SHEFFIELD CHILDREN'S NHS FOUNDATION TRUST

DEPARTMENT OF CLINICAL CHEMISTRY AND NEWBORN SCREENING

USER'S HANDBOOK FOR METABOLIC INVESTIGATIONS

APRIL 2020

Do Not Use This Edition after March 2021

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Department of Clinical Chemistry and Newborn Screening

SHEFFIELD CHILDREN'S NHS FOUNDATION TRUST
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SHEFFIELD S10 2TH

Website

http://www.sheffieldlab.org.uk

Telephone numbers & enquiries

Hospital switchboard: 0114 271 7000

	Direct Telephone
Camilla Scott (Head of Department, Consultant Clinical Scientist)	2717404
Lynne Wolstenholme (PA to Camilla Scott and Professor J. Bonham)	2717318
Mr Philip Craddock – Laboratory Manager	2717444
Alison Lenthall (PA to Mr P Craddock)	2717340
Duty Clinical Scientist	Bleep No 095
(From outside the hospital please dial the switchboard and request bleep 095)	

Metabolic Section

Result enquiries	2717445 / metabolic.sch@nhs.net
Claire Hart (Principal Clinical Scientist, Metabolic Lead)	2717307
Sharon Colyer (Principal Clinical Scientist)	2717307
Louisa Ann Smith / Stephen McSweeney (Chief Biomedical Scientist)	2717445

Tissue Culture Section

Joanne Croft (Principal Clinical Scientist, Tissue Culture and Enzyme Assay Lead)	2717267
Dr Simon Olpin (Joint Head of Dept, Consultant Clinical Scientist, Tissue Culture and Enzyme Assay)	2717267
Prenatal diagnosis enquiries	2717267

Newborn Screening Section

Dr Lynette Shakespeare (Screening Lead Scientist)	2717302
Ben Sholademi (Senior Clinical Scientist)	2717346
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NORMAL LABORATORY OPENING TIMES

Monday to Friday
9:00am- 5:00pm

Outside of these hours the on-call Clinical Biochemist can be reached via the hospital switchboard.

REQUESTS FOR ANALYSES

Legible request forms (see below) must accompany all samples.
Every sample for which an analysis is required, other than those for routine newborn screening, must be accompanied by a FULLY COMPLETED laboratory request form signed by the doctor making the request and giving his/her bleep number. It is also important to include the ***time*** and ***date*** on which the sample was collected plus clinical details.

THE COMPLETION OF REQUEST FORMS

All samples including DBS samples must be accompanied by a request form (except DBS sample for Newborn Screening or DBS samples for monitoring amino acids.

All request forms *must* contain a minimum of the following essential information:

1. Full name (initials will be classed as missing information)
2. DoB (age only will be classed as missing information)
3. At least one of the following:
    - Hospital number
    - A/E or Majax number
    - NHS number
    - Clinical Genetics Family ID
4. Name of the requesting consultant (or referring laboratory)
5. Location where results are to be sent.
6. Test required.
7. Requesting hospital/location.
8. Sample type.

The following information is also *highly* desirable

9. Name of the person collecting/obtaining the sample.
10. Date & time sample(s) taken (particularly if more than one sample is likely to obtained on the same day)
11. Clinical details (full and appropriate clinical details including circumstances that may increase the risk of infection, provisional diagnosis and current drug therapy.
12. Patient's address including postcode.
13. Patient's sex.
14. Clinician's bleep number.

Clinical details and the patient's age are particularly important in requesting so that laboratory staff may:

1. Understand the reason for the request.
2. Interpret the results.
3. Consider the need for further investigations.
4. Advise and assist the clinical staff concerning the results obtained.

For urgent or telephoned requests, it is helpful to have the signature of the medical officer and the legible printed name for urgent or telephoned results.

Tests can be added verbally by telephone if the sample and form have already been received in the laboratory and there is sufficient and suitable sample for the additional test remaining.

SPECIMEN CONTAINERS

Please ensure that specimens are in suitable containers, otherwise they may be rejected for analysis.

Plasma samples – maximum **height** of the container should not exceed 55mm.
Urine samples – maximum **height** of the container should not exceed 100mm, width should not exceed 30mm.

PLEASE DO NOT SEND SAMPLES IN MICROCUPS OR TUBES WITH PUSH ON CAPS – THEY WILL NOT BE ACCEPTED.
These are a health and safety risk to us and also result in the loss of sample volume when we transfer them to an acceptable container.

Please do not use carrier tubes without the inner tube being labelled, we regard these as unlabelled samples and they will be rejected.

LABELLING OF PATHOLOGICAL SAMPLES

When collecting and labelling samples, the criteria for patient identification (outlined earlier) must be followed. **Sample and request form information *must* also be compatible**. Samples will only be accepted for analysis if minimum criteria are met. **This responsibility lies with the person collecting the sample.** Failure to meet these requirements may result in the sample being rejected.

Minimum Criteria
As defined by laboratory policy all pathological samples sent to the laboratory **must** contain a minimum of the following information:

1. Surname/family name.
2. Forename (or Baby, Twin One/Two, Triplet One/Two/Three etc, if forenames have not been given. Initials will be classed as missing information)
3. At least one of the following:

    • Date of birth (age only will be classed as missing information)
    • Hospital registration number
    • A/E or Majax number
    • NHS number

And ideally for samples being tested for patient monitoring purposes the following must also be included:

    • Date sample taken
    • Sample type

Aliquoted samples e.g. separated plasma or serum

Must contain at least **two** of the following identifiers:

- ***NHS number (****Important identifier)*
- A/E number
- Hospital registration number
- Surname/family name and forename (or Baby, Twin 1 etc, if forenames have not been given)
- Date of birth
- Requesting laboratory number

Legal Responsibilities

In signing a request form the person making the request assumes responsibility under Section 7 of the Health and Safety at Work Act and will be assumed to be familiar with its requirements in relation to danger of infection.

To fulfil these regulations you must comply with the following:

1 All samples must be in a sealed plastic bag and the request form placed in the separate compartment provided.
2 Full and appropriate clinical details and danger of infection labels on both request form and sample are required from Category 3 risk patients.
3 Samples from patients with suspected and proven HIV infection must also be enclosed in a cardboard box.
4 Data on request form may be stored on laboratory computer files. It is assumed the person completing the form has done so in accordance with the requirements of the Data Protection Act 1984.

The attention of medical staff is drawn to the warning notice printed upon each laboratory request form concerning specimens which might carry a risk of infection. The doctor completing the request should also indicate on the form if the patient has a communicable disease such as rubella, for the protection of any laboratory staff who might attend the patient.

The service provided by the laboratory is governed by the Law of England and Wales.

