NHS
Greater Glasgow and Clyde

WEST OF SCOTLAND CENTRE FOR GENOMIC MEDICINE | Laboratory Genetics

Information for Users [PRE-4]

The Service

The Laboratory Genetics department, forms part of the West of Scotland Centre for Genomic Medicine and provides a comprehensive diagnostic genetic service for the patients of the West of Scotland (population >2.7 million) and specialised testing for particular disorders to the whole of Scotland, the UK and overseas. The West of Scotland Centre for Genomic Medicine also includes the Clinical Genetics Service, which is co-located.

The laboratory is situated on Level 2 of the Laboratory Medicine Building at the Queen Elizabeth University Hospital, Glasgow and encompasses cytogenetics and molecular diagnostic testing for the specialist diagnosis and/ or monitoring of patients with constitutional (prenatal and postnatal) and acquired (malignancy) genetic abnormalities in hereditary genetic disease, solid tumours as well as adult and childhood leukaemia.

The laboratory is a member of the Scottish Genetics Laboratories Consortium and the Scottish Molecular Pathology Consortium, with laboratories also located in Aberdeen, Dundee and Edinburgh. The laboratories in each of these four centres are funded by National Services Division of NHS Scotland and are commissioned to work together to provide a comprehensive genetics service to the patients of Scotland. In addition, the laboratory sources genetic testing from other laboratories when required ensuring our patients have access to specialist genetic tests from other UK accredited laboratories, where appropriate.

The Laboratory Genetics department is an accredited laboratory. The scope of services offered for laboratory testing is accredited by the United Kingdom Accreditation Service (UKAS) to ISO 15189:2012 standards (Medical Laboratory 8290).

Laboratory's Mission Statement

To provide and further develop a high quality diagnostic genetics service for those disorders where there is demand, using the most effective technological approaches whilst working within national and professional guidelines. To securely store DNA and frozen cell samples from individuals with genetic disorders for use in future diagnoses. To distribute and receive samples within the Scottish Genetics Laboratories Consortium and the Scottish Molecular Pathology Consortium, ensuring the best use of the available resources and expertise for the diagnostic genetic testing for the patients of Scotland.

Information for Users

Contents

Contacting the laboratory

Postal address for correspondence and samples

West of Scotland Centre for Genomic Medicine
Laboratory Genetics
Level 2B
Laboratory Medicine
Queen Elizabeth University Hospital
Glasgow
G51 4TF

Website address

http://www.nhsggc.org.uk/about-us/professional-support-sites/west-of-scotland-genetic-services/laboratory-genetics/#

Other ways of contacting the laboratory

Tel: 0141 354 9300
Email: Genetic.Laboratories@ggc.scot.nhs.uk

The department's email account is monitored daily, and is suitable for the receipt of patient-identifiable information. Patient identifiable information should only be sent to the laboratory from secure accounts such as nhs.uk or nhs.net accounts. Do NOT send patient identifiable information to the laboratory from any other email provider.

Department working hours

Monday to Friday 9.00 a.m. – 5.00 p.m.
Saturday 9.00 a.m. – 12.00 p.m.

The laboratory is only open to receive specimens on a Saturday morning, no scientific staff are available to deal with enquires. The laboratory does not offer an out of hours service but it may be possible to arrange the analysis of urgent samples out with these times, by prior arrangement.

Laboratory Staff

Head of Service for Laboratory Genetics

Nicola Williams, Consultant Clinical Scientist
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Deputy Head of Service for Laboratory Genetics

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Compliance and Resource Programme Manager

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Email: stuart.imrie@ggc.scot.nhs.uk

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Technical Programme Manager

Rachael Ellis, Principal Clinical Scientist
Tel: 0141 354 9331
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Other Senior Scientific Staff, Compliance Programme

Training officer, Lorna Crawford, Principal Clinical Scientist Tel: 0141 354 9289
Quality Manager, Caroline Devlin, Principal Clinical Scientist Tel: 0141 354 9299

Other Senior Scientific Staff, Germline Programme

Germline Principal Clinical Scientist, Vera Cerqueira Tel: 0141 354 9287
Germline Principal Clinical Scientist, Kathryn Love Tel: 0141 354 9289

Other Senior Scientific Staff, Somatic Programme

Somatic Principal Clinical Scientist, Sandra Chudleigh Tel: 0141 354 9110
Somatic Principal Clinical Scientist, Avril Morris Tel: 0141 354 9324

Other Senior Scientific Staff, Technical Programme

Laboratory Manager, Thomas Kerr, Principal Biomedical Scientist Tel: 0141 354 9408

Other Senior Scientific Staff, Development Programme

Development Manager, Laura Miller, Principal Clinical Scientist Tel: 0141 354 9286

Voicemail

When diverted to voicemail, please leave a message and your contact telephone number. Someone from the department will get back to you as soon as possible.

Complaints

Should you have any comments, suggestions, cause for concern or complaints about the service you receive from the laboratory, please contact the Head of Service, Deputy Head of Service, Compliance and Resource Programme Manager or Quality Manager, using the contact details above.

Sending a sample to the laboratory

Reasons for referral

The laboratory uses various analysis techniques to carry out tests for a wide range of hereditary and acquired genetic disorders (haematological malignancy and solid tumours).

The types of investigation include:

- Confirmation/exclusion of a diagnosis for hereditary and acquired disorders.
- Carrier testing and risk assessment in families with a known genetic disorder.
- Presymptomatic/predictive testing in individuals at risk of a late-onset hereditary genetic disorder.
- Prenatal diagnosis of hereditary genetic conditions where appropriate.
- Pharmacogenetic testing to determine drug treatment options.
- Diagnostic tests to classify malignant diseases e.g. lymphoma, sarcoma.
- Diagnostic testing/monitoring of haematological malignancies.

The laboratory offers testing for a range of 'core' disorders plus a set of more specialist services for which samples are received on a supra-regional or national basis (see Laboratory Test Directory tables below for details).

Where tests are not available in our laboratory we will send DNA samples to other accredited UK genetic laboratories for testing for a large range of hereditary genetic disorders following appropriate approval from our Clinical Genetics Service (see below). Please contact the laboratory for details of access and availability of tests.

Details of services not currently available in the UK can be found on the web site www.orpha.net and www.genetests.org or by contacting the laboratory.

Each request accepted by the laboratory for testing is considered an agreement between the user and laboratory. Terms and Conditions of Service are available to read on our website (see above).

Gate-keeping and funding of tests

Access to many tests provided by other laboratories is restricted to specific referring specialities or clinicians. Clinicians may have to provide specific referral criteria and complete patient information forms, before these tests can be requested. Please contact the laboratory for details.

Please note that specimens referred out-with Scotland for testing will have a cost implication. Authorisation for testing for germline disorders is in consultation with our Clinical Genetics Service and for high value referrals approval is granted by the Scottish Genetics Laboratory Consortium clinical representatives. Following approval any associated costs will be met by National Services Division (NSD) of NHS Scotland. However in some instances, authorisation for testing may be declined and therefore any associated cost must be met by the referring clinician/ clinical service. Specimens referred out-with Scotland for somatic cancer are not funded by NSD.

