REGIONAL MOLECULAR DIAGNOSTICS SERVICE USER MANUAL

Additional Information & Cross References	
Replaces Document Number	**N/A**
Change Management	**N/A**
Related Documents	**C-345 BTL User Manuals**

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REGIONAL MOLECULAR DIAGNOSTICS SERVICE USER MANUAL

LABORATORY SERVICES

- The Regional Molecular Diagnostics Service (RMDS) offers services for Germline and Somatic testing to improve diagnosis, treatment options and management of patients with cancer, haematological conditions and rare genetic disorders.

RMDS GERMLINE SERVICE

The RMDS Germline Service is divided into Constitutional Cytogenetics and Molecular Genetics.

GERMLINE CONSTITUTIONAL CYTOGENETICS

- Constitutional Cytogenetics is composed of the Prenatal and Developmental Delay Sections.

- The **Prenatal Section** performs cytogenetic and molecular cytogenetic analysis (if required) on amniotic fluid and chorionic villus samples for pregnancies at increased risk of a chromosome anomaly. Molecular cytogenetic analysis on fetal tissue for intrauterine deaths, neonatal deaths and stillbirths; and products of conception for recurrent miscarriages. Fetal tissue may also be cultured for storage/onward referral for metabolic investigations. The Prenatal Section also performs cytogenetic and molecular cytogenetic analysis on individuals with indeterminate gender, family history of chromosome anomaly and primary infertility.

- The **Developmental Delay Section** performs cytogenetic and molecular cytogenetic analysis (including microarray) on blood samples for a wide range of conditions including:
  - Congenital abnormalities or dysmorphism
  - Delayed puberty
  - Females with short stature
  - Autism spectrum disorder
  - Developmental delay (motor or growth)
  - Learning difficulties (moderate to severe)
  - Microdeletion syndromes

GERMLINE MOLECULAR GENETICS

- Molecular Genetics is composed of the Metabolic, Neurogenetic, Familial Cancer, Rare Genetic Disorders and Molecular Haematology Sections.

- The **Metabolic Section** performs molecular genetic analysis on samples to aid diagnosis of a wide range of metabolic conditions including cystic fibrosis, Fabry disease, familial expansile osteolysis, and phenylketonuria; and to predict carriers of these diseases, assess recurrence risk and offer testing to at risk family members.

- The **Neurogenetic Section** performs molecular genetic analysis on samples to aid diagnosis of a range of neurogenetic conditions including muscular dystrophy, Prader-Willi/Anglemans, and triplet disorders (e.g. Huntington disease, myotonic dystrophy, Fragile X); and offer testing to at risk family members.

- The **Familial Cancer Section** performs molecular genetic analysis on samples to aid diagnosis of a range of hereditary cancers including breast cancer and colon cancer; and offers testing to at risk family members.

- The **Rare Genetic Disorders Section** performs molecular genetic analysis on samples to aid diagnosis of a range of genetic conditions including cardiac and lipid conditions such as hypertrophic cardiomyopathy and familial hypercholesterolaemia; and to predict carriers of these diseases.

- The **Molecular Haematology Section** performs molecular genetic analysis on samples to aid in the diagnosis of blood disorders such as red blood cell disorders and coagulation disorders.

RMDS SOMATIC SERVICE

The RMDS Somatic Service is divided into the Haemato-oncology Cytogenetics, Haemato-oncology Molecular and Solid Tumour Sections.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- The **Haemato-oncology Cytogenetics Section** performs cytogenetic and molecular cytogenetic analysis on bone marrow and blood samples for acquired genetic changes associated with haematological malignancies.

- Detection of these genetic changes may:
  - Aid diagnosis and classification
  - Provide prognostic information

- Help monitor disease status following treatment, during remission, or after bone marrow transplantation

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- The **Haemato-oncology Molecular Section** performs molecular diagnostic tests on blood and bone marrow to detect mutations associated with haematological malignancies. The presence or absence of these mutations may aid in the diagnosis and classification of disease and provide prognostic information. Minimum residual disease following treatment, during remission or after transplantation can be quantitatively monitored.

SOMATIC SOLID TUMOUR

- The **Solid Tumour Section** performs molecular marker and expression analysis on formalin fixed paraffin embedded (FFPE) and cell free (cf) DNA isolated from plasma, to identify specific gene alterations and antigen expression, in a range of cancer types to facilitate prognostic, predictive and targeted treatment decisions.

HOURS OF LABORATORY SERVICES

- Monday to Friday (excluding public holidays) - 9:00 a.m. to 5:00 p.m.
- No out of hours service is available.

CONTACT DETAILS

Regional Molecular Diagnostics Service (Germline)	
Constitutional Cytogenetics & Molecular Genetics Belfast Trust Laboratories A Floor Tower Block Belfast City Hospital 51 Lisburn Road BELFAST BT9 7AB GeneticsLabs@belfasttrust.hscni.net	028 950 48281
Regional Molecular Diagnostics Service (Somatic)	
Haemato-oncology Cytogenetics Belfast Trust Laboratories A Floor Tower Block Belfast City Hospital 51 Lisburn Road BELFAST BT9 7AB GeneticsLabs@belfasttrust.hscni.net	028 950 48281
Haemato-oncology Molecular Belfast Trust Laboratories C Floor Tower Block Belfast City Hospital 51 Lisburn Road BELFAST BT9 7AB MolecularHaemLab@belfasttrust.hscni.net	028 95040914
Solid Tumour Belfast Trust Laboratories A Floor Tower Block Belfast City Hospital 51 Lisburn Road BELFAST BT9 7AB NIMPL@belfasttrust.hscni.net	028 950 42849 075 919 87216
Head of Regional Molecular Diagnostics Service (Germline)	028 950 45264

Dr Shirley Heggarty, Consultant Clinical Scientist shirley.heggarty@belfasttrust.hscni.net	
Head of Regional Molecular Diagnostics Service (Somatic) Dr Mark Catherwood, Consultant Clinical Scientist mark.catherwood@belfasttrust.hscni.net	028 950 48138 028 9097 1517
Manager of Regional Molecular Diagnostics Service Dr Louise McArt Louise.McArt@belfasttrust.hscni.net	02895040822
Quality Officer of Regional Molecular Diagnostics Service Michael Gribben michael.gribben@belfasttrust.hscni.net Joan McKinney joan.mckinney@belfasttrust@hscni.net	02895046851 02895046273
Secretaries of Regional Molecular Diagnostics Service (Germline)	028 950 48040 028 950 47844
Germline Constitutional Cytogenetics **Enquiries** Constitutional Cytogenetics **Scientific Staff** Simon McCullough (Head of Constitutional Cytogenetics) Louise Rauch (Prenatal Section Head) Dr Laura Taggart (Developmental Delay Section Head) **Operational Manager** Judith Briggs	 028 950 48040 028 950 49371 028 950 42090 028 961 54009 028 950 46113

Germline Molecular Genetics	

Enquiries Molecular Genetics	 028 950 40878
Scientific Staff Peter Logan (Deputy Head of Germline) Dr Rosalind Martin (Metabolic Disorders Section Head) Dr Claire Byrne (Familial Cancer Section Head) Dr Pádraig Hart (Rare Genetic Disorders Section Head) Vacant (Molecular Haematology Section Head) Dr William Wright (Neurogenetic Section Head)	 028 950 48077 02895041979 028 950 48155 028 950 48301 02895042139
Operational Manager Borghert Jan Borghmans	028 950 48048
<u>Somatic Haemato-oncology Cytogenetics</u>	
Enquiries Haemato-oncology Cytogenetics	 028 950 47984 028 950 42034
Scientific Staff Amy Logan (Deputy Head of Somatic) Kathryn McAuley (Haemato-oncology Section Head)	 028 950 47984 028 950 42034
Operational Manager Judith Briggs	028 950 46113
<u>Somatic Haemato-oncology Molecular</u>	
Enquiries Haemato-oncology Molecular	 028 950 40914
Scientific Staff Dr Mark Catherwood (Head of Somatic)	 028 950 48138 028 909 71517
Julie McGimpsey (Clinical Scientist) Andrew Hindley (Biomedical Scientist)	028 96152870 028 96152877
Operational Manager Patricia Higgins	02896153021

<u>Somatic Solid Tumour</u>	
Enquires Solid Tumour	 028 950 42849

	075 919 87216
Scientific Staff	
Dr Beatriz Cutillas-Moreno (Solid Tumour Section Lead)	028 909 75799
Dr Clare Crean (Clinical Scientist)	028 909 72721
Dr Anthony Abladey (Clinical Scientist)	028 909 72721
Operational Manager	
Patricia Higgins	02896153021

CLINICAL STAFF

- The RMDS works closely with the Regional Clinical Genetics Service which is located on the A Floor, Tower Block, Belfast City Hospital.

- Consultant Haematologists support the RMDS Germline Molecular Haematology Section and are based in the Northern Ireland Haemophilia Comprehensive Care Centre, C Floor, Tower Block, Belfast City Hospital.

REGIONAL CLINICAL GENETICS SERVICE CONTACT DETAILS

Genetic Nurses/Counsellors	
Sianan MacParland	028 950 48042
Siobhan Harding-Lester	028 950 47240

Gemma Corbett	028 950 47684
Janice Scott	028 950 48022
Rachel Hardy	028 950 48326
Courtney Forgeng	028 950
Lucy Simpson	4522502896154292
Megan Pries	02895048477
Saralynne Boyle	02895043924
Elena Owens	02896150707
Consultant Clinical Geneticists	
Prof Patrick J Morrison	028 961 54693
Dr Shane McKee	028 950 48326
Dr Tabib Dabir	028 950 45225
Dr Deirdre Donnelly	028 950 47240
Dr Gillian Rea	028 950 47684
Dr Caoimhe McKenna	028 950 48042
Dr Ciaran McCarthy	028 961 54693
Specialist Trainees	
Dr Mairead Hegarty	028 950 45225

HAEMATOLOGISTS CONTACT DETAILS

Consultant Haematologists (Haemostasis)	
Dr Gary Benson	028 950 47977
Dr Claire Corrigan	028 950 45634 / 40444
Dr Richard Gooding	028 950 45634 / 40444
Somatic Haemato-oncology Molecular	
For clinical queries please contact: Haematology On-call Registrar/Consultant	028 903 29241 (BCH switchboard)

MOLECULAR PATHOLOGISTS CONTACT DETAILS

Consultant Molecular Pathologists	
Prof Manuel Salto-Tellez	028 909 72178
Prof Jacqueline James	028 909 75781

QUALITY ASSURANCE

- The RMDS (Medical Laboratory No. 8952) is accredited by the 'United Kingdom Accreditation Service' (UKAS). The RMDS is inspected by UKAS against the standards 'Medical laboratories – Requirements for quality and competence (ISO 15189:2022). The Schedule of Accreditation (i.e. list of accredited tests) can be found on the UKAS website: https://www.ukas.com/search-accredited-organisations/.

- The RMDS participates in all available external quality assessment schemes offered by 'Genomics Quality Assessment' (GenQA) and 'United Kingdom National External Quality Assessment Service' (UKNEQAS) for the tests delivered by the service.

COMMENTS / COMPLAINTS

- The RMDS adheres to the Belfast Health & Social Care Trust 'Policy and Procedure for the Management of Comments, Concerns, Complaints and Compliments' (TP 45/10).

- The RMDS welcomes feedback from health care professionals and patients on ways to improve the service.

- Feedback can be sent to a Quality Officer, Michael Gribben & Joan McKinney, at the above address, or by e-mail to:

michael.gribben@belfasttrust.hscni.net
joan.mckinney@belfasttrust@hscni.net

CLINICAL ADVICE

- Please ring the RMDS enquiries numbers listed in the 'Contact Details' section above for advice on:
  - Sending samples
  - Requesting the most appropriate tests (particularly in urgent cases)
  - Interpretation of patients' results

- Interpretative comments are added to reports, where appropriate.

- Please email the RMDS Duty Scientists using the generic Germline and Somatic emails listed in the 'Contact Details' section above, if information on the following is required:
  - Clinical indications and limitations of examination procedures
  - Estimates of measurement uncertainty of examination procedures

- For guidance on offering, or providing, clinical expertise about the results of Direct to Consumer (DTC) genomic or genetic testing please refer to the Royal College of General Practitioners' and the British Society for Genetic Medicine's 'Position Statement on Direct to Consumer Genomic Testing' (October 2019).

DATA PROTECTION

- The RMDS ensures confidentiality of patient information is maintained by adhering to a number of guidelines and policies including the Belfast Health & Social Care Trust 'Policy on the Data Protection and Protection of Personal Information' (BHSCT/PPI (06)).

REQUEST FORM

Encompass is a Northern Ireland solution for digitisation of the patient care record. The system is in the process of being rolled out regionally and all test requests should be ordered through the system, however, during the transition period paper request forms will be accepted.

Patient consent will be collected within Encompass, however during the transition period, paper copies of consent will still be accepted.

If it is necessary to complete a request form, please use the guidance below.

GERMLINE CONSTITUTIONAL CYTOGENETICS

- For Germline Constitutional Cytogenetics tests listed in the 'RMDS Test Repertoire' table below, please complete a 'Genetic Testing Request Form' or request testing electronically through EPIC.

- The form (with integral plastic sealable envelope) is available either singly or in books of 25 and can be obtained by contacting the RMDS.

