Genetics and Molecular Pathology Laboratory Services User Information Manual

Latest update 01/2024

Change summary

1) Added
   a) Updated details around CF testing. Kit now detected 68 mutations rather than 50.

Please note

1. As a dynamic department, there are a number of tests and processes that are being developed or amended between accreditation visits. The accreditation status of a test is added to all laboratory reports.

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Medical Genetics – Phone Numbers

General enquiries	01224 553820 OR 01224 553893
Clinical Genetics	01224 552120
Prof Zosia Miedzybrodzka Service Clinical Director and consultant in Clinical Genetics	01224 552120
Dr Christine Bell Head of Laboratory Genetics and Molecular Pathology Laboratories	01224 550681
Dawn O'Sullivan Deputy Head of Laboratory Genetics and Molecular Pathology Laboratories	01224 553821

Laboratory Address

Specimens should be sent to:

Genetics and Molecular Pathology Laboratory Services
Polwarth Building
Medical School
Foresterhill
Aberdeen
AB25 2ZD

Laboratory email address

gram.molgen@nhs.scot

Laboratory website

http://www.nhsgrampian.org/medicalgenetics

Laboratory Hours

Monday – Friday 0900 - 1700 **(there is no out of hours service)**

Medical Genetics Service

Medical Genetics offers a range of laboratory services including; cytogenetic, molecular cytogenetic and molecular genetic investigations on various sample types. Details of these tests and sample requirements are detailed below.

The laboratory is a UKAS accredited medical laboratory No. 8141. The laboratory operates in compliance with ISO 15189 'Medical laboratories — Requirements for quality and competence'.

The laboratory's scope of accreditation can be viewed on the UKAS website

https://www.ukas.com/find-an-organisation/

Please note that due to the rapidly growing repertoire of tests and continual improvement in assays, some available tests may not yet be accredited by UKAS (e.g. whole exome sequencing, new RNA fusion assay). A statement is added to all reports where the test used is not accredited.

Consent for Genetic Testing

Genetic test results may have implications for relatives and families. DNA samples are normally stored when current diagnostic testing is complete. These issues should be discussed with patients, parents or guardians prior to sending a sample for a genetic test. Telephone advice and consent forms are available from the Department of Clinical Genetics (tel. 01224 552120).

Contacting Medical Genetics Laboratory Services

For general enquiries, requests for results and to discuss particular cases please email the Duty Scientist (gram.molgen@nhs.scot) or phone 01224 553893 or 01224 553820. The Duty Scientist may not always be available immediately, however, a mail box service is available on this extension and is regularly checked.

Comments or Complaints

If you are unhappy with any aspect of the service you receive please contact the laboratory on 01224 550682, by email (laboratory email address above) or letter (see address above). We will try to resolve the problem as quickly as possible.

If for any reason, you would prefer not to speak to a member of staff, you can contact a member of the Feedback Service about making a complaint:

Log on to http://www.nhsgrampian.org

Select 'Working with us'

Select 'Contact us'

Click on 'comments or complaints'

The feedback page will be displayed

Collection of Samples

Criteria for sample acceptance

The reason for having sample acceptance criteria is to maintain patient safety. For NHSG referrals please refer to the Laboratory Medicine Clinical Unit Sample Acceptance Policy which is available on the intranet

http://nhsgintranet.grampian.scot.nhs.uk/depts/Laboratories/Pages/Policies%20and%20Guidelines.aspx

Samples which are not compliant with this policy will be rejected. The requirements of the policy are summarised below.

NB. For anonymised samples use a proper coded identifier.

For referrals from out with NHSG the requirements are summarised below

Completion of Referral Form

Required information:

- Patient CHI number
- Full name
- Address (including postcode)
- Date of birth
- Sex
- Specimen type
- Date and time of taking specimen
- Full clinical abstract
- Referring consultant's full name
- Place to which result is to be sent

Referral forms for different indications can be found on the website (http://www.nhsgrampian.org/medicalgenetics).

Sample Containers

Required information:

- Full name of patient
- Patient CHI number or date of birth
- Date of collection of specimen

Use of the correct specimen container is essential. Samples arriving in the wrong type of container will be rejected.

The correct type of container for each sample type or investigation is detailed in subsequent sections of this document. Certain sample types must be transported in sample tubes containing transport medium, these are supplied by the laboratory upon request (ARI only).