Consent

All genetic testing requires appropriate consent. The laboratory assumes that when sending a sample consent has been obtained by the referring clinician. Testing and/or storage of genetic material must be discussed with the patient with a summary of clinical consent recorded in the patient's health record.For further information and guidance, please refer to *'Consent and Confidentiality in genomic medicine -Guidance on the use of genetic and genomic information in the clinic* which is available as a download from the British Society of Genetic Medicine website at www.bsgm.org.uk.

Products of conception requiring post-mortem and/ or sensitive disposal must be accompanied by the necessary paperwork supplied by local pathology department.

The department is committed to protecting personal information and complies with NHSGGC policies and the principles of the Data Protection Act.

Referral information

Test request forms are available on request by emailing Genetic.Laboratories@ggc.scot.nhs.uk or by calling the laboratory on 0141 354 9300. Test request forms are also available for printing at http://www.nhsggc.org.uk/about-us/professional-support-sites/west-of-scotland-genetic-services/laboratory-genetics/.

A test proforma must be completed for certain disorders, these are available for printing at http://www.nhsggc.org.uk/about-us/professional-support-sites/west-of-scotland-genetic-services/laboratory-genetics/ (see Laboratory Test Directory tables below for details of tests which will require a completed proforma).

Referral forms must be legible and should contain the patient's surname, forename, date of birth/ CHI number and postcode along with the reason for referral/ analysis/ test requested and a name and address for the referring clinician for reporting purposes. Referral forms received with insufficient information may be rejected.

Where no test is currently available for a referred disorder, the specimen will be accepted for DNA/ RNA extraction and storage. The laboratory may accept samples collected for R&D projects following prior discussion and agreement with the Head of Laboratory.

Verbal requests for testing must be followed up in writing.

After receipt and processing of the primary sample for testing, and assuming appropriate material has been stored by the laboratory, additional testing may be requested. Please contact the laboratory to discuss (see page 4 and 5 for appropriate contact details).

Specimen labels

All specimens should be clearly labelled with surname, forename and date of birth/ CHI number and must match those supplied on the test referral form. If the specimen label does not match the information that is supplied on the test referral form, the ***sample will be discarded***.

Please ensure other labels e.g. those which are added to the specimen tube by other laboratories, ***do not obscure the original specimen label*** containing the patient identifiers (name and date of birth/ CHI number) or the specimen ***may be rejected***.

Unsuitable specimens

Samples arriving in an unsuitable condition will not be processed and will therefore be rejected by the laboratory. Unsuitable conditons includes but is not limited to, samples sent in the wrong container, samples significantly delayed in transport, clotted blood samples or blood samples in an inapproriate blood tube and a broken sample tube. In such circumstances the ***sample will be discarded*** a repeat specimen will be requested if appropriate.

Specimens from patients with blood borne viruses (Hepatitis and HIV)

If a sample is known or suspected to be affected with HIV, Hepatitis B or Hepatitis C, it is no longer a requirement to label the specimen container as 'danger of infection' or 'high risk'.

Specimens from patients with Creutzfeldt Jakob Disease

Specimens from individuals with a confirmed or suspected diagnosis of Creutzfeldt Jakob Disease (CJD) must be labelled as 'danger of infection' or 'high risk', with the CJD status clearly indicated

on the referral form. These specimens are not processed by the laboratory for DNA extraction or tissue culture, instead they are sent to the the CJD Surveillance Unit in Edinburgh for DNA extraction prior to testing.

Specimens from patients with other suspected Group 3 and 4 pathogenic infections

For patients with a suspected or known TB infection, please contact the laboratory to discuss. The laboratory ***cannot*** process specimens from patients who have or are suspected as having any other Group 3 or Group 4 pathogenic infections (other than those specified above).

Packaging and transportation

It is the responsibility of those taking and dispatching specimens to the laboratory to ensure that these samples are sent in accordance with any national guidelines and/ or local policies for packaging, labelling and transport of biological material.

Specimens sent internally using the Greater Glasgow and Clyde specimen transport system should be placed in sealed plastic bag containing absorbent material, with the accompanying referral form placed in a separate compartment.

Blood and fluid specimens sent through the post should be packaged in accordance with PI 650 and UN3373 regulations. Specimens should be wrapped in absorbent material and then placed inside a rigid leak-proof primary receptacle, which should then be placed inside a rigid leak-proof secondary receptacle e.g. bio-bottle. The package must then be placed into outer package and should be clearly labelled with the laboratory's address and the sender details. The outer packaging must also be clearly labelled with the words 'BIOLOGICAL SUBSTANCE – CATEGORY B'.

All samples should be sent to the laboratory as soon as possible after being taken. If this is not possible, we would recommend storage at 4-8^{o}C for blood specimens, and at room temperature for bone marrow, amniotic fluid, CVS and tissue specimens, until you are able to send to the laboratory. Please note that DNA/ RNA quality may be affected by delays in transit which may compromise testing.

Turnaround times

The target turnaround times for each test we provide are shown in the Laboratory Test Directories below.

The laboratory aims to report both urgent and non-urgent samples within the stated times, however due to the complex nature of some of our tests occasionally it is not possible do so.

Please contact the laboratory before sending urgent referrals, including prenatal requests for hereditary genetic disorders (there is no need to call the laboratory for non-urgent referrals). Urgent requests will be processed as quickly as possible depending on the techniques required. Prenatal samples are ***always*** processed urgently and we aim to report these within the target reporting time of 3 working days for routine molecular tests but may be reported up to 14 days for prenatal arrays.

Reporting of Results

Reports for the majority of Greater Glasgow & Clyde referrals and for many of our feeder health boards are issued using Clinical Portal/SCI store. All others are sent as paper reports to the referring clinician as specified on the test referral form. Reports for referrals marked as urgent can be telephoned following special arrangement with the laboratory, however telephone reporting is not available routinely for urgent referrals. Under certain circumstances reports may be available by email but only following prior arrangement with the Head of Laboratory. Please contact the laboratory for further information.

Acute lymphoblastic leukaemia minimal residual disease (MRD) results are reported directly to the referring clinician and the relevant Clinical Trials Units when appropriate.

Conditions and tests listed in the Laboratory Testing Directories are accredited by UKAS to either ISO 15189:2012 standard or CPA standards. Where a test is out with scope of accreditation, it is marked with ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation**.* For such tests, the opinion and interpretation of results and reports are also outside the scope of UKAS accreditation and are detailed as so on the patients report.

