# Newborn Screening & Biochemical Genetics

West Midlands Laboratory Service for Newborn Bloodspot Screening and Inherited Metabolic Disorders

**Handbook for Users**

<table>
<thead>
<tr>
<th>General Contact numbers:</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMD Duty BMS (results and enquiries)</td>
</tr>
<tr>
<td>IMD Duty Biochemist (clinical queries, interpretation)</td>
</tr>
<tr>
<td>Newborn Bloodspot Screening Service</td>
</tr>
</tbody>
</table>

Please check whether this is the current version of this handbook at: [https://bwc.nhs.uk/our-pathology-services](https://bwc.nhs.uk/our-pathology-services)
Newborn Screening & Biochemical Genetics

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1 Introduction to Newborn Screening & Biochemical Genetics

Services Provided
The Department of Newborn Screening and Biochemical Genetics at Birmingham Women’s and Children’s NHS Foundation Trust (BWC) provides laboratory services as defined by the UK NHS Blood Spot Screening Programme and by NHS England for Metabolic Disorders (Laboratory Services). It additionally includes highly specialised Biochemical testing for inherited metabolic disorders, accessible to patients and clinicians worldwide. The department may refer some tests externally. Please see section 9 for further details.

Service Scope
Newborn Screening
The West Midlands Newborn Screening Centre at BCH provides newborn bloodspot screening for congenital hypothyroidism, sickle cell disease, cystic fibrosis, phenylketonuria (including the investigation of biotin defects), medium chain acyl CoA dehydrogenase deficiency, maple syrup urine disease, pyridoxine non-responsive homocystinuria, glutaric aciduria type 1, and isovaleric acidaemia. Please refer to the separate Public Health England newborn screening handbook for further details: https://www.gov.uk/government/publications/health-professional-handbook-newborn-blood-spot-screening

Biochemical Genetics
The Biochemical Genetics laboratories provide biochemical and enzyme testing with result interpretation for the diagnosis, monitoring and clinical care of patients with inherited metabolic disorders, which are rare but serious conditions. The laboratory professionals are part of a wide multidisciplinary IMD team comprising clinical, nursing, dietetic, pharmacy and psychology staff. We have facilities for tissue banking and the culture and storage of skin fibroblasts, chorionic villus cells and amniotic fluid cells.

Antenatal Diagnosis
In liaison with the Regional Genetics Laboratory and Clinical Genetics Service we act as a centre for advice on antenatal testing options for inherited metabolic disorders and co-ordinate sample handling and the reporting of results. We attempt the audit of all antenatal diagnoses and record and report the results on an annual basis.

Advisory Service
Duty biochemists for Newborn Screening and Biochemical Genetics are available for all queries concerning test selection and effective utilisation, clinical advice, result interpretation and urgent requests. Refer to the ‘Contacting the Laboratory’ section for contact details.
Service Standards/Quality Assurance
The Department of Newborn Screening and Biochemical Genetics is a UKAS accredited medical laboratory no. 9948 to ISO15189:2012. Our accreditation is limited to those activities described in our Schedule of Accreditation, which can be found at https://www.ukas.com/wp-content/uploads/schedule Uploads/00007/9948%20Medical%20Single.pdf. Tests not in scope and therefore unaccredited (and unaccredited tests referred to other laboratories) are indicated with the symbol † in the repertoire tables.

The quality of our service is maintained by recognised effective internal quality control measures and by participation in the External Quality Assessment (EQA) schemes provided by UKNEQAS, ERNDIM and CDC. Where schemes are not available, we participate in small interlaboratory comparison schemes with other laboratories where possible. The staff working within the department are fully qualified, HCPC registered (where required), specialised and experienced, providing a quality service. A high quality service is maintained by frequently looking at feedback from user meetings, audits and user satisfaction surveys.

Please refer to our Quality Policy for further information.

Service Commitment
The Department of Newborn Screening and Biochemical Genetics is committed to providing laboratory services of the highest quality within the resources available, and to continually evaluate and improve all aspects of the service. The department endeavours to:

- Provide accurate and timely results
- Provide advice on testing algorithms, sample requirements, result interpretation
- Meet the needs of our users
- Respond to feedback
- Improve the service on an ongoing basis
- Provide training for undergraduate and postgraduate Biomedical Scientists, Clinical Scientists and Clinicians

The laboratory is one of 17 stakeholders in the National Metabolic Biochemistry Network (http://www.metbio.net).

The purpose of this handbook is to provide information on the IMD laboratory service including test repertoire, specimen requirements and details on accessing our service. It also provides some guidance on investigating patients for suspected IMD.
2 Information Governance

Data Protection
Information is a vital asset both in terms of the clinical management of individual patients and the efficient management of services and resources. It plays a key part in clinical governance, service planning and performance management.

Your personal data is data which by itself or with other data available to us can be used to identify you. We are Birmingham Women’s and Children’s NHS Foundation Trust, the data controller. Our Trust is registered with the Information Commissioner’s Office (ICO) to process personal and special categories of information under the General Data Protection Regulation (GDPR) and Data Protection Act 2018 (subject to parliamentary approval) and our registration number is Z6078102.

The department complies with the Trust policies relating to the handling, use and protection of personal information:

- We only ask for information that we need to allow interpretation of results
- We protect the information and ensure only those staff who need to see the information can access it
- We share the information only when we need to for patient case, for example sending the information to another laboratory for testing
- The data will be stored in accordance with The retention and storage of pathological records and specimens (5th edition) Guidance from The Royal College of Pathologists and the Institute of Biomedical Science, April 2015. We do not store any information for any longer than is absolutely necessary.

For more information, please click on the following link to read the Trusts Privacy Policy. This data protection and privacy policy sets out how we will use your personal data when you access our website. You can contact our Data Protection Officer at Birmingham Children’s Hospital, Steelhouse Lane, Birmingham B4 6NH if you have any questions.

https://bwc.nhs.uk/privacy-policy

Complaints
Pathology Services operates a complaints system in line with the Trusts Complaints Policy ‘Making Experiences Count Policy’.

Complaints, comments or feedback regarding the services provided by pathology can be made verbally or in writing (letter or email). Please contact the Pathology Services Manager or the Quality Manager.

If you feel that your concerns have not been put right you can make a formal complaint:

https://bwc.nhs.uk/complaints
3 Patient Information

Testing is available to patients via appropriate healthcare professionals and is guided by clinical assessment. Under certain circumstances, the laboratory may undertake additional relevant testing dependent on the clinical information provided and the results of other analyses. Any additional testing performed will remain within the remit of the investigation of inherited metabolic disorders.

All patient information is held securely under the provisions of the UK Data Protection Act 1998. Results are communicated directly to the requesting healthcare professional, usually via the referring laboratory. Results may only be accessed by healthcare professionals directly involved in the care of the patient. The laboratory cannot currently provide results directly to patients; the relevant healthcare professional should be contacted for all result enquiries.

Relevant patient information can be requested from your healthcare professional and is provided at consultation. Useful websites include:

- NHS Newborn Screening Programme [http://newbornbloodspot.screening.nhs.uk/public](http://newbornbloodspot.screening.nhs.uk/public)

Lab Tests Online (for non-IMD biochemistry tests) [http://labtestsonline.org.uk/](http://labtestsonline.org.uk/)

4 Service Location & Availability

Location of the Department

<table>
<thead>
<tr>
<th>Laboratory postal address</th>
<th>Delivery address for couriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathology Reception</td>
<td>Pathology Reception</td>
</tr>
<tr>
<td>Newborn Screening</td>
<td>Newborn Screening</td>
</tr>
<tr>
<td>&amp; Biochemical Genetics</td>
<td>&amp; Biochemical Genetics</td>
</tr>
<tr>
<td>Paediatric Laboratory Medicine</td>
<td>Paediatric Laboratory Medicine</td>
</tr>
<tr>
<td>Birmingham Children's Hospital</td>
<td>Birmingham Children's Hospital</td>
</tr>
<tr>
<td>Steelhouse Lane</td>
<td>Whittall Street</td>
</tr>
<tr>
<td>Birmingham</td>
<td>Birmingham</td>
</tr>
<tr>
<td>B4 6NH</td>
<td>B4 6DH</td>
</tr>
</tbody>
</table>

Service Hours

Normal Working Hours

The laboratories are open for the receipt and processing of routine samples and for result reporting and advice from 09:00-17:10h Monday to Friday (except Bank Holidays).

