2022_03

SCOTTISH GENETICS LABORATORY CONSORTIUM

GENOMIC TEST DIRECTORY

FOR

RARE AND INHERITED DISEASE

NHS SCOTLAND

NHS National Services Scotland

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INTRODUCTION

NHS SCOTLAND LABORATORY GENETIC SERVICES

NHS Scotland genetics services are delivered through four regional genetics centres in Aberdeen, Dundee, Edinburgh and Glasgow. Each centre offers a closely integrated laboratory and clinical service. NHS National Services Scotland commission the four genetics laboratories in Scotland work as a formal consortium arrangement, to deliver equitable, high quality genetic testing service for Scotland. All laboratories are accredited by United Kingdom Accreditation Service (UKAS) in accordance with the recognized ISO 15189:2012 standard.

Molecular genetics testing was nationally designated in 1985 and cytogenetics in 2009. Molecular pathology testing services was nationally commissioned as a single designated multi-site national specialist service from 1 April 2013.

Genetics and molecular pathology services are evolving with the workload increasing each year, as new advances increase the range of conditions which can be tested for. In molecular genetics there are a small number of 'core' tests performed in all four centres, with the majority of tests being performed in one laboratory for all of Scotland. The service undertakes testing for over 200 conditions.

PURPOSE OF DOCUMENT

The Scottish Genetics Laboratory Consortium Genomic Test Directory for Rare and Inherited Disease contains a list of all services currently available in Scotland.

This document will be reviewed annually.

NHS SCOTLAND GENETIC LABORATORY CONTACT DETAILS

- **Aberdeen (NHS Grampian)**
  Address: Genetics and Molecular Pathology Laboratory Services, Polwarth Building, Foresterhill, Aberdeen AB25 2ZD
  Email address: gram.molgen@nhs.scot
  Website: https://www.nhsgrampian.org/service-hub/north-of-scotland-medical-genetics

- **Dundee (NHS Tayside)**
  Address: East of Scotland Regional Genetics Service, Level 6, Ninewells Hospital, Dundee DD1 9SY
  Email address: Tay.esrg@nhs.scot
  Website: https://www.nhstayside.scot.nhs.uk/OurServicesA-Z/Genetics/PROD_295540/index.htm

- **Edinburgh (NHS Lothian)**
  Address: South East Scotland Genetic Service, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU
  Email address: edinburgh.dna@nhslothian.scot.nhs.uk / wgh.cytogenetics@nhslothian.scot.nhs.uk
  Phone : 0131 537 1116 / 0131 537 1940
  Website:https://services.nhslothian.scot/clinicalgeneticsservice/GeneticLaboratoryServices/Pages/default.aspx

- **Glasgow (NHS Greater Glasgow & Clyde)**
  Address: West of Scotland Centre for Genomic Medicine, Laboratory Genetics, Level 2B Laboratory Medicine & FM Building, Queen Elizabeth University Hospital, Glasgow G51 4TF
  Email address: Genetic.Laboratories@ggc.scot.nhs.uk
  Website: https://www.nhsggc.org.uk/about-us/professional-support-sites/laboratory-medicine/laboratory-disciplines/laboratory-genetics/#

TEST REQUESTING

Testing will be delivered either locally or nationally according to the test directory. However, samples should be taken and sent to your **LOCAL** genetics laboratory with the appropriate completed genetics referral form (or proforma if required). For local sample acceptance policies and referral forms, please see the local laboratory website.

Services are provided for the clinical indications listed when referred from the appropriate specialties.

SAMPLE REQUIREMENTS

For most rare and inherited disease genomic tests with the exception of karyotyping, an EDTA blood sample is required. For karyotyping tests, a lithium heparin blood sample is required.

Other sample types may be required for some services including:

- Urine samples may be required for some mitochondrial tests.
- Appropriate fresh tissue samples from post mortems for various tests.

For specific sample requirements, please see the local laboratory website.

TESTING METHODOLOGY

Different methods are utilised depending on the scope of testing. These methods include techniques to detect a single variant up to genome wide screens. The different methods include:

- PCR
- Sanger sequencing
- Next Generation Sequencing (NGS) panels – vary in size from a small to large number of genes
- Fragment analysis
- Multiplex Ligation Probe Amplification (MLPA)
- Karyotype
- Microarray
- Chromosome breakage

SCOPE AND RANGE OF TEST

The scope and range of testing refers to the extent of testing and the types of variant that will be detected.

The scope of testing includes:

- Targeted testing – testing of specific region(s)
- Whole gene screen – sequence of coding region of relevant gene(s)
- Whole gene screen and copy number – sequence of coding region and assessment of exon level copy number
- Genome wide – detection of large scale rearrangements

The types of variants detected includes:

- Small sequence variants
    - Single nucleotide variants (SNVs)
    - Insertions / deletions (indels)
- Copy number variants (CNVs)
    - Exon level
    - genome wide level
- Repeat expansions
- Aneuploidy
- Genome wide rearrangements

The targets tested refer to the genes / regions tested for the particular clinical indication.

Testing is provided for the affected individual only in most cases. If parental samples are required for Trio analysis, this will be stated in the test information.

REPORTING TIMES

Reporting times are listed based on calendar days. These range from 3 to 112 days depending on urgency and complexity of testing. Where more urgent testing is required than what is stated for treatment decisions, please contact the laboratory providing testing to discuss.

CLINICAL CONSENT AND COUNSELLING IMPLICATIONS

It is the referring clinician's responsibility to ensure that testing and /or storage of genetic material is discussed with the patient and that a summary of clinical consent is included in the patient's health record. Further information regarding consent can be found at https://www.bsgm.org.uk/healthcare-professionals/confidentiality-and-genetic-information. The patient should discuss and understand the following:

- **Family implications**

  The results of my test may have implications for other members of my family. I acknowledge that my results may sometimes be used to inform the appropriate healthcare of others. This could be done in discussion with me, or in such a way that I am not personally identified in this process.

- **Uncertainty**

  The results of my test may reveal genetic variation whose significance is not yet known. Deciding whether such variation is significant may require sharing of information about me including (inter)national comparisons with variation in others. I acknowledge that interpretation of my results may change over time as such evidence is gathered.

- **Unexpected information**

  The results of some tests may reveal a chance of a disease in the future, and nothing to do with why I am having this test. This may be found by chance, while focusing on the reason for my test, and I may then need further tests to understand what this means for me. If these additional findings are to be looked for, I will be given more information about this.

- **DNA storage**

  Normal laboratory practice is to store the DNA extracted from my sample even after the current testing is complete. My sample might be used as a 'quality control' for other testing, for example, that of family members.

- **Data storage**

  Data from my test will be stored to allow for possible future interpretations.

- **Health records**

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

CARDIOLOGY

ANDERSEN-TAWIL SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*KCNJ2, KCNJ5*	56
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Ventricular arrhythmia and /or prolonged QTc
- Periodic paralysis
- Distinctive facial and skeletal features

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Neurology
- Paediatric Neurology

ARRHYTHMIA PANEL

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*KCNQ1, KCNH2, KCNE1, KCNE2, KCNJ2, SCN5A, RYR2, DSC2, DSG2, DSP, PKP2, ABCC9, AKAP9, ANK2, CACNA1C, CACNA2D1, CACNB2, CALM1, CALM2, CASQ2, CAV3, DES, DPP6, GJA1, GJA5, GPD1L, HCN4, JUP, KCNA5, KCND3, KCNE5, KCNE3, KCNJ5, KCNJ8, LMNA, NOS1AP, NPPA, PLN, RANGRF, SCN10A, SCN1B, SCN2B, SCN3B, SCN4B, SLMAP, SNTA1, TGFB3, TMEM43, TRDN, TRPM4*	*112*
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Out of Hospital Cardiac Arrest with no known cause
- Sudden cardiac death with negative post mortem

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology in discussion with Clinical Genetics

ARRHYTHMOGENIC CARDIOMYOPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*PKP2, DSG2, DSC2, DSP, SCN5A, ABCC9, DES, HCN4, JUP, LMNA, PLN, RYR2, TGFB3, TMEM43*	112
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- A possible, borderline or definite diagnosis according to 2010 modified Task Force criteria
- Fibrosis & fatty replacement of myocardium affecting one or both ventricles seen on Echocardiogram or Post mortem investigations
- Clinical phenotype considered to be compatible with ACM (e.g. dilated cardiomyopathy, arrhythmia, heart failure)

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology

ATRIAL FIBRILLATION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*SCN5A, ABCC9, GJA1, GJA5, HCN4, KCNA5, KCNE5, NPPA, SCN2B, SCN4B*	56
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Atrial fibrillation detected at young age with family history of atrial fibrillation or sudden cardiac death

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics

BARTH SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*TAZ*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Cardiomyopathy
- Neutropenia
- Fatigue & general muscle weakness
- Growth / feeding issues

REQUESTING SPECIALTIES

- Cardiology
- Clinical Genetics
- Paediatrics

BRUGADA SYNDROME AND SODIUM CHANNEL DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*SCN5A, CACNA1C, CACNA2D1, CACNB2, GPD1L, HCN4, KCND3, KCNE3, KCNE5, KCNJ8, RANGRF, SCN1B, SCN2B, SCN3B, SCN10A, SLMAP, TRPM4*	112
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Cardiac arrest in the absence of secondary causes, most commonly at night
- Arrhythmia triggered by fever
- Type 1 Brugada ECG
- Atrial arrhythmia, sinus node dysfunction, or conduction disease, with or without QT prolongation predominantly in children and young people.

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics

CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA (CPVT)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*RYR2, CALM1, CALM2, CASQ2, DPP6, TRDN*	56
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Ventricular fibrillation or polymorphic VT.
- Bi-directional VT on exercise.
- Resuscitated from cardiac arrest, or syncope compatible with tachyarrhythmia especially related to physical activity, or acute emotion, in the presence of an unremarkable ECG (e.g. normal QT interval), and in the absence of structural heart or coronary artery disease.
- Family history of premature sudden cardiac death particularly due to physical activity or emotion.

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology in discussion with Clinical Genetics

DILATED CARDIOMYOPATHY (DCM)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ACTC1, ACTN2, BAG3, CSRP3, DES, DMD, DSP, FLNC, LAMP2, LMNA, MYBPC3, MYH7, MYL2, MYL3, NKX2-5, PLN, RBM20, SCN5A, TNNC1, TNNI3, TNNI3K, TNNT2 , TPM1, TTN (N2-B* isoform*), VCL*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Left ventricular failure with echocardiographic/MRI evidence of dilated cardiomyopathy (REQUIRED)
- Patients with left ventricular dilatation due to coronary artery disease or haemochromatosis do not require genetic testing with this panel.
- If other potential precipitants are present - hypertension, hypo / hyperthyroidism, myocarditis, peripartum, alcohol abuse, exposure to cardiotoxic drugs, then expert advice should be sought prior to genetic testing.
- Family history of skeletal myopathy, cardiomyopathy or related sudden death – please provide details (including the diagnosis) of the affected relatives.
- Pathologically confirmed non-ischaemic dilated cardiomyopathy at post mortem.

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology in discussion with Clinical Genetics

HEART BLOCK

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*SCN5A, HCN4, LMNA, TRPM4*	56
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Heart block (see also Brugada and sodium channel disease)
- Syncope associated with heart block

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics

HYPERTROPHIC CARDIOMYOPATHY (HCM)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ACTC1, ACTN2, CSRP3, FHL1, FLNC, GLA, JPH2, LAMP2, MYBPC3, MYH7, MYL2, MYL3, PLN, PRKAG2, TNNC1, TNNI3, TNNT2, TPM1, TTR*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- ECG or echocardiographic/MRI evidence of hypertrophic cardiomyopathy (REQUIRED)
- No evidence of hypertensive or valvular heart disease sufficient to cause cardiac hypertrophy
- Family history of skeletal myopathy, cardiomyopathy or related sudden death – please provide medical details of the affected relatives.
- Pathologically confirmed HCM at post mortem with no history of hypertension or evidence of valvular heart disease sufficient to cause cardiac hypertrophy.

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology in discussion with Clinical Genetics

LONG QT SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV*	*KCNQ1*, KCNH2*, KCNE1*, KCNE2*, SCN5A, KCNJ2, ANK2, AKAP9, CACNA1C, CALM1, CALM2, CAV3, KCNJ5, NOS1AP, SCN4B, SNTA1, TRPM4*	112
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Abnormal ECG (QTc ≥440ms in males, ≥460ms in females)
- Syncope or apparent seizures compatible with ventricular tachyarrhythmia, especially relating to stress or high emotion, physical activity including swimming, sudden loud noise or at rest or in bed.
- Exclude other causes of QT prolongation (e.g. QT prolonging drugs, electrolyte or calcium disturbance, hypothyroidism, ischaemia, dilated cardiomyopathy)
- Family history of unexplained premature sudden cardiac death, syncope or seizures among immediate family members.

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology in discussion with Clinical Genetics

MARFAN SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*FBN1, TGFBR1, TGFRB2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features of Marfan syndrome giving a Ghent systemic score of ≥ 7 in an adult over 18 years
- In children, clinical features of Marfan syndrome giving a lower Ghent score following assessment in a clinical service with expertise in the diagnosis of Marfan syndrome.
- Clinical features suggestive of Loeys-Dietz syndrome
- Ectopia lentis if other causes such as homocystinuria (due to cystathionine beta-synthase deficiency) have been excluded.
- Aortic sinus dilatation, defined as z score >3 for body surface area in children, and > 2 for body surface area in adults. See also Thoracic Aortic Aneurysm and Dissection.
- Thoracic aortic aneurysm or dissection. See also Thoracic Aortic Aneurysm and Dissection.

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics

PAEDIATRIC CARDIOMYOPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*AARS2, ABCC9, ACAD9, ACADVL, ACTA1, ACTC1, ACTN2, AGK, AGL, ALMS1, ALPK3, ARSB, ATP5D, ATPAF2, BAG3, BRAF, CACNA1C, CBL, CDH2, COA5, COA6, COX10, COX14, COX15, COX20, COX6B1, CPT2, CSRP3, DES, DMD, DNAJC19, DOLK, DSC2, DSG2, DSP, EMD, EPG5, FAH, FHL1, FHOD3, FKTN, FLNC, GAA, GLB1, GUSB, HADHA, HADHB, HCN4, HRAS, IDH2, IDS, IDUA, JPH2, JUP, KRAS, LAMP2, LMNA, LRPPRC, LZTR1, MAP2K1, MAP2K2, MIB1, MLYCD, MRPL44, MUT, MYBPC3, MYH6, MYH7, MYL2, MYL3, MYPN, NDUFA1, NDUFA10, NDUFA11, NDUFA2, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4, NDUFAF5, NDUFB11, NDUFB3, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS6, NDUFS7, NDUFS8, NDUFV1, NDUFV2, NEXN, NF1, NKX2-5, NONO, NRAS, NUBPL, PCCA, PCCB, PDLIM3, PKP2, PLN, PNPLA2, PPA2, PPCS, PPP1CB, PPP1R13L, PRKAG2, PTPN11, RAF1, RBM20, RIT1, RYR2, SCN5A, SCO1, SCO2, SDHA, SDHAF1, SDHD, SGCD, SHOC2, SLC22A5, SLC25A20, SLC25A4, SOS1, SOS2, SURF1, TAZ, TBX5, TMEM126B, TMEM43, TMEM70, TNNC1, TNNI3, TNNI3K, TNNT2, TPM1, TSFM, TTN, TTR, VCL*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Child (under 16) with cardiomyopathy where no other non-genetic cause has been found, and there is no family history of Adult Onset Cardiomyopathy.
- If there is a family history of "non-syndromic" adult onset cardiomyopathy (dilated, hypertrophic) then the relevant adult cardiomyopathy panel should be considered instead.
- If there are features of a specific "non-syndromic" cardiomyopathy such as Arrhythmogenic Cardiomyopathy, then the Arrhythmogenic Cardiomyopathy panel should be considered instead.
- If the cardiomyopathy is one of multiple features of a likely multisystem disorder suggestive of Noonan syndrome or a Rasopathy, then the Noonan/Rasopathy panel should be considered instead.
- If the cardiomyopathy is one of multiple features of a likely multisystem disorder not suggestive of Noonan syndrome or a Rasopathy, please seek expert advice as a broader spectrum test may be appropriate. To be finalised with NICCs.

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology in discussion with Clinical Genetics

SHORT QT SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*KCNQ1, KCNH2, KCNJ2*	56
Family member testing		as indicated above			14
Proforma required?		YES	Cardiac Arrhythmia Proforma (see centre website)		

REFERRAL CRITERIA

- Abnormal ECG (QTc ≤360ms in males, ≤370ms in females)
- Syncope compatible with tachyarrhythmia or cardiac arrest.
- A family history of SCD at age < 40 years

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics

THORACIC AORTIC ANEURYSM & DISSECTION (TAAD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ACTA2, BGN, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, EFEMP2, ELN, FBN1, FBN2, FLCN, FLNA, LOX, MED12, MYH11, MYLK, NOTCH1, PLOD1, PRKG1, SKI, SLC2A10, SMAD2, SMAD3, SMAD4, SMAD6, TGFB2, TGFB3, TGFBR1 , TGFBR2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Thoracic aortic aneurysm* or dissection with onset before age 60 and no classical cardiovascular risk factors
- Aneurysm or dissection of any part of the aorta during pregnancy
- Clinical features of Marfan syndrome giving a Ghent systemic score of ≥ 7 in an adult over 18 years
- Aortic sinus dilatation, defined as z score >3 for body surface area in children, and > 2 for body surface area in adults.
- Clinical features suggestive of Loeys-Dietz syndrome
- High clinical suspicion of a condition predisposing to aortic/arterial disease AND diagnostic testing for other conditions such as Ehlers Danlos syndrome (where indicated) has not identified a cause
- Any deceased individual with a thoracic aortic aneurysm* or dissection detected at autopsy meeting one of the above criteria and who have relatives who will benefit from cascade testing using a genetic diagnosis

*Thoracic aortic aneurysm defined as:
• In children: z score >2 for body surface area
• In adults: z score > 2 for body surface area or dilatation >38 mm

REQUESTING SPECIALTIES

- Cardiologist with expertise in ICC
- Clinical Genetics
- Pathology in discussion with Clinical Genetics
- Cardiothoracic surgery in discussion with clinical genetics

CHROMOSOME BREAKAGE

ATAXIA TELANGIECTASIA (& AT-LIKE)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Whole genome screen	Chromosomes 7 & 14	Chromosomes 7 & 14	28
Aberdeen	NGS	Whole gene screen	SNVs, indels	*ATM, MRE11*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of ataxia telangiectasia – elevated serum AFP levels and ≥1 of the following criteria:
    - Progressive gait and truncal ataxia with onset between 1-4 years old, Ocular motor apraxia, Ocular telangiectasia, Chorea and dysarthia, Frequent infections (Immunodeficiency), Malignancy

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Oncology in discussion with Clinical Genetics

ATAXIA WITH OCULOMOTOR APRAXIA & HYPOALBUMINEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*APTX*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of ataxia with oculomotor apraxia & hypoalbuminemia

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

BLOOM SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Chromosome breakage analysis*	Whole genome screen	Aneuploidy	Genome wide	28
Aberdeen	NGS	Whole gene screen	SNVs, indels	*BLM*	56
Family member testing		as indicated above			14
Proforma required?		NO			

*5ml lithium heparin blood sample required. Send guaranteed next day delivery directly to Aberdeen laboratory, preferably on Monday-Wednesday. If possible, please also send an anonymised control blood (5ml lithium heparin) with completed control form (available on centre website).