- A form (paper or electronic) must accompany each sample and be comprehensively completed.

- Patient identification labels should be used, if available.

- It is essential that the following patient information is captured on the form:
  - Surname
  - Forename
  - Health & Care Number
  - DOB
  - Gender
  - Referring Consultant
  - Dept/Ward/Hospital

- It is essential that the tests requested are indicated on the form by:
  - Ticking the appropriate boxes in the section:
    - Blood LI-HEP TUBE
    - Blood EDTA TUBE
    - OTHER SAMPLE TYPES
  - Entering the tests in the relevant section
  - If more than one test is requested, please indicate the order of testing.

- The form must include the reason for testing.

- Identity of the person collecting the primary sample, including time and date of collection can be recorded where relevant

- The form must include for intrauterine deaths, neonatal deaths and stillbirths the:
  - Baby as the patient, however the mother's details should also be provided
  - Cellular Pathology Laboratory reference number and sampling details

- The form must include for miscarriages the:
  - Details of the history/number of miscarriages
  - Details if a fetus was identified in the miscarried tissue
  - Cellular Pathology Laboratory reference number and sampling details

Patient Consent

- All genetic testing requires patient consent, for which there is a patient consent section (Record of Discussion regarding testing and/or storage of genetic material) on the form.

- It is the responsibility of the referring clinician to ensure that the patient signs the 'Record of Discussion regarding testing and/or storage of genetic material' section.

- If the 'Record of Discussion regarding testing and/or storage of genetic material' section is not completed and signed, the clinician, by submitting a sample, confirms that informed consent from the patient has been obtained for testing and storage.

- Consent is assumed unless otherwise stated.

- Identity of the person collecting the primary sample, including time and date of collection can be recorded where relevant

GERMLINE MOLECULAR GENETICS

- For Germline Molecular Genetic tests listed in the 'RMDS Test Repertoire' table below, please complete a 'Genetic Testing Request Form' or request testing electronically through EPIC.

- The form (with integral plastic sealable envelope) is available either singly or in books of 25 and can be obtained by contacting the RMDS.

- A form (paper or electronic) must accompany each sample and be comprehensively completed.

- Patient identification labels should be used, if available.

- It is essential that the following patient information is captured on the form:
  - Surname
  - Forename
  - Health & Care Number
  - DOB
  - Gender
  - Referring Consultant
  - Dept/Ward/Hospital

- It is essential that the tests requested are indicated on the form by:
  - Ticking the appropriate boxes in the section:
    - Blood LI-HEP TUBE
    - Blood EDTA TUBE
    - OTHER SAMPLE TYPES
  - Entering the gene panels/tests in the relevant section
  - If more than one test is requested, please indicate the order of testing.

- The form must include:
  - The disease to be tested for and the exact test, if known
  - Any relevant test results, if known, i.e.:
    - Familial hypercholesterolaemia - lipid profile
    - Cystic fibrosis - sweat test (where available) and immunoreactive trypsin test results (neonatal samples)
  - The status of the patient (Affected/Possibly affected/Possible carrier/etc)
  - Family history of the disease and names of affected or carrier relatives
  - Variant details, if available

- Identity of the person collecting the primary sample, including time and date of collection can be recorded where relevant

Patient Consent

- All genetic testing requires patient consent, for which there is a patient consent section (Record of Discussion regarding testing and/or storage of genetic material) on the form.

- It is the responsibility of the referring clinician to ensure that the patient signs the 'Record of Discussion regarding testing and/or storage of genetic material' section.

- If the 'Record of Discussion regarding testing and/or storage of genetic material' section is not completed and signed, the clinician, by submitting a sample, confirms that informed consent from the patient has been obtained for testing and storage.

- Consent is assumed unless otherwise stated.

Familial Cancer Section:

- For cancer gene panel requests please ensure that the appropriate R panel is requested in Encompass as indicated in 'RMDS Test Repertoire' table below.

Molecular Haematology Section:

- For haemochromatosis (HFE) requests please indicate on the request form that the patient has met the appropriate 'Hereditary Haemochromatosis Testing Criteria' as listed below in 'Testing Criteria' section.

- Please include all relevant family history of HFE.

Patient Consent for Genetic Testing for Heritable Bleeding Disorders

- Please refer to the UKHCDO 'INFORMATION ON GENETIC TESTING AND CONSENT FORM FOR PATIENTS AND FAMILIES WITH DISORDERS OF BLOOD CLOTTING'in the 'Testing Criteria' section below.

- Consent is assumed unless otherwise stated.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- For Somatic Haemato-oncology Cytogenetic tests listed in the 'RMDS Test Repertoire' table below, please complete a 'Genetic Testing Request Form'.

- The form (with integral plastic sealable envelope) is available either singly or in books of 25 and can be obtained by contacting the RMDS.

- A form must accompany each sample and be comprehensively completed.

- Patient identification labels should be used, if available.

- It is essential that the following patient information is captured on the form:
  - Surname
  - Forename
  - Health & Care Number
  - DOB
  - Gender
  - Referring Consultant
  - Dept/Ward/Hospital

- It is essential that the tests requested are indicated on the form by:
  - Ticking the appropriate boxes in the section:
    - Bone marrow in BM transport media (supplied by laboratory)
    - Blood LI-HEP TUBE
    - Blood EDTA TUBE
    - OTHER SAMPLE TYPES
  - Entering the tests in the relevant section
  - If more than one test is requested, please indicate the order of testing.

- Samples referred, where a suspected diagnosis is not clearly indicated on the form, will not automatically be analysed:
  - A pre-analysis haematological outcome form will be emailed to the referring clinician, requesting further clinical information, and if chromosome analysis is required.

  - If this information is not returned within 10 days of this email being sent, the sample will be reported as not analysed.

- Samples referred for plasma cell neoplasms will not be processed for prognostic FISH until a confirmed diagnosis is received:
  - An email will be sent to the referring clinician requesting this information following receipt of the sample.
  - If this information is not returned within 10 days of this email being sent, the sample will be reported as not analysed.

- Identity of the person collecting the primary sample, including time and date of collection can be recorded where relevant

Patient Consent

- Consent is assumed unless otherwise stated

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- For Haemato-oncology Molecular tests listed in the 'RMDS Test Repertoire' table below, please complete a 'RMDS Somatic - Haemato-Oncology Molecular Request Form' (LF 390 354).

- The form is available to referrers from the Belfast Trust Laboratories via Q-Pulse or to referrers from outside of the Belfast Trust Laboratories by contacting the RMDS.

- A form must accompany each sample and be comprehensively completed.

- Patient identification labels should be used, if available.

- It is essential that the following patient information is captured on the form:
  - Surname
  - Forename
  - Health & Care Number
  - DOB
  - Sex
  - Referring Consultant
  - Dept/Ward/Hospital

- It is essential that the tests requested are indicated on the form by:
  - Ticking the appropriate boxes in the section:
    - Bone marrow in RPMI
    - Blood EDTA TUBE
    - Other sample type
  - Selecting the tests in the relevant section

- Identity of the person collecting the primary sample, including time and date of collection can be recorded where relevant

Patient Consent

- Consent is assumed unless otherwise stated

SOMATIC SOLID TUMOUR

FFPE Sample:

- For Somatic Solid Tumour tests listed in the 'RMDS Test Repertoire' table below, requiring a FFPE sample, complete the 'RMDS Somatic - Solid Tumours Test Request Form, (LF 390 014).

- The form is available to referrers from the Belfast Trust Laboratories via Q-Pulse or to referrers from outside of the Belfast Trust Laboratories by contacting the RMDS.

- A form must accompany each sample and be comprehensively completed.

- Patient identification labels should be used, if available.

- It is essential that the following patient information is captured on the form:
  - Health & Care Number
  - Pathology Number
  - Surname
  - Forename
  - Sex
  - DOB
  - Consultant
  - Department
  - Ward

- It is essential that the tests requested are indicated on the form by:
  - Ticking the appropriate 'Request' box against the clinical indication

  N.B. Please indicate if the request is urgent.

- Identity of the person collecting the primary sample, including time and date of collection can be recorded where relevant

cfDNA Blood Sample:

- For Somatic Solid Tumour tests listed in the 'RMDS Test Repertoire' table below, requiring a cfDNA blood sample, please complete the 'RMDS Somatic - Request Form for cfDNA Samples' (LF 390 037).

- The form is available to referrers from the Belfast Trust Laboratories via Q-Pulse or to referrers from outside of the Belfast Trust Laboratories by contacting the RMDS.

- A form must accompany each sample and be comprehensively completed.

- Patient identification labels should be used, if available.

- It is essential that the following patient information is captured on the form:
  - Health & Care Number
  - Hospital Number
  - Surname
  - Forename
  - Gender
  - DOB
  - Consultant
  - Department
  - Ward
  - Clinical details

N.B. Please indicate if the request is urgent or non-urgent.

SAMPLES

SAMPLE LABELLING

GERMLINE CONSTITUTIONAL CYTOGENETICS

- All samples require the following information:
  - Patient's full name
  - Patient's date of birth
  - Patient's Health & Care Number
  - Date and time the sample was taken

- Patient identification labels should be used, if available.

- The sample and request form must have a minimum of 2 matching patient identifiers.

GERMLINE MOLECULAR GENETICS

- As for Germline Constitutional Cytogenetics

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- As for Germline Constitutional Cytogenetics

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- As for Germline Constitutional Cytogenetics

SOMATIC SOLID TUMOUR

- As for Germline Constitutional Cytogenetics

- All FFPE blank sections, accompanying H&E stained slides and if applicable tumour positive IHC slides (e.g. TTF1 or p40), require the Pathology Block number and part ID.

- Pencil must be used to label blank slides for molecular testing as most pen/markers are soluble in chemicals used during downstream processing.

SAMPLE TYPE

- For information on sample type required please refer to the 'RMDS Test Repertoire' table below.

SAMPLE COLLECTION

- For information on sample collection requirements please refer to the 'RMDS Test Repertoire' table below.

SAMPLE TRANSPORTATION

GERMLINE CONSTITUTIONAL CYTOGENETICS

- Samples should be received by the RMDS as soon as possible after sampling and preferably within 24-48 hours as delays may compromise the result.
- Chorionic villus samples cannot be received in the RMDS after 12pm on Thursday.
- If a delay in transport to the RMDS is anticipated, please store the samples at 4°C and record this on Encompass or the accompanying request form.
- Samples must be packaged and sent to the RMDS so as to comply with the current regulations on the transport and postage of biological materials.
- The following transportation documents are available from the RMDS on request:
  - Pneumatic Tube Transport of Clinical Specimens (C-17)
  - Transport of Specimens to the Laboratory (C-18)
  - Health & Safety Rules for Porters & Couriers (C-43)

GERMLINE MOLECULAR GENETICS

- See Germline Constitutional Cytogenetics above.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- See Germline Constitutional Cytogenetics above.

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- Samples should be received by the RMDS as soon as possible after sampling and preferably within 24 hours as delays may compromise the result.

- If a delay in transport to the RMDS is anticipated, please store the samples at room temperature.

- Samples must be packaged and sent to the RMDS so as to comply with the current regulations on the transport and postage of biological materials.

- The following transportation documents are available from the RMDS on request:
  - Pneumatic Tube Transport of Clinical Specimens (C-17)
  - Transport of Specimens to the Laboratory (C-18)
  - Health & Safety Rules for Porters & Couriers (C-43)

Samples requiring RNA extraction *e.g. BCR::ABL1 (monitoring/diagnosis) or Acute myeloid leukaemia measurable residual disease (AML MRD) (monitoring / diagnosis*) must be received by the RMDS within 24 hours of sampling and by 3 pm Fridays and before Bank Holidays. Samples received after this time will not be processed as RNA quality cannot be guaranteed.

SOMATIC SOLID TUMOUR

FFPE Sample:

- FFPE blank slides must be pre-incubated at 60^{O}C for 1 hour before sending.

- FFPE samples should be sent in a Cytomailer and as soon as possible after sectioning and drying.

cfDNA Blood Sample:

- cfDNA blood samples should be received no later than 16:00hrs. If this is not possible, retain samples at source, at room temperature, and send the following morning. Record this on Encompass or the accompanying request form.

- Do NOT transport cfDNA blood samples on ice, send under room temperature conditions.

- The laboratory must be notified via email or telephone prior to sending the sample.

SAMPLE REJECTION

- Samples will be rejected if they are:
  - Unlabelled or inadequately labelled
  - In the wrong container/tube
  - On the wrong slide type
  - In an expired container/tube
  - Of inadequate size or volume
  - Badly clotted
  - Delayed in transit
  - Broken/leaking
  - Inappropriately referred
  - If the patient details on the sample do not match those on Encompass or the accompanying request form

  N.B. Precious samples may be accepted if a repeat sample would cause distress to the patient e.g. Bone marrow aspirate for haemato-oncology molecular testing. The sample will be processed with the understanding that the responsibility lies with the clinician signing the required documentation.

HIGH RISK SAMPLES

- The RMDS must be informed of any known or potential hazards associated with samples.

- Samples and packaging must be clearly labelled as BIOHAZARD with a Category 3 label affixed to the sample and request form.

- The nature of the hazard must be indicated on the request form or Encompass e.g. Hepatitis B, HIV.

For some types of sample, and specific categories of hazard, a restricted range of services may be offered.

