User handbook
Liver Pathology

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Author	Simon Hammond
Authorised by	Maesha Deheragoda
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INSTITUTE OF LIVER STUDIES

LIVER PATHOLOGY

USER HANDBOOK

Pathology Services:
Immunosuppressive Drug Monitoring (IDM - Clinical Biochemistry)
Hepatitis Testing (HTS - Virology)
Histopathology (HIS)
Liver Molecular Genetics (LMG)

Contents

GENERAL INFORMATION

Liver Pathology is part of the Institute of Liver Studies at King's College Hospital and is under the control of Viapath group LLP. Viapath Group LLP is a limited liability partnership between Guy's and St Thomas' NHS Foundation Trust, King's College Hospital NHS Foundation Trust and Synlab. Viapath Analytics and Viapath Services sit within the Viapath Group: Liver pathology sits within Viapath Analytics. The corporate functions of strategy, management, finance, human resources and commercial are managed within the Viapath Group. Viapath Services manage the laboratory facilities, systems, equipment, consumables and maintenance. Viapath Analytics manages the operations, diagnostics, research and development and clinical innovation.

The postal address is:-
Liver Pathology
Institute of Liver Studies
3rd Floor, Cheyne Wing
King's College Hospital
Denmark Hill, London SE5 9RS

The Institute of Liver Studies encompasses the clinical service and academic activities (undergraduate and postgraduate teaching and overlapping research) in adult and paediatric hepatology, hepatobiliary surgery and liver transplantation at King's. It was established in 1966 and is the largest specialist center in Europe for the treatment of Liver disease. Patients both from the UK and abroad are admitted for treatment. Annually 10,000 outpatient appointments are held and approximately 230 liver transplants are performed. Institute of Liver Studies consists of Todd, Dawson and Howard wards, the Liver Transplant Theatre, the Liver Intensive Therapy Unit, the Liver Outpatients' Department, Liver Endoscopy, Paediatric hepatology and the Laboratories (Liver Pathology and Academic laboratories).

Liver Pathology provides a specialist diagnostic and drug monitoring service for the clinical management of liver patients. Although Liver Pathology primarily supports Adult and Paediatric Liver services, it also provides specialist services to other departments at King's and/or referring clinicians outside of King's.

Liver Pathology comprises of four services:

a) Clinical Biochemistry - Immunosuppressive Drug Monitoring Service (IDM)
b) Virology - Hepatitis Testing Service (HTS)
c) Histopathology Service (HIS)
d) Liver Molecular Genetics (LMG)

All offer ISO15189:2012 accredited tests.

CONTACTS

Liver Laboratory Director is Dr M Deheragoda
Telephone: 020 3299 1208
Email: maesha.deheragoda@nhs.net

Immunosuppressive Drug Monitoring Service
Clinical-lead is Professor N Heaton
Service- lead is Dr P Morgan
Telephone: 020 3299 3147
E-mail: kch-tr.KCHIDMService@nhs.net

Hepatitis Testing Service
Clinical-lead is Dr K Agarwal
Service-lead is Dr S Moses
Service Manager is Dr D Shang
Telephone: 020 3299 3732
Email: dazhuang.shang@nhs.net

Histopathology Service
Service and Clinical-lead is Dr M Deheragoda
Service Manager is Mr J Croud
Fax 020 3299 3125
Email: james.croud@nhs.net

Liver Molecular Genetics Service
Clinical-lead is Professor R Thompson
Service Manager is Mr S Allouni
Telephone: 020 3299 2253
Email: KCH-tr.KCHLMG@nhs.net

Quality/Risk Manager is Mr S Hammond
Telephone: 020 3299 4814
Email: simon.hammond@nhs.net

Training Officer is Mr M Bruce
Telephone: 020 3299 3732
Email: matthew.bruce@nhs.net

General enquiries about Liver Pathology Service should be made to the Liver Laboratory Director. Enquiries about clinical aspects of the services should be made to the service-specific Service-lead or Clinical-lead.

SAMPLE HANDLING AND TRANSPORTATION

HANDLING BIOLOGICAL SAMPLES

1. All blood and tissue samples from patients should be considered as 'infectious risk'. They must be handled with great care.

2. Any spillages must be cleared up IMMEDIATELY and any possible contamination through cuts, finger pricks etc. reported as per local procedure.

3. 'Biological spill kits' and suitable disinfectant should be used to clear any biological fluid spillages. 'Chemical spill kit' should be used to clear chemical spills.

4. Staff employed by Viapath LLP sign contracts with to ensure ethical conduct and confidentiality is maintained in handling human samples, tissues and remains. This policy also applies to bank and agency staff.

SAMPLE COLLECTION AND LABELLING

When collecting samples from a patient, the clinician should positively identify the patient and check that any necessary preparation has been completed. All samples must be clearly labelled with the patient's identity. A minimum of two identifiers (name, hospital/NHS number or date of birth) are normally required to positively identify a sample. Samples that do not meet this standard may be accepted at the discretion of the service lead if the samples are regarded as 'unrepeatable'. The sample collector, date and time of collection should also be included with the sample request. All materials used in the sample collection process should be disposed of carefully in accordance with trust policy.

TRANSPORTATION OF BIOLOGICAL SAMPLES

1. All samples must be transported in the appropriate container (advice can be sought from service-specific Service-lead.)
2. Sample/specimens sent by post or courier must be correctly labeled and packaged (using UN 3373 compliant conditions) and addressed to service-specific Service-lead.

In case of emergency, please contact Quality/Risk Manager or Laboratory Director in Liver Pathology.

Making sample requests

The department requires all samples are accompanied with a formal request for analysis, whether this is in the form of a paper request, or one made electronically. Solely verbal requests for analysis will not be accepted. The only exception to this is when a verbal request is made to add additional tests to a sample already accepted for analysis.

The sample request should also include clear contact details for the requesting clinician. This is required so as to facilitate contact with the sample referrer if it is necessary to clarify any issues relating to the request for analysis.

Patient consent

All patients should give their consent to have samples collected for laboratory analysis. The patient should also be informed that it may be necessary to refer their samples on to another laboratory for analysis. If this proves necessary the department will only share the clinical information that is relevant to the sample request.

IMMUNOSUPPRESSIVE DRUG MONITORING (IDM)

The IDM service supports prescribed immunosuppressive therapy of adult and paediatric patients. Selective and sensitive analysis of Tacrolimus, Ciclosporin, Mycophenolic acid, Sirolimus and Everolimus is offered using liquid chromatography-tandem mass-spectrometry. Additionally the laboratory provides a service for measuring the anti-viral Ribavirin. Interpretative advice is also provided to aid optimal clinical management of patients.