REFERRAL CRITERIA

- Clinical phenotype suggestive of Bloom syndrome – growth deficiency, sun-sensitive, telangiectatic, hypo- and hyperpigmented skin
- Confirmed diagnosis from chromosome breakage analysis

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

CEREBRO-OCULO-FACIO-SKELETAL SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*ERCC1, ERCC2, ERCC6*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Cerebro oculo facio skeletal syndrome – microcephaly, congenital cataracts, severe mental retardation, facial dysmorphism, arthrogryposis

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

COCKAYNE SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*ERCC6, ERCC8*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical diagnosis of Cockayne syndrome – mental retardation, microcephaly, progressive neurologic & retinal degeneration, skeletal abnormalities, gait defects, sun sensitivity

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

DUANE-RADIAL RAY & IVIC SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*SALL4*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Duane-radial ray & IVIC syndrome – upper limb anomalies, ocular anomalies, renal anomalies

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

FANCONI ANAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Chromosome breakage analysis*	Whole genome screen	Chromosome breakage	Whole genome	28
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV (limited genes*)	*BRCA2, BRIP1, ERCC4, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, PALB2, RAD51C, SLX4*	56
Family member testing		as indicated above			14
Proforma required?		NO			

*5ml lithium heparin blood sample required. Send guaranteed next day delivery directly to Aberdeen laboratory, preferably on Monday-Wednesday. If possible, please also send an anonymised control blood (5ml lithium heparin) with completed control form (available on centre website).

REFERRAL CRITERIA

- Clinical phenotype suggestive of Fanconi anaemia – persistent or recurrent pancytopenia, short stature, abnormal skin pigmentation, skeletal malformations of the upper and lower limbs, microcephaly, and ophthalmic and genitourinary tract anomalies.
- Confirmed diagnosis from chromosome breakage analysis

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

GROWTH FAILURE IN EARLY CHILDHOOD

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNVs	*ACAN, ANKRD11, BLM, BRAF, BRCA2, BRIP1, CBL, CCDC8, CDKN1C, CUL7, ERCC4, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FGFR3, HMGA2, HRAS, IGF1, IGF1R, IGF2, KRAS, LZTR1, MAP2K1, MAP2K2, NBN, NRAS, OBSL1, PALB2, PIK3R1, PLAG1, PPP1CB, PTPN11, RAF1, RIT1, SHOC2, SLX4, SOS1, SOS2, SRCAP, TOP3A, TRIM37, UBE2T*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Height/length more than 3 standard deviations below the mean at the age of at least 2 years.

REQUESTING SPECIALTIES

- Clinical Genetics

HOLT-ORAM SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*TBX5*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Holt-Oram Syndrome – Congenital heart defect/cardiac conduction disease and upper limb malformation

REQUESTING SPECIALTIES

- Clinical Genetics

IMMUNODEFICIENCY-CENTROMERIC INSTABILITY-FACIAL ANOMALIES SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Whole genome screen	Chromosomes 1, 9 & 16	Chromosomes 1, 9 & 16	28
Aberdeen	NGS	Whole gene screen	SNVs, indels	*DNMT3B*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Immunodeficiency-Centromeric Instability-Facial Anomalies Syndrome

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

LIG4 SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*LIG4*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of LIG4 syndrome – immunodeficiency, developmental delay, growth delay

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

MEIER-GORLIN SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*ORC1, ORC4, ORC6, CDT1, CDC6*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Meier-Gorlin syndrome – severe intrauterine & postnatal growth retardation, microcephaly, bilateral microtia, aplasia or hypoplasia of patellae

REQUESTING SPECIALTIES

- Clinical Genetics

NATURAL KILLER CELL AND GLUCOCORTICOID DEFICIENCY WITH DNA REPAIR DEFECT

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*MCM4*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of a Natural killer Cell & Glucocorticoid deficiency with DNA repair defect – growth retardation, microcephaly, decreased numbers of natural killer cells, recurrent infection, respiratory failure

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

NIJMEGEN BREAKAGE SYNDROME (& NBS-LIKE)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Whole genome screen	Chromosomes 7 & 14 studies	Chromosomes 7 & 14	28
Aberdeen	NGS	Whole gene screen	SNVs, indels	*NBN, RAD50*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Nijmegen Breakage Syndrome – microcephaly, growth retardation, immunodeficiency
- Confirmed diagnosis from chromosome breakage analysis

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

ROBERTS-SC PHOCOMELIA SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Karyotype	Whole genome screen	Aneuploidy	Genome wide	28
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*ESCO2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Roberts / SC phocomelia syndrome – growth retardation, extremity malformations, craniofacial anomalies, developmental delay, cardiac anomalies, renal anomalies

REQUESTING SPECIALTIES

- Clinical Genetics

ROTHMUND-THOMSON / RAPADILINO / BALLER-GEROLD

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*RECQL4*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Rothmund Thomson / Rapadilino / Baller-Gerold

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

SECKEL SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*ATR, RBBP8, CEP152, CENPJ*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Seckel Syndrome – growth retardation, microcephaly with mental retardation, characteristic facial appearance

REQUESTING SPECIALTIES

- Clinical Genetics

TAR SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*RBM8A*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Thrombocytopenia-absent radius syndrome

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

TOWNES-BROCKS SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*SALL1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Townes-Brocks Syndrome – triad of imperforate anus, dysplastic ears & thumb malformations

REQUESTING SPECIALTIES

- Clinical Genetics

TRICOTHIODYSTROPHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*ERCC2, ERCC3, MPLKIP, GTF2H5*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical diagnosis of Tricothiodystrophy – brittle, sulfur-deficient hair which displays a diagnostic alternating light and dark banding pattern

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

ULNAR-MAMMARY SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*TBX3*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Ulnar-Mammary Syndrome – posterior limb deficiencies or duplications, mammary gland hypoplasia and / or dysfunction, abnormal dentition, delayed puberty in males, genital anomalies

REQUESTING SPECIALTIES

- Clinical Genetics

WARSAW BREAKAGE SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*DDX11*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Warsaw Breakage Syndrome

REQUESTING SPECIALTIES

- Clinical Genetics

WERNER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*WRN*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Werner syndrome – accelerated aging, bilateral cataracts, diabetes mellitus, osteoporosis, premature arteriosclerosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

XERODERMA PIGMENTOSUM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*XPA, XPC, ERCC1, ERCC3, ERCC4, ERCC5, DDB2, POLH*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical diagnosis of Xeroderma Pigmentosum – XP-related features in eye, neurological systems or related cancer

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

CONNECTIVE TISSUE DISORDERS

CONNECTIVE TISSUE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ABCC6, ACTA2, ACVR1, ADAMTS2, ALPL, ATP6V0A2, B3GALT6, B4GALT7, BMP1, CBS, CHST14, COL11A1, COL1A1, COL1A2, COL2A1, COL3A1, COL5A1, COL5A2, CRTAP, ELN, FBLN5, FBN1, FBN2, FKBP10, FKBP14, IFITM5, LEPRE1 (P_3H_1), LRP5, MYLK, NOTCH1, NOTCH2, PKD2, PLOD1, PLOD2, PPIB, PRDM5, RIN2, SERPINF1, SERPINH1, SLC2A10, SLC39A13, SMAD3, SP7, TGFB2, TGFBR1, TGFBR2, TNXB, ZNF469*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- See criteria for Ehlers-Danlos Syndrome, Stickler Syndrome / Cleft Palate
- Please contact the laboratory to discuss indications not included by above criteria

REQUESTING SPECIALTIES

- Clinical Genetics

EHLERS DANLOS SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ADAMTS2, B3GALT6, B4GALT7, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, CHST14, PLOD1, FKBP14, RIN2, PRDM5, ZNF469, SLC39A13, TNXB, C1R, C1S*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Referral criteria as per Malfait et al (2017) Am J Med Genetics 175C:8-26
- Includes following subtypes:
    - Classic 1 and 2, classic-like 1, arthrochalasia 1 and 2, cardiac valvular, dermatosparaxis, kyphoscoliotic 1 and 2, musculocontractural 1, periodontal 1 and 2, spondylodysplastic 1, 2 and 3 and vascular
    - Combined osteogenesis imperfecta and Ehlers-Danlos syndrome 2, Macrocephaly, alopecia, cutis laxa, and scoliosis
    - Brittle cornea syndrome 1 and 2
- Samples for Hypermobile EDS will not be accepted as the genetic basis is unknown

REQUESTING SPECIALTIES

- Clinical Genetics

STICKLER SYNDROME / CLEFT PALATE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ANKRD11, COL11A1, COL11A2, COL2A1, COL9A1, COL9A2, COL9A3, FLNA, FLNB, FOXE1, FOXC2, IRF6, IRF7, PLOD3, SATB2, SLC26A2, SOX9, TP63, TBX1, TBX22*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Two or more of the following:
  - Retinal detachment or: High myopia with onset before 6 years
  - Cleft palate
  - Vitreous abnormality
  - Joint hypermobility or premature joint degeneration
  - Sensorineural hearing loss
  - Facial features (flat midface with depressed nasal bridge, reduced nasal protrusion, anteverted nares and micrognathia)

REQUESTING SPECIALTIES

- Clinical Genetics

DEVELOPMENTAL DISORDERS

ANEUPLOIDY SCREENING – NON-INVASIVE PRENATAL TESTING (NIPT)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Targeted screen	Aneuploidy	Chromosomes 13, 18, 21	7
Proforma required?	YES	NIPT request form			

REFERRAL CRITERIA

- Higher chance biochemical screen result (>1:150) OR
- Previous trisomy 13, 18 or 21
- Pregnancy must be >10 weeks gestation confirmed by ultrasound scan

EXCLUSION CRITERIA

NIPT is not an appropriate test if any of the following are not excluded:

- Fetal demise / vanishing twin
- Blood transfusion within 4 months
- Transplant surgery within 1 year
- Immuno / stem cell therapy within 1 year
- Maternal malignancy within 1 year
- Known maternal chromosome anomaly

REQUESTING SPECIALTIES

- Obstetrics
- Clinical Genetics

ANEUPLOIDY TESTING – PRENATAL (AF / CVS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	QF-PCR	Targeted screen	STRs	Chromosome markers 13, 18, 21, X/Y	3
Proforma required?		NO			

REFERRAL CRITERIA

- Higher chance biochemical screen result (>1:150) OR
- High chance Non-Invasive Prenatal Test (NIPT) result OR
- Abnormalities detected on ultrasound scan OR
- Previous trisomy detected OR
- Family history of known single gene disorder (referral through Clinical Genetics only)
- Family history of known chromosomal rearrangement (referral through Clinical Genetics only)

REQUESTING SPECIALTIES

- Obstetrics
- Clinical Genetics

ANEUPLOIDY TESTING – PRENATAL (AF / CVS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Microarray	Whole genome screen	CNV	Whole genome	14
Proforma required?		NO			

REFERRAL CRITERIA

- One or more abnormalities detected on ultrasound scan e.g. structural heart malformations, possible tracheoesphageal fistula, possible duodenal atresia, cleft lip, structural renal malformations, bladder extrophy, absent radius - unilateral or bilateral, pleural effusion OR
- An isolated nuchal translucency NT ≥ 3.5 mm when crown-rump length measures from 45 mm to 84 mm (at approximately 11 weeks 0 days to 13 weeks 6 days).

REQUESTING SPECIALTIES

- Obstetrics
- Clinical Genetics

ANEUPLOIDY / MICRODUPLICATION / MICRODELETION NEONATAL SCREENING (URGENT)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	QF- PCR	Targeted screen	STRs	Chromosomes 13, 18, 21, X/Y	5
	Microarray	Whole genome screen	CNV	Whole genome	14
Proforma required?		NO			

REFERRAL CRITERIA

- Features suggestive of Trisomy 13, 18 or 21
- Congenital malformation/abnormalities
- Ambiguous genitalia
- Dysmorphic features
- Failure to thrive

REQUESTING SPECIALTIES

- Neonatologists
- Clinical Genetics

ANEUPLOIDY / MICRODUPLICATION / MICRODELETION POSTNATAL SCREENING (ROUTINE)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	QF- PCR	Targeted screen	STRs	Chromosomes 13, 18, 21, X/Y	28
	Microarray	Whole genome screen	CNV	Whole genome	
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical suspicion of mosaic Trisomy 13, 18 or 21
- Features of sex chromosome abnormality

REQUESTING SPECIALTIES

- Clinical Genetics
- Obstetrics

ANGELMAN SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	MLPA	Targeted screen	CNV Methylation abnormalities	15q11-13 markers	28
Glasgow	Sanger	Whole gene screen	SNVs, indels	*UBE3A*	56
Glasgow	PCR	Targeted screen	STRs	Microsatellite markers	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Severe developmental delay and intellectual disability
  - Seizures
  - Microcephaly
  - Severe speech impairment
  - Gait ataxia and/or tremulousness of the limbs

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

BECKWITH WIEDEMANN SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	MLPA	Targeted screen	CNV Methylation abnormalities	11p15 markers	28
Glasgow	PCR	Targeted screen	STRs	Microsatellite markers	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Macrosomia
  - Hemihyperplasia and/or macroglossia
  - Omphalocele (exomphalos) or umbilical hernia
  - Embryonal tumour (e.g. Wilms tumor, hepatoblastoma, neuroblastoma, rhabdomyosarcoma) in childhood

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

CHARGE SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger	Whole gene screen MLPA	SNVs, indels Exon level CNV	*CHD7*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Coloboma
  - Choanal atresia or stenosis
  - Cleft palate with or without cleft lip
  - Cranial nerve dysfunction or anomaly
  - Characteristic ear malformations
  - Tracheoesophageal fistula or oesophageal atresia
  - Cardiovascular malformation
  - Genital hypoplasia

REQUESTING SPECIALTIES

- Clinical Genetics

CONGENITAL ABNORMALITIES, MULTIPLE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Microarray	Whole genome screen	Structural variants CNV	Whole genome	14
	Karyotype				
Proforma required?		NO			

REFERRAL CRITERIA

- Multiple abnormalities present at birth

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

CORNELIA DE LANGE, ATYPICAL

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*NIPBL, SMC1A, SMC3, HDAC8, RAD21, ANKRD11, KMT2A, AFF4, NAA10*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Normal Karyotype or array CGH
- Characteristic facial appearance (including long eyelashes, upturned nose, long philtrum)
- Post-natal growth delay
- Developmental delay

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

DEVELOPMENTAL DELAY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Microarray	Whole gene screen	CNV	Whole genome	28
Proforma required?		NO			

REFERRAL CRITERIA

- Significant delay in one or more of the following developmental areas
  - Gross motor
  - Vision and fine motor
  - Hearing, speech and language
  - Social, emotional and behavioural

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

DEVELOPMENTAL DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	DDG2P	112
Family member testing		as indicated above			14
Proforma required?		NO	DECIPHER entry required		

REFERRAL CRITERIA

- Unexplained intellectual disability or global developmental delay where clinical features are suggestive of an underlying monogenic disorder requiring sequencing and targeted genetic testing is not possible
- Microarray analysis has previously been performed on a sample from the proband
- Samples from a proband plus both parents (trio) are required

REQUESTING SPECIALTIES

- Clinical Genetics

Di GEORGE (22q11 DELETION) SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Microarray / MLPA	Targeted screen	CNV	Di George Critical Region	28 Urgent 5 Prenatal 14
Proforma required?		NO			

REFERRAL CRITERIA

- Heart abnormalities detected on ultrasound scan OR
- Congenital heart defect consistent with Di George syndrome (e.g. ventricular septal defect, tetralogy of Fallot, interrupted aortic arch and truncus arteriosus).
- Palatal anomalies (e.g. velopharyngeal incompetence, submucous cleft palate or bifid uvula).

REQUESTING SPECIALTIES

- Cardiology
- Clinical Genetics
- Obstetrics
- Paediatrics

DISORDERS OF SEXUAL DEVELOPMENT (DSD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Microarray	Whole genome screen	CNV	Whole genome	28
Glasgow	NGS	Whole gene screen	SNVs, indels	*AMH, AMHR2, ANOS1, AR, ARX, ATRX, CBX2, CHD7, CUL4B, CYB5A, CYP11A1, CYP11B1, CYP17A1, CYP19A1, DHCR7, DHH, DMRT1, FEZF1, FGF8, FGFR1, FOXL2, FSHB, GATA4, GNRH1, GNRHR, HSD17B3, HSD3B2, INSL3, KISS1R, LHB, LHCGR, MAMLD1, MAP3K1, NR0B1, NR3C1, NR5A1, POR, PROK2, PROK2, RSPO1, RXFP2, SEMA3E, SOX2, SOX3, SOX9, SOX10, SPRY4, SRD5A2, SRY, STAR, TAC3, TACR3, TSPYL1, WDR11, WNT4, WT1*	112
Family member testing		as indicated above (Glasgow)			14
Proforma required?		YES	DSD referral form (see centre website)		

REFERRAL CRITERIA

- Ambiguous genitalia and/or impalpable gonads at birth OR
- Delayed puberty in adolescence
- No chromosomal abnormalities detected by karyotype analysis.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Paediatrics

FRAGILE X

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Edinburgh Glasgow	PCR & TPPCR	Targeted screen	Triplet repeat expansion	*FMR1*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features characteristic of fragile X syndrome or other *FMR1*-related disorder
    - Typical fragile X syndrome manifestations in females: learning difficulty (usually mild, IQ often 80-85, but can be moderate or severe LD)
    - Typical fragile X syndrome manifestations in males: moderate to severe developmental delay / learning difficulty (IQ if measured would be 35-70)
- Family history of Fragile X

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

INFERTILITY, MALES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Karyotype	Whole genome screen	Structural variants, CNV	Whole genome	28
Aberdeen Dundee Edinburgh Glasgow	ARMS	Targeted screen	SNVs, indels	50 common mutations	28
Dundee Edinburgh Glasgow	PCR	Targeted screen	Y chromosome markers	AZFa, AZFb, AZFc	28
Proforma required?		NO			

REFERRAL CRITERIA

- Karyotype - Unexplained infertility who are going to undergo infertility treatment
- Y Chromosome microdeletions - Patients with non-obstructive azoospermia or severe oligospermia where testicular sperm extraction (TESE)/microdissection TESE (mTESE) is considered and outcome of testing will inform eligibility for (m)TESE and success of sperm retrieval
- Cystic Fibrosis - Male infertility associated with obstructive azoospermia, AND
    - CBAVD (or isolated CUAVD) diagnosed from expert clinical examination, OR
    - CBAVD identified at incidental herniotomy

REQUESTING SPECIALTIES

- Clinical Genetics
- Fertility clinics

INFERTILITY, FEMALES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Karyotype	Whole genome screen	Structural variants, CNV	Whole genome	28
Aberdeen Edinburgh Glasgow	PCR	Targeted screen	Triplet repeat expansion	*FMR1*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Four consecutive months of unexplained amenorrhoea (primary or secondary), AND
- Elevated serum FSH of >30IU/L on two separate occasions at least 6 weeks apart, AND
- Age of onset is ovarian failure, AND
- Non genetic causes have been excluded including presence of thyroid and adrenal auto-antibodies

REQUESTING SPECIALTIES

- Clinical Genetics
- Fertility clinics

KLINEFELTER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Karyotype	Whole genome screen	CNV	Whole genome	28
	Microarray				
Proforma required?		NO			

REFERRAL CRITERIA

- Primary hypogonadism
- Cryptorchidism
- Gynaecomastia
- Infertility

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Fertility clinics

MICRODELETION / MICRODUPLICATION SYNDROMES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Microarray	Whole genome screen	CNV	Whole genome	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical suspicion of a common microdeletion syndrome to include but not restricted to: 1p36 deletion syndrome, Wolf-Hirschhorn syndrome, Cri-du-Chat syndrome, Sotos syndrome, Saethre-Chotzen syndrome, Williams-Beuren syndrome, Williams-Beuren duplication syndrome, Langer-Giedion syndrome, Rubinstein-Taybi syndrome, Miller-Dieker syndrome, Smith-Magenis syndrome.