URGENT REQUESTS

Urgent requests must be arranged with the laboratory by telephone (0114 271 7445 / 7307) so that if there is any delay in receipt, steps can be taken to locate the sample. Ideally urgent requests should be discussed with a clinical scientist so that the appropriate action for the clinical circumstances can be planned and taken. Urgent samples which arrive in the laboratory without prior arrangement run the risk of being delayed, as they will be analysed routinely.
Out of routine hours metabolic tests are not performed.
In extreme and urgent circumstances some tests may be performed out of hours, but only after discussing with the Consultant Clinical Scientist who can be contacted via the hospital switchboard.

SPECIMEN TRANSPORT

Specimens must be sent to the laboratory contained in a transparent leak proof plastic bag. The request form must be separated from the specimen. Any label indicating a danger of infection must be shown on the request form.

Urgent samples must be arranged with this laboratory before dispatch and ***sent by courier or taxi.***

Non-urgent samples
Suitable postal or other delivery arrangements must be made by the sending laboratory. Samples must be sent direct to the laboratory; we cannot undertake to collect samples from rail stations or other collection points. Details of sample preservation and packaging are given below. Charges are detailed on pages 17-37.

Post Office regulations require that all pathological samples are sent by first class post. The use of second class letter or parcel post is specifically forbidden. Padded

envelopes used alone without a suitable inner container are not permitted. The regulations (RML 12/87) are summarised below.

1. Hazard group 4 pathogens are prohibited, other pathological specimens may be sent provided that they comply with the regulations.

2. Specimens may be sent by qualified medical, dental or veterinary practitioners, a registered nurse, a recognised laboratory or institution.

3. Members of the public may not send such specimens unless requested to do so by one of the above who must supply them with the required packaging and instructions.

4. Only first class letter or Datapost may be used.

5. There is a range of acceptable packaging but the following must be observed.

    - Every specimen must be in a primary container hermetically sealed or otherwise securely closed. The capacity of the primary container must not exceed 50 mL unless specifically permitted. The primary container must be wrapped in enough absorbent material to absorb all possible leakage, and sealed in a leakproof plastic bag.

6. The container and its immediate packaging must be placed in one of the following:

    a) a polypropylene clip-down container
    b) a cylindrical light-metal container
    c) a strong cardboard box with a full-depth lid
    d) the appropriate groove in a two piece polystyrene box, empty spaces must be filled with absorbent material, the box must be secured with self-adhesive tape.

7. A padded outer bag is recommended.

8. Soft absorbent packaging must be used between samples to prevent contact.

9. Written agreement from the Post Office is required for non-standard packaging.

10. The outer packaging must be labelled ‘PATHOLOGICAL SPECIMEN - FRAGILE WITH CARE’ with the name and address of sender.

11. Therapeutic and diagnostic materials such as blood products are accepted under the same conditions.

12. Packets found in the post which contravene the regulations will be detained and may be destroyed. Any person who sends deleterious substances without conforming to the regulations may be liable to prosecution.

Please note. Infectious pathology samples may only be transported in packaging which meets the U.N. class 6.2 specifications and the 602 packaging requirements. These new packaging requirements are described below:

BASIC TRIPLE PACKAGING SYSTEM.

The system consists of three layers as follows:

Primary receptacle
A labelled primary watertight, leak-proof receptacle containing the sample. The receptacle is wrapped in enough absorbent material to absorb all fluid in case of breakage.

Secondary receptacle
A second durable, watertight, leak-proof receptacle to enclose and protect the primary receptacle(s). Several wrapped primary receptacles may be placed in one secondary receptacle. Sufficient additional absorbent material must be used to cushion multiple primary receptacles.

Outer shipping package
The secondary receptacle is placed in an outer shipping package which protects it and its contents from outside influences such as physical damage and water while in transit.

Information concerning the sample, such as data forms, letters and other types of information that identify or describe the sample and the identity of the shipper and receiver should be taped to the outside of the secondary receptacle.

Newborn Screening Dried Blood Spot (Guthrie) Cards

By common consent these regulations are deemed inappropriate for dried blood specimens on Newborn Screening (Guthrie) cards. The blood spots should be allowed to **dry thoroughly before packing** the card placed in the transparent paper (Glassine) envelope provided (not plastic as this may cause the specimen to “sweat”) and sent, by first class post, in a stout envelope as if it were a normal letter or in a newborn screening pre paid envelope according to local arrangements.

Please accompany all dried blood spot samples other than those for routine newborn screening, for instance those for acylcarnitine analysis, with a fully completed laboratory request form.

Tissue Culture

For skin biopsies sent from external hospitals within the Trent Inherited Metabolic Disease Group a request form with full clinical details and test request is required. Sample transport at room temperature, normal first class post to Clinical Chemistry Department to arrive ideally no later than 4.30pm Mon – Fri. Please contact laboratory if sample to arrive on the weekend (0114 271 7445 or 271 7267).

For skin biopsies sent from external hospitals outside the Trent Inherited Metabolic Disease Group, please contact the Tissue Culture laboratory prior to sample collection to discuss sample collection details and turnaround times. A request form with full clinical details and test request is required.

Please note turnaround times (TAT) are flexible when applied to cultured cell assays. As different patient cell lines grow at different rates. In general for most assays starting from a skin biopsy the TAT is 8-12 weeks

Sample Storage

With the exception of post mortem dried blood sample and bile samples, samples will only be stored for a maximum of 6 months before being discarded, unless (from the laboratory's perspective) the results from the sample have contributed to diagnosis.

Post Mortem DBS and bile samples

Please note that all samples taken at post mortem for dried blood spots and bile analysis, usually for acylcarnitines, will be returned to the originating laboratory along with the analytical report. Samples can then be stored or destroyed depending on the circumstances of the specific case. This change in protocol came into effect on 01.01.16.

SPECIALISED SERVICES

Investigation of Inborn Errors of Metabolism

A service is provided for the detection, diagnosis and monitoring of patients with inborn errors of metabolism. Analyses performed include (full details are found in the table starting on page 17):

Acylcarnitine profile (includes free carnitine)
Amino acids
Bile Salts
Biotinidase
Cholestanol
Collagen Cross Links
7 and 8 Dehydrocholesterol
Dimethylglycine
Ethylmalonic acid (quantitative)
Free fatty acids
Galactitol
Galactosaemia Screen
2-hydroxyglutaric acid chirality (D or L)
Glycosaminoglycans (screen and electrophoresis)
Hexanoylglycine (quantitative)
Homocysteine (total)
Homocystine (free)
HVA/VMA (quantitative)
3-hydroxybutyrate
Isovalerylglycine (quantitative)
Lactate (CSF)
Methylmalonate (quantitative)
Organic acids
Orotic acid (quantitative)
Phenylalanine
Phytanic acid
Phytosterols
Pipecolic Acid
Plasmalogens (C_{16} and C_{18})
Pristanic Acid
Sulphocysteine
Trimethylamine and oxide (Fish Odour Syndrome)
Very long chain fatty acids

Qualitative urine screening tests for glucose, reducing substances, cystine and homocystine, are also available.

It is important that requests for the investigation of inborn errors of metabolism are accompanied by adequate clinical information including drugs being taken at the time of sampling. If the relevant clinical information is detailed, the laboratory should be contacted by letter or telephone.