IDM SERVICE PERSONNEL AND CONTACT DETAILS

Professor Nigel Heaton	Professor in Transplant Surgery and Clinical-lead
Dr Phillip Morgan	Consultant Clinical Scientist

Contact details: Telephone 020 3299 3147; Fax, 020 3299 3641;
E-mail: kch-tr.KCHIDMService@nhs.net

HOURS OF WORK (OUT OF HOURS, BANK HOLIDAYS)

0900 to 1730, Monday to Friday. One day each Bank holiday weekend
There is **no** routine provision of on-call/out-of-hours service

CLINICAL ADVICE

Clinical advice is available during service hours from:

- Clinical Scientists providing the service at a level commensurate with their seniority and expertise. Please phone 020 3299 3147 and ask for Dr Phillip Morgan in the first instance
- Paediatric liver nurse specialists for Paediatric liver patients. Please phone 020 3299 3774
- Lead-Clinician in Liver Transplantation and Hepato-biliary Pancreatic Surgery

TESTS PROVIDED and TURNAROUND TIMES

- Ciclosporin blood concentrations (Monday to Friday)
- Tacrolimus blood concentrations (Monday to Friday)
- Mycophenolic acid (MPA) plasma concentrations (Monday to Friday)
- Sirolimus blood concentrations (Monday to Friday)
- Everolimus blood concentrations (Monday to Friday)
- Ribavirin (RBV) plasma concentrations (at least monthly)

We regularly turn around 95% of immunosuppressive drug tests within 24h of receipt; same day reporting is targeted for specimens received by 2.30 pm. For ribavirin a turn-around time of 3-4 weeks is expected.

SAMPLE REQUIRED: (per test)
The customary single blood sample used for monitoring is the trough drug level, taken just before subsequent dose and at a constant interval (**12h** for Tacrolimus, Ciclosporin, Mycophenolic acid and Everolimus; **24h** for Sirolimus) from the time of the previous dose.

Ciclosporin / Tacrolimus / Sirolimus / Everolimus: 2ml EDTA-anticoagulated whole blood

Mycophenolate: 0.5 ml EDTA-plasma (preferred) or 2ml EDTA-anticoagulated whole blood
(N.B. Serum and citrate or fluoride-oxalate anticoagulated samples are **NOT** appropriate and therefore NOT acceptable)

Ribavirin: 0.5 mL of EDTA plasma is required. The sample **MUST** be immediately placed in a refrigerator and **MUST** be separated within **2 hours** of collection. The plasma should be stored at 4^{o}C for no longer than 2 weeks. The service **MUST** be contacted before sending samples to the service to discuss appropriate methods of transport. Haemolysed samples are not acceptable.

PATIENT PREPARATION
No patient preparation is required.

REQUESTS FOR IDM TESTING
Referrers should provide (by the KCH electronic patients records system if appropriate)

- The patient's Forename and Family Name and their Date of Birth
- The patient's Hospital number and NHS number (if available) and their gender
- The test requested
- The most recent **drug dose (in mg)** and the **time and date of that dose**
- The time and date of the blood sample taken for testing
- The legible Name of the requesting healthcare professional and a contact number
- The clear address to which the report of the result should be sent
- Any other pertinent information e.g., co-medication; liver dysfunction; infectivity
- For ribavirin assay, in addition to the information above, the length of time on therapy should be stated as well as the HCV genotype.

Super–urgent assay requests will be considered from the Consultant managing the patient. Requests for pharmacokinetic profiles **must** be discussed with the service providers.

During intravenous therapy with Ciclosporin or Tacrolimus, take samples from sites distant from those used for drug administration and **NOT** from plastic infusion sets to which the drugs adhere strongly. Mycophenolic acid samples must be taken at least 10 minutes after the infusion has stopped. Provide full details of the intravenous drug regimen.

STABILITY

Tacrolimus, Ciclosporin, Sirolimus and Everolimus are stable in blood for several days at ambient temperatures ~ 20°C. Mycophenolic acid is most stable in plasma despatched to the IDM laboratory. Erroneous results may result in blood samples containing mycophenolic acid and stored at ambient temperatures.

Ribavirin is unstable in whole blood at room temperature and to a lesser extent at 4ºC. Levels decrease over the first 6 – 8 hours after collection then increase markedly. Sample collection requirements are detailed above. No sample will be analysed that has not been collected correctly.

TIME LIMITS FOR REQUESTING ADDITIONAL TESTS

Samples are stored frozen for at least 4 months 7 days after testing. Additional tests must be ordered within 7 days of original request. Within this time limit, plasma separated for mycophenolic acid testing can NOT be used to test other immunosuppressants. Frozen whole blood can be used for other immunosuppressant assays although it is not recommended for mycophenolic acid. No retrospective ribavirin testing is undertaken.

RESULTS (TURNAROUND TIME)

Results are usually despatched within 24 working hours of receipt (immunosuppressants) or 1 month (ribavirin):

- by phone (020 3299 3147) but are divulged only to the official healthcare representative of the patient. Please have your / patient identifiers ready.
- by fax (upon request)
- electronically via EPR within King's College Hospital (KCH).
- as printed reports including the last five results - issued by second class mail to referrers
- by e-mail to NHSmail accounts

THERAPEUTIC RANGES

Numerous variables determine the drug level targeted e.g. graft type or drug indication, time after transplant, immunosuppressive co-medication, clinical and graft function. IDM staff can assist setting patient-specific targets within the ranges:

Tacrolimus: <1 – 12 µg/l for 12h trough concentrations

Ciclosporin:	<20 – 350 µg/l for 12h trough concentrations
Mycophenolic acid:	1 – 3.5 mg/l for 12h trough concentrations
Sirolimus:	2 – 15 µg/l for 24h trough concentrations
Everolimus:	3 – 8 µg/L for 12 hr trough concentrations suggested for immunosuppression. Therapeutic range for anti-tumour use has not been established
Ribavirin:	Probable target of 2 – 3 mg/L, this will be determined as part of a study of the clinical use of this monitoring.

SUGGESTED FREQUENCY OF IDM TESTING

The frequency at which IDM is performed generally decreases with time after transplant i.e., three to five times (children) weekly immediately after transplant, decreasing to once three or six monthly in long-term stable patients. Testing should be performed if:

- immunosuppressive drug dosage is increased or decreased;
- graft rejection or dysfunction is suspected / diagnosed;
- drug-related side-effects are detected
- co-medication affecting immunosuppressants is introduced, tapered or withdrawn;
- the brand or formulation of immunosuppressant is changed
- liver or renal function additionally deteriorates or improves;
- non-adherence is suspected;
- diarrhoea or persistent severe gastrointestinal dysfunction occurs.