Clinical advice and interpretation

For clinical advice contact:

Hereditary Genetic Disease	
Clinical Genetics Duty Consultant	0141 354 9300
Lymphoma testing (by arrangement only)	
Dr John Goodlad, Consultant Pathologist	0141 354 9418
Neuropathology testing (by arrangement only)	
Dr Zoltan Hanzely	0141 354 9492
Sarcoma testing (by arrangement only)	
Dr Amanda Murphy, Consultant Pathologist	0141 354 9497
Dr Elaine MacDuff, Consultant Pathologist (Adult)	0141 354 9511
Haemato-oncology (Paediatrics)	
Professor Brenda Gibson, Consultant Haematologist	0141 201 9307
Haemato-oncology (Adults)	
Dr Mark Drummond, Consultant Haematologist	0141 301 7712
Laboratory testing advice and report interpretation	
Nicola Williams, Head of Laboratory Service	0141 354 9313
Paul Westwood, Deputy Head of Laboratory Service	0141 354 9312
Senior scientific staff or duty scientist	0141 354 9300

Quality control and accreditation

The laboratory participates in appropriate external quality assessment schemes run by GenQA (Genomics Quality Assessment), EMQN (European Molecular Genetics Quality Network) and other appropriate UK and European EQA schemes to cover the scope of testing. Details of performance in these EQA schemes can be obtained by contacting the Quality Manager. Where an Accredited EQA scheme or formal inter laboratory comparison (ILC) programme is not available (e.g. for a rare disorder, or a new technique) the laboratory chooses an alternative approach to provide objective evidence for determining the acceptability of examination results. The laboratory also conforms to the best practice guidelines issued by EMQN and the Association for Clinical Genomic Science (ACGS), which is a constituent organisation of the British Society of Genetic Medicine (BSGM).

The scope of services offered for laboratory testing is accredited by the United Kingdom Accreditation Service (UKAS) to ISO 15189:2012 standards (Medical Laboratory 8290). The UKAS symbol appears on relevant report templates. Where tests are out with scope and therefore not accredited, this is clearly detailed on the relevant report.

Specimen requirements for germline (constitutional) investigations

Blood samples for postnatal germline (constitutional) disorders

Blood for molecular DNA investigations should be collected in potassium EDTA (KE) tubes. Blood for cytogenetics chromosome investigation should be collected in Lithium Heparin tubes. If requesting both molecular DNA and cytogenetic investigations, TWO blood specimens are required; one Lithium Heparin tube and one EDTA (KE) tube.

EDTA (KE) specimen tube	Volume of whole blood
Adult	3ml
Paediatric	3ml
Newborn	1ml

Lithium Heparin specimen tube	Volume of whole blood
Adult	3ml
Paediatric	3ml
Newborn	1ml

Blood samples for postnatal germline (constitutional) microarray analysis

TWO blood specimens are required; one Lithium Heparin tube and one EDTA (KE) tube.

EDTA (KE) plus Lithium Heparin specimen tube	Volume of whole blood
Adult	3ml (in each tube)
Paediatric	3ml (in each tube)
Newborn	1ml (in each tube)

Note: Please contact the laboratory if the patient has previously had a bone marrow transplant since this could affect the results of germline genetic testing.

DNA from other laboratories for hereditary genetic disorders

A minimum of 2µg of DNA is required for a simple PCR and up to 20µg for gene sequencing analysis. DNA should be supplied in water or TE buffer at a concentration of ≥20µg/ml. Please see the Laboratory Test Directory for further information.

Amniotic fluids for chromosome and DNA investigations (including QF-PCR)

Families with DNA or cytogenetic abnormalities (i.e. hereditary genetic disorders or hereditary chromosome abnormalities) may require work-up prior to offering prenatal diagnosis. It is therefore important that the laboratory is alerted as early as possible when the specimen is expected for prenatal diagnosis requiring molecular DNA or cytogenetic investigations. Please telephone the laboratory as soon as possible to discuss, giving the patient details along with the nature of the genetic abnormality. There is no need to telephone the laboratory for routine QF-PCR testing.

Two samples are required for amniotic fluid prenatal diagnosis. For immediate processing, specimens must be received before 12.30pm or they may not be processed until the following day.

Specimen type	Specimen container
15-20mls amniotic fluid samples	Sterile 20ml universal
3ml maternal blood	EDTA (KE) specimen tube

Three samples are required for amniotic fluid prenatal diagnosis from pregnancies with an abnormal ultrasound scan. For immediate processing, specimens must be received before 12.30pm or they may not be processed until the following day.

Specimen type	Specimen container
15-20mls amniotic fluid samples	Sterile 20ml universal
3ml maternal blood	EDTA (KE) specimen tube
3ml paternal blood	EDTA (KE) specimen tube

Chorionic villus biopsy for chromosome and DNA investigations (including QF-PCR)

Families with DNA or cytogenetic abnormalities (i.e. hereditary genetic disorders or hereditary chromosome abnormalities) may require work-up prior to offering prenatal diagnosis. It is therefore important that the laboratory is alerted as early as possible when the specimen is expected for prenatal diagnosis requiring molecular DNA or cytogenetic investigations. Please telephone the laboratory as soon as possible to discuss, giving the patient details along with the nature of the genetic abnormality. There is no need to telephone the laboratory for routine QF-PCR testing.

Two samples are required for chorionic villus biopsy prenatal diagnosis.

Specimen type	Specimen container
10 – 20 mg of villus for most referrals (see below)	Sterile 20ml universal containing transport medium (see below)
3ml maternal blood	EDTA (KE) specimen tube

Three samples are required for chorionic villus biopsy prenatal diagnosis from pregnancies with an abnormal ultrasound scan.

Specimen type	Specimen container
10 – 20 mg of villus for most referrals (see below)	Sterile 20ml universal containing transport medium (see below)
3ml maternal blood	EDTA (KE) specimen tube
3ml paternal blood	EDTA (KE) specimen tube

The villus biopsy sample should be placed in a sterile universal containing sterile CVS transport medium (supplied by the laboratory, please contact us directly for further information). If additional testing is requested, for example for biochemical diagnosis, additional fetal material may be required and will require prior discussion with the laboratory before sampling.

For immediate processing, specimens must be received before 12.30pm or they may not be processed until the following day. Specimens received later in the day will miss the 12.30pm cut-off for QF-PCR testing but will be processed the following day.

Fresh or frozen tissue specimens

Products of conception or post-mortem samples should be sent to the laboratory in a dry well sealed container. Fresh tissue biopsies should be transported to the laboratory in sterile tissue culture medium (available on request), an internal tissue such as rib or pericardium is optimal for

culture purposes. DNA can be extracted from fresh and frozen tissue specimens and the optimal tissue type for DNA extraction is spleen or lung. Frozen tissue specimens should be transported on dry ice. Fresh and frozen tissue specimens should be sent to the laboratory immediately after sampling.

Pre-implantation genetic diagnosis

This service is run in partnership with the Assisted Conception Service at the Glasgow Royal Infirmary. Patients are referred through one of the four regional clinical genetics services or directly from the Assisted Conception Service.

Other specimen types

Venous blood sampling for molecular DNA investigations is the preferred specimen of choice, but occasionally this may not be appropriate. In these circumstances we may be able to extract DNA from other types of specimens such as buccal swabs or saliva samples, however other specimen types may yield insufficient DNA quality or quantity for some tests. ***Please contact the laboratory for further information prior to sampling for other specimen types.***

RNA studies

The extraction of RNA from some specimen types is available following discussion with the laboratory. ***Please telephone the laboratory prior to sampling for RNA studies.***

DNA and RNA storage

DNA/ RNA extracted from all referrals is retained for storage unless the request card indicates that permission for storage is denied. When storage is denied, the DNA/ RNA specimen is destroyed following testing. The laboratory can also store DNA and/ or RNA from patients on request (for example where no specific test is currently available).

