External Handbook

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Department of Chemical Pathology
Great Ormond Street Hospital for Children

Great Ormond Street Hospital for Children
NHS Foundation Trust

Chemical Pathology Services

External User Guide

Updated May 2023

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INTRODUCTION

Chemical Pathology, Great Ormond Street Hospital for Children NHS Foundation Trust (GOSH), is a specialist medical laboratory accredited by UKAS to ISO15189:2012 and provides a wide range of Chemical Pathology analyses with a special interest in the diagnosis and monitoring of inborn errors of metabolism. For current information on the scope of our accreditation please visit www.ukas.com

The laboratory is fully staffed between 9 am and 5.30 pm Monday to Friday and staff will be available for any enquiries you may have. For sample requirements and general enquiries not dealt with by this guide or for results, please contact the general enquiries line or visit our website at www.gosh.nhs.uk/labs

General information on pathology tests can be found at http://labtestsonline.org.uk/

For advice on investigations, explanations of tests or procedures, clinical advice and interpretation or to request an urgent analysis, the duty biochemist is available on bleep 020 7405 9200 (hospital switchboard) bleep 0589 and by email: duty.biochemists.distribution@gosh.nhs.uk during normal working hours. The duty biochemist can also be contacted via the hospital switchboard, out of hours.

This handbook contains details of the tests currently performed in house for external users. There are a number of investigations that are available to GOSH Clinicians provided by external referral laboratories; details of which can be found in the Internal User's Guide (CCL002).

Sample reception
Chemical Pathology Reception
Paediatric Laboratory Medicine
Camelia Botnar Building
Great Ormond Street Hospital for Children
Great Ormond Street
London
WC1N 3JH

Senior Staff		
Dr Alistair Horman alistair.horman@gosh.nhs.uk	Consultant Clinical Scientist *Co-Clinical Lead*	☎ 020 7813 8321 (DD)
Ms Helen Aitkenhead helen.aitkenhead@gosh.nhs.uk	Consultant Clinical Scientist *Co-Clinical Lead, Director of Newborn Screening*	☎ 020 7813 8318 (DD)
Mrs Christine Morris christine.morris@gosh.nhs.uk	Lead Laboratory Manager *Paediatric Laboratory Medicine*	☎ 020 7813 8664 (DD)
Mrs Katie Harvey katie.harvey@gosh.nhs.uk	Principal Clinical Scientist *Enzyme Laboratory*	☎ 020 7829 7843 (DD)
Ms Helen Prunty helen.prunty@gosh.nhs.uk	Principal Clinical Scientist *Metabolic Laboratory*	☎ 020 7813 8319 (DD)
Dr Amanda Lam amanda.lam@gosh.nhs.uk	Principal Clinical Scientist *Metabolic Laboratory*	
Dr Steve Krywawych steve.krywawych@gosh.nhs.uk	Principal Clinical Scientist	☎ 020 7405 9200 x 6758
Prof Simon Heales simon.heales@gosh.nhs.uk	Associate Professor of Clinical Chemistry	

Mr Daley Aofolaju daley.aofolaju@gosh.nhs.uk	Chief Biomedical Scientist *Blood Sciences / Special Routine*	☎ 020 7405 9200 x 0214
Dr Derek Burke derek.burke@gosh.nhs.uk	Chief Biomedical Scientist *Enzyme Laboratory*	☎ 020 7405 9200 x5290
Mr Ade Ifederu adeboye.ifederu@gosh.nhs.uk	Chief Biomedical Scientist *Head of Newborn Screening*	☎ 020 7405 9200 x5290
Ms Julie Leakey julie.leakey@gosh.nhs.uk	Chief Biomedical Scientist *Metabolic Laboratory*	☎ 020 7405 9200 x0480
Mrs Tejwurree Ramgoolam tejwurree.ramgoolam@gosh.nhs.uk	Chief Biomedical Scientist *Deputy Head of Newborn Screening*	☎ 020 7405 9200 x5290

DEPARTMENT SECTIONS AND PHONE NUMBERS

RESULTS ENQUIRIES/GENERAL ENQUIRIES	Email: gos-tr.chemicalpathology@nhs.net
Departmental Office	☎ 020 7829 8662 (note: email preferred)
CLINICAL ADVICE	☎ 020 7405 9200 bleep 0589 Email: duty.biochemists.distribution@gosh.nhs.uk

Metabolic / Enzyme Laboratory Reception	☎ 020 7405 9200 ext 7874
Metabolic Laboratory	☎ 020 7405 9200 ext 5225
Enzyme Laboratory	☎ 020 7762 6751 (DD) or 020 7405 9200 ext 1785 Email: gos-tr.ENZYME@nhs.net
Blood Sciences Reception	☎ 020 7405 9200 ext 5009
Automated Routine Laboratory	☎ 020 7405 9200 ext 5710
Newborn Screening Laboratory	☎ 020 7829 8383 (DD) Email: gos-tr.enquiriesgosnbs@nhs.net

REQUESTING

The test request from an external user acts as formal acceptance of testing and creates an agreement with the requester.

It is assumed that all necessary patient consent (and ethical approval if applicable) has been obtained by the Health Professional requesting the tests prior to sampling.

A request giving the following information must accompany the specimen (apart from newborn screening tests), a minimum of three identifiers are required:-

Patient ID:
surname or family name
forename or personal name
date of birth (many reference ranges are age dependent)
sex (some reference ranges are sex related)
patients reference i.e. Hospital number, laboratory, NHS number

Specimen: type, date and time of collection

Test(s) required:

Clinical details: as full as possible including medication, diet, fasting or fed sample

Sender: name of sender, address for report and invoice
urgent contact, name, phone number (if different from sender)

Please use our special 'Chemical Pathology' Request Form and an 'Enzyme Screen' Request form (see appendix 4). This will enable us to perform the most appropriate investigations and provide comprehensive interpretive reports based on the information provided.

Labelling of Specimens
Specimens should be legibly labelled with a minimum of three patient identifiers (see above) along with the date and time of collection, type of specimen and specimen reference. To avoid results being wrongly attributed to patients, unlabelled samples or samples that do not match the name on the request form cannot be processed by the laboratory.

Protection of Personal Information
All staff have a legal obligation to ensure that any confidential information they come into contact with is kept secure and confidential at all times. Where a member of staff receives a request for information relating to an individual, staff must ensure that any disclosure of confidential information is fully justified and in compliance with the Data Protection Act 1998 or Common Law Duty of Confidentiality.

SAMPLE COLLECTION/HANDLING

Requirements for sample collection, processing and transportation are listed under individual analytes further on in this handbook. Please note that the preferred sample type is stated; however other sample types may also be suitable. Please contact us for further information.

Abbreviations used:				
	Li hep	Lithium heparin	L	Liver
	Plain	Plain container	M	Muscle
	RBC	Erythrocytes	F	Fibroblasts
	WBC	Leucocytes	FB	Fetal blood
	S	Serum	VL	Vacuolated lymphocytes
	P	Li hep plasma	CV	Chorionic villus
	B	Whole blood	CCV	Cultured chorionic villus
	BS	Blood spot	AF	Amniotic fluid

Order of Draw / Collection sequence

Order	Tube	Additive
1	Green	Sodium citrate
2	Brown	Serum gel
3	White	Serum
4	Orange	Lithium heparin
5	Red	EDTA
6	Blue	EDTA for blood transfusion
7	Yellow	Sodium fluoride

STORAGE

Samples should be sent to us as soon as possible after collection. However, if storage is unavoidable, guidance for sample storage is given under individual tests.