The suggested frequency of ribavirin monitoring has not been determined. However data in the literature suggests monitoring on each occasion a sample is taken for HCV viral load, and given the long half-life of the drug monitoring after cessation of treatment for adverse effects may be required.

SAMPLE REFERRAL

IDM does not refer samples to other laboratories for analysis.

HEPATITIS TESTING SERVICE (HTS)

The virology hepatitis testing service provides diagnostic tests for hepatitis A, B, C, D, and E to support the hepatitis out-patient clinics, liver in-patients, liver transplantation and liver intensive care, as well as GP's and other hospitals.

Hours of Service

From 9am to 5pm, Monday to Friday. No routine service is provided outside these hours. The HTS is closed on public holidays.

For requests internal to King's, outside normal working hours specimens may be left in the designated fridge in the HTS laboratory.

Clinical Advice

Clinical advice is available during service hours from:

- Clinical Scientists providing the service at a level commensurate with their seniority and expertise. Please phone 020 3299 3732 and ask for Dr Dazhuang Shang in the first instance
- Dr Sam Moses (Consultant Virologist and Service Lead for the HTS)
- Dr Kosh Agarwal (Lead Clinician/Consultant Hepatologist)

Specimen Submission Guidelines

Specimens

All specimens must be labelled with the following:-

- Patient's full name and/or unique patient identifier (Hospital number and/or NHS number)
- Date of Birth
- Sender's lab reference number (requests external to KCH only)
- Date of specimen collection
- Time of specimen collection (desirable)

Request Forms

For Users external to KCH, a fully completed request form must accompany all specimens. Your own locally available request form is acceptable or an HTS request form is available on request from the lab.

For requests internal to KCH, orders should be placed via electronic patients records (EPR) using the 'Hepatitis Markers – Liver Unit' order form. Alternatively, paper requests can be placed using the dedicated HTS request form (packs of request forms are available from the HTS on request)

Both electronic and paper requests **must** match the information on the specimen and must include the following information:

- Patient's full name and/or unique patient identifier (Hospital number and/or NHS number)
- Date of birth
- Gender
- Sender's lab reference number (requests external to KCH only)
- Sample type (serum/EDTA plasma) (requests external to KCH only)
- Date of specimen collection
- Test(s) required
- A secure postal address to which the results will be sent (results may be sent to a secure email address on prior arrangement with the Lab)
- A contact telephone/extension number
- A contact name
- Relevant clinical information

PLEASE NOTE: specimens or request forms received without the minimum essential identification criteria may be rejected and/or may lead to a delay in reporting. Unlabelled specimens cannot be processed and may be discarded.

Requests that do not meet the above criteria may on occasion be accepted at the discretion of the Service Lead if the samples are regarded as 'unrepeatable'. Reports will indicate the nature of the problem and any possible consequence of this.

Specimen Transportation

Specimens sent by post or by courier must be in a sealed container, surrounded by sufficient absorbent material to absorb any fluid should a breakage occur, sealed in a plastic bag and placed in an approved outer container which meets current postal or other transport regulations.

The sender is responsible for ensuring that clinical specimens are transported in a way that complies with UK postal, courier or international safety regulations

For further information on the transport of infectious materials please refer to the following web page:

http://www.dft.gov.uk/vca/dangerousgoods/dangerous-goods-offi.asp

Specimen Collection/Processing/Factors Affecting Tests

Patient preparation:
No patient preparation is required

Serology tests:
Fresh whole blood should be left at room temperature to clot. Samples should be separated as soon as possible after collection (within 24 hours). Do not freeze whole blood samples as this can cause haemolysis of the red blood cells which may affect the results of serological assays.

Serum or plasma samples should be stored at 2-8°C for up to 5 days then should be frozen at -20°C or lower until referral. Samples should be frozen and thawed a maximum of three times as multiple freeze-thaw cycles may degrade the target analyte resulting in false negative results or inaccurate quantitation.

Certain assays (e.g. Delta Ab (Total) assay) require serum only – plasma samples are not suitable.

Samples which are grossly haemolysed, hyperlipaemic, heat-inactivated or which contain obvious microbial contamination are not suitable for testing and should not be sent.

Molecular tests:
Serum or EDTA plasma should be separated within 24 hours of collection. Separated samples should be sent as soon as possible or frozen at -20°C or lower until referral.

Multiple freeze-thaw cycles should be avoided as this may result in under-quantification of viral load.

Samples which are grossly haemolysed, hyperlipaemic or which contain obvious microbial contamination are not suitable for testing and should not be sent.

Please note: viral loads may decrease if specimens are not processed and stored appropriately.
Sample volume requirements:
Please refer to the 'Tests provided' table for information on minimum serum/plasma volumes required for each test.

Internal KCH requests:
A 5-10mL sample of both clotted and EDTA whole blood are required. Samples should be delivered to the HTS as soon as possible after collection, either via Central Specimen Reception (CSR) or brought directly to the Laboratory. If necessary, whole blood samples may be stored at 2 – 8^{o}C over-night for delivery the following morning.

Rejection Criteria
Samples may be rejected if:-

- They are the incorrect sample type for required test(s)
- They have leaked in transit
- They are of insufficient volume*
- They are grossly haemolysed, hyperlipaemic, heat-inactivated or contain obvious microbial contamination
- The information on the request form and sample do not match or if there is insufficient information on either the sample or form
- The specimen has not been processed/stored appropriately prior to referral or if there is a significant delay in specimen receipt

*where appropriate low volume samples may be tested at a dilution; reports will indicate the potential effect of this on assay sensitivity

If a specimen is rejected the referring laboratory will be notified of the rejection and the reason(s) why by telephone

Tests

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HAVAb (IgM)	Daily	2	The HAVAb-IgM assay is used for the qualitative detection of IgM antibody to hepatitis A virus (IgM anti-HAV) in human serum and plasma. To aid diagnosis of acute or recent hepatitis A viral infection.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	200µL serum/EDTA Plasma	N/A
HAVAb (IgG)	Daily	2	The HAVAb-IgG assay is used for the qualitative detection of IgG antibody to hepatitis A virus (IgG anti-HAV) in human serum and plasma. The presence of IgG anti-HAV (with nonreactive IgM anti-HAV) indicates past infection with hepatitis A virus (HAV) or vaccination against HAV.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	200µL serum/EDTA Plasma	N/A

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HBsAg	Daily	2	The HBsAg assay is used for the qualitative detection of hepatitis B surface antigen in human serum and plasma. The assay is used to identify current HBV infection and is also used to monitor the status of infected individuals in combination with other hepatitis B serological markers	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	300µL serum/EDTA plasma	N/A

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HBsAb	Daily	2	The anti-HBs assay is used for quantitative determination of antibody to Hepatitis B surface antigen (anti-HBs) in human serum and plasma. Anti-HBs assays are used to monitor the success of Hepatitis B vaccination. They are also used to monitor the convalescence and recovery of Hepatitis B infected individuals; presence of anti-HBs after acute HBV infection and loss of HBsAg can be a useful indicator of disease resolution. Based on the World Health Organisation recommendation, an Anti-HBs concentration ≥ 10 mIU/mL is regarded as being protective against Hepatitis B viral infection.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	300µL serum/EDTA plasma	Range of quantitation 0.00 to 1000mIU/mL. Samples >1000mIU/mL can be manually diluted 1/100 though this is not routinely performed. Samples with anti-HBs concentrations greater than or equal to 10.0 mIU/mL are considered reactive.