Test directory for hereditary (germline) investigations

The laboratory's testing list, specimen type and turnaround times for each disorder are listed below. Prenatal diagnosis is available for the majority of hereditary genetic disorders following a referral or discussion with Clinical Genetics (telephone 0141 354 9222/ 9228).
Conditions and tests listed below are accredited by UKAS to ISO 15189:2012 standards. Where a test is out with scope of accreditation, it is marked with ****Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***.

Condition and test description	Turnaround Time	Specimen	Notes
Angelman Syndrome			
• Testing for 15q11-13 deletion mutations and methylation abnormalities	28 days	EDTA	
• Family studies using microsatellite markers	28 days		
• Screening for *UBE3A* gene mutations	56 days		or 2µg DNA
• Prenatal diagnosis	3 days	AF or CVS plus maternal EDTA	Please contact the laboratory prior to testing

Bardet-Biedl Syndrome			
• Testing for the p.M390R *BBS1* gene mutation	28 days	EDTA	
Beckwith-Weidemann Syndrome			
• 11p15 methylation analysis	28 days	EDTA	
• Family studies using microsatellite markers	28 days		
Birt-Hogg-Dube Syndrome			
• Screening for *FLCN* gene mutations	56 days	EDTA	or 2µg DNA
• Predictive testing for *FLCN* gene mutations	14 days		
Breast Cancer (acquired, including somatic BRCA1 And BRCA2 testing)			
Specimen requirements and test information is detailed in the solid tumour section below (pages 23-25).			
Breast Cancer (hereditary), mainstream referrals			
• Screening using NGS for *BRCA1, BRCA2, PALB2, PTEN, STK11, TP53, ATM (targeted testing only) and CHEK2 (targeted testing only)* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
Breast Cancer and Ovarian Cancer (hereditary), clinical genetics referrals only			
• Screening using NGS for *BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53, ATM (targeted testing only) and CHEK2 (targeted testing only)* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Predictive testing for *BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53, ATM (targeted testing only) and CHEK2 (targeted testing only)* gene mutations	14 days		
Breast Cancer, Ovarian and Colorectal Cancer (hereditary), clinical genetics referrals only			
• Screening using NGS for *APC, BMPR1A, BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, MUTYH, NTHL1, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53, ATM (targeted testing only) and CHEK2 (targeted testing only)* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Predictive testing for *APC, BMPR1A, BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, MUTYH, NTHL1, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53, ATM (targetted testing only) and CHEK2 (targeted testing only)* gene mutations	14 days		

CADASIL			
• Screening for *NOTCH3* gene mutations	56 days	EDTA	or 3µg DNA
• Predictive testing for *NOTCH3* gene mutations	14 days		
CHARGE Syndrome			
• Screening for *CHD7* gene mutations	56 days	EDTA	or 5µg DNA
• Family studies for *CHD7* gene mutations	28 days		
Chromosomes, aneuploidy screening (chromosomes and QF-PCR)			
• Postnatal QF-PCR testing for trisomy 13, 18, 21, X & Y	3 days	EDTA & LiHep	
• Postnatal karyotype analysis (only to confirm abnormal QF-PCR result)	28 days		Urgent results TAT 10 days
• Prenatal QF-PCR testing for trisomy 13, 18, 21, X & Y	3 days	AF or CVS plus maternal EDTA	
• Prenatal SNP microarray analysis	14 days		Structural anomaly on ultrasound scan
• Prenatal karyotype analysis (only to confirm abnormal QF-PCR result)	14 days		
Chromosomes, inherited structural abnormalities			
• Karyotype analysis	28 days	LiHep	
• SNP microarray analysis	28 days	EDTA	May be subject to approval by clinical genetics
Chromosomes, other including multiple congenital abnormalities			
• SNP microarray analysis	28 days	EDTA	May be subject to approval by clinical genetics
• Karyotype analysis (only to confirm abnormal SNP microarray >5Mb when appropriate)	28 days	LiHep	
Chromosomes, pregnancy loss			
• Pregnancy loss QF-PCR testing for trisomy 13, 15, 16, 18, 21, 22, X & Y	28 days	Fetal tissue	'Recurrent' classed as 3 or more miscarriages. Testing of parental blood specimens is not available.
• SNP microarray analysis	28 days		
Colorectal cancer (hereditary)			
• MSI testing	14 days	FFPE	<60 years only Specimen requirement and testing details available in solid tumour section below (pages 23 – 25)

Chondrodysplasia Punctata			
• Screening using NGS for *AGPS, ARSE, EBP, GNPAT, PEX7* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Family studies for *AGPS, ARSE, EBP, GNPAT, PEX7* gene mutations	28 days		
Congenital Hypothyroidism			
• Screening for *TSHR*, *TPO* and *TG* gene mutations	56 days	EDTA	or 8µg DNA
• Family studies for *TSHR*, *TPO* and *TG* gene mutations	28 days		
Cowden Syndrome			
• Screening for *PTEN* gene mutations	56 days	EDTA	or 2µg DNA
• Predictive testing for *PTEN* mutations	14 days		
Cystic Fibrosis, including CFTR-related disorders			
• Testing for 50 'common' *CFTR* gene mutations	28 days	EDTA	
• Carrier testing for *CFTR* gene mutations	28 days		
• Screening for *CFTR* gene rare mutations may be available upon request for some referrals	N/A		Please contact the laboratory
• Cystic Fibrosis Newborn Screening (p.F508del, p.G542*, p.G551D and c.489+1G>T common *CFTR* mutations)	7 days	Blood spot	
Developmental Delay (including Fragile X syndrome)			
• Testing for the Fragile X syndrome *FMR1* gene expansion	28 days	EDTA	
• SNP microarray analysis	28 days		
• Testing for common microdeletion/ microduplication syndromes	28 days		
DICER1 syndrome			
• Screening using NGS for *DICER1* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Predictive testing for *DICER1* gene mutations	14 days		
DiGeorge Syndrome			
• Testing for the common 22q microdeletions	28 days	EDTA	5 days if urgent newborn
• Prenatal diagnosis	3 days	AF or CVS plus maternal EDTA	Please contact the laboratory prior to testing

