mr THY Man BSc	Medical Laboratory Assistant

GENERAL INFORMATION

Background

The Neuroimmunology & CSF Laboratory (NICL) is a fully accredited (CPA UK) clinical consultant-led laboratory within the University College London Hospitals NHS Foundation Trust. It is located on the 9th Floor of the Institute of Neurology (IoN), next to the National Hospital for Neurology & Neurosurgery (NHNN) in Queen Square. The laboratory is part of the Queen Square Division within the Trust.

The laboratory provides an analytical service for the routine examination of cerebrospinal fluid (CSF) for the NHNN that includes triaging material between other laboratories within the Pathology Directorate. It forms a single of point of contact for all work carried out on CSF within NHNN.

In addition, the laboratory provides specialist analytical services and associated clinical advice for referring laboratories throughout the United Kingdom and abroad with on-going research programmes supplementing and continuously enhancing the service provision. The NICL is dedicated to the analysis of CSF to aid in the diagnosis of neurological diseases such as inflammatory demyelinating disorders and dementia and also provides a specialist autoantibody service for immunological disorders affecting the central and peripheral nervous system.

Access to services

The Laboratory is open between the hours 9.00 – 17.00 Monday to Friday.

NOTE: The Laboratory does NOT operate an out-of-hours service

Please arrange in advance if a sample is to arrive in the lab after 4.30pm (020 3448 3814)

Internal (NHNN) requests

After 5pm CSF samples from NHNN are processed in the Whitfield St Labs (UCLH). The requesting Doctor must: Bleep the on-call Microbiology BMS in advance and arrange sample transport to Whitfield St.

- At 6.00pm there is a specimen pick-up at the NHNN basement Specimen Reception (Ext: 83198)
- From 7.00pm to midnight there is an hourly specimen pick-up from the NHNN front desk
- After midnight specimen transport is by the Medical Courier (0207 307 9383), a budget code will be needed to organise this.

POSTAL ADDRESS & CONTACTS

Address

Neuroimmunology & CSF Laboratory
Institute of Neurology (NHNN) Box 76
Queen Square
London WC1N 3BG

Telephone

020 3448 3814 Main laboratory (General analytical and result enquiries)

020 3448 3812	Ms Jan Johnson	jan.johnson@uclh.nhs.uk	(Office Manager)
020 3448 4198	Dr Viki Worthington	viki.worthington@uclh.nhs.uk	(CDG, NAbs)
020 3448 3542	Dr Miles Chapman	miles.chapman@uclh.nhs.uk	(CSF biomarkers)
020 3448 3842	Dr Andrew Church	andrew.church@uclh.nhs.uk	(Autoantibodies)

Fax (safe haven) 020 3448 3797

SAMPLE HANDLING AND TRANSPORTATION

With the exception of samples for CSF biomarkers for neurodegeneration (see below), samples may be transported to the laboratory under normal postal regulations for the transport of pathological specimens (UN3373). We do not offer an out-of-hours service, therefore please post samples at the beginning of the week to avoid delays at weekends and bank holidays.

Special requirements for sample collection and handling

Serum: To help avoid haemolysis during transit all serum samples from external labs should be centrifuged and separated before sending.

Oligoclonal bands: A paired serum sample is essential for interpretation, preferably taken on same day (or within 14 days of the CSF). The CSF and serum should be sent together.

CSF biomarkers for neurodegeneration: CSF must be collected in polypropylene tubes (NOT polystyrene) then centrifuged, separated and the supernatant frozen in aliquots (one for each test required) preferably within one hour of the LP. The CSF must remain frozen and be transported to the NICL on dry ice. See Appendix 1. If in doubt please contact the laboratory viki.worthington@uclh.nhs.uk for advice before taking sample.

Xanthochromia: Supernatant from centrifuged CSF should be protected from light during storage and transport. *(Annals of Clinical Biochem 2008; 45: 238-244).* To aid result interpretation please note any deviations from protocol on the request form.

High risk samples: All high risk (e.g. HIV, Hep B, Hep C, CJD) specimens and the accompanying form must be clearly labelled and marked with biohazard stickers.