Requesting additional tests and sample retention

If the sample is still available and sufficient in volume and is viable, additional tests may be added by phone. However requestor may be asked to send a further request form with details of the test required.

Samples are retained in accordance to the Guidelines published by the Royal College of Pathologists and the Institute of Biomedical Science: *the retention and storage of pathological records and specimens (5th edition, 2015)*. All samples are stored for a minimum of 48 hours after the report has been issued; most samples are stored for at least two weeks and many are stored for longer periods. Please contact us for further advice.

PACKING

The packing requirements for samples are specified under each analyte further on in the booklet.

General and room temperature

All specimens must be in leak-proof containers. Seal cap of container with 'parafilm' or similar waterproof tape. Wrap each container with sufficient absorbent material to completely absorb the contents in case of breakage. There should be no contact between containers. Place the container(s)

and packing in plastic bag and seal the bag. Place the sealed bag, together with the request form, in a rigid fibre or plastic outer case. The outer case should be sealed with tape.

NOTE – the request form must **not** be inside the plastic bag with the specimen.

Ice
Pack specimens as above. Place the ice in a leak-proof container (use a plastic bottle or bag). Ice should not come into direct contact with the specimen container to avoid risk of contamination or labels becoming illegible. Place the ice and specimen(s) in a plastic outer container and seal with waterproof tape. Include sufficient ice to cover any possible delays in delivery.

Ice packs are suitable for **a journey time of less than 6 hours**. However, **DO NOT place ice packs from –20 °C freezer immediately next to whole blood or cells.**

Dry Ice [Solid CO_2]
Pack the specimens as above. The outer pack must be an insulator and be permeable to CO_2, e.g. expanded polystyrene. State "CONTAINS SOLID CO_2" on the outside. Seal outer case with tape. Include sufficient solid CO_2 to cover any possible delays in delivery.

TRANSPORT

First class post

When sending specimens by first class post, the packaging MUST comply with UN3733 packaging regulations and postal regulations.

The package must be labelled 'PATHOLOGICAL SPECIMEN' and may only be sent 1st class letter post. Where first class post is indicated this assumes that delivery will be made by the next day. Please DO NOT POST on Friday or before a UK Bank Holiday.

Courier or express delivery.
A reliable service should be used and instructed to take the specimens to the Reception in Chemical Pathology in the Camelia Botnar Laboratories Building.

TURNAROUND TIME

Turnaround time given is the anticipated time taken between sample receipt and report under normal operating conditions. Where the assays are batched and performed infrequently, the time is given as a range up to the maximum anticipated time. However, on occasions, the turnaround time may be longer if the result requires confirmation or further analysis is required. Time taken for sample transport and posting the report should be added to this. Where appropriate, abnormal results will be phoned, or emailed to the sending laboratory.
In cases where results are required more urgently, please contact the relevant section or the duty biochemist (bleep 0589) to discuss your requirements (prior to sending specimens) so that samples can be fast tracked.

REPORTING

An **on-line Results Portal** is available for all the users to access their reports and check the status of requested tests. The service is fully secure and free of charge.
To arrange access to GOSHOutreach, please email gos-tr.Outreach@nhs.net
Authorised reports can also be printed and dispatched by first class post to the requesting organisation as required. Please contact us at gos-tr.chemicalpathology@nhs.net

NEWBORN SCREENING

Blood spot assays to screen for phenylketonuria (PKU), congenital hypothyroidism (CHT), medium chain acyl coA dehydrogenase deficiency (MCADD), sickle cell disorders, cystic fibrosis (CF), maple syrup urine disease (MSUD), isovaleric acidaemia (IVA), glutaric aciduria type 1 (GA1) and homocystinuria (HCU) in the newborn period are available as part of the NHS Newborn Blood Spot Screening Programme.
Sample requirement: 4 good blood spots collected on day 5 (day of birth = day 0) on a standard screening card, dried at room temperature, and enclosed in a glassine cover. Please provide the dates of birth and sampling as well as the baby's NHS number as these are mandatory fields. Send at room temperature by post immediately to the North Thames Newborn Screening Laboratory.

CHANGES TO METHODS INCLUDING REFERENCE INTERVALS

The performance of our methods is under constant review to ensure that we continue to provide a high-quality service. Occasionally we will change our method and / or reference intervals as part of this quality improvement. When we change methods or reference intervals, details of the change will be made on the patient reports. Also our users may be notified via email, via the Results portal, multi-disciplinary team meetings or in a letter depending on the change.

COMPLAINTS PROCEDURE

The Chemical Pathology Department makes every effort to maintain a high standard of service at all times. However, mistakes do occur and we are happy to receive any comments and to try to resolve any complaints quickly. If you have a complaint, please speak in the first instance to a member of the Senior Staff team whose contact numbers can be found on page 3 and 4. If this fails to meet your requirements, please state that you wish to speak to a more senior member of staff or to a member of the Trust's Patient Safety and Complaints Team.

FACTORS AFFECTING THE PERFORMANCE OF TESTS AND THEIR INTERPRETATION

METABOLIC INVESTIGATIONS

What samples?
It is important to check the fluid in which the metabolites of interest most obviously accumulate, e.g. urine for organic acids. The next part of this booklet indicates the sample type required for the investigations offered. When indicated (e.g. because of metabolite instability), it is necessary to make arrangements with the laboratory prior to collecting the sample.

When?
The time of the sample collection is crucial where characteristic metabolites accumulate only intermittently in the samples. Whenever possible, patients should be investigated during periods when they are unwell. Samples should be taken as soon as possible after admission, before changes in treatment and diet lead to the disappearance of relevant metabolites.

Sample integrity
Bacterial activity in poorly preserved samples produces a rise in pH and can lead to both the appearance of bacterial metabolites and the breakdown of important components, especially sugars and some amino acids. Samples with a high pH may not be analysed for this reason. Faecal contamination of urine produces a similar effect. Dilute urine makes the detection of urinary constituents unreliable and samples with creatinine concentration >1 mmol/L are preferred.

Diet
Some metabolic disorders are related to a particular dietary intake or are produced only in the fasting state. Investigations should be carried out, as far as possible, on samples taken at the time the patient was symptomatic. Dietary restrictions or feeding may cause characteristic metabolites to disappear and result in false negative results. Dietary metabolites may interfere with organic acid, amino acid or carbohydrate chromatograms. Patients receiving intravenous amino acid mixture may have amino aciduria, amino acidaemia or organic aciduria. Information on the type of diet and the timing of the sample in relation to meals will aid in the interpretation of these complex analyses.

Drugs
Drugs influence metabolic investigations by analytical interference or by modifying metabolic processes. Details of all medication should be provided with metabolic investigations.

Exchange transfusions / blood transfusions
These may affect the analytes measured in blood and especially erythrocytes. When requesting tests in such patients, check whether adequate time has lapsed since the last transfusion. For assays of enzymes and metabolites in erythrocytes, the time interval should be 6 weeks.