Out of Hours Service

Out-of-hours analytical services are available for plasma ammonia and plasma/CSF lactate as part of the Blood Sciences: Clinical Chemistry on-call service at BCH.

No other analytical services are routinely available out-of-hours but, in emergency, specific tests may be provided if clinically justified and if staff are available. If analytical or advisory services are required out of hours please contact the on-call Consultant Biochemist in the first instance (via the BCH switchboard, Telephone 0121 333 9999).
Sending a Specimen
Information on sending specimens collected within Birmingham Children’s Hospital can be obtained from the Hospital Laboratory Handbook located on the Intranet.

Specimens collected at sites outside Birmingham Children’s Hospital should, where possible, be sent via the blood sciences/clinical chemistry department in the originating hospital. In some cases specimens for certain tests may require immediate transport by courier or taxi. Specific needs are listed in the specimen requirement section of the table in this handbook. If using a courier or taxi please request that the specimens are delivered to the Paediatric Laboratory Medicine Block entrance at Whittall Street (not to the main hospital post room).

5 Specimen Collection, completion of the request form and management of urgent and additional requests

Consent
Unless written consent is required for a particular test or investigation (this will be documented in the test details), the laboratory assumes that informed consent for testing to be carried out has been given at the time of the request form has been completed.

It is the responsibility of the requesting doctor to obtain consent for specimen collection and the tests requested. It is implicit in the receipt of the request form that consent has been obtained. We never request more sample than we need to but where there is material left over after laboratory testing, it may be used for other purposes such as quality assurance or audit, under the provisions of the Human Tissue Act 2004. Specific research is regulated separately by the ethics committee. Consent for the use of tissue requires that patients must be given the option to refuse permission for spare material to be used. When this occurs, each request to the laboratory must be clearly marked so that specimens are not used for other purposes.

There may be specific requirements for written consent for DNA tests sent to other countries, please contact the molecular genetics laboratory for further information.

Specimen Collection (including the preparation of the patient)
Phlebotomy services are provided at Birmingham Children’s Hospital for inpatients and outpatients. Specimen collection requirements are provided in the relevant tables of this handbook.

Instructions for patient collected samples
For specimens collected by patients and/or their parents/carers (e.g. urine or bloodspot/capillary blood samples), instruction leaflets and training are available and provided on request.

Instructions for the completion of the request form
The laboratories have well established acceptance criteria which need to be present for samples to be accepted and processed. All essential items need to be present on the form to ensure that patients are uniquely identified so that results are not allocated to the wrong patient, and that the correct test can be performed and reported to the correct clinician and sent to the correct location.
It is the responsibility of the requesting clinician to complete the correct request form fully. Errors or incomplete information WILL result in the delay in specimen processing and reporting.

To comply with laboratory procedures, we will only accept samples where all mandatory information and minimum patient identifiers are provided. The following essential information is required:

<table>
<thead>
<tr>
<th>Essential Criteria</th>
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</thead>
<tbody>
<tr>
<td>NHS Number / Hospital Registration Number</td>
</tr>
<tr>
<td>Surname</td>
</tr>
<tr>
<td>Forename</td>
</tr>
<tr>
<td>Date of Birth</td>
</tr>
<tr>
<td>Identification and location of requestor</td>
</tr>
<tr>
<td>Investigation required</td>
</tr>
<tr>
<td>Date and time of collection</td>
</tr>
<tr>
<td>Specimen Type, where appropriate the anatomical site of origin</td>
</tr>
<tr>
<td>Relevant clinical information</td>
</tr>
<tr>
<td>Fasting or dietary status</td>
</tr>
<tr>
<td>The date of the onset of symptoms or date of contact</td>
</tr>
<tr>
<td>Details of antibiotic therapy and drug therapy</td>
</tr>
<tr>
<td>Biohazard warning label</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Desirable Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient address</td>
</tr>
<tr>
<td>Recent transfusion history (where relevant)</td>
</tr>
<tr>
<td>Any anticoagulant agents administered</td>
</tr>
<tr>
<td>Contact phone number / bleep</td>
</tr>
<tr>
<td>Indication of the urgency of the request</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Medical Specialty</td>
</tr>
<tr>
<td>NHS/PP category</td>
</tr>
</tbody>
</table>

**Specimen labelling and minimum data set**

The specimen must be labelled with the following information:

1. Surname
2. And two from
   - Forename
   - Date of Birth
   - Registration number
   - Referring laboratory specimen number

Note: for samples in small cryotubes, due to space constraints two patient identifiers are acceptable: surname, and one from date of birth, registration number, referring laboratory specimen number.

The following information is desirable:

- Date and time of specimen collection
- Forename
- Date of birth
- Sex
- Sample type
Urgent Specimens
Urgent requests can often be dealt with more quickly if there is prior discussion with the team. If your request is urgent please contact the Duty Metabolic Biochemist (mobile via switchboard: 0121 333 9999).

High Risk Specimens
We do not routinely analyse high-risk specimens without prior discussion. Please contact the Duty Metabolic Biochemist before sending such specimens.

Specimen Storage
Plasma and urine specimens are stored frozen for 3 months prior to disposal. Tissue specimens are stored for 30 years.

Add-on Tests
To request additional tests on specimens already received by the laboratory, please telephone to discuss whether sufficient specimen is remaining and is suitable for analysis. For requests added subsequent to receipt of the specimen, turnaround times are from the date of test request. A specific request form for this purpose must be used. This is available at https://bwc.nhs.uk/download.cfm?doc=docm93jijm4n2211.docx

Criteria for acceptance and rejection of samples
Request forms and specimens are the key source of data for any department. The details on the request form, form the information that is entered onto the Laboratory computer system, Telepath which enables results to be available on the Laboratory reporting system ICE. If any detail is missing on either the request form or sample, there is a risk that the specimen may be rejected. The criteria is clearly stated in ‘Instructions for completion of the request form’ and ‘Sample labelling and minimum data set’

Specimen rejection
We do not analyse incorrectly or inadequately labelled specimens and/or request forms (see above). Specimens that are inadequately labelled, in the incorrect anticoagulant or preservative, or are received too late after sampling will not usually be analysed and a report will be issued to this effect. If appropriate, unsatisfactory specimens will be stored with routine specimens for 3 months.
6 Transportation of samples to the laboratory
All specimens must be handled with care and treated by all personnel as a potential infection risk. However, additional precautions are required for samples that are deemed to be high risk.

Low Risk Diagnostic Specimens (UN3373):
The majority of specimens collected and transported to the pathology departments do not present a significant risk of infection to staff handling them. These may be considered “low risk” diagnostic specimens. Such specimens will normally be packaged in a primary container (e.g. blood tube, swab tube, specimen pot), and an outer secondary container (a sealed pathology transport bag or sealed plastic bag). All specimens must be accompanied by an accurately, fully completed pathology request form which must preferably be integral and external to the bag. The tertiary container used to transport specimens around and between hospitals may vary in design, but must comply with the P60 specification outlined in this Policy.