Further investigation of some disorders requires the use of cultured fibroblasts. The following are routinely available:-

- Screen for disorders of long-or medium-chain fatty acid oxidation This screen will detect defects of carnitine transport and deficiency of carnitine-palmitoyltransferase types 1 and 2, carnitine acylcarnitine translocase deficiency, very-long- or medium-chain acyl-CoA dehydrogenases, long-chain 3-hydroxyacyl-CoA dehydrogenase and other disorders of the trifunctional enzyme complex and mild to severe multiple acyl-CoA dehydrogenation defects (ethylmalonic-adipic aciduria and glutaric aciduria type 2).

* Carnitine-acylcarnitine translocase
* Glutaryl-CoA dehydrogenase (for glutaric aciduria type 1)
* Palmitoyl carnitine transferase Type I and II
* Propionyl-CoA carboxylase (for propionic acidaemia)
* Pyruvate Carboxylase
* 3-Methylcrotonyl-CoA carboxylase
* Release of $^{14}CO_2$ or ^{14}C-incorporation from various substrates for the detection of isovaleric acidaemia, MSUD and other disorders
* Very long-chain fatty acids

Enquire for disorders not listed.

In general the laboratory will advise on the need for tissue based assays and make the necessary preliminary arrangements.

Pre-natal Diagnoses

Prenatal diagnosis may be performed in a variety of ways:

* Metabolite analysis on amniotic fluid (or occasionally chorionic villus or cultured fetal cells). We currently provide metabolite analyses for the diagnosis of Smith Lemli Opitz Syndrome.

* Enzyme assay on chorionic villus (fresh or cultured) or cultured amniotic fluid cells. Most of the assays listed above for fibroblasts can be used with cultured amniotic fluid cells or chorionic villus material.

* DNA analysis

Prenatal diagnosis for other disorders is usually available in the UK but some conditions will require samples to be sent overseas.

Careful consideration of the technical aspects (timing, material and route, time of result and reliability) is an essential part of preparatory counselling and prenatal diagnosis should be arranged well in advance if possible. Reliable prenatal diagnoses requires that the initial diagnosis has been clearly established and it is important to appreciate the need for rigorous investigation even when the index case presents in a terminal phase with little hope of useful intervention.

Newborn Screening

The screening laboratory in Sheffield covers all babies born in the East Midlands SHA, South Yorkshire and South Humberside portion of the Yorkshire and Humber SHA (Derbyshire, Leicestershire, Lincolnshire, Northamptonshire, Nottinghamshire, Rutland, and South Yorkshire). Testing is for phenylketonuria (phenylalanine), congenital hypothyroidism (TSH), cystic fibrosis (immunoreactive trypsin), medium chain acyl CoA dehydrogenase deficiency (octanoylcarnitine), sickle cell disorders (haemoglobin profile), maple syrup urine disease (leucine), homocystinuria (methionine), isovaleric acidaemia (isovalerylcarnitine) and glutaric aciduria type 1 (glutarylcarnitine).

Dried blood spot samples are collected on day 5 of life (day of birth is day 0). Results are sent out to the appropriate Child Health Records Department for entry into the Child Health Records Computer and checking against birth lists screen.
This service is largely separate from the routine analytical services offered in the hospital and in general it is NOT appropriate to enquire directly of the Newborn Screening Laboratory for a test result. If an abnormal result has been found then, as soon as it has been confirmed, the patient's Family Practitioner and designated clinician for that disorder will have been informed. **If you have clinical suspicion of hypothyroidism it is better to initiate your own investigations since the neonatal test is only a screening assay and in any case will not detect secondary hypothyroidism. Similarly, suspicion of MCADD, MSUD, GA1 and IVA should always be vigorously pursued in the newborn period and separate investigations (including urinary organic acid analysis and acyl carnitine profile) are indicated. Please bleep the duty biochemist if further advice on relevant investigations is required. Please note, Immunoreactive trypsin is not always abnormal in cystic fibrosis patients with meconium ileus.**

Reference (normal) ranges

Reference ranges are provided for guidance in clinical decision making, rather than for prescriptive use. They are conventionally set to give the range of values which would be found in approximately 95% of a 'normal' population. They are derived from results obtained by this Department and from other sources. Reference ranges for blood refer to serum or plasma samples unless stated otherwise.

Changes during growth and development create age-related reference ranges for most analytes. Detailed ranges are kept in the Department and information upon them may be obtained from one of the Duty Clinical Scientists.

For the day to day interpretation of results age-related reference ranges have been condensed to cover generally recognised stages of development. These are generally printed automatically by the laboratory computer when the result is generated.

Newborn: First 7 days of life for term baby.

Neonate: First month of life for a term baby. Ranges may not apply to pre-term or small-for-dates babies.

Infant: Normally from the second month to one year, neonates are included in these ranges if not separately quoted.

Child: Normally one year to adolescence, neonates and infants are included in these ranges if not separately quoted.

Adult: From the end of adolescence

Accuracy and Imprecision (Uncertainty of Measurement) of Results

These are monitored and controlled by our quality assurance procedures. When patients are being repeatedly tested the significance of any apparent change in their results depends upon many factors including biological variability (intrapersonal variation) and the imprecision with which an analysis is performed (analytical variation). To aid in the interpretation of consecutive results imprecision data can be generated from laboratory quality control data, which can then be used to determine whether two results are significantly different, or within the bounds of analytical variation.
As a first approximation a result has a 95% probability (using a level of $p< 0.05$) of being genuinely different from a previous result for the same patient if the results differ by more than the quoted imprecision (2.8 times the analytical standard deviation).

For example:

Plasma urea result on day 1 = 6.0 mmol/L

Plasma urea result on day 2 = 6.8 mmol/L

Difference (day 2- day 1) = 0.8 mmol/L

Imprecision estimate for Urea = 0.84 mmol/L

Because the difference between the two results is less than the imprecision estimate there is a less than 5% chance that these results are statistically different. Of course, even if there is a significant analytical change between consecutive results this may well be within expected biological variation and consequently have little significance for the patient. It should be noted that analytical imprecision is not constant over the reportable range. Should you wish to discuss the significance of results further please contact the Clinical Scientist (Bleep 095).

TURNAROUND TIMES

Turnaround times for each assay are given in the table of analytes (page 18). Occasionally TATs may be delayed following a bank holiday or other exceptional circumstances but we aim for 95% of samples to be analysed within the stated TAT or less. This is monitored on a quarterly basis and remedial action taken when it is not achieved. While the TAT given represents the standard time taken to analyse a sample and produce a result we will always do our best to obtain a more timely result when analysis is urgent clinically or a specific diagnosis strongly suspected. Should this be the case please contact the Duty Biochemist or a Metabolic Section Clinical Scientist to discuss your needs.

If an assay is withdrawn or unavailable for any reason, or we expect any significant delay in the usual turnaround time, we will notify users of the service as soon as possible.