PATIENT SAMPLE AND REQUEST FORM IDENTIFICATION CRITERIA

It is the responsibility of the requester to ensure that samples are correctly labelled and that request forms are completed to the agreed standard.

The following outlines the information required by the Laboratory

Sample Tube

Essential

- Patient's full name or proper coded identifier
- Patient's date of birth
- Hospital (or NHS) number
- Date of sampling

Request Form

Essential

- Patient's full name or proper coded identifier
- Patient's date of birth
- Patient's hospital (or NHS) number
- Date of sampling
- Return address (hospital & department) for the report
- Tel. No. (& Bleep) for urgent results
- Tests required
- Sample type
- Relevant clinical details (to aid interpretation of results)

Desirable

- Patient's sex
- Name of the consulting physician

Patient's date of birth - Essential as the interpretation of some of tests is critically age-dependent.

Name of the consulting physician – Required for billing in some cases.

All details on both sample and request form must be completely legible. Specimens that are equivocally or illegibly labelled will not normally be accepted for analysis unless we receive written agreement from the Consulting Physician or Head of Department of the referral laboratory to accept full responsibility.

NICL TEST LIST

Routine CSF Analysis	**Sample type: CSF & Serum**	**TaT: STAT**	**NHS Price: £59**
Test for: Suspected CNS disease. Note: Includes cell count and differential, glucose, lactate, total protein, IgG, CSF albumin, serum albumin and QAlb. Specimen requirements: CSF in plain polypropylene tube and CSF in fluoride oxalate tube. Blood in plain tube and blood in fluoride oxalate tube. Minimum sample volume: 500μL in each tube. Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN Methodology: Microscopy, enzymology, nephelometry. EQA: UK NEQAS CSF Proteins and Biochemistry.			
Oligoclonal Bands (IgG)	**Sample type: CSF & Serum**	**TaT: 7 working days**	**NHS Price: £45**
Test for: Suspected CNS inflammation. Particularly demyelinating syndromes such as multiple sclerosis. Alternative name: OCB. Specimen requirements: Both CSF and a paired serum are essential for interpretation of results. CSF and blood samples will only be tested if they are taken within 14 days of each other. Minimum sample volume: 250μL in each tube. Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN Methodology: Isoelectric focusing. EQA: UK NEQAS CSF IgG Oligoclonal Bands			
Xanthochromia & Ferritin	**Sample type: CSF**	**TaT: STAT**	**NHS Price: £58**
Test for: Intracranial haemorrhage such as subarachnoid haemorrhage. Alternative name: Haem pigments. Specimen requirements: CSF in plain polypropylene tube. Minimum sample volume: 200μL. Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN. CSF must be protected from light to avoid bilirubin degradation *(Annals of Clinical Biochem 2008; 45: 238-244)* Methodology: Spectrophotometry and nephelometry for CSF ferritin. EQA: UK NEQAS CSF Haem Pigments			
Total Tau-Protein & Amyloid Beta$_{1-42}$	**Sample type: CSF**	**TaT: 20 working days**	**NHS Price: £132**
Test for: Investigation of dementias including Alzheimer's Disease. Alternative name: Tau. Aβ$_{1-42.}$ CSF biomarkers for neurodegeneration/ for the investigation of cognitive impairment. Note: Elevation of total-tau is seen in several neurodegenerative conditions (including Alzheimer's disease) but also in stroke and encephalitides. Very high total tau levels are seen in diseases with rapid ongoing neuronal degeneration/destruction. Reduction in CSF Aβ$_{1-42}$ is associated with deposition of β-amyloid in the brain, but has also been reported in neuroinflammatory conditions. Ratio of total tau:Aβ$_{1-42}$ aids interpretation of results. Specimen requirements: CSF in plain polypropylene tube. Minimum sample volume: 500μL in separate polypropylene tubes for each test. Special precautions/Transport: Unhaemolysed CSF MUST be collected in polypropylene tubes, centrifuged, separated and the supernatant frozen on the same day as the LP. Samples from outside NHNN must be transported frozen on dry ice. For long term storage CSF must be kept frozen at -80^{o}C. Important note: Aβ$_{1-42}$ may be artificially low if samples are not processed correctly. See Appendix 1. Methodology: ELISA EQA: Alzheimer's Association EQA Scheme (European)			
Phospho-Tau	**Sample type: CSF**	**TaT: 25 working days**	**NHS Price: £66**
Test for: Investigation of dementias including Alzheimer's Disease. Elevated phospho-tau levels indicate tangle pathology as seen in Alzheimer's disease and are not usually seen in other conditions. Alternative name: P-Tau			