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

MOLAR PREGNANCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee Edinburgh	QFPCR	Targeted screen	STRs	Chromosome markers 13, 18, 21, X/Y	28
Dundee	FISH	Targeted screen	CNV	*CEPX*, Y and 12 markers	2
Proforma required?		NO			

REFERRAL CRITERIA

- Molar pregnancy may be suspected during routine booking scan, or at emergency presentation in clinic. In the majority of cases, molar pregnancy is suspected after pathological analysis of products of conception (POC), initially reviewed at local regional pathology departments.
- Pathological suspicion of Hydatidiform Mole prompts referral to the Hydatidiform Mole Follow-Up Service (HMFUS), based within Ninewells Hospital, Dundee. HMFUS provides a national service for all women in Scotland.
- Diagnosis of a molar pregnancy is achieved by MDT which includes gynaecology, pathology and genetics, coordinated via HMFUS.
- For more information visit https://www.nss.nhs.scot/specialist-healthcare/specialist-services/hydatidiform-mole/

Genetic testing in isolation

- In some cases, a complete homozygous mole can be identified solely by genotyping using QF-PCR in the absence of any parental samples. If maternal samples are provided, further molar genotypes such as complete heterozygous complements, associated with a complete hydatidiform mole, and diandric triploidy associated with partial moles, may be identified. Mosaic and chimeric moles may be harder to interpret.
- FISH testing will not differentially distinguish between normal diploid pregnancies and diandric diploid complements, associated with complete moles. Or differentiate between diandric and dygnic triploidy and therefore should not be offered as a sole test for diagnosis of molar pregnancy.

REQUESTING SPECIALTIES

- Pathology

PRADER-WILLI SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	MLPA	Targeted screen	CNV Methylation abnormalities	15q11-13 region	28
Glasgow	PCR	Targeted screen	STRs	Microsatellite markers	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Severe hypotonia and/or feeding difficulties in early infancy
  - Global developmental delay
  - Hypogonadism
  - Excessive eating with central obesity if uncontrolled in childhood

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

RECURRENT MISCARRIAGE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	QF- PCR	Targeted screen	STRs	Chromosomes 13, 18, 21, X/Y	28
	Microarray	Whole genome screen	CNV	Whole genome	
Proforma required?		NO			

REFERRAL CRITERIA

- Tissue from 3rd or subsequent consecutive miscarriage

REQUESTING SPECIALTIES

- Fetal Medicine
- Pathology

SILVER-RUSSELL SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	MLPA	Targeted screen	CNV Methylation abnormalities	11p15 region	28
Glasgow	PCR	Targeted screen	STRs	Microsatellite markers	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Postnatal growth failure
  - Small for gestational age
  - Characteristic facies
  - Limb asymmetry
  - Feeding difficulties

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

SMITH-LEMLI-OPITZ

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger	Whole gene screen	SNVs, indels	*DHCR7*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Prenatal and postnatal growth restriction
  - Microcephaly
  - Moderate-to-severe intellectual disability
  - Malformations that may include distinctive facial features, cleft palate, cardiac defects, underdeveloped external genitalia in males, postaxial polydactyly, syndactyly of the toes
  - Elevated serum concentration of 7-dehydrocholesterol (7-DHC)

REQUESTING SPECIALTIES

- Clinical Genetics

UNIPARENTAL DISOMY, CHROMOSOME 14

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	PCR	Targeted screen	STRs	Chromosome 14 microsatellite markers	28 Prenatal 3
Proforma required?		NO			

REFERRAL CRITERIA

- Prenatal testing is available for:
  - Balanced carriers of Robertsonian translocations
  - Fetuses with a familial or de novo balanced Robertsonian translocation that contains chromosome 14
  - Fetuses with a normal karyotype where a parent is a carrier of a Robertsonian translocation that contains chromosome 14
- Postnatal testing is available in patients with a clinical suspicion of maternal uniparental disomy of chromosome 14.

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

X-INACTIVATION STUDIES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	PCR	Targeted screen	Methylation analysis	*AR* CAG trinucleotide repeat	28
Proforma required?		NO			

REFERRAL CRITERIA

- Possible manifesting carrier of an X-linked recessive condition

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

ENDOCRINOLOGY

ALBRIGHT'S HEREDITARY, PSEUDOHYPOPARATHYROIDISM / PSEUDOPSEUDOHYPOPARATHYROIDISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*GNAS*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Individuals with a clear clinical diagnosis of Albright hereditary osteodystrophy, pseudohypoparathyroidism or pseudopseudohypoparathyroidism based on clinical and biochemical assessment
- Note: Imprinting defects are not tested for.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

ANDROGEN INSENSITIVITY SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*AR*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Undermasculinisation of external genitalia at birth OR
- Abnormal secondary sexual development in puberty OR
- Infertility in individuals with a 46,XY karyotype.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

ASYMPTOMATIC FASTING HYPERGLYCAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*GCK*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Asymptomatic fasting hyperglycaemia: fasting glucose 5.5-8mmols/L

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Obstetrics
- Paediatrics

CARNEY COMPLEX

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*PRKAR1A*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see website)		

REFERRAL CRITERIA

- Two or more of the features from the list below (with histological confirmation where relevant) OR
- One feature from the list below (with histological confirmation where relevant) and an affected first degree relative:
    - Spotty skin pigmentation with typical distribution (lips, conjunctiva, vaginal and penile mucosa)
    - Myxoma (cutaneous and mucosal)
    - Cardiac myxomas
    - Breast myxomatosis or fat-suppressed MRI suggestive of this finding
    - PPNAD or paradoxical positive response of urinary glucocorticosteroid excretion to dexamethasone administration during Liddles test
    - Acromegaly due to GH-producing adenoma
    - Large cell calcifying Sertoli cell tumour (LDDST) or characteristic calcification on testicular ultrasound
    - Thyroid carcinoma or multiple, hypoechoic nodules on thyroid ultrasound in a young patient
    - Psammomatous melanotic schwannomas (PMS)
    - Blue nevus, epithelioid blue nevus
    - Breast ductal adenoma
    - Osteochondromyxoma

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology
- Endocrinology

CONGENITAL HYPERINSULINISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels exon level CNV (selected genes)	*ABCC8, AKT2, CACNA1D, GCK, GLUD1, GPC3, HADH, HNF1A, HNF4A, INSR, KCNJ11, KDM6A, KMT2D, PMM2, SLC16A1, TRMT10A*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Hypoglycaemia accompanied by one of the following, with no identifiable cause:
  - During an episode of hypoglycaemia there is a requirement for the glucose infusion to be at a rate of >8mg/kg/min, OR
  - Detectable serum insulin or c-peptide when the blood glucose is <3mmol/l, OR
  - Suppressed or undetectable serum fatty acids and ketone bodies
- Urgent neonatal requests can be accommodated. Please contact the laboratory to discuss. Where possible, clinicians are asked to submit samples from the probands parents for the DNA to be stored to allow prompt follow-up of variants

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Paediatrics

CONGENITAL HYPOTHYROIDISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*NKX2-1 (TITF1)*	56
Dundee	NGS	Whole gene screen	SNVs, indels	*DUOX2, DUOXA2, FOXE1, GLIS3, GNAS, HESX1, IGSF1, IRS4, IYD, LHX3, LHX4 NKX2-1, OTX2, PAX8, POU1F1, PRKAR1A, PROP1, SECISBP2, SLC16A2, SLC26A4, SLC5A5, TBL1X, TG ,THRB, THRA, TRHR, TPO, TSHR, TSHB*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Congenital hypothyroidism, thyroid hypoplasia or agenesis with or without syndromic features, OR
- Thyroid dyshormonogenesis, OR
- Raised serum thyroid stimulating hormone (TSH) level:
  - With enlarged thyroid gland, OR
  - In the absence of thyroid autoantibodies

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

CONGENITAL NEPHROGENIC DIABETES INSIPIDUS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*AQP2*, *AVPR2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

CONGENITAL OVERGROWTH DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AKT2*, *BRWD3*, *CDKN1C*, *CHD8*, *DIS3L2*, *DNMT3A*, *EZH2*, *GPC3*, *MTOR*, *NFIB*, *NFIX*, *NSD1*, *OFD1*, *PDGFRB*, *PIK3CA*, *PTEN*, *RNF125*, *SETD2*, *SUZ12*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with clinical features suggestive of:
  - Atypical Beckwith-Wiedemann syndrome, Classical Beckwith-Wiedemann syndrome, Simpson-Golabi-Behmel syndrome, Sotos syndrome, Weaver syndrome
- Overlapping investigations: Beckwith-Wiedemann syndrome, Microdeletion/Microduplication Syndromes

REQUESTING SPECIALTIES

- Clinical Genetics

FAMILIAL HYPERPARATHYROIDISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AP2S1, CASR, CDC73, CDKN1B, GCM2, GNA11, MEN1, RET* (exons 5, 8, 10, 11, 13-16)	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Primary hyperparathyroidism (unexplained hypercalcaemia with PTH high or in the upper normal range, and calcium clearance: creatinine clearance ratio > 0.02) which meets ONE of the criteria below:
    - Presenting before the age of 35, OR
    - Presenting at any age with ONE of:
        - Proven multi-glandular involvement, OR
        - Hyperplasia on histology, OR
        - Ossifying fibroma(s) of the maxilla and / or mandible, OR
        - At least one first degree relative with unexplained hyperparathyroidism
- Testing in other contexts e.g. where age of onset is not clear or with a later onset but strong family history is also appropriate.
- Overlapping indications:
    - Familial Hypocalciuric hypercalcaemia test should be used where there is hypercalcaemia (and inappropriately normal or raised PTH) with hypocalciuria (calcium clearance: creatinine clearance ratio < 0.02)
    - Multiple Endorine Neoplasia Type 1 & Type 4
    - Multiple Endocrine Neoplasia Type 2A
    - Hyperparathyroidism-Jaw Tumour Syndrome/Parathyroid carcinoma

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

FAMILIAL HYPOCALCIURIC HYPERCALCAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AP2S1, CASR, CDC73, CDKN1B, GCM2, GNA11, MEN1, RET (exons 5, 8, 10, 11, 13-16)*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Individuals with hypercalcaemia with hypocalciuria (calcium clearance: creatinine clearance ratio < 0.02), with normal and/or elevated PTH
- Overlapping indications:
    - Familial hyperparathyroidism test should be used for hypercalcaemia (with normal or raised PTH) with calcium clearance: creatinine clearance ratio > 0.02 in the presence of an appropriate clinical indication (see Familial Hyperparathyoridism panel)
- Note that the same gene panel is used for FHH and Familial Hyperparathyroidism referrals.

REQUESTING SPECIALTIES

- Clinical Biochemistry
- Clinical Genetics
- Endocrinology
- Nephrology

FAMILIAL HYPOPARATHYROIDISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AIRE*, *CASR*, *GATA3*, *GCM2*, *GNA11*, *PTH*, *TBCE*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Individuals with non-syndromic hypoparathyroidism with low calcium levels and low or inappropriately normal serum PTH, with no detectable cause.
- Any individual with clinical features suggestive of an *AIRE* disorder.
- Testing of patients who are normocalcaemic may occasionally be appropriate after consultation with an expert in calcium homeostasis

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

FAMILIAL ISOLATED PITUITARY ADENOMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*MEN1, CDKN1B, AIP*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Individuals with one of the following:
  - Any pituitary adenoma <20 years
  - Any pituitary macroadenoma <30 years of age
  - Isolated pituitary adenoma developing under the age of 35, with at least one first degree relative with an isolated pituitary adenoma
- Overlapping clinical indications:
  - Multiple Endocrine Neoplasia Type 1 & Type 4 (included in this panel – MEN1 and CDKN1B genes)

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

FAMILIAL NEUROHYPOPHYSEAL DIABETES INSIPIDUS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*AVP*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

GLUCOCORTICOID REMEDIABLE ALDOSTERONISM (GRA)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	PCR	Targeted screen	Fusion gene	*CYP11B1*, *CYP11B2* fusion gene detection	28
Proforma required?		NO			

REFERRAL CRITERIA

- Hypertension presenting in childhood to early adulthood

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

HYPERPARATHYROIDISM-JAW TUMOUR SYNDROME / INHERITED PARATHYROID CARCINOMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels Exon level CNV* *Only available on request, not routinely offered	*CDC73*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- All Patients with parathyroid carcinoma
- Clinical phenotype of HPT-JT (i.e. primary hyperparathyroidism and ossifying fibroma or maxilla and mandible
- Or ≥1 HPT-JT manifestation and a first degree relative with ≥1 HPT-JT manifestation
- HPT-JT manifestations include primary hyperparathyroidism (including parathyroid adenoma and carcinoma) and ossifying fibroma of the mandible and maxilla

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

HYPERTHYROIDISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ALB, SECISBP2, SLC16A2, THRA, THRB, TSHR, TTR*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Hyperthyroidism where common causes have been excluded:
  - Clinical exclusion of common causes such as toxic solitary nodules or multinodular goitre, AND
  - Graves disease excluded by negative TSH receptor autoantibodies when the patient is biochemically hyperthyroid, AND
  - Patient presenting below the age of 18 OR patient has a first degree relative with unexplained hyperthyroidism

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

HYPOGONADOTROPHIC HYPOGONADISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*ANOS1, CHD7, CUL4B, FEZF1, FGF8, FGFR1, FSHB, GNRH1, GNRHR, KISS1R, NR0B1, PROK2, PROK2R, SEMA3E, SOX2, SOX10, SPRY4, TAC3, TACR3, WDR11*	112
Family member testing		as indicated above			14
Proforma required?		YES	DSD referral form (see centre website)		

REFERRAL CRITERIA

- Clinical history of Hypogonadism

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

HYPOPHOSPHATEMIC RICKETS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*CYP27B1, CYP2R1, DMP1, ENPP1, FAM20C, FGF23, PHEX, SLC34A1, SLC34A3, VDR*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Hypophosphataemia with no identifiable cause, with evidence of decreased renal phosphate reabsorption, which has or could lead to presentation with rickets

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

MONOGENIC DIABETES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ABCC8, AKT2, APPL1, CEL, CISD2, DCAF17, DNAJC3, DYRK1B, GATA4, GATA6, GCK, HNF1A, HNF4A, HNF1B, INS, INSR, KCNJ11, LMNA, NEUROD1, PAX6, PCBD1, PDX1, PIK3R1, PLIN1, POLD1, PPARG, PPP1R15B, RFX6, SLC29A3, TRMT10A, WFS1, ZBTB20, ZFP57,* mitochondrial MIDD variant m.3243A>G	112
Family member testing		as indicated above			14
Proforma required?		YES	Monogenic diabetes 33 gene NGS panel proforma (see centre website)		

REFERRAL CRITERIA

- Individuals meeting any one of the following criteria:
  - Minimum two generation family history of diabetes with at least one individual diagnosed under the age of 35 years with BMI less than 30, negative GAD and IA2 autoantibodies and detectable C-peptide, OR
  - High risk of MODY based on MODY calculator http://www.diabetesgenes.org/content/mody-probability-calculator, OR
  - Diabetes in conjunction with cystic renal disease and/or congenital anomaly of the kidney or urinary tract (likely HNF1B), OR
  - Diabetes in conjunction with other extra-pancreatic features suggestive of monogenic diabetes. e.g. deafness, congenital heart disease, epilepsy, diabetes insipidus, developmental delay etc.
  - Post-pubertal children or adults with insulin resistance:
    - Severely elevated plasma insulin (typically greater than 150pmol/L in non-diabetic non-obese subject), AND
    - Clinical features consistent with severe insulin resistance, e.g. polycystic ovarian syndrome, acanthosis nigricans, diabetes with high insulin requirements, post-prandial hypoglycaemia, OR
    - Post-pubertal severe insulin resistance with plasma adiponectin >5mg/l, OR
  - Clinical features of lipodystrophy, including:
    - Abnormal fat distribution (with abdominal fat preservation), AND
    - Acanthosis nigricans and/or very high insulin requirement, AND
    - Impaired glucose tolerance/diabetes

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Paediatrics

MULTIPLE ENDOCRINE NEOPLASIA (TYPE 1, TYPE 4)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	*MEN1, CDKN1B, AIP*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Testing of individual affected with endocrine abnormalities where the individual +/- family history meets one of the following criteria:
    - Multiple endocrine neoplasia type 1 (MEN1). The proband has:
        - Parathyroid multiglandular disease (hyperplasia/ adenomas) (<35 years), OR
        - Any pituitary adenoma or insulinoma (< 20years), OR
        - Pituitary macroadenoma (<30 years), OR
        - ≥2 MEN1-related endocrine abnormalities (any age), OR
        - ≥1 MEN1-related endocrine abnormality and ≥1 MEN1-related non-endocrine tumours (any age), OR
        - ≥1 MEN1-related endocrine abnormality and a first degree relative has ≥1 MEN1-related endocrine abnormality
- MEN1-related endocrine abnormalities include:
    - Parathyroid hyperplasia/multiglandular adenomas
    - Pituitary tumors
    - Endocrine tumors of the gastro-entero-pancreatic (GEP) tract
    - Carcinoid tumors
    - Adrenocortical tumors
- MEN1-related non-endocrine tumours include:
    - facial angiofibromas
    - collagenomas
    - meningioma
- Overlapping clinical indications:
    - Familial Hyperparathyroidism
    - Familial Pituitary Adenoma (FIPA)

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

MULTIPLE ENDOCRINE NEOPLASIA (TYPE 2A, TYPE 2B) AND MEDULLARY THYROID CARCINOMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	*RET* (exons 5, 8, 10, 11, 13, 14, 15, 16)	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Testing of individual (proband) affected with endocrine abnormalities where the individual +/- family history meets one of the following criteria. The proband has:
    - MTC (any age), OR
    - ≥2 MEN2-related endocrine abnormalities (any age), OR
    - ≥1 MEN2-related endocrine abnormality and a first degree relative with ≥1 MEN2-related endocrine abnormality
- MEN2-related endocrine abnormalities include: Medullary Thyroid Carcinoma (MTC), Phaechromocytoma/paraganglioma, Parathyroid adenoma/hyperplasia, Hirschprungs disease
- Overlapping clinical indications:
    - Phaeochromocytoma and paraganglioma panel

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

PHAEOCHROMOCYTOMA AND PARAGANGLIOMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels Exon level CNV in relevant genes	*SDHA, SDHB, SDHC; SDHD, SDHAF2, VHL, MAX, TMEM127, RET* (exons 5, 8, 10, 11, 13 to 16)*, FH*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Testing of individual (proband) affected with cancer where the individual +/- family history meets one of the following criteria. The proband has:
  - Unilateral phaeochromocytoma (<60 years), OR
  - Paraganglioma of the head and neck (<60 years), OR
  - Sympathetic, metastatic or abdominal, thoracic, pelvic paraganglioma (any age), OR
  - Bilateral phaeochromocytoma (any age), OR
  - Phaeochromocytoma and renal cell carcinoma (any age), OR
  - Phaeochromocytoma / paraganglioma (any age) AND ≥1 relative (first / second / third degree relative) with phaeochromocytoma / paraganglioma / renal cell cancer (any age)
- Individuals with clinical features associated with Neurofibromatosis Type 1 can also be tested for variants in *NF1.*
- Overlapping clinical indications:
  - Multiple Endocrine Neoplasia Type 2 (tested for within this panel: *RET* gene)