High Risk Infectious Specimens (UN2114):
Some patients may be suffering from, or be suspected of having a disease which may present higher risk to staff. Legislation requires specimens from such patients to be identifiable.
- The specimen containers and pathology transport bags used for these specimens will be identical to those used for routine specimens. The identification of risk associated with these specimens will be by the use of “DANGER OF INFECTION” labels.
- It is the legal responsibility of the person who requests the laboratory examination of the specimen to ensure that both the request form and the container are correctly labelled to indicate a danger of infection. “DANGER OF INFECTION” labels must only be used for specimens which are suspected of or are known to contain pathogens.

Air Tube
All sample containers must be properly closed and packaged in a dedicated sealed specimen bag with absorbent padding attached to the request form. Excessive numbers of samples should not be packed into a pod as this may cause the lid to open during transportation.

It is the responsibility of the sender to ensure that:
- The sample is labeled, packed appropriately and is accompanied by the relevant paperwork.
- The air tube sample carrier is secured properly before transport.
- The air tube sample carrier is sent to the correct ‘system’ address

The sample(s) should be secured in the air tube carrier pod and the lid is closed;

Instructions for sending samples from an external source
Specimens collected outside the hospital should be delivered using the correct packaging that complies with national guidelines and sent via hospital transport, courier or taxi. The department should be notified in advance of any urgent or special requests.
7 Examinations offered by the laboratory
This section of the handbook explains which examinations are offered by the laboratory, including (as appropriate) information concerning samples required, sample volumes, special precautions, biological reference intervals and clinical decision values.

Testing Guidelines
The National Metabolic Biochemistry Network provides information about testing and guidelines for metabolic disorders: 
http://www.metbio.net/metbioGuidelines.asp

Group Tests and Profiles
Some tests will detect a wide range of disorders that produce abnormalities in the particular group of analytes, e.g. amino acids, organic acids, acylcarnitines, mucopolysaccharides & very long chain fatty acids. This type of “Group Test” is often used as a first line test.

In other cases we have combined tests into a profile that is aimed at detecting disorders with a particular symptom or pattern of symptoms e.g. hepatosplenomegaly, hereditary optic atrophy.

A request for a urine “metabolic screen” will normally be interpreted by the laboratory as requiring urine amino acids, organic acids and “spot tests”. However if the clinical information supplied suggests other tests could be appropriate these may be added by the Duty Metabolic Biochemist.

Test Repertoire
The volume, specimen type and storage/transport requirements are detailed in the following tables. If the test you require is not included in our repertoire please contact us or visit the National Metabolic Biochemistry Website: http://www.metbio.net/metbioAssays.asp

Test Cost
Within the West Midlands region the laboratory IMD services are provided by NHS England as part of specialist services commissioning.
### Newborn Bloodspot Screening tests

<table>
<thead>
<tr>
<th>Metabolite Test (Method)</th>
<th>Investigation</th>
<th>Specimen type/ volume</th>
<th>Specific needs</th>
<th>Storage/ Transport</th>
<th>Turnaround time in working days (90&lt;sup&gt;th&lt;/sup&gt; centile)</th>
<th>EQA scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylalanine and Tyrosine (FIA-MSMS)</td>
<td>Phenylketonuria (PKU)</td>
<td>4x bloodspots</td>
<td>Refer to national guidelines for specimen acceptance criteria</td>
<td>Room temperature</td>
<td>3 (for initial screening process)</td>
<td>UKNEQAS CDC</td>
</tr>
<tr>
<td>C8 and C10 carnitines (FIA-MSMS)</td>
<td>Medium chain acyl-CoA dehydrogenase deficiency (MCADD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5 carnitine (FIA-MSMS)</td>
<td>Isovaleric acidaemia (IVA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5-DC carnitine (FIA-MSMS)</td>
<td>Glutaric aciduria type-1 (GA1)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leucine – total (FIA-MSMS)</td>
<td>Maple Syrup Urine Disease (MSUD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methionine (FIA-MSMS)</td>
<td>Classical Homocystinuria (HCU)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TSH (Immunooassay)</td>
<td>Congenital Hypothyroidism (CHT)</td>
<td></td>
<td></td>
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<tr>
<td>IRT (Immunooassay)</td>
<td>Cystic Fibrosis (CF)</td>
<td></td>
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<tr>
<td>CFTR – four common mutations (QPCR)</td>
<td>Cystic Fibrosis (CF)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Haemoglobin variants (HPLC)</td>
<td>Sickle Cell Disease (SCD) and Haemoglobin Variants</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

HPLC = High Pressure Liquid Chromatography, FIA = Flow injection analysis, MSMS = Tandem Mass Spectrometry, QPCR = quantitative polymerase chain reaction