Sample Collection

Asepsis in the collection of specimens is essential. A specimen should be placed in a correctly labelled sterile container, and should reach the laboratory within the intervals indicated (indicated in the subsections below).

High Risk Samples

A high risk sample is one known or suspected of carrying a harmful pathogen e.g. HepB, HIV, HepC, Parvovirus B19, Creutzfeldt-Jacob disease (CJD).

The laboratory is dependent on the referring clinician ensuring that such a sample has a Danger of Infection sticker attached to the request and/or sample container. This label should also be visible to those transporting the sample.

Agreement to send such a sample should have been made with a senior member of the laboratory staff by the referring clinician, prior to any such sample being taken.

Medical Genetics operates containment level of 2+

For a full list of dangerous pathogens, their hazard group and their required containment level, please refer to the Approved List of Biological Agents on the HSE website;

https://www.hse.gov.uk/pubns/misc208.pdf

NB Samples at high risk of Tuberculosis (TB) require Containment level 3 and therefore cannot be processed.

Infection Hazards

Please help to minimise the risk to laboratory staff and porters by:

- Discarding cracked tubes or those with tops off
- Avoiding overfilling and contaminating the outside of containers
- Making sure that tubes and bottles are securely stoppered

Sample Transportation

Portering Service

Sample containers should be placed in a zip lock specimen bag and associated paperwork (referral form, clinical letter or consent form) should be placed in the **outer** pocket of this bag.

Postal Service

Packaging requirements are detailed on the HSE website:

https://www.hse.gov.uk/index.htm

Search for: Transportation of infectious substances

Protection of Personal Information

NHS Grampian complies fully with the provisions and obligations of the Data Protection Act 2018 in storing and processing your information. The purpose of the Data Protection Act 2018 is to control how personal information is used by organisations, businesses or the government to protect people's rights and confidentiality in relation to how information about them is handled.

For more information

Log on to http://www.nhsgrampian.org
Select 'Working with us'
Select 'Our Privacy Notice'
Click the link to the 'Privacy Notice'

Referrals for Chromosome Diagnosis

The laboratory can give an effective service if referrals are restricted to those cases where there is a good clinical reason for the examination. The duty scientist will be happy to discuss the investigation of individual patients before samples are taken. A full clinical abstract should accompany each sample so that the laboratory can judge which procedures are required.

Time limit for requests for extra tests

It is policy to store fixed cell suspension (where available) for a period of 1 year. Additional FISH testing can be requested during this period – contact the laboratory to check availability of cell suspension.

Germline samples

Blood Chromosome Diagnosis

- Sterile lithium heparin tube (match the volume of the tube to the volume of the sample)
- 5 - 10 ml (adult) or 1-2ml (child) of venous blood
- Post-mortem cardiac blood and cord blood are also acceptable
- Roll the sample gently to prevent clotting.
- The sample should reach the Laboratory within 24 hours

Fanconi Anaemia Testing

- Sterile lithium heparin tube (match the volume of the tube to the volume of the sample)
- 5 - 10 ml (adult) or 2.5ml (child) of venous blood

In addition to the patient sample send a control sample (5 – 10ml of venous blood) when available

Prenatal Diagnosis

Rapid prenatal diagnosis is a molecular test (QF-PCR) used to detect common autosome aneuploidies (13, 18 and 21) and sex chromosome aneuploidy. **NB** blood staining of amniotic fluid samples can hamper the rapid prenatal test and patients should be advised of this. QF-PCR is performed on all prenatal samples received in the laboratory. Karyotype analysis will only be performed for those where a positive result is obtained using QF-PCR. For abnormal scan (ABSCAN) cases, microarray analysis will be performed following a negative QF-PCR result.

Prenatal samples should be forwarded to the laboratory as soon as possible after being taken. If for any reason there is a delay in transportation the samples should be kept at room temperature.

Amniotic Fluid

Amniocentesis can be performed after 15+0 weeks gestation. If the sample requires microarray analysis (ABSCAN or increased nuchal translucency), ≥16 week gestation is preferred.

Prolonged inactivity of the mother, prior to the test, should be avoided to prevent settling of the amniotic fluid cells.

A sample of about 20ml (total volume) of amniotic fluid is required. The containers required can be obtained from the laboratory.