Other factors include
Age of specimen
Time of specimen separation
Specimen storage
Specimen haemolysis, icterus and lipaemia
Fasting state

BIOCHEMICAL INVESTIGATION OF A SUDDEN INFANT DEATH

If an inborn error of metabolism is suspected in an infant who died suddenly, collect the following samples as soon as practicable to minimize post mortem changes; blood spots, bile spots, plasma, urine, CSF, aqueous humor. Blood stained CSF and urine should be spun and separated immediately and this should be recorded. Freeze at –20 °C. Skin biopsy can also be taken (see fibroblasts). Please discuss the request with the duty biochemist on 020 7405 9200 bleep 0589 before sending the samples.

METABOLIC INVESTIGATION IN A MORIBUND CHILD

The diagnosis of metabolic disease cannot be made after death unless the correct specimens have been appropriately collected. If metabolic disease is suspected and the child seems likely to die before a diagnosis can be made, it would be advisable to collect the following specimens:

Blood - 10 ml in a heparinised tube. Separate plasma promptly. Freeze the bulk of the plasma, the remaining plasma and red cells should be kept at 4 °C.

Urine - 20 ml in a plain container and deep freeze.

Blood spots for acylcarnitines

Bile spots for acylcarnitines

DNA - If the condition is one in which DNA studies are likely to be helpful, take 10ml blood into an EDTA tube and deep freeze the whole blood.

Tissue biopsies (liver, muscle, heart) – Label the plain container with the type of tissues prior to taking the biopsies. Pre-cool a plain container in the deep freeze. Obtain dry ice, liquid nitrogen or a freezing pack. Make a small boat with a piece of aluminium foil and place it on the dry ice / freezing mixture. Take the biopsy (as many cores as possible, minimum two) and put it immediately in the boat, it should freeze immediately and thereafter should be not allowed to thaw at any time. Wrap up the core in the foil and put it in the pre-chilled container, making sure that the cap is tight and immediately replace in the deep freeze (-40 °C or lower). A small part should be put into glutaraldehyde and if necessary some into formalin, but the majority should be frozen for chemistry and enzymology.

Skin Biopsy - See fibroblasts (appendix 1, page 26)

Please note if you are sending ‘chain of evidence’ samples, please discuss with the duty biochemist prior to sending.

ASSAY DIRECTORY

Codes

Tests highlighted in turquoise are analysed in the Metabolic Laboratory
Test highlighted in green are analysed in the Enzyme Laboratory
Tests highlighted in yellow are analysed in the Routine Laboratory
Tests highlighted in pink are analysed in the Routine Laboratory

AMINO ACID DISORDERS

Test	Sample requirement	Sample handling	Turnaround
Amino acids			
Plasma	0.5 ml li hep plasma	Separate ASAP. Freeze immediately. Send frozen	1 – 2 w by HPLC 1 – 3 w by IEC
Urine	2 ml fresh random urine	Freeze immediately. Send frozen	3 – 6 w
CSF	0.2 ml clear CSF	Freeze immediately. Send frozen	1 – 2 w
Blood spot - branched chain	4 blood spots on std card	Send by first class post.	4 d
Homocysteine			
Plasma	0.5 ml li hep plasma	Separate ASAP. Freeze immediately. Send frozen	1 – 2 w
Urine	2 ml fresh random urine	Freeze immediately	3 – 6 w
Succinylacetone	2 ml fresh random urine	Freeze immediately. Send frozen	2 - 4 w
Sulphocysteine	2 ml fresh random urine	Freeze immediately. Send frozen	3 – 6 w

CARBOHYDRATE METABOLISM DISORDERS

Galactose/ Fructose metabolism Disorders

Test	Type	Sample handling		Turnaround
Reducing substances Sugar chromatography	U	2 ml fresh random urine	Freeze immediately. Send frozen	up to 2 w 3 – 6 w
Galactose -1-phosphate uridyl-transferase [Gal-1-PUT]	RBC	2 ml li hep whole blood. No transfusion prior 6 wk	Send whole blood at ambient temp. to reach lab ideally within 48 h of collection	2 - 4 w
Galactose-1 Phosphate	RBC	2 ml li hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h of collection	4–6 w
Fructose-1-P aldolase	L	liver biopsy	Freeze immediately. Send frozen without thawing	4-6 w

Glycogen Storage Disorders (GSD)

Test	Type	Sample handling		Turnaround
Ia Glucose-6-phosphate hydrolase	L	Fresh liver biopsy	Contact enzyme lab prior to sampling. Do not freeze.	4-6 w
Ib Glucose-6-phosphate translocase	L	Fresh liver biopsy	Contact enzyme lab prior to sampling. Do not freeze.	4-6 w
II α-1,4-glucosidase (acid maltase) ** CRIM testing available*	BS, WBC	Blood spots, 5 ml li hep blood	Send whole blood at ambient temp. to reach lab ideally within 24 h collection	4-6 w
III glycogen debrancher	WBC	5-10 ml li hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h collection	4-6 w
	M, L	muscle / liver biopsy	Freeze immediately Send frozen	4-6 w
	F	skin biopsy into culture Medium or saline	Send at ambient temp. Do not freeze	4-6 w
IV glycogen brancher	WBC	5-10 ml li hep whole blood	Send whole blood at ambient temp. to reach lab within 18 h of collection	4-6 w
	M, L	muscle / liver biopsy	Freeze immediately Send frozen	4-6 w
	F	skin biopsy into culture Medium or saline	Send at ambient temp. Do not freeze	4-6 w
V phosphorylase	M	muscle biopsy	Freeze immediately Send frozen	4-6 w
VI phosphorylase	WBC	5-10 ml lip hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h collection	4-6 w
	L	liver biopsy	Freeze immediately Send frozen	4-6 w
VII phospho fructokinase	M	muscle biopsy	Freeze immediately Send frozen	4-6 w
IX phosphorylase b Kinase	RBC	5 ml li hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h collection	4-6 w
	L	liver biopsy	Freeze immediately Send frozen	4-6 w

***Pompe CRIM testing** – contact the Enzyme Laboratory Tel:* 020 7405 9200 ext 6751/1785

Glycolytic enzymes

Test	Type	Sample handling		Turnaround
Fructose-1,6 bisphosphatase	WBC	5-10 ml lip hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h of collection	4-6 w
	L	liver biopsy	Freeze immediately Send frozen	4-6 w
Phospho-glucomutase	WBC	5 ml li hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h of collection	4-6 w
	M, L	muscle / liver biopsy	Freeze immediately Send frozen	4-6 w

FATTY ACID OXIDATION DEFECT / HYPOGLYCAEMIA

Test	Type	Sample handling		Turnaround
3-(B)Hydroxy-butyrate (BOHB)	P	0.3 ml li hep plasma	Freeze immediately. Send frozen. Provide glucose result for interpretation.	1 - 2 w
Free fatty acids (non-esterified fatty acids, NEFA)	P	0.3 ml li hep plasma	Freeze immediately. Send frozen. Provide glucose result for interpretation.	1 - 2 w
Acetoacetate	B	perchloric acid supernatant	Freeze immediately (see appendix for protocol). Send frozen	1 – 2 w
Organic acids	U	2 ml fresh random urine	Freeze immediately. Send frozen	2 – 4 w
Acylcarnitines	BS	4 blood spot on standard card	Send by first class post	1 - 2 w