### Metabolite tests

<table>
<thead>
<tr>
<th>Metabolite Test (Method)</th>
<th>Investigation</th>
<th>Specimen type/ volume</th>
<th>Specific needs</th>
<th>Storage</th>
<th>Transport</th>
<th>Turnaround time in working days (90&lt;sup&gt;th&lt;/sup&gt; centile)</th>
<th>EQA scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-Dehydrocholesterol screen (Spectrophotometric)</td>
<td>Smith-Lemli-Opitz Syndrome</td>
<td>VP 0.5mL plasma or serum</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>ERNDIM</td>
<td></td>
</tr>
<tr>
<td>Acyl carnitines incl. free carnitine (FIA-MSMS)</td>
<td>Fatty acid oxidation defects Organic acid disorders</td>
<td>VB (Heparin 0.5mL) or BS VP (0.2mL)</td>
<td>Please send plasma AND blood spots</td>
<td>Room temperature</td>
<td>Room temperature</td>
<td>15 days</td>
<td>ERNDIM CDC</td>
</tr>
<tr>
<td>Amino Acids – Quantitative (AAA)</td>
<td>Amino acid disorders and urea cycle defects</td>
<td>VP (Heparin 0.5mL)</td>
<td>Preferably send a fasting sample.</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>ERNDIM UKNEQAS</td>
</tr>
<tr>
<td>Metabolite Test (Method)</td>
<td>Investigation</td>
<td>Specimen type/volume</td>
<td>Specific needs</td>
<td>Storage</td>
<td>Transport</td>
<td>Turnaround time in working days (90th centile)</td>
<td>EQA scheme</td>
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<tr>
<td>Newborn Screening &amp; Biochemical Genetics</td>
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<tr>
<td></td>
<td></td>
<td>CSF 0.5mL</td>
<td>Blood stained CSF is unsuitable for analysis.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>U (2mL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Blood stained CSF is unsuitable for analysis.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amino Acids (Qualitative) (HVE)</td>
<td>Renal transport disorders</td>
<td>U (2mL)</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>7 days</td>
<td>ERNDIM</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Pterins (HPLC)</td>
<td>Biopterin deficiency disorders</td>
<td>6x10mm BS (1x10mm extra BS if phenylalanine result is not provided)</td>
<td>Ideally collect when blood phenylalanine is increased. Bloodspots made from anti-coagulated blood are NOT acceptable.</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Carnitine – free (FIA – MSMS)</td>
<td>Carnitine status and transport disorders</td>
<td>U (0.5mL), VP (Heparin 0.2mL)</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>ERNDIM CDC</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
<tr>
<td>Cystine (AAA)</td>
<td>Cystinuria</td>
<td>U (0.5mL)</td>
<td>Store frozen prior to shipment.</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>ERNDIM</td>
<td></td>
</tr>
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<td></td>
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</tr>
<tr>
<td>Free Fatty Acids &amp; 3-Hydroxybutyrate (Enzymatic)</td>
<td>Hypoglycaemia</td>
<td>VP (Fluoride-Oxalate 0.5mL)</td>
<td>Please state fasting status.</td>
<td>Store frozen prior to shipment.</td>
<td>Room temperature</td>
<td>3 days</td>
<td>ERNDIM RANDOX</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Galactose-1-Phosphate – Quantitative (Enzymatic)</td>
<td>Galactosaemia monitoring</td>
<td>Whole VB (Heparin 1mL)</td>
<td>The sample must be received within 24 hours of collection. (If this is not possible, cells can be washed and sent frozen – please contact our laboratory for details)</td>
<td>Room temperature</td>
<td>Room temperature</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>Glycosaminoglycans (Spectrophotometric and electrophoresis)</td>
<td>Mucopolysaccharides</td>
<td>U (5mL)</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days (1D)</td>
<td>ERNDIM WILLINK MPS SCHEME</td>
<td></td>
</tr>
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</tr>
<tr>
<td>Homocystine – free (HPLC)</td>
<td>Homocystinuria</td>
<td>VP (Heparin 0.5mL)</td>
<td>See sulphur-containing amino acids</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen</td>
<td>15 days</td>
<td>ERNDIM</td>
</tr>
<tr>
<td>Metabolite Test (Method)</td>
<td>Investigation</td>
<td>Specimen type/ volume</td>
<td>Specific needs</td>
<td>Storage</td>
<td>Transport</td>
<td>Turnaround time in working days (90th centile)</td>
<td>EQA scheme</td>
</tr>
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</tr>
<tr>
<td>Homocysteine – total (HPLC-MSMS)</td>
<td>Homocystinuria</td>
<td>VP 0.2mL (or BS for monitoring known patients)</td>
<td>Separate within 30 minutes of collection</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>7 days - DBS 10 days – plasma</td>
<td>ERNDIM</td>
</tr>
<tr>
<td>Methylmalonic acid – Quantitative (GCMS)</td>
<td>Methylmalonic aciduria Not for B12 deficiency</td>
<td>VP (Heparin 1mL) U (1mL)</td>
<td></td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>ERNDIM (plasma only)</td>
</tr>
<tr>
<td>Nitisinone – NTBC (HPLC-MSMS)</td>
<td>Tyrosinaemia type-1 (therapeutic drug monitoring)</td>
<td>VS or VP (Heparin 1mL)</td>
<td>Collect specimen pre-dose</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td>†Oligosaccharides (TLC)</td>
<td>Oligosaccharidoses</td>
<td>U (1mL)</td>
<td></td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td>Organic Acid Analysis (GCMS)</td>
<td>Organic acid disorders and urea cycle defects</td>
<td>U (5mL)</td>
<td></td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>10 days</td>
<td>ERNDIM</td>
</tr>
<tr>
<td>Orotic Acid – Quantitative (GCMS)</td>
<td>Urea cycle defects</td>
<td>U (5mL)</td>
<td></td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>ERNDIM</td>
</tr>
<tr>
<td>Oxalate (Enzymatic)</td>
<td>Renal stones – Oxalosis</td>
<td>VP (EDTA 1mL)</td>
<td>Plasma must be separated within 30 minutes of venepuncture</td>
<td>Store frozen prior to shipment</td>
<td>Must be sent frozen</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>U (5mL)</td>
<td>Acidify urine to pH&lt;2 within 30 mins of voiding, or collect 24h urine into acid containing bottle</td>
<td>Send frozen if possible</td>
<td></td>
<td></td>
<td>ERNDIM WEQAS</td>
</tr>
<tr>
<td>Phenylalanine &amp; tyrosine (FIA-MSMS)</td>
<td>Phenylketonuria &amp; tyrosinaemia (monitoring)</td>
<td>2x10mm BS</td>
<td></td>
<td>Store frozen prior to shipment.</td>
<td>Room temperature</td>
<td>3 days</td>
<td>UKNEQAS CDC</td>
</tr>
<tr>
<td>Phosphoethanolamine (AAA)</td>
<td>Hypophosphatasia</td>
<td>U (5mL)</td>
<td></td>
<td>Store frozen prior to shipment.</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>ERNDIM</td>
</tr>
<tr>
<td>Phytanic &amp; Pristanic acids (GCMS)</td>
<td>Peroxisomal disorders</td>
<td>VP (Heparin, Fluoride-Oxalate or EDTA 1mL)</td>
<td></td>
<td>Store frozen prior to shipment</td>
<td>Send at room temperature</td>
<td>15 days</td>
<td>ERNDIM</td>
</tr>
<tr>
<td>Reducing substances (Colourimetric)</td>
<td>Renal reabsorption. Gl absorption/transport/metabolism</td>
<td>U (5mL)</td>
<td></td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>3 days</td>
<td>N/A</td>
</tr>
</tbody>
</table>

†Faeces (liquid)
<table>
<thead>
<tr>
<th>Metabolite Test (Method)</th>
<th>Investigation</th>
<th>Specimen type/ volume</th>
<th>Specific needs</th>
<th>Storage</th>
<th>Transport</th>
<th>Turnaround time in working days (90th centile)</th>
<th>EQA scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Succinylacetone (HPLC-MSMS)</td>
<td>Tyrosinaemia type-1</td>
<td>VS or VP (Heparin 1mL) 2x10mm BS</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>ERNDIM</td>
<td></td>
</tr>
<tr>
<td>Sugar chromatography of mono &amp; disaccharides (TLC)</td>
<td>Renal reabsorption. Gl absorption/ transport/ metabolism</td>
<td>U (5mL)  Faeces (liquid)</td>
<td>Only routinely analysed if reducing substances positive</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td>Sulphur-containing Amino Acids: Quantitative free cystine, free homocystine and methionine (AAA)</td>
<td>Homocystinuria</td>
<td>VP (Heparin 0.5mL)</td>
<td>Separate within 30 minutes of collection and deproteinise immediately (Deproteinising solution available on request)</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen</td>
<td>15 days</td>
<td>ERNDIM</td>
</tr>
<tr>
<td>Sulphocysteine – also request free and total homocyst(e) (AAA)</td>
<td>Sulphite oxidase/ molybdenum cofactor deficiency</td>
<td>VP (Heparin 0.5mL)</td>
<td>See sulphur-containing amino acids</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td>Transferrin Isoforms (HPLC)</td>
<td>Congenital Disorders of Glycosylation</td>
<td>VS or VP 0.5 mL</td>
<td>None</td>
<td>Room temperature</td>
<td>25 days</td>
<td>ERNDIM</td>
<td></td>
</tr>
<tr>
<td>Very long chain fatty acids (GCMS)</td>
<td>Peroxisomal disorders</td>
<td>VP (Heparin, Fluoride-Oxalate or EDTA 2mL)</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>ERNDIM</td>
<td></td>
</tr>
<tr>
<td>White Cell Cystine (HPLC-MSMS)</td>
<td>Cystinosis</td>
<td>VB (Heparin 5mL for monitoring, 10mL for diagnosis)</td>
<td>Prior arrangement essential</td>
<td>Do not freeze</td>
<td>Send whole blood to arrive before 1pm on the day of sampling</td>
<td>15 days</td>
<td>ERNDIM</td>
</tr>
</tbody>
</table>

BS = bloodspot, U = urine, VB = venous blood, VS = venous serum, VP = venous plasma (anticoagulant stated). AAA = Amino Acid Analyser, HPLC = High Pressure Liquid Chromatography, FIA = Flow injection analysis, MSMS = Tandem Mass Spectrometry, GCMS = Gas Chromatography Mass Spectrometry, TLC = thin layer chromatography, N/A = no EQA scheme available. *Test not included in UKAS accreditation scope

For tests not performed by this laboratory (i.e. those tests not listed in the table), please contact us to discuss the most appropriate referral laboratory for testing and relevant specimen handling requirements.
Lysosomal Enzyme Tests

Lysosomal Enzyme Assays
Assays are typically performed on leucocytes isolated from whole blood collected into EDTA. All samples should be received in our Department within 24 hours of collection to ensure an optimum yield of cells. Samples must arrive Mon-Thu or by 10am Friday at the latest, i.e. collect Mon-Thu if to be sent overnight or Mon-Wed if to come via standard transport from another hospital. Please do not use first or second-class post. Samples can be stored overnight at +4°C but DO NOT FREEZE OR SEPARATE. The volume of blood required varies according to the number and type of tests requested. For these reasons it is important to contact the laboratory prior to taking the sample. Some enzymes can be measured on plasma or blood spots as an initial screen but any abnormal result should be confirmed on leucocytes isolated from whole blood. Unless pre-agreed we will test plasma or bloodspots in the first instance.

