

**WILLINK BIOCHEMICAL GENETICS UNIT**  
**Genetic Medicine, 6<sup>th</sup> Floor, Pod 1, St Mary's Hospital, Oxford Road,**  
**Manchester, M13 9WL**  
**Tel. 0161-70-12137/8; Fax 0161-70-12303**

**A USER'S GUIDE TO THE SERVICE AND  
DIAGNOSTIC TESTS AVAILABLE**

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**INTRODUCTION**

The Willink Biochemical Genetics Unit is based at the Central Manchester Hospitals Foundation Trust within the Genetic Medicine Division. Close integration of laboratory investigation and clinical management within the Unit has led to the development of a unique service aimed at the prevention of mental retardation by the early diagnosis and appropriate management of children and adults affected by inherited biochemical defects.

The Unit is housed in a purpose-built building completed in 2009. The clinic area and office suite is in the same area. The unit contains the laboratories responsible for the Region's newborn screening programme as well as a wide range of biochemical and molecular investigations. There is very close liaison between the clinicians and scientists responsible for the service.

Clinical interpretation of results is essential when investigating for rare disorders. Clinicians sending samples are contacted personally about their patients when positive or important negative diagnoses are made. Four consultant paediatricians provide a 24-hour on-call service for metabolic patients. Advice regarding investigations is available at all times by contacting the paediatricians, the consultant clinical scientist or other senior scientists in the laboratory.

There are a number of specialist metabolic clinics held each week. Outreach clinics are also held in Bradford, Liverpool, Bristol, Cardiff, Belfast and Dublin. All clinics are consultant-led and patients are seen initially by the consultant staff. The medical staff is supported by specialist nurses based in the Unit, the Unit's Chief Dietician and a senior Clinical Psychologist. In-patients are managed on Ward 85 at the Children's Hospital in Central Manchester. Patients on enzyme replacement therapy transfusions are managed at the Elective Treatment Centre.

The laboratory also provides a diagnostic service for the adult LSD clinic situated at Salford Royal Hospital. The clinical service there is led by consultant with a special interest in inherited metabolic disorders.

# 1 GENERAL INFORMATION

## 1.1 POSTAL ADDRESS

**Willink Unit  
Genetic Medicine  
6<sup>th</sup> Floor  
St Mary's Hospital  
Oxford Road  
Manchester  
M13 9WL**

Telephone: 0161 70 12137/8  
Fax: 0161 70 12303

## WEBSITE ADDRESS

[www.mangen.co.uk/biochemical-genetics.asp](http://www.mangen.co.uk/biochemical-genetics.asp)

Request forms can be down-loaded from this site (See Use of Laboratory section).

## 1.2 WHERE TO FIND US

The Unit is situated on the sixth floor in Pod 1 of Genetic Medicine at St Mary's Hospital, Oxford Road, Manchester. Access by foot can also be made from Hathersage Road. Access to the unit is through the Children's Hospital and is signposted.

## 1.3 KEY PERSONNEL

The Unit has four consultant paediatricians Dr. Ed Wraith, Dr. John Walter, Dr. Simon Jones and Dr Andrew Morris. They can be contacted through the Unit office, Tel. 0161-70 12137/8.

Laboratory Director is Lorraine Gaunt.

Contact may also be made by email: [forename.surname@cmft.nhs.uk](mailto:forename.surname@cmft.nhs.uk)

Outside normal working hours the on-call paediatrician is available via the hospital switchboard (0161-276-1234).

## 1.4 POPULATION SERVED

The laboratory performs the newborn screening service for Phenylketonuria and MCADD for the North West of England but also serves as a reference laboratory for inherited metabolic disorders for this area. It is a NCG designated national referral centre for lysosomal storage disorders and accepts samples referred from other centres throughout the world.

## 1.5 LABORATORY HOURS

The laboratory is open:

Mondays to Thursdays	8.30am to 5.30pm
Fridays	8.30am to 5.00pm

The Unit is closed on official UK Public Holidays.

## USE OF THE LABORATORY

### 1.6 REQUESTS TO THE LABORATORY

Requests for tests done by this laboratory should be sent from a referring doctor. Routine requests should be sent to the laboratory by the methods relevant to the test as stated in the handbook. Urgent and out of hours requests must be made by first contacting the consultant on duty or laboratory director, via the hospital switchboard tel: 0161 276-1234.

The request form must be completed with all required information. The specimen container must also be fully identified with the patient name, date of birth, identification number and the date / time of sample collection.

The Willink Laboratory has its own request form (available on the laboratory website) but will accept requests for tests written on other forms or by letter from the referring doctor, provided that all relevant information is given. The information given should include:

- Patient name in full
- Identification number eg hospital number or NHS number
- Date of Birth
- Sex
- Consultant or referring doctor's name
- Name and address to where reports should be sent
- Date and time of specimen
- Date and time of sending sample

Specimens which are sent from another laboratory must be identified with the referral laboratory number. This number should also be on the request form.

Specimen containers are identified with the information for each test. These can be obtained from local pathology sources.

### 2.2 COLLECTION OF SPECIMENS

The laboratory does not provide its own specimen collection service, other than for those patients attending a Willink Unit clinic session under one of our consultants.

### 2.3 TRANSPORT TO THE LABORATORY

Samples are accepted at the laboratory from hospital porters for hospital internal samples, by hand, by external post and by courier.

The hospital porters collect from each ward three times a day, morning and afternoon, and deliver samples to pathology sample reception where they are redistributed. It must be noted, however, that some samples will need to be delivered directly to the laboratory and not wait for the porter service (see appropriate test requirements).

Samples delivered by hand must be brought upstairs to the laboratory hatch and not left at the reception desk. Urgent samples from outside the hospital should be delivered by taxi or courier and must be delivered directly to the unit, not to elsewhere within the hospital.

Many samples from outside the hospital may be delivered by first class post (see relevant sample and test information if this is allowed).

Samples must be sent direct to the laboratory, we cannot undertake to collect samples from rail stations, airports or other collection points.