QUALITY ASSURANCE

The Department participates in national and international external quality assurance schemes to monitor the accuracy and precision of its analyses. Internal quality control is used to check the validity of results on a day to day basis.

It is important that the laboratory be informed at once if results appear inconsistent with a patient's condition or are at variance with previous results.

External Quality Assurance Schemes:

The laboratory's policy is to participate in ISO 17043 accredited schemes wherever they are available. However the reality is that for most of the specialist metabolic assays no such scheme exists. The majority of our assays are covered by schemes offered by ERNDIM (European Research Network for evaluation and improvement of Diagnosis in IEMs) which is a European wide collaborative project to provide EQA material for esoteric assays. ERNDIM is internationally recognised as a quality provider of EQA schemes and is working towards ISO 17043 accreditation.

The Metabolic Section participates in the following EQA Schemes:

EQA Scheme	Assays Covered
UKNEQAS Urinary Catecholamines	VMA/HVA
UKNEQAS Quantitative Amino Acids	Phenylalanine,Tyrosine, Branched Chain Amino Acids
ERNDIM Quantitative Amino Acids	All amino acids
ERNDIM Special Assays in DBS	Free carnitine, phenylalanine, tyrosine, valine, leucine, isoleucine, methionine
ERNDIM Acylcarnitines in serum (quantitative)	Acylcarnitines including free carnitine
ERNDIM Acylcarnitines in DBS (qualitative)	Acylcarnitines with emphasis on diagnosis / interpretation
ERNDIM Quantitative Organic Acids in Urine	MMA, EMA, Isovalerylglycine, Hexanoylglycine
ERNDIM Special Assays in Urine	Free carnitine, orotic acid, GAGs, VMA / HVA, pipecolic acid, sulphocysteine, galactitol
ERNDIM Special Assays in Serum	FFA and 3-hydroxybutyrate, VLCFA, phytanate, pristanate, 7-dehydrocholesterol, total homocysteine, cholestanol, pipecolic acid
ERNDIM Qualitative Organic Acids	Qualitative Organic Acid profile
ERNDIM MPS Scheme	Quantitative / Qualitative analysis for MPS disorders (GAG/ creat ratio and GAG electrophoresis)
ERNDIM Diagnostic Proficiency Scheme	Test of laboratory's overall ability to apply the correct tests to a sample given clinical details and to correctly ascertain the diagnosis.

There are a number of assays for which no EQA scheme exists. The following assays are covered by sample exchange schemes with other laboratories in the UK or internationally.

Trimethylamine
Biotinidase
Galactosaemia screen
Plasmalogens
Phytosterols

There are two assays which currently have no EQA scheme and no sample exchange scheme;

1. Urinary collagen cross-links –Previous EQA scheme now defunct, in preliminary phase of agreeing sample exchange with another UK laboratory.
2. Bile Acids – no other UK provider. Currently seeking other labs in Europe.

We assure quality for both assays by running regular iQC samples and a positive (affected patient) control is run with every batch of collagen cross links. Bile acid results can be compared with known affected patients and results can be correlated with the results of other complementary assays.

Where poor performance on an EQA scheme occurs we undertake to inform any affected users in a timely fashion.

A-Z TEST LIST (Metabolic Section)

Abbreviations:

CDPX2	Chondrodysplasia punctata (X-linked)
CTX	Cerebrotendinous Xanthomatosis
DBS	Dried blood spot
EMA	Ethylmalonic Acid
GAG	Glycosaminoglycan
GA1	Glutaric Aciduria Type 1
GA2	Glutaric Aciduria Type 2 (aka MADD)
HHH Syndrome	Hyperammonaemia, hyperornithinaemia and homocitrullinuria syndrome
HVA	Homovanillic acid
IVA	Isovaleric Acidaemia
IEM	Inborn error of metabolism
LiHep	Lithium heparin
MADD	Multiple AcylCoA dehydrogenase deficiency (aka GA2)
MCADD	Medium chain AcylCoA dehydrogenase deficiency
MMA	Methylmalonic aciduria (also methylmalonic acid)
MPS	Mucopolysaccharide disorder
NKH	Non-ketotic hyperglycinaemia
PA	Propionic Acidaemia
PDE	Pyridoxine Dependent Epilepsy
RCDP	Rhizomelic chondrodysplasia punctata
SCAD	Short chain AcylCoA dehydrogenase deficiency
SLO	Smith Lemli Opitz Syndrome
VMA	Vanilylmandelic acid
VLCFA	Very long chain fatty acids
X-ALD	X-linked adrenoleukodystrophy

Our UKAS Schedule of Accreditation can be found by entering our accreditation number (10139) on the search page of the UKAS website. The schedule includes information on methodology / equipment used.
https://www.ukas.com/search-accredited-organisations/

All tests listed below are within the scope of accreditation except for the following highly specialised and rarely performed assays;

- **2-hydroxyglutarate chirality**
- **Hair Amino Acids**
- **Methylmalonic acid in amniotic fluid**