Dilated Cardiomyopathy			
• Screening for *DES* gene mutations	56 days	EDTA	or 2µg DNA
• Predictive testing for *DES* gene mutations	14 days		
• Screening for *LMNA* gene mutations	56 days		or 2µg DNA
• Predictive testing for *LMNA* gene mutations	14 days		
Disorders of Sexual Development			
• Mutation screening by NGS using a 56 gene panel **(gene list available on Laboratory Genetics web link, please see page 4)**	112 days	EDTA	or 5µg DNA, *proforma required*
• Mutation screening by NGS using a 21 gene subpanel for hypogonadotropic hypogonadism **(gene list available on Laboratory Genetics web link, please see page 4)**	112 days		
• Family studies for variants identified by the 56 gene panel	28 days		
• SNP microarray analysis	28 days		
Dihydropyrimidine dehydrogenase deficiency (DPYD)			
• Testing for c.1905+1G>A, p.D949V), p.I560S and c.1129-5923C>G *DPYD* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	EDTA	*proforma required*
Duchenne/ Becker Muscular Dystrophy			
• Testing for deletion/ duplication mutations in the *DMD* gene	28 days	EDTA	
• Screening for *DMD* gene mutations	56 days		or 8µg DNA
• Carrier testing for *DMD* gene mutations	28 days		
• Prenatal diagnosis	3 days	AF or CVS plus maternal EDTA	Please contact the laboratory prior to testing
Epilepsy			
• Mutation screening by NGS using a 104 gene panel **(gene list available on Laboratory Genetics web link, please see page 4)**	112 days	EDTA	or 5µg DNA, *proforma required*
• Family studies for variants identified by the 104 gene panel	28 days		
• Screening for *SCN1A*, *PCDH19*, *SLC2A1*, *CDKL5*, *STXBP1*, *MECP2*, *PRRT2*, *POLG*, *KCNQ2, CACNA1A* gene mutations	56 days		or 8µg DNA, *proforma required*
• Family studies for *SCN1A*, *PCDH19*, *SLC2A1*, *CDKL5*, *STXBP1*, *MECP2*, *PRRT2*, *POLG*, *KCNQ2, CACNA1A* gene mutations	28 days		
• SNP microarray analysis	28 days		

Episodic ataxia			
• Screening for *CACNA1A* gene mutations	56 days	EDTA	or 5µg DNA
• Family studies for *CACNA1A* gene mutations	28 days		
Familial hemiplegic migraine			
• Screening using NGS for *ATP1A2, CACNA1A, PRRT2, SCN1A* and *SLC2A1* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Family studies for *ATP1A2, CACNA1A, PRRT2, SCN1A* and *SLC2A1* gene mutations	28 days		
Fibrodysplasia Ossificans Progressiva			
• Testing for the p.R206H *ACVR1* gene mutation	28 days	EDTA	
Fragile X syndrome			
• Testing for the Fragile X syndrome *FMR1* CGG repeat expansion	28 days	EDTA	
• Prenatal diagnosis	3 days	AF or CVS plus maternal EDTA	Please contact the laboratory prior to Testing
Fragile X Tremor Ataxia Syndrome (FXTAS)			
• Testing for the Fragile X syndrome *FMR1* CGG repeat expansion	28 days	EDTA	
Gorlin syndrome (Basal cell nevus syndrome)			
• Screening using NGS for *PTCH1* and SUFU gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Predictive testing for *PTCH1* and *SUFU* gene mutations	14 days		
Hereditary Ataxia			
• Mutation screening by NGS using a 107 gene panel **(gene list available on Laboratory Genetics web link, please see page 4)** ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	112 days	EDTA	or 5µg DNA, *proforma required*
• Family studies for variants identified by the 107 gene panel	28 days		
Hereditary Haemochromatosis (HFE related)			
• Testing for the p.C282Y *HFE* gene mutation, followed by reflex testing for the p.H63D *HFE* gene mutation	28 days	EDTA	

Hereditary Spastic Paraplegia			
• Mutation screening by NGS using a 20 gene panel, stage 1 test **(gene list available on Laboratory Genetics web link, please see page 4).** *ATL* and *SPAST* copy number analysis by MLPA. ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Mutation screening by NGS using a 41 gene panel, stage 2 test **(gene list available on Laboratory Genetics web link, please see page 4)** ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	112 days		
• Family studies for variants identified by the 62 genes stage 1 and stage 2 panels	28 days		
Infertility			
• *CFTR* gene mutations analysis for the 50 'common' variants	28 days	EDTA & LiHep	Males only
• Y chromosome marker analysis using *AZFa, AZFb* and *AZFc*	28 days		Males only
• Karyotype analysis	28 days		Males and females
Inflammatory bowel disease			
• Testing for the p.G460A, p.A719G and p.G238C common *TPMT* gene mutation	14 days	EDTA	
Lesch Nyhan Syndrome			
• Screening for *HPRT1* gene mutations	56 days	EDTA	or 2µg DNA
• Family studies for *HPRT1* gene mutations	28 days		
Li-Fraumeni Syndrome			
• Screening for *TP53* gene mutations	56 days	EDTA	or 2µg DNA
• Predictive testing for *TP53* gene mutations	14 days		
Limb Girdle Muscular Dystrophy			
• Screening for *DES* gene mutations	56 days	EDTA	or 2µg DNA
• Family studies for *DES* gene mutations	28 days		
• Screening for *FKRP* gene mutations	56 days		or 2µg DNA
• Family studies for *FKRP* gene mutations	28 days		
Malignant Melanoma (acquired)			
Specimen requirement and testing details available in solid tumour section below (pages 18-20).			

Malignant Melanoma (hereditary)			
• Screening using NGS for BRCA2, *CDKN2A*, *CDK4*, *POT1* and *BAP1* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 2µg DNA, *proforma required*
• Predictive testing for *BRCA2*, *CDKN2A*, *CDK4*, *POT1* and *BAP1* gene mutations	14 days		
Medium-chain acyl-CoA dehydrogenase deficiency (MCADD)			
• Screening for *ACADM* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 2µg DNA
• Family studies for *ACADM* gene mutations	28 days	EDTA	
Microdeletion/ Microduplication syndromes			
• SNP microarray analysis	28 days		Following a negative targeted test result
Myotonic Dystrophy (type 1)			
• Testing for the *DMPK* CTG repeat expansion	28 days	EDTA	3 days for Newborns
• Prenatal diagnosis	3 days	AF or CVS plus maternal EDTA	Please contact the laboratory prior to testing
Neurodegeneration with Brain Iron Accumulation (NBIA)			
• Mutation screening by NGS using a 21 gene panel, **(gene list available on Laboratory Genetics web link, please see page 4)** ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Family studies for variants identified by the 21 gene panel	28 days		
Neurofibromatosis type 2 (NF2) and Schwannomatosis			
• Screening using NGS for *LZTR1, NF2* and *SMARCB1* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Predictive testing for *LZTR1, NF2* and *SMARCB1* gene mutations	14 days		
Ovarian Cancer (hereditary), mainstream referrals			
• Screening using NGS for *BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, RAD51C and RAD51D* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*