Split the sample as follows:

- 2ml in a sterile, labelled centrifuge tube, accompanied (in the same sample bag) by a 5ml sample of maternal blood in an EDTA tube (for rapid prenatal diagnosis). A 5ml paternal blood sample should also be received when the sample is being referred due to an ABSCAN (for microarray analysis).
- 10-18ml in a sterile, labelled universal container (for karyotype / microarray analysis)
- 5ml sample of maternal blood in an EDTA tube. A 5ml paternal blood sample should also be received when the sample is being referred due to an ABSCAN (for microarray analysis).

A separate referral form should accompany each portion of the sample.

Trophoblastic Villi (CVS)

Chorionic villus sampling (CVS) can be performed between 11+0 and 14+6 weeks gestation.

A supply of sterile flasks containing CVS transport medium is available on request from the laboratory. These must be used on the day that they are prepared and for that reason the laboratory should be informed in advance of taking the sample. Place each aspirate in a separate transport flask and label each flask.

- 10-20mg of tissue are required

- 5ml sample of maternal blood in an EDTA tube. A 5ml paternal blood sample should also be received when the sample is being referred due to an ABSCAN (for microarray analysis).

Solid Tissue (Biopsy and Necropsy)

From stillbirths, neonatal deaths, etc., a surface-sterilised skin sample 10 mm long and 2 mm wide is placed into the medium. Samples from abortions and products of conception (POC) should also be sent in transport medium. Recognisable fetal parts and fetuses over 2cm in length should be sent to Pathology in the first instance. If required, they will then forward appropriate material for analysis. Samples should be delivered to the laboratory as soon as possible after being taken.

- For POC samples, a 5ml sample of maternal blood in an EDTA tube should be sent along with the sample where possible.

Samples will be analysed by QF-PCR and microarray analysis.

Tissue Samples requiring cell culture

Tissue samples (e.g. skin biopsies requiring fibroblast culture) are now cultured in the NHS Glasgow Genetics Laboratory. Prior to any such sample being taken, please phone the Aberdeen Genetics laboratory to arrange collection of tissue transport media the day before procedure (media can be stored overnight in the fridge if required).

- Skin biopsies should ideally be taken at the beginning of the week (samples should arrive at the laboratory before 2pm on Wednesday, to allow for transport to Glasgow).
- Collect tissue transport media from the Genetics laboratory (Room: 2:008).
- Place skin biopsy directly into tissue transport media and label tube with patient details.
- Send this sample back to the Genetics laboratory.
- Aberdeen Genetics laboratory will arrange for the sample to be forwarded onto the Glasgow laboratory for cell culture (next day delivery).

Referrals for Molecular Cytogenetics (FISH)

- Molecular cytogenetics can be carried out on all sample types
- Collect these samples as for Chromosome Diagnosis
- The **same** sample can be used for **both** cytogenetic and molecular cytogenetic analysis

The request for molecular cytogenetics must be clearly marked on the referral form.

Molecular cytogenetic testing can also be undertaken on formalin fixed paraffin embedded (FFPE) sections of either 2 or 4 microns thick (depending on cellularity).

Referrals for microarray analysis.

(For prenatal microarray samples see Prenatal Diagnosis section above)

Microarray analysis is available for patients with learning difficulties, developmental delay, epilepsy and multiple congenital abnormalities.

- EDTA tube
- 5ml of venous blood

Depending on the findings of the microarray analysis, it may be necessary to obtain samples from BOTH parents and a second sample from the patient to complete the study.

Oncology Samples

All samples should arrive at the laboratory before 3.00 pm. To allow the investigation of slowly growing cells, it is preferable that samples are not sent on a Friday. Samples for molecular oncology must be received as soon as possible after sampling, and must also be received during normal working hours, to allow appropriate storage prior to further processing. On a Friday, they should not arrive after 4.00 pm, to allow time for appropriate processing.

Bone Marrow Chromosome Diagnosis

- Sterile tubes containing oncology medium (available on request from the laboratory - limited shelf life which is indicated on the tube)
- The sample of bone marrow should be placed in a tube and gently inverted to prevent clotting
- Deliver the sample to the laboratory at once

Blood Chromosome Diagnosis

- Sterile tubes containing oncology medium (available on request from the laboratory - limited shelf life which is indicated on the tube)
- 10 ml (adult) or 1-2ml (child) of venous blood should be placed in the tube
- Roll gently, to prevent clotting
- Should reach the Laboratory as soon as possible after being taken.