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Acylcarnitine profile (including Free Carnitine) – Plasma	For the diagnosis of fatty acid oxidation disorders & some organic acidaemias including but not limited to; Primary Carnitine deficiency, SCADD, MCADD, MADD (GA2), VLCADD, CPT2, CPT1, LCHADD, PA, MMA, b-ketothiolase, IVA, 3HMGCoA-lyase deficiency, Biotinidase deficiency, GA1, Malonic aciduria	LiHep plasma 0.5ml (0.1) Serum and fluoride can also be used but NOT EDTA	Store at -20C, Send first class post	Free Carnitine = 15-53 µmol/L All other ranges given on report where relevant.	5-14 days	**PLASMA is the preferred sample type except for ?CPT1 when a DBS may be the best sample type**	£72.78 (£57.67)
Acylcarnitine profile (including Free Carnitine) -DBS	As above	Guthrie card, 2 full spots MUST be sent with a request form	Send by first class post	Free Carnitine = 5-35 µmol/L All other ranges given on report where relevant.	5-14 days	**ALWAYS treat Guthrie card as if it is a sample container and send a completed REQUEST FORM with it.** **DO NOT send to Newborn Screening lab**	£72.78 (£57.67)
Acylcarnitine profile - DBS (POST MORTEM)	As above	Guthrie card, 2 full spots	Send first class post	Reference Ranges and Interpretation given on report as relevant.	4-6 weeks		£72.78 (£57.67)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Acylcarnitine profile - Bile (POST MORTEM)	As above	Guthrie card, 2 full spots	Send first class post	Reference Ranges and Interpretation given on report as relevant.	4-6 weeks		£72.78 (£57.67)
Amino Acids -Plasma	For the diagnosis of amino acid and urea cycle disorders	Lithium heparin plasma 0.5 ml (0.15)	Store at -20, Send by first class post.	Reference ranges vary by age and are provided with report – contact lab for separate summary document if required.	5-14 days		Full quantitation £87.69 Part quantitation £62.82
Amino Acids – Blood Spots	For monitoring of select patients receiving dietary treatment for specific IEMs. Contact lab.	Guthrie card, 2 full spots.	Send by first class post.	N/A	5-14 days		£62.82
Amino Acids – CSF (paired with plasma)	Diagnosis of NKH (non-ketotic hyperglycinaemia) and the Serine synthesis disorders.	CSF sample in plain tube 0.5ml (0.15) Unsuitable if bloodstained	Store at -20 Send by first class post.	Interpretation given on report	5-14 days	Requires a **PAIRED** plasma sample to be sent with the CSF sample (for these purposes a sample taken within a few hours is sufficient)	£87.69
Amino Acids- Hair	For the diagnosis of **Trichothiodystrophy** syndrome only	50mg of hair (a small lock)	Send by first class post	Interpretation provided with report	2 months	This assay is very rarely carried out – please contact laboratory before sending a sample	£203.75 (£101.67)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Amino Acids – Urine (SCREEN)	Basic screen for a variety of amino acid disorders but not suitable if an amino acid / urea cycle disorder is being seriously considered.	10ml (2ml) random urine or aliquot from 24 hour urine collection (no preservative)	Store at -20 Send by first class post	Qualitative	3-6 weeks	Includes reducing substances, CNNP and dipstix tests. Please include information on current therapy	£68.25
Amino Acids – Urine (QUANTITATIVE)	Most amino acid disorders are better diagnosed by a plasma sample however urine analysis is essential for the diagnosis of Cystinuria, Hartnup's, HHH syndrome, Lysinuric Protein Intolerance and Prolidase deficiency.	5 ml aliquot in plain container Very dilute or deteriorated samples (Creat <0.8 mmol/L, nitrite positive) may not be analysed.	Store at -20 Send by first class post	Reference ranges vary by age and are provided with report – contact lab for separate summary document if required.	21 days	Diagnosis of **Prolidase Deficiency** requires analysis pre and post acid hydrolysis of a urine sample. Please contact lab to discuss if being considered as a diagnosis.	Full quantitation £87.69 Part quantitation £62.82
Bile Salts / Acids - Plasma	For the diagnosis of the primary bile acid biosynthesis disorders, for further investigations of probable Peroxisomal disorders, and for diagnosis of Cerebrotendinous Xanthomatosis (specific bile alcohols, see also entry for Cholestanol)	LiHep plasma 0.5ml	Store at -20 Send by first class post	Interpretation provided with report	3-6 weeks	**NOT** for the diagnosis of **cholestasis of pregnancy** 4 primary bile salts are quantitatively measured with additional qualitative analysis looking for the presence of abnormal bile acid / salt intermediates	£72.78 (£57.67)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Bile Salts/Acids- Urine	As above	2ml urine	Store at -20 Send by first class post	Interpretation provided with report	3-6 weeks	As above	£72.78 (£57.67)
Biotinidase	Diagnosis of Biotinidase Deficiency	Lithium heparin plasma 0.5ml (0.1)	Store at -20 Send by first class post	u/L Child/adult 2.5 – 10.5	5-14 days	Patients with Biotinidase deficiency may also show abnormalities in organic acid and acylcarnitine profiles but this can be variable	£56.64
Carnitine (Free) – see acylcarnitine profile	-	-	-	-	-	-	-
Carnitine (Free) – Paired PLASMA and URINE	For the diagnosis of **Primary Carnitine Deficiency** (also known as Carnitine transporter deficiency) ONLY	1ml urine 0.5ml LiHep plasma (paired)	Store at -20 Send by first class post	Interpretation given with report (normal is typically >98%)	5-14 days	Fractional tubular reabsorption of free carnitine is calculated. Please take samples BEFORE giving the patient carnitine if at all possible.	£72.78 (£57.67)
Catecholamine metabolites - see VMA /HVA	-	-	-	-	-	-	-
Cholestanol	For the diagnosis of Cerebrotendinous Xanthomatosis (CTX)	Lithium heparin plasma or serum 1ml (0.3)	Store at -20 Send by first class post	µmol/L 3-16	3-6 weeks	The bile alcohols associated with CTX (cholestane-tetrol-glucuronide, cholestane-pentol-glucuronide, cholestane-hexol-glucuronide) can be detected by the Bile Acids/ Salts test	£99.41 (£49.76)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Collagen Cross-links (pyridinoline / deoxypyridinoline)	For the diagnosis of PLOD 1 Defects / Ehlers-Danlos Type VI (also known as Kyphoscoliotic ED) only	Urine, fresh sample in plain container, **protect from light** 1ml (min)	Store at -20 Send by first class post	Interpretation given with report	6-8 weeks		£103.73
Cystine –Urine (includes lysine, ornithine, arginine)	For the diagnosis of Cystinuria (renal stones).	Urine 5 ml aliquot in plain container	Store at -20 Send by first class post	Interpretation given with report	21 days	Analysis is the same as urine quantitative amino acids	£62.82
7-Dehydrocholesterol	For the diagnosis of Smith-Lemli-Opitz syndrome (and other disorders of sterol metabolism via sterol profile)	Lithium heparin plasma 1 ml (0.3)	Store at -20 Send by first class post	µmol/L Reference range < 2 Affected range >5	3-6 weeks	Includes quantitative measurement of 8-dehydrocholesterol and cholesterol. Also includes a full sterol profile which can detect the presence of **Desmosterol**, **Lathosterol, Lanosterol, 8,(9)-cholestenol, and the 4-methyl-sterols**	£99.41 (£49.76)
7-Dehydrocholesterol – Amniotic fluid	For prenatal diagnosis of Smith-Lemli-Opitz syndrome	10 ml Amniotic fluid for prenatal diagnosis- (contact lab prior to collection)	Contact laboratory prior to collection of sample	Interpretation given on report	N/A	**MUST** contact laboratory prior to taking a sample to arrange analysis. Please provide information on proband.	Amniotic fluid £385.50 (£193.57)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
8-Dehydrocholesterol	Secondary metabolite in SLO, primary metabolite in diagnosis of Conradi-Hunermann-Happle (X-linked Chondrodysplasia punctata, CDPX2).	Lithium heparin plasma 1 ml (0.3)	Store at -20 Send by first class post	µmol/L Reference range <3	3-6 weeks	Includes quantitative measurement of 8-dehydrocholesterol and cholesterol. Also includes a full sterol profile which can detect the presence of **Desmosterol**, **Lathosterol, Lanosterol, 8,(9)-cholestenol, and the 4-methyl-sterols**	£99.41 (£49.76)
Dimethylglycine	Diagnosis of Dimethylglycinuria (alternative but extremely rare cause of fish odour like syndrome). Also used for monitoring of treatment in Glutaric Aciduria Type 2 and betaine therapy.	Urine 2ml aliquot in a plain container.	Store at -20 Send by first class post	Interpretation given with report	3-6 weeks		£53.97 (£27.34)
Ethylmalonic acid	Confirmation of diagnosis / monitoring of SCAD deficiency or other disorders with elevated EMA.	Urine 5ml aliquot in a plain container	Store at -20 Send by first class post	µmol/mmol creatinine Reference range <15	5-14 days		£77.00 (£39.06)
Fish Odour Syndrome – see Trimethylaminuria	-	-	-	-	-	-	-