Pancreatic Cancer (hereditary)			
• Screening using NGS for BRCA2, *CDKN2A*, *CDK4*, *MLH1, MSH2, MSH6, PALB2, STK11* and *TP53* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Predictive testing for *BRCA2*, *CDKN2A*, *CDK4*, *MLH1, MSH2, MSH6, PALB2, STK11* and *TP53* gene mutations	14 days		
Phenylketonuria			
• Screening for *PAH* gene mutations	56 days	EDTA	or 2µg DNA
• Family studies for *PAH* gene mutations	28 days		
Prader Willi Syndrome			
• 15q11-13 methylation analysis	28 days	EDTA	3 days for newborns
• Family studies using microsatellite markers	28 days		
• Prenatal diagnosis	3 days	AF or CVS plus maternal EDTA	Please contact the laboratory prior to Testing
Pre-implantation Genetics Diagnosis			
• FISH testing for familial chromosome abnormality and embryo sexing	1 day		
Premature Ovarian Failure			
• Testing for the Fragile X syndrome *FMR1* CGG repeat expansion	28 days	EDTA	
Primary Ciliary Dyskinesia			
• Mutation screening by NGS using a 29 gene panel **(gene list available on Laboratory Genetics web link, please see page 4)** ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	112 days	EDTA	or 5µg DNA, *proforma required*
• Family studies for variants identified by the 29 gene panel	28 days		
Rett Syndrome and Rett-like Sydrome			
• Screening for *MECP2* and *CDKL5* gene mutations	56 days	EDTA	or 2µg DNA
• Family studies for *MECP2* and *CDKL5* gene mutations	28 days		
Rhabdoid tumour			
• Screening using NGS for *SMARCA4* and *SMARCB1* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Predictive testing for *SMARCA4* and *SMARCB1* gene mutations	14 days		

Short Stature, including Turner syndrome			
• Screening for *SHOX* gene mutations	56 days	EDTA	or 2µg DNA
• SNP microarray analysis	28 days		
• Karyotype analysis, when Turner syndrome is suspected	28 days	Li Hep	Females only
Sickle Cell Anaemia (HbS variant)			
• Newborn screening for p.E7V *HBB* gene mutation	7 days	Blood spot	
Silver Russell Syndrome			
• 11p15 methylation analysis	28 days	EDTA	
• Family studies using microsatellite markers	28 days		
Smith-Lemli-Opitz Syndrome			
• Screening for *DHCR7* gene mutations	56 days	EDTA	or 2µg DNA
• Family studies for *DHCR7* gene mutations	28 days		
Surfactant Metabolism Dysfunction			
• Screening using NGS for *ABCA3, NKX2-1, SFTPB* AND *SFTPC* gene mutations ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	56 days	EDTA	or 5µg DNA, *proforma required*
• Carrier testing for *ABCA3, NKX2-1, SFTPB* AND *SFTPC* gene mutations	28 days		
X-inactivation Studies			
• Methylation analysis of the *AR* CAG trinucleotide repeat (Xq12)	28 days	EDTA	

Specimen requirements for solid tumour investigations

Fresh Tissue specimens

Cytogenetics investigations (including FISH) from fresh tissue ideally require a 1cm piece of fresh tumour however, smaller pieces of tissue may be sufficient. Alternatively, a fine needle aspirate (FNA) or core biopsy with as much available material as possible should be sent for testing.

Fresh tissue samples should be placed in a sterile universal containing sterile tumour transport medium (supplied by the laboratory, please contact us directly for further information) and sent to the laboratory without delay.

Specimens taken on a Saturday or Sunday should be kept at room temperature and transported to the laboratory first thing on the Monday morning.

FFPE tissue specimens

Molecular investigations (DNA, RNA and FISH) from FFPE referrals should be performed using an identified tumour specific FFPE tissue block.

When molecular DNA/RNA investigations involving PCR are required, the identified tumour specific FFPE tissue block should be sent directly to the laboratory for sectioning to prevent cross contamination of the extracted DNA/ RNA specimen. The tumour cellularity (% tumour content) of the referred specimen **must** be detailed on the tumour request form. Targeted DNA extraction is

available on request or is performed routinely when tumour load is low (<30% tumour versus normal tissue). If targeted DNA extraction is required, please send a stained H&E slide to the laboratory from the same tumour block clearly marking the tumour location using a permanent marker pen. Please contact the laboratory for further information.

DNA and RNA storage

DNA/ RNA extracted from all referrals is retained for storage unless the request card indicates that permission for storage is denied. When storage is denied, the DNA/ RNA specimen is destroyed following testing.

Test directory for cancer investigations

The laboratory's testing list, specimen type and turnaround times for each disorder are listed below.

Conditions and tests listed below are accredited by UKAS to ISO 15189:2012 standards. Where a test is out with scope of accreditation, it is marked with ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***.

An estimation of the % tumour cell population is required for all samples submitted for testing so the appropriate DNA extraction protocol can be used. If tumour content is <30%, a stained H&E slide is required and will be noted below ***H&E required for <30% tumour***.

Some testing may identify genetic mutations not listed in the table below. These results will be reported following the standard laboratory reporting policy.

Condition and test description	Turnaround Time	Specimen requirements and notes
Breast Cancer (acquired)		
• *ERBB2* (*HER2*) FISH testing for cases scored as 2+ by ICC	14 days (1 week if urgent)	2x Superfrost, Surgipath Apex or Bond Plus blank slides cut at 4µm.
Breast Cancer (hereditary)		
Specimen requirements and test information is detailed in the germline section above (pages 13-21).		
Colorectal cancer (acquired and hereditary)		
• Testing using NGS for *KRAS* gene mutations (codons 12, 13, 59, 61, 117, 146) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	FFPE block ***H&E required for <30% tumour*** MSI – FFPE block and normal colorectal tissue, testing available to <50 years only or on request by Clinical Genetics/ Consultant Pathologist
• Testing using NGS for *NRAS* gene mutations (codons 12, 13, 59, 61) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
• Testing using NGS for *BRAF* gene mutations (codon 600) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
• MSI testing	14 days	

Glioma, high grade		
• *MGMT* methylation analysis	14 days	*MGMT*, IDH1, IDH2 - 2X targeted H&E, 10x Superfrost, Surgipath Apex or Bond Plus blank slides cut at 8µm. 1p/19q FISH – 1x targeted H&E, 5x Superfrost, Surgipath Apex or Bond Plus blank slides cut at 3µm. Tests selected in consultation with consultant pathologist.
• Testing using NGS for *BRAF* gene mutations (codon 600) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
• Testing *using NGS* for *IDH1* gene mutations (codon 132) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
• Testing using NGS for *IDH2* gene mutations (codon 172) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
• FISH testing for 1p and 19q	14 days	
Head and Neck Cancer, Squamous		
• HPV PCR testing for types 16 and 18	7 days	FFPE block
Lung Cancer, Non-Small Cell (acquired)		
• Targeted testing using NGS for *EGFR* gene mutations (exons 18, 19, 20, 21) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	FFPE block required for EGFR testing
• FISH testing for *ALK* rearrangement	14 days	1x targeted H&E, 2x Superfrost, Surgipath Apex or Bond Plus blank slides cut at 4µm and FFPE block required for *ALK* or *ROS1* testing.
• FISH testing for *ROS1* rearrangement ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
Lymphoproliferative Disease (LPD), including Lymphoma		
• PCR testing for *IGH* and *IgK* clonality	14 days	PCR – FFPE block or EDTA or fresh tissue FISH – FFPE block or fresh tissue or FNA Karyotype – fresh tissue or FNA Bone marrow testing is also available, please see haematological malignancy section below (page 26-28) Tests selected in consultation with consultant pathologist.
• PCR testing for *TCRG* and *TCRB* clonality	14 days	
• PCR testing for MYD88 p.L265P	14 days	
• FISH testing for *MYC*, *IGH-MYC*, *IGH-BCL2*, *BCL6*, *IGK*, *IGL*, *IGH*, *MALT1*, *BIRC3/MALT1*, *BCL2* and *IGH-CCND1* (B cell)	3 days for MYC 14 days for all other FISH	
• Karyotype analysis	28 days	
Malignant Melanoma (acquired)		
• Testing using NGS for *BRAF* gene mutations (codon 600) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	FFPE block ***H&E required for <30% tumour***
Malignant Melanoma (hereditary)		
Specimen requirements and test information is detailed in the germline section above (pages 31-21).		