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

PIGMENTED NODULAR ADRENOCORTICAL DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ARMC5*, *PDE11A*, *PDE8B*, *PRKAR1A*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Primary pigmented nodular adrenocortical disease, OR
- Clinical diagnosis of ACTH-independent Cushing syndrome of unknown aetiology.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

PRIMARY HYPERALDOSTERONISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*KCNJ5*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Hypertension presenting in childhood (under 10 years of age)

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

RENAL CYSTS & DIABETES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels Exon level CNV	*HNF1B*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition.
- Overlapping indication: Monogenic Diabetes. Full Monogenic diabetes panel will be added for all patients with diabetes with or without renal cysts unless requested otherwise.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Fetal Medicine
- Nephrology
- Paediatrics
- Renal

SEVERE EARLY ONSET OBESITY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ALMS1, ARL6, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, CEP19, GNAS, LEP, LEPR, MC4R, MKKS, MKS1, MYT1L, NTRK2, PCSK1, PHF6, POMC, SDCCAG8, SIM1, TTC8, VPS13B*	112
Family member testing		as indicated above			14
Proforma required?		YES	Obesity proforma (see centre website)		

REFERRAL CRITERIA

- BMI >3.5 SDS
- Age of onset below 5 years
- No significant developmental delay or dysmorphic features (referral to Clinical Genetics required as other testing may be more appropriate)

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Obesity specialist

THYROID HORMONE RESISTANCE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*THRB*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Clinical and biochemical picture consistent with thyroid hormone resistance with or without a relevant family history

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

VON HIPPEL LINDAU SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels Exon level CNV	*VHL*	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Testing of individual (proband) affected with VHL-related tumours where the individual/family history meets one of the following criteria:
    - Retinal angioma, spinal or endolymphatic sac tumour (<40 years), OR
    - Cerebellar haemangioblastoma (<60 years), OR
    - ≥2 VHL-related tumours (any age), OR
    - ≥1 VHL-related tumour and a first degree relative with ≥1 VHL-related tumour (where one of the tumours is retinal angioma / hemangioblastoma)
- Deceased affected individual (proband) where (i) the individual +/- family history meets one of the above criteria, (ii) appropriate tissue is available (tumour or normal), and (iii) no living affected individual is available for genetic testing
- VHL-related tumours comprise: Retinal angioma, Spinal or cerebellar hemangioblastoma, adrenal or extra-adrenal phaeochromocytoma, Renal cell carcinoma, multiple renal and/or pancreatic cysts, endolymphatic sac tumors, papillary cystadenomas of the epididymis or broad ligament, neuroendocrine tumour of the pancreas
- Overlapping clinical indications:
    - Phaeochromocytoma and paraganglioma

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

EYES

ABCA4 ASSOCIATED OPHTHALMIC CONDITIONS (incl. STARGARDT DISEASE, CONE-ROD DYSTROPHY, FUNDUS FLAVIMACULATUS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ABCA4*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of *ABCA4* associated ophthalmic conditions

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

ALBINISM & NYSTAGMUS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*AP3B1, CACNA1A, CACNA1F, CASK, FRMD7, GPR143, HPS1, HPS3, HPS4, HPS5, HPS6, LRMDA, LYST, OCA2, PAX6, RAB27A, SACS, SETX, SLC24A5, SLC38A8, SLC45A2, TYR, TYRP1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Albinism & Nystagmus

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

ANTERIOR SEGMENT DYSGENESIS (ASD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ADAMTS18, ALDH18A1, ATOH7, B3GLCT, BEST1, BMP7, CHRDL1, CHST6, COL4A1, COL8A2, CRYGC, CYP1B1, DCN, EYA1, FBN1, FOXC1, FOXE3, FOXL2, GJA1, GNPTG, GSN, KERA, KRT12, KRT3, LAMB2, LCAT, LMX1B, LTBP2, MYOC, NOTCH2, OPTN, PAX3, PEX2, PIKFYVE, PITX2, PITX3, PRDM5, PXDN, RAB18, RAB3GAP1, RAB3GAP2, SEC23A, SH3PXD2B, SIX3, SLC16A12, SLC4A11, SLC4A4, TACSTD2, TGFBI, UBIAD1, VSX1, WDR36, ZEB1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Anterior Segment Dysgenesis – glaucoma, iris hypoplasia, vascularization and opacity in the cornea, corectopia, polycoria, ectopia lentis, cataracts

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

BARDET-BIEDL SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ARL6, BBS1, BBS2, BBS4, BBS5, BBS7, BBS9, BBS10, BBS12, LZTFL1, MKKS, MKS1, SDCCAG8, TMEM67,TTC8*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Bardet-Biedl Syndrome (≥4 primary features or 3 primary features & ≥2 secondary features
    - Primary features: Retinal dystrophy, Renal abnormalities, Obesity, Polydactyly, Learning difficulties, Hypogonadism in males
    - Secondary features: Speech disorder / delay, Strabismus / cataracts / astigmatism, Brachydactyly / syndactyly, developmental delay, Polyuria / polydipsia, Ataxia / poor coordination / imbalance

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology
- Ophthalmology in discussion with Clinical Genetics

BEST DISEASE, VITELLIFORM MACULAR DYSTROPHY (VMD), AR BESTROPHINOPATHY (ARB)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*BEST1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Best disease, Vitelliform Macular dystrophy (VMD), AR bestrophinopathy - reduced vision and an early, significant reduction in electro-oculogram (EOG) light rise

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

BRITTLE CORNEA SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*PRDM5, ZNF469*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of isolated Brittle Cornea Syndrome (can also be a feature in Ehlers-Danlos Syndrome, see Connective Tissue Disorders) – Thinning of the cornea, myopia, blue sclera, retinal detachment

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

CHOROIDERAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*CHM*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Choroideraemia - consistent with X-linked ocular disorder, degeneration of choriocapillaris, retinal pigment epithelium and retinal photoreceptor

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

CONGENITAL CATARACTS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ADAMTS10, AGK, AGPS, ALDH18A1, B3GLCT, BCOR, BFSP1, BFSP2, CHMP4B, COL11A1, COL18A1, COL2A1, COL4A1, CRYAA, CRYAB, CRYBA1, CRYBA4, CRYBB1, CRYBB2, CRYBB3, CRYGC, CRYGD, CRYGS, CYP27A1, CYP51A1, DHCR7, DNMBP, EED, EIF2B2, EPHA2, ERCC2, ERCC3, ERCC6, ERCC8, FAM126A, FOXE3, FTL, FYCO1, GALK1, GALT, GCNT2, GEMIN4, GJA3, GJA8, GNPAT, GTF2H5, HMX1, HSF4, HTRA2, INPP5K, JAM3, LCAT, LIM2, LONP1, LSS, MAF, MAN2B1, MIP, MSMO1, MYH9, NDP, NF2, NHS, OCRL, OPA3, P3H2, PAX6, PEX1, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PITX3, PXDN, RAB18, RAB3GAP1, RAB3GAP2, SC5D, SIL1, SLC2A1, SLC33A1, SRD5A3, TDRD7, TFAP2A, VIM, VSX2, WFS1, WRN, XYLT2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of congenital cataracts

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

CORNEAL ABNORMALITIES (incl. CORNEAL DYSTROPHY & BCS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ADAMTS18, ALDH18A1, B3GLCT, CHRDL1, CHST6, COL17A1, COL8A2, DCN, GJA1, GRHL2, GSN, HMX1, KERA, KRT12, KRT3, LCAT, MIR184, OVOL2, PIK3R1, PIKFYVE, PRDM5, PXDN, RAB18, RAB3GAP1, RAB3GAP2, SLC16A12, SLC4A11, STS, TACSTD2, TCF4, TGFBI, UBIAD1, ZEB1, ZNF469*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of corneal abnormalities

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

CORNEAL DYSTROPHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*CHST6, COL17A1, COL8A2, DCN, GRHL2, GSN, KERA, KRT12, KRT3, LCAT, MIR184, OVOL2, PIKFYVE, PRDM5, SLC4A11, STS, TACSTD2, TCF4, TGFBI, UBIAD1, ZEB1 , ZNF469*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Corneal Dystrophy

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

EYE MOVEMENT DISORDER

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ADAMTS10, ADAMTS17, CYP1B1, FOXC1, FOXD3, FOXE3, JAG1, LTBP2, MYOC, PITX2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of an eye movement disorder

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

FAMILIAL EXUDATIVE VITRORETINOPATHY (FEVR)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ATOH7, FZD4, LRP5, NDP, TSPAN12*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Familial Executive Vitroretinopathy – vision loss or blindness, retinal detachment, strabismus, leukocoria

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

GLAUCOMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ADAMTS10, ADAMTS17, CPAMD8, CREBBP, CYP1B1, DDX58, FOXC1, FOXE3, IFIH1, LMX1B, LTBP2, MYOC, OCRL, PAX6, PITX2, SBF2, SH3PXD2B, TEK*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Glaucoma

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

MACULAR DYSTROPHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels	*PRPH2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of monogenic Macular Dystrophy – loss of central vision

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

OCULAR MALFORMATIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ACTB, ACTG1, ALDH1A3, BCOR, C12ORF57, CHD7, COL4A1, FOXC1, FOXE3, CHD7, GJA8, ITPA, ITPR1, MAB21L1, MAB21L2, NAA10, OTX2, PAX2, PAX6, PITX2, PITX3, RAB18, RAB3GAP1, RAB3GAP2, RARB, RAX, RBP4, SALL2, SALL4, SHH, SIX3, SMCHD1, SMOC1, SOX2, STRA6, TBC1D20, VAX1, VSX2, YAP1, ZEB2, ZIC2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Microphthalmia or anophthalmia or uveoretinal coloboma where there is evidence to support a likely monogenic cause, for example bilateral disease, consanguinity or additional ocular and non-ocular features, OR
- Aniridia

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics
- Paediatrics

OCULOCUTANEOUS ALBINISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*GPR143, HPS1, HPS3, HPS4, HPS5, LRMDA, LYST, OCA2, SLC24A5, SLC45A2, TYR, TYRP1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Oculocutaneous Albinism – very light skin and light coloured irises, decreased sharpness of vision, nystagmus, strabismum, photophobia

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

OPTIC ATROPHY TYPE 1

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS MLPA	Whole gene screen	SNVs, indels Exon level CNV	*OPA1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Optic Atrophy type 1 – vision loss, difficulty distinguishing between colours, pallor of the optic nerve. May also have sensorineural hearing loss, ataxia, myopathy

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

OPTIC NEUROPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ACO2, C12orf65, C19orf12, CISD2, DNM1L, MFF, MFN2, NR2F1, OPA1, OPA3, RTN4IP1, SLC25A46, SLC52A2, SPG7, SSBP1, TMEM126A, WFS1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of an Optic Neuropathy

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

RETINAL DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ABCA4, ABHD12, ACO2, ADAM9, ADAMTS18, ADGRV1, AGBL5, AHI1, AIPL1, AIRE, ALMS1, ARHGEF18, ARL2BP, ARL6, ATF6, ATOH7, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, BEST1, C1QTNF5, C8orf37, CABP4, CACNA1F, CACNA2D4, CAPN5, CC2D2A, CDH23, CDH3, CDHR1, CEP164, CEP290, CEP78, CERKL, CFAP410 (C21orf2), CFH, CHM, CIB2, CLN3, CLN5, CLN6, CLN8, CLRN1, CNGA1, CNGA3, CNGB1, CNGB3, CNNM4, COL18A1, COL4A1, CRB1, CRX, CSPP1, CTNNB1, CTSD, CWC27, CYP4V2, DHDDS, EFEMP1, ELOVL4, ERCC6, ERCC8, EYS, FAM161A, FLVCR1, FZD4, GNAT1, GNAT2, GNPTG, GPR143, GPR179, GRK1, GRM6, GUCA1A, GUCA1B, GUCY2D, HARS, HCCS, HGSNAT, HMX1, IDH3A, IDH3B, IFT140, IKBKG, IMPDH1, IMPG1, IMPG2, INPP5E, IQCB1, KCNJ13, KCNV2, KIAA1549, KIF11, KIZ, KLHL7, LCA5, LRAT, LRIT3, LRP2, LRP5, LZTFL1, MAK, MERTK, MFRP, MFSD8, MKKS, MKS1, MYO7A, NDP, NMNAT1, NPHP1, NPHP3, NPHP4, NR2E3, NRL, NYX, OAT, OFD1, OPN1LW, OPN1MW, OTX2, PANK2, PCARE (c20rf71), PCDH15, PCYT1A, PDE6A, PDE6B, PDE6C, PDE6G, PEX1, PEX2, PEX7, PHYH, PLA2G5, POC1B, PPT1, PRCD, PROM1, PRPF3, PRPF31, PRPF4, PRPF6, PRPF8, PRPH2, PRPS1, RAB28, RAX2, RBP3, RBP4, RCBTB1, RD3, RDH12, RDH5, REEP6, RGS9, RHO, RLBP1, RP1, RP1L1, RP2, RP9, RPE65, RPGR, RPGRIP1, RPGRIP1L, RS1, SAG, SCAPER, SDCCAG8, SLC24A1, SLC38A8, SNRNP200, SPATA7, SRD5A3, TIMM8A, TIMP3, TMEM237, TOPORS, TPP1, TRIM32, TRPM1, TSPAN12, TTC8, TTLL5, TUB, TULP1, USH1C, USH1G, USH2A, VCAN, VPS13B, WDPCP, WDR19, WHRN, ZNF408, ZNF423*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic Retinal disorder
- Where clinical testing indicates a subset of genes should be tested, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.
- Please note, *ORF15* sequencing is not currently available in the Aberdeen laboratory. Where testing is required, please send to the Manchester laboratory.

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

USHER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*MYO7A, USH1C, CDH23, PCDH15, USH1G, ADGRV1, DFNB31 (WHRN), USH2A*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Usher Syndrome – retinitis pigmentosa and sensorineural hearing loss.
- If clinical presentation is mainly hearing loss, testing should be performed in Dundee

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

X-LINKED CONGENITAL NYSTAGMUS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*FRMD7*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of X-linked Congenital Nystagmus – nystagmus presenting within first 6 months of life

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

X-LINKED JUVENILE RETINOSCHISIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*RS1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

Can be performed prior to Retinal Degeneration panel if required

REFERRAL CRITERIA

- Clinical features suggestive of X-linked Juvenile Retinoschisis

REQUESTING SPECIALTIES

- Clinical Genetics
- Ophthalmology in discussion with Clinical Genetics

GASTROHEPATOLOGY

CHOLESTASIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ABCB11, ABCB4, ABCC2, AKR1D1, ALDOB, AMACR, ATP8B1, BAAT, BCS1L, CLDN1, CYP27A1, CYP7A1, DCDC2, FAH, HSD3B7, JAG1, MYO5B, NOTCH2, NPC1, NPC2, NR1H4, PEX1, PEX12, PEX26, PEX6, SERPINA1, SLC25A13, TALDO1, TJP2, UGT1A1, VIPAS39, VPS33B*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Neonatal conjugated hyperbilirubinaemia where multifactorial and infective causes have been excluded
- Unexplained cholestasis developing <18 years old
- Unexplained cholestasis >18 years old where other causes excluded

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastroenterology
- Hepatology
- Paediatrics

CRIGLER-NAJJAR SYNDROME, TYPE 1 AND 2

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	Promoter variant	*UGT1A1*, TA Allele7 (A[TA]7TAA)	28
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals with unconjugated hyperbilirubinaemia in the absence of haemolysis, where a molecular diagnosis will contribute to management
- Urgent requests for neonates are processed in 5 days.

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastroenterology
- Hepatology
- Paediatrics

GILBERT SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Fragment	Targeted screen	Promoter variant	TA Allele7 (A[TA]7TAA)	28
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals with mild unconjugated hyperbilirubinaemia in the absence of haemolysis, where a molecular diagnosis will contribute to management

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastrohepatology
- Paediatrics

HIRSCHSPRUNG DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*RET* as a single gene, or 8 gene panel: *EDN3, EDNRB, KIF1BP, L1CAM, PHOX2B, RET, SOX10,ZEB2*	56 - RET 112 -panel
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Diagnosis of Hirschsprung disease (HSCR) and at least one of the following:
  - Family history of HSCR, at least 1 affected first or second degree relative, OR
  - HSCR occurring as part of a syndrome or with other anomalies associated with the listed genes

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastroenterology
- Hepatology
- Paediatrics

PANCREATITIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*SPINK1, PRSS1*	56
Aberdeen Dundee Edinburgh Glasgow	ARMS	Targeted screen	SNVs, indels	*CFTR* common mutations	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Recurrent acute pancreatitis
- Chronic pancreatitis
- 1st episode of acute pancreatitis <18 years old
- 1st episode of acute pancreatitis with a first degree relative who has also had pancreatitis
- Secondary causes excluded (e.g. excessive alcohol, gallstones)

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastroenterology
- Hepatology
- Lipidology
- Paediatrics

PORPHYRIAS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ALAD*, *ALAS2*, *CPOX*, *FECH*, *HMBS*, *PPOX*, *UROD*, *UROS*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical diagnosis of porphyria with suspected monogenic cause

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastroenterology
- Hepatology

WILSON DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*ATP7B*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Wilson disease – high liver copper, high urinary copper, high free copper, low caeruloplasmin

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastroenterology
- Hepatology

HAEMATOLOGY

ANTITHROMBIN DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*SERPINC1*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Antithrombin activity and/or antigen below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

BERNARD-SOULIER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs	*GP1BA, GP1BB, GP9*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Platelet function testing suggestive of Bernard Soulier syndrome

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

COAGULATION & FIBRINOLYSIS PANEL

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs	*F2, F5, F7, F8, F9, F10, F11, F12, F13A1, F13B, FGA, FGB, FGG, GGCX, KLKB1, KNG1, LMAN1, MCFD2, SERPINE1, SERPINF2, THBD, VKORC1, VWF*	84
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Suspected congenital unexplained bleeding disorder, meeting both of
  - normal coagulation factors or deficiency of multiple coagulation factors
  - life long significant bleeding history (eg OBS >9), or personal bleeding history and family history of bleeding
- **Note:** specific genes are available as sub-panels where there is a highly suggestive phenotype such as Factor II, V or XIII deficiency

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

COMBINED FACTOR V AND VIII DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs (plus exon level CNV for *F8* where appropriate)	*F5, F8, LMAN1, MCFD2*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Factor V and factor VIII levels below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

DIAMOND BLACKFAN ANAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*RPL5, RPS10, RPL11, RPL35A, RPS7, RPS19, RPS24, RPS26, GATA1, RPS17*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of Diamond Blackfan Anaemia – Presenting in the 1st year of life. Normochromic macrocytic anaemia, reticulocytopenia and nearly absent erythroid progenitors in the bone marrow.