Samples sent by post should follow the appropriate packaging requirements of the postal system used (see below).

#### PACKAGING OF SAMPLES FOR TRANSPORT

Samples must be sent to the laboratory in a special closed polythene bag which allows the sample and the accompanying request form to be kept separated. Samples with a category 3 infection risk must be clearly marked with a yellow CATEGORY 3 RISK sticker on the request form.

Samples being delivered by post should follow the guidelines set down. 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 Data post may be used.
- 5 There is a range of acceptable packaging but the following must be observed.
- 6 Every specimen must be in a primary container hermetically sealed or otherwise securely closed. The capacity of the primary container must not exceed 50mL unless specifically permitted. The primary container must be wrapped in enough absorbent material to absorb all possible leakage, and sealed in a leak-proof bag.
- 7 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 adhesive tape.
- 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 'BIOLOGICAL SUBSTANCE, CATEGORY B' and show an open diamond with UN 3373 across its centre. The package should also show the name and address of the sender as well as the delivery address.
- 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 650 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 travel.

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.

NB Containers received with samples

As we receive a great number of samples for testing from outside the hospital, we also receive a great number of transport containers. It is now our laboratory policy that all re-usable sample transport containers received **with postage paid return labels** will be returned to the initiating laboratory. All other containers will be disposed of.

## **NEWBORN SCREENING CARDS**

By common consent these regulations are deemed inappropriate for dried blood specimens on Newborn Screening 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 in a stout envelope as if it were a normal letter, first class post.

## **2.4 RESULTS**

Reports from samples taken within the hospital will be issued to the appropriate ward.

Reports from samples sent from another hospital will be sent to the referring hospital's pathology department.

Reports from samples sent from abroad will be sent to the referring clinician, initially by email with a follow up written report sent by mail.

Reports are issued without delay, usually within 24 hours of results being obtained.

Positive diagnostic results are communicated to the referring consultant by our duty consultant by telephone.

Telephone results are followed by written results within 24 hours.

The referring laboratory is also informed of positive diagnostic results by a senior member of the appropriate section.

Urgent results, such as for prenatal diagnoses, may be communicated by secure fax transmission. These will always be followed by a written report sent within 24 hours.

Results will not be communicated to patients or their relatives or to any unauthorised person with the following exception:

Phenylalanine levels of treated PKU patients may be given to parents if authorised by doctor / dietician.

## **3 OUT OF HOURS SERVICE**

Urgent investigations will only be performed following discussion with one of our consultants. They may be contacted via the hospital switchboard, Tel 0161 276 1234. (see general information and notes on tests available)

## **4 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.

**General information and notes on tests available*****Urgent investigations - organic acid and amino acid disorders.***

Patients with suspected amino acid or organic acid disorders may require urgent studies in order to implement appropriate treatment. These patients often present in the neonatal period with failure to thrive, vomiting, lethargy, hyperventilation, seizures and hypotonia. There may be metabolic acidosis, respiratory alkalosis, hypoglycaemia, hypocalcaemia and/or deranged liver function tests. Blood ammonia and lactate may be raised.

For organic and amino acid screen, as well as acylcarnitines, please send 10ml fresh urine and 2ml heparinised blood or a blood card with 4 spots of blood. Results should be available the same day assuming samples arrive in good time (before 11am) and the laboratory has been warned of the urgent sample. It is important that full clinical details are given including details of metabolic acidosis, jaundice, blood ammonia and drug history. For disorders of fat oxidation e.g. MCAD deficiency, it is important that urine is collected at the time of hypoglycaemic stress. Urgent investigations will normally only be performed following discussions with one of our consultants

***Galactosaemia screen***

Patients with unexplained or prolonged jaundice should be screened for classical galactosaemia. The condition is often accompanied by septicaemia, has an incidence of around 1 in 45,000 births and is exacerbated by lactose - containing milk. Reducing substances are not always found in urine and therefore a Beutler screening test should be carried out. Approx. 0.2-0.5ml heparinised blood should be sent directly to the lab. Note the test is not valid if the patient has undergone a recent blood transfusion (within 4 months). The test could also give a false positive result with G-6-PD deficiency. Transfused patients would require Gal-1-P analysis on whole heparinised blood (5ml). Since these samples require immediate processing it is important to warn the lab of any Gal-1-P analyses.

***Sudden unexplained infant deaths***

Some metabolic disorders may result in sudden infant death or SUDI. Disorders of fat oxidation especially MCAD deficiency has been linked with SIDS, however the incidence of this disorder is probably not significantly higher than that generally present in Caucasians particularly North Europeans, i.e. 1 in 10,000. To investigate these disorders in SUD infants, please collect urine (5ml by supra pubic stab if necessary) or failing this CSF for organic acid analysis and cardiac blood (5ml EDTA) for DNA analysis. Approx. 90% MCAD deficient patients carry a common (985A>G) mutation. It is also recommended that a dried blood spot is taken, onto a standard newborn screening card, for tandem mass spectrometry of acylcarnitines. Tissue for culture should only be collected where there is a strong possibility of fat oxidation defect, i.e. fatty liver on gross examination. A small (approx. 2-3mm<sup>3</sup>) piece of skin and fascia should be collected aseptically into sterile tissue culture medium.

***Lysosomal disorders***

The lysosomal enzyme screen covers some 17 different disorders, mostly the sphingolipid and glycoprotein storage disorders. Mucopolysaccharidoses are initially screened by urinary MPS electrophoresis. Some disorders require specific tests not covered in the screen. These disorders include Pompe, Niemann-Pick type C, Sialic Acid Storage Disease and Sialidosis. Where the enzyme and MPS screens are negative but there is evidence of an underlying storage disorder (visceromegaly, vacuolated/foam cells in bone marrow or blood) further tests should be discussed with the laboratory.