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Free fatty acids	See Intermediary metabolites	-	-	-	-	-	-
Galactitol	For the diagnosis of Classical Galactosaemia, Galactosaemia due to UDP-galactose epimerase deficiency, and Galactokinase deficiency.	Urine 2ml in plain container	Store at -20 Send by first class post	Interpretation given with report	5-14 days	First line test for Galactokinase deficiency. Alternative test for galactosaemia when patient has been transfused in previous 3 months. Results will be less abnormal if patient on galactose free diet.	£97.87 (£49.76)
Galactosaemia screen – Whole Blood	Screening test for diagnosis of Classical Galactosaemia (Galactose-1-phosphate uridyl transferase deficiency only)	LiHep whole blood 0.5ml (0.1) Do not separate (although the remaining red cell pellet left after plasma has been removed can be used) **(EDTA samples not accepted)**	Store in fridge, send by first class post	Qualitative. Normal samples fluoresce after 1 hr of incubation with substrate, failure to fluoresce after 4 hrs incubation indicates Galactoasemia (fluorescence at intermediate times can be due to sample deterioration or variant / mild forms).	1 week	The test is a quick screening rest for Galactosaemia, it is not fully diagnostic (which requires qualitative enzyme assay and galactose-1-phosphate measurement) **Test not valid if there has been a transfusion in the previous 3 months**. In this circumstance send urine for **GALACTITOL**	£38.55
Galactosaemia screen - DBS	As above	2 full spots on Guthrie card	Store at room temperature send by first	As above	1 week	As above	£38.55

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
			class post.				
Galactose-1-phosphate uridyl transferase – see Galactosaemia Screen	-	-	-	-	-	-	-
Glycine – Plasma (see Plasma Amino acids)	-	-	-	-	-	-	-
Glycine –CSF (see CSF amino acids)	-Diagnosis of NKH (non-ketotic hyperglycinaemia)	-	-	-	-	-	-
Glycosaminoglycans (GAGs)	Screening test for Mucopolysaccharide disorders (Hurler, Huler-Scheie, Hunter, Sanfilippo, Morquio, Maroteaux-Lamy, Sly)	Urine 10 mls random sample (no preservative) Dilute (creat <1.0mmol/L) or deteriorated samples (nitrite/protein positive) are not processed	Store at -20 Send by first class post	µmol/mmol creatinine 0-4 w 22.1-40.8 1-3 m 9.2-38.8 3-6m 11.9-34.5 6-12m 4.2-30.5 1-2y 6.8-21.7 2-3y 9.7-19.5 3-5y 6.2-15.4 5-7y 6.2-12.1 7-9y. 4.1-10.8 9-11y. 4.5-10.8 11-13y 2.8-10.4 13-15y 2.0-7.6 >15 y 1.7-4.4	5-14 days	A normal result cannot rule out an MPS disorder. If an MPS disorder is seriously considered clinically then GAG electrophoresis is required as a minimum.	Included in organic acid / urine amino acid screen.
Hexanoylglycine	Primarily used for confirmation / rule out in MCAD screening. May have value in	Urine 2 mls random sample (no preservative)	Store at -20 Send by first class post	µmol/mmol creatinine 0.1-1.1	5-14 days	Lab **MUST** be contacted before sending sample	£173.22 (£87.17)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
	other circumstances.						
HMMA (see HVA / VMA)	-	-	-	-	-	-	-
Homocysteine (Total)	For diagnosis and monitoring of Classical Homocystinuria and other disorders of homocysteine metabolism such the remethylation defects and cobalamin metabolism disorders	Lithium heparin or EDTA Plasma Fasting sample (overnight) Collect 3mls blood spin and separate from cells within 60 minutes	Store at -20 Send by first class post	µmol/L Child/adult Male 0-18 Female 0-16	5-14 days	This is the most sensitive test for "homocystinuria" –urine testing is inadequate due to high renal threshold causing low sensitivity.	£38.55
Homocystine (free)	For diagnosis of Classical homocystinuria – **HOWEVER this is not the recommended test- please send plasma sample for Total Homocysteine**	Urine 5 ml aliquot in plain container	Store at -20 Send by first class post	µmol/mmol creatinine Result on report	21 days	In theory free homocysteine can be detected in urine (in the quantitative urine amino acid profile) – however because of a high renal threshold and a tendency to stick to protein the amount detectable in urine is very low in comparison to total body burden. It is a very insensitive test.	£62.82
HVA (see VMA / HVA)	-	-	-	-	-	-	-
3-Hydroxy Butyrate	See intermediary metabolites	-	-	-	-	-	-