FACTORS WHICH AFFECT RESULT QUALITY

GERMLINE CONSTITUTIONAL CYTOGENETICS

- The factors listed below MAY affect the quality of results:
  - Samples not taken under sterile conditions
  - Samples not received by the RMDS within 24-48 hours of sampling
  - Chorionic villus samples not collected in transport medium supplied by the RMDS
  - Solid tissue samples not collected in sterile saline or transport media supplied by the RMDS

GERMLINE MOLECULAR GENETICS

- The factors listed below MAY affect the quality of the results:
  - Samples from patients who have had bone marrow transplantation
  - Samples not taken under sterile conditions
  - Samples not received by the RMDS within 24-48 hours of sampling

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- The factors listed below MAY affect the quality of results:
  - Samples not taken under sterile conditions
  - Samples not received by the RMDS within 24-48 hours of sampling; 24 hours for bone marrow samples
  - Bone marrow samples not collected in transport media supplied by the RMDS

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- The factors listed below MAY affect the quality of results:
  - Samples not received by the RMDS within 24 hours of sampling in the case of *BCR::ABL*1 (monitoring/diagnosis) testing & Acute myeloid leukaemia measurable residual disease (AML MRD) (monitoring / diagnosis).

SOMATIC SOLID TUMOUR

- The factors listed below MAY affect the quality of results:
  - Decalcified or bone specimens **have not** been validated for use with any of the IHC antibodies/FISH probes and are deemed **unsuitable** for genomic analysis too. However, if these are the only specimen available, testing will be attempted, but results must be interpreted with caution.
  - Blank slides NOT incubated at 60^{O}C for 1 hour
  - Poor quality FFPE sections - inadequate fixation, section folding, incorrect section thickness
  - FFPE sample with high levels of melanin, necrosis, inflammation or mucin
  - FFPE material from FFPE blocks which are ≥10 years old
  - cfDNA blood sample(s) stored incorrectly below room temperature

ADDITIONAL / SUPPLEMENTARY TESTS

GERMLINE CONSTITUTIONAL CYTOGENETICS

- All requests for additional/supplementary tests on existing samples must be made in writing or by email to the RMDS.
- Telephone requests are not accepted until written confirmation is received.
- Cell suspensions are stored during the course of an investigation and are available for additional/supplementary testing during this time.
- If an additional/supplementary test is requested after the final report has been issued, a new sample may be required.
- In cases where a congenital abnormality is detected, it is often necessary to test parental samples before issuing a final report.
- In cases where mosaicism is detected, a repeat sample or a sample from a different tissue/site may be requested for confirmation.

GERMLINE MOLECULAR GENETICS

- All requests for additional/supplementary tests on existing samples must be made in writing or by email to the RMDS.
- Telephone requests are not accepted until written confirmation is received.
- Excess DNA is permanently stored after the requested tests have been completed (consent for DNA storage is assumed unless stated otherwise).

- If a previous sample has been submitted with consent for DNA storage, supplementary tests relevant to the original referral reason can be requested without submitting a further sample or re-consenting the patient.

- However, a new test request for another condition must have appropriate consent.

- It is advisable to check with the RMDS to ensure that sufficient DNA of good quality remains in storage.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- All requests for additional/supplementary tests on existing samples must be made in writing or by email to the RMDS.

- Telephone requests are not accepted until written confirmation is received.

- Cell suspensions from patients with haematological malignancies may be kept long term and are available for additional/supplementary testing.

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- All requests for additional/supplementary tests on existing samples must be made in writing or email to the RMDS.

- Telephone requests are not accepted until written confirmation is received.

SOMATIC SOLID TUMOUR

- All requests for additional/supplementary tests on existing samples must be made in writing or by email to the RMDS.

- Telephone requests are not accepted until written confirmation is received.

- DNA from patients previously tested is stored long term and is available for additional/supplementary molecular based testing if sufficient DNA remains.

Please note that stored DNA extracted using Cobas Extraction Method (samples extracted 2013 - June 2021) cannot be used for NGS testing.

REPORTING

GERMLINE CONSTITUTIONAL CYTOGENETICS

Prenatal Section:

- Reports will be uploaded to EPIC (manually to Media tab/automated to Labs tab) and alerted to the referring clinician.
- Results will NOT routinely be issued by phone.
- Urgent results can be phoned through or emailed as PDF documents (within the hscni.net email system) to the referring clinician on request.
- Solid tissue reports will be provided to both the obstetrician and the pathologist.

Developmental Delay Section:

- Reports will be uploaded to EPIC (manually to Media tab/automated to Labs tab) and alerted to the referring clinician.
- Results will NOT routinely be issued by phone.
- Urgent results can be phoned through or emailed as PDF documents (within the hscni.net email system) to the referring clinician on request.
- FISH results on urgent bloods are available within 3 days of sample receipt and will be verbally reported. On completion of chromosome analysis or microarray, as required, a report will be issued.

GERMLINE MOLECULAR GENETICS

Metabolic, Neurogenetic, Familial Cancer, Rare Genetic Disorders & Molecular Haematology Sections:

- Reports will be uploaded to EPIC (manually to Media/Automated to Labs tab) and alerted to the referring clinician (with the exception of predictive Huntington disorder reports).
- Results will NOT routinely be issued by phone.

- Urgent results can be phoned through or emailed as PDF documents (within the hscni.net email system) to the referring clinician on request.

- Detected variants are assessed at the time of reporting according to the 'American College of Medical Genetics' (ACMG) / 'Association for Clinical Genomic Science' (ACGS) best practice guidelines (Richards et al, 2015, Genet Med 17: 405-24: https://www.acgs.uk.com/media/12533/uk-practice-guidelines-for-variant-classification-v12-2024.pdf).

- Variant nomenclature conforms to 'Human Genome Variation Society' (HGVS) guidelines (www.HGVS.org).

Sequence variants of no or unlikely clinical significance are omitted from the reported results.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- Reports will be uploaded to EPIC (manually to Media tab/automated to Labs tab) and alerted to the referring clinician.

- Urgent results can be phoned through to the referring clinician on request.

- FISH results for urgent samples are available within 2-3 days of sample receipt. However, a copy of these results is only issued by post with the final chromosome analysis report.

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- All reports are automatically uploaded to NIECR/Encompass.

SOMATIC SOLID TUMOUR

- Reports are uploaded to NIECR/Encompass.

- Paper reports are NOT issued.

- Results will NOT routinely be issued by phone.

- Urgent results can be phoned through or emailed as PDF documents (within the hscni.net email system) to the referring clinician on request.

- Private patient results will be emailed via encrypted email to the referring private hospital Cellular Pathology Laboratory.

TEST TURNAROUND TIMES

- For information on test turnaround times please refer to the 'RMDS Test Repertoire' table below.

- The 'Reporting Time Guideline' is an approximate guide to the availability of results and applies from the date of receipt of the sample in the RMDS or the date at which information required to determine appropriate testing is received.

REFERRAL LABORATORY TESTS

GERMLINE CONSTITUTIONAL CYTOGENETICS

- Tests which are clinically necessary, but are either not currently carried out in-house or unable to be performed by the RMDS due to capacity issues, can be arranged to be sent to a referring laboratory.

- Samples will be sent to a referring laboratory, providing the test is offered by NHS England's National Genomic Test Directory.
  - These tests can be very expensive and the RMDS reserves the right to request that referrers pay for them.
  - Samples will be prioritised based on clinical need and may be placed on a waiting list.
  - Where specific 'Testing Criteria' are defined, referrers MUST ensure that patients meet these criteria and that the appropriate forms are supplied with the sample or a request is made in Encompass indicating how the patient meets the criteria.

GERMLINE MOLECULAR GENETICS

- See Germline Constitutional Cytogenetics above.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS

- For tests not offered by the RMDS, it is the responsibility of the referring clinician to send these tests to the appropriate referral laboratory. The RMDS will return any such samples sent to them.

SOMATIC HAEMATO-ONCOLOGY MOLECULAR

- For tests not offered by the RMDS, it is the responsibility of the referring clinician to send these tests to the appropriate referral laboratory. The RMDS will return any such samples sent to them.

SOMATIC SOLID TUMOUR

- For tests not offered by the RMDS, it is the responsibility of the referring Cellular Pathology Laboratory to send these tests to the appropriate referral laboratory. The RMDS will return any such samples sent to them.

UKAS ACCREDITATION

ALL TESTS LISTED ARE ACCREDITED UNLESS OTHERWISE STATED

The Regional Molecular Diagnostics Service (RMDS) has been approved by the United Kingdom Accreditation Service (UKAS) to manage a flexible scope of accreditation for selected examination procedures. Tests can be added / modified without the requirement to apply for an extension to scope through UKAS. New tests and targets will managed internally by RMDS.

The below processes are accredited under a flexible scope of accreditation:

Sanger Sequencing (Fluorescent sequencing)
Repeat Fragment Detection
MLPA
ARMS
WES
NGS

Examination procedures currently not UKAS accredited:
FISH
Karyotyping & G-banding (Chromosome Analysis)
Dihydropyrimidine Dehydrogenase Deficiency LAMP
Somatic Haemato-Oncology Molecular Section Tests
Somatic Solid Tumour Section Tests

RMDS TEST REPERTOIRE

GERMLINE CONSTITUTIONAL CYTOGENETICS - PRENATAL SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Congenital Abnormality Detected on Ultrasound Scan Suggestive of a Chromosome Anomaly ***Family History of a Chromosome Anomaly*** ***Raised Serum Screen/Non-invasive Prenatal Test Result Indicating an Increased Risk of a Chromosome Anomaly***	**20-30ml Amniotic Fluid** in sterile plastic universal or **10-30mg Chorionic Villus** in transport media supplied by the RMDS – tests on this sample must be prearranged by contacting the RMDS or **1-2ml Lithium Heparin Cord Blood**	**QF-PCR (R401)** (aneuploidy) • Down Syndrome • Edwards Syndrome • Patau Syndrome • Sex Chromosome Aneuploidy	3 working days	•Rapid prenatal diagnosis using an aneuploidy QF-PCR test.
		Chromosome Analysis (R297) (karyotyping)	17 days Amniotic Fluid	•Chromosome analysis may not exclude mosaicism or subtle chromosome rearrangement. •Chorionic Villus is currently sent to a referral laboratory for testing.
		Microarray (R022)	14 days	•Microarray may not exclude mosaicism and does not detect balanced rearrangements. •Microarray testing is only available in the presence of Congenital Abnormality on Ultrasound Scan.
		Culture (R322) (onward referral for mitochondrial investigation)		•Please contact the RMDS.

GERMLINE CONSTITUTIONAL CYTOGENETICS - PRENATAL SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Intrauterine Deaths ***Neonatal Deaths*** ***Stillbirths***	**5mm^3 Skin and Muscle Biopsy** and/or **1 cm^3 Placental Tissue** **For stillbirths 1-2ml EDTA cord blood or cardiac stab blood is acceptable** (please indicate the blood site on the 'Genetic Testing Request Form' or in Encompass test request) Intrauterine deaths, neonatal deaths and stillbirths should be sent to Cellular Pathology Laboratory where: •Pathologist will collect sample described above in 5ml sterile saline or in transport media supplied by RMDS •Forward sample to RMDS for testing N.B. Tissue should not be formalin fixed	**QF-PCR (R318)**	42 days	•For diagnosis of triploidy & aneuploidy for chromosomes 13, 15, 16, 18, 21, 22, X & Y. •All referrals from this group of patients must be from a consultant obstetrician or pathologist or following discussions with Regional Clinical Genetics Service.
		Microarray (R022)	42 days	•Microarray may not exclude mosaicism and does not detect balanced rearrangements. •Microarray is only available if there are congenital abnormalities detected at post mortem.
		Culture (R322) (for storage)		•As required.

GERMLINE CONSTITUTIONAL CYTOGENETICS - PRENATAL SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Indeterminate Gender	**1-4ml Lithium Heparin Blood** and **4ml EDTA Blood**	**FISH (R026)** (where appropriate)	<3 days	• Chromosome analysis will be performed if FISH or microarray testing is abnormal.
		Chromosome Analysis (R297) (karyotyping)	14 days	
		Microarray (R028)	14 days	
Family History of Chromosome Anomaly ***Primary Infertility***	**4ml Lithium Heparin Blood**	**Chromosome Analysis (R297)** (karyotyping)	3 mths	

GERMLINE CONSTITUTIONAL CYTOGENETICS - PRENATAL SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Recurrent Miscarriage *(3 or more)*	**Products of Conception: 2-4mm^3 Placental Villus Tissue** Products of conception should be sent to Cellular Pathology Laboratory where: •Pathologist will collect sample described above in 5ml sterile saline or in transport media supplied by RMDS •Forward sample to RMDS N.B. Tissue should not be formalin fixed	**QF-PCR (R318)**	42 days	•For diagnosis of triploidy & aneuploidy for chromosomes 13, 15, 16, 18, 21, 22, X & Y. •All referrals from this group of patients must be from a consultant obstetrician or pathologist or following discussions with Regional Clinical Genetics Service.

Recurrent Miscarriage:

- The RMDS will follow NHS England test directory guidance for recurrent miscarriage referrals. The guidance is found in the test directory under the clinical indications R318 and R297.
- Parental testing is now advised, only when an unbalanced structural chromosomal abnormality is found in the products of conception.
- In the absence of products of conception material, please contact the RMDS by email.