Specimen requirements: CSF in plain polypropylene tube.
Minimum sample volume: 500μL in polypropylene tube.
Special precautions/Transport: Unhaemolysed CSF MUST be collected in polypropylene tubes, centrifuged, separated and the supernatant frozen on the same day as the LP. Samples from outside NHNN must be transported frozen on dry ice. For long term storage CSF must be kept frozen at -80°C. See Appendix 1.
Methodology: ELISA
EQA: Alzheimer's Association EQA Scheme (European)

14-3-3	**Sample type: CSF**	**TaT: 25 working days**	**NHS Price: £20**

Test for: Investigation of neurodegenerative disorders
Alternative name: CSF protein 14-3-3
Specimen requirements: CSF in plain polypropylene tube.
Minimum sample volume: 500μL.
Special precautions/Transport: Unhaemolysed CSF MUST be collected in polypropylene tubes, centrifuged, separated and the supernatant frozen on the same day as the LP. Samples from outside NHNN must be transported frozen on dry ice. For long term storage CSF must be kept frozen at -80°C.
Methodology: Western Immunoblotting
EQA: None available

S100b	**Sample type: CSF**	**TaT: 25 working days**	**NHS Price: £40**

Test for: Investigation of neurodegenerative and neuroinflammatory disorders
Alternative name: S100beta
Specimen requirements: CSF in plain polypropylene tube.
Minimum sample volume: 500μL.
Special precautions/Transport: Unhaemolysed CSF MUST be collected in polypropylene tubes, centrifuged, separated and the supernatant frozen on the same day as the LP. Samples from outside NHNN must be transported frozen on dry ice. For long term storage CSF must be kept frozen at -80°C.
Methodology: ELISA
EQA: None available

Lactate	**Sample type: CSF**	**TaT: STAT**	**NHS Price: £5**

Test for: Metabolic disturbance and possible infection.
Specimen requirements: CSF in fluoride oxalate tube. Blood in fluoride oxalate tube.
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: Enzymology
EQA: UK NEQAS CSF Proteins and Biochemistry.

Neurofilament heavy chain	**Sample type: CSF**	**TaT: 40 working days (under review)**	**NHS Price: £40**

Test for: Investigation of neurodegenerative and neuroinflammatory disorders
Alternative name: NfH, pNfH
Specimen requirements:
Minimum sample volume: 500μL
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN.
Methodology: ELISA
EQA: None

HIV CSF Cognitive Panel	**Sample type: CSF**	**TaT: 25 working days**	**NHS Price: £380**

Test for: Investigation of cognitive decline in cases of HIV.
Includes CSF biomarkers: Total tau. $A\beta_{1-42.}$ S100b. Ferritin. Neopterin.
Specimen requirements: CSF in plain polypropylene tube.
Minimum sample volume: 250-500μL in separate polypropylene tubes for each test.
Special precautions/Transport: Unhaemolysed CSF MUST be collected in polypropylene tubes, centrifuged, separated and the supernatant frozen on the same day as the LP. Samples from outside NHNN must be transported frozen on dry ice. For long term storage CSF must be kept frozen at -80°C. Important note: $A\beta_{1-42}$ may be artificially low if samples are not processed correctly. See Appendix 1.