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
2-Hydroxy Glutaric Acid Chirality (D or L)	To differentiate between L-2-hydroxyglutaric aciduria and D-2-hydroxyglutaric aciduria	Urine 5 ml aliquot in plain container	Store at -20 Send by first class post	Qualitative. Interpretation given with report.	3-6 weeks	Please send sample with organic acid profile showing elevated excretion of 2-hydroxy glutaric acid (or request us to do OA analysis first)	£413.87 (£206.94)
Intermediary Metabolites	Includes glucose, lactate, free fatty acids and 3-hydroxybutyrate.	Fluoride plasma sample 0.5ml	Send by first class post	Results for FFA and 3-OHbutyrate can only be interpreted in context of each other and glucose result. Therefore no ranges are provided for these parameters. Interpretation given on report	1 week	Part of fasting hypoglycaemia screen. Follow emergency protocol below: Take 2 ml blood in fluoride heparin and **obtain the first urine sample passed** for organic acid analysis.	£56.64 for full profile. Free fatty acids or 3-hydroxybutyrate individually are £18.71 each
Lactate (CSF)		CSF Fluoride bottle, 0.2ml	Send by first class post	Neonate <3.0mmol/L Child 0.9-1.8 mmol/L Adult 0.6-2.4 mmol/L	1 week	CSF lactate may be clearly abnormal in some patients with mitochondrial disorders even when plasma is normal / borderline.	£19.22
Methylmalonic Acid – Amniotic Fluid	For prenatal diagnosis later in pregnancy for the purposes of knowing that a baby is affected before birth so that appropriate	Amniotic Fluid-**CONTACT LAB TO DISCUSS BEFORE SENDING**	**CONTACT LAB TO DISCUSS**	Interpretation given with report	N/A	**MUST CONTACT LAB TO DISCUSS** Prenatal diagnosis for MMA by the measurement of MMA in amniotic fluid is now	£385.50 (£193.57)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
	plans can be put in place.					very rarely done and where a termination is being contemplated we would recommend mutational analysis.	
Methylmalonic Acid - Urine	For diagnosis and monitoring of patients with methylmalonic aciduria, Cobalamin defects or Vitamin B12 deficiency	Urine 5-10ml (1.0) aliquot in plain container	Store at -20 Send by first class post	µmol/mmol creatinine Child 1-8 Adult 0.2-2.4	14-21 days		£77.00 (£39.06)
Mucopoly-saccharides – GAG electrophoresis	Screening test for Mucopolysaccharide disorders (Hurler, Huler-Scheie, Hunter, Sanfilippo, Morquio, Maroteaux-Lamy, Sly)	Urine 10ml aliquot in plain container **Very dilute (creatinine <0.8) and deteriorated samples (nitrite/protein positive) are not analysed.**	Store at -20 Send by first class post	Qualitative. Interpretation given with report.	6-8 weeks	Can identify vast majority of patients with MPS and narrow down which disorder but final confirmation requires enzyme assay	£113.39
Organic Acids	For the diagnosis of or as a pointer to diagnosis in a wide range of IEMs, including but not limited to classic organic acidurias (MMA, PA, IVA), b-ketothiolase, fumarate	Urine 10ml aliquot in a plain container. DO NOT USE BORIC ACID PRESERVATIVE	Store at -20 Send by first class post	Qualitative. Interpretation given with report.	5-14 days	Given the number of disorders that can be diagnosed by organic acid analysis it is particularly important that clinical details or information on which particular disorder is suspected (where	£97.35 (£48.73)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
	hydratase, malonic aciduria, mevalonate kinase def, GA1, 3-HMGCoA-lyase def, biotinidase deficiency, some amino acid disorders including Tyrosinaemia type1, fatty acid oxidation disorders, some urea cycle disorders (raised orotic acid), pyroglutamic aciduria (secondary and primary) etc					relevant) is provided in order to aid interpretation, tailor report and include appropriate caveats. If you are not sure if the disorder under consideration is covered by OA analysis please contact that lab to discuss.	
Orotic Acid	For diagnosis and monitoring of patients with urea cycle disorders or hereditary orotic aciduria.	Urine 10ml aliquot in plain container	Store at -20 Send by first class post	µmol/mmol creatinine Infant/child/adult < 3.5	5-14 days	Orotic acid can be detected in urine organic acid profile but the quantitative test is more sensitive and allows comparison between samples.	£82.86 (£41.74)
Phenylalanine – Plasma (see Plasma Amino Acids)	-	-	-	-	-	-	-
Phenylalanine –Blood spot	For monitoring of known patients only – please contact lab.	-	-	-	-	-	-
Phosphoethanolamine	For the diagnosis of Hypophosphotasia	Urine 5 ml aliquot in plain container	Store at -20 Send by first class post	µmol/mmol creatinine “Normal range” is <10 but results above this are not necessarily	21 days		£62.82

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
				significant depending on age /context. Interpretation given with report			
Phytanate – see VLCFA	-	-	-	-	-	-	-
Phytosterols	For the diagnosis of Phytosterolaemia / Sitosterolaemia. Includes the measurement of **campesterol, stigmasterol and sitosterol.**	Lithium heparin plasma or serum 1ml (0.3)	Store at -20 Send by first class post	Campesterol: 0-13 µmol/L Stigmasterol: 0-4 µmol/L Sitosterol: 0-29 µmol/L	3-6 weeks		£99.41 (£49.76)
Pipecolic Acid –CSF	For the diagnosis of **Pyridoxine Dependent Epilepsy (Antiquitin deficiency).** Also used for further investigation of patients with probable **Peroxisomal disorders**	CSF 0.5ml (0.2)	Store at -20 Send by first class post	0.009 – 0.12 µmol/L	3-6 weeks	Please indicate on request form whether querying PDE or Peroxisomal disorder. For the diagnosis of PDE CSF is the best sample type, followed by plasma and then urine. For peroxisomal disorders plasma samples suffice.	£173.22 (£87.17)
Pipecolic Acid - Plasma	As above	Lithium heparin/EDTA Plasma or serum 0.5ml (0.2)	Store at -20 Send by first class post	< 10.8 µmol/L (<1 week old) < 2.46 µmol/L (>1 week old)	3-6 weeks	As above	£173.22 (£87.17)

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Pipecolic Acid -Urine	As above	Urine 5 ml (1ml)	Store at -20 Send by first class post	0.55 – 24.1 µmol/mmol creat (<6 months old) 0.01 – 1.54 µmol/mmol creat (>6 months old)	3-6 weeks	As above	£173.22 (£87.17)
Plasmalogens	For confirmation of diagnosis / further characterisation of patients with probable Peroxisomal Biogenesis disorders or Rhizomelic Chondrodysplasia Punctata (RCDP)	Red blood cell pellet 2 mls EDTA red blood cells, spin and take off plasma (including buffy coat), wash x3 with equal volume normal saline	Store at -20 (washed RBC only) and send frozen (dry ice). Can send by first class post if will arrive day after sample taken (in which case do not freeze)	Interpretation given with report.	3-6 weeks	Please provide information on clinical context and information on VLCFA results in order to facilitate appropriate interpretation.	£173.22 (£87.17)
Pristanate – see VLCFA	-	-	-	-	-	-	-
Sitosterols – see phytosterols	-	-	-	-	-	-	-
Sterols – see 7-dehydrocholesterol, 8-dehydrocholesterol, cholestanol or phytosterols as appropriate	-	-	-	-	-	-	-
Sulphocysteine (this replaces the urine sulphite test)	For the diagnosis of Sulphite Oxidase or Molybdenum Cofactor deficiency	Urine, no preservative, 5ml (1ml)	Store at -20 Send by first class post	µmol/mmol creatinine Ref range <10	3-6 weeks	If diagnosis is strongly suspected in a newborn please contact lab to request urgent analysis.	£77.00

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
Trimethylamine	Diagnosis of Fish Odour Syndrome, also known as Trimethylaminuria, (FMO3 gene defect)	Urine 10 aliquot of acidified (HCl) 24 hour collection or 10 ml random urine acidified to pH 2 with HCl prior to dispatch. **Please note nitrite positive samples will not be analysed.**	Store at -80 Send by first class post	Free TMA/ creat ratio: < 7.7 µmol/mmol crt TMA-N-Oxide / creat ratio: < 119 µmol/mmol crt % N-Oxidation: > 94% Additionally interpretation will be given with report	6-8 weeks	TMAU is associated with ingestion of certain foods so it is important to collect this sample at the time of the odour. For this we recommend a dietary 'Choline Load' before sample collection using foods known to produce the odour eg beans, eggs, liver. **Suggested Procedure**: at 13:00 and 19:00 a high choline meal containing (eg 2 eggs + 400g baked beans or other beans – can reduce quantity for children). Then; 1. Start '24 hour' urine collection the day after the choline load and collect urine until the end of the day *or* 2. collect a single 20ml sample first thing in the morning after the choline load if 24hr collection is impractical (e.g. in young children)	£146.59 (£72.78)
VMA / HVA	Primarily used for the investigation and monitoring of neuroblastoma	Urine, 10ml aliquot of acidifed (HCl) 24 hour collection or 10ml random urine accepted	Store at -20 Send by first class post	µmol/mmol creatinine Infant: HVA 4 - 25 VMA 2 -12	5-14 days		£83.47