Group Tests of Lysosomal Enzymes
Hepatosplenomegaly Profile (5mL EDTA)
Leucocyte sphingomyelinase (Niemann-Pick disease type A & B)
Leucocyte β-glucosidase (Gauches disease)
Leucocyte acid esterase (Wolman disease & Cholesteryl Ester Storage disease)
Plasma chitotriosidase (Non specific screen for some lysosomal disorders such as Gaucher disease and Niemann-Pick disease type C – screening test only).

Leucodystrophy Profile (10mL EDTA)
Leucocyte arylsulphatase A (Metachromatic leucodystrophy)
Leucocyte β-galactocerebrosidase (Krabbe leucodystrophy).

Gangliosidosis Profile (5mL EDTA)
Leucocyte β-galactosidase (GM1 Gangliosidosis & Galactosialidosis)
Leucocyte total hexosaminidase (Sandhoff disease)
Leucocyte hexosaminidase A (Tay-Sachs disease).

Dysmorphic Profile (10mL EDTA)
(See http://www.metbio.net/metbioGuidelines.asp for guidelines)
Plasma I-cell Screen (Mucolipidosis II & III)
Plasma aspartylglucosaminidase (Aspartylglucosaminuria)
Leucocyte arylsulphatase A (Multiple Sulphatase Deficiency)
Plasma /Leucocyte β-glucuronidase (MPS VII)
Leucocyte β-galactosidase (GM1-gangliosidosis & galactosialidosis)
Plasma/ Leucocyte α- & β-mannosidase (α- & β-mannosidosis)
Plasma/ Leucocyte α-fucosidase (α-fucosidosis)

Batten Disease Profile (10mL EDTA)
Leucocyte palmitoyl protein thioesterase 1 (CLN1)
Leucocyte tripeptidyl peptidase 1 (CLN2)

Foetal/Neonatal Hydrops Profile (10mL EDTA)
(See http://www.metbio.net/metbioGuidelines.asp for guidelines).
Leucocyte β-glucosidase (Gaucher Disease)
Plasma/ Leucocyte β-glucuronidase (MPS VII)
Leucocyte β-galactosidase (GM1 gangliosidosis & galactosialidosis),
Leucocyte sphingomyelinase (Niemann-Pick A & B)
Leucocyte acid esterase (Wolman’ disease & Cholesteryl Ester Storage disease)
Leucocyte arylsulphatase A (Metachromatic leucodystrophy)
Plasma chitotriosidase (Non specific screen for some lysosomal disorders such as Gaucher disease and Niemann-Pick disease type C – screening test only).
## Enzyme tests in blood (whole blood, bloodspots, red blood cells, leucocytes, plasma and serum)

<table>
<thead>
<tr>
<th>Blood Enzyme Test</th>
<th>Investigation</th>
<th>Specimen type/ volume</th>
<th>Specific needs</th>
<th>Storage</th>
<th>Transport</th>
<th>Turnaround time in working days (90th centile)</th>
<th>EQA scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid Esterase / Lysosomal Acid Lipase (LAL)</td>
<td>Wolman/Cholesteryl Ester Storage Disease/Lysosomal Acid Lipase deficiency</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DBS (EDTA)*</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>α-N-Acetyl-galactosaminidase</td>
<td>Schindler Disease</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DBS (EDTA)*</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>α-Galactosidase A</td>
<td>Fabry Disease Males only</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DBS (EDTA)*</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>α-Fucosidase</td>
<td>Fucosidosis</td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>α-Mannosidase</td>
<td>α-Mannosidosis</td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td>α-Glucosidase (Acid Maltase)</td>
<td>GSD II, Pompe Disease</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DBS (EDTA)*</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Arylsulphatase A</td>
<td>Metachromatic Leucodystrophy</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td>Blood Enzyme Test</td>
<td>Investigation</td>
<td>Specimen type/ volume</td>
<td>Specific needs</td>
<td>Storage</td>
<td>Transport</td>
<td>Turnaround time in working days (90th centile)</td>
<td>EQA scheme</td>
</tr>
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<tr>
<td>Aspartylglucosaminidase</td>
<td>Aspartylglucosaminuria</td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>β-Galactocerebrosidase</td>
<td>Krabbe Leucodystrophy</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td>(Galactosylceramidase)</td>
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</tr>
<tr>
<td>β-Galactosidase</td>
<td>GM1 Gangliosidosis</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DBS (EDTA)*</td>
<td>Store frozen prior to shipment</td>
<td>Room temperature</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-Glucosidase (Glucocerebrosidase)</td>
<td>Gaucher Disease</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td></td>
</tr>
<tr>
<td>β-Glucuronidase</td>
<td>Sly Disease, MPS VII</td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>β-Mannosidase</td>
<td>β-Mannosidosis</td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Biotinidase</td>
<td>Biotinidase deficiency</td>
<td>VP (Heparin 1mL)</td>
<td>Store frozen prior to shipment</td>
<td>Courier or taxi</td>
<td>10 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Chitotriosidase</td>
<td>Screen for lysosomal disorders</td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>10 days</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Blood Enzyme Test</td>
<td>Investigation</td>
<td>Specimen type/ volume</td>
<td>Specific needs</td>
<td>Storage</td>
<td>Transport</td>
<td>Turnaround time in working days (90th centile)</td>
<td>EQA scheme</td>
</tr>
<tr>
<td>----------------------------------------</td>
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</tr>
<tr>
<td><strong>†Dihydropteridine Reductase (DHPR)</strong></td>
<td><strong>Dihydropteridine Reductase Deficiency</strong></td>
<td>2x10mm BS</td>
<td>Bloodspots made from anti-coagulated blood are NOT acceptable. A blood transfusion within 6 weeks prior to sampling may invalidate results</td>
<td>Store frozen prior to shipment.</td>
<td>Room temperature</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Fumarylacetoacetate Lyase</strong></td>
<td>Tyrosinaemia Type 1</td>
<td>VB (EDTA 10mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>Please enquire</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Fructose 1,6 Bisphosphatase</strong></td>
<td>Fructose 1,6 Bisphosphatase deficiency</td>
<td>VB (EDTA 10mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>Please enquire</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Galactose-1-phosphate uridyl transferase screen</strong></td>
<td><strong>Galactosaemia</strong></td>
<td>VB (Heparin 0.5mL)</td>
<td>A blood transfusion within 6 weeks prior to sampling may invalidate results</td>
<td>Store frozen prior to shipment.</td>
<td>For receipt within 24h of collection</td>
<td>3 days</td>
<td>CDC</td>
</tr>
<tr>
<td><strong>Hexosaminidase A</strong></td>
<td><strong>Tay-Sachs Disease</strong></td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>See below</td>
<td>ERNDIM~</td>
</tr>
<tr>
<td><strong>Hexosaminidase (Total)</strong></td>
<td><strong>Sandhoff Disease</strong></td>
<td>VP/VS Heparin, EDTA, Clotted 0.2mL</td>
<td>Store frozen prior to shipment</td>
<td>Send frozen if possible</td>
<td>15 days</td>
<td>See below</td>
<td>ERNDIM~</td>
</tr>
<tr>
<td><strong>Palmitoyl Protein Thioesterase 1</strong></td>
<td><strong>CLN1 (Batten)</strong></td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
<td>ERNDIM~</td>
</tr>
</tbody>
</table>
## Blood Enzyme Test