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HBsAg Confirmatory	Weekly	5	The HBsAg Confirmatory assay is used for the confirmation of the presence of hepatitis B surface antigen (HBsAg) in human serum or plasma by means of specific antibody neutralization.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	500µL serum/EDTA plasma	N/A
HBsAg Quantitation	2-4 times weekly	3	The quantitative HBsAg assay is used for the quantitative determination of hepatitis B surface antigen (HBsAg) in human serum and plasma. Quantitation of HBV is increasingly used in the monitoring of treatment for HBV with studies suggesting the use of HBsAg as a biomarker for the prognosis and response to therapy.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	300µL serum/EDTA plasma	LOD 0.05 IU/mL. On-board auto-dilution 1/500 gives a range of 175 to 124,925 IU/mL. Samples with an initial result of <175 IU/mL are routinely re-tested neat to give an accurate HBsAg level. Samples with an initial result of >124,925 IU/mL can be be further diluted manually if required.

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HBeAg	Daily	2	The HBeAg assay is used for the qualitative detection of hepatitis B e antigen (HBeAg) in human serum and plasma and is indicated for use as an aid in the diagnosis and monitoring of hepatitis B viral infection.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	300µL serum/EDTA plasma	N/A
HBeAb	Daily	2	The Anti-HBe assay is used for the qualitative detection of antibody to hepatitis B e antigen (anti-HBe) in human serum and plasma and is indicated as an aid in the diagnosis and monitoring of hepatitis B viral infection.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	300µL serum/EDTA plasma	N/A

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HBcAb (IgM)	Daily	2	The anti-HBc IgM assay is used for the qualitative detection of IgM antibody to hepatitis B core antigen (anti-HBc IgM) in human serum and plasma and is indicated for use as an aid in the diagnosis of acute or recent hepatitis B viral infection	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	200µL serum/EDTA Plasma	N/A
HBcAb	Daily	2	The anti-HBc II assay is used for the qualitative detection of antibody to hepatitis B core antigen (anti-HBc) in human serum and plasma. The presence of Anti-HBc indicates current or past HBV infection. In the absence of information about any other HBV markers, detectable levels of anti-HBc may indicate current HBV infection or resolved infection (natural immunity)	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	200µL serum/EDTA Plasma	N/A

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HBV DNA Quantitative (Not currently accredited)	4-5 times weekly	3	The HBV DNA assay is an *in vitro* nucleic acid amplification test for the quantitation of Hepatitis B Virus (HBV) DNA in human plasma and serum. The primary use of the test is as an aid in the management of patients with chronic HBV infection undergoing anti-viral therapy. The assay can be used to measure HBV DNA levels at baseline and during treatment to aid in assessing response to treatment. Results must be interpreted within the context of relevant clinical and laboratory findings.	Cobas 6800	1.5mLs EDTA plasma preferred or serum.	Lower Limit of Quantitation (LLOQ) 10 IU/mL range of quantitation <1.00E1 to >1.0E9 IU/mL

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HBV Drug Resistance Mutation (not currently accredited)	2-3 times monthly	20	The HBV Drug Resistance Mutation Screen is used to detect anti-viral resistance mutations in patients undergoing treatment for HBV infection by the determination of nucleotide mutations that lead to amino acid changes responsible for resistance to HBV antiviral drugs.	The HBV Drug Resistance Mutation Screen is an *in vitro* nucleic acid amplification and direct sequencing test.	1.5mLs EDTA plasma preferred or serum.	LOD 200 IU/mL. It is recommended that only samples with a VL >/= 200 IU/mL be referred for testing; samples with a lower VL may be sent but amplification cannot be guaranteed.
HBV Genotype (not currently accredited)	2-3 times monthly	20	The HBV Genotyping Test is intended for use as an aid in the management and treatment of patients infected with hepatitis B virus. The assay utilizes nucleic acid amplification and direct sequencing for the determination of HBV genotypes A-H in human serum or plasma.	The HBV Genotyping Test is an *in vitro* nucleic acid amplification and direct sequencing test.	1.5mLs EDTA plasma preferred or serum	LOD 200 IU/mL. It is recommended that only samples with a VL >/= 200 IU/mL be referred for testing; samples with a lower VL may be sent but amplification cannot be guaranteed.

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HCV Ab	Daily	2	The anti-HCV assay is a used for the qualitative detection of antibody to hepatitis C virus (anti-HCV) in human serum and plasma. The assay is used as an aid in the diagnosis of Hepatitis C infection and as a screening test to prevent transmission of Hepatitis C virus (HCV). The presence of anti-HCV indicates that an individual may have been previously exposed to HCV or that they are currently infected with HCV.	Abbott ARCHITECT: automated chemiluminescent microparticle immunoassay (CMIA)	300µL serum/EDTA plasma	

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HCV Genotype (not currently accredited)	Weekly	4	The HCV Genotyping assay is used for the identification of HCV genotypes 1 to 6 and subtypes a and b of genotype 1 in human serum or plasma. Determination of HCV genotype helps guide treatment decisions (type/duration) in patients being considered for anti-viral treatment	The VERSANT HCV Genotype assay is an *in vitro* line probe assay (LiPA)	1.5mLs EDTA plasma preferred or serum	

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HCV RNA Quantitative (Not currently accredited)	3-4 times weekly	3	The HCV RNA assay is an *in vitro* nucleic acid amplification test for the quantitation of Hepatitis C Virus (HCV) RNA genotypes 1 to 6 in human EDTA plasma or serum. The test is intended as an aid in the diagnosis of current HCV infection and in the management of patients with chronic HCV in conjunction with clinical and laboratory markers of infection. The test can be used to assess viral response to antiviral treatment (response guided therapy) as measured by changes of HCV RNA levels in serum or EDTA plasma.	Cobas 6800	1.5mLs EDTA plasma preferred or serum	Lower Limit of Quantitation (LLOQ) 15IU/mL; range of quantitation <1.50E1 IU/mL to >1.00E8 IU/mL