Test	Clinical Utility	Sample Type and Volume (min in brackets)	Storage / Sending requirements	Reference Ranges	TAT	Comments / Notes	Price (Price for East Mids and South Yorks in brackets)
				1-5 yrs: HVA 2 -15 VMA 2 - 9 > 5 yrs: HVA 2 -13 VMA 1- 7			
Very Long Chain Fatty Acids (VLCFA) – includes C26, C24, C22, C26/C22, C24/C22, phytanate and pristanate	For investigation / diagnosis of peroxisomal disorders such X-ALD, Zellweger syndrome, Infantile Refsum's, Adult Refsum's, RCDP, D-bifunctional protein deficiency etc NB Diagnosis of **VLCAD deficiency** requires Acylcarnitine analysis as this is a fatty acid oxidation disorder NOT a peroxisomal disorder	Lithium or EDTA Plasma, or serum 0.5 ml (0.3)	Store at -20 Send by first class post	µmol/L C22 15-112 C24 14-80 C26 0.33-1.50 C24/C22 0.44-0.97 C26/C22 0.005-0.03 Pristanate 0 – 1.88 Phytanate 0.2-19.3	3-6 weeks	This is the first line test for the investigation of patients with suspected peroxisomal disorders. Almost all patients will show some abnormality with exception of some forms of RCDP which only have abnormal plasmalogens and some very rare variant / mild PEX gene defects.	£90.98 (£45.44)

Tissue Culture and Enzyme Assay

Most enzyme assays on cultured cells at Sheffield Children's NHS Foundation Trust are performed on cultured skin fibroblasts. These can be sent as either a skin biopsy or as cultured fibroblasts.

For skin biopsies sent from external hospitals a request form with full clinical details and test request is required. Sample transport at room temperature, normal first class post to Clinical Chemistry Department to arrive ideally no later than 4.30pm Mon – Fri. Please contact laboratory if sample to arrive on the weekend (0114 271 7445 or 271 7267).

For cultured fibroblasts, please send samples with the aim of them arriving Mon – Fri. A request form with full clinical details and test request is required.

Please note: turnaround times (TAT) are flexible when applied to cultured cell assays as different patient cell lines grow at different rates. In general for most assays starting from a skin biopsy the TAT is 8-12 weeks.

Reference ranges are not provided in the table below. Patient reports will contain the relevant reference range.

Please note: there are no EQA schemes available for the enzyme assays performed by the laboratory.

The following tests are free of charge for patients living in districts covered by the East Midlands and South Yorkshire Newborn Screening Contracts.

Test	Clinical Utility	Comments / Notes	Price (£)
TISSUE CULTURE			
Establishing a primary culture from skin biopsy, growing under sterile conditions (mycoplasma -free), cryopreservation and retention	To enable fatty acid oxidation flux assay, specific enzyme assay, cryopreservation of cells for future analysis, including molecular analysis. Cultured cells are not subject to secondary effects of post mortem.	Please send skin biopsy in a pot of sterile culture medium. Can be placed in the fridge overnight if posting straight away is not possible. **DO NOT freeze.**	£362.99
Growing on of fibroblast cell line for assay when received as cells from outside laboratory	As above.	Ensure flasks are filled completely with medium (no air bubbles) and are well insulated. Continue to grow cells at sending lab in case there are any issues. Cells MUST be mycoplasma free (see below).	£229.35
Recovery of cryopreserved cultured cells and growing on	For further studies.	Please contact the lab on 0114 2717267.	£79.16
Onward dispatch of living culture (carriage extra at cost): Within the UK: Abroad:	For studies not performed at Sheffield Children's NHS Foundation Trust	Please contact the lab on 0114 2717267.	 £61.27 £110.61
ASSAYS ON CULTURED CELLS			
$^{14}CO_2$ or ^{14}C-incorporation assays (isovaleric etc)	Isovaleric acid incorporation is used to confirm the diagnosis of isovaleric acidaemia. It can also be used to aid in the diagnosis of patients with 3-hydroxy-3methylglutaryl (HMG) CoA lyase deficiency.		£379.64
3-Methylcrotonyl-CoA Carboxylase	Specific enzyme assay for 3-Methylcrotonyl-CoA Carboxylase		£382.00

Test	Clinical Utility	Comments / Notes	Price (£)
Carnitine Palmitoyl Transferase Type I	Specific enzyme assay for CPT1. Can be requested directly or added on following performance of the tritiated flux assay		£602.72
Carnitine Palmitoyl Transferase Type II	Specific enzyme assay for CPT2. Can be requested directly or added on following performance of the tritiated flux assay		£429.09
Carnitine Acylcarnitine Translocase (CATR)	Specific enzyme assay for Carnitine Acylcarnitine Translocase (CATR).		£551.62
Carnitine Transporter Assay	To aid in the diagnosis of primary carnitine deficiency		£294.57
Fatty acid oxidation flux assay (tritiated myristate, palmitate and oleate in parallel)	For diagnosis of fatty acid oxidation defects.		£338.01
Glutaryl CoA dehydrogenase	To aid in the diagnosis of Glutaryl CoA dehydrogenase (GA1) deficiency. To exclude GA1 in cases of suspected non-accidental injury.		£392.18
L-leucine $^{14}CO_2$ release	To aid in diagnosing/confirming maple syrup urine disease (MSUD)		£379.64
L-Valine $^{14}CO2$ release	Valine oxidation is a useful assay for detecting BCAT2 deficiency		£379.64
Propionyl CoA carboxylase	To aid with confirming diagnosis of Propionic Acidaemia.		£392.18
Pyruvate Carboxylase	Should be considered in any child presenting with lactic acidosis and neurological abnormalities.		£382.00
Very long-chain fatty acids in cultured cells (fibroblasts, amniotic fluid cells or chorionic villus cells)	To aid with the work up of patients with suspected peroxisomal defects.		£411.20

NOTES

a) Cultured fibroblasts submitted for assay MUST be mycoplasma-free. If your local cytogenetics laboratory cannot ensure this then please send skin biopsy directly to us for culture. Cultures that are infected when received will be discarded.

b) The prices shown are indicative only. For some assays there are substantial reductions for multiple samples received at one time e.g. for family studies.

c) For prenatal diagnoses using cultured amniotic fluid cells or chorionic villus, reference material, cultured under the same conditions as the suspect sample, should be supplied by the referring centre. The above prices are increased by 40% for prenatal diagnosis or 70% if recovered cryopreserved material (e.g. the index case) is included as a positive control.

d) The prices shown do not include VAT, not usually applicable within the NHS. It may be applied to users outside the NHS dependent on current VAT rules.