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Specimen type/volume</th>
<th>Specific needs</th>
<th>Storage</th>
<th>Transport</th>
<th>Turnaround time in working days (90th centile)</th>
<th>EQA scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Porphobilinogen (PBG) synthase inhibition</strong></td>
<td>No longer available – replaced by succinyl acetone (VP/BS)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sphingomyelinase</strong></td>
<td>Niemann-Pick disease types A &amp; B</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
</tr>
<tr>
<td><strong>Steroid Sulphatase</strong> (aryl sulphatase C)</td>
<td>X-linked ichthyosis, Multiple sulphatase deficiency</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Tripeptidyl Peptidase 1</strong></td>
<td>CLN2 (Batten)</td>
<td>VB (EDTA 5mL)</td>
<td>Do not freeze</td>
<td>For receipt within 24h of collection</td>
<td>15 days</td>
<td>ERNDIM~</td>
</tr>
</tbody>
</table>

BS = bloodspot, U = urine, VB = venous blood, VS = venous serum, VP = venous plasma (anticoagulant stated). *abnormal results require confirmation in leucocytes. ~ERNDIM scheme is performed on fibroblasts and the range of enzymes tested varies from year to year. N/A = no scheme available.
Tissue and Fibroblast Tests

Cell Culture
Skin biopsies should be collected in a sterile manner (See Appendix) and transported unfrozen in tissue culture medium guaranteed to reach us within 24 hours of being taken. A guideline for sampling and storage is available. Skin biopsies will be cultured (in most cases) and the cultured fibroblasts grown will be cryopreserved in liquid nitrogen and stored for 30 years (unless earlier disposal is specifically requested). Similarly all cultured chorionic villus cells and cultured amniotic fluid cells will be cryopreserved and stored for 30 years.

Tissue Specimens
Tissue specimens (e.g. liver, muscle, duodenum) should be collected in small cryotubes (which can be provided) and, ideally, frozen at the bedside in liquid nitrogen or on dry ice. If this is not available the tubes should be put on water ice and immediately transferred to the coldest freezer available. Transport to our laboratory can then be arranged at a convenient date. Frozen tissue samples should be transported on dry ice. Where tissue specimens are stored a report is issued to this effect.

<table>
<thead>
<tr>
<th>Tissue and Fibroblast Enzyme Tests</th>
<th>Investigation</th>
<th>Specimen type/ volume</th>
<th>Specific needs</th>
<th>Storage</th>
<th>Transport</th>
<th>Turnaround time</th>
<th>EQA scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>†Citrulline Incorporation</td>
<td>Citrullinaemia &amp; Argininosuccinic Aciduria</td>
<td>SB (Culture)</td>
<td>Sterile collection</td>
<td>Culture medium Do not freeze</td>
<td>Room temperature</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>†Butyrate 14CO₂ Release</td>
<td>Short Chain Fatty Acid Oxidation Defects</td>
<td>SB (Culture)</td>
<td>Sterile collection</td>
<td>Culture medium Do not freeze</td>
<td>Room temperature</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>Duodenal Disaccharidases</td>
<td>Inherited Lactase/Sucrase Isomaltase Deficiency</td>
<td>Duodenal Tissue &gt;10mg</td>
<td>Freeze immediately</td>
<td>Coldest freezer available</td>
<td>Courier or taxi on dry ice</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>Fructose 1,6 Bisphosphatase</td>
<td>Fructose Bisphosphatase Deficiency</td>
<td>Liver (Two Trucut Wedges) &gt;10 mg</td>
<td>Freeze immediately</td>
<td>Coldest freezer available</td>
<td>Courier or taxi on dry ice</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>Fumarylacetoacetate Lyase</td>
<td>Tyrosinaemia Type 1</td>
<td>SB (Culture)</td>
<td>Sterile collection</td>
<td>Culture medium Do not freeze</td>
<td>Room temperature</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver (Two Trucut Wedges) &gt;10 mg</td>
<td>Freeze immediately</td>
<td>Coldest freezer available</td>
<td>Courier or taxi on dry ice</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>Tissue Enzyme Test</td>
<td>Investigation</td>
<td>Specimen type/ volume</td>
<td>Specific needs</td>
<td>Storage</td>
<td>Transport</td>
<td>Turnaround time</td>
<td>EQA scheme</td>
</tr>
<tr>
<td>----------------------------------------</td>
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<td>----------------------------------------</td>
<td>----------------</td>
<td>--------------------------------</td>
<td>---------------------------</td>
<td>-----------------</td>
<td>------------</td>
</tr>
<tr>
<td>Glycine Cleavage Enzyme System</td>
<td>Non-Ketotic Hyperglycinaemia</td>
<td>Liver (Two Trucut Wedges) &gt;10 mg</td>
<td>Freeze immediately</td>
<td>Coldest freezer available</td>
<td>Courier or taxi on dry ice</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>†Isovaleric Acid Incorporation</td>
<td>Isovaleric Acidaemia &amp; Hydroxymethylglutaric Aciduria</td>
<td>SB (Culture)</td>
<td>Sterile collection</td>
<td>Culture medium Do not freeze</td>
<td>Room temperature</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>†Leucine $^{13}$CO$_2$ Release</td>
<td>Maple Syrup Urine Disease</td>
<td>SB (Culture)</td>
<td>Sterile collection</td>
<td>Culture medium Do not freeze</td>
<td>Room temperature</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>Myristate/Oleate Fatty Acid Oxidation Flux Assays ($^{3}$H Release)</td>
<td>Medium &amp; Long Chain Fatty acid oxidation defects</td>
<td>SB (Culture)</td>
<td>Sterile collection</td>
<td>Culture medium Do not freeze</td>
<td>Room temperature</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
<tr>
<td>†Ornithine Incorporation</td>
<td>Hyperornithinaemia with Gyrate Atrophy of the Retina (HOGA) &amp; Hyperammonaemia with Hyperornithinaemia &amp; Homocitrullinuria (HHH)</td>
<td>SB (Culture)</td>
<td>Sterile collection</td>
<td>Culture medium Do not freeze</td>
<td>Room temperature</td>
<td>Please enquire</td>
<td>N/A</td>
</tr>
</tbody>
</table>

SB = skin biopsy. N/A = no scheme available. †test not included in UKAS accreditation scope
8 Reports, turnaround times and availability of clinical advice

Key factors affecting test performance
Many factors can affect biochemical results; diurnal rhythm, exercise, fasting status, drug therapy, method of specimen collection (e.g. venous or capillary), haemolysis and biological variation. Some drugs interfere with certain analyses therefore it is helpful to provide a list of current therapy on the request form accompanying the specimen. If specimens are not stored and transported as indicated in the tables below, results of some analytes may be affected. If urine specimens show signs of deterioration a repeat specimen is usually requested because diagnostic abnormalities may not be apparent.

Interpretation of Results
For qualitative tests, a written explanation of the observed result(s) is provided on the report. For quantitative tests that produce a numerical result, the appropriate biological reference interval or clinical decision value is provided on the final report to guide interpretation. Reference intervals are not provided in this handbook because: the majority are age and/or sex related; their significance may be dependent on the results of other investigations; they may not be appropriate under certain clinical scenarios; they may therefore be misleading or misinterpreted. Reference intervals and advice on result interpretation are available from the duty biochemist.