Other Sample Types:

- If it is not possible to obtain a tissue sample, then FFPE tissue slides and/or buccal cells may be sent for FISH testing, only by arrangement with RMDS.

GERMLINE CONSTITUTIONAL CYTOGENETICS - DEVELOPMENTAL DELAY SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Congenital Abnormalities or Dysmorphism in Neonate Consistent with Aneuploidy	**1-4ml Lithium Heparin Blood**	**FISH (R026)** (where appropriate)	<3 days	•Aneuploidy includes: - Down syndrome - Edwards syndrome - Patau syndrome •May proceed to microarray analysis if result normal.
		Chromosome Analysis (R297) (karyotyping)	14 days	
Congenital Abnormalities or Dysmorphism in Neonate NOT Consistent with Aneuploidy	**1-4ml EDTA Blood**	**Microarray (R028)**	14 days	
Delayed Puberty ***Female with Short Stature*** ***Autism Spectrum Disorder*** ***Developmental Delay*** ***Learning Difficulties*** ***Microdeletion Syndromes***	**4ml EDTA Blood**	**Microarray**	42 days	• **R377** For autism / developmental delay / learning difficulties • **R028** For delayed puberty / Short stature females / Microdeletion syndromes

GERMLINE CONSTITUTIONAL CYTOGENETICS - DEVELOPMENTAL DELAY SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Follow Up Analysis	**4ml Lithium Heparin Blood** and/or **4ml EDTA Blood** (as indicated by RMDS)	**FISH (R298)** (as required)	42 days (from receipt of FISH probe)	•Follow up analysis of proband, parents and other relatives (as required) will be detailed in preliminary report.
		Chromosome Analysis (R297) (karyotyping) (as required)	42 days	
		Microarray (R028/R377) – see above (as required)	3 mths	

GERMLINE MOLECULAR GENETICS - METABOLIC SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Cystic Fibrosis (CF) ***R184 Screen*** ***R185 Carrier Testing***	**4-8ml EDTA Blood**	**ARMS** **CF Base test** (50 CFTR variants and the intron 8 poly T/TG tract c.1210-12(5/7/9T))	4 wks	•Detects approximately 90% of Northern Irish variants.
		Fluorescent sequencing (CFTR exons)	8 wks	•Analysis of family variants not detected by the CF Base kit.
		Full gene sequencing & **Dosage analysis**	>6 mths	•Arranged at an external accredited laboratory.
Cystic Fibrosis Neonatal Screen ***R253***	**Guthrie Card**	**ARMS** **CF Lite4 test** (4 most common variants and extended variant screen by CF Base as required)	1 wk	•Neonatal screening test. •Detects approximately 80% of Northern Irish variants.
Dihydropyrimidine Dehydrogenase Deficiency (DPYD) ***Genotyping***	**4-8ml EDTA Blood**	**LAMP** Not UKAS accredited	14 days	•Patients requiring fluoropyrimidine chemotherapy treatment (for dosage guidance).
		Fluorescent sequencing		
		ARMS		
Fabry Disease (α-galactosidase A deficiency) ***R335***	**4-8ml EDTA Blood**	**NGS WES and MLPA dosage analysis**	12 wks	•MLPA analysis may be batched.

GERMLINE MOLECULAR GENETICS - METABOLIC DISORDERS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Familial Expansile Osteolysis (FEO)	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** (exon 1 of TNFRSF11A (RANK) gene for FEO)	8wks	•Predictive testing for known family variant.
		Cascade testing for at risk relatives	8wks	
Homocystinuria (cystathionine β-synthase deficiency)	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** (exon 8 of CBS gene - detects the most common p.(Gly307Ser) and p.(Ile278Thr) variants and other exon 8 variants)	8 wks	•Cascade testing only for confirmed family variants.
Hurler Syndrome / Mucopolysaccharidosis (MPS I) R277	**4-8ml EDTA Blood**	**Targeted fluorescent sequencing screen** (IDUA)	4 wks	•Screen for Mucopolysaccharidosis I •(Screen for common NI variants only)
Myophosphorylase deficiency (McArdles disease)	**4-8ml EDTA Blood**	**Targeted fluorescent sequencing screen (PGYM)**	**4 wks**	
I-Cell Disease / Mucolipidosis Type 2 (ML II) R289	**4-8ml EDTA Blood**	**Targeted fluorescent sequencing screen** (GNPTAB)	4 wks	•Screen for Mucolipidosis II •(Screen for common NI variants only)

GERMLINE MOLECULAR GENETICS - METABOLIC DISORDERS SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Identity Testing and Maternal Cell Contamination (MCC) Assay for Prenatal Testing R321	**4-8ml EDTA Blood**	**Multi locus multiplex STR-PCR assay**	4 wks	•Identity testing only performed to confirm other test results or for twin studies. •MCC testing carried out in parallel with prenatal diagnostic test or to exclude MCC from sample types at increased risk of MCC such as cord blood.
Phenylketonuria (PKU) R283	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** (all exons of PAH)	12 wks	•Detects majority of Northern Irish variants ~99%.
		Partner carrier testing	12 wks	•Detects ~99% of Northern Irish variants.
		Carrier testing for relatives of PKU patients	4 wks	•Various single variant tests.

N.B.

- For infants 1-2ml EDTA Blood may be sent.
- If it is difficult to obtain an EDTA Blood, please contact the RMDS to discuss sending an alternative sample (e.g. Buccal Cell Scrapings or Saliva).
- **DO NOT SEND AN ALTERNATIVE SAMPLE UNLESS THIS HAS BEEN DISCUSSED WITH THE RMDS.**

GERMLINE MOLECULAR GENETICS - NEUROGENETIC SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Azoospermia Factor (AZF)	**4-8ml EDTA Blood**	**MLPA (R411)** (Y chromosome microdeletions)	8 wks	•Infertility investigations.
Charcot-Marie-Tooth Syndrome Type 1A (CMT1A) ***&*** ***Hereditary Neuropathy with Liability to Pressure Palsy (HNPP)***	**4-8ml EDTA Blood**	**MLPA (R077)**	8 wks	•Detects common PMP22 duplications (CMT1A) and deletions (HNPP).
		Cascade testing for at risk relatives	8 wks	•Predictive testing for known family variant.
Dentatorubral-Pallidoluysian Atrophy (DRPLA)	**4-8ml EDTA Blood**	**Fluorescent gene specific triplet repeat PCR**	8 wks	
Duchenne / Becker Muscular Dystrophy (DMD / BMD)	**4-8ml EDTA Blood**	**MLPA (R073)** (all exons)	8 wks	•Detects all whole exon deletion and duplication variants (65 -80% of all DMD variants).
Fragile X Syndrome ***&*** ***Fragile X - Associated Tremor/Ataxia Syndrome (FXATS)*** ***&*** ***Premature Ovarian Insufficiency (POI)***	**4-8ml EDTA Blood**	**Fluorescent gene specific triplet repeat PCR AmplideX™ FMR1 PCR kit (R053)**	8 wks	•Detects normal, pre and full variant alleles. •Fragile X tests no longer carried out as a frontline screening test. •Now only performed for developmental delay referrals following a normal microarray result (on request) or for patients with other relevant clinical features such as ataxia or POI, or family history as appropriate.

GERMLINE MOLECULAR GENETICS - NEUROGENTICS DISORDERS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Friedreich Ataxia	**4-8ml EDTA Blood**	**Fluorescent gene specific triplet repeat PCR** & **TP-PCR** (FXN expansion variants)	8 wks	•Detects the majority of triplet repeat expansions in affected patients and carriers but cannot detect other rare sequence variations.
Huntington Disease (HD)	**4-8ml EDTA Blood**	**Fluorescent gene specific triplet repeat PCR** & **TP-PCR (R068)** **Cascade testing** for at risk relatives	4 wks 4 wks	•Detects normal alleles and the majority of pathogenic expansion alleles (>35). •Referrals only accepted from Regional Clinical Genetics Service.
Kennedy Syndrome	**4-8ml EDTA Blood**	***Fluorescent gene specific triplet repeat PCR***	8 wks	•Detects normal alleles and pathogenic expansion alleles.
Myotonic Dystrophy Type 1 (DM1)	**4-8ml EDTA Blood**	**Fluorescent gene specific triplet repeat PCR** & **TP-PCR (R072)** **Cascade testing** for at risk relatives	8 wks 8 wks	•Detects normal alleles (<38 repeats) and pathogenic expansion alleles (>50 repeats). •Accurate repeat sizing in the affected range may not be possible. •Predictive testing for known family variant.
Prader Willi / Angelman Syndromes	**4-8ml EDTA Blood**	**MS-MLPA dosage and methylation test (R048/R047)**	8 wks	•Detects the majority of cases due to deletion disomy and imprinting defects. •Cannot distinguish between disomy and imprinting defects.

N.B.

- For infants 1-2ml EDTA Blood may be sent.
- If it is difficult to obtain an EDTA Blood, please contact the RMDS to discuss sending an alternative sample (e.g. Buccal Cell Scrapings or Saliva).
- **DO NOT SEND AN ALTERNATIVE SAMPLE UNLESS THIS HAS BEEN DISCUSSED WITH THE RMDS.**

GERMLINE MOLECULAR GENETICS - FAMILIAL CANCER SECTION TESTS – TARGETED CANCER PANEL

Referrals are only accepted from approved mainstreaming consultants or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Isolated Breast Cancer *(R208)*	**4-8ml EDTA Blood**	**NGS Panel** (BRCA1, BRCA2) Not UKAS accredited **Dosage analysis** (BRCA1, BRCA2)	12 wks	• Please use Encompass **R208** to make a request. • In general testing for BRCA1 and BRCA2 only should be limited to cases where it is requested by referring consultant or patient choice.
Inherited Breast Cancer *(R208)*	**4-8ml EDTA Blood**	**NGS Panel** (ATM, BRCA1, BRCA2, CHEK2, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53) **Dosage analysis** (ATM, BRCA1, BRCA2, CHEK2, PALB2, PTEN, RAD51C, RAD51D, STK11, TP53)	12 wks	• Please use Encompass **R208** to make a request. • Any patient meeting the testing criteria with a family history of breast cancer only is eligible.

GERMLINE MOLECULAR GENETICS - FAMILIAL CANCER SECTION TESTS – TARGETED CANCER PANEL

Referrals are only accepted from approved mainstreaming consultants or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Inherited Breast and Ovarian Cancer *(R208)*	**4-8ml EDTA Blood**	**NGS Panel** (ATM, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53) **Dosage analysis** (ATM, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53)	12 wks	• Please use Encompass **R208** to make a request. • Any patient meeting the testing criteria with a family history (FRD/ SDR/TDR) of breast, ovarian or CRC may be offered a breast and ovarian cancer panel. •
Isolated Ovarian Cancer *(R207)*	**4-8ml EDTA Blood**	**NGS Panel** (BRCA1, BRCA2) **Dosage analysis** (BRCA1, BRCA2)	12 wks	• Please use Encompass **R207** to make a request. • In general testing for BRCA1 and BRCA2 only should be limited to cases where it is requested by referring consultant or patient choice.

GERMLINE MOLECULAR GENETICS - FAMILIAL CANCER SECTION TESTS – TARGETED CANCER PANEL

Referrals are only accepted from approved mainstreaming consultants or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Inherited Ovarian Cancer (without breast cancer) *(R207)*	**4-8ml EDTA Blood**	**NGS Panel** (BRCA1, BRCA2, BRIP1, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, RAD51C, RAD51D) **Dosage analysis** (BRCA1, BRCA2, BRIP1, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, RAD51C, RAD51D)	12 wks	• Please use Encompass **R207** to make a request. • Any patient meeting the testing criteria with a family history of ovarian cancer only is eligible
Inherited Breast and Ovarian Cancer *(R208 or R207)*	**4-8ml EDTA Blood**	**NGS Panel** (ATM, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53) **Dosage analysis** (ATM, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, RAD51C, RAD51D, STK11, TP53)	12 wks	• Please use Encompass **R208** or **R207** to make a request if a family history of breast cancer becomes apparent when reviewing an ovarian cancer family. • Patients with a personal or family history (FRD/ SDR/TDR) of ovarian or CRC may be offered a breast and ovarian cancer panel

GERMLINE MOLECULAR GENETICS - FAMILIAL CANCER SECTION TESTS – TARGETED CANCER PANEL

Referrals are only accepted from approved mainstreaming consultants or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Inherited Polyposis *(R414)*	**4-8ml EDTA Blood**	**NGS Panel** (APC, MUTYH) **Dosage analysis** (APC, MUTYH)	12 wks	• Please use Encompass **R414** to make a request. • In general testing for APC / MutYH only should be limited to cases where it is requested by referring consultant or patient choice.
Inherited Colorectal Cancer (with or without polyposis) *(R211)*	**4-8ml EDTA Blood**	**NGS Panel** (APC, BMPR1A, EPCAM, MLH1, MSH2, MSH6, MUTYH, NTHL1, PMS2, POLD1, POLE, PTEN, SMAD4, STK11) **Dosage analysis** (APC, BMPR1A, EPCAM, MLH1, MSH2, MSH6, MUTYH, NTHL1, PMS2, POLD1, POLE, PTEN, SMAD4, STK11)	12 wks	• Please use Encompass **R211** to make a request.Any patient meeting the testing criteria with a family history