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

ERYTHROCYTOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*EGLN1, EPAS1, EPO, EPOR, HBA1, HBA2, HBB, VHL*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Idiopathic erythrocytosis with:
  - No acquired JAK2 variants
  - Secondary causes excluded
  - Young onset and/or family history

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

FACTOR VII DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger MLPA	Whole gene screen	SNVs Exon level CNV	*F7*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Factor VII level below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

FACTOR X DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger MLPA	Whole gene screen	SNVs Exon level CNV	*F10*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Factor X level below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

FACTOR XI DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger MLPA	Whole gene screen	SNVs Exon level CNV	*F11*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Factor XI level below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

FIBRINOGEN DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs	*FGA*, *FGB*, *FGG*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Diagnosis of hypo-, a- or dys- fibrinogenaemia with a reduced antigenic and/or functional fibrinogen level on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

GLANZMANN THROMBASTHENIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs	*ITGA2B*, *ITGB3*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Platelet function testing suggestive of Glanzmann thrombasthenia

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

HAEMOCHROMATOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Glasgow	ARMS (D & G) Sanger (A)	Targeted screen	SNVs	*HFE* p.C282Y & p.H63D	28
Proforma required?		NO			

REFERRAL CRITERIA

- Raised serum ferritin and transferrin saturation

REQUESTING SPECIALTIES

- Clinical Genetics
- GPs
- Haematology

HAEMOGLOBINOPATHY
(incl. SICKLE CELL DISEASE, ALPHA AND BETA THALASSAEMIAS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger	Whole gene screen	SNVs, indels	*HBB, HBA*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features indicative of likely thalassaemia or other clinically significant haemoglobinopathy.

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

HAEMOPHILIA A

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS MLPA Inversion PCR	Whole gene screen	SNVs Exon level CNV Inversions *	*F8*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

* Inversion testing includes recurrent inversions with breakpoints within *F8* intron 1 and 22 and is only included for severe haemophilia A, or moderate haemophilia A where no other causative variant is identified

REFERRAL CRITERIA

- Factor VIII level below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

HAEMOPHILIA B

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*F9*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Factor IX level below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

INHERITED BONE MARROW FAILURE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*BRCA2, BRIP1, CTC1, DKC1, ELANE, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, G6PC3, GATA1, GATA2, GFI1, HAX1, MPL, NHP2, NOP10, PALB2*, RAD51C, RPL11, RPL35A, RPL5, RPS10, RPS17, RPS19, RPS24, RPS26, RPS7, RUNX1, SBDS, SLX4, SRP72, TERT, TINF2, WAS, WRAP53*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of an inherited bone marrow failure disorder

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

IRON REGULATION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ABCB7, ALAS2, ATP7B, BMP6, CP, CYBRD1, FTL, GBA, GLRX5, HAMP, HFE, HFE2, SLC11A2, SLC25A38, SLC40A1, TF, TFR2, TMPRSS6*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Juvenile Haemochromatosis (<30years) with severe iron overload in liver AND/OR heart. Raised serum ferritin >1000ug/L and transferrin saturation >90%
- Juvenile Haemochromatosis >30 years with unexplained severe haemochromatosis and HFE negative
- Ferroportin disease: raised serum ferritin with normal transferrin saturation and evidence of reticuloendothelial iron staining on liver biopsy or splenic iron overload on MRI and HFE mutations negative
- Haemochromatosis: raised serum ferritin and transferrin saturation C282Y negative
- Hereditary Hyperferritinemia cataract syndrome: High and constant levels of serum ferritin unresponsive to iron depletion and no signs of iron overload and no relevant clinical symptoms apart from visual impairment by cataract
- Biochemical evidence of unexplained iron overload and lack of homozygous/compound homozygous HFE mutations
- Iron Refractory Iron Deficiency Anaemia (IRIDA): Very low mean corpuscular volume (MCV) and low serum iron and low transferrin saturation, normal ferritin or ferritin levels in the lower limits of normal, no response to oral iron treatment

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

MYELODYSPLASTIC SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*SRP72, GATA2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggestive of monogenic Myelodysplastic syndrome

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

NEUTROPENIA CONSISTENT WITH ELANE MUTATIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*ELANE*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Isolated neutropenia suggestive of ELANE pathogenic variants.

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

PLATELET PANEL

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ABCG5, ABCG8, ACTB, ACTN1, ANKRD26, ANO6, AP3B1, AP3D1, ARPC1B, BLOC1S3, BLOC1S6, CDC42, CYCS, DIAPH1, DTNBP1, ETV6, FERMT3, FLI1, FLNA, FYB1, GBA, GATA1, GFI1B, GNE, GP1BA, GP1BB, GP6, GP9, HOXA11, HPS1, HPS3, HPS4, HPS5, HPS6, ITGA2B, ITGB3, KDSR, LYST, MECOM, MPIG6B, MPL, MYH9, NBEA, NBEAL2, P2RY12, PLA2G4A, PLAU, RASGRP2, RBM8A, RNU4ATAC, RUNX1, SLFN14, SRC, STIM1, STXBP2, TBXA2R, TBXAS1, THPO, TUBB1, VIPAS39, VPS33B, VWF, WAS*	84
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Suspected congenital (macro)thrombocytopenia or thrombocytopathy
- Confirmed platelet function defect (other than Glanzmann Thrombasthenia or Bernard Soulier syndrome pattern)
- Life long significant bleeding history (eg OBS >9), or personal bleeding history and family history of bleeding

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

PROTEIN C DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*PROC*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Protein C level below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

PROTEIN S DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*PROS1*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Protein S level below the normal range on at least two occasions

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

RED CELL ENZYMES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ALDOA, AK1, G6PD, GCLC, GPI, GSR, GSS, HK1, NT5C3A, PFKM, PKLR, TPI1, CYB5R3*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical presentation or biochemical enzyme deficiency highly suggestive of a specific red cell enzyme deficiency

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

RED CELL MEMBRANOPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*AK1, ANK1, EPB41, EPB42, RhAG, SLC2A1, SLC4A1, SPTA1, SPTB, XK*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Phenotypic presentation highly suggestive of a gene included in the current panel.

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

SCHWACHMAN-DIAMOND SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*SBDS*, *DNAJC21*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical phenotype suggestive of Schwachman-Diamond Syndrome

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

SICKLE CELL ANAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Targeted screen	SNVs	*HBB* p.(Glu7Val)	28 Prenatal 3
Edinburgh	Sanger	Targeted screen	SNVs	*HBB* p.(Glu7Val)	28 Prenatal 3
Glasgow	Sanger	Targeted screen (incl. newborn screening)	SNVs	*HBB* p.(Glu7Val)	28 Prenatal 3 Newborn screening 7
Proforma required?		NO			

REFERRAL CRITERIA

- Sickle cell anaemia diagnosed by Haemaology test
- For prenatal testing, both parents to be confirmed as carrier by genetics prior to offering invasive prenatal test. Please contact the laboratory to discuss
- Newborn screening (Glasgow)
    - Newborns who have undergone a blood transfusion prior to the blood spot sample being taken.

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Obstetrics

THROMBOPHILIA (FACTOR V LEIDEN & PROTHROMBIN)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee EdinburghMP*	Sanger (A) ARMS (D) Real time PCR (E)	Targeted screen	SNVs	*F5* p.R534Q *F2* c.*97G>A	28
Proforma required?		NO			

*Performed by Edinburgh Molecular pathology, see https://edinburghlabmed.co.uk/node/1728

REFERRAL CRITERIA

- Venous thromboembolic event less than 40 years, with no apparent secondary causes
- Family history of venous thromboembolic events

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

THROMBOSIS PANEL

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs	*ADAMTS13, F2, F5, HRG, PIGA, PLG, PROC, PROS1, SERPINC1, SERPIND1, THBD*	84
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Significant personal and family history of thrombosis
- Normal protein C, protein S and antithrombin levels

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

VON WILLEBRAND DISEASE (VWD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS MLPA	Whole gene screen	SNVs Exon level CNV	*VWF*	56
Family member testing		as indicated above			14
Proforma required?		YES	Molecular Haematology request form (see centre website)		

REFERRAL CRITERIA

- Type 1/3 VWD: VWF antigen and/or activity below 30 IU/dL on at least two occasions
- Type 2 VWD: VWF antigenic or activity levels suggestive of type 2 VWD, with or without suggestive platelet function or multimer results.

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology

HEARING LOSS

AMINOGLYCOSIDE RELATED DEAFNESS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNV	m.1555A>G	28 or 5
Proforma required?		NO			

REFERRAL CRITERIA

- Significant exposure to aminoglycosides posing risk of ototoxicity
- This indication would be relevant to:
    - Individuals in whom aminoglycoside therapy may be required
    - Individuals who have been exposed to aminoglycosides in whom mt.1555A>G status needs to be determined because of concern regarding hearing loss
- Note TAT is quicker for imminent treatment decisions

REQUESTING SPECIALTIES

- Clinical Genetics
- Any specialty considering aminoglycoside treatment

BRANCHIOOTORENAL (BOR) SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels, Exon level CNV (*EYA1*)	*EYA1, SIX1, SIX5*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition.
- Referrals should be discussed with Clinical Genetics.

REQUESTING SPECIALTIES

- Audiology
- Clinical Genetics
- Nephrology

HEARING LOSS, SYNDROMIC & NON SYNDROMIC

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ABHD12, ACTG1, ADGRV1 (GPR98), ALMS1, ATP6V1B1, BCS1L, BSND, CABP2, CCDC50, CDH23, CEACAM16, CHD7, CIB2, CLDN14, CLPP, CLRN1, COCH, COL11A2, COL4A5, COL4A6, DIAPH1, DNMT1, DSPP, EDN3, EDNRB, EPS8, ESPN, ESRRB, EYA1, EYA4, FGF3, GATA3, GIPC3, GJB2, GJB3, GJB6, GPSM2, GRHL2, GRXCR1, GSDME (DFNA5), HOXA2, HSD17B4, ILDR1, KARS, KCNE1, KCNJ10, KCNQ1, KCNQ4, KIT, LARS2, LHFPL5, LOXHD1, LRTOMT, MARVELD2, MASP1, MITF, MSRB3, MYH14, MYH9, MYO15A, MYO3A, MYO6, MYO7A, OPA1, OSBPL2, OTOA, OTOF, OTOG, OTOGL, P2RX2, PAX2, PAX3, PCDH15, PDZD7, PJVK (DFNB59), PNPT1, POU3F4, POU4F3, PRPS1, PTPRQ, RDX, SALL1, SALL4, SERAC1, SERPINB6, SIX1, SIX5, SLC17A8, SLC26A4, SLC26A5, SLC4A11, SMPX, SNAI2, SOX10, SOX2, STRC, SYNE4, TBC1D24, TECTA, TIMM8A, TMC1, TMIE, TMPRSS3, TPRN, TRIOBP, USH1C, USH1G, USH2A, WFS1, WHRN (DFNB31)*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Discussion with Clinical Genetics is required before testing.
- Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family

REQUESTING SPECIALTIES

- Audiology (with Clinical Genetics approval)
- Clinical Genetics

NON-SYNDROMIC HEARING LOSS – *DFNB1*

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels (GJB2) Deletions (GJB6)	*GJB2*, *GJB6*	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with congenital, sensorineural hearing loss which is confirmed, bilateral and has no syndromic features.

REQUESTING SPECIALTIES

- Audiology
- Clinical Genetics
- Paediatrics

PENDRED SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*SLC26A4*, *FOXI1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
  - Autosomal recessive deafness also associated with thyroid goiter
  - Abnormal cochlea or enlarged vestibular aqueduct is considered the most likely presentation of Pendred Syndrome
- Note that *FOXI1* is analysed if a single heterozygous variant is detected in *SLC26A4*.

REQUESTING SPECIALTIES

- Audiology
- Clinical Genetics
- Paediatrics

USHER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ADGRV1, CDH23, CIB2, CLRN1, MYO7A, PCDH15, PDZD7, USH1C, USH1G, USH2A, WHRN*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition. Referrals should be discussed with Clinical Genetics.
- If clinical presentation is mainly ophthalmic, testing should be performed in Aberdeen

REQUESTING SPECIALTIES

- Clinical Genetics

WAARDENBURG SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*PAX3, MITF, SOX10, SNAI2, EDNRB, EDN3, KIT*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition.

REQUESTING SPECIALTIES

- Clinical Genetics

WOLFRAM SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*WFS1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition.
- Available as single gene analysis via targeted Monogenic Diabetes NGS panel

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

IMMUNOLOGY

ADENOSINE DEAMINASE DEFICIENCY (ADAD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*ADA2 (CECR1)*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Polyarteritis nodosa, childhood onset
- Early-onset recurrent ischemic stroke and fever
- Livedo racemosa
- Low IgM
- Hypogammaglobulinaemia
- Lymphopenia
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology

ANHYDROTIC ECTODERMODYSPLASIA WITH ID

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*IKBKG (NEMO), NFKBIA (IKBA)*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Anhidrotic ectodermal dysplasia
- Various infections (bacteria, mycobacteria viruses & fungi)
- Colitis
- Variable defects of skin, hair & teeth.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

ALPHA 1 ANTITRYPSIN DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger	Whole gene screen	SNVs, indels	*SERPINA1*	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Plasma concentration of alpha-1-antitrypsin below normal range, AND
    - Prolonged neonatal jaundice with an inconclusive alpha-1-antitrypsin phenotyping result, OR 2. Mutation analysis will inform reproductive choice, OR
    - Adult with cirrhosis or emphysema where a genetic diagnosis would influence management following an inconclusive alpha-1-antitrypsin phenotyping result
- Referrals for testing will be triaged by the Genomic Laboratory; testing should be targeted at those where a genetic or genomic diagnosis will guide management for the proband or family.

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastroenterology
- Hepatology
- Respiratory Medicine

ASSOCIATION WITH GI INFLAMMATION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ADAM17, AICDA, AP3B1, B2M, BTK, CBL, CD40LG, CORO1A, CTC1, CTPS1, CYBA, CYBB, DCLRE1C, DOCK8, FERMT1, FOXP3, GUCY2C, HPS1, HPS4, HPS6, ICOS, IFNGR1, IFNGR2, IKBKG, IL10RA, IL2RA, ITGB2, MAGT1, NCF1, NCF2, NCF4, NF1, PIK3CD, PIK3R1, PTEN, PYCARD, SKIV2L, SLC37A4, STK4, TTC37, VPS13B, WAS*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Rheumatology

AUTOINFLAMMATORY DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACP5, ADA2 (CECR1), ADAM17, ADAR1, AP1S3, CARD14, COPA, IFIH1, IL1RN, IL36RN, LPIN2, MEFV, MVK, NOD2, NLCR4, NLRP1, NLRP3, NLRP12, OTULIN, PLCG2, POLA1, PSMB8, PSTPIP1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SH3BP2, SLC29A3, TMEM173, TNF1IP3, TNFAIP3, TNFRSF1A, TREX1, USP18*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Autoinflammatory disorders.
- For specific Autoinflammatory disorders subpanels (Monogenic Autoinflammatory diseases, Recurrent inflammation, Systemic inflammation with urticarial rash, Others, Sterile inflammation predominant on the bone / joints, Sterile inflammation predominant on the skin, Type 1 interferonopathies), please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology
- Rheumatology

BACTERIAL AND PARASITIC INFECTIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACT1 (TRAF3IP1), APOL1, CARD9, HMOX1, IRAK1, IRAK4, MYD88, NBAS, NCSTN, PSEN, PSENEN, RANBP2, RPSA, STAT1, IL17F, IL17RA, 1L17RC, TIRAP*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Bacterial and Parastic infections.
- For specific Bacterial and parasitic infections subpanels (Predisposition to invasive bacterial infections, Predisposition to parasitic and fungal infections, Hydradenitis suppurativa, Acute liver failure due to NBAS deficiency, Acute necrotising encephalopathy), please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

BACTERIAL INFECTIONS, AUTOINFLAMMATION, AMYLOPECTINOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*HOIL1 (RBCK1), HOIP1 (RNF31)*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Bacterical infections, Autoinflammation, Amylopectinosis.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

CALCIUM CHANNEL DEFECTS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ORAI1, STIM1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Autoimmunity
- EDA
- Non-progressive myopathy
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

CHRONIC GRANULOMATOUS DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CYBA, CYBB, NCF1, NCF2, NCF4*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Early onset of severe and recurrent infections affecting initially the natural barriers of the organism (lungs, lymph nodes, skin), and eventually inner structures (liver, spleen, bones, brain, and +++ hepatic abscess).
- Autoinflammatory phenotype.
- IBD.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology

COMBINED IMMUNODEFICIENCIES (CVID)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*B2M, BCL11B, CD3G, CD8A, CIITA, DOCK8, IL21 ,LAT, LCK, MAGT1, MAP3K14, MSN, OX40 (TNFRSF4), RFX5, RFXANK, RFXAP,RHOH, STK4, TAP1, TAP2, TAPBP, TRAC, UNC119, ZAP70*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Generally less profound than SCID.
- For specific CVID subpanels (Low CD4 / MHCII expression absent, Low CD4 / MHCII expression present, Low CD8, Low B cells, Ig often normal, Ig low, Normal Ig with poor specific antibody response), please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

COMPLEMENT DEFICIENCIES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*C1QA, C1QB, C1QC, C1R, C1S, C2, C3, C4A, C4B, C5, C6, C7, C8A, C8B, C8G, C9, CD55, CD59, CFB, CFD, FCN3, MASP2, PFC (CFP), SERPING1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Complement deficiencies.
- For specific Complement deficiencies subpanels (Disseminated Neisserial infections, Recurrent pyogenic infections, SLE-like syndrome, Low susceptibility to infection), please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology
- Rheumatology

CONGENITAL THROMBOCYTOPENIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ARPC1B, WAS, WIPF1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Recurrent bacterial and viral infections
- Bloody diarrhoea
- Excema
- Vasculitis
- For specific Congenital thrombocytopenia subpanels (Wiskott Aldrich Syndrome, WIP deficiency, *ARPC1B* deficiency), please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

DEFECTS OF VITAMIN B12 AND FOLATE METABOLISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*MTHFD1, SLC46A1, TCN2*	56 or 112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Megablastic anaemia.
- Ig decreased.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

DNA REPAIR DEFECTS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ATM, BLM, CDCA7, DNMT3B, GINS1, HELLS, LIG1, MCM4, NBS1 (NBN), PMS2, POLE1, POLE2, NSMCE3, ERCC6L2, RNF168, ZBTB24*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of DNA repair defects
- For specific DNA repair defects subpanels (Ataxia telangiectasia, Nijmegen breakage syndrome, Bloom syndrome, *PMS2* deficiency, Immunodeficiency with centromeric instability & facial anomalies, *MCM4* deficiency, *RNF168* deficiency, *POLE1* deficiency, *POLE2* deficiency, *NSME3* deficiency, *ERCC6L2* (Hebo) deficiency, Ligase 1 deficiency. *GINS1* deficiency), please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

DYSKERATOSIS CONGENITA (DKC)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CTC1, DKC1,PARN, NOLA2 (NHP2), NOLA3 (NOP10), RTEL1, SAMD9, SAMD9L, SNM1B / APOLLO (DCLRE1B), STN1, TERC, TERT, TINF2, TPP1, WRAP53*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Myelodysplasia
- Defective telomere maintenance
- Exclude other causes: Fanconi Anaemia, Diamond-Blackfan
- For specific Dyskeratosis congenita panels (Dyskeratosis congenital, Coats plus syndrome, Others), please refer to GEN FORM 215 Primary Immunodeficiency Request form on website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

FAMILIAL HLH DUE TO PRF1 VARIANTS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*PRF1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Fever
- Cytopenias
- Increased activated Tc
- Decreased to absent NK and CTL activities cytotoxicity.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website.