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
Delta Ab (Total)	Weekly	8	The Delta Ab (Total) assay is used for the qualitative determination of total antibodies to hepatitis delta antigen in human serum only. Detection of total anti-HD antibodies represents the preferred method for identification of possible HDV infection.	The DIA PRO Delta Ab (total) assay is a simultaneous competitive assay based on the ELISA technique (Enzyme-Linked Immunosorbent Assay).	200µl serum or EDTA plasma	N/A
Delta Ab (IgM)	2-4 times monthly	8	The Delta Ab (IgM) assay is used for the qualitative detection of IgM antibody to HDV in human serum and plasma. The assay is intended to aid in the diagnosis of HDV and to provide information on the course and prognosis of the infection.	The DIA PRO Delta Ab (IgM) assay is an immunometric assay based on the antibody capture ELISA technique (Enzyme-linked Immunosorbent Assay).	200µl serum or EDTA plasma	n/A

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
Delta RNA Quantitative	Weekly	8	The Quantitative HDV RNA is intended to be used as an aid in the diagnosis of current HDV infection and in the management of patients infected with HDV undergoing anti-viral therapy	The quantitative HDV RNA assay is an *in vitro* reverse transcription and real time PCR amplification test for the quantification of HDV RNA in human serum or plasma.	600µL EDTA plasma preferred or serum	LOD 6.40E2 copies/mL; range of quantitation 6.40E2 to 6.40E7 copies/mL
HEV Ab (IgM)	Weekly	5	The HEV-IgM assay is intended to be used as an aid in the diagnosis and management of hepatitis E infection.	The Fortress Diagnostics HEV-IgM assay is an enzyme-linked immunosorbent assay (ELISA) for the qualitative detection of IgM-class antibodies to hepatitis E virus in human serum or plasma.	100µL serum/EDTA plasma	N/A

Test	Test Schedule	Target Turnaround Time (working days)	PURPOSE OF TEST	METHOD	MINIMUM SAMPLE REQUIREMENTS	Limit of Detection (LOD)/RANGE OF QUANTITATION
HEV Ab (IgG)	Weekly	5	The HEV-IgG assay is intended to be used as an aid in the diagnosis of hepatitis E infection and in HEV prevalence studies among the population.	The Fortress Diagnostics HEV-IgG assay is an enzyme-linked immunosorbent assay (ELISA) for the qualitative detection of IgG-class antibodies to hepatitis E virus in human serum or plasma.	100µL serum/EDTA plasma	N/A
HEV RNA Qualitative	Weekly	5	The Qualitative HEV RNA assay is intended to be used as an aid in the diagnosis and management of hepatitis E infection.	Cobas 6800	1mL EDTA plasma	Contact Lab
HEV RNA Quantitative (Not currently accredited)	Weekly	5	The Quantitative HEV RNA is intended to be used as an aid in the management of patients infected with HEV and in patients undergoing HEV anti-viral therapy	Real-time PCR using StepOnePlus.	500µL serum/EDTA plasma	50 IU/ml

For further information on any of the above tests please contact the Laboratory directly

Minimum sample requirements include sufficient volume for repeat testing in the event of assay failure. Smaller volumes may be sent at Sender's discretion.

We aim to turnaround >95% of test results within these target times. Turnaround times are from day of specimen receipt to issue of reports in working days. Depending on demand, tests may be performed more frequently than detailed under Test Schedule

Please note: these turnaround times are based on a single test per sample, where multiple tests are requested on a sample the turnaround time of the sample is likely to be that of the test with the longest turnaround time

Urgent requests internal to KCH:
Specimens should be brought directly to the HTS Laboratory. Requirements for testing and results turnaround should be discussed with a senior member of HTS staff. Urgent requests for most serological tests can be completed the same working day if received in the Laboratory before 14:00.

Urgent requests from external Users:
Please contact the Laboratory directly to discuss.

Requests for Additional Tests: Time Limits and Retention of Specimens
If additional testing is required on a sample previously sent to the HTS, please contact the Lab directly. Specimens are normally retained for several years after analysis but further testing may not be possible due to insufficient sample volume, specimen viability or other factors. The HTS will be able to advise on the suitability of the original specimen for further testing.

Sample Referral
When required, samples will be referred for testing to external accredited referral laboratories.
Where it is not possible to determine HCV genotype in-house samples are referred to:
Public Health England
Virus Reference Department
61 Colindale Avenue
London
NW9 5EQ
vrdqueries@phe.gov.uk; Tel: 020 8327 6017

Reports
Authorised patient reports will be printed and delivered by post. Printed reports include results for the last four samples on the patient.

Results may be emailed to a secure email address on prior arrangement with the Laboratory.

For requests internal to KCH placed electronically, results will be available via EPR. Printed patient reports are available on request.

Quality Assurance in the HTS

External Quality Assessment (EQA):
The HTS participates in all available proficiency testing schemes relevant to our test portfolio. These include schemes run by the UK National External Quality Assurance Scheme (NEQAS), Quality Control for Molecular Diagnostics (QCMD) and INSTAND. Details of participation in specific schemes are available on request.

Internal Quality Assessment (IQA):
The quality of our Service is also monitored by our IQA re-test scheme. This involves the selection of previously tested and reported samples for anonymised/blind re-testing. After re-testing, the results for IQA samples are unblinded and are assessed against the originally reported results. Any inconsistencies are fully investigated and, where appropriate, corrective measures are implemented.

EQA and IQA performance outcomes are discussed at monthly HTS Lab Meetings and monthly Quality Meetings.

HISTOPATHOLOGY (HIS)

The Histopathology Service provides full diagnostic support to clinicians and surgeons caring for adult and paediatric patients with liver, biliary tree or pancreatic disorders and is renowned as a referral centre both nationally and internationally.

The department comprises 4.5 Consultant Histopathologists and a team of Biomedical Scientists who handle 4500 specimens (approx.) annually including liver biopsies, whole or part of organs resection specimens, and referrals for expert opinion from other centres. There is also an active postgraduate pathology teaching programme.

The department offers a rapid diagnostic service for small biopsies, and a 24/7 service for frozen section diagnosis.