If oncology medium is not available sterile lithium heparin tubes will suffice, please match the volume of the tube to the volume of the sample.

Effusion Chromosome Diagnosis

- Sterile tubes containing oncology medium (available on request from the laboratory – limited shelf life which is indicated on the tube)
- Place the aspirate in the medium.
- It is essential that the sample is delivered to the laboratory as soon as possible after being taken.

Molecular Cytogenetic (FISH) Analysis of Oncology Samples

A number of FISH tests are available for oncology samples for bone marrows, bloods or FFPE sections. Collect the samples as outlined above and indicate clearly on the referral form that molecular investigation is required.

Cytogenetic Sample Turnaround Times

Turnaround times are dependent on the sample type. National guidelines on reporting times are followed where possible and are summarised below. The quoted turnaround times are for conventional and molecular cytogenetics.

Sample type	Recommended turnaround time (calendar days)
Amniotic fluid (full karyotype)	14
Amniotic fluid (trisomy screen)*	3
Blood (routine)	28
Blood (urgent)	10
CVS (full karyotype)	14
CVS (trisomy screen)*	3
FISH constitutional	28
Microarray analysis postnatal†	28
prenatal†	14
Oncology routine (karyotype or FISH)	21
Oncology urgent (karyotype or FISH)	14
Expedited urgent FISH e.g. PML-RARA (APML), BCR-ABL1 (CML)	3
Solid tissue (trisomy screen)*	3

*Also see section- 'Referrals for DNA diagnosis'

95% of samples should have an issued final report within these times

† Microarray testing is not accredited

Referrals for DNA (and RNA) Diagnosis

The laboratory offers a service of DNA (and RNA) extraction and analysis for genetic diseases and cancer diagnosis and management. These are summarised in the table below. Clinical enquiries should be directed first to the ON-CALL Clinical Geneticist (01224 552120).

The duty scientist can be contacted to provide information on the laboratory service and sample collection and storage.

Time limit for requests for extra tests

Providing DNA (or RNA) is available, extra tests can be requested at any time after receipt of the original sample. Please contact the laboratory to check if sufficient sample remains for testing.

Sample Requirements

- Samples of blood (5-10 ml from adults and 1 – 5ml from children) in an EDTA tube
- Unfixed tissue (50-100 mg) in a sterile container are suitable for DNA extraction.

NB DNA cannot be successfully extracted from clotted blood.

Rapid Aneuploidy screening, QF-PCR

- Rapid prenatal diagnosis is achieved by extracting DNA from a 2ml aliquot of amniotic fluid or enzyme digested villi from a CVS (see Cytogenetics requirements above for these sample types).
- A 5ml sample of maternal blood in an EDTA tube is required to complete these studies.
- Samples should be forwarded to the laboratory as soon as possible after sampling (see prenatal samples above for details of sample collection).

NB blood staining of amniotic fluid samples can hamper the rapid prenatal test and patients should be advised of this.

Rapid aneuploidy screening of tissue samples is available (see solid tissue samples above for details of sample collection).

cfDNA for circulating tumour DNA testing

Samples from immediate ARI area

- Blood samples (10-12mls) collected in EDTA vacutainers
- Must arrive at the laboratory within 4 hours of sample collection and no later than 4.00pm

Samples out with Aberdeen

- Blood samples (10mls) collected in Streck cell-free BCT
- Forward to the lab as soon as possible
- Must be kept at room temperature, not refrigerated

FFPE Tumour testing (both DNA-based & RNA-based PCR analysis)

For both diagnostic purposes and directing treatment stratification in solid tumours.

- 5μM FFPE sections cut using a sterile microtome blade and mounted on plain glass slides (number of sections required indicated on request form dependent upon individual test)

Blood/Bone Marrow Molecular Genetic Analysis (both qualitative and quantitative RNA-based & DNA-based PCR analysis)

For both diagnostic purposes and post-treatment follow-up monitoring of molecular abnormalities detected at diagnosis in haematological neoplasms

- EDTA tube
- 10-20ml venous blood (or 5ml bone marrow aspirate as appropriate)
- Gently invert to prevent clotting
- Deliver the sample to the laboratory within 24 hours, if possible, especially when RNA extraction is required.