Mesothelioma		
• FISH testing for *CDKN2A/CEP9*	14 days	1x targeted H&E, FFPE block
Ovarian cancer		
• Testing using NGS for BRCA1/BRCA 2 gene mutations	**42 days***	FFPE block ***H&E required for <30% tumour*** *TAT agreed locally with oncology to fit treatment pathway
Papillary thyroid cancer		
• Testing using NGS for *BRAF* gene mutations (codon 600) ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14days	FFPE block ***H&E required for <30% tumour***
Sarcoma		
• PCR testing for *SS18-SSX1, SS18-SSX2, EWSR1-FLI1, PAX3-FOXO1, PAX7-FOXO1,* and *FUS-CREB3L2*	14 days	PCR – FFPE block or EDTA or fresh tissue FISH – FFPE block or fresh tissue or FNA Karyotype – fresh tissue or FNA Tests selected in consultation with consultant pathologist.
• FISH testing for *SS18, EWSR1, FOXO1*, *PAX7-FOXO1*, *PAX3-FOXO1*, *FUS*, *DDIT3 and MDM2* ***Please note that the MDM2 test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
• Karyotype analysis	28 days	
Solid tumour, other		
• Karyotype analysis	28 days	Fresh tissue or FNA
• FISH testing	28 days	To aid characterisation of chromosome abnormality
Uveal melanoma		
• FISH testing for copy number changes on chromosomes 3, 6 and 8	14 days	1x targeted H&E, FFPE block

Specimen requirements for haematological malignancy investigations

Paediatric acute lymphoblastic leukaemia MRD specimens

Minimal residual disease (MRD) testing is available at diagnosis and relapse using a blood (when WCC > $20x10^6$) or a bone marrow specimen. For diagnostic testing either a blood or a bone marrow specimen is appropriate. For MRD monitoring at follow up time points only a bone marrow is acceptable. Specimens must be collected in ACD specimen tubes.

Specimen type	Specimen container
5 – 10ml blood (when WCC > $20x10^6$)	ACD specimen tube
3 – 5ml bone marrow	ACD specimen tube
Trephine	Transport media

Please contact the laboratory on 0141 354 9110 prior to sending a sample for MRD testing, giving details of the patient's name and date of birth so we can ensure the specimen arrives safely.

There is some evidence that sample site and volume may affect MRD detection. For this reason careful attention to sampling technique is required. Please obtain marrow as follows: the aspirate needle should be passed fresh into two sites (this can be done by re-angling the needle; new skin punctures are not required). From each site the first 1ml of marrow should be aspirated using a 2ml syringe. The samples from each site can be combined into a single ACD specimen tube.

Adult and paediatric haemato-oncology specimens

Bone marrow is the preferred specimen for most haematological malignancy testing. Peripheral blood specimens may provide a result where there are circulating blast cells and/ or the white blood cell count is >20x10^9/l. Bone marrow trephine specimens are also acceptable, in cases of dry tap or where aspiration is difficult.

For cytogenetic karyotype and FISH investigations, specimens should be collected in bone marrow transport medium supplied by the laboratory. The specimens should be well mixed to prevent clotting and then transported to the laboratory immediately after collection.
The transport medium is supplied in sterile 20ml universal tubes and should be stored at 4-8^{o}C. Please do not use after the expiry date on the universal tube or if it appears cloudy/ contaminated.

When an urgent diagnosis is required (e.g. APML, CML), FISH can also be performed using an EDTA or LiHep blood specimen. **Please phone the lab on 0141 354 9290 before sending the specimen.**

For molecular DNA and RNA investigations, specimens should be collected in sterile tubes containing potassium EDTA (KE). The specimen should be well mixed to prevent clotting and then transported to the laboratory immediately after collection. It is essential that specimens which require RNA extraction arrive in the laboratory within 24 - 48 hours of sampling. Tests which involve RNA analysis may be compromised if the specimen arrives more than 48 hours after sampling.

Test required	Specimen type and notes
Karyotype & FISH	• 1-3ml bone marrow (in supplied marrow medium) • Or 5ml blood (LiHep) • Or trephine (in supplied marrow medium)
Karyotype, FISH & PCR (including RQ-PCR)*	• 1-3ml bone marrow (in supplied marrow medium) • Or 5ml blood (LiHep) • Or trephine (in supplied marrow medium) Plus • 1-3ml bone marrow (EDTA) • Or 5ml blood (EDTA) for routine PCR • Or 20ml blood (EDTA) for RQ-PCR • Or trephine (in supplied marrow medium)
FISH only, CLL and Myeloma	• CLL, 20ml blood (EDTA) • Myeloma, 1-3ml bone marrow (EDTA)
FISH urgent, CML and APML	• 1-3ml blood (EDTA or LiHep or bone marrow) ***Follow up bone marrow required for karyotyping***
PCR alone (including RQ-PCR)	• 1-3ml bone marrow (EDTA) • Or 5ml blood (EDTA) for routine PCR • Or 20ml blood (EDTA) for RQ-PCR • Or trephine

*****Please note that all new diagnoses of acute myeloid leukaemia require both a cytogenetics sample for karyotype/FISH analysis and an EDTA sample for PCR analysis*

Chimerism testing

Blood samples are the preferred specimen for Chimerism studies, bone marrow can also be tested if required. Chimerism testing is available for both paediatric and adult samples.

Chimerism	• Pre-transplant (donor and recipient), 5ml blood EDTA
	• Post-transplant whole sample analysis, 5ml blood EDTA or 1-3ml bone marrow EDTA
	• Post-transplant lineage specific analysis, 20ml blood EDTA or 1-3ml bone marrow EDTA

DNA and RNA storage

DNA/ RNA extracted from all referrals is retained for storage unless the request card indicates that permission for storage is denied. When storage is denied, the DNA/ RNA specimen is destroyed following testing. DNA/ RNA for post-diagnostic acquired samples, i.e. monitoring specimens, is stored for 6 months.