Reports
Within BWC, reports will be available electronically on ICE following authorisation and paper copy reports will follow. For users external to BWC, paper reports will be posted to the requesting laboratory.

Turnaround Times
Turnaround times quoted are the anticipated times between specimen receipt in our laboratory and reporting under normal operating conditions. The turnaround times of all tests are monitored. Results will normally be returned via the local laboratory at the requesting hospital. The times taken for the specimen to reach the laboratory and for the report to reach the requesting clinician are not included. When appropriate, abnormal results will be telephoned to the requesting physician.

Telephone
Duty Metabolic Biochemist (clinical advice) 07795 828617
Daytime (mobile): 0121 333 9942
Out of hours: 0121 333 9999

Duty Biomedical Scientist (IMD results) 0121 333 9942

Enzymes and Tissue Culture Fax Number 0121 333 9902 0121 333 9911

Email bwc.imdlab@nhs.net

Internet https://bwc.nhs.uk/our-pathology-services
## Staff Contact Details

<table>
<thead>
<tr>
<th>Scientific Staff</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mrs Mary Anne Preece</strong></td>
<td>Consultant Biochemist &amp; Head of Department</td>
</tr>
<tr>
<td><strong>Mary Anne Preece</strong></td>
<td>Director of Newborn Screening and Laboratory IMD</td>
</tr>
<tr>
<td><strong>0121 333 9940</strong></td>
<td><strong><a href="mailto:maryanne.preece@nhs.net">maryanne.preece@nhs.net</a></strong></td>
</tr>
</tbody>
</table>

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| **Lead Biomedical Scientist**    | **Consultant Biochemist** |
| **NSBG**                         | **Newborn Screening, Pterins** |
| **0121 333 9938**                | **0121 333 9927** |
| **russell.denmeade@nhs.net**     | **philippa.goddard@nhs.net** |

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| **Principal Clinical Scientist** | **Senior Clinical Scientist** |
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| **jessica.schroeder@nhs.net**    | **greg.toulson@nhs.net** |

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| **Principal Clinical Scientist** | **Senior Biomedical Scientist** |
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| **Mrs Yvette Taylor**            | **Ms Emilie Terry** |
| **Senior Biomedical Scientist**  | **Quality Lead** |
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| **yvette.taylor2@nhs.net**       | **emilieterry@nhs.net** |

## Consultant Metabolic Paediatricians

- **Dr Suresh Vijay**
  - suresh.vijay1@nhs.net

- **Dr Saikat Santra**
  - s.santra@nhs.net

## Consultants Metabolic Physicians (adults)

- **Dr Julian Raiman**
  - Julian.Raiman@nhs.net

- **Dr Srividya Sreekantam**
  - ssreekantam1@nhs.net

- **Dr Tarek Hiwot**
  - tarekegn.hiwot@uhb.nhs.uk

- **Dr Charlotte Dawson**
  - charlotte.dawson@uhb.nhs.uk

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**Birmingham Children’s Hospital**: 0121 333 9908

**University Hospital Birmingham**: 0121 627 1627 ext 51592
9 Work Referred Away

Work Referred Away
The department regularly refers specimens to other specialist centres in order to provide a comprehensive diagnostic service. Most medical laboratories to which samples are referred are UKAS accredited. However, many research laboratories (including those abroad) are either not accredited or their accreditation status is unknown. The performance of referral laboratories is routinely monitored.

Where work has been done in other centres, this is made clear on our laboratory report. A list of referral laboratories is given in appendix D.
Appendix A: Guidelines on Technique of Skin Biopsy for Inherited Metabolic Disorders

When a sample of the skin is required for fibroblast culture for investigations for inherited metabolic disorders, a minor surgical procedure is undertaken in order to obtain a suitable biopsy sample. Skin biopsy taken via a punch device as detailed below is the preferred method; other methods include a shave biopsy or surgical excision. Under normal circumstances biopsies should not be taken without prior arrangement with the laboratory: Department of Newborn Screening and Biochemical Genetics, Birmingham Children’s Hospital, Tel No. 0121 333 9942.

NOTE THAT A SKIN BIOPSY IS OFTEN COLLECTED FOR HISTOLOGICAL ANALYSIS AND THAT THE SAMPLE HANDLING FOR THIS IS DIFFERENT. Please contact your local histopathology department for advice.

This procedure may be performed on the Ward, outpatients or in the operating theatre, by a trained Health care professional (any training should include the practical procedure, psychological aspects). A local anaesthetic is used when carrying out the procedure, rarely; oral sedation may also be required. An aseptic non-touch technique should be employed throughout the procedure. Consent must be obtained following BCH policy. Ensure the Skin Biopsy Consent form is signed and filed in the patient notes detailing consent to the procedure, analysis and storage of cells and asking whether patient/parents agree to subsequent storage of cells for quality control, comparison purposes and/or research. Information given should include the rationale for the biopsy, procedure and risks involved, side effects such as healing and scarring and a time line to expected results. The possibility of contamination or poor growth and repeat biopsy should be discussed where possible. Should a repeat biopsy be required referral to the play specialists may be appropriate.

Equipment
- Plastic apron
- Sterile gloves
- Sterile dressing pack
- 25 Fg needle (orange)
- 23 Fg needle (blue)
- 2 ml syringe
- A labelled skin biopsy cryotube (Obtainable from IMD laboratory Ext 9942)
- 4mm Punch Device
- Lignocaine 1%
- Local anaesthetic and appropriate covering/dressing (Ametop gel or Emla cream)
- Normal saline sachet
- ChloraPrep Sepp (Chlorhexidine 2% in 70% alcohol)
- Steristrips
- Small Mepore dressing
- Sterile scissors or scalpel blade

Sample requirements
A skin biopsy should be collected using a 4mm punch; smaller diameter punches may give insufficient sample for reliable culture. The inner sides of the forearm or posterior aspect just above the elbow are the preferred sites.
Appendix A cont’d: Guidelines on Technique of Skin Biopsy for Inherited Metabolic Disorders

Technique

- Apply local anaesthetic cream or gel to the biopsy site (following consultation with the family re allergies) and cover with appropriate dressing. Leave for a minimum of 30 minutes.1,5,6,13
- Position the child, continue to maintain the dignity of the child whilst placing them in a comfortable position with the potential biopsy area exposed. Small children/infants can lie or sit on an adult’s lap. Ensure a young child has his/her favourite cuddly toy or comforter with him/her throughout.2,13
- Prepare equipment and wash hands, put on apron and sterile gloves.4,7,10,14
- Remove local anaesthetic cream and dressing and clean any residual cream from site.5
- Sterilise the site with ChloraPrep Sepp, wait for the area to dry.7,11
- Prepare local anaesthetic withdrawing from ampoule with blue needle, inject lignocane1% using orange needle. Placement of lignocaine should be intradermally with the majority subcutaneously such that an area 1.5 x1cm is affected.14
- Wait 2-3 minutes.
- Clean area vigorously with normal saline using non woven swabs from dressing pack, and dry.
- Pull the skin tight, introduce the punch and rotate 360 degrees with the cutting edge carrying the punch down onto the tissue (the guard will prevent deep penetration).15
- Withdraw the punch whilst applying pressure to site with a non-woven swab (found in dressing pack).
- Remove specimen using sterile forceps and scissors or scalpel. Without touching the biopsy, transfer immediately into the skin biopsy cryotube. Replace the screw cap.
- Apply pressure to wound with non woven swab until cessation of bleeding
- Apply Steristrips over wound.4
- Cover with Mepore or another suitable dressing.4
- Provide family with after care instructions, including analgesic dose should this be required.4,12,13
- Dispose of equipment and waste per BCH policy.14
- Send the sample immediately to the laboratory with a fully completed request form4,11 and the lower part of the Skin Biopsy Consent form.