For single gene DNA-based tests (e.g. JAK2 or MYD88)

- EDTA tube
- 4-6ml venous blood

Storage of DNA (and RNA) Samples

When current diagnostic testing is complete, DNA (and RNA) samples are retained in storage in the NE Scotland DNA bank unless otherwise directed. These issues should be discussed with patients, parents or guardians prior to sending a sample for a genetic test. Telephone advice and consent forms are available from the Department of Clinical Genetics (tel. 01224 552120).

Scottish Strategic Network for Genomic Medicine

Genetic testing services are delivered through four regional centres based in Aberdeen, Dundee, Edinburgh and Glasgow. These genetics laboratories collaborate through the Scottish Strategic Network for Genomic Medicine (SSNGM). In addition to the disorders listed below many other conditions can be tested through SSNGM. The Scottish Genomic Test Directory for Rare and Inherited Disease contains a list of all services currently available in Scotland (https://www.genomics.nhs.scot/test-directories/). Tests available in Scotland include: Prader Willi / Angelman syndrome, Huntington disease, SCA and Duchenne MD. Please refer to the Clinical Genetics Service (01224 552120) for information.

For information on haemophilia, haemoglobinopathies, connective tissue disorders, rare cystic fibrosis mutation or any other genetic disorder not mentioned contact the laboratory on 01224 553893 or the Clinical Genetics Service on 01224 552120.

Please also refer to the ACGS website https://www.acgs.uk.com

Genetic Disease Analysis Services Available:

Disorder	Service	Genes	Can be referred by	Reporting time (calendar days)*
Acute Lymphoblastic Leukaemia (ALL)	Karyotype		Haematologist	14
	FISH	*BCR::ABL1*	Haematologist	3
	FISH	*KMT2A rearrangement; ETV6::RUNX1, TCF3::PBX1, TCF3::HLF, PDGFRB, FIP1L1::PDGFRA, ABL1, ABL2*	Haematologist	14
	Microarray **	*Ploidy and large copy number changes as well as targeted analysis of EBF1, IKZF1, CDKN2A, CDKN2B, PAX5, ETV6, BTG1, RB1 and PAR1 regions.*	Haematologist	14
	Targeted screen by Fusion gene NGS panel	*Including BCR::ABL1, KMT2A rearrangement; ETV6::RUNX1, TCF3::PBX1 and TCF3::HLF*	Haematologist	14
	Rt-q PCR (MRD)	*BCR::ABL1*	Haematologist	21

Acute Myeloid Leukaemia (AML)	Karyotype		Haematologist	14
	FISH	*PML::RARA as required / indicated*	Haematologist	3
	FISH	*As required / indicated*	Haematologist	14
	Targeted screen by Fusion gene NGS panel	*Including BCR::ABL1, PML::RARA, RUNX1::RUNX1T1, CBF::MYH11 and KMT2A rearrangement*	Haematologist	14
	RT-PCR / DNA-based PCR	*FLT3 ITD & TKD*	Haematologist	7
	RT-PCR	*NPM1*	Haematologist	14
	Targeted screen by NGS panel (intensive treatment-eligible / relapsed AML patients)	*ASXL1, BCOR, CALR, CEBPA, CSF3R, DNMT3A, EZH2, FLT3, GATA2, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NPM1, NRAS, PTPN11, RUNX1, SETBP1, SF3B1, SRSF2, STAG2, TET2, TP53, U2AF1, WT1, ZRSR2*	Haematologist	28