GERMLINE MOLECULAR GENETICS - FAMILIAL CANCER SECTION TESTS – TARGETED CANCER PANEL

Referrals are only accepted from approved mainstreaming consultants or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
NICE Lynch Pathway and Inherited MMR Deficiency (Lynch syndrome) *(R210)*	**4-8ml EDTA Blood**	**NGS Panel** (EPCAM, MLH1, MSH2, MSH6, PMS2) **Dosage analysis** (EPCAM, MLH1, MSH2, MSH6, PMS2)	12 wks	• Please use Encompass **R210** to make a request. • In general testing for Lynch associated genes only should be limited to cases where it is requested by referring consultant or patient choice.
Paraganglioma and phaeochromyctoma *(R223)* *plus* ***Multiple endocrine neoplasia type 2*** *(R218)* ***Neurofibromatosis type 1*** *(R222)* ***Von Hippel Lindau Syndrome*** *(R225)*	**4-8ml EDTA Blood**	**NGS Panel** (FH, MAX, MEN1, NF1, PRKAR1A, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL) **Dosage analysis** (FH, MAX, MEN1, NF1, PRKAR1A, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL)	12 wks	• Please use Encompass **R223** to make a request. • Any patient meeting the testing criteria

GERMLINE MOLECULAR GENETICS - FAMILIAL CANCER SECTION TESTS – TARGETED CANCER PANEL

Referrals are only accepted from approved mainstreaming consultants or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Familial Melanoma *(R254)*	**4-8ml EDTA Blood**	**NGS Panel** (BAP1, BRCA2, CDK4, CDKN2A (p14), CDKN2A (p16)) **Dosage analysis** (FH, MAX, MEN1, NF1, PRKAR1A, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, TMEM127, VHL)	12 wks	• Please use Encompass **R254** to make a request. • Any patient meeting the testing criteria

GERMLINE MOLECULAR GENETICS - FAMILIAL CANCER SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Cancer Gene Testing *(see Targeted Cancer Panel for gene list)* **R242 Predictive R240 Confirmation**	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** & **MLPA**	4 wks	• Please use Encompass **R242 (Predictive) or R240 (Confirmation)** •Cascade testing for at risk relatives – Predictive and confirmation testing for known family variants (accepted from Regional Clinical Genetics Service only).
TP53 **R216**	**4-8ml EDTA Blood**	**Fluorescent sequencing single gene screen** *(TP53)*	8 wks	• Please use Encompass **R216** •Detects coding region and splice junction variants. •Dosage analysis is available for TP53, only on request if clinically indicated (sent to Referral Laboratory for testing).
Von Hippel-Lindau Syndrome (VHL) ***R225***	**4-8ml EDTA Blood**	**Fluorescent sequencing single gene screen** *(VHL)*	8 wks	• Please use Encompass **R225** •Detects coding region and splice junction variants. •Dosage analysis is available for VHL only on request if clinically indicated (sent to Referral Laboratory for testing)

- For infants 1-2ml EDTA Blood may be sent.
- If it is difficult to obtain an EDTA Blood, please contact the RMDS to discuss sending an alternative sample (e.g. Buccal Cell Scrapings or Saliva).
- **DO NOT SEND AN ALTERNATIVE SAMPLE UNLESS THIS HAS BEEN DISCUSSED WITH THE RMDS.**

GERMLINE MOLECULAR GENETICS – RARE GENETIC DISORDERS SECTION TESTS – CARDIAC

Referrals are only accepted from an appropriate clinical consultant from the Inherited Cardiac Conditions Service or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Long QT Syndrome (LQTS) (R127)	**4-8ml EDTA Blood**	**WES Panel** (CACNA1C, CALM1, CALM2, CALM3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, SCN5A)	12 wks	•Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Brugada Syndrome (BrS) (R128)	**4-8ml EDTA Blood**	**WES Panel** (SCN5A)	12 wks	•Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing	4 wks	•Predictive testing for known family variants.
Catecholaminergic Polymorphic VT (R129)	**4-8ml EDTA Blood**	**WES Panel** (CALM1, CALM2, CALM3, CASQ2, RYR2, TRDN)	12 wks	•Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.

GERMLINE MOLECULAR GENETICS – RARE GENETIC DISORDERS SECTION TESTS – CARDIAC

Referrals are only accepted from an appropriate clinical consultant from the Inherited Cardiac Conditions Service or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Hypertrophic Cardiomyopathy - teen and adult (HCM) (R131)	**4-8ml EDTA Blood**	**WES Panel** (ACTC1, ACTN2, CACNA1C, CSRP3, FHL1, FHOD3, FLNC, GLA, JPH2, LAMP2, MYBPC3, MYH7, MYL2, MYL3, PLN, PRKAG2, TNNC1, TNNI3, TNNT2, TPM1, TTR)	12 wks	•Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Dilated Cardiomyopathy - teen and adult (R132)	**4-8ml EDTA Blood**	**WES Panel** (ACTC1, ACTN2, BAG3, CDH2, DES, DMD, DOLK, DSC2, DSG2, DSP, EMD, FLNC, JUP, LAMP2, LMNA, MYBPC3, MYH7, NEXN, NKX2-5, PKP2, PLN, RBM20, RYR2, SCN5A, TMEM43, TNNC1, TNNI3, TNNI3K, TNNT2, TPM1, TTN, VCL)	12 wks	•Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.

GERMLINE MOLECULAR GENETICS – RARE GENETIC DISORDERS SECTION TESTS – CARDIAC

Referrals are only accepted from an appropriate clinical consultant from the Inherited Cardiac Conditions Service or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Arrythmogenic cardiomyopathy (R133)	**4-8ml EDTA Blood**	**WES Panel** (CDH2, DES, DSC2, DSG2, DSP, FLNC, JUP, LMNA, PKP2, PLN, TMEM43)	12 wks	•Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Sudden Cardiac death (R138)	**4-8ml EDTA Blood**	**WES Panel** (ACTC1, ACTN2, BAG3, CACNA1C, CALM1, CALM2, CALM3, CASQ2, CDH2, CSRP3, DES, DMD, DOLK, DSC2, DSG2, DSP, EMD, FHL1, FHOD3, FLNC, GLA, HCN4, JPH2, JUP, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, LAMP2, LMNA, MYBPC3, MYH7, MYL2, MYL3, NEXN, NKX2-5, PKP2, PLN, PRKAG2, RBM20, RYR2, SCN5A, TMEM43, TNNC1, TNNI3, TNNI3K, TNNT2, TPM1, TRDN, TTN, TTR, VCL)	12 wks	•Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.

GERMLINE MOLECULAR GENETICS – RARE GENETIC DISORDERS SECTION TESTS – CARDIAC

Referrals are only accepted from an appropriate clinical consultant from the Inherited Cardiac Conditions Service or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Thoracic aortic aneurysm or dissection (R125)	**4-8ml Blood**	**WES Panel** **(ABL1, ACTA2, ASPH, BGN, CBS, COL1A1, COL3A1, COL5A1, COL5A2, EFEMP2, ELN, FBLN5, FBN1, FBN2, FKBP14, FLNA, IPO8, LOX, MFAP5, MYH11, MYLK, NOTCH1, PLOD1, PMEPA1, PRKG1, SECISBP2, SKI, SLC2A10, SMAD2, SMAD3, SMAD4, SMAD6, TGFB2, TGFB3, TGFBR1, TGFBR2,**	12 wks	• Patient should meet the specified criteria and have seen cardiologist or clinical geneticist.
		Cascade testing for at risk relatives	4 wks	• Predictive testing for known family variants.

GERMLINE MOLECULAR GENETICS – RARE GENETIC DISORDERS SECTION TESTS - LIPID

Referrals are only accepted from a consultant clinical biochemist or associated speciality nurse or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Familial Hypercholesterolaemia (FH) (R134)	**4-8ml EDTA Blood**	**WES Panel** (APOB, APOE, LDLR, LDLRAP1, PCSK9)	12 wks	•**Criteria Score** required. •See **Wales Score Calculator tool**
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Familial Defective Apolipoprotein B-100 (FDB)	**4-8ml EDTA Blood**	**Fluorescent sequencing**	4 wks	•Predictive testing for known family variants.
		Cascade for at risk relatives	4 wks	Predictive testing for known family variants.
Apolipoprotein E (APOE)	**4-8ml EDTA Blood**	**Fluorescent sequencing** for E2/E2 status (APOE codon 176 (prev KA 158))	4 wks	•Type III Hyperlipidaemia. •ApoE4 status not reported.
Sitosterolaemia (R323)	**4-8ml EDTA Blood**	**WES Panel** (ABCG5 & ABCG8)	12 wks	•**Criteria** required. Elevated plasma β-sitosterol with development of Xanthomata before 30yrs).
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.

GERMLINE MOLECULAR GENETICS – RARE GENETIC DISORDERS SECTION TESTS – LIPID

Referrals are only accepted from a consultant clinical biochemist or associated speciality nurse or Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Familial Chylomicronaemia Syndrome (FCS) (R324)	**4-8ml EDTA Blood**	**WES Panel** (APOE, APOA5, APOC2, LPL, CREB3L3, GPD1, GPIHBP1, LMF1)	12 wks	•**FCS Criteria Score** required. •Fasting TG>20 with no secondary causes.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Lysosomal Acid Lipase Deficiency (R325)	**4-8ml EDTA Blood**	**WES Panel** (LIPA)	12 wks	•**Criteria** required. •Biochemically established deficiency of Lysosomal Acid Lipase.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
CETP Deficiency (CETP) ***LCAT Deficiency (LCAT)*** ***Lipoprotein Lipase (LPL) Deficiency etc*** *(R387)*	**4-8ml EDTA Blood**	**WES Panel** (APOA1, APOA4, APOA5, APOC2, APOC3, CETP, LCAT, LPL)	12 wks	•Individual genes analysed by request.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.

GERMLINE MOLECULAR GENETICS – RARE GENETIC DISORDERS SECTION TESTS

Referrals are only accepted from Regional Clinical Genetics

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Acutely Unwell Children with a Likely Monogenic Disorder (R14)	**4-8ml EDTA Blood**	**Trio WES**	12 wks	•Trio, gene-agnostic analysis of WES

N.B.

- For infants 1-2ml EDTA Blood may be sent.
- If it is difficult to obtain an EDTA Blood, please contact the RMDS to discuss sending an alternative sample (e.g. Buccal Cell Scrapings or Saliva).
- **DO NOT SEND AN ALTERNATIVE SAMPLE UNLESS THIS HAS BEEN DISCUSSED WITH THE RMDS**

GERMLINE MOLECULAR GENETICS - MOLECULAR HAEMATOLOGY SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Factor V Leiden (FVL) & Prothrombin G20210A (PT20) R240	**4-8ml EDTA Blood**	**Cobas Factor II and Factor V Test**	6 wks	•Activated Protein C resistance (APC) result must be positive for test to be performed. Please state APC result when requesting. •Contact Haemostasis Clinical Team for further advice on 028 95040444.
Haemophilia A (Factor VIII Deficiency) R117	**4-8ml EDTA Blood**	**WES Panel** (F8)	12 wks	•Patient should meet the specified criteria and have been reviewed by haematology. •May also include screening for F8 intron 1 and F8 intron 22 inversion in new patient with severe haemophilia A.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Haemophilia A (F8 Gene: Intron 1 Inversion) R117	**4-8ml EDTA Blood**	**PCR & Gel Electrophoresis Genotyping** (F8 intron 1)	4 wks	•F8 Gene: Intron 1 Inversion. •Predictive testing for known family variant.
Haemophilia A (F8 Gene: Intron 22 Inversion) R117	**4-8ml EDTA Blood**	**PCR & Gel Electrophoresis Genotyping** (F8 intron 22)	4 wks	•F8 Gene: Intron 22 Inversion. •Predictive testing for known family variant.

GERMLINE MOLECULAR GENETICS - MOLECULAR HAEMATOLOGY SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Haemophilia B (Factor IX Defiiency) R118	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** (F9)	12 wks	• Patient should meet the specified criteria and have been reviewed by haematology.
		Cascade testing for at risk relatives	4 wks	• Predictive testing for known family variants.
Von Willebrand Disease (VWD) R121	**4-8ml EDTA Blood**	**WES** (VWF)	12 wks	•Patient should meet the specified criteria and have been reviewed by haematology. •
		Cascade testing for at risk relatives	4 wks	• Predictive testing for known family variants.
Hereditary Haemorrhagic Telangiectasia (HHT) (R186)	**4-8ml EDTA Blood**	**WES Panel** (ACVRL1, ENG, EPHB4, GDF2, RASA1, SMAD4)	12 wks	• Patient should meet the specified criteria and have been reviewed by an appropriate Consultant.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.

GERMLINE MOLECULAR GENETICS - MOLECULAR HAEMATOLOGY SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Inherited Factor VII Deficiency R116	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** (F7)	12 wks	•Patient should meet the specified criteria and have been reviewed by haematology.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Inherited Factor X Deficiency R119	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** (F10)	12 wks	•Patient should meet the specified criteria and have been reviewed by haematology.
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Inherited Factor XI Deficiency R120	**4-8ml EDTA Blood**	**Fluorescent sequencing screen** (F11)	12 wks	•Patient should meet the specified criteria and have been reviewed by haematology. •
		Cascade testing for at risk relatives	4 wks	•Predictive testing for known family variants.
Hereditary Haemochromatosis (HFE) R95	**4-8ml EDTA Blood**	**LAMP**	6 wks	Referrals accepted from consultant hepatologists, paediatricians, gastroenterologists, nephrologists, haematologists, specialist physicians and GPs where referrals meet the testing criteria – see Hereditary Haemochromatosis Testing Criteria (below in 'Testing Criteria' section).