Test directory for haematological malignancy investigations

The laboratory's testing list, specimen type and turnaround times for each disorder are listed below. 26

Conditions and tests listed below are accredited by UKAS to ISO 15189:2012 standards. Where a test is out with scope of accreditation, it is marked with ***Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation**.*

Condition and test description	Turnaround Time	Specimen requirements and notes
Acute Lymphoblastic Leukaemia (ALL)		
• Karyotype analysis	14 days	Karyotype – bone marrow or trephine in marrow medium or LiHep blood FISH – bone marrow or trephine in marrow medium or LiHep blood PCR – EDTA bone marrow or EDTA blood or trephine
• FISH testing for *ETV6-RUNX1, KMT2A, BCR-ABL1, PBX1-TCF3, PDGFRB, ABL1, ABL2*	7 days (3 days if urgent)	
• PCR testing for *BCR-ABL* (quantitative and qualitative), *ETV6-RUNX1, TCF3-PBX1, SIL-TAL1, MLL-AF4, MLL-AF6 and MLL-AF9*	14 days (7 days if urgent)	
Acute Lymphoblastic Leukaemia (ALL), Minimal Residual Disease (MRD)		
• *IgH/TCR* gene rearrangement work-up	Up to 28 days	Bone marrow or blood collected in an ACD tube
• MRD patient specific monitoring (day 29 and week 14)	7 days	

Acute Myeloid Leukaemia (AML)		
• Karyotype analysis	14 days	Karyotype – bone marrow or trephine in marrow medium or LiHep blood FISH – bone marrow or trephine in marrow medium or LiHep blood ***For APML cases please phone the lab on 0141 354 9290 before sending the specimen.*** PCR – EDTA bone marrow or EDTA blood or trephine
• FISH testing for *PML-RARA, RUNX1-RUNX1T1 and CBFB*	3 days ***(Same day for PML-RARA if sample arrives before 1pm.)***	
• PCR testing for *BCR-ABL* (quantitative and qualitative), *RUNX1-RUNX1T1, CBFB-MYH11* inv(16), *PML-RARA (quantitative and qualitative), FLT3-ITD, FLT3-TKD and NPM1.* ****Please note that the FLT3-TKD test and quantitative BCR-ABL reported to the International Scale are not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation***	14 days	
• Mutation screening by NGS using a 28 gene targetted panel **(gene list available on Laboratory Genetics web link, please see page 4)** ****Please note that this test is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation28***	28 days	PCR – EDTA bone marrow or EDTA blood
Chimerism		
• Testing for chimerism following bone marrow transplant	7 days	EDTA blood or D+EDTA
Leukaemia, other		
• Karyotype analysis	21 days	Karyotype – bone marrow or trephine in marrow medium or LiHep blood FISH - bone marrow or trephine in marrow medium or LiHep blood
• FISH testing to aid characterisation of chromosome abnormality	7 days	
Lymphoproliferative Disease (LPD), including Chronic Lymphoblastic Leukaemia (CLL), Lymphoma and Myeloma		
• Karyotype analysis	21 days	Karyotype and/ or FISH (NHL) – bone marrow or trephine in marrow medium or LiHep blood FISH (CLL) – EDTA blood FISH (Myeloma) - EDTA marrow PCR – EDTA bone marrow or EDTA blood or trephine FFPE testing is also available for lymphoma, see solid tumour section above (pages 18-20) Tests selected in consultation with consultant haematologist/ pathologist.
• FISH testing for CLL,*TP53* and *ATM* routinely with *IGH-CCND1*,13q14, 13q34, and 12 centromere available in cases with a differential diagnosis	21 days (3 days if urgent)	
• FISH testing for Myeloma, *IGH-FGFR3*, *IGH-MAF*, *TP53, ATM, CDKN2C* and *CKS1B*	21 days	
• FISH testing for non-Hodgkins' lymphoma, *MYC*, *IGH-MYC*, *IGH-BCL2*, *BCL6*, *IGK*, *IGL*, *IGH*, *MALT1*, *BIRC3/MALT1*, *BCL2* and *IGH-CCND1*	14 days (3 days if urgent)	
• PCR testing for *IGH* and *IgK* clonality	14 days	
• PCR testing for *TCRG* and *TCRB* clonality	14 days	
• PCR testing for *MYD88* p.L265P	14 days	
• Screening for *TP53* gene mutations	28 days	

Myeloproliferative Disorders (MPD), including Chronic Myeloid Leukaemia (CML)		
• Karyotype analysis	21 days	Karyotype – bone marrow or trephine in marrow medium or LiHep blood FISH – bone marrow or trephine in marrow medium or LiHep blood PCR – EDTA bone marrow or EDTA blood or trephine
• FISH testing for *BCR-ABL1, FIPL1-CHIC2-PDGFRA, 20q deletion*	7 days (3 days if urgent)	
• PCR testing for *BCR-ABL1* (quantitative and qualitative), *JAK2* p.(V617F), *CALR* exon 9 insertions and deletions, *MPL* p.(W515L). ***Please note that the quantitative BCR-ABL reported to the International Scale is not currently UKAS accredited and interpretations expressed herein are outside the scope of UKAS accreditation**	14 days (7 days if urgent)	
• PCR testing for *JAK2* exon 12 insertions and deletions	14 days (7 days if urgent)	
Myelodysplastic Syndrome (MDS)		
• Karyotype analysis	21 days	Karyotype – bone marrow or trephine in marrow medium or LiHep blood FISH – bone marrow or trephine in marrow medium or LiHep blood PCR – EDTA bone marrow or EDTA blood or trephine.
• FISH testing for monosomy 5/5q-, monosomy 7/7q- and 20q-	3 days	
• Screening for *TP53* gene mutations for 5q – syndrome	28 days	

Testing for other disorders

Some of the genes or genetic abnormalities listed in the test directories above may also be applicable to other disorders. Please contact the laboratory if you would like to discuss testing for any of these genes or genetic abnormalities, in relation to an alternative disorder.

Testing for other genetic disorders is also available from the Scottish Genetics Consortium Laboratories network. For further information please contact these laboratories directly or refer to their User Handbooks (using the web links below).
Contact details for the other Scottish Genetics Consortium Laboratories are:

North East Scotland Genetics Service (Aberdeen)
Medical Genetics Laboratory,
Polwarth Building, Medical School,
Foresterhill, Aberdeen, AB25 2ZA
Tel: 01224 550682
http://www.nhsgrampian.org/nhsgrampian/gra_display_simple_index.jsp?pContentID=7219&p_applic=CCC&p_service=Content.show&

East Scotland Genetics Service (Dundee)
Level 6, Ninewell's Hospital and Medical School,
Dundee, DD1 9SY
Tel: 01382 632035
https://www.nhstayside.scot.nhs.uk/OurServicesA-Z/Genetics/PROD_295540/index.htm

South East Scotland Genetics Service (Edinburgh)
David Brock Building, Western General Hospital,
Crewe Road,Edinburgh, EH4 2XU
Tel: 0131 537 1270
http://www.nhslothian.scot.nhs.uk/Services/A-Z/ClinicalGeneticsService/GeneticLaboratoryServices/Pages/default.aspx