References

1. Olpin S. What are Biopsies, Cultures and Assays and what information do they provide? CLIMB update 2008;3:11-14
2. NMC. Professional code of conduct. April 2008.
8. BCH. Consent, Tissue and Bodily fluids policy. 2006.
9. BCH. Seeking and obtaining consent to treatment, examination and research with Children, Young People and those with “Parental Responsibility”. February 2006.
10. BCH. Policy for effective and appropriate hand hygiene. October 2006.
14. BCH. Policy for the management of risks associated with needle stick injuries and mucous membrane exposures to blood and body fluids. January 2007
APPENDIX B: Guidelines for Emergency Specimen Collection (Inherited Metabolic Disorder Suspected)

In life-threatening situations, where an inherited disorder is thought to be likely (either from family history, results of preliminary investigations or clinical presentation) appropriate specimens should be collected. At the earliest opportunity contact the metabolic laboratory duty biochemist (0121 333 9864) to discuss appropriate investigations. If possible, urine and blood specimens should be taken before death. Skin and tissue specimens, if not taken pre-mortem, should be taken as soon as possible after death. If any of the samples are taken after death it is extremely important to record accurately both the time of death and when the samples were taken. Appropriate storage as detailed below is essential. Local laboratories should make arrangements for suitable storage and transport of tissues to the specialist laboratory.

Urine
Urine, however little is extremely useful. Ideally 5-10ml should be stored. Collect into a bottle with no preservative and store deep frozen (-20°C or lower). If the specimen is contaminated with blood, centrifuge to remove cells before freezing the supernatant.

Blood
Collect 5-10ml in lithium heparin and 0.5ml in fluoride oxalate: separate the plasma as soon as possible and store the plasma deep frozen (-20°C). Store the packed red cells at +4°C (do not freeze). If DNA analysis is likely to be required, store a further 5-10ml of whole blood (EDTA) in a plastic tube at +4°C.

Skin (for fibroblast culture)
Skin taken up to 24 hours after death is likely to be viable provided it is not infected. Take a skin biopsy and place it in tissue culture medium which is available from us or a suitable transport medium (obtainable from most Virology or Cytogenetics Departments). In emergency, sterile isotonic saline can be used, but do not use agar. The specimen should be stored at +4°C before despatch. Do not freeze. See Appendix A for further details. Transport to BCH by taxi or hospital transport to reach us within 24hours of collection. Sterility is of paramount importance when taking skin biopsy specimens, especially at necropsy. Tissue culture medium and a protocol are available on request.

Tissue specimens (liver, heart muscle, skeletal muscle, duodenum)
Please ensure that these specimens are labelled with the type of tissue as well as the patient details.

Label the tubes prior to taking the specimens. Biopsies should only be taken if there is a strong clinical suspicion of a primary defect in one of these tissues. It is very important that blood and urine specimens are also taken and not just tissue specimens. Necropsy tissue specimens are suitable usually only for biochemical analysis if taken within two hours of death.

Two or three needle biopsy specimens of tissue should be taken and placed in a small plastic tube. Immediately place a small piece of plastic film over the top of the specimen to prevent the biopsy drying out, cap the tube and snap freeze in liquid nitrogen (or solid CO₂) and store in the coldest freezer available. If liquid nitrogen or solid CO₂ are not available specimens must be stored immediately in the coldest freezer available. Please note that the collection procedures for tissue for biochemical analyses are not necessarily appropriate for histological tests and your local Histopathology Department should be contacted if specimens are required for histological analysis. Please contact the IMD service before sending samples and transport frozen specimens on solid CO₂ (dry ice).

Cerebrospinal fluid
Sometimes a cerebrospinal fluid specimen may be useful. Collect a 1ml specimen. If blood stained, centrifuge and separate the supernatant. Store deep frozen.
APPENDIX C: Sudden Unexplained Deaths in Infancy (SUDI)

SUDI investigations should be carried out in all children less than 2 years of age who die suddenly and whose death is unexplained. This covers the investigation for:
- Inherited Metabolic Disorders
- Police Purposes (i.e. Forensic Laboratory and Radiology)

in children who die:
- at home
- en route/shortly after arrival at hospital
- in hospital (Coroner’s case)

Summary of Samples Required

**Blood** (heart stab) for;
**Blood culture (Pedplus/F)** – *Pedplus/F bottles* are designed to take 0.5 – 5.0 ml blood. The greater the sample volume, the more likely that bacteraemia can be detected.

**Lithium heparin specimen** (at least 0.5ml)

**Guthrie card spots** – These should ideally be prepared using fresh non-anticoagulated blood. From the syringe place 4 drops of blood directly onto a labelled neonatal screening blood test card provided in the SUDS kit.

**Urine** (bladder stab)
Place into a sterile plastic universal container. If urine is unobtainable, but the nappy is wet, place the nappy in a plastic bag, seal and label.

**Naso-pharyngeal swab** for virology
The swab should be cut off, using scissors, into a bottle of viral transport medium.

**Skin** for fibroblast culture.
See the guidelines for skin biopsy protocol (Appendix A)
At BCH, medium for skin biopsies are located in the refrigerator outside the resuscitation room in the emergency department.

**Tests carried out will be:**

**Plasma**
- acyl carnitines, quantitative amino acids

**Blood spots**
- acyl carnitines

**Urine**
- depends upon specimen volume; if >5 mL organic acids will be analysed

**Skin biopsy**
- will be banked for subsequent fibroblast culture if indicated by metabolic results; if not cultured, all biopsies are stored for 3-4 months and then discarded
APPENDIX D: Laboratories to which Tests are Routinely Referred

Addenbrookes Hospital  
Biochemical Genetics Unit  
Box 247  
Hills Road  
Cambridge, CB2 2QQ

Great Ormond Street Hospital  
Department of Chemical Pathology  
Great Ormond Street  
London  
WC1N 3JH

University College London Hospitals  
Department of Clinical Biochemistry  
60 Whitfield St  
London  
W1T 4EU

Bristol Royal Infirmary  
Department of Clinical Biochemistry  
Bristol  
BS2 8HW

University Hospital of Wales  
Department of Medical Biochemistry  
Heath Park  
Cardiff  
CF14 4XW

Kings College Hospital  
Dept of Clinical Chemistry  
Denmark Hill  
London  
SE5 9RS

Sheffield Childrens Hospital  
Department of Clinical Chemistry  
Western Bank  
Sheffield  
S10 2TH

Pole Biologie-Pathologie-Pharmacie  
Service de Virologie  
Bâtiment Jean Dausset - 6 étage, Hopital Cochin  
27 rue du Faubourg Saint Jacques  
Paris  
France

Guy's & St Thomas' Hospital,  
Purine Research Laboratory  
4th Floor  
North Wing  
Westminster Bridge Road  
London  
SE1 7EH

Academisch Medisch Centrum  
Laboratorium Genetische Metabole Ziekten  
Room FO-132A  
Meibergdreef 9  
Amsterdam  
The Netherlands

Neurometabolic Unit  
Box 105  
National Hospital (UCLH Trust)  
Queen Square  
London  
WC1N 3BG

Potsdam MVZ GbR  
Institute fuer Medizinishe Diagnostik Berlin  
Nicolaistrasse 22  
Berlin  
Germany

Southmead Hospital  
Department of Clinical Biochemistry  
Blood Sciences Laboratories  
Southmead Hospital  
Bristol  
BS10 5NB

Willink Biochemical Genetics Unit Genetic  
Medicine, 6th Floor, St Mary’s Hospital, Oxford  
Road, Manchester, M13 9WL