***Peroxisomal disorders***

Plasma very long chain fatty acid analysis remains the most useful screening test for these conditions. VLCFA concentrations are significantly increased in general peroxisomal disorders such as Zellweger syndrome as well as in rare peroxisomal  $\beta$ -oxidation disorders. In X-linked adrenoleukodystrophy the C26/C22 ratio is less markedly raised. Where disorders such as Zellweger are strongly suspected it is important to also request plasmalogens on erythrocytes. Fibroblast assays may be required to confirm the diagnosis. Please note that phytanic acid levels will only be abnormally raised after sufficient dietary intake i.e. older patients.

***Prenatal diagnosis***

Prenatal diagnosis is available for a number of metabolic disorders. For all cases a firm biochemical diagnosis must be established in the proband, since a similar test is likely to be used for prenatal studies. Studies in the parents/obligate heterozygotes may also be necessary to exclude low enzyme activities or pseudo deficiencies which may compromise the interpretation of prenatal results. Advice should be sought from the laboratory on the type of sample best suited for diagnosis and optimum gestational age. Direct enzyme assay of CVS is usually the preferred approach but for some disorders amniocentesis may be more appropriate.

<b>REPertoire OF ALL AVAILABLE TESTS</b>
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The following pages list the various diagnostic tests available from this Unit. Not listed are details of samples from newborn infants for PKU screening, which is carried out in this laboratory for the 'old North Western' Health Region and operates through the health visitors and midwives. The test which is carried out at 6-10 days by the tandem mass spectrometry method, also picks up certain other amino acid disorders. Listed below is the code used for different types of sample for investigation; the necessary volumes are shown for individual tests. Turnaround times and reference ranges are given where appropriate.

EDTA = EDTA Blood	HEP = Heparinised Blood
P = Plasma	U = Urine
CC = Cultured Skin Fibroblasts	L = Liver
CSF = Cerebrospinal fluid	AF = Amniotic Fluid
AFC = Cultured Amniotic Fluid Cells	CVS = Chorionic Villus Sample
	DBS = Dried Blood Spots
CCV = Cultured Chorionic Villi	

If further details are required please do not hesitate to contact the laboratory. **Tissue culture costs will have to be added separately where cultured cells are required.**

### ALL REQUESTS MUST GIVE AGE, SEX, CLINICAL DETAILS AND RELATED THERAPY

Test	Required specimen & volume	Special precautions	Turnaround time	Reference ranges	Section
<b>CARBOHYDRATE DISORDERS</b>					
Sugar Chromatography	5ml U	None	3 working weeks	Qualitative	Metabolites
$\alpha$ -glucosidase <i>Pompe (GSDII)</i>	5ml EDTA	Must reach laboratory within 48 hours	1 working week	3 – 20 $\mu$ mol/g.h. - acarbose	Lysosomal
Beutler Test <i>Galactosaemia</i>	0.5 ml HEP	Must reach laboratory within 24 hours	3 working days	Qualitative	Metabolites
Galactose-1-phosphate <i>Galactosaemia monitoring</i>	5ml HEP	Must reach laboratory within 24 hours	3 working weeks	5 – 10 $\mu$ g/ml packed red cells	Metabolites
<b>AMINO ACID DISORDERS</b>					
2-D TLC (see footnote to table)	5ml U, no preservative	None	3 working weeks	Qualitative	Metabolites
Quantitative amino acids	3ml HEP	Must be sent on ice or deproteinised with internal standard	3 working weeks	Quoted on report	Metabolites
White cell cystine <i>Cystinosis</i>	5ml HEP	Must be sent immediately on ice	3 working weeks	<0.1-0.2 nmole cyst / mg protein	Metabolites

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Pterins <i>PKU Variants</i>	U	Contact lab prior to collection. Special conditions apply.	4 weeks	Age-dependent, quoted on report	Metabolites
Orotic acid <i>Urea cycle defects</i>	2ml U	None	4 weeks	<5 µmol / mmol creatinine	Metabolites
<sup>14</sup> C-citrulline incorporation <i>Citrullinaemia and arginosuccinic aciduria</i>	CC, AFC, CCV	Contact lab prior to dispatch to discuss test	Dependent on culture time	Controls quoted	Metabolites
<sup>14</sup> C-leucine oxidation <i>Maple syrup urine disease</i>	CC, AFC	Contact lab prior to dispatch to discuss test.	Dependent on culture time	Controls quoted	Metabolites
<sup>14</sup> C-methionine synthesis <i>Homocystinuria remethylation</i>	CC, AFC, CCV	Contact lab prior to dispatch to discuss test.	Dependent on culture time	Controls quoted	Metabolites
<b>ORGANIC ACID DISORDERS</b>					
Organic acids by GC-MS	5ml U	Full drug history	3 working weeks	Qualitative	Metabolites
Pyruvate carboxylase	CC, AFC, CCV, CVS	Contact lab prior to dispatch to discuss test.	Dependent on culture time	Fibroblasts 6-40 nmol/h/mg	Metabolites
Propionyl-CoA carboxylase <i>Propionic aciduria</i>	CC, AFC, CCV, CVS	Contact lab prior to dispatch to discuss test.	Dependent on culture time	40-100nmol/h/mg (fibroblasts)	Metabolites
Methylmalonic-CoA mutase <i>Methylmalonic aciduria</i>	CC, AFC, CCV, CVS	Contact lab prior to dispatch to discuss test.	Dependent on culture time	Fibroblasts 207-1730 pmol/min/mg	Metabolites
<sup>14</sup> C-propionate incorporation <i>Propionic and Methylmalonic aciduria defects in B12 Metabolism</i>	CC, AFC, CCV, CVS	Contact lab prior to dispatch to discuss test.	Dependent on culture time	Assay Controls quoted	Metabolites
Methylcrotonyl-CoA carboxylase	CC, AFC, CCV	Contact lab prior to dispatch to discuss test.	Dependent on culture time	2.5-12nmol/h/mg (fibroblasts)	Metabolites
HMG-CoA lyase <i>3-hydroxy 3-methylglutaric aciduria</i>	CC, AFC, CCV	Contact laboratory prior to dispatch to discuss test.	Dependent on culture time	0.52-3.96nmol/min/mg protein	Metabolites
Biotinidase <i>Multiple carboxylase</i>	2-3ml HEP	To reach lab within 24	2 working	Plasma 4-12nmol/min	Metabolites