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Acute Myeloid Leukaemia (Diagnosis) M80	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** only if circulating blasts present	**Chromosome Analysis** (karyotyping)	14 days	• Please indicate if the patient is being considered for a clinical trial. • Additional FISH testing may be carried out according to clinical trial requirements. • Other FISH tests may be performed if indicated by chromosome analysis.
		FISH - to confirm specific abnormality found by chromosome analysis or as indicated by morphology RUNX1T1-RUNX1 CBFB-MYH11 MECOM (formerly EVI1) KMT2A (formerly MLL) PML-RARA	Result available in 2-3 days but reported with chromosome analysis result	
Acute Myeloid Leukaemia (Follow Up) M80	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** only if circulating blasts present	**Chromosome Analysis** (karyotyping)	21 days	• Only if abnormal at diagnosis. • Chromosome analysis and/or FISH carried out depending on abnormalities identified at disease diagnosis. • Full chromosome analysis is carried out in cases of suspected relapsed disease. • FISH analysis is not carried out on patients with APL. MRD analysis is carried out by the Haemato-oncology Molecular Section, C Floor, Tower Block, BCH, for patients with APL.
		FISH - using relevant probe(s) to target diagnostic abnormality		

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Aplastic Anaemia M83	**1-2ml Bone Marrow** in transport media supplied by RMDS	**Chromosome Analysis** (karyotyping)	21 days	•Chromosome analysis can be attempted on blood if bone marrow aspirate is a dry tap.
B-Cell Precursor Lymphoblastic Leukaemia (Diagnosis) M91	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** only if circulating blasts present	**Chromosome Analysis** (karyotyping) **FISH** BCR::ABL1 ETV6-RUNX1 (if ≤25 years) KMT2A (formerly MLL) Hyperdiploidy / Hypodiploidy Panel*, TCF3* & ABL class fusions* (* if indicated)	14 days Result available in 2-3 days but reported with chromosome analysis result	•Please indicate if the patient is being considered for a clinical trial. •Additional FISH testing may be carried out according to clinical trial requirements. •Other FISH tests may be performed if indicated by chromosome analysis.
B-Cell Precursor Lymphoblastic Leukaemia (Follow Up) M91	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** only if circulating blasts present	**Chromosome Analysis** (karyotyping) **FISH**	21 days	•Only if abnormal at diagnosis. •Chromosome analysis and/or FISH carried out depending on abnormalities identified at disease diagnosis. •Full chromosome analysis carried out in cases of suspected relapsed disease.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Bone Marrow Transplant (Sex Matched)	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood**	**Chromosome Analysis** (karyotyping) **FISH** – using relevant probe(s) to target diagnostic abnormality	21 days	•Only if abnormal clone at diagnosis. •Please provide donor sex if known.
Bone Marrow Transplant (Sex Mismatched)	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood**	**FISH** XY	21 days	•Only if donor sex mismatched. •Please provide donor sex if known.
Chronic Lymphocytic Leukaemia M94	**4-5ml EDTA Blood**	**FISH** ATM/TP53 12 centromere/13q14/13q34 & IGH-CCND1 (on request)	21 days	•FISH may also be carried out on blood smears if sufficient lymphocytes present. •ATM/TP53 prognostic FISH carried out on CD19+ cell fraction on confirmed cases if treatment is required. •FISH for 13q, 12 centromere & IGH::CCND1 can be carried out on request

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Chronic Myeloid Leukaemia (Diagnosis) M84	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood**	**Chromosome Analysis** (karyotyping)	14 days	•*BCR::ABL1 FISH analysis is only carried out where indicated by chromosome analysis (e.g. where variant translocations have been identified) •Other FISH tests may be performed if indicated by chromosome analysis.
		FISH BCR::ABL1*	Result available in 2-3 days but reported with chromosome analysis result	
Chronic Myeloid Leukaemia (Follow Up) M84	**1-2ml Bone Marrow** in transport media supplied by RMDS	**Chromosome Analysis** (karyotyping)	21 days	•Chromosome analysis is only performed where the disease progression is suspected. •MRD analysis is carried out by the Haemato-oncology Molecular Section, C Floor, Tower Block, BCH.
MDS/MPN M224 ***Juvenile myelomonocytic Leukaemia (JMML) M88***	**1-2ml Bone Marrow** in transport media supplied by RMDS	**Chromosome Analysis** (karyotyping)	21 days	•Other FISH tests may be performed if indicated by chromosome analysis. •*unless carried out by Q PCR
		FISH BCR::ABL1*		

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Eosinophilia M85	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood**	**Chromosome Analysis** (karyotyping) and/or **FISH** PDGFRA PDGFRB BCR::ABL1 (if requested) FGFR1 JAK2 ETV6	21 days	•PDGFRA only carried out on PB. •Additional tests carried out on BMA. •Other FISH tests may be performed if indicated by chromosome analysis
Mantle Cell Lymphoma M102	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** or **Bone Marrow Smears** or **Blood Smears**	**FISH** IGH-CCND1	21 days	•CD5+ CD200 - by flow cytometry.

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Myelodysplastic Syndrome M82	**1-2ml Bone Marrow** in transport media supplied by RMDS	**Chromosome Analysis** (karyotyping) **FISH** 5p/5q 7cen/7q MECOM TP53	21 days	•FISH is performed only if chromosome analysis fails. •Other FISH tests may be performed if indicated by chromosome analysis. •Chromosome analysis can be attempted on blood if bone marrow aspirate is a dry tap. •
Myelofibrosis M85	**1-2ml Bone Marrow** in transport media supplied by RMDS	**Chromosome Analysis** (karyotyping) **FISH** BCR::ABL1*	21 days	•Chromosome analysis can be attempted on blood if bone marrow aspirate is a dry tap. •*unless carried out by Q PCR
Myeloproliferative Neoplasms *Polycythaemia Vera / Essential Thrombocythaemia* ***M85***	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood**	**FISH** BCR::ABL1*	21 days	•Chromosome analysis can be performed only on request. •*unless carried out by Q PCR

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Plasma Cell Dyscrasia M92	**1-2ml First Tap Bone Marrow** in transport media supplied by RMDS	**FISH** CDKN2C (1p32.3) / CKS1B (1q21) P53 Deletion IGH And if appropriate: IGH/CCND1 IGH/FGFR3 IGH/MAF IGH/MAFB	21 days	• Prognostic FISH carried out on CD138 purified cell fraction on confirmed cases of multiple myeloma. • Bone marrow aspirates received in the RMDS after 12pm on Friday will be processed on the following Monday.
T-Cell Precursor Lymphoblastic Leukaemia (Diagnosis) M91	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** only if circulating blasts present	**Chromosome Analysis** (karyotyping)	14 days	• Please indicate if the patient is being considered for a clinical trial. • Additional FISH testing may be carried out according to clinical trial requirements. • Other FISH tests may be performed if indicated by chromosome analysis.
		FISH BCR::ABL1 KMT2A TCRA/D ABL class fusions	Result available in 2-3 days but reported with chromosome analysis result	
T-Cell Precursor Lymphoblastic Leukaemia (Follow Up) M91	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** only if circulating blasts present	**Chromosome Analysis** (karyotyping)	21 days	• Only if abnormal at diagnosis. • Chromosome analysis and/ or FISH carried out depending on abnormalities identified at disease diagnosis. • Full chromosome analysis carried out in cases of suspected relapsed disease.
		FISH - using relevant probe(s) to target diagnostic abnormality		

SOMATIC HAEMATO-ONCOLOGY CYTOGENETICS SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
T-Cell Prolymphocytic Leukaemia M113	**1-2ml Bone Marrow** in transport media supplied by RMDS or **4-5ml Lithium Heparin Blood** only if circulating blasts present	**Chromosome Analysis** (karyotyping) **FISH** TRA/D ATM/TP53	21 days	•Other FISH tests may be performed if indicated by chromosome analysis.

N.B.

- FISH tests specified are not exhaustive and further FISH testing may be initiated if indicated by results of chromosome analysis or disease subtype.
- Where both chromosome analysis and FISH is required, this can be carried out on the same sample.

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Acute Lymphocytic Leukaemia (ALL) (Diagnosis / Monitoring) *(M91)*	**10-20ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**RT-qPCR** (t(9;22) BCR::ABL1) Not UKAS accredited	14 days	• **Samples must arrive in the laboratory within 24 hours of sampling.** Samples received after this time will not be processed as RNA quality cannot be guaranteed. • Patient's full clinical details are essential.
		Fluorescent Sequencing Screen BCR::ABL1 Tyrosine Kinase Domain Mutation Studies Not UKAS accredited	28 days	• BCR::ABL1 % must be **≥ 10%** for analysis to be performed. • See **Request for TKI Discontinuation Form** (below in 'Testing Criteria' section).

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Acute Myeloid Leukaemia (AML) (Diagnosis / Monitoring) *(M80)*	**10-20ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**RT-qPCR** (t(15;17) PML::RARA, t(8;21) RUNX1-RUNX1T1, inv(16) CBFB-MYH11, t(9;22) BCR::ABL1, NPM1 MRD) Not UKAS accredited	14 days	• **Samples must arrive in the laboratory within 24 hours of sampling.** Samples received after this time will not be processed as RNA quality cannot be guaranteed. • Patient's full clinical details are essential.
		Fragment analysis (FLT3-ITD, NPM1 Diagnostic) Not UKAS accredited	7 days	
		Myeloid NGS Gene Panel Not UKAS accredited	42 days	• Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
B Cell Non-Hodgkin Lymphoma *(M95)*	**5x10µm Paraffin Embedded Tissue** or **Fresh Tissue** or **5ml Peripheral Blood** in EDTA or **5ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**PCR & Fragment Analysis** Immunoglobulin Gene Rearrangements Not UKAS accredited	14 days	
		Fluorescent Sequencing Screen (IgHV) Not UKAS accredited	14 days	
		Myeloid NGS Gene Panel (TP53) Not UKAS accredited	42 days	Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).
		RT-qPCR (MYD88) Not UKAS accredited	14 days	

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Blastic Plasmacytoid Dendritic Cell Neoplasm *(M90)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**Myeloid NGS Gene Panel** Not UKAS accredited	42 days	• Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).
Chronic Lymphocytic Leukaemia (CLL) *(M94)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**Fluorescent Sequencing Screen** *(*IgHV) Not UKAS accredited	14 days	
		Myeloid NGS Gene Panel (TP53) Not UKAS accredited	42 days	Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Chronic Myeloid Leukaemia (CML) (Diagnosis / Monitoring) *(M84)*	**10-20ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**RT-qPCR** (t(9;22) BCR::ABL1) Not UKAS accredited	14 days	• **Samples must arrive in the laboratory within 24 hours of sampling.** Samples received after this time will not be processed as RNA quality cannot be guaranteed. • Patient's full clinical details are essential. See **Request for TKI Discontinuation Form** (below in 'Testing Criteria' section).
		Fluorescent Sequencing Screen t(9;22) BCR::ABL1 Tyrosine Kinase Domain Mutation Studies Not UKAS accredited	28 days	• BCR::ABL1 % must be ≥ 10% for analysis.

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Hairy Cell Leukaemia *(M108)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**RT-qPCR** (BRAF V600E) Not UKAS accredited	14 days	
Juvenile Myelomonocytic Leukaemia *(M88)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**Myeloid NGS Gene Panel** Not UKAS accredited	42 days	• Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).
Lymphoplasmacytic Lymphoma/Waldenstrom Macroglobulinaemia *(M104)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**RT-qPCR** (MYD88) Not UKAS accredited	14 days	

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Myeloproliferative Neoplasm (MPN) *(M85)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**RT-qPCR** (JAK2 V617F) Not UKAS accredited	28 days	• Test must be requested by a Haematologist. • JAK2 V617F is initial screen performed. • Subsequent reflex testing for CALR Exon 9, MPL Exon 10 and JAK2 Exon 12 mutations is carried out as per **Molecular Diagnosis of Myeloproliferative Neoplasms (MPN)** (see below in 'Testing Criteria' section).
		Fluorescent Sequencing Screen (CALR Exon 9, MPL Exon 10, JAK2 Exon12) Not UKAS accredited	56 days	
		RT-qPCR (t(9;22) BCR::ABL1) Not UKAS accredited	14 days	• **Samples must arrive in the laboratory within 24 hours of sampling.** Samples received after this time will not be processed as RNA quality cannot be guaranteed. • Patient's full clinical details are essential.
		Myeloid NGS gene panel Not UKAS accredited	42 days	• Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Systemic Mastocytosis *(M86)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**RT-qPCR** (c-KIT) Not UKAS accredited	14 days	
T Cell Non-Hodgkin Lymphoma *(M111)*	**5x10µm Paraffin Embedded Tissue** or **Fresh Tissue** or **5ml Peripheral Blood** in EDTA or **5ml Bone Marrow** in RPMI supplied by supplied by Haematology Flow Cytometry Laboratory	**PCR & Fragment Analysis** T-Cell Receptor Gene Rearrangements Not UKAS accredited	14 days	

SOMATIC HAEMATO-ONCOLOGY MOLECULAR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Transient Abnormal Myelopoiesis *(M81)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**Myeloid NGS Gene Panel** Not UKAS accredited	42 days	• Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).
Myelodysplasia *(M82)*	**5ml Peripheral Blood** in EDTA or **1-3ml Bone Marrow** in RPMI supplied by Haematology Flow Cytometry Laboratory	**Myeloid NGS Gene Panel** Not UKAS accredited	42 days	• Reason for request must meet **Myeloid NGS Acceptance Criteria** (below in 'Testing Criteria' section).