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

HAEMOPHAGOCYTIC LYMPHOHISTOPCYTOSIS (HLH) & EBV SUSCEPTIBILITY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*AP3B1, AP3D1, CD27, CD70, CTPS1, DNASE2, FAAP24, ITK, LYST, MAGT1, PRF1, PRKCD, RAB27A, RASGRP1, RLTPR (CARMIL2), SH2DIA, SLC29A3, STX11, STXBP2, UNC13D, XIAP*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of HLH & EBV susceptibility.
- For specific Hemophagocytic Lymphohistocytosis HLH & EBV susceptibility panels (Chediak Higashi syndrome, Griscelli syndrome type 2, Hermansky Pudiak Syndrome type 10, H ermansky Pudiak Syndrome type 2, Familial HLH Syndromes, Susceptibility to EBV, EBV associated HLH), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology
- Rheumatology

HENNEKAM-LYMPHANGIECTASIA-LYMPHEDEMA SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CCBE1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Lymphangiectasia and lymphedema with facial abnormalies and other dysmorphic features.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

HEPATIC VENO-OCCLUSIVE DISEASE WITH IMMUNODEFICIENCY (VODI)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*SP110*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Hepatic veno-occlusive disease.
- *Pneumocystis jirovecii* pneumonia
- CMV
- Candida
- Thrombocytopenia
- Hepatosplenomegaly
- Cerebrospinal leukodystrophy
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

HEREDITARY AMYLOIDOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*APOA1, APOA2, APOA4, APOC2, APOC3, APOE, FGA, GSN, IL31RA, LYZ, TTR, UNC13D*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Hereditary Amyloidosis.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Rheumatology

HEREDITARY ANGIOEDEMA, TYPES I & II

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*SERPING1*	56
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*SERPING1, Factor XII, PLG, ANGPT1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Hereditary angioedema
- Spontaneous activation of the complement pathway with consumption of C4/C2.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology

HYPER IgE SYNDROMES (HIES)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*PGM3*, *SPINK5*, *STAT3*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Hyper IgE syndromes (HIES).
- For specific Hyper IgE syndromes (AD-HIES / Job syndrome, Comel Netherton syndrome, PGM3 deficiency), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

HYPOGAMMAGLOBULINAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ATP6AP1, BLNK, BTK, CD19, CD20 (MS4A1), CD79A, CD79B, CD81, IGHM, IGLL1, IKZF1 (IKAROS), IRF2BP2, MOGS, NFKB1, PIK3CD, PIK3R1, PTEN, TCF3, TNFRSF13B (TACI), TNFRSF13C (BAFFR), TRNT1, TTC37, TWEAK (TNFSF12)*	56 or 112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- IgG, IgA and / or IgM decreased
- Exclude second causes: drugs [Hx], myeloma [bone marrow], lymphoma. Ig loss (not hypo-IgM) in urine, gastro-intestinal or skin.
- For specific Hypogammaglobulinaemia subpanels (B absent, B>1% Common Variable Immunodeficiency phenotype), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

ID WITH MULTIPLE INTESTINAL ATRESIAS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*TTC7A*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Bacterial (sepsis), fungal, viral infections
- Multiple intestinal atresias, often with intrauterine polyhydramnios and early demise, some with SCIDphenotype.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

IMMUNO-OSSEOUS DYSPLASIAS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*EXTL3, MYSM1, RMRP, RNU4ATAC, SMARCAL1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Immuno-Osseous Dysplasias
- For specific Immuno-osseous dysplasias subpanels (Cartilage Hair Hypoplasia, Schimke syndrome, MYSM1 deficiency, MOPD1 deficiency, EXLT3 deficiency), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology

INTERFERONOPATHY / SLS / AGS / COMPLEMENT

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACP5, ADAM17, C1QA, C1QB, C1QC, C1R, C2, C3, C5, C6, C7, C8A, C8B, C9, CFH, CFHR5, CFI, CFP, DNASE1, DNASE1L3, IFIH1, IRF8, RASGRP1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SNORD118, TREX1, USP18*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Interferonopathy/ SLS / AGS / Complement disorders.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website.

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology
- Rheumatology

KABUKI SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*KDM6A, KMT2D (MLL2)*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Typical facial abnormalies
- Cleft or high arched palate
- Skeletal abnormalities
- Short stature
- Intellectual disability
- Congenital heart defects
- Recurrent infecons (otitis media, pneumonia) in 50% of patients
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

MENDELIAN SUSCEPTIBILITY TO MYCOBACTERIAL DISEASE (MSMD) AND VIRAL INFECTION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CXCR4 (WHIM), CYBB, FCGR3A, IFIH1, IFNAR2, IFNGR1, IFNGR2, IL12B, IL12RB1, IRF3, IRF7, IRF8, ISG15, JAK1, RORC, STAT1, STAT2, TBK1, TICAM1 (TRIF), TLR3, TMC6, TMC8, TRAF3, TYK2, UNC93B1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Mendelian Susceptibility to Mycobacterial Disease (MSMD) and Viral infection.
- For specific Mendelian Susceptilibility to Mycobacterial disease (MSMD) and viral infection subpanels (MSMD sever phenotypes, MSMD moderate phenotypes, Epidermodysplasia verruciformis (HPV), Predominant suscebtibility to viral infection – Herpes simplex Encephalitis, Predisposition to severe viral infection), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

MISCELLANEOUS AUTOINFLAMMATORY CONDITIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ADA2, AIRE, AP1S3, CASP10, CASP8, COPA, COL7A1, CPT2, FAS, FASLG, FLNA, HTR1A, IL10, IL10RB, IL12B, IL12RB1, IL1RN, IL36RN, ISG15, LACC1, LPIN2, LRBA, LYN, MASP2, MAT2A, MBL2, MEFV, MVK, MYD88, NLRC4, NLRP1, NLRP12, NLRP3, NLRP6, NLRP7, NOD2, NRAS, OTULIN, PRKCD, PLCG2, POMP, PRG4, PSMA3, PSMB4, PSMB8, PSMB9, PSTPIP1, RAG1, RANBP2, SCN9A, SERPING1, SH2D1A, SH3BP2, TMEM173, TNFAIP3, TNFRSF11A, TNFRSF1A, TRAP1, TRNT1, USB1, WDR1*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website.

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology
- Rheumatology

NEUTROPENIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*C16ORF57 (USB1), CLPB, COH1 (VPS13B), CSF3R, DNAJC21, ELANE, G6PC3, G6PT1 (SLC37A4), GFI1, HAX1, HYOU1, JAGN1, LAMTOR2, MKL1 (MRTFA), SBDS, SMARCD2, TAZ, VPS45, WAS, WDR1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Neutropenia.
- For specific Neutropenia subpanels (Schwachman-Diamond Syndrome, G6PC3 deficiency, Glycogen storage diasease type 1b, Cohen syndrome, Barth Syndrome, Clericuzio syndrome, VPS45 deficiency, P14/LAMTOR2 deficiency, JAGN1 deficiency, 2-Methylglutaconic aciduria, SMARCD2 deficiency, WDR1 deficiency, HYOU1 deficiency, No syndrome associated), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

OTHER ANTIBODY DEFICIENCIES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*AICDA*, *CARD11*, *IGKC*, *INO80*, *MSH6*, *UNG*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Other Antibody Deficiencies.
- For specific Other antibody deficiencies subpanels (Hyper IgM Syndromes; Isotype, Light Chain, or Functional Deficiencies; High Bc), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

PURINE NUCLEOSIDE PHOSPHORYLASE DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*PNP*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Autoimmune hemolytic anaemia
- Neurological impairment.
- Hypouricemia.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

SEVERE COMBINED IMMUNODEFICIENCY (SCID)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ADA, AK2, CD3D, CD3E, CD247, CORO1A, DCLRE1C (ARTEMIS), FOXN1, IL2RG, IL7R, JAK3, LIG4, NHEJ1, PRKDC, PTPRC, RAG1, RAG2*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- CD3 T cell lymphopenia: CD3+ T cells <300/µl.
- For specific SCID subpanels (SCID T-B+ CD19 normal, SCID T-B- CD19 low), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

STAT5B DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*STAT5B*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Growth-hormone insensitive dwarfism
- Dysmorphic features
- Eczema
- Lymphocytic interstitial pneumonitis
- Autoimmunity
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

STROKE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CBS*, *CST3*, *GLA*, *HTRA1*, *NOTCH3*, *ADA2*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Stroke.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website.

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology
- Rheumatology

SYNDROMES ASSOCIATED WITH AUTOIMMUNITY AND OTHERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*AIRE, BACH2, CASP8, CASP10, CTLA4, FADD, FOXP3 (IPEX), IL2RA, IL10, IL10RA, IL10RB, ITCH, JAK1, LRBA, NFAT5, PEPD, STAT3, TNFRSF6 (FAS), TNFSF6 (FASLG), TPP2, ZAP70*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Syndromes associated with autoimmunity and others.
- For specific Syndrome associated with Autoimmunity and others subpanels (Syndromes with autoimmunity with increased CD4-CD8-TCRα/β ALPS, Syndromes with autoimmunity with occasionally increased CD4-CD8-TCRα/β, Syndromes with autoimmunity without increased CD4-CD8-TCRα/β and without regulatory T Cell defects, Syndromes with autoimmunity without increased CD4-CD8-TCRα/β and with regulatory T Cell defects, Immune dysregulation with Colitis), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

SYNDROMES ASSOCIATED WITH CONGENITAL DEFECTS OF PHAGOCYTES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACTB, CEBPE, CSFR2A, CSFR2B, CTSC, FERMT3 (LADIII), FPR1, GATA2, G6PD, ILGB2 (LAD1), RAX2, SLC35C1 (LADII)*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Syndromes associated with Congenital Defects of Phagocytes.
- For specific Syndrome associated with congenital defects of phagocytes subpanels (Papillion-Lefevre, Localised juvenile periodontitis, β-Actin, Leukocyte adhesion deficiency / LAD, MonMac syndrome, Specific granule deficiency, Pulmonary alveolar proteinosis, RAC2 deficiency, G6PD deficiency Class 1), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

THYMIC DEFECTS WITH CONGENITAL ANOMALIES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CDH7, SEMA3E, TBX1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Thymic Defects with Congenital Anomalies.
- For specific Thymic defects with Congenital anomalies subpanels (TBX1 deficiency, Charge syndrome), please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

VASCULOPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACTA2, BMPR2, COL3A1, COL4A1, COL5A1, COL5A2, EFEMP2, ELN, FBN1, FBN2, FOXE3, GUCA1B, LMNA, LOX, MFAP5, MYH11, MYLK, NOTCH1, PLOD1, PRKG1, RHOD, RNF213, SKI, SLC2A10, SMAD2, SMAD3, SMAD4, STX11, STXBP2, TGFB2, TGFB3, TGFBI, TGFBR1, YY1AP1*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Vasculopathy.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website.

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology
- Rheumatology

VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE (VEO-IBD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ADAM17, AICDA, CD40LG, BTK, CD3G, ZAP70, WAS, CYBA, CYBB, NCF1, NCF2, NCF4, DOCK8, EPCAM (Sanger only), FOXP3, GUCY2C, HPS1, HPS4, HPS6, ADA, IL2RG, LIG4, DCLRE1C, RAG2, IL10, Il10RA, IL10RB, ITGB2, LRBA, ICOS, PIK3R1, PLCG2, RET, SH2D1A, XIAP, SKIV2L, TTC37, SLC37A4, STAT1, STAT3, STXBP2*	112
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Clinical features suggestive of a monogenic cause of Very Early Onset Inflammatory Bowel Disease (VEO-IBD).
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website.

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology
- Rheumatology

VICI SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*EPG5*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Agenesis of the corpus callosum
- Cataracts
- Cardiomyopathy
- Skin hypopigmentaon
- Intellectual disability
- Microcephaly
- CMC
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Haematology
- Immunology

X-LINKED CGD

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*CYBB*	56
Family member testing		as indicated above			14
Proforma required?		YES	GEN FORM 215 Primary Immunodeficiency Request form (see centre website)		

REFERRAL CRITERIA

- Suggestive of X linked transmission.
- Early onset of severe and recurrent infections affecting initially the natural barriers of the organism (lungs, lymph nodes, skin), and eventually inner structures (liver, spleen, bones, brain, and +++ hepatic abscess).
- Autoinflammatory phenotype.
- IBD.
- Please refer to GEN FORM 215 Primary Immunodeficiency Request form on centre website and IUIS 2017 (J Clin Immunol., 2018 38:129–143).

REQUESTING SPECIALTIES

- Clinical Genetics
- Immunology

INHERITED CANCER

COLORECTAL CANCER

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*APC, BMPR1A, MBD4, MLH1, MSH2, MSH3, MSH6, MUTYH, NTHL1, PMS2, POLD1* (exons 4-12), *POLE* (exons 3-13), *PTEN, RNF43, SMAD4, STK11*	56
Family member testing		as indicated above			14
Proforma required?		YES	Colorectal cancer gene panel proforma (see centre website)		

REFERRAL CRITERIA

- Living affected individual (proband) with colorectal cancer with:
  - a. Diagnosed aged <30 OR
  - b. Personal/family history of colorectal cancers reaching Amsterdam Criteria ($\geqslant$3 cases over $\geqslant$2
- Deceased affected individual (proband) where (i) the individual +/- family history meets one of the above criteria, (ii) appropriate tissue is available (tumour or normal) and (iii) no living affected individual is available for genetic testing.
- The proband's cancer and majority of reported cancers in the family should have been confirmed

REQUESTING SPECIALTIES

- Clinical Genetics

COWDEN SYNDROME / PTEN HAMARTOMA TUMOUR SYNDROME (PHTS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Glasgow	NGS	Whole gene screen	SNVs, indels Exon level CNV	*PTEN*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Proband and / or family history meets one of the following criteria:
  - Mucocutaneous lesions comprising
    - ≥ 6 facial papules, of which ≥ 3 are trichilemmoma
    - Cutaneous facial papules AND oral mucosal papillomatosis
    - Oral mucosal papillomatosis AND acral keratosis
    - ≥6 palmoplantar keratosis
  - Cerebellar dysplastic gangliocytoma (Adult Lhermitte-Duclos disease)
  - ≥2 major criteria of which should be macrocephaly
  - ≥1 major criteria and ≥ 1 PTEN-HTS-related mucocutaneous lesion
  - ≥1 major and ≥ 3 minor criteria
  - Macrocephaly ≥99th centile AND ≥ 1 minor criteria
  - ≥ 1 PHTS-related mucocutaneous lesion
  - ≥ 4 minor criteria
  - ≥ 1 major criteria, AND ≥ 2 first / second degree relatives each with:
    - ≥ 1 major criteria, OR ≥ 1 PHTS-related mucocutaneous lesion, OR
    - ≥ 2 minor criteria (multiple cases of breast cancer are not eligible for inclusion)

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology
- Neurology
- Paediatrics

DICER1 SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*DICER1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Testing of affected individual (proband) where the individual has one of the following diagnoses:
    - Pleuropulmonary blastoma or Lung cyst(s) in childhood, especially if multi-septated, multiple or bilateral; Thoracic, uterine, cervical or ovarian embryonal rhabdomyosarcoma; Cystic nephroma; Genitourinary sarcoma including undifferentiated sarcoma in childhood; Ovarian Sertoli Leydig tumour; Gynandroblastoma; Genitourinary/gynaecologic neuroendocrine tumors; Childhood-onset multinodular goitre or differentiated thyroid cancer (papillary or follicular); Ciliary body medulloepithelioma; Nasal chondromesenchymal hamartoma; Pineoblastoma; Pituitary blastoma, OR
- Testing of affected individual where there is a combination of two of the following diagnoses, either both in one affected individual or in two affected first degree relatives;
    - Lung cyst(s) in adults; Wilms tumor; Multinodular goiter or differentiated thyroid cancer; Embryonal rhabdomyosarcoma other than thoracic or gynaecologic; Poorly differentiated neuroendocrine tumour; Undifferentiated sarcoma; Macrocephaly

REQUESTING SPECIALTIES

- Clinical Genetics

FAMILIAL MELANOMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*BAP1*, *BRCA2*, *CDKN2A*, *CDK4*, *POT1*	56
Family member testing		as indicated above			14
Proforma required?		YES	Inherited cancer proforma (see centre website)		

REFERRAL CRITERIA

- Testing of phenotypically affected individual (proband) where the individual +/- family history meets one of the following criteria. The proband has:
  - ⩾2 melanomas in situ age < 30 OR
  - Melanoma in situ AND >/= 2 relatives (first / second / third degree) with melanoma in situ OR
  - Melanoma in situ AND >/= 1 first degree relative with melanoma in situ; one individual has multiple melanomas in situ OR
  - 1 Melanoma in situ OR melanoma in situ and atypical moles AND >/=1 first degree relative with pancreatic cancer < 60 OR
  - Atypical moles AND >/= 2 relatives (first / second degree relatives) with melanoma in situ

REQUESTING SPECIALTIES

- Clinical Genetics
- Oncology

GORLIN SYNDROME (BASAL CELL NEVUS SYNDROME)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*PTCH1, SUFU*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Living individual affected (proband) where the individual history meets:
  - ⩾ 2 major and ⩾ 1 minor criteria OR
  - ⩾ 1 major and ⩾ 3 minor criteria
- Major criteria:
  - Lamellar (sheet-like) calcification of the falx or clear evidence of calcification in an individual younger than age 20 years
  - Jaw keratocyst: odontogenic keratocyst histologically
  - Palmar/plantar pits (two or more)
  - SHH medulloblastoma, confirmed on tumour testing
  - Multiple basal cell carcinomas (BCCs) (>5 in a lifetime) or BCC before age 30 years
- Minor criteria:
  - Childhood medulloblastoma where SHH pathway in tumour has not been investigated (also called primitive neuroectodermal tumor [PNET])
  - Lympho-mesenteric or pleural cysts
  - Macrocephaly (OFC >97th centile)
  - Cleft lip/palate
  - Vertebral/rib anomalies observed on chest x-ray and/or spinal x-ray; bifid/splayed/extra ribs; bifid vertebrae
  - Preaxial or postaxial polydactyly
  - Ovarian/cardiac fibromas
  - Ocular anomalies (cataract, developmental defects, and pigmentary changes of the retinal epithelium)

REQUESTING SPECIALTIES

- Clinical Genetics

HEREDITARY BREAST CANCER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Glasgow	NGS	Whole gene screen	SNVs, indels Exon level CNV	*BRCA1, BRCA2, TP53, PTEN, PALB2, STK11, CHEK2, ATM, RAD51C, RAD51D*	56
Family member testing		as indicated above			14
Proforma required?		YES	Glasgow laboratory only (see centre website)		

REFERRAL CRITERIA

- Breast Cancer diagnosed <40 years
- Bilateral breast cancer, both <60 years
- Triple negative breast cancer, <60 years
- Male breast cancer, any age
- Two 1st degree relatives both diagnosed before the age of 45 years
- Manchester score of 15 / CanRisk score of 10%

REQUESTING SPECIALTIES

- Breast Surgeons
- Clinical Genetics
- Oncology

HEREDITARY BREAST / OVARIAN CANCER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Glasgow	NGS	Whole gene screen	SNVs, indels Exon level CNV	*BRCA1, BRCA2, TP53, PTEN, PALB2, STK11, RAD51C, RAD51D, BRIP, MSH2, MSH6, MLH1, CHEK2, ATM*	56
Family member testing		as indicated above			14
Proforma required?		YES	Glasgow laboratory only (see centre website)		

REFERRAL CRITERIA

- Breast and Ovarian cancer, any age
- Breast cancer (meeting breast panel criteria) with family history of ovarian cancer
- High-grade epithelial ovarian cancer, any age with a family history of breast cancer
- Manchester score of 15 / CanRisk score of 10%

REQUESTING SPECIALTIES

- Clinical Genetics
- Oncology

HEREDITARY OVARIAN CANCER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Glasgow	NGS	Whole gene screen	SNVs, indels Exon level CNV	*BRCA1*, *BRCA2*, *RAD51C*, *RAD51D*, *BRIP*, *MSH2*, *MSH6*, *MLH1*, *PALB2*	56
Family member testing		as indicated above			14
Proforma required?		YES	Glasgow laboratory only (see centre website)		

REFERRAL CRITERIA

- High-grade non-mucinous ovarian cancer, any age

  N.B. *BRCA1* and *BRCA2* testing in the tumour is also available, specifically for platinum sensitive high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer (FIGO stage III or stage IV). Please refer to the Scottish Molecular Pathology Laboratory Consortium Genomic Test Directory.