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<i>deficiency</i>		hours	weeks	/ml	
Acyl carnitines (Includes free Carnitine)	1ml HEP or dried blood spot	None	2 working weeks	Free carnitine 20-40µM, values quoted for specific acyl carnitines	Metabolites
<b>LYSOSOMAL STORAGE DISEASES</b>					
Lysosomal enzyme screen <i>17 different lysosomal storage disorders (see page 21)</i>	5ml EDTA	To reach the laboratory within 72 hours	4 working weeks	See individual enzymes	Lysosomal
<b>Mucopolysaccharidosis</b>					
2-D electrophoresis of GAGs <i>Mucopolysaccharidoses</i>	5-10ml fresh U, 10ml AF	None	3 working weeks	Qualitative	Lysosomal / MPS
Oligosaccharide screen	2-3ml U	To reach the laboratory within 72 hours	3 working weeks	Qualitative	Lysosomal / MPS
Quantitative sialic acid <i>Sialic acid storage disease, Sialidosis, Galactosialidosis</i>	2-3ml U, CC, AFC, CCV, white cells. Age of patient <b>must</b> be specified	To reach the laboratory within 72 hours	4 weeks	Age-matched controls quoted	Lysosomal / MPS
<b>MPS enzyme assays</b>					
α-iduronidase <i>MPS I, Hurler syndrome, Scheie syndrome, Hurler/Scheie syndrome</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	2 working weeks.	White cells 10 <sup>-5</sup> -50 µmol/g.h Other tissues, assay control values quoted	Lysosomal
Iduronate sulphatase <i>MPS II, Hunter syndrome</i>	2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	Assay control values quoted	Lysosomal
Heparan sulphamidase <i>MPS IIIA Sanfilippo A syndrome</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	Assay control values quoted	Lysosomal
α-N-acetylglucosaminidase <i>MPS IIIB Sanfilippo B syndrome</i>	2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks time	Assay control values quoted	Lysosomal
Acetyl-CoA:α-glucosaminide N-	5ml EDTA, CC, AFC,	To reach the laboratory within 72	3 working weeks	Assay control values	Lysosomal

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acetyltransferase <i>MPS IIIC Sanfilippo C syndrome</i>	CCV, CVS	hours		quoted	
Galactose-6-sulphatase <i>MPS IVA Morquio syndrome</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks.	Assay control values quoted	Lysosomal
$\beta$ -galactosidase <i>MPS IVB, Morquio syndrome &amp; GM1-gangliosidosis</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks.	White cells 100-400 $\mu\text{mol/g.h.}$ Other tissues assay control values quoted	Lysosomal
Arylsulphatase B <i>MPS VI Marateaux-Lamy syndrome</i>	10ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks.	Assay control values quoted	Lysosomal
$\beta$ -glucuronidase <i>MPS VII Sly's syndrome</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks.	White cells 100 – 800 $\mu\text{mol/g.h.}$ Other tissues assay control values quoted	Lysosomal
Multiple sulphatases <i>Multiple sulphatase deficiency</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	See individual sulphatase values for white cells, other tissues assay controls quoted	Lysosomal
<b>Other enzyme assays</b>					
Aspartylglucosaminidase <i>Aspartylglucosaminuria</i>	5ml EDTA, 2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks.	Plasma 10 – 60 $\mu\text{mol/l.h.}$ Other tissues, assay controls quoted	Lysosomal
N-acetyl $\alpha$ -neuraminidase <i>Sialidosis</i>	CC, AFC, CCV.	To reach the laboratory within 72	3 working weeks following	Assay controls	Lysosomal

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		hours	completion of culture	quoted	
$\alpha$ -fucosidase <i>Fucosidosis</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 50 – 200 $\mu\text{mol/g.h.}$ Other tissues assay controls quoted	Lysosomal
$\alpha$ -mannosidase <i><math>\alpha</math>-Mannosidosis</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 100 – 800 $\mu\text{mol/g.h.}$ Other tissues assay controls quoted	Lysosomal
$\beta$ -mannosidase <i><math>\beta</math>-Mannosidosis</i>	5ml EDTA, 2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	Plasma 200-1500 $\mu\text{mol/l.h.}$ Other tissues, controls quoted	Lysosomal
Multiple hydrolases <i>ML II &amp; III</i>	5ml EDTA, 2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	2 working weeks	See other plasma hydrolase assays	Lysosomal
$\beta$ -hexosaminidase A (MUGS) <i>Tay-Sachs disease</i>	5ml EDTA, 2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	2 working weeks	Plasma 50 – 200 $\mu\text{mol/l.h.}$ other tissues assay controls quoted	Lysosomal
$\beta$ -hexosaminidase A & B <i>Sandhoff disease</i>	5ml EDTA, 2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	2 working weeks	Plasma 600– 3500 $\mu\text{mol/l.h.}$ other tissues assay controls quoted	Lysosomal
Galactocerebrosidase <i>Krabbe Leucodystrophy</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 0.4 – 4 $\mu\text{mol/g.h.}$ other tissues	Lysosomal

				assay controls quoted	
Arylsulphatase A <i>Metachromatic Leucodystrophy</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 50 – 200 $\mu\text{mol/g.h.}$ other tissues assay controls quoted	Lysosomal
$\alpha$ -galactosidase <i>Fabry disease</i>	5ml EDTA, 2ml P, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	1 working week	Plasma 3 – 20 $\mu\text{mol/l.h.}$ white cells 10 –50 $\mu\text{mol.g.h.}$ , other tissues assay controls quoted	Lysosomal
$\beta$ -glucosidase <i>Gaucher disease</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 1- 5 $\mu\text{mol/g.h.}$ other tissues assay controls quoted	Lysosomal
Chitotriosidase <i>Marker for some lysosomal storage disorders, monitoring Gaucher patients on treatment</i>	5ml EDTA, 2 ml P	To reach the laboratory within 72 hours	2 working weeks	4 – 80 $\mu\text{mol/l.h.}$	Lysosomal
N-acetyl- $\alpha$ -galactosaminidase <i>Schindler disease</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 15-70 $\mu\text{mol/g.h.}$ other tissues assay controls quoted	Lysosomal
Sphingomyelinase <i>Niemann-Pick A and B</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 1 – 8 $\mu\text{mol/g.h.}$ other tissues assay controls quoted	Lysosomal
Acid esterase <i>Wolmans disease and cholesteryl ester storage</i>	5ml EDTA, CC, AFC, CCV, CVS	To reach the laboratory within 72 hours	3 working weeks	White cells 350 – 2000 $\mu\text{mol/g.h.}$	Lysosomal