Adult Granulosa Cell Tumour (AGCT)	Targeted screen**	*FOXL2 (c.402C>G p.(Cys134Trp) missense variant) **	Oncologist/ Pathologist	14
Arrhythmia – Out of Hospital Cardiac Arrest (OOHCA) or Sudden Cardiac Death (SCD)	Mutation screen	*50 gene panel: KCNQ1, KCNH2, KCNE1, KCNE2, KCNJ2, SCN5A, TYT2, DSC2, DSG2, DSP, PKP2, ABCC9, AKAP9, ANK2, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CASQ2, CAV3, DES, DPP6, GJA1, GJA5, GPD1L, HCN4, JUP, KCNA5, KCND3, KCNE5, KCNE3, KCNJ5, KCNJ8, LMNA, NOS1AP, NPPA, PLN, RANGRF, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SLMAP, SNTA1, TGFB3, TMEM43, TRDN, TRPM4*	Clinical geneticist/ cardiologist/ pathologist	112
	Predictive test, mutation known		Refer to clinical genetics	14
Arrhythmogenic Cardiomyopathy	Mutation screen	*PKP2, DSG2, DSC2, DSP, SCN5A, ABCC9, DES, HCN4, JUP, LMNA, PLN, RYR2, TGFB3, TMEM43*	Clinical geneticist/ cardiologist/ pathologist	112
	Predictive test, mutation known		Refer to clinical genetics	14
Atrial Fibrillation (AF)	Mutation screen	*SCN5A, ABCC9, GJA1, GJA5, HCN4, KCNA5, KCNE5, NPPA, SCN2B, SCN4B*	Clinical geneticist/ cardiologist/ pathologist	56
	Predictive test, mutation known		Refer to clinical genetics	14
Breast/ovarian*/prostate* cancer (For prostate cancer referrals, prostate cancer referral form to be completed)	Mutation screen	Breast Cancer: *BRCA1, BRCA2, PALB2, PTEN, STK11, TP53, ATM, CHEK2* Ovarian Cancer: *BRCA1, BRCA2, BRIP1, MLH1, MSH2, MSH6, RAD51C, RAD51D*	Clinical geneticist, consultant oncologist	Routine: 56 Urgent: 21
	Predictive test, mutation known	Breast & Ovarian Cancer: *BRCA1, BRCA2, PALB2, PTEN, STK11, TP53, BRIP1, MLH1, MSH2, MSH6, RAD51C, RAD51D, ATM, CHEK2* *Prostate Cancer**: BRCA1, BRCA2, CHEK2, ATM, PALB2, TP53, MLH1, MSH2, MSH6, RAD51D, PMS2, EPCAM, HOXB13*	Refer to clinical genetics	14
Breast cancer	FISH	*HER2*		14

Brugada	Mutation screen	*SCN5A, CACNA1C, CACNA2D1, CACNB2, GPD1L, HCN4, KCND3, KCNE3, KCNE5, KCNJ8, RANGRF, SCN1B, SCN2B, SCN3B, SCN10A, SLMAP, TRPM4*	Clinical geneticist/ cardiologist/ pathologist	112
	Predictive test, mutation known		Refer to clinical genetics	14
Charcot Marie Tooth disease	Mutation screen	*PMP22 MLPA, MPZ, Cx32, PMP22, MFN2* *Further extended testing available in Glasgow laboratory.*	Clinical geneticist/ neurologist	56
	Predictive test, mutation known		Refer to clinical genetics	14
Chromosome breakage / Bone Marrow Failure disorders**	Mutation screen by NGS panel	*Subpanels analysed from SOPHiA Whole Exome (See Rare & inherited disease test directory)*	Haematologists, clinical geneticists	56 (up to 10 genes) or 112 (>10 genes)
	Predictive test, mutation known		Refer to clinical genetics	14
Chronic Myeloid Leukaemia (CML)	Rt-q PCR (MRD)	*BCR/ABL1*	Haematologist	21
	Targeted screen	*BCR/ABL1 kinase domain mutation*	Haematologist	21
Colorectal Cancer	Mutation screen** (tumour)	*KRAS codons 12, 13, 59, 61, 117 & 146*	Oncologist/ Pathologist	14
		NRAS codons 12, 13, 59, 61, 117 & 146		
		BRAF codon 600		
		MSI testing		
		MLH1 promoter hypermethylation **		
CPVT	Mutation screen	*RYR2, CALM1, CALM2, CASQ2, DPP6, TRDN*	Clinical geneticist/ cardiologist/ pathologist	56
	Predictive test, mutation known		Refer to clinical genetics	14

Cystic fibrosis	Mutation screen**: 68 mutations +/- intron 8 poly-T	*CFTR*	Hospital specialists	28 non urgent 7 urgent
DPYD for 5-Fluorouracil (5-FU) toxicity **	Targeted screen** – 4 SNPs	*DPYD (c.1236G>A, c.1679T>G, c.1905+1G>A and c.2846A>G)*	Oncologist	7
Eye disorders**	Mutation screen by NGS panel / Sanger	*Subpanels analysed from SOPHiA Whole Exome (See Rare & inherited disease test directory)*	Opthalmologists; clinical geneticists	56 (up to 10 genes) or 112 (>10 genes)
	Predictive test, mutation known		Refer to clinical genetics	14
Factor V Leiden	1691 G > A mutation	*F5*	Any physician	28
Familial Hypercholesterolaemia	Mutation screen**	*LDLR, ApoB Ex26, ApoE, PCSK9*	Clinical geneticist/ consultant lipidologist	56
	Predictive test, mutation known		Refer to clinical genetics	14
Fragile X A	FRAXA expansion	*FMR1*	Hospital specialists	28 non urgent 7 urgent
Gastrohepatology disorders**	Mutation screen by NGS panel / Sanger	*Subpanels analysed from SOPHiA Whole Exome (See Rare & inherited disease test directory)*	Gastrohepatology specialists; clinical geneticists	56 (up to 10 genes) or 112 (>10 genes)
	Predictive test, mutation known		Refer to clinical genetics	14