Diagnostic fast
All the above investigations to be carried out at the beginning and end of the fast under close medical supervision in a Hospital unit experienced in carrying out these tests (not advisable in patients under 18 months or under 5 kg in weight)

LACTATE / PYRUVATE DISORDERS

Test	Type	Sample handling		Turnaround
Lactate	P	2 ml fluoride oxalate plasma	Separate plasma assay ASAP	6 h
	B	perchloric acid precipitation (see appendix for protocol)	Freeze immediately Send frozen	1 – 2 w
	CSF	0.2 ml clear CSF	Freeze immediately Send frozen	1 – 2 w
Lactate/Pyruvate ratio	B	perchloric acid precipitation (see appendix for protocol)	Freeze immediately Send frozen	1 – 2 w
	CSF	perchloric acid precipitation (see appendix for protocol)	Freeze immediately Send frozen	1 – 2 w

LYSOSOMAL STORAGE DISORDERS (LSD)

Initial investigations/monitoring

Test	Type	Sample handling		Turnaround
Glycosaminoglycans	U	5 ml fresh random urine	Send at ambient temp. by special post	up to 4 w
Sialic acid*	U	5 ml fresh random urine	Send at ambient temp. by special post	up to 4 w
Globotriaosylceramide (ceramide trihexoside) (GL3/GB3/CTH)**	U	5 ml fresh random urine	Send at ambient temp. by special post	up to 4 – 6 w
Lyso-globotriaosyl-ceramide **	P	0.5 ml li hep plasma	Send to reach lab within 24 h of collection For best results, freeze plasma immediately. Send frozen.	up to 6 – 8 w
Glucose tetra-saccharide, Glc4/Hex4	U	1 ml fresh random urine	Store and send frozen/ chilled if possible	up to 4 – 6 w
Vacuolated lymphocytes	B	2 ml EDTA whole blood (see page 22)	Send at ambient temp. by special post (done in	Contact histopathology

			Histopathology)	at GOSH. Tel: 020 7829 8663. Fax: 020 7813 1170.

** Measured in a research laboratory in Institute of Child Health, UCL
* Contact the laboratory before sending a sample.

Individual enzyme

Assays available individually for the diagnosis of lysosomal storage disorders are listed below with samples suitable for the assay. Turnaround is 4-6 weeks

Disease	Assay	Tissue
Mucopolysaccharidoses		
I-Hurler	α-iduronidase	WBC, F
II-Hunter	iduronate-sulphatase	WBC, P, F
IIIA-Sanfilippo A	heparan sulphamidase	WBC, F
IIIB-Sanfilippo B	α–N-acetyl-glucosaminidase	WBC, P, F
IIIC-Sanfilippo C	N-acetyltransferase	WBC, F
IIID-Sanfilippo D	N-acetyl-glucosamine-6-sulphatase	WBC, F
IVA-Morquio A	N-acetyl galactosamine-6-sulphatase	WBC, F
IVB-Morquio B	β-galactosidase	WBC, F
VI-Maroteaux-Lamy	arylsulphatase B	WBC, F
VII-Sly	β-glucuronidase	WBC, P, F
Multiple enzyme defects		
Mucolipidosis II (I-cell)	multiple hydrolases	P, VL, F
Mucolipidosis III (pseudo Hurler)	multiple hydrolases	P, VL, F
Multiple sulphatidosis	multiple sulphatases	WBC, P, F
Gangliosidoses		
G_{M1} gangliosidosis	β-galactosidase	WBC, VL, F
G_{M2} gangliosidoses:		
Tay Sachs / B1 variant	hexosaminidase A	WBC, P, F
Sandhoff	total β-hexosaminidase	WBC, P, F
Leucodystrophies		
Krabbe	galactocerebrosidase	WBC, F
Metachromatic	arylsulphatase A	WBC, F
Glycoproteinoses		
Fucosidosis	α-fucosidase	WBC, P, VL, F
α-Mannosidosis	α-mannosidase	WBC, P, VL, F
β-Mannosidosis	β-mannosidase	P, WBC, F, VL
Schindler	α-N-acetyl galactosaminidase	P, WBC, F
Sialidosis	α-neuraminidase	WBC, VL, F
Aspartylglucosaminuria	aspartylglucosaminidase	P, F
Galactosialidosis	α-neuraminidase/ β-galactosidase	WBC, VL, F
Other lipid storage disorders		
Fabry	α-galactosidase	WBC, P, F
Gaucher	β-glucosidase	WBC, F
	chitotriosidase	P
Niemann-Pick A & B	sphingomyelinase	WBC, VL, F,
Wolman & cholesteryl ester storage disease (CESD)	acid esterase (lysosomal acid-lipase/LAL)	WBC, VL, F,
Neuronal ceroid lipofuscinoses (*Batten disease****)***		
Infantile (INCL, NCL1, CLN1)	palmitoyl protein thioesterase	WBC, F

Classic late infantile (LINCL, NCL2, CLN2)	tripeptidyl peptidase I	WBC, F
Transport defects		
Cystinosis	cystine	WBC, F
Sialic acid storage	sialic acid	U, VL, F

NB: **Prenatal diagnosis** is available for these disorders. Contact the laboratories to discuss if required.

Grouped Enzyme Screens for Lysosomal Disorders

The lysosomal storage disorders can be grouped according to clinical features and a group of enzyme assays can be carried out on a single blood sample which provides both white blood cells and plasma for analysis. The clinical signs of a lysosomal storage disease may eventually develop to give a classic picture but diagnosis at an earlier stage can be more difficult, e.g. while Type II Gaucher disease leads to hepato/splenomegaly, neurological signs may be more obvious initially. To meet this and other concerns all patients have plasma chitotriosidase measured to exclude Gaucher disease and other LSDs. Palmitoyl protein thioesterase and tripeptidyl peptidase I which are deficient in infantile (INCL, NCL1, CLN1) and classic late infantile (LINCL, NCL2, CLN2) neuronal ceroid lipofuscinosis are assayed in all patients under 16 years with neurological problems, and also in adult patients if these disorders are suspected.

The profile of enzymes in a 'screen' unless specifically requested may vary depending on clinical details provided (or discussed) or the results of other investigations or tests.'

It is important that the laboratory is given full clinical details in order to carry out the appropriate combination of tests. Turnaround time is 6 - 8 weeks
Note: Some diseases may present under more than one heading.

Neurodegenerative screen
Evidence of neurological regression, hypotonia, fits, etc.

Disease	Enzyme
G_{M1} gangliosidosis	β-galactosidase
G_{M2} gangliosidoses:	
Tay Sachs / B1 variant	hexosaminidase A
Sandhoff	total β-hexosaminidase
Krabbe leucodystrophy	galactocerebrosidase
Metachromatic leucodystrophy	arylsulphatase A
Fucosidosis	α-fucosidase
α-Mannosidosis	α-mannosidase
β-Mannosidosis	β-mannosidase
Schindler	α-N-acetyl galactosaminidase
MPS VII-Sly	β-glucuronidase
I cell disease	I cell screen

Plasma chitotriosidase is assayed in all patients to exclude Gaucher disease

All patients under 16 years of age are tested for:

Infantile neuronal ceroid lipofuscinosis(INCL, NCL1, CLN1)	palmitoyl protein thioesterase
Classic late infantile neuronal ceroid lipofuscinosis (LINCL, NCL2, CLN2)	tripeptidyl peptidase I

Dysmorphic screen
The first line test for a dysmorphic child is screening for a mucopolysaccharidosis by urine GAGs. The following enzymes are indicated if a mucopolysaccharidosis is excluded.