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<i>disease</i>		hours		other tissues assay controls quoted	
Filipin staining (Cholesterol esterification) <i>Niemann-Pick C</i>	CC	None	2 working weeks after culture	Qualitative	Lysosomal
Transferrin electrofocusing <i>Carbohydrate-deficient glycoprotein disorders</i>	1ml clotted blood	To reach the laboratory within 48hours	4 working weeks	Qualitative	Lysosomal
<b>PEROXISOMAL DISORDERS</b>					
Very Long Chain Fatty Acids <i>General peroxisomal disorders, VLCFA oxidation defects and X-linked ALD</i>	5ml EDTA or 2ml P	To reach the laboratory within 72 hours	4 working weeks	C26 / C22 <0.033 C24 / C22 0.65 – 1.05	Metabolites
Phytanic and Pristic acids <i>Refsum disease, RCDP and other peroxisomal disorders</i>	5ml EDTA or 2ml P	To reach the laboratory within 72 hours	4 working weeks	<16umol/L	Metabolites
Plasmalogens <i>RCDP and general peroxisomal disorders</i>	5ml EDTA	To reach the laboratory within 72 hours	2 months	Ref. values quoted	Metabolites
<b>OTHER DISORDERS</b>					
Arylsulphatase C (Steroid sulphatase) <i>X-linked Ichthyosis</i>	5ml EDTA	To reach the laboratory within 72 hours	4 working weeks	In-assay controls quoted	Lysosomal
7-dehydrocholesterol <i>Smith-Lemli-Opitz syndrome</i>	2ml EDTA	None	4 working weeks	<10µmol/L	Metabolites
<b>TISSUE CULTURE</b>					
Initiation of culture	Skin biopsy, amniocytes or CVS	To reach the laboratory within 48hours	Dependent on cell growth	NA	CMFT Cytogenetics Laboratory
Maintenance of cultures initiated elsewhere	CC, AFC, CCV	To reach the laboratory within	NA	NA	Tissue Culture

		48hours			
Cryogenic storage in cell bank	NA	NA	NA	NA	CMFT Central Culture Bank
<b>PRENATAL DIAGNOSIS</b>					
<b>ALWAYS CONTACT LABORATORY PRIOR TO SAMPLING</b>	CVS, cell free amniotic fluid, cultured cells.	To be transported in culture medium, at room temperature and to reach the laboratory within 72 hours.	Dependent on assay needed. Up to 2 working weeks. Many assays will be within 72 hours of receipt. Check with lab for reporting time expected for individual assays.	Dependent on analysis. Control values included in the analysis are quoted.	Various.

**Footnote:-**

All samples **must** be accompanied by relevant clinical details. This is especially so for **urine amino acids, organic acids mucopolysaccharides and all samples for prenatal diagnosis. Reports will not be sent out where samples are received without clinical details** as an accurate interpretation is not possible without them.

**CONTACT NAMES AND NUMBERS FOR EACH LABORATORY SECTION**

Laboratory Director	Lorraine Gaunt	0161 70 66553
Metabolites and Newborn Screening	Jackie Till / Teresa Wu	0161 70 12140/2
Lysosomal Storage Disorders.	Heather Church/Karen Tylee	0161 70 12307/6

Members of staff can be contacted by email at the general trust email addresses of

[forename.surname@cmft.nhs.uk](mailto:forename.surname@cmft.nhs.uk)

**FURTHER INFORMATION****LYSOSOMAL STORAGE DISEASES**

The following enzyme analyses are performed as a group lysosomal disorder screening test. The minimum sample required is **5ml** of whole blood in an EDTA specimen tube. Please post specimens early in the week to avoid samples being delayed over the weekend. All relevant clinical information should be provided with the sample. The following enzymes are routinely assayed. -----

**Lysosomal enzyme screen – N.B. does not screen for MPS disorders**

Plasma chitotriosidase	(non-specific marker for lysosomal storage disorders)
Plasma $\beta$ -hexosaminidase	(Sandhoff disease, I-cell disease)
Plasma $\beta$ -mannosidase	( $\beta$ -Mannosidosis, I-cell disease)
Plasma $\beta$ -hexosaminidase A [MUGS]	(Tay-Sachs disease)
Plasma aspartylglucosaminidase	(Aspartylglucosaminuria)
Leucocyte $\beta$ -glucuronidase	(Sly disease, MPS VI)
Leucocyte $\beta$ -galactosidase	(GM1-gangliosidosis)
Leucocyte $\alpha$ -mannosidase	( $\alpha$ -Mannosidosis)
Leucocyte $\alpha$ -galactosidase	(Fabry disease)
Leucocyte $\alpha$ -fucosidase	(Fucosidosis)
Leucocyte acid esterase	(Wolman/cholesterol ester storage disease)
Leucocyte arylsulphatase A	(Metachromatic Leucodystrophy)
Leucocyte $\beta$ -glucosidase (Gaucher disease)	(Gaucher disease)
Leucocyte sphingomyelinase	(Niemann-Pick types A & B)
Leucocyte galactocerebrosidase	(Krabbe Leucodystrophy)
Leucocyte N-acetyl- $\alpha$ -galactosaminidase	(Schindler disease)

**MUCOPOLYSACCHARIDE DISORDERS****Urine screen - Mucopolysaccharide 2-dimensional electrophoresis**

This should be the first diagnostic test performed for MPS disorders. Urine should be sent prior to or with samples for enzyme analysis. Enzyme analysis will normally only be performed when an abnormal mucopolysaccharide pattern has been identified in urine. Routinely all urine samples are also tested for abnormal oligosaccharides or sialic acid containing conjugates by t.l.c.