Glucocorticoid remediable aldosteronism GRA	Chimaeric gene product	*CYP11B1, CYP11B2*	Hospital specialists	28
Haemochromatosis (familial)	C282Y and H63D mutations	*HFE*	Any physician	28
Hairy cell leukaemia **	Targeted screen	*BRAF V600E*	Haematologist	14
Heart block	Mutation screen	*SCN5A, HCN4, LMNA, TRPM4*	Clinical geneticist/ cardiologist/pathologist	56
	Predictive test, mutation known		Refer to clinical genetics	14
Hyperlipidaemia Type III	Mutation screen	*ApoE codons 130, 176*	Clinical geneticist, consultant lipidologist	28
Hypertriglyceridaemia	Mutation screen	*LPL, ApoC2, ApoA5, GPI-HBP1, LMF1*	Clinical geneticist, consultant lipidologist	56
	Predictive test, mutation known		Refer to clinical genetics	14
Li Fraumeni	Mutation screen	*TP53*	Clinical geneticist, consultant oncologist	56
	Predictive test, mutation known		Refer to clinical genetics	14
Long QT syndrome	Mutation screen	*KCNQ1, KCNH2, KCNE1, KCNE2, SCN5A, KCNJ2, ANK2, AKAP9, CACNA1C, CALM1, CALM2, CAV3, KCNJ5, NOS1AP, SCN4B, SNTA1, TRPM4*	Clinical geneticist/ cardiologist/ pathologist	112
	Predictive test, mutation known		Refer to clinical genetics	14

Lung Cancer	Mutation screen (tumour)**	*EGFR exons 18-21*	Oncologist/ Pathologist	14
		KRAS codons 12, 13, 61		
		BRAF codon 600		
	Fusion gene screen (tumour) **	*ALK, ROS and RET gene fusions*		
	ctDNA EGFR common mutations	*EGFR*		~~14~~ **7**
Lymphoproliferative Disease	CLL - FISH	*TP53* *IGH::CCND1 if required as part of differential diagnosis*	Pathologist / Haematologist	21
	CLL – Whole gene screen **	*TP53*	Pathologist / Haematologist	21
	Myeloma - FISH	*IGH::FGFR3, IGH::MAF, IGH::MAFB, TP53, ATM, CDKN2C and CKS1B*	Pathologist / Haematologist	21
	LPL – targeted screen	*MYD88 (L265P)*	Pathologist / Haematologist	21
Lymphoma	FISH	*MYC, BCL2, BCL6, IGH::CCND1, MALT1*	Haematologist/ Pathologist	21
	Karyotype	*If required*	Haematologist	21
	Clonality	*IGH, IGK, TCRB and TCRG rearrangement*	Haematologist/ Pathologist	21
Melanoma	Mutation screen** (tumour)	*BRAF codon 600*	Oncologist/ Pathologist	14
		*NRAS codons 12, 13, 59, 61 ** *		
		*KIT exons 9, 11, 13, 17 ** *		
Mesothelioma	FISH	*CDKN2A::CEP9*	Oncologist/ Pathologist	21