REQUESTING SPECIALTIES

- Clinical Genetics
- Oncology

HEREDITARY PROSTATE CANCER

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS *HOXB13* Sanger	Whole gene screen	SNVs, indels Exon level CNV	**BRCA1, BRCA2, ATM, HOXB13* ***BRCA1, BRCA2, CHEK2, ATM, TP53, MLH1, MSH2, MSH6, RAD51D, PMS2, EPCAM, HOXB13. PALB2* included where there is a family history of breast cancer	56
Family member testing		as indicated above			14
Proforma required?		YES	Prostate cancer proforma (see centre website)		

REFERRAL CRITERIA

- A man with prostate cancer diagnosed below the age of 50 years*
- A man with metastatic prostate cancer diagnosed below 60 years with one first degree relative (a brother or a father) diagnosed with prostate cancer below 60 years*
- A man diagnosed with metastatic prostate cancer with two first degree relatives (or one first and one second degree relative who are all first degree relatives of each other) with prostate cancer (patient and two brothers/ patient + 1 brother and father/ patient, father and father's brother/ patient, father & father's father)*
- A man with prostate cancer who has a family history of cancer with a Manchester score greater than or equal to 15**

REQUESTING SPECIALTIES

- Clinical Genetics
- Oncology in discussion with Clinical Genetics

JUVENILE POLYPOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS MLPA	Whole gene screen	SNVs, indels Exon level CNV	*SMAD4*, *BMPR1A*	56
Family member testing		as indicated above			14
Proforma required?		YES	Colorectal cancer gene panel proforma (see centre website)		

REFERRAL CRITERIA

- Juvenile polyposis syndrome:
  - a. ⩾ 5 juvenile polyps of the colorectum, OR
  - b. ⩾ 2 juvenile polyps throughout the GI tract, OR
  - c. ⩾ 1 juvenile polyp and a first / second degree relative has juvenile polyp, OR criteria

REQUESTING SPECIALTIES

- Clinical Genetics
- Oncology

LI-FRAUMENI SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Glasgow	NGS	Whole gene screen	SNVs, indels Exon level CNV	*TP53*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Proband and / or family history meets one of the following criteria:
  - Rhabdomyosarcoma (≤5 years)
  - Adrenocortical cancer (any age)
  - Choroid plexus cancer (any age)
  - Breast cancer (≤30 years)
  - Triple positive breast cancer (≤35 years)
  - ≥2 LFS-related cancers* (both occurring ≤46 years; 2 breast cancers not eligible)
  - ≥1 LFS-related cancer* with ≥1 1st / 2nd degree relative with ≥1 LFS-related cancer* (one case ≤46 years, the other ≤56 years; 2 breast cancers not eligible)
  - Cancer with ≥2 1st / 2nd degree relatives with cancer (sarcoma ≤45 years, any cancer ≤45 years and sarcoma or any cancer ≤45 years)

  * Sarcoma of bone/soft tissue, breast cancer, brain cancer, adrenocortical cancer or any childhood cancer (occurring ≤ 18 years)

REQUESTING SPECIALTIES

- Clinical Genetics
- Oncology

LYNCH SYNDROME (HNPCC)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS MLPA	Whole gene screen	SNVs, indels Exon level CNV	*MLH1, MSH2, MSH6, PMS2, EPCAM* (del exons 8-9), *POLD1* (exons 4-12), *POLE* (exons 3-13)	56
Family member testing		as indicated above			14
Proforma required?		YES	Colorectal cancer gene panel proforma (see centre website)		

REFERRAL CRITERIA

- Clinical Criteria for germline testing in an affected individual
  - a. The proband has a dMMR tumour where results of BRAF and/or MLH1 hypermethylation testing suggest Lynch syndrome
  - b. The proband is diagnosed with colorectal cancer $\leqslant$ 40 , irrespective of the dMMR status of the tumour
  - c. The affected proband comes from a modified Amsterdam criteria positive family irrespective of the dMMR status of the tumour
  - d. (Wimmer score =>3)

- Clinical Criteria for germline testing in an unaffected individual
  - a. First degree relative affected with Lynch-related cancer, AND
  - b. Family history of colorectal cancer/Lynch-related cancers reaches Amsterdam Criteria ($\geqslant$3 cases over $\geqslant$2 generations with $\geqslant$1 case affected $\leqslant$50 years) AND
  - c. Tumour sample analysis from affected family member has been attempted and is not possible, failed, indeterminate or indicates MMR deficiency (via IHC or MSI), AND
  - d. Somatic sequencing is not possible, or failed, AND
  - e. No living affected individual is available for genetic testing

REQUESTING SPECIALTIES

- Clinical Genetics

MEDULLARY THYROID CANCER

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Targeted screen	SNVs, indels	*RET* (exons 5, 8, 10, 11, 13, 14, 15, 16)	56
Family member testing		as indicated above			14
Proforma required?		YES	Endocrine disorders proforma (see centre website)		

REFERRAL CRITERIA

- Medullary thyroid cancer (MTC) at any age.
- See entry for Multiple Endocrine Neoplasia Type 2A, Type 2B and Medullary Thyroid Cancer

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology

PEUTZ-JEGHERS SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS MLPA	Whole gene screen	SNVs, indels Exon level CNV	*STK11*	56
Family member testing		as indicated above			14
Proforma required?		YES	Colorectal cancer gene panel proforma (see centre website)		

REFERRAL CRITERIA

- Living affected individual (proband) where the individual +/- family history meets one of the criteria.
    - 1. ≥2 PJS-type hamartomatous polyps, OR
    - 2. ≥1 PJS-type hamartomatous polyp and characteristic mucocutaneous pigmentation, OR
    - 3. Characteristic mucocutaneous pigmentation age
    - 4. Sex cord tumours with annular tubules (SCAT) at any age
    - 5. Adenoma malignum of the cervix at any age
    - 6. ≥1 PJS-type hamartomatous polyp, AND ≥1 first / second degree relative with: a. ≥1 PJS-like feature, OR b. ≥2 PJS-related cancers (the two cancers can be in the same or different relatives), OR
    - 7. Characteristic mucocutaneous pigmentation, AND ≥1 first / second degree relative with: a≥1 PJS-like feature, OR b. ≥2 PJS-related cancers (the two cancers can be in the same or different relatives)
- Deceased affected individual (proband) where (i) the individual +/- family history meets one of the above criteria, (ii) appropriate tissue is available (tumour or normal), and (iii) no living affected individual is available for genetic testing PJS-like features: characteristic mucocutaneous pigmentation, PJS-type hamartomatous polyps PJS-related cancers: epithelial colorectal, gastric, pancreatic, breast, and ovarian cancers, sex cord tumors with annular tubules (SCTAT), adenoma malignum of the cervix, and Sertoli cell tumors (LCST) of the testes
- The majority of polyps should be histologically confirmed

REQUESTING SPECIALTIES

- Clinical Genetics

POLYPOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*APC*, *BMPR1A*, *MBD4*, *MSH3*, *MUTYH*, *NTHL1*, *POLD1* (exons 4-12), *POLE* (exons 3-13), *PTEN*, *RNF43*, *SMAD4*, *STK11*, *GREM1* (upstream dup)	56
Family member testing		as indicated above			14
Proforma required?		YES	Colorectal cancer gene panel proforma (see centre website)		

REFERRAL CRITERIA

- ≥5 polyps and colorectal cancer (<60 years) OR
- ≥10 polyps (age <60 years), OR
- ≥20 polyps (age ≥ 60 years), OR
- ≥5 polyps AND first degree relative with ≥5 polyps OR CRC (age <60years), OR
- ≥10 polyps (age ≥ 60 years) AND first degree relative with ≥5 polyps OR CRC (age <60years).

Please note small hyperplastic rectal polyps can be ignored/not included in the count.

Additional testing for:

- Desmoid tumour (*APC* and *MUTYH*)
- CHRPEs (*APC* only)
- Mosaic FAP: indicated if phenotype consistent with a diagnosis of FAP or attenuated FAP and result will impact on clinical management of relatives.

REQUESTING SPECIALTIES

- Clinical Genetics

RENAL CANCER

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels, Exon level CNV for *FLCN*, *VHL*, *SDHB*	*BAP1*, *FH*, *FLCN*, *MET*, *PTEN*, *SDHB*, *VHL*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals with:
  - Renal cancer (≤ 40 years), OR
  - Type 2 papillary renal cancer (≤50 years), OR
  - Bilateral/multifocal or unusual pathology renal cancer (any age), OR
  - Renal cancer AND first / second degree relative with renal cancer
  - Renal cancer and features of an inherited renal cancer syndrome

REQUESTING SPECIALTIES

- Clinical Genetics

RHABDOID TUMOUR

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*SMARCA4*, *SMARCB1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Child with atypical teratoid / rhabdoid tumouor (ATRT) or malignant rhabdoid tumour (MRT) showing loss of SMARCB1 on immunohistochemistry OR
- Small cell carcinoma of the ovary, hypercalcaemic type (SCCOHT) (any age)

REQUESTING SPECIALTIES

- Clinical Genetics

METABOLIC

AMINO ACID DISORDERS & DISORDERS OF NEUROTRANSMISSION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ABAT, ALDH18A1, ALDH5A1, ALDH7A1, AMT, ASPA, CBS, CTH, D2HGDH, DBH, DDC, FAH, GABRG2, GCDH, GCH1, GLDC, GLRA1, HGD, L2HGDH, MAT1A, OAT, PAH, PCBD1, PNPO, QDPR, SLC25A22, SLC6A19, SLC7A7, SUOX*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype suggests an amino acid disorder or disorder of neurotransmission
- Biochemical testing supportive (abnormal urine or plasma amino acid profile, abnormal urine organic amino acid profile)
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

BATTEN DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*TPP1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Batten disease
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

BIOTINIDASE DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*BTD*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals where newborn screening or biochemical findings indicate multiple carboxylase deficiency.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

BIOTIN-THIAMINE-RESPONSIVE BASAL GANGLIA DISEASE (BTBGD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*SLC19A3*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of BTBGD
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

CARNITINE PALMITOYLTRANSFERASE II DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*CPT2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Carnitine Palmityltransferase II deficiency
- Biochemical tests supportive of diagnosis (Hypoketotic hypoglycaemia)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

CEREBRAL FOLATE TRANSPORT DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*FOLR1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Cerebral Folate Transport Deficiency
- Biochemical tests supportive of diagnosis (Vitamin B9 deficiency)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

CITRULLINAEMIA TYPE 1

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*ASS1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Citrullinaemia Type 1
- Biochemical tests supportive of diagnosis (Abnormal plasma amino acid profile)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

COBALAMIN C DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*MMACHC*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Cobalamin C Deficiency
- Biochemical tests supportive of diagnosis (Vitamin B12 deficiency)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

CREATINE DEFICIENCY SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels	*GATM, GAMT, SLC6A8*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Creatine Deficiency Syndrome
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

DISORDERS ASSOCIATED WITH HYPERAMMONAEMIA / FATTY ACID OXIDATION / KETOGENESIS / KETOLYSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACADM, ACADS, ACADVL, ARG1, ASL, ASS1, CPS1, CPT1A, CPT2, ETFA, ETFB, ETFDH, GLUD1, HADHA, HADHB, HMGCL, HMGCS2, IVD, MMAA, MMAB, MMACHC, MMADHC, MUT, NAGS, OAT, OTC, OXCT1, PCCA, PCCB, SLC22A5, SLC25A13, SLC25A15, SLC25A20, SLC7A7, SLC52A2, SLC52A3*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Disorders associated with Hyperammonaemia / Fatty Acid Oxidation / Ketogenesis / Ketolysis (e.g. encephalopathy, severe vomiting or loss of consciousness)
- Biochemical tests supportive of diagnosis (Plasma ammonia >150umol/L or Hypoketotic hypoglycaemia or severe ketoacidosis)
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

DISORDERS OF CARBOHYDRATE METABOLISM (incl. GLYCOGEN STORAGE DISORDERS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*AGL, ALDOA, ENO3, EPM2A, FBP1, G6PC, G6PC3, GAA, GALE, GALK1, GALT, GBE1, GYG1, GYS1, GYS2, LAMP2, LDHA, NHLRC1, PFKM, PGAM2, PGK1, PGM1, PHKA1, PHKA2, PHKB, PHKG2, PRKAG2, PYGL, PYGM, SLC2A2, SLC37A4*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a disorder of carbohydrate metabolism
- Biochemical or haematological tests supportive of diagnosis (e.g. Abnormal liver function, abnormal muscle physiology, hypoglycaemia, hypobilirubinaemia, presence of urinary reducing substances, reduced GALT, GALE activity in blood, abnormal CSF:blood glucome ratio)
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

FABRY DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger	Whole gene screen	SNVs, indels	*GLA*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- In males: clinical and laboratory features characteristic of Fabry disease following alpha-galactosidase A enzyme testing
- In females: clinical features characteristic of Fabry disease

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

FAMILIAL HYPERCHOLESTEROLAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV* (**LDLR* only)	*LDLR,APOE, PCSK9, APOB, LDLRAP1*	56
Family member testing		as indicated above			14
Proforma required?		NO	Optional FH proforma on centre website		

REFERRAL CRITERIA

- Total cholesterol >7.5 mmol/l (>6.7mmol/l in a child < 16 years) or LDL cholesterol >4.9 mmol/l (>4 mmol/l in a child < 16 yrs)

AND one or more of the following:

- Tendon xanthomas in the index individual or Tendon xanthomas in a 1st or 2nd degree relative
- Family history of myocardial infarction: in 2nd degree relative <50 yrs or in 1st degree relative < 60 yrs
- . Family history of raised total cholesterol: >7.5mmol/l in an adult 1st or 2nd degree relative or >6.7 mmol/l in a child or sibling < 16 yrs

Secondary causes of hypercholesterolaemia should be excluded (diabetes, thyroid disease, abnormal LFTs). If in doubt, please seek advice from your local lipid clinic.

REQUESTING SPECIALTIES

- Cardiologists
- Clinical Genetics
- GPs
- Lipidology
- Metabolic

FANCONI-BICKEL SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*SLC2A2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Fanconi Bickel Syndrome
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

FATTY ACID OXIDATION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACADM, ACADS, ACADVL, CPT1A, CPT2, ETFA, ETFB, ETFDH, HADHA, HADHB, HMGCL, HMGCS2, IVD, MMAA, MMAB, MMACHC, MMADHC, OXCT1, SLC22A5, SLC25A20, SLC52A2, SLC52A3*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a Fatty Acid Oxidation disorder
- Biochemical tests supportive of diagnosis
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic
- Neurology

GALACTOSAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*GALT*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Galactosaemia
- Biochemical tests supportive of diagnosis (Increase galactose in blood)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

GAUCHER DISEASE (B-GLUCOCEREBROSIDASE DEFICIENCY)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*GBA*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Gaucher disease
- Biochemical tests supportive of diagnosis (Decreased glucocerebrosidase enzyme levels)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

GLUTARIC ACIDAEMIA TYPE 1

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*GCDH*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Glutaric Acidaemia Type 1
- Biochemical / newborn screen test supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

GLYCEROL KINASE DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*GK*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Glycerol Kinase Deficiency
- Biochemical tests supportive of diagnosis (Glycerol peak in urine sample)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

GLYCOGEN STORAGE DISEASE 1A

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*G6PC*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Glycogen Storage Disease 1A
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

HOMOCYSTINURIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CBS, MMADHC, MTHR, MTR, MTRR*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Homocysteinuria
- Biochemical tests supportive of diagnosis (High homocysteine levels in blood)

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

HYPERLIPIDAEMIA, TYPE III

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Targeted screen	SNVs	*APOE* (Codons p.130 and p.176)	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Hyperlipidaemia Type III, e.g. accelerated atherosclerosis
- Biochemical tests supportive of diagnosis (Elevated cholesterol and triglycerides)

REQUESTING SPECIALTIES

- Clinical Genetics
- Lipidology

HYPERTRIGLYCERIDAEMIA / FAMILIAL CHYLOMICRONAEMIA SYNDROME / LIPOPROTEIN LIPASE DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV* (**LPL* only)	*LPL, LMF1, APOC2, APOA5, GPI-HBP1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of hypertriglyceridaemia, e.g. recurrent pancreatitis,eruptive xanthomas, lipaemia retinalis.
- Biochemical tests supportive of diagnosis (Elevated triglycerides >20mmol/L)

REQUESTING SPECIALTIES

- Clinical Genetics
- Gastrohepatology
- Lipidology

HYPOBETALIPOPROTEINAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ANGPTL3, APOB, MTTP, PCSK9, SAR1B*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Hypobetalipoproteinaemia
- Biochemical tests supportive of diagnosis (Undetectable / low levels of ApoB)

REQUESTING SPECIALTIES

- Clinical Genetics
- Lipidology

LYSOSOMAL STORAGE DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*AGA, ARSA, ARSB, ASAH1, CLN3, CLN5, CLN6, CLN8, CTNS, CTSA, CTSD, CTSK, DNAJC5, FUCA1, GAA, GALC, GALNS, GBA, GLA, GLB1, GM2A, GNE, GNPTAB, GNPTG, GNS, GUSB, HEXA, HEXB, HGSNAT, IDS, IDUA, LIPA, MAN2B1, MANBA, MCOLN1, MFSD8, NAGA, NAGLU, NEU1, NPC1, NPC2, PPT1, PSAP, SGSH, SLC17A5, SMPD1, SUMF1, TPP1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a Lysosomal storage disorder
- Biochemical tests supportive of diagnosis (Abnormal urine MPS, oligosaccharide screen, white cell enzyme analysis)
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

MAPLE SYRUP URINE DISEASE (MSUD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*BCKDHA, BCKDHB, DBT*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Maple Syrup Urine Disease
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

MEDIUM CHAIN ACYL-COA DEHYDROGENASE DEFICIENCY (MCADD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger	Whole gene screen	SNVs, indels Exon level CNV	*ACADM*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of MADD
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic
- Paediatrics

METACHROMATIC LEUKODYSTROPHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*ARSA*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Metachromatic Leukodystrophy
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

MUCOPOLYSACCHARIDOSIS TYPE 1 (HURLER / SCHEIE SYNDROME)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*IDUA*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Mucopolysaccharidosis Type 1
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