Methodology: Various

Asialotransferrin (Beta2-transferrin)	**Sample type: Unknown fluid**	**TaT: 6 working days**	**NHS Price: £50**

Test for: CSF leak in unknown fluids, for example in CSF rhinorrhea or otorrhea.
Alternative name: Tau transferrin. Also referred to as 'Tau'. However, this is **NOT** the same biomarker as tau-protein; the dementia biomarker (see above). To avoid confusion please do **NOT** use the term 'tau protein' when requesting this test.
Specimen requirements: Unhaemolysed fluid in a SMALL plain tube.
Note: Please do not use large containers for small fluid volumes as evaporation will lead to processing difficulties.
Minimum sample volume: 100μL.
Special precautions/Transport: First class post. Please store frozen if not posting immediately.
Methodology: Electrophoresis or isoelectric focusing
EQA: UK NEQAS CSF Beta2 Transferrin

Anti-ACh Receptor Antibodies	**Sample type: Serum**	**TaT: 15 working days**	**NHS Price: £20**

Test for: Autoimmune Myasthenia Gravis
Alternative name: Acetylcholine receptor autoantibodies.
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: ELISA
EQA: UK NEQAS Acetyl Choline Receptor Antibodies.

Anti-Basal Ganglia Antibodies	**Sample type: Serum**	**TaT:10 working days**	**NHS Price: £68**

Test for: Sydenham's chorea
Alternative name: ABGA
Note: Includes antibodies to enolase, pyruvate kinase, aldolase.
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: Western Immunoblotting
EQA: None available

Anti-Neuronal Antibodies	**Sample type: Serum**	**TaT: 10 working days**	**NHS Price: £40**

Test for: Paraneoplastic neurological syndromes
Alternative name: PNS antibodies
Note: Includes antibodies to Hu, Yo, Ri, Ma1, Ma2, CV2, amphyphysin, Sox1, Tr, PCA2.
With Zic4 and Gephyrin by prior arrangement.
Specimen requirements: serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: Indirect immunofluorescence, Western and recombinant immunoblotting.
EQA: UK NEQAS for Paraneoplastic Antibodies

Anti-Glycolipid Antibodies	**Sample type: Serum**	**TaT: 10 working days**	**NHS Price: £40**

Test for: Autoimmune peripheral neuropathies
Alternative name: Anti-ganglioside antibodies.
Routine screen: Includes antibodies to GM1, GD1a, GD1b, GT1b, GQ1b
Additional screen available on request (£40): Includes antibodies to GA1, GM2, GM3, GD3, GT1a
Sulphatides available on request (£20): Antibodies to sulphatides
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: ELISA
EQA: NEQAS Pilot Scheme

Anti-MAG Antibodies	Sample type: Serum	TaT: 21 working days	NHS Price: £50

Test for: Autoimmune neuropathies associated with myeloma and IgM paraprotein
Alternative name: Anti-Myelin Associated Glycoprotein Antibodies
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: ELISA
EQA: None available

Anti-GAD Antibodies	Sample type: Serum	TaT: 10 working days	NHS Price: £40

Test for: Autoimmune diabetes and autoimmune stiff person syndrome
Alternative name: Anti-Glutamic Acid Decarboxylase Antibodies
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: ELISA
EQA: UK NEQAS for Paraneoplastic Antibodies

Anti-Recoverin Antibodies	Sample type: Serum	TaT: 40 working days	NHS Price: £68

Test for: Paraneoplastic retinopathy
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: Western immunoblot
EQA: None available

Anti-NMDA Receptor Antibodies	Sample type: Serum	TaT: 10 working days	NHS Price: £40

Test for: Autoimmune encephalitis
Alternative name: Anti-N-methyl-D-aspartate receptor antibodies
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: Indirect immunofluorescence
EQA: None available

Neutralising Antibodies to b-Interferon	Sample type: Serum	TaT: 21 working days	NHS Price: £90

Test for: Monitoring multiple sclerosis patients on beta-interferon therapy
Alternative name: NAbs
Note: Binding antibodies do not necessarily neutralise the bioactivity of beta-interferon. This bioassay measures antibodies that bind and neutralise beta-interferon activity.
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: Luciferase bioassay
EQA: None available

Vascular Endothelial Growth Factor	Sample type: Serum	TaT: 21 working days	NHS Price: £55

Test for: POEMS syndrome and myeloma. POEMS: peripheral neuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes.
Alternative name: VEGF
Specimen requirements: Serum
Minimum sample volume: 500μL.

Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: ELISA
EQA: None available

Transferrin Glycoforms	**Sample type: Serum**	**TaT: 9 working days**	**NHS Price: £50**

Test for: Congenital disorders of glycosylation (CDG). This is NOT a test for alcohol abuse or haemochromatosis.
Alternative name: CDG screen
Note: This test may be unreliable in neonates younger than three weeks due to the presence of maternal transferrin. Recent transfusion may invalidate the result.
Specimen requirements: Serum
Minimum sample volume: 500μL.
Special precautions/Transport: Samples should be unhaemolysed & transported by first class post from outside NHNN
Methodology: Isoelectric focusing
EQA: ERNDIM CDG Scheme

TURNAROUND TIMES

The target turnaround time is for 90% of tests requested and is given as the number of working days from receipt to result authorisation, it is the within laboratory TaT as postal delays are not taken into account. All urgent results (e.g. all xanthochromia and positive beta-2 transferrins) are relayed by telephone or fax (safe haven), if possible, prior to a hardcopy of the report being sent in the post.

NOTE: Prices quoted are for NHS requests; these are a guide only and may be subject to change in the future.

SUGGESTIONS AND COMPLAINTS

Suggestions about our service may be raised at any time with the Laboratory Manager viki.worthington@uclh.nhs.uk or when completing our annual user satisfaction survey. Suggestions will be discussed and evaluated at departmental meetings.

All complaints will be dealt with in compliance with the UCLH Complaints Policy. The Laboratory Manager will investigate and issue a response as soon as possible.

PATIENT CONSENT

For samples referred from outside the UCLH Trust it is a requirement that there is patient consent to disclose clinical information and family history to relevant healthcare professionals as required for the purposes of diagnosis and patient management. On receipt of a referred sample for testing, as part of the service agreement, the NICL assumes that this consent has been given.

APPENDIX 1

Testing for total tau protein and amyloid beta in CSF

Sample requirements:

Unhaemolysed CSF MUST be collected in polypropylene tubes, centrifuged, separated and the supernatant frozen at -80^{o}C on the same day of lumbar puncture.
Please freeze in separate aliquots for each test (in polypropylene tubes - minimum volume 0.5mL per tube).
Note: Results may be unreliable if polystyrene tubes are used.

Polypropylene Universal tube: e.g. Sarstedt Product code 63.9922.254.
Polypropylene sample tube: e.g. Elkay 021-4204-500. Lids are extra and can be bought in a variety of colours. (We use yellow lids, Elkay 021-4800-506)

Sample transport:

Samples must be sent frozen, on dry ice (solid CO_2), preferably at the beginning of the week to avoid delays at weekends and bank holidays. Samples need to arrive in Neuroimmunology before 5 pm. The samples need to remain frozen until analysis.

For enquiries contact:

Dr Miles Chapman (Biomedical Scientist)
Tel: 020 3448 3542
Email: miles.chapman@uclh.nhs.uk

Dr Viki Worthington (Clinical Scientist)
Tel: 020 3448 4198
Email: viki.worthington@uclh.nhs.uk

APPENDIX 2

Testing for neutralising antibodies to interferon-beta in serum

Sample requirements:

For interferon-beta neutralising antibody testing we require a serum sample (1-2ml minimum), with cells removed.

Sending samples within the UK:

These may be sent at ambient temperature by first class post, preferably at the beginning of the week to avoid delays at weekends and bank holidays.

Sending samples from overseas:

These should be frozen and sent on dry ice (solid CO_2), preferably at the beginning of the week to avoid delays at weekends and bank holidays. Please notify Dr Viki Worthington by email in advance (see address below).

The following information should be included with each sample:

The name of the consultant.
The address (including department) to send the report to.
The basic demographics of the patient.
The type of interferon-beta product that the patient is receiving.
When interferon-beta therapy was started.

For enquiries contact:

Dr Viki Worthington (Clinical Scientist)
Tel: 020 3448 4198
Email: viki.worthington@uclh.nhs.uk