**GLYCOPROTEIN AND SIALIC ACID STORAGE DISORDERS****Urinary oligosaccharide screen - Oligosaccharide t.l.c**

Analysis by t.l.c. of urinary oligosaccharides stained with orcinol and resorcinol for abnormal oligosaccharides or sialic acid containing conjugates. Test is not always easy to interpret but complements lysosomal enzyme and urinary MPS screens. Useful for some oligosaccharide/glycoprotein disorders.

**PEROXISOMAL DISORDERS**

The following investigations can all be carried out on the same 5ml EDTA sample.

**Very Long Chain Fatty Acids**

*Screening for Zellweger, other general peroxisomal disorders, X-ALD and VLCFA oxidation defects by GC-MS*

**Phytanic acid and Pristanic acid**

*Refsum disease, rhizomelic chondrodysplasia punctata, other peroxisomal disorders*

**Plasmalogens**

*RCDP (especially) and general peroxisomal disorders e.g. Zellweger*

**PRENATAL DIAGNOSES**

You should **always** contact the unit **prior** to prenatal sampling. Direct analysis of uncultured chorionic villus is not universally appropriate, and for some disorders, prenatal diagnosis is not yet available. It is important that biochemical diagnosis has been established in the proband and if this has not been done in this laboratory, it may be necessary to confirm the diagnosis on a fresh sample (for which the charge may be waived) or to verify a diagnosis made elsewhere before accepting the sample. It may also be necessary to study enzyme activities in parents/obligate heterozygotes prior to prenatal studies. We would be happy to provide advice on appropriate samples for each condition, the amount required and the best gestational age for sampling. We **do not** charge for advice given over the telephone, so please contact us with any clinical or technical enquiries.

**The charge for prenatal diagnosis by direct analysis of chorionic villi or cultured amniotic fluid cells is as listed above under the specific test plus £55.14. Where cultured amniocytes or cultured chorionic villus cells are required, the appropriate culture charge must be added.**

**TISSUE CULTURE**

For some conditions it is necessary to carry out enzyme or *in situ* radiochemical incorporation/oxidation studies on cultured cells. Skin biopsies for these studies must be taken with great care to avoid primary contamination of the fibroblast culture. An aseptic technique must be used with sterile instruments. The biopsy is best taken from the inside aspect of the forearm, which should first be cleaned with a suitable antiseptic such as alcohol, Hibitane or chlorhexidine. It may also be necessary to use a local anaesthetic. The tissue may be taken by punch biopsy or with a sterile scalpel blade, when it is sometimes helpful to raise a small area of skin with a fine needle. The biopsy should not be full thickness or too large, but about 1mm by 3-4mm in area and dropped immediately into sterile tissue culture medium, making sure that the biopsy is well immersed. At post-mortem there is always a greater risk of contamination, particularly when a large biopsy is taken. An internal tissue such as fascia may be preferred.

Sufficient cells for study should be available after about 2-5 weeks in culture. All cultures are checked for mycoplasma contamination and subsequently banked in a cryogenic store.

For cultures that are sent here for study it is important that they are first checked for mycoplasma or other contaminants.

**RETENTION OF MATERIAL FOR FURTHER ANALYSIS**

The Willink laboratory has a written policy for the retention of various clinical samples for future analysis should this be required. This policy is based on the Report of the Working Party of the Royal College of Pathologists, 3<sup>rd</sup> Edition 2005, entitled THE RETENTION AND STORAGE OF PATHOLOGICAL RECORDS AND ARCHIVES..

**NORMAL DIAGNOSTIC SAMPLES – TIME OF STORAGE PRIOR TO DISPOSAL**

URINE	4 weeks after final report is issued
WHOLE BLOOD (Beutler test)	48 hours after final report is issued
SERUM	48 hours after final report is issued
PLASMA	up to 4 weeks after final report is issued, however samples for quantitative amino acid analysis are deprotenised on arrival and are thus unsuitable for other analyses.
WHITE CELL PREPARATIONS	48 hours after final report is issued, however, once cells are lysed, labile enzymes are rapidly degraded rendering samples inappropriate for further analysis.
CSF	48 hours after final report is issued
MUSCLE BIOPSIES	4 weeks after final report is issued
BLOOD SPOTS	25 years after final report is issued for newborn screening samples, 6 months for others
CULTURED FIBROBLASTS	Stored in the cell bank for a period of 2 years. Positive samples are stored for up to 30 years.
CULTURED AMNIOCYTES OR CHORIONIC VILLI	Stored in the cell bank for a period of 2 years. Positive samples are stored for up to 30 years.