HISTOPATHOLOGY SERVICE PERSONNEL AND CONTACT DETAILS

Consultants

Dr Maesha Deheragoda Consultant Histopathologist and Clinical Lead in Histopathology
Telephone: 020 3299 4525
E-mail: Maesha.deheragoda@nhs.net
Dr Rosa Miquel Consultant Histopathologist
Telephone: 020 3299 3734
E-mail rosa.miquel@nhs.net
Dr Yoh Zen Consultant Histopathologist
Telephone: 020 3299 4627
E-mail: yoh.zen@nhs.net
Dr Eva Sticova Consultant Histopathologist
Telephone: 020 3299 3734
E-mail: eva.sticova@nhs.net
Dr Claudia Mestre Consultant Histopathologist
Telephone: 020 3299 8275
E-mail: claudia.mestre@nhs.net

Office

Caroline Robinson PA to Consultant Histopathologists
Telephone: 020 3299 9000 ext 31208; Fax: 020 3299 3125;
E-mail: caroline.robinson10@nhs.net

Laboratory

James Croud Chief Biomedical Scientist and Service Manager
Telephone: 020 3299 2237;
E-mail: james.croud@nhs.net

Enquiries

Results (verbal reports)	Ext 31208
Current and previous cases	Ext 31208
Clinical advice / Urgent results	Ext 31208
Technical enquiries (e.g. specimen handling)	Ext 32237

HOURS OF WORK (OUT OF HOURS, BANK HOLIDAYS)

Laboratory and office personnel can be reached between 0900 - 1700 weekdays. Specimen reception with consultation and results supply are generally unavailable outside those hours. Specimen drop-off is available at any time. A consultant on-call rota exists; in emergencies or other unusual situations, a consultant can be reached by telephone at any time (365 / 24 / 7) either through their mobiles or 0203 299 9000 (King's College Hospital switchboard).

SERVICE PROVIDED

- Histological examination of adult and paediatric liver biopsy specimens and of surgical hepatobiliary and pancreatic specimens (Whipple's procedure), in particular, those arisen from liver transplantation and hepatobiliary surgical services; brush cytology (biliary tree) and fine-needle aspiration (pancreas).
- Wide range of special staining techniques.
- Immunohistochemical and electron microscopic investigations.
- Selected in situ hybridisation (EBER)
- Frozen sections (available outside normal working hours).
- Expert clinical and technical advice.
- Second opinion on referred cases.
- Participation at MDMs for HPB cancers, hepatocellular carcinomas and neuroendocrine neoplasms.
- Arranging and presenting adult and paediatric liver and paediatric gastrointestinal pathology histology meetings
- Tissue processing, staining and histological examination of liver biopsy specimens on contract basis for regional institutions.
- Photography of specimens

PATIENT PREPARATION

No patient preparation is required.

SPECIMEN HANDLING REQUIREMENTS

If malignancy or metabolic disorder (including drug reaction) is suspected, consultation before biopsy/resection may be in order to ensure that tissue can be appropriately processed (sampling for transmission electron microscopy; specialty fixatives). Please speak with one of the consultant histopathologists when planning the biopsy to ensure that tissue is appropriately harvested / stored / fixed.All specimens are to be brought to the Liver Histopathology specimen reception.
Large surgical specimens may be submitted without formalin (fresh) to facilitate tissue freezing during working hours 09:00-17:00 Monday to Friday. A biomedical scientist or MLA is informed of all specimens arriving fresh to the lab so that a Consultant pathologist can be informed, Out of working hours, procedures in LP-HIS-FM-33-Formalin out of hours v1.1 should be followed. This notice is displayed in the specimen reception area.
Otherwise, specimens must be immersed in an adequate amount of 10% formal saline in a large plastic bucket (available in Theatre 3 or in the histology laboratory) and brought to the laboratory as soon as possible.
Note that the penetration of formalin into liver tissue is slow and all specimens must therefore be treated as potentially infectious.

Specimen pots must be labelled with patient name, alphanumeric hospital patient identifier, and patient date of birth.
Failure to fill in a consultation-request form completely, or failure to label specimen pots properly may delay specimen processing and impede interpretation of findings.

ROUTINE LIVER BIOPSY (NEEDLE)

- The tissue core should be immediately placed (left floating without blotting paper) in a perspex container with 10% formal saline which is available on the ward or in the laboratory and brought directly to the histology laboratory in the Institute of Liver Studies accompanied by an EPR request form or, when not possible, a liver histology request form (pink) which is available in the respective wards or in the laboratory.
- The exception to this is paediatric liver biopsies where metabolic or other familial liver disease is suspected. A small sample for snap freezing which can be later sent for genetic testing by the clinical team may be undertaken. In these cases, the procedure in LP-HIS-SOP-55-Receipt and storage of paediatric liver samples for cryopreservation is followed.
- Adult liver biopsies may be accompanied by a sample in RNA-later solution as part of the second pass biopsy protocol. These samples are submitted along with the formalin fixed biopsy specimen so that both can be assigned the same accession number.

- All forms should carry the name and contact details of the doctor to whom the report is to be made, and a brief clinical summary.
- Specimen pots must be labelled with patient name, alphanumeric hospital patient identifier, and patient date of birth.
- Failure to fill in a consultation-request form completely, or failure to label specimen pots properly may delay specimen processing and impede interpretation of findings

URGENT PROCESSING
Is available for limited numbers of a few small classes of specimen (generally biopsy material). It must be approved for any particular specimen by both a consultant who clinically attends the patient from whom the specimen comes and a consultant histopathologist. An approved specimen must reach the laboratory by 13:30 to qualify for “urgent processing”.

FROZEN SECTIONS
Frozen section examination is exceptionally performed on needle biopsy specimens. Larger blocks of tissue are usually required. For routine requests during working hours contact the laboratory on ext. 32237, or for out of hours work contact the duty pathologist via the Transplant Co-ordinators by air call. Surgical specimens for frozen section analysis are sent without formalin to the laboratory accompanied by a member of theatre staff who must inform a member of the laboratory staff that a frozen section is required.
Frozen sections on needle core biopsies for transplant donor assessment are always to be agreed in advance with the Consultant Liver Histopathologist on call, via the transplant co-ordinators. These specimens are sent in normal saline or UW solution accompanied by a request form bearing the ODT number, Case ID, donor date of birth and Hospital of origin.

ELECTRON MICROSCOPY
Small portions (1mm) of tissue must be immediately immersed in small vial containing appropriate EM fixative (readily available in the Lab) and brought to the lab along with the formalin fixed biopsy so that they can be assigned the same accession number.

CYTOLOGY SPECIMENS
The lab’s SOP LP-HIS-SOP-44-Cytology sample collection protocol covers the collection procedure for different types of cytology sample. The specimen is brought straight to the liver histopathology laboratory. If the sample arrives out of hours, the instructions on the sign in specimen reception, LP-HIS-FM-28-Out of Hours cytology sample sign, are followed.