SOMATIC SOLID TUMOUR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Breast Carcinoma	**FFPE sample** 2x3-4µm unstained sections incubated on positively charged TOMO slides PLUS H&E and HER2 IHC slide	**ERBB2 (HER2) FISH** M3 Not UKAS accredited	14 days	**Decalcified or bone samples are not suitable for IHC, FISH or molecular based tests. Testing will be attempted if it is the only sample available.**
	FFPE sample 4x3µm unstained sections incubated on positively charged TOMO slides	**PD-L1 IHC** (SP142) M234 Not UKAS accredited	14 days	•PD-L1 testing in TNBC: •**ALL IHC requests must be sent to the Institute of Pathology, RVH.** •PD-L1 142 testing can only be requested on Advanced/Metastatic **Triple Negative Breast Cancer** Patients. •Metastatic decalcified or bone samples and liver samples are not suitable. •Cytology samples cannot be tested for PD-L1 142. •If metastatic sample cannot be tested the primary breast sample can be tested.
	FFPE sample 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**NGS Panel** (PIK3CA, NTRK1, NTRK3) **(Metastatic Breast Cancer patients)** M3 Not UKAS accredited	14 days	NGS Panel- Metastatic Breast Cancer patients (HER2 IHC negative & HR Positive)

SOMATIC SOLID TUMOUR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Cholangiocarcinoma M220	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**NGS Panel** (IDH1, IDH2, FGFR2, NTRK 1, NTRK 3, MSI) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for molecular based tests. Testing will be attempted if it is the only sample available.**
Colorectal Carcinoma M1	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**NGS Panel** (BRAF, KRAS, NRAS, MSI, NTRK1, NTRK3) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for molecular based tests. Testing will be attempted if it is the only sample available.**

SOMATIC SOLID TUMOUR SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Endometrial Cancer M215	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**NGS Panel** (TP53, POLE, NTRK, MSI) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for molecular based tests. Testing will be attempted if it is the only sample available.**
Gastric / Oesophageal Cancer M236/M237	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E 4x3µm unstained section incubated on positively charged TOMO slides	**NGS Panel** (MSI, NTRK1, NTRK3) Not UKAS accredited **HER2 IHC** Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for IHC or molecular based tests. Testing will be attempted if it is the only sample available.** • **ALL IHC requests must be sent to the Institute of Pathology, RVH.** • PD-L1 22C3 testing is currently not available in RMDS for gastric oesopghageal cancer patients. This test must be organised by the referring Pathologist.

SOMATIC SOLID TUMOUR SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Lung Adenocarcinoma - Advanced/ Metastatic M4	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E 4x3µm unstained sections incubated on positively charged TOMO slides	**PD-L1 IHC** (SP263) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for IHC or molecular based tests. Testing will be attempted if it is the only sample available.** • **ALL IHC requests must be sent to the Institute of Pathology, RVH.** • Please send labelled tumour positive IHC slides (e.g. TTF1) alongside ALL cytology samples. • FFPE sections for testing should be serial sections. • Samples requiring both IHC and molecular based tests should be sectioned for 1xH&E first, then for molecular based tests and then sectioned for IHC based tests (e.g. Lung adenocarcinoma, section 1 H&E, sections 2-6 NGS, sections 7-10 PD-L1).
		NGS Panel (ALK, EGFR, ERBB2, BRAF, KRAS, MET, NTRK1, NTRK3, ROS1, RET) Not UKAS accredited		
	EDTA 2xRoche cfDNA Collection Tubes filled to the indicated line (supplied by RMDS)	**cfDNA EGFR Cobas** Not UKAS accredited	14 days	• Please use Encompass or **RMDS Somatic – Request Form for cfDNA Samples (LF 390 037)** • Please see Sample Transportation section above. • Please contact the RMDS before sending the samples.

SOMATIC SOLID TUMOUR SECTION TESTS

Disease	Sample Type & Collection Requirements	Tests Available	Reporting Time Guideline	Comment
Lung Squamous Cell Carcinoma - Advanced/ Metastatic M4	**FFPE sample** 4x3µm unstained sections incubated on positively charged TOMO slides	**PD-L1 IHC** (SP263) Not UKAS accredited **NGS Panel** (ALK, EGFR, ERBB2, BRAF, KRAS, MET, NTRK1, NTRK3, ROS1, RET) Not UKAS accredited	14 days	• **Decalcified bone samples are not suitable for IHC or molecular based tests. Testing will be attempted if it is the only sample available.** • **ALL IHC requests must be sent to the Institute of Pathology, RVH.** • Send tumour positive IHC slides (e.g. p40) alongside ALL cytology samples. • Samples requiring both IHC and molecular based tests should be sectioned for 1xH&E first, then for molecular based tests and then sectioned for IHC based tests (e.g. Lung adenocarcinoma, section 1 H&E, sections 2-6 NGS, sections 7-10 PD-L1).
Malignant Melanoma M7	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**BRAF Cobas** Not UKAS accredited **NGS Panel** (BRAF, KIT, NRAS, NTRK1, NTRK3) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for molecular based tests. Testing will be attempted if it is the only sample available.**

SOMATIC SOLID TUMOUR SECTION TESTS				
Disease	**Sample Type & Collection Requirements**	**Tests Available**	**Reporting Time Guideline**	**Comment**
Ovarian Cancer M2	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**NGS Panel** (BRCA1, BRCA2, TP53) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for molecular based tests. Testing will be attempted if it is the only sample available.**
Prostate Cancer M218	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**NGS Panel** (BRCA1, BRCA2, TMPRSS2, NTRK1, NTRK3, MSI) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for molecular based tests. Testing will be attempted if it is the only sample available.**
Thyroid Cancer M9	**FFPE sample** 5x5µm unstained sections incubated on uncoated Superfrost slides PLUS an H&E	**NGS Panel** (BRAF, NRAS, KRAS HRAS, TP53, NTRK1, NTRK3, RET*) Not UKAS accredited	14 days	• **Decalcified or bone samples are not suitable for molecular based tests. Testing will be attempted if it is the only sample available.** • ***** Please note that the main purpose of this test is the detection of BRAF V600 variants and that this assay does not cover the majority of sequence variants in the RET gene.

TESTING CRITERIA

HEREDITARY HAEMOCHROMATOSIS (HFE) TESTING CRITERIA

Referrals are accepted from consultant hepatologists, paediatricians, gastroenterologists, nephrologists, haematologists, specialist physicians and GPs providing the patient meets the following criteria:

- Diagnosis of haemochromatosis in a first degree relative i.e. Parent, partner, child or sibling
- Unexplained raised serum ferritin with normal FBC and Fasting TS >300µg/l and >50% male or >200µg/l and >40% female, respectively
- Age limit for testing amended to >16 years of age (no minors will be tested)
- Specialist physician indicates an exceptional case
- Referral from hospital
- Extended family testing is not recommended for compound heterozygotes C282Y/H63D

NORTHERN IRELAND FH GENOTYPING SCREENING CRITERIA FORM

PATIENT NAME:

H&C NUMBER:

Family History	**1st / 2nd Degree Relative:** • known with premature (<60yrs) CHD • known with premature (<45yrs) CHD • known with LDL-C >4.9 mmol/l (or total chol > 7.5 mmol/l) • <18 yrs with LDL-C >4.0 mmol/l (or total chol > 6.7 mmol/l) Please specify relation to index case:	1 2 1 2
Physical Examination	• Tendon xanthomata (in patient or 1st / 2nd degree relative) • Premature corneal arcus (<50yrs - no score for arcus senilis)	6 4
Clinical History	• Patient with premature CHD (<45yrs) • Patient with premature CHD (<50yrs) • Patient with premature CHD (<60yrs) • Patient with premature (<60yrs) strokes and/or peripheral vascular disease	4 3 2 1
Untreated LDL-Cholesterol Concentrations (mmol/l)*	• LDL-C ≥ 8.5 • LDL-C 6.5 – 8.4 • LDL-C 5.0 – 6.4 • LDL-C 4.0 – 4.9	8 5 3 1
Fasting TG (mmol/l)	• TG ≥ 3.0	Minus 2

PATIENT SCORE:

The highest score is circled from each section and the overall score is obtained by totalling all scores together. **If the score is 6 or greater, the patient should be offered genetic testing for FH.**
If the score is below 6 FH genetic testing may be offered at the discretion of the Lipid Clinic Consultant.

* *If no untreated level is available, information on adjustment of LDL-C for treatment can be found in Atherosclerosis 2015;240:190-196 (table reproduced below)*

Based on Wales FH scoring criteria (Atherosclerosis 2015;240:190-196)

Statin/dose (mg)	Correction factor
Ezetimibe	
10	1.2
Pravastatin	
10	1.2
20	1.3
40	1.5
Pravastatin + Ezetimibe	
10 + 10	1.5
20 + 10	1.6
40 + 10	1.7
Simvastatin	
10	1.4
20	1.6
40	1.7
80	1.9
Simvastatin + Ezetimibe	
10 + 10	1.9
20 + 10	2.0
40 + 10	2.3
80 + 10	2.4

Statin/dose (mg)	Correction factor
Atorvastatin	
10	1.6
20	1.8
40	2.0
80	2.2
Atorvastatin + Ezetimibe	
10 + 10	2.0
20 + 10	2.2
40 + 10	2.2
80 + 10	2.5
Rosuvastatin	
5	1.8
10	1.9
20	2.1
40	2.4
Rosuvastatin + Ezetimibe	
10 + 10	2.5
20 + 10	2.7
40 + 10	3.3

REQUEST FOR TKI DISCONTINUATION FORM

(available from the RMDS)

Revision Number	2.0	Document Number	LF 390 325
Author/Reviewer	J McGimpsey	Authoriser	A Hindley
Active Date	27/06/2024	Page Number	Page 1 of 1
Effective Date	N/A	Document Type	Laboratory Form
RMDS Somatic - Request for TKI Discontinuation			

This form **MUST** be completed once for each patient discontinuing TKI.

Completed forms should be attached to the laboratory request form and returned with monitoring samples to the Haem-Onc Molecular Laboratory, C Floor, Tower Block BCH or returned via e-mail to MolecularHaemLab@belfasttrust.hscni.net

If a completed form is not received, samples may not be processed.

Patient Identification

Complete or affix addressograph	
Name	
Hospital No. or H&C	
DOB	
Hospital	
Consultant	
Ward	

Does the patient meet the criteria for discontinuation of TKI? Yes / No

Print: .....

Sign: ..... Date.....

Criteria for Discontinuation[1]

- Patient has been on continuous treatment for at least 3 (preferably 5) years.
- Sustained BCR-ABL response of ≤0.01% throughout the last 24 months prior to discontinuation, verified by a minimum of four consecutive RT-qPCR results (at least 3 months apart).
- Decision to stop endorsed by MDT.

Reference:

Smith, G., Apperley, J., Milojkovic, D., Cross, N.C.P., Foroni, L., Byrne, J., Goringe, A., Rao, A., Khorashad, J., de Lavallade, H., Mead, A.J., Osborne, W., Plummer, C., Jones, G., Copland, M. and (2020), A British Society for Haematology Guideline on the diagnosis and management of chronic myeloid leukaemia. Br. J. Haematol., 191: 171-193. https://doi.org/10.1111/bjh.16971

Belfast Health and Social Care Trust
caring supporting improving together

Belfast Trust Laboratories
Regional Molecular Diagnostics Service

MYELOID NGS ACCEPTANCE CRITERIA

Regional Molecular Diagnostics Service

Belfast Health and Social Care Trust
caring supporting improving together

Regional Molecular Diagnostics Service (Somatic)

Myeloid Gene Panel- Testing **20/05/2025**

Dear Service User,

Genetics and genomics are playing an increasingly important role in the diagnosis and management of patients with haematological neoplasms[1,2]. Next-generation sequencing (NGS) panels aim to facilitate a standardised approach to testing and provide equity of access. The detection of genetic variants identified in the DNA from patients with myeloid malignancies contribute to the diagnosis, prognosis and treatment of patients.

A key component of this approach is the definition of eligibility criteria for specific tests to ensure appropriate usage from both clinical and financial perspectives. To facilitate this the following referral Criteria will be use to implement Myeloid Gene Panel testing:

Referral Criteria

The panel is designed for use in patients with a **CONFIRMED** diagnosis of:

- Acute myeloid leukaemia
- Myelodysplasia
- Chronic neutrophillic leukaemia
- Chronic myeloproliferative disease unclassifiable
- Chronic/ Juvenile myelomonocytic leukaemia
- MPN with myelofibrosis/primary myelofibrosis
- Triple-negative Essential thrombocythaemia.

This test is not suitable for referrals for mastocytosis and a separate request for C-KIT D816V is required.
This test is not suitable for minimal residual disease monitoring.

Referrals which do not meet this referral criteria will not be processed.