Metabolic disorders**	Mutation screen by NGS panel / Sanger	*Subpanels analysed from SOPHiA Whole Exome (See Rare & inherited disease test directory)*	Metabolic specialists; neurologists (some referrals), clinical geneticists	56 (up to 10 genes) or 112 (>10 genes)
	Predictive test, mutation known		Refer to clinical genetics	14
Myelodysplastic Syndrome	Karyotype		Haematologist	21
	FISH	*Monosomy 5/5q-, Monosomy 7/7q-,TP53 (on 5q- syndrome)*	Haematologist	21
	Whole gene screen **	*TP53*	Haematologist	21
	Targeted screen by NGS panel (transplant-eligible MDS patients, MDS/MPN overlap)	*ASXL1, BCOR, CALR, CEBPA, CSF3R, DNMT3A, EZH2, FLT3, GATA2, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NPM1, NRAS, PTPN11, RUNX1, SETBP1, SF3B1, SRSF2, STAG2, TET2, TP53, U2AF1, WT1, ZRSR2*	Haematologist	28
Myelofibrosis	Karyotype		Haematologist	21
	Targeted screen by DNA-based diagnosis	*JAK2 (V617F), CALR (exon 9 ins/del), MPL (W515L)*	Haematologist	21
	Targeted screen by NGS panel (transplant-eligible PMF)	*ASXL1, BCOR, CALR, CEBPA, CSF3R, DNMT3A, EZH2, FLT3, GATA2, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NPM1, NRAS, PTPN11, RUNX1, SETBP1, SF3B1, SRSF2, STAG2, TET2, TP53, U2AF1, WT1, ZRSR2*	Haematologist	28
Myeloproliferative disorders, including	Karyotype - CML		Haematologist	14

Chronic Myeloid Leukaemia (CML)	Karyotype - MPD		Haematologist	21
	FISH - CML	*BCR::ABL1*	Haematologist	3
	FISH - MPD	*BCR::ABL1, FIP1L1::PDGFRA, PDGFRB*	Haematologist	21
	Targeted screen by Fusion gene NGS panel - CML	*Including BCR::ABL1*	Haematologist	14
	Targeted screen by Fusion gene NGS panel / DNA-based PCR – MPD/CML differential diagnosis	*JAK2 (V617F), JAK2 (exon 12), CALR (exon 9 ins/del), MPL W515L), KIT (D816V)*	Haematologist	21
	Targeted screen by NGS panel (atypical MPN)	*ASXL1, BCOR, CALR, CEBPA, CSF3R, DNMT3A, EZH2, FLT3, GATA2, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NPM1, NRAS, PTPN11, RUNX1, SETBP1, SF3B1, SRSF2, STAG2, TET2, TP53, U2AF1, WT1, ZRSR2*	Haematologist	28
Myotonic dystrophy type 2 (DM2)	DM2 gene expansion	*CNBP (ZNF9)*	Hospital specialists	28
Neuroblastoma	FISH	*MYCN*	Oncologist/ Pathologist	*3*
Ovarian cancer (high grade serous)	Mutation screen**	*BRCA1 & BRCA2*	Pathologist / Oncologist	56
Primary Immune Deficiencies (PID referral form to be completed with referral, on Q-Pulse and website)	Mutation screen by NGS panel / Sanger	*>200 immunology associated genes*	Immunologists; clinical geneticists	56 (up to 10 genes)
				or 112 (>10 genes)
	Predictive test, mutation known			14

Prothrombin 20210A	20210A mutation	*F2*	Hospital specialist	28
PTEN Hamartoma Tumour Syndrome (PHTS) (Cowdens)	Mutation screen	*PTEN*	Clinical geneticist, consultant oncologist	56
	Predictive test, mutation known		Refer to clinical genetics	14
Renal cell carcinoma	Microarray **	Whole chromosome or whole chromosome arm copy number gains and / or losses.	Oncologist/ Pathologist	21
	FISH	*TFE3*	Oncologist/ Pathologist	21
RNF135	Mutation screen	*RNF135*	Refer to clinical genetics	56
Rapid Aneuploidy Detection	Prenatal	*Chromosomes 13, 18 and 21 & sex chromosomes*	Hospital specialist	3
	Neonatal			10
	Routine			28
Sarcoma	*FISH*	*EWSR1, SS18*	Oncologist/ Pathologist	14
	FISH	*FUS, MDM2, FOXO1*	Oncologist/ Pathologist	21
Sickle cell anaemia	Common mutation E7V	*HBB*	Refer to clinical genetics	28 non urgent
				7 urgent
Torsion dystonia	3bp deletion in TOR1A gene	*TOR1A*	Refer to clinical genetics	28
Thyroid carcinoma	Mutation screen (tumour) **	*BRAF codon 600*	Oncologist/ Pathologist	14

*Reporting times are set by national agreement with the National Services Division. For any prenatal diagnosis (except trisomy screen) the contracted time is 95% within 10 calendar days.

** These (updated) tests have not yet been submitted for accreditation.