MUCOLIPIDOSIS II & III ALPHA / BETA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*GNPTAB*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Mucolipidosis II & III Alpha / Beta.
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

MULTIPLE ACYL-CoA DEHYDROGENASE DEFICIENCY (MADD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ETFDH, ETFA, ETFB, SLC52A2, SLC52A3*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of MADD
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic
- Neurology

NEURONAL CEROID LIPOFUSCINOSIS (NCL)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*CLN3, CLN5, CLN6, CLN8, CTSD, DNAJC5, KCTD7, MFSD8, PPT1, TPP1*	56
Family member testing		as indicated above			14
Available genes: See website					
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Neuronal Ceroid Lipofuscinosis
- Haematological / Biochemical tests supportive of diagnosis (Demonstration of vacuolated lymphocytes, presence of pathological inclusions on tissue biopsies, deficient enzyme activity)
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic
- Neurology

NIEMANN-PICK DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*NPC1, NPC2, SMPD1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Niemann Pick Disease
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

NIEMANN-PICK DISEASE TYPES A & B

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*SMPD1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Niemann Pick Disease Types A & B
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

NIEMANN-PICK DISEASE TYPES C1 & C2

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*NPC1, NPC2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Niemann Pick Disease Type C
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

NON KETOTIC HYPERGLYCINAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ALDH7A1, AMT, GLDC, PPT1, TPP1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Non ketotic hyperglycinaemia
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

ORGANIC ACIDAEMIAS & COFACTOR / VITAMIN DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ABCD4, ACSF3, AMN, AUH, BCKDHA, BCKDHB, BTD, CUBN, DBT, DHFR, DNAJC19, FOLR1, GIF, HCFC1, HLCS, IVD, LMBRD1, LPIN1, MCCC1, MCCC2, MCEE, MLYCD, MMAA, MMAB, MMACHC, MMADHC, MTHFD1, MTHFR, MTR, MTRR, MUT, OPA3, PCCA, PCCB, PRDX1, SLC19A3, SLC46A1, SLC52A3, SUCLA2, SUCLG1, TAZ, TCN2, TMEM70*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of an organic acidaemia or cofactor / vitamin disorder
- Biochemical tests supportive of diagnosis (abnormal results of urine organic acid or amino acid screen, anaemia, unexplained deficiency of a specific vitamin)
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

ORNITHINE AMINOTRANSFERASE DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*OAT*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Ornithine Aminotransferase Deficiency
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

ORNITHINE TRANSCARBAMULASE DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS MLPA	Whole gene screen	SNVs, indels Exon level CNV	*OTC*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of Ornithine Transcarbamulase Deficiency

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

PEROXISOMAL DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ABCD1, ACOX1, AGPS, AGXT, AMACR, CAT, DNM1L, GNPAT, HSD17B4, PEX1, PEX2, PEX3, PEX5, PEX6, PEX7, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX26, PHYH, SCP2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of a Peroxisomal disorder
    - At least 2 of the following: Hypoptonia / developmental delay, Characteristic facial dysmorphism, Characteristic X-ray findings (e.g. stippling), Retinal dystrophy / sensorineural hearing loss, Liver dysfunction
- Biochemical tests supportive of diagnosis (Increased plasma very long chain fatty acids +/- erythrocyte membrane plasmalogens)
- Where biochemical testing indicates testing of a single gene, please indicate this on the referral form and testing can be performed by either NGS or Sanger sequencing.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

PHENYLKETONURIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*PAH*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Elevated blood phenylalanine and low levels or absence of phenylalanine hydroxylase enzyme.
- Diagnosis of Phenylketonuria by Newborn screening.

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

POMPE DISEASE / GLYCOGEN STORAGE DISEASE TYPE 2

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*GAA*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Pompe disease
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

PROPRIONIC ANAEMIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*PCCA, PCCB*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Proprionic Anaemia
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

REFSUM DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*PEX7, PHYH*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Refsum disease
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

SUCCINIC SEMIALDEHYDE DEHYRDOGENASE DEFICIENCY (SSADH)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*ALDH5A1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Succinic Semialdehyde Dehydrogenase Deficiency (SSADH)
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

TANGO2-RELATED METABOLIC ENCEPHALOPATHY & ARRHYTHMIAS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen Long Range PCR	SNVs, indels Ex3-9 deletion	*TANGO2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of *TANGO2*-related metabolic encephalopathy & arrhythmias

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

TAY-SACHS DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*HEXA*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Tay-Sachs Disease
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

TRIMETHYLAMMINURIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger	Whole gene screen	SNVs, indels	*FMO3*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of Trimethyamminuria
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

VLCAD DEFICIENCY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	NGS	Whole gene screen	SNVs, indels Exon level CNV	*ACADVL*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of VLCAD Deficiency
- Biochemical tests supportive of diagnosis

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic

MITOCHONDRIAL

LEBER HEREDITARY OPTIC NEUROPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	Common LHON mitochondrial DNA variants (m.3460G>A, m.11778G>A, m.14484T>C)	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual suspected clinical diagnosis of Leber hereditary optic neuropathy
    - Bilateral painless subacute visual failure at a young age
    - Optic disk atrophy
    - Optic nerve dysfunction and absence of other retinal diseases

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic
- Neurology
- Ophthalmology

MITOCHONDRIAL DISORDERS (MERRF, NARP, DEAFNESS AND CARDIOMYOPATHY)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	Common mitochondrial DNA variants MT-TL1:m.3243A>G MT-TK:m.8344A>G MT-ATP6:m.8993T>G/C Plus others relevant to phenotype	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Possible mitochondrial disorder caused by mitochondrial DNA variants including individuals with clinical features suggestive of:
    - chronic progressive external ophthalmoplegia (CPEO)
    - Kearns-Sayre syndrome
    - myoclonic epilepsy with ragged red fibres (MERRF)
    - neuropathy, ataxia and retinitis pigmentosa (NARP)
    - maternally inherited Leigh syndrome (MILS)

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Metabolic
- Neurology
- Ophthalmology

MITOCHONDRIAL ENCEPHALOPATHY, LACTIC ACIDOSIS, AND STROKE-LIKE EPISODERS (MELAS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	MTTL1 m. 3243A>G	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- The most common initial symptoms are seizures, recurrent headaches, stroke-like episodes, cortical vision loss, muscle weakness, recurrent vomiting, and short stature
- Please send a urine sample for adults.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Metabolic
- Neurology

MITOCHONDRIAL INHERITED DIABETES AND DEAFNESS (MIDD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNV	MTTL1 m. 3243A>G	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Adult onset sensorineural hearing loss and diabetes or family history suggestive of a diagnosis of maternally inherited diabetes and deafness.
- Please send a urine sample for adults.

REQUESTING SPECIALTIES

- Clinical Genetics
- Endocrinology
- Metabolic

MUSCULOSKELETAL

BECKER MUSCULAR DYSTROPHY (BMD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	MLPA	Targeted screen	Exon level CNV	*DMD*	28
	Sanger	Whole gene screen	SNVs, indels	*DMD*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Progressive symmetric muscle weakness
  - Increase in serum concentration of creatine kinase (CK)
  - Calf hypertrophy
  - Cardiomyopathy

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics
- Neurology

CHONDRODYSPLASIA PUNCTATA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*AGPS, ARSE, EBP, GNPAT, PEX7*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Stippling involving the epiphyses of the long bones and vertebrae, the trachea and distal ends of the ribs seen on x-ray OR rhizomelia with stippling involving the epiphyses knee, hip, elbow, and shoulder
- OR biochemical evidence of Chondrodysplasia punctata

REQUESTING SPECIALTIES

- Clinical Genetics

DUCHENNE MUSCULAR DYSTROPHY (DMD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	MLPA	Targeted screen	Exon level CNV	*DMD*	28
	Sanger	Whole gene screen	SNVs, indels	*DMD*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Highly elevated serum concentration of creatine kinase (CK)
  - Delay in motor milestones/frequent falls.
  - Positive Gowers' sign
  - Progressive symmetric muscle weakness

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics
- Neurology

FGFR3 RELATED SKELETAL DYSPLASIA (incl. ACHONDROPLASIA, HYPOCHONDROPLASIA, THANATOPHORIC DYSPLASIA, MUENKE SYNDROME)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Sanger	Targeted screen	SNVs, indels	*FGFR3* (exons 7, 10, 13, 15, 19)	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features strongly suggestive of *FGFR3*-related skeletal dysplasias

REQUESTING SPECIALTIES

- Clinical Genetics
- Neonatology
- Orthopaedics
- Paediatrics

FIBRODYSPLASIA OSSIFICANS PROGRESSIVA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger	Targeted screen	SNVs	*ACVR1* (p.R206H)	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Congenital malformations of the great toes i.e.hallux valgus, malformed first metatarsal, and/or monophalangism.
- Progressive heterotopic ossification

REQUESTING SPECIALTIES

- Clinical Genetics
- Orthopaedics
- Paediatrics

HEREDITARY MULTIPLE OSTEOCHONDROMAS / MULTIPLE EXOSTOSES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*EXT1, EXT2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Growths of multiple osteochondromas

REQUESTING SPECIALTIES

- Clinical Genetics
- Orthopaedics
- Paediatrics

LIMB GIRDLE MUSCULAR DYSTROPHY (LGMD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger	Whole gene screen	SNVs, indels	*DES, FKRP*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Progressive weakness and atrophy of the Limb-Girdle muscles AND/OR
- Cardiomyopathy

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology
- Paediatrics

MYOTONIC DYSTROPHY TYPE 1 (DM1)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Edinburgh Glasgow	PCR & TP-PCR	Targeted screen	Triplet repeat expansion	*DMPK*	28 Prenatal 3
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype that could be consistent with (or "that raises suspicion of") myotonic dystrophy type 1. Suggestive features include
  - Hypotonic infant with or without joint contractures
  - Muscle myotonia
  - Muscle weakness
  - Presenile cataracts
  - Temporal muscle wasting and / or frontal balding
  - Adverse anaesthetic reaction
  - Family history of Myotonic Dystrophy
  - Unexplained excessive somnolence or cardiac conduction system abnormalities with additional features as above.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology
- Ophthalmology
- Paediatrics

MYOTONIC DYSTROPHY TYPE 2 (DM2)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	PCR & QP-PCR	Targeted screen	4bp repeat expansion	*ZNF9*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical phenotype consistent with a diagnosis of Myotonic Dystrophy Type 2 – muscle pain and stiffness, progressive muscle weakness (predominantly proximal and axial), myotonia

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

OCULOPHARYNGEAL MUSCULAR DYSTROPHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	PCR and Sanger	Targeted screen	Repeat expansion, SNV	*PABPN1* – GCN repeat expansion and c.35G>C	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features strongly suggestive of oculopharyngeal muscular dystrophy.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology
- Ophthalmology

OSTEOGENESIS IMPERFECTA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*BMP1, COL1A1, COL1A2, CREB3L1, CRTAP, FAM46A, FKBP10, IFITM5, P3H1 (LEPRE1), PLOD2, PLS3, PPIB, SERPINF1, SERPINH1, SP7, SPARC, TMEM38B, WNT1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Multiple fractures of long bones without significant trauma AND at least two of the following:
  - Wormian bones
  - Blue / grey sclera
  - Hearing loss
  - Ribs, broad and breaded, thin & irregular
  - Short stature
  - Dentinogenesis imperfect
  - Triangular face & narrow thorax
  - Round faces & short barrel-shaped chest

REQUESTING SPECIALTIES

- Clinical Genetics

OSTEOPETROSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*AMER1, ANKH, CA2, CLCN7, CTSK, FAM20C, FERMT3, LEMD3, LRP5, OSTM1, PTH1R, RASGRP2, SNX10, SOST, TCIRG1, TGFB1, TNFRSF11A, TNFSF11, TYROBP*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Characteristic radiographic changes

REQUESTING SPECIALTIES

- Adult Orthapaedics
- Clinical Genetics
- Paediatricis specialising in bone marrow transplantation, haematology, metabolic disease or orthapaedics

PRIMORDIAL DWARFISM, MICROCEPHALY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*NKRD11, ASPM, ATR; ATRIP, ATRX, BLM, CASK, CDC45, CDC6, CDKN1C, CDK5RAP2, CDT1, CENPE, CENPF, CENPJ, CEP135, CEP152, CEP63, CREBBP, DNA2, DNMT3A, DONSON, DPP6, DYRK1A, EP300, GMNN, IGF1, IGF1R, KIF11, KMT2A, KNL1, LARP7, LIG4, MCPH1, MRE11, NBN, NDE1, ORC1, ORC4, ORC6, PCNT, PHC1, PLK4, PNKP, POC1A, POLE, RAD50, RBBP8, RNU4ATAC, SMARCAL1, SRCAP, STIL, TCF4, TOP3A, TRAIP, TUBGCP6, VPS13B, WDR4, WDR62, XRCC4*	112
Family member testing		as indicated above			14
Proforma required?		YES	Primordial Dwarfism and Microcephaly gene panel referral proforma (see centre website)		

REFERRAL CRITERIA

- Normal microarray
- No history of intrauterine infection, birth hypoxia, teratogens
- OFC smaller than -3SD

REQUESTING SPECIALTIES

- Clinical Genetics

PROXIMAL SYMPHALANGISM

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*GDF5, NOG1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features strongly suggestive of proximal symphalangism

REQUESTING SPECIALTIES

- Clinical Genetics

RASOPATHIES
(incl. NOONAN, COSTELLO, CFC, LEGIUS SYNDROMES, NF1 AND NSML)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*BRAF, CBL, HRAS, KRAS, LZTR1, MAP2K1, MAP2K2, MRAS, NF1, NRAS, PPP1CB, PTP11, RAF1, RIT1, SHOC2, SOS1, SPRED1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- At least 2 of the suggestive clinical features:
  - Early feeding difficulty / failure to thrive
  - Relative macrocephaly
  - Short stature
  - Developmental disability

- At least 1 of:
  - Cardiomyopathy
  - Congenital heart disease
  - Arrhythmia
  - Suggestive malignancy (bladder carcinoma, Rhabdomyosarcoma, Leukaemia, phaeochromocytoma)
  - Skin abnormalities (hyperkeratosis, café au lait patches, ulerythema oophorogenes, keratosis pilaris, excess palmar skin)

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

SHORT STATURE, INCLUDING TURNER SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	Karyotype	Whole genome screen	Structural rearrangements CNV	Whole genome	28
	Microarray	Whole genome screen	CNV	Whole genome	28
Glasgow	Sanger	Whole gene screen	SNVs, indels	*SHOX*	56
Proforma required?		NO			

REFERRAL CRITERIA

- Disproportionate short stature

Other specific features may include

- Premature Ovarian Failure (Turner syndrome)
- Mesomelia and/or Madelung deformity (SHOX-deficiency disorders)

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

SKELETAL DYSPLASIA
(incl. KNIEST DYSPLASIA, CZECH DYSPLASIA, SPONDYLOPERIPHERAL DYSPLASIA, SPONDYLOENCHONDRODYSPLASIA, ACHONDROGENESIS, TYPE II OR HYPOCHONDROGENESIS, SPONDYLOEPIMETAPHYSEAL DYSPLASIA, WEILL-MARCHESANI SYNDROME 1)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ACAN, ACP5, ADAMTS10, ADAMTSL2, AGPS, ALPL, ANKH, ARSE, B3GALT6, BMP1, BMPR1B, CA2, CANT1, CDC6, CDKN1C, CDT1, CHST3, CLCN7, COL10A1, COL11A1, COL11A2, COL1A1, COL1A2, COL2A1, COL9A1, COL9A2, COL9A3, COMP, CRTAP, CTSK, CUL7, CYP27B1, DHCR24, DLL3, DYM, DYNC2H1, EBP, EIF2AK3, ENPP1, ESCO2, EVC, EVC2, FAM20C, FGF23, FGFR1, FGFR2, FGFR3, FKBP10, FLNA, FLNB, GDF5, GNPAT, GPC6, HSPG2, IFT122, IFT140, IFT43, IFT80, IHH, KAT6B, LBR, LEPRE1, LIFR, LMX1B, LRP5, LTBP2, MATN3, MMP9, NEK1, NPR2, OBSL1, ORC1, ORC4, ORC6, OSTM1, PAPSS2, PCNT, PEX7, PHEX, PLOD2, PPIB, PTH1R, RMRP, RNU4ATAC, ROR2, RUNX2, SBDS, SERPINF1, SERPINH1, SHOX, SLC26A2, SLC34A3, SLC35D1, SLC39A13, SMAD4, SMARCAL1, SNX10, SOX9, TCIRG1, TGFB1, TNFRSF11A, TNFRSF11B, TNFSF11, TRAPPC2, TRIP11, TRPV4, TTC21B, VDR, WDR19, WDR35, WISP3, WNT5A, XYLT1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Antenatal evidence (Ultrasound or other imaging modality) or Postnatal evidence of skeletal dysplasia (X ray and clinical examination)
- Multiple joint involvements (e.g. ephyseal or metaphyseal abnormalities)
- Short limbs (Long bone length-3SD below mean or serial measurement at or below 5th centile)
- Narrow thorax
- Poly and/or Oligodactyly
- Syndactyly
- Limb reduction defects
- Fractures of long bones
- Poor mineralisation of calvarium or spine

REQUESTING SPECIALTIES

- Clinical Genetics

SPINAL AND BULBAR MUSCULAR ATROPHY (SBMA)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	PCR & TP-PCR	Targeted screen	Triplet repeat expansion	*AR*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of SBMA

REQUESTING SPECIALTIES

- Clinical Genetics

NEUROLOGY

AICARDI-GOUTIERES SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ADAR, IFIH1, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, TREX1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals with a clinical presentation of the condition:
  - Newborns with a combination of features including enlarged liver and spleen (hepatosplenomegaly), elevated blood levels of liver enzymes, decreased platelets and neurological abnormalities. No evidence of viral infection
  - Children with encephalopathy, sterile pyrexias and seizures, developmental regression, microcephaly, white blood cells in CSF, calcification of the brain, spasticity, dystonia and hypotonia
  - Isolated 'spastic paraparesis'
  - Singleton Merten syndrome
  - Bilateral striatal necrosis
  - Familial chilblain lupus

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

NEUROMUSCULAR ARTHROGRYPOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*ACTA1, ADAMTS10, ANTXR2, ASCC1, ASXL1, B3GALNT2, B4GAT1, BICD2, CHAT, CHRNA1, CHRNB1, CHRND, CHRNE, CHRNG, CHST14, CNTNAP1, COL12A1, COL6A1, COL6A2, COL6A3, COLQ, DAG1, DNM2, DOK7, DPAGT1, DYNC1H1, ECEL1, ERCC6, ERCC8, EXOSC3, FAM20C, FBN2, FGFR2, FKBP10, FKRP, FKTN, GBA, GBE1, GLDN, GLE1, GMPPB, ADGRG6, HSPG2, ISPD, KLHL40, KLHL41, LAMA2, LARGE1, LMOD3, MAGEL2, MPZ, MTM1, MUSK, MYBPC1, MYH2, MYH3, MYH7, MYH8, NALCN, NEB, PEX1, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PFKM, PIEZO2, PLOD1, PLOD2, POMGNT1, POMGNT2, POMK, POMT1, POMT2, POR, PRG4, RAPSN, RYR1, SCARF2, SCN4A, SKI, SLC5A7, SMAD4, STAC3, SYNE1, TMEM5, TNNI2, TNNT1, TNNT3, TPM