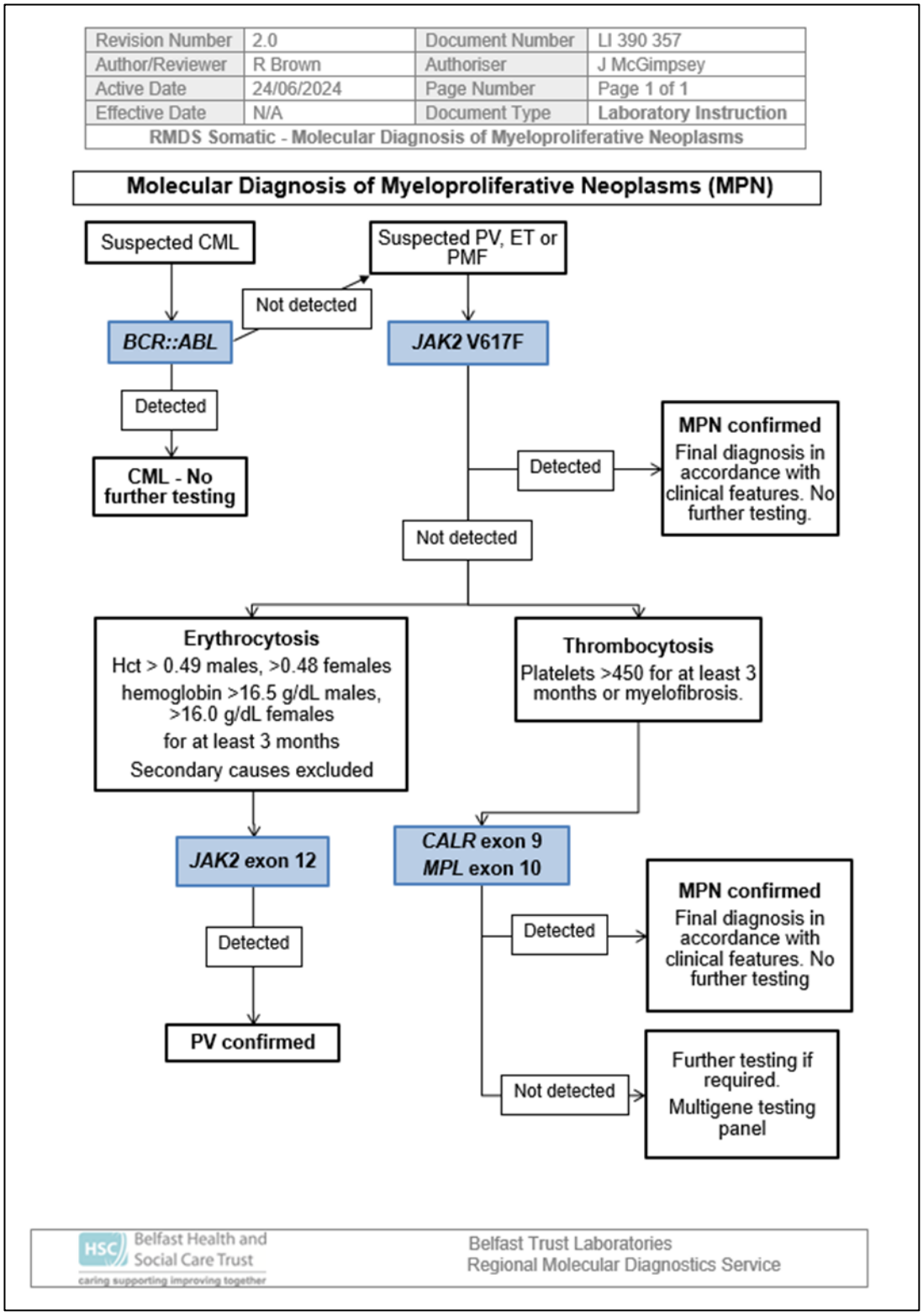
If you require further information please contact:

Amy Logan/Mark Catherwood
Regional Molecular Diagnostics Service (Somatic)
Amy.logan@belfasttrust.hscni.net /mark.catherwood@belfasttrust.hscni.net

1. Cross NCP *et al*. 2021. Br J Haematol. 2021 Nov;195(3):338-351.
2. Khoury JD *et al*. 2022 Leukemia. 2022 Jul;36(7):1703-1719.

Genetics: email: GeneticsLabs@belfasttrust.hscni.net (HSCNI secure e-mail) or nirgs.bhsct@nhs.net (NHS secure e-mail).
Molecular haematology : MolecularHaemLab@belfasttrust.hscni.net
NIMPL: NIMPL@belfasttrust.hscni.net

MOLECULAR DIAGNOSIS OF MYELOPROLIFERATIVE NEOPLASMS (MPN)



INFORMATION ON GENETIC TESTING AND CONSENT FORM FOR PATIENTS AND FAMILIES WITH DISORDERS OF BLOOD CLOTTING

Disorders of blood clotting can cause bleeding or thrombosis. These disorders may run in families and your healthcare professional will have explained how this affects your family. The purpose of this information sheet is to explain the reasons why you are being offered genetic testing and includes the consent form you will be asked to sign before these are performed.

Genetic tests may answer the following questions:

- If you are known to have a bleeding or thrombotic disorder, what is the genetic change that has caused the condition in your case?
- Are you a carrier of a bleeding or thrombotic disorder?

Introduction

Why do we resemble our parents? How does a single cell grow into a whole human? Genetics is the science that tries to answer these questions. Humans, like every other living creature, are made up of cells. We all start off as one cell at the time of fertilisation. This cell contains two sets of genes, one from our mother and one from our father. These genes are made of a chemical called DNA and each cell holds about two metres of it. For ease of storage and access, the genes in DNA are packaged up into 46 chromosomes. As the single cell divides the genes are copied so that every new cell possesses the full complement of genetic material (DNA).

Humans have approximately 20,000 genes stretched out along their DNA. Each gene acts as the recipe for the production of a protein and together they make up the recipe book or blue print for you and me. Different genes or recipes are read at different times in different cells in response to the requirements of our bodies.

Sometimes genes, like recipes or blueprints, may have spelling mistakes in them or have bits missing. When this happens, the proteins are either not produced or are abnormal. Genes with these mistakes or variants can cause genetic disorders. Since genes are passed on from one generation to the next, genetic disorders often run in families. These mistakes can arise when a cell does not accurately copy its DNA. A mistake or variation in a single DNA letter can lead to disease but some variants have no harmful effects.

Genetic testing can tell us which people in your family have the condition. In some conditions there are individuals who don't show the clinical effects themselves but might pass the disorder on to their own children. These are referred to as 'carriers'. Simple tests of the defective clotting protein can sometimes tell us if a person is affected by the disorder or is a carrier. In carriers these tests are often normal and genetic testing may be the only way of identifying them. With modern genetic testing it is usually possible to locate the

faulty genetic change in each family, although this can sometimes take time. Sometimes the same genetic change is seen in unrelated families with the same disorder and sometimes a unique genetic change is found in a particular family.

1. **What is the purpose of obtaining a blood sample?** It is very useful to know what the exact change is in the DNA that is causing the disorder in you/your child. Sometimes this helps us to understand better how the disorder may respond to treatment in the future. Measurement of the blood clotting factor level or platelet testing does not always clearly indicate if there is a genetic change present or not. Analysis of the DNA is a more accurate way of telling this. For this a blood sample is required from which the DNA can be extracted. A second sample may be taken from you on a separate occasion to confirm the result of the initial test.

2. **Where will the blood sample be tested?** The tests needed to detect a change ('spelling mistake' or bit missing) in DNA are specialised. Some of them are performed locally, but depending upon the nature of the disorder, it may be necessary to send your blood sample away to one of a small number of specialised laboratories. In all these laboratories there are strict regulations in place to ensure complete confidentiality of your details.

3. **How long will the test take?** The answers to genetic tests often take some time to obtain. The healthcare professional explaining the test to you will discuss the likely time course, as this varies with the disorder. It may take several months or years if you have one of the less common or more complicated disorders.

4. **How long will my blood sample be stored?** It is usual practice to store DNA samples indefinitely for several reasons. Sometimes it may not be possible with existing methods to find the genetic change in your family. In this case, the DNA will be stored until new tests are available. Other new tests relevant to the disorder may arise in the future and further analysis of your sample may then be required. Sometimes when testing family members is it useful to have the samples from other family members available for confirmation.

5. **What are the risks of genetic testing?** In addition to information on the inheritance of the disorder that we are testing for, the results from these genetic tests may sometimes inadvertently provide other information about family relationships, such as paternity. If it is found, for example, that an individual's parent is different from that assumed by the family, this may cause significant psychological problems and this may cause harm to the person being tested and other family members.

   The studies performed will often be specific for the disorder in your family. These types of tests will not exclude all forms of possible coagulation disorders.

Some genetic testing can be completed using a 'panel'. This is where multiple genes are tested at the same time and is helpful to investigate patients who have an unknown cause for their bleeding or thrombotic condition. If your blood is to be tested using the 'bleeding panel', for example, it is important to know that there are a small number of genes on the panel which are known to be associated with other disorders such as cancer. If a genetic change is found that is known to cause another disorder separate to the one for which the test was done, that is referred to as an 'incidental finding'. Only incidental findings that are considered important for your own health or that of a relative are reported back to your care team. Your healthcare professional will discuss the implications of the test with you prior to you agreeing to a blood sample. If you would prefer not to know about changes in these other genes, you should discuss with your healthcare professional whether there are alternative ways of doing the test.

The results of some genetic tests are inconclusive, which means that we might find a change in a gene but do not know whether it is the cause of a disease. These changes to genes are known as 'variants of uncertain significance' (VUS). As more data accumulate over time, a VUS may be found to be unimportant and non-disease causing or alternatively may be found to be the cause of a certain disease. If this occurs and your report changes, we will contact you.

6. **What else might be done with my blood sample?** We might want to use your sample to help develop or refine genetic tests for coagulation disorders. In such cases your blood samples would be used in a completely anonymous way so that the results could not be linked back to you.

7. **Who gets to know about the results?** The results will be told to you personally. Your family doctor will be told about the result.

8. **Why might it be useful for other members of my family to know about the results?** Information about the genetic disorder in you/your child is likely to be of benefit to other members of your family. It may, for example, be used to discover if a woman is a carrier and therefore if there is a risk of passing on the disorder to her children. With your permission we would like to be able to make the information about your genetic change available to doctors looking after other people in your family if they ask.

9. **Are my genetic results going to be stored anywhere other than in my hospital and GP case records?** There are local and national confidential databases within the NHS, which keep information about genetic disorders of coagulation. We would like use these to record the information about your gene change. <u>These databases are secure and protected and your personal information will not be sent outside the NHS.</u> In addition to this, anonymised details of genetic variants are stored in

international databases so that the results from many people can be evaluated in a co-ordinated manner. This is to improve our ability to interpret genetic variants in the future and to benefit other people who may have a similar disorder.

10. **Will having this genetic test affect my insurance premiums?** No. The Department of Health has agreed with the Association of British Insurers that results from genetic tests that provide information about possible future risk (predictive tests) should not be used to determine premiums except for tests for Huntington's Disease. You should answer all questions on the insurance application form honestly and accurately and include information about your diagnosed blood clotting disorder where asked for.

If you would like to have your blood tested please read and sign the consent form on the next page. If you require further information, or you are unclear about what you have been told, please ask for clarification or more help.

RECORD OF DISCUSSIONS regarding testing and storage of genetic material

I have discussed genetic/genomic testing with my healthcare professional and understand that:

Family and wider implications
The results of my test may have implications for me and members of my family. I understand that my results may also be used to help the healthcare of others nationally and internationally, through a process that will not personally identify me.

Uncertainty
The results of my test may reveal genetic variation whose significance is not yet known. To decide whether findings are significant for myself or others, my data may be compared in confidential databases to other patients' results across the country and internationally. I understand that this could change what my results mean for me and my treatment over time.

Unexpected information and Incidental findings
The results of my test may also reveal unexpected results that are not related to why I am having this test. These may be found by chance and I may need further tests to understand their significance.

DNA storage
Normal NHS laboratory practice is to store the DNA extracted from my sample after my current testing is complete. My DNA might be used for future analysis and/or to ensure that other testing, for example, that of my family members, or testing performed at other NHS laboratories is of high quality.

Data storage
The data from my test will be securely stored so that it can be looked at again in the future if necessary.

Health records
Results from my test and my test report will be part of my patient record.

Note of other specific issues discussed (*e.g. specific items not consented to*):

I agree to genetic/genomic investigations for the purpose of: (insert reason for test)

Signatures:

---	---	---
Patient/Guardian	**Healthcare professional's name**	**Healthcare professional's signature**

Date _____/_____/_____

Affix sticky label or fill in details
Patient name: _____
Hospital No. : _____
Date of birth _____/_____/_____

TEST GLOSSARY

ARMS – Amplification Refractory Mutation System
FISH - Fluorescence In Situ Hybridization
IHC - Immunohistochemistry
LAMP – Loop-mediated Isothermal Amplification
MLPA - Multiplex Ligation-dependent Probe Amplification
MS-MLPA - Methylation Specific – MLPA
NGS - Next Generation Sequencing
PCR – Polymerase Chain Reaction
QF-PCR – Quantitative Fluorescence - PCR
RT-qPCR – Real-Time Quantitative PCR
STR-PCR - Short Tandem Repeat - PCR
TP-PCR - Triplet Repeat Primed - PCR
WES – Whole Exome Sequencing