Disease	Enzyme
G_{M1} gangliosidosis	β-galactosidase
Sialidosis	α-neuraminidase
Galactosialidosis	α-neuraminidase/ β-galactosidase

Fucosidosis	α-fucosidase
α-Mannosidosis	α-mannosidase
I cell disease	I cell screen
β-Mannosidosis	β-mannosidase
MPS VII-Sly	β-glucuronidase
Multiple sulphatidosis	arylsulphatase A
Aspartylglucosaminuria	aspartylglucosaminidase
Schindler	α-N-acetyl galactosaminidase

Plasma chitotriosidase is assayed in all patients to exclude Gaucher disease

Hepato/splenomegaly screen: for those patients with hepatomegaly and or splenomegaly suspected of having a lysosomal storage disorder.

Disease	Enzyme
G_{M1} gangliosidosis	β-galactosidase
Sialidosis	α-neuraminidase
Galactosialidosis	α-neuraminidase/ β-galactosidase
Gaucher	β-glucosidase
Niemann-Pick A & B	sphingomyelinase
Wolman & CESD	acid esterase (lysosomal acid-lipase/LAL)
Fucosidosis	α-fucosidase
α-Mannosidosis	α-mannosidase
I cell disease	I cell screen
β-Mannosidosis	β-mannosidase
MPS VII-Sly	β-glucuronidase

In all patients with hepato/splenomegaly plasma chitotriosidase is assayed

Cherry red spot screen: for patients with a cherry red spot on the macula.

Disease	Enzyme
G_{M1} gangliosidosis	β-galactosidase
G_{M2} gangliosidoses:	
Tay Sachs / B1 variant	hexosaminidase A
Sandhoff	total β-hexosaminidase
Niemann-Pick A	sphingomyelinase
Sialidosis	α-neuraminidase
Galactosialidosis	α-neuraminidase/ β-galactosidase
Krabbe leucodystrophy	galactocerebrosidase

Angiokeratoma screen: for patients with an angiokeratoma.

Disease	Enzyme
Fabry	α-galactosidase
Fucosidosis	α-fucosidase
Sialidosis	α-neuraminidase
Galactosialidosis	α-neuraminidase/ β-galactosidase
Adult G_{M1} gangliosidosis	β-galactosidase
α-Mannosidosis	α-mannosidase
β-Mannosidosis	β-mannosidase
Schindler	α-N-acetyl galactosaminidase
Aspartylglucosaminuria	aspartylglucosaminidase

DNA Analysis

The Enzyme Laboratory works closely with the Clinical Molecular Genetics Laboratory at Great Ormond Street Hospital to offer mutational analysis for many of the lysosomal storage disorders. It is essential to test for the presence of the polyA mutation encoding a **pseudodeficiency** of arylsulphatase A in all patients with low arylsulphatase A activity. For other disorders the Enzyme Laboratory will advise if mutational analysis is available and/or appropriate when a diagnosis is made.

PRENATAL DIAGNOSIS

Prenatal diagnosis is available for the following disorders. It is important that the diagnosis in the index case has been confirmed in an appropriate tissue and ideally enzyme levels in the parents should be measured to exclude pseudodeficiencies etc. The tissues suitable for assay are stated in the table. **It is <u>essential</u> to contact the Enzyme Laboratory (020 7405 9200 ext 1785) before taking any samples for prenatal diagnosis to discuss your requirements and transport arrangements**. It may take time to have suitable controls available for the assay so advance notice of an up-coming prenatal can ensure a quicker turnaround time.

For chorionic villus specimens, it is our policy to assay the villi directly, where appropriate, and then to check equivocal results or confirm diagnosis of an unaffected fetus on cultured cells.

Direct and cultured cell assays are charged separately and an additional charge is made for the cell culture. For amniotic fluid samples where the assay is performed on cultured cells, the cost of the cell culture is charged additionally.

LYSOSOMAL STORAGE DISORDERS

Mucopolysaccharidoses, mucolipidoses and multiple sulphatidosis

Following amniocentesis, electrophoresis of amniotic fluid glycosaminoglycans (GAGs) is carried out on all pregnancies at risk for a mucopolysaccharidosis, mucolipidoses II and III or a multiple sulphatidosis.

Disorder	Enzyme	Samples
Mucopolysaccharidoses		
I Hurler / Scheie	α-iduronidase	CV, CCV, CAC
II Hunter	iduronate sulphatase	CV, CCV, AF, CAC
IIIA-Sanfilippo A	heparan sulphamidase	CV, CCV, CAC
IIIB-Sanfilippo B	α-glucosaminidase	CV, CCV, CAC
IIIC-Sanfilippo C	N-acetyltransferase	CV, CCV, CAC
IVA-Morquio A	N-ac galactosamine-6-sulphatase	CV, CCV, CAC
IVB-Morquio B	β-galactosidase	CV, CCV, CAC
VI-Maroteaux-Lamy	arylsulphatase B	CV, CCV, CAC
VII-Sly	β-glucuronidase	CV, CCV, AF, CAC
Mucolipidosis II (I-cell)	multiple lysosomal hydrolases	CCV, AF, CAC
Mucolipidosis III (pseudo-Hurler)	multiple lysosomal hydrolases	CCV, AF, CAC
Multiple sulphatidosis	multiple sulphatases	CV, CCV, AF, CAC,
Lipidoses		
GM1 gangliosidosis	β-galactosidase	CV, CCV, CAC
GM2 gangliosidoses:		
Tay Sachs	hexosaminidase A	CV, CCV, CAC
Sandhoff	total β-hexosaminidase	CV, CCV, AF, CAC
Krabbe leucodystrophy	galactocerebrosidase	CV, CCV, CAC
Metachromatic leucodystrophy	arylsulphatase A	CV, CCV, CAC
Fucosidosis	α-fucosidase	CV, CCV, CAC
β-Mannosidosis	β-mannosidase	CV, CCV, CAC
α-Mannosidosis	α-mannosidase	CV, CCV, CAC

Schindler	α-N-acetyl galactosaminidase	CV, CCV, CAC
Sialidosis	neuraminidase	CV, CCV, CAC
Galactosialidosis	α-neuraminidase/ β-galactosidase	CV, CCV, CAC
Fabry	α-galactosidase	CV, CCV, AF, CAC
Gaucher	β-glucosidase	CV, CCV, CAC
Niemann-Pick A & B	sphingomyelinase	CV, CCV, CAC
Wolman & CESD	acid esterase (lysosomal acid-lipase/LAL)	CV, CCV, CAC
Other lysosomal disorders		
Sialic acid storage	sialic acid	CV, CCV, AF, CAC
Cystinosis	cystine	CV, CCV, CAC
Pompe (GSD type II)	α-glucosidase	CV, CCV, CAC
Neuronal ceroid lipofuscinoses		
Infantile (INCL, NCL1, CLN1)	palmitoyl protein thioesterase	CV, CCV, CAC
Classic late infantile (LINCL, NCL2, CLN2)	tripeptidyl peptidase I	CCV, CAC
Glycogen storage disorders		
GSD II (Pompe)	α-glucosidase	CV, CCV, CAC
GSD IV	brancher	CV, CCV, CAC
Urea cycle disorders		
OCT deficiency	ornithine carbamoyl transferase	fetal liver
CPS deficiency	carbamoyl phosphate synthase	fetal liver
Arginase deficiency	arginase	FB
Argininosuccinate lyase deficiency	argininosuccinate lyase	FB