**ALPHABETICAL LIST OF METABOLIC CONDITIONS FOR WHICH  
SPECIFIC DIAGNOSTIC TESTS ARE AVAILABLE IN THIS LABORATORY.**

	Page No(s)
Adrenoleukodystrophy X-linked	9,16,22
Argininosuccinicaciduria	11
Aspartylglucosaminuria	12,14, 22
Carbohydrate-deficient glycoprotein syndrome	16
Biotinidase deficiency	12
Citrullinaemia	11
Cholesterol ester storage disease	12,16,22
Cystinosis	11
Fabry disease	12, 15
Farber disease – discuss with laboratory	
Fucosidosis	12, 14, 22
Galactosaemia	9, 10, 17
Galactosialidosis	12
Gaucher disease	12, 15, 18, 22
GM1-gangliosidosis	12, 13, 22
Hereditary fructose intolerance	11, 17
Homocystinuria (CS deficiency and remethylation defects)	11
Hunter disease (MPS II)	12, 13, 19
Hurler (and Scheie) disease (MPS I)	13, 19
Hydroxymethylglutaric aciduria	12
I-cell disease (mucopolipidosis II, and ML III)	12, 14, 19, 22
Krabbe disease	12, 15, 22
Mannosidosis ( $\alpha$ -mannosidase deficiency)	12, 14, 22
Mannosidosis ( $\beta$ -mannosidase deficiency)	12, 14, 22
Maple syrup urine disease	11
Maroteaux-Lamy disease (MPS VI)	12, 13
Metachromatic leukodystrophy	12, 15, 19, 22,
Methylcrotonyl-CoA carboxylase deficiency	12
Methylmalonic aciduria (mutase deficiency and B12 defects)	11, 12
Mitochondrial disorders and mitochondrial cardiomyopathy	9, 18, 23
Morquio disease types A and B (MPS IVA and B)	12, 13, 20
mtDNA deletions	9, 17, 23
Mucopolysaccharidosis	9, 12, 13
Multiple sulphatase deficiency	12, 14
NARP (neurogenic muscle weakness ataxia and retinitis pigmentosa)	17
Niemann-Pick disease	9, 12, 15, 16, 18, 22
Phenylketonuria (classical, pterin defects, DHPR deficiency)	11
Pompe (GSD II)	10
Propionic acidaemia	11, 12
Pyruvate carboxylase deficiency	11
Refsum disease	16, 23
Rhizomelic chondrodysplasia punctata	16, 23
Sandhoff disease	12, 15, 22
Sanfilippo diseases types A,B and C (MPS IIIA, B, C)	12, 13, 19
Schindler disease	12, 16, 22
Sialic acid storage disease (Salla disease)	12
Sialidosis (mucopolipidosis I)	12, 14
Sly disease (MPS VII)	12, 13
Smith-Lemli-Opitz syndrome	17
Sudden infant death syndrome (SIDS)	9
Tay-Sachs disease	12, 15, 22
Urea cycle defects	11
Wolman disease	12, 16, 22
X-linked Ichthyosis	16, 17

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**ALPHABETICAL LIST OF ALL TESTS PERFORMED IN THE LABORATORY**

	Page No(s)
Acetyl-CoA: $\alpha$ -glucosaminide N-acetyltransferase	13
Acid esterase	16, 22
Acyl carnitines	9, 12
Amino acids -urine	9, 11
Amino acids quantitative	9, 11
Arylsulphatase A	15, 22
Arylsulphatase B	13
Aryl sulphatase C (steroid sulphatase)	17
Aspartylglucosaminidase	14, 22
Beutler test (galactose-1-phosphate uridyl transferase)	10
Biotinidase	12
Carnitine, Free	12
Chitotriosidase	15
$^{14}\text{C}$ -Citrulline incorporation	11
7-dehydrocholesterol	17
Filipin staining (Cholesterol esterification)	16
$\alpha$ -fucosidase	14, 22
Galactocerebrosidase	15, 22
Galactose-1-phosphate	9, 11
Galactose-1-phosphate uridyl transferase - see Beutler test	9, 10
Galactose - 6-sulphatase	13
$\alpha$ -galactosidase	15, 22
$\beta$ -galactosidase	13, 22
$\alpha$ -glucosidase	10
$\beta$ -glucosidase	15, 22
$\beta$ -glucuronidase	13, 22
Heparan sulphamidase	13
$\beta$ -hexosaminidase A	15, 22
$\beta$ -hexosaminidase A & B	15, 22
HMG-CoA lyase	12
Homocysteine – total plasma concentration	11
Iduronate sulphatase	13
$\alpha$ -iduronidase	13
$^{14}\text{C}$ -Leucine oxidation	11
Lysosomal enzyme screen	9, 12, 22
$\alpha$ -mannosidase	14, 22
$\beta$ -mannosidase	14, 22
Methylcrotonyl-CoA carboxylase	12
Methylmalonyl-CoA mutase	12
Mucopolysaccharide urine screen	9, 12, 22
Mucopolipidosis II/III (multiple hydrolases, I-cell)	14, 19
Multiple sulphatases	14
N-acetyl- $\alpha$ -galactosaminidase	16, 22
$\alpha$ -N-acetylglucosaminidase	13
N-acetyl $\alpha$ -neuraminidase	14
Oligosaccharide / sialic acid screen	12, 22
Organic acids	9, 11
Orotic acid	11
Phytanic acid and Pristanic acid	9, 16, 23
Plasmalogens	16, 23
Prenatal diagnosis	10, 20, 24
$^{14}\text{C}$ -Propionate incorporation	12
Propionyl-CoA carboxylase	11
Pterins	11
Pyruvate carboxylase	11
Sialic acid, quantitative	12

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Sphingomyelinase	16, 22
Steroid sulphatase – see aryl sulphatase C	
Sugar Chromatography	10
Tissue culture: Initiation of cell culture from skin biopsy, amniocytes or chorionic villi and storage of cells in cryogenic cell bank	20, 24
Tissue culture: Maintenance of cultures initiated elsewhere until investigations are completed and cryogenic storage of cells	20, 24
Very Long Chain Fatty Acids	16, 23
White cell cystine	11

**APPENDIX 1****REFERRAL LABORATORIES USED BY THE WILLINK LABORATORY**

When the Willink Laboratory does not perform a particular test, samples can often be referred to other laboratories world wide. The Willink Laboratory has a list of approved referral laboratories to which it sends samples for analysis. If a particular test is required, please contact the Willink Laboratory to discuss whether that test is covered by one of our approved referral laboratories or if preliminary testing needs to be performed by ourselves.