SPECIMENS RECEIVED OUT OF HOURS

All specimens must be in fixative, unless they are for transplant donor frozen section assessment. Instructions for adding formalin to surgical specimens and for storage of cytology specimens is displayed on the wall in specimen reception. All specimen details must be recorded in the specimens left out of hours form (LP-HIS-FM-66-Specimens left out of hours form) which is on the desk in specimen reception.

REFERRAL FOR SECOND OPINION

Slides bearing stained and /or unstained sections and / or paraffin blocks must be accompanied by the original histopathology report for correct patient identification, adequate clinical information and the Doctor to be appraised of findings (e-mail address and both telephone and facsimile numbers will speed up the process). Unless the referring Hospital holds an SLA agreement with the laboratory, the request for second opinion must be made in writing and agreed with one of the Consultant staff.

"Wet tissue" (in formalin or in specialty fixatives) is handled on a contract basis for regional institutions and, on occasion, for consultation specimens from abroad. Similar labelling procedures apply. Duplicate sets of slides bearing stained sections or images illustrating pertinent findings are generally supplied to referring institutions or histopathologists.

REQUESTS FOR HISTOPATHOLOGY

All specimens sent to the laboratory must be accompanied by a request form. This may be hand written or generated and printed from EPR records. Note that we are not able to print forms from EPR in the laboratory.

The request form **must** include the following information:

- Name, date of birth and hospital number
- ID and location of requesting individual
- Date and time of specimen collection
- Type of specimen and anatomical site of origin
- Relevant clinical information
- Identification of priority status
- Origin of patient (NHS / Private / Non UK EU)
- Location(s) to which the results are to be sent

TIME LIMITS FOR REQUESTING ADDITIONAL TESTS

Paraffin blocks are stored indefinitely, so there is no time limit for requesting additional tests on these samples

REPORTING OF RESULTS (TURNAROUND TIME)

- Targeted turnaround time agreed with users is:

i) Written reports for needle and small biopsy specimens are available within 2 working days. Transplant related biopsy material is available within 1 working day.
ii) Written reports for large specimens requiring fixation and multiple tissue blocks are available within 7 working days. Written definitive reports authorised by one of the consultants are immediately posted onto EPR and indicated as “authorised” in the limited access filemaker database.

- Oral reports on routine specimens received before 5.00pm are normally available after 4.00pm on the following day.
- Frozen section reports are usually made by phone within 30 minutes of receipt of the specimen.
- Other urgent reports can be made within four hours if the specimen reaches the laboratory before 1.30pm.
- Discussions at the microscope of cases of particular interest / importance are encouraged. The most suitable time is between 4.30pm and 5.30pm on weekdays.
- Cases referred during the previous week are reviewed by one of the Consultants on Tuesdays at 9.00am (selected Adult cases) and Thursday at 10.00am (all paediatric cases) in the Institute Seminar Room and the Alex Mowat seminar room respectively.
- Complex specimens can take longer to report

At discretion, a consultant histopathologist may telephone or otherwise make contact with a physician or surgeon named on a consultation-request form to communicate results. Such communications are in their nature preliminary. Written definitive reports, authorised as correct and signed by the consultant responsible, are posted on a limited-access database (Filemaker) at that time. Posting on a wider-access database (EPR) generally follows shortly.

SAMPLE REFERRAL

Samples that require electron microscopy are referred to the Sheffield Teaching Hospitals NHS foundation trust for sample processing, with the electron micrographs being returned to KCH for interpretation. Samples may also be sent to the Viapath Histopathology laboratory for Immunohistochemistry with antibodies that are not routinely stocked by the department. Full details for indications for referral can be found in LP-HIS-SOP-34-Histopathology referrals.

LIVER MOLECULAR GENETICS SERVICE (LMG)

The Liver Molecular Genetics service conducts genetic tests and provides interpretation of results for inherited conditions. The technology employed includes next generation sequencing, Sanger sequencing and qPCR. Laboratory scientists provide specialist interpretation of genetic findings and contribute to local MDM. The service currently offers next generation sequencing tests for inherited causes of Cholestasis and Wilson disease for internal and external clinical services. The laboratory also stores DNA for the liver transplant service and provides tests for inherited causes of Intestinal Failure, HFE and some low definition low definition HLA genotypes for internal services.

LIVER MOLECULAR GENETICS PERSONNEL AND CONTACT DETAILS

Professor Richard Thompson Consultant Paediatric Hepatologist and Clinical-lead
Mr Sammi Allouni Clinical Scientist and Service Manager

Telephone: 020 3299 2253; Fax: 020 3299 3641
Email: KCH-tr.KCHLMG@nhs.net

HOURS OF WORK (OUT OF HOURS, BANK HOLIDAYS)

0900 to 1730 Monday to Friday excluding Bank Holidays
There is **no** routine provision of on-call/out-of-hours service..

CLINICAL ADVICE

Clinical advice is available during service hours from:

- Clinical Scientists providing the service at a level commensurate with their seniority and expertise.
- Lead-Clinician in Liver Molecular Genetics

Please phone 020 3299 2253 and ask for Sammi Allouni in the first instance

PLEASE NOTE: specimens or request forms received without the minimum essential identification criteria may be rejected and/or may lead to a delay in reporting. Unlabelled specimens cannot be processed and may be discarded.

Requests that do not meet the above criteria may on occasion be accepted at the discretion of the Service Lead if the samples are regarded as ‘unrepeatable’. Reports will indicate the nature of the problem and any possible consequence of this.

TESTS PROVIDED

- Cholestasis Gene Panel (includes Alagille Syndrome)

NGS panel of the 27 main genes known to cause inherited cholestasis Reports are fully interpretative.

- Wilson disease genetics

NGS testing of the *ATP7B* gene known to cause Wilson disease. Reports are fully interpretative.

- Family mutation / mutation confirmation

Polycystic liver disease

Pancreatitis

Hirsprung disease – familial

Intestinal failure

Sanger sequencing of known mutations for phase analysis, carrier testing, prenatal analysis and confirmation of research findings.

- Ankylosing spondylitis / joint disease association genetics

SSP genotyping of HLA B*27 alleles (not currently accredited)

- Bechet's disease genetics

SSP genotyping of HLA B*51 alleles (not currently accredited)

- Coeliac disease association genetics

SSP genotyping of HLA DQ2 and DQ8 alleles plus DQA1*05 (not currently accredited)

- Abacavir sensitivity genetics

SSP genotyping of HLA B*5701 alleles (not currently accredited)

SAMPLE VOLUME REQUIREMENTS

For all tests:

Adults: 5 -10ml of peripheral blood in EDTA.
Paediatrics: 1-2ml of peripheral blood in EDTA

Tissue samples are accepted for donor typing, please contact the lab for further details.