ORGANIC ACID DISORDERS

Test	Type	Sample handling	Turnaround
Organic acids incl. methylmalonate	5 ml fresh random urine	Freeze immediately. Send frozen	2 – 4 w
N-acetylaspartate	5 ml fresh random urine	Freeze immediately. Send frozen	2 – 4 w
Biotinidase	0.2 ml li hep plasma	Freeze ASAP. Send frozen	1 – 2 w

PEROXISOMAL DISORDERS

Very long chain fatty acids includes phytanate & pristanate	0.5 ml li hep plasma or EDTA	Separate immediately. Send by 1st class post.	2 – 4 w

UREA CYCLE DISORDERS

Amino acids	P	0.5 ml li hep plasma	Separate ASAP. Freeze immediately. Send frozen	1 – 2 w
Organic acids includes orotic acid	U	2 ml fresh random urine	Freeze immediately. Send frozen	2 – 4 w
N-acetylglutamate Synthase	Discuss with enzyme lab			up to 6 w
Arginase	RBC	5 ml li hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h of collection	up to 6 w
	L	liver biopsy	Freeze immediately. Send frozen	up to 6 w
Argininosuccinate Lyase	RBC	5 ml li hep whole blood	Send whole blood at ambient temp. to reach lab ideally within 24 h of collection	up to 6 w
	L	liver biopsy	Freeze immediately. Send frozen	up to 6 w
Carbamoyl Phosphate synthase	L	liver biopsy	Freeze immediately. Send frozen	up to 6 w
Ornithine carbamoyl Transferase	L	liver biopsy	Freeze immediately. Send frozen	up to 6 w

OTHER INHERITED METABOLIC DISORDERS

Hypophosphatasia

Phospho-ethanolamine	U	2 ml fresh random urine	Freeze immediately. Send frozen	3 – 6 w

Disaccharidase Deficiencies

Enzymes * (* not included in current scope of accreditation)	jejunum	2 mg jejunum biopsy	Snap freeze in liquid N2. Send frozen on solid dry ice. Also see appendix 1.	up to 8 w
Sugar chromatography	stool	walnut size stool	Freeze immediately. Send frozen	3 – 6 w

Glycerol kinase deficiency

Organic acids, includes glycerol	U	2 ml fresh random urine	Freeze immediately. Send frozen	2 – 4 w
Glycerol kinase	F	skin biopsy into culture medium or saline	Send at room temperature. Do not freeze	up to 10w

Creatine Biosynthesis/Transport Defects

Test	Type		Sample handling	Turnaround
Creatine Guanidinoacetate	U and P	0.5 ml fresh random urine 0.2 ml li hep plasma	Freeze immediately. Send frozen Separate ASAP. Freeze immediately. Send frozen	4 w

NEUROBLASTOMA SCREEN

HVA	U	2 ml fresh random urine	Freeze ASAP. Send frozen	3 d
VMA	U	2 ml fresh random urine	Freeze ASAP. Send frozen	3 d

OTHER TESTS

Hormones

ACTH	P	0.5 ml EDTA plasma	Separate and freeze plasma / serum immediately after collection. Send frozen	1 w
Antimullerian hormone (AMH)	P, S	0.5 ml EDTA plasma or serum	Separate and freeze plasma / serum immediately after collection. Send frozen	up to 1 m
C-peptide	S	0.3 ml serum	Separate serum. Send on ice. Provide concurrent plasma glucose result if interpretation is required.	1 - 3 d
17-hydroxyprogesterone	P	0.5 ml li hep plasma	Separate and freeze plasma immediately after collection. Send frozen.	2 w
Inhibin B	P, S	0.5 ml li hep plasma or serum	Separate and freeze plasma / serum immediately after collection. Send frozen	up to 1 m
Insulin	S, P	0.3 ml serum/plasma	Separate plasma. Send on ice. Provide concurrent plasma glucose result if interpretation is required.	1 - 3 d
TSH	BS	4 blood spots on std card	Send by first class post.	1 - 3 d

Metals

Copper	P	0.4 ml li hep plasma	Separate plasma ASAP	1-2 w
Manganese	P	0.5 ml whole blood in Trace metal container	Send whole blood by first class post	2 – 4 w
Selenium	P	0.4 ml li hep plasma	Separate plasma ASAP Send by first class post	1-2 w
Zinc	P	0.4 ml li hep plasma	Separate plasma ASAP Send by first class post	1-2 w

Renal tubular markers

Retinol binding Protein [RBP]	U	1 ml fresh random urine	Freeze soon after collection	1 - 3 w
N-acetylglucosaminidase [NAG]	U	1 ml fresh random urine	Send by 1st class post	1 - 3 w

Others

Busulphan	P	1 ml EDTA blood at 0, 0.5, 1, 1.5, 2, 4, 7 h	Arrange with the GOSH metabolic lab prior to sampling. Send samples immediately to local Lab. Samples must be separated and freeze plasma locally ASAP. Label samples clearly with time of collection.	Same day. Must be pre-booked.
Immunoreactive trypsinogen (IRT)	BS	4 blood spots on std card	Send by first class post.	1 - 3 d
Lipase	S, P	0.3 ml serum/plasma	Separate serum/plasma. Send by first class post.	1 d
Sugar chromatography	U F	2 ml random urine walnut size stool	Freeze immediately. Send frozen	3 – 6 w

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APPENDIX 1
Special Enzyme Assays

It is important that full clinical details (especially presence or absence of neurological features, hepatosplenomegaly, dysmorphic features) are given on the request form so that appropriate assays can be carried out. Please let us know if the mother is pregnant as we can advise on prenatal diagnosis.

Sample requirements
Enzyme assays are classified under separate diagnostic groups with abbreviations for samples where appropriate. These abbreviations are explained below.

WBC (leucocytes) for white cell enzymes
Unless specified, enzymes are assayed according to the clinical details given. Blood transfusion within 4 weeks may interfere with the result and sampling at this time is best avoided if possible.

Send 5 – 10 ml well mixed blood in lithium heparin (minimum of 5mls). The sample must not contain any clots; heparinise the syringe if the patient is difficult to bleed. Send the whole blood sample to reach the laboratory ideally within 24 hours of sample collection (the shorter the interval, the better the quality of the sample). For most enzymes up to 48 hours is acceptable. However WBC cystine it is **essential** that the **sample is received within 24 hours**. Send by courier or Royal Mail Special Next Day delivery to arrive before 14:30 on a normal working day. Please avoid sending samples on a Friday in case of delays in transport.

The turnaround time for these assays is approximately 6 weeks.

RBC (erythrocytes)
Blood transfusion in the previous 6 weeks invalidates results.

Send 2 ml heparinised blood to arrive in the laboratory within 24 hours of sample collection, **except for galactokinase which has to be assayed on the day of sample collection and should be arranged with the enzyme laboratory at least a day in advance.** Send by courier or Royal Mail Special Next Day delivery.

P (plasma) I cell screen etc.
Send 1 ml plasma from a lithium heparin blood sample, to reach the laboratory within 24 hours of collection. Send by courier or Royal Mail Special Next Day delivery.

F (fibroblasts) from skin biopsies
Taking a skin biopsy:

Proceed under aseptic conditions. Have sterile culture medium ready. The forearm and axilla are suitable sites. Swab the skin with alcohol or chlorhexidine (not iodine or betadine). Approximately 0.2 ml to 0.4 ml of 0.5% lignocaine or similar local anaesthetic is injected intradermally and just subcutaneously. Take a 3 mm punch biopsy (full thickness skin) or ellipse 4 mm x 2 mm, immediately transfer the skin to the culture medium. IN EXCEPTIONAL circumstances, sterile dextrose / saline may be used. Keep at 4 °C or room temperature (DO NOT FREEZE) and send by courier or datapost. Fill the container to the top to avoid any airlock.

Storage: 4-8 ^{o}C for 24 hours in sterile saline, 3 to 5 days in sterile culture medium. It will take up to 6 weeks to grow fibroblasts.

U (urine)
Send 5 ml urine. Keep frozen until dispatched and send by 1st class post. This is used for our metabolic assays, not enzymes. Dilute urines (creatinine <1.0mmol/L) and infected urines (pH >8.0) are unsuitable.

L (liver) M (muscle) J (jejunal)
Contact the enzyme laboratory for instructions before taking liver and muscle biopsies as some assays require the biopsy in an unfrozen state. These assays are only available with prior arrangement and when the tissue sample can be delivered to this laboratory within 1 hour after being taken. Unfrozen samples must be transported in a sealed container on wet ice.

For most enzyme assays, including disaccharidases, a frozen biopsy is required. After wrapping in aluminium foil, the sample must be frozen **immediately,** using solid CO_2 or liquid nitrogen, then placed in a labelled plastic bag. The sample must be stored and transported frozen. **It is essential that the sample remains frozen at all times until it is assayed.**

APPENDIX 2:

Perchlorate Precipitation of Samples for Lactate/Pyruvate Ratios and Acetoacetate

For each sample, prepare 2 tubes each with 500 µl of ice cold 0.46 mol/L perchloric acid, keep cold at the bedside on an ice pack. Collect blood into a lithium heparin tube or CSF into a plain tube and IMMEDIATELY pipette 100 µl of the sample into each of the perchloric acid tubes. Mix vigorously, transport to the laboratory on the ice pack. Centrifuge within 10 minutes at 4°C, 3000 rpm for 5 minutes. Freeze supernatant in separate tubes and transport frozen. Any delay in sample precipitation will result in rapid deterioration of the analyte level. Our method requires that the proportion and concentration of perchloric acid is strictly adhered to in order to produce reliable results. Manufacturers supply perchloric acid at a variety of strengths. Please prepare the working perchloric acid as specified below:

NB: For β-hydroxybutyrate / acetoacetate ratio, a separate unprecipitated plasma sample should be sent.

Stock perchloric acid Supplied by manufacturer	Preparation of 0.46 mol/L perchloric acid
60 % w/w (SG 1.54)	2.50 ml stock made up to 50 ml with distilled water
70 % w/w (SG 1.70)	1.94 ml stock made up to 50 ml with distilled water

Keep the working reagent in a plastic bottle at 4 °C.

APPENDIX 3
External Quality Assessment Scheme Participation

ORGANISER	SCHEME	ANALYTES
ERNDIM	Special Assays in Urine	Creatine, free carnitine, guanidinoacetate, HVA, lactate, mucopolysaccharides, orotate,
	Special Assays in Serum	Biotinidase, creatine, guanidinoacetate, homocysteine, NEFA, 3-OHButyrate, lactate, pyruvate, VLCFAs
	Quantitative Organic Acids	
	Amino Acids	Plasma amino acids
	Proficiency Testing	Urine only - includes interpretation.
	Acylcarnitines	Blood spot acylcarnitines
	Interpretative Organic Acids	Organic acids - analysis & interpretation
	Cystine in White Blood Cells	White cell cystine
	Lysosomal Enzymes in Fibroblasts	Lysosomal enzymes
	Urine Mucopolysaccharides	GAGs
WILLINK	Urine Mucopolysaccharides	GAGs
CDC NEWBORN SCREENING	Carnitines	Blood spot acylcarnitines
	Blood spot Leucine	Blood spot leucine
WYE VALLEY	Reducing Substances	Reducing substances
UKNEQAS	Clinical Chemistry	Lipase
	Specific Proteins	Alpha-1-antitrypsin, caeruloplasmin
	Paediatric Bilirubin	TBil, conj.Bili
	Peptide Hormones	AMH, ACTH
	Guildford Peptides	Insulin, C-peptide, IGF-1, IGFBP3
	Newborn Screening	IRT, TSH
	Peptides II	Intact PTH, ACTH
	Steroid Hormones	17-hydroxyprogesterone, DHEAS, androstenedione
	Sweat Testing	Sweat test (sweat chloride & conductivity)
	Catecholamines	VMA HVA
	CSF Proteins & Biochemistry	CSF lactate
	Tacrolimus, Sirolimus, Ciclosporin	Tacrolimus, Sirolimus, Ciclosporin
	Trace Elements	Cu, Zn, Se, Blood Mn.
WEQAS	Ammonia	Ammonia

APPENDIX 4
Chemical Pathology and Enzyme laboratory request forms

(overleaf)

Great Ormond Street Hospital for Children NHS Foundation Trust

Great Ormond Street Hospital
Chemical Pathology External Laboratory Request Form

Chemical Pathology
Camelia Botnar Laboratories
Great Ormond Street Hospital
London WC1N 3JH
UNITED KINGDOM

Telephone: +44 (0)207 829 8662
Clinical: Bleep 0589 Generic e-mail:
Duty.Biochemists@gosh.nhs.uk
Fax: +44 (0)207 829 8624
Website: http://www.labs.gosh.nhs.uk

For Laboratory Use Only

Sample prepped by:

Enzyme Unit
Contacts: Katie Harvey / Derek Burke
Telephone: +44 (0)207 405 9200
ext. 1785 (Lab) 7843 (Clinical)
E-mail: gos-tr.ENZYME@nhs.net
See enzyme specific request form:
http://www.labs.gosh.nhs.uk (see lab handbook)

Metabolic Unit
Contacts: Helen Prunty/ Julie Leakey
Telephone: +44 (0)207 405 9200
ext. 5225 (Lab) 8319 (Clinical)
E-mail: metabolic.gosh@nhs.net

Chemical Pathology
Contacts: Helen Aitkenhead/ Daley Aofolaju
Telephone: +44 (0)207 405 9200
ext. 5710/0415 (Lab) 8318 (Clinical)
E-mail: gos-tr.chemicalpathology@nhs.net

Patient Details

Surname:		**Specimen Date & Time:**	Date:	Time:
Forename:		**Referring Dept & Hosp:**		
Date of birth :		Referral Lab No:		
Sex	M F	Referral Lab Tel No.:		
Hospital No:		Secure Fax Number:		
NHS No:		E-mail for reports (if available):		
Hospital & Ward:		Order number (If applicable):		
Consultant & Ext/Bleep:		Sample Comments: E.g. Sample type, frozen, etc.		

Assay / investigation required: N.B See full list of available tests on website http://www.labs.gosh.nhs.uk	Address for reports:	Address for invoice:

Clinical details: (ESSENTIAL)
Please specify if test is for monitoring (state disorder) or diagnostic.

FAO: Katie Harvey / Derek Burke
Enzyme Laboratory
Chemical Pathology
Camelia Botnar Laboratories
Great Ormond Street Hospital
London WC1N 3JH
UNITED KINGDOM

Telephone: +44 (0)207 405 9200 ext. 1785/6751
Fax: +44 (0)207 829 8624
E-mail: gos-tr.ENZYME@nhs.net
Website: http://www.labs.gosh.nhs.uk

For Enzyme Laboratory use only
Date / Time received:
Lab number:
Comments

TO BE COMPLETED BY REQUESTING CLINICIAN / LABORATORY

GREAT ORMOND STREET HOSPITAL ENZYMOLOGY SCREENS/TESTS

Surname:	**NHS No:**	**Referring Dept. & Hospital:**	**Address for reports/billing:**
Forename:	**Hospital & Ward:**		.....
Sex: M / F	**Consultant:**	**Referral Lab no:**	.....
DOB:	**Consultant ext./bleep:**	**Referral Lab Tel no:**	.....
Hospital No:	**Specimen date & time:**	**Secure Fax Number:**	**Order Number (if applicable)**

Clinical details (ESSENTIAL, if no details included specimen will not be prioritised):

Please tick:

☐ Hepatosplenomegaly ☐ Hypoglycaemia ☐ Cardiomyopathy ☐ Developmental Delay ☐ Dysmorphic ☐ Skeletal Dysplasia ☐ Myopathy ☐ Hydrops
☐ Ocular Abnormalities ☐ Angiokeratoma ☐ Vacuolated Lymphocyte Positive

Further information related to clinical details ticked above or any additional clinical details:

.....
.....

See user handbook (on website) for the list of diseases / enzymes tested in each enzyme screen and for sample handling and delivery instructions.

ENZYME SCREEN/TEST 8-10ml well mixed lith hep blood	Tick
Neurodegenerative screen (Suggest also consider urine sialic acids)	
Dysmorphic screen (please also request urine GAGs)	
Hepato / Splenomegaly screen	
Glycogen storage disease screen (state if glycogen brancher is also required)	
Galactosaemia Test (Galactose-1-Phosphate Uridyltransferase)	
Cystinosis Test /Monitoring (WBC cystine) to be received within 24 hrs	
Fabry Disease Testing (Patient's sex MUST be stated)	
Pompe Disease Testing* (bloodspot clearly labelled for Pompe testing)	

ENZYME TEST	Tick
Chitotriosidase (Gaucher monitoring) 2 mL plasma	
Galactose-1-Phosphate (galactosaemia monitoring) 2 mL blood	
Lyso-Gb3 (for Fabry disease monitoring or 2nd line diagnostic testing) 2 mL plasma	
5 mL urine fresh or frozen	
Urine Glycosaminoglycans (if MPS IV is suspected also send blood)	
Urine Sialic acid	
Urine Glucose Tetrasaccharide (Glc4 for Pompe Disease monitoring)	
Urine Gb3 (CTH, GL3, for Fabry Disease monitoring)	

Other Enzyme Tests or Further Comments:

***Please note: For urgent request or if infantile Pompe disease is suspected it is ESSENTIAL to call the laboratory prior to sending the specimen to enable it to be prioritised.**

ENZYME LABORATORY ENZYME SCREENS

Neurodegenerative screen*:

Disorder	Deficient Enzyme
G_{M2} gangliosidosis - Tay-Sachs/B1 variant	β-Hexosaminidase A
G_{M2} gangliosidosis – Sandhoff Disease	Total β-hexosaminidase
G_{M1} gangliosidosis	β-Galactosidase
Krabbe Leucodystrophy	Galactocerebrosidase
Metachromatic Leucodystrophy	Arylsulphatase A
Gaucher disease	Chitotriosidase +/- β-glucosidase
Fucosidosis	α-Fucosidase
α-Mannosidosis	α-Mannosidase
MPS VII (Sly Disease)	β-Glucuronidase
β-Mannosidosis	β-Mannosidase
Schindler's Disease	α-N-Acetylgalactosaminidase
I-Cell (Mucolipidoses II)	I-cell screen
Infantile neuronal ceroid lipofuscinosis*	Palmitoyl protein thioesterase
Late infantile neuronal ceroid lipofuscinosis*	Tripeptidyl peptidase I

*These enzymes are only included in the full screen (added when patients are <16 years) or if specifically requested

Dysmorphic screen:**

Disorder	Deficient Enzyme
G_{M2} gangliosidosis - Tay-Sachs/B1 variant	β-Hexosaminidase A
G_{M2} gangliosidosis – Sandhoff Disease	Total β-hexosaminidase
G_{M1} gangliosidosis	β-Galactosidase
Fucosidosis	α-Fucosidase
α-Mannosidosis	α-Mannosidase
MPS VII (Sly Disease)	β-Glucuronidase
Multiple sulphatase	Arylsulphatase A
Sialidosis	α-Neuraminidase
β-Mannosidosis	β-Mannosidase
Schindler's Disease	α-N-Acetylgalactosaminidase
I-Cell (Mucolipidoses II)	I-cell screen
Aspartylglucosaminuria	Asp-N-acetylglucosaminidase
Gaucher disease	Chitotriosidase

****Urine GAGs should also be requested to exclude MPS**

Hepato/ Splenomegaly Screen:

Disorder	Deficient Enzyme
G_{M2} gangliosidosis - Tay-Sachs/B1 variant	β-Hexosaminidase A
G_{M2} gangliosidosis – Sandhoff Disease	Total β-hexosaminidase
G_{M1} gangliosidosis	β-Galactosidase
Fucosidosis	α-Fucosidase
α-Mannosidosis	α-Mannosidase
Niemann Pick A & B	Sphingomyelinase
Sialidosis	α-Neuraminidase
β-Mannosidosis	β-Mannosidase
MPS VII (Sly Disease)	β-Glucuronidase
Schindler's Disease	α-N-Acetylgalactosaminidase
I-Cell (Mucolipidoses II)	I-cell screen
Lysosomal Acid Lipase Deficiency (Wolman and CESD)	Lysosomal Acid Lipase (Acid Esterase)
Gaucher disease	Chitotriosidase +/- β-glucosidase

Glycogen Storage Disease Screen*:**

Disorder	Deficient Enzyme
Glycogen Storage Disease III (GSD III)	Glycogen Debrancher (RBC glycogen also typically abnormal)
Glycogen Storage Disease IX (GSD IX)	Phosphorylase B Kinase (typically RBC glycogen and phosphorylase a/total phosphorylase ratio abnormal)
Glycogen Storage Disease VI (GSD VI)	Glycogen Phosphorylase (although deficiency may be seen in liver only)

***Glycogen brancher enzyme can be added to the screen (no additional blood required) if specifically requested.

Fabry Disease Testing includes WBC α-galactosidase testing, plasma α-galactosidase is also included for females and if WBC levels are deficient.