**The majority of UK laboratories to which samples are referred are CPA accredited. However, many of those from Europe and around the world are either not accredited or their accreditation status is unknown.**

**The Willink Laboratory makes every effort to appraise the laboratories to which it refers samples. This not only includes personal knowledge of the personnel carrying out the tests but also the international reputation of laboratories and their record of publications in reputable peer reviewed internationally renowned journals. Many laboratories do not quote turn around times as they are University bases research laboratories. However we find their turnaround times to be acceptable in the context of the disorder being investigated. In the absence of accredited laboratories, we have little option but to send samples from patients with vary rare disorders to laboratories that often provide a service unique world wide.**

**APPROVED REFERRAL LABORATORIES AND TESTS OFFERED**

Sheffield Children's Hospital\*

Clinical Chemistry

Western Bank

Sheffield S10 2TH

UK

Contact: Dr. Simon Olpin

Phone: 0114 271 7000

Email: [simon.olpin@sch.nhs.uk](mailto:simon.olpin@sch.nhs.uk)

Tests provided: Fatty Acid Oxidation ( $\beta$ -oxidation) studies on cultured skin fibroblasts.

Scottish Molecular Genetics Consortium\*\*\*

Ninewells Hospital

Dundee

UK

Contact: Dr. David Soudie

Phone: 01382 632035

Tests provided: Molecular analysis of Crigler-Najjar Syndrome

Purine Laboratory Guy's Hospital\*

Department of Chemical Pathology

Thomas Guy House

Guy's Hospital

London SE1 9RT

Phone: 020 7188 8008

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Tests provided: Urinary purine and pyrimidine analysis. Molybdenum Cofactor Deficiency Mutation analysis.

Oxford Genetics Unit\*\*\*

South Parks Road  
Oxford OX1 3QU  
UK

Contact: DR. G.K. Brown

Phone: 01865 275214

Fax: 01865 275318

Email: [garry.brown@bioch.ox.ac.uk](mailto:garry.brown@bioch.ox.ac.uk)

Tests provided: pyruvate dehydrogenase in cultured skin fibroblasts.

Newcastle Mitochondrial Diagnostic Service\*\*\*

University of Newcastle upon Tyne  
Framlington Place  
NE2 4HH  
UK

Contact: Dr. R.W. Taylor

Phone: 0191 222 8334

Fax: 0191 222 8553

Email: [r.w.taylor@ncl.ac.uk](mailto:r.w.taylor@ncl.ac.uk)

Tests provided: Mitochondrial respiratory chain enzymes in muscle.

Molecular and Medical Genetics Oregon\*\*\*

Oregon Health and Science University  
2525 S.W. 3<sup>rd</sup> Avenue,  
Portland OR 97210  
USA

Mersey and Cheshire Molecular Genetics Laboratory\*

Liverpool Women's Hospital  
Crown Street  
Liverpool L8 7SS  
UK

Contact: Roger Mountford

Phone: 0151 702 4228

Fax: 0151 702 4226

Email: [roger.mountford@lwh-tr.nwest.nhs.uk](mailto:roger.mountford@lwh-tr.nwest.nhs.uk)

Laboratory de Neurochimie\*\*\*

Bat 3B Center Hospitalier Lyon-Sud  
Pierre Benite Cedex  
F-69495  
France

Contact : Dr. Marie Vanier

Tests provided: Cholesterol esterification studies on cultured skin fibroblasts and prenatal diagnoses.

John F. Kennedy Institute\*\*\*  
Gl. Landevei 7 Postbox 1480  
Glostrup  
DK-2600  
Denmark  
Contact: Prof. Nina Horn

Institute of Laboratory Medicine Gothenburg\*\*\*  
Sahlgrenska University Hospital  
Gothenburg  
S-41345  
Sweden  
Contact: Dr. E Holme

Institute of Laboratory Medicine\*\*\*  
Ingolstadter Landstrasse 1  
Neuherberg  
85764  
Germany  
Fax: 49 89 3187 2397  
Email: [monika.ebbhardt@gsf.de](mailto:monika.ebbhardt@gsf.de)

Institute of Child Health\*  
30 Guilford Street  
London  
WC1N 1EH  
UK  
Contact: Prof. P. Clayton  
Tests provided: Plasma bile acids

Institut für Humangenetik München\*\*\*  
Des Klinikums rechts der Isar  
Der Technischen Universität München  
Germany  
Contact: Dr. Tim Strom  
Phone: 089 4140 6381  
Fax: 089 4140 6382  
Email: <http://ihg.gsf.de>

Guy's Regional Genetics Centre\*  
Guy's Hospital  
St Thomas Street  
London SE1 9RT  
UK  
Contact: Marie Jackson  
Tests provided: Batters Enzymes

Department of Paediatrics\*\*\*  
The Hammersmith Hospital  
Du Cane Road  
London  
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W12 0HS

UK

Contact: Dr. A Manzur

Clinical Chemistry\*\*

University Medical Centre De Boelelaan

HV Amsterdam

1081

The Netherlands

Contact: Dr. C Jacobs

Phone: 31 20 444 2416

Fax: 31 20 444 0305

Email: [C.Jakobs@vumc.nl](mailto:C.Jakobs@vumc.nl)

Chemical Pathology Block 20\*\*\*

St James' University Hospital

Beckett Street

Leeds

LS9 7TF

UK

Contact: Colin Evans

Bristol Biochemical Genetics Unit\*

Westbury-on-Tryn

Southmead Hospital

Bristol

BS10 5NB

UK

Contact: Dr. Anny Brown

Phone: 0117 959 5565

Fax: 0117 959 1792

Tests provided: Galactosaemia mutation analysis.

Birmingham Clinical Chemistry\*

Birmingham Children's Hospital

Steelhouse Lane

Birmingham

B4 6NH

UK

Basler Kinderspital\*\*\*

Roemergasse 8

Basel

Postfach CH 4005

Switzerland

Contact: Prof. Brian Fowler

Defects of Homocystine metabolism.

Aarhus Research Unit for Molecular Medicine\*\*\*

Aarhus University

Aarhus

Denmark

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Contact: Prof. B.S. Andresen  
Phone: 45 894 95142  
Fax: 45 894 96018  
Email: [BRAGE@KI.AU.DK](mailto:BRAGE@KI.AU.DK)

Institute of Neurology\*  
9<sup>th</sup> Floor  
Queens Square  
London  
WC1N 3BG  
UK

\* CPA UK Accredited Laboratory  
\*\* Accredited by Equivalent National Organisation  
\*\*\* Not Accredited or Accreditation status unknown.