PATIENT PREPARATION
No patient preparation is required.

REQUESTS FOR LIVER MOLECULAR GENETICS TESTING

A fully completed request form electronic or paper must accompany each sample. **Incomplete request forms may result in sample rejection.**

- Routine samples originating from within King's College Hospital (KCH) should either be sent via main pathology reception or brought directly to the Liver Unit laboratories.
- KCH samples should be requested via the EPR system. Tests can be found under Liver Laboratories orders or they can be searched for using the test name or by keywords.
- For external referrals or if EPR is unavailable request forms can be downloaded from the laboratory. External laboratory 'sendaway' referral forms are accepted.
- All samples from outside King's College NHS Trust must be accompanied by a written acceptance of the charges for testing and a clear indication of the person and/or department to whom the invoice should be sent.

Both electronic and paper requests **must** match the information on the specimen and should include the following information:

- Patient's full name and/or unique patient identifier (Hospital number and/or NHS number)
- Date of birth
- Gender
- Sender's lab reference number (requests external to KCH only)
- Sample type
- Date of specimen collection
- Test(s) required
- Pregnancy status (if relevant)
- Indication for testing and any clinical details that may influence the interpretation of results, e.g. medication, transfusion history, relevant laboratory results, family history and any previous genetic results.
- A secure address to which the results will be sent

EDTA samples which are grossly haemolysed or obviously clotted are not suitable for testing and should not be sent.

URGENT REQUESTS

Urgent requests internal to KCH:
Specimens should be brought directly to the LMG Laboratory. Requirements for testing and results turnaround should be discussed with a senior member of LMG staff.

Urgent requests from external users:
Please contact the Laboratory directly to discuss.

REQUESTS FOR ADDITIONAL TESTS, TIME LIMITS AND RETENTION OF SPECIMENS**.**
Verbal requests for extra testing are not accepted. Additional requests must be made on a request form.

Samples are stored for a maximum of 30 years after testing.

If additional testing is required on a sample previously sent to LMG, please contact the lab directly. Specimens are normally retained for several years after analysis but further testing may not be possible due to insufficient sample volume, specimen viability or other factors. LMG will be able to advise on the suitability of the original specimen for further testing.

CONSENT

- It is the referring clinician's responsibility to ensure that the patient/carer knows the purpose of the test and that a specimen may be stored for future diagnostic tests.

- Consent for DNA testing and storage must be obtained from the patient by the referring clinician prior to referral of the sample. All genetic testing requires consent. This is not the responsibility of the laboratory staff. For more information on consent please see the guidelines from the Joint Committee on Medical Genetics.

- The clinical genetics and genomics laboratory adheres to Trust policies and Caldicott principles to safeguard all patient information. Diagnostic

material is stored according to The Royal College of Pathologists' guidelines.

- Surplus diagnostic material from all referrals is retained for quality assurance purposes and may be used anonymously for the development of new tests unless consent for this is expressly denied on the request form.

SAMPLE TRANSPORT

Specimens should be delivered to the laboratory as soon as possible after they are taken to ensure the quality of the specimen and the success of the results. Blood sample should be sent at room temperature (15°C - 25°C) and must arrive in the laboratory within 7 days from being taken. DO NOT FREEZE. DNA samples in a suitable buffer can be sent at room temperature (15°C - 25°C) and should arrive in the laboratory within 7 days of being sent. Consider using local DNA extraction and sendaway services if sending samples from overseas.

For samples sent by post or by courier. All packaging should conform to PI650 standards.

SAMPLE REJECTION

All samples must be clearly labelled with the patient's identity. A minimum of two identifiers (name, hospital/NHS number or date of birth) are required to positively identify a sample. A completed request form (electronic/paper) must accompany all samples.

Samples may be rejected if:-

- They are the incorrect sample type for required test(s)
- They have leaked in transit
- They are of insufficient volume
- They are grossly haemolysed, or obviously clotted when in anticoagulant.
- The information on the request form and sample do not match or if there is insufficient information on either the sample or form.
- The specimen has not been processed/stored appropriately prior to referral or if there is a significant delay in specimen receipt

If a specimen is rejected the referring laboratory will be notified of the rejection and the reason(s) why by given by telephone

PLEASE NOTE: specimens or request forms received without the minimum essential identification criteria may be rejected and/or may lead to a delay in reporting. Unlabelled specimens cannot be processed and may be discarded.

Requests that do not meet the above criteria may on occasion be accepted at the discretion of the Service Lead if the samples are regarded as 'unrepeatable'. Reports will indicate the nature of the problem and any possible consequence of this.

FACTORS KNOWN TO AFFECT THE PERFORMANCE OF THE EXAMINATION

The quality and quantity of extracted DNA will be affected if samples are collected incorrectly, stored at extreme temperatures, or delayed in transit. This may result in the failure of the test. EDTA samples which are grossly haemolysed or obviously clotted will not yield sufficient DNA for analysis. Samples with abnormal WBC or abnormal clotting may not be apparent until processing and are also unlikely to yield sufficient DNA for analysis.

Failure to provide a reason for testing and further clinical details will limit the interpretation of the result. Providing a detailed family history and evidence of any previous genetic test results in the family is particularly important for guiding appropriate genetic analysis and interpreting the results, failure to provide these may result in delay, less interpretation on the report and/or less targeted testing.

Blood samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic blood or marrow transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype is expected to revert to that of the recipient within 1 week (Adams et al (1992) Blood 80:551). For individuals who have received allogeneic blood or marrow transplantation, a pre-transplant DNA specimen is recommended for testing. For individuals who have received an organ transplantation and are being tested for a disorder with an aetiology in the donor organ, please contact the laboratory to discuss the suitability of DNA testing.

RESULTS (TURNAROUND TIME)

- Results are available on EPR, in a printed format and over the telephone. Results are despatched immediately after authorisation.

- Turnaround times:

For NGS based tests we aim to have 95% of results reported within 112 working days.

For mutation confirmations and phase analysis we aim to have 95% of results within 20 working days.

For disease association typing we aim to have 95% of results within 10 working days.

If samples are Urgent please phone the lab.

SAMPLE REFERRAL
LMG does not refer samples to other laboratories for clinical analysis.

PATIENT CONFIDENTIALITY
In accordance with local policies and the data protection act, the department has an absolute commitment to maintaining patient confidentiality under all circumstances.

COMPLAINTS
The department has a complaints procedure in place, a copy of which is available on request. When raising a complaint the initial point of contact should be the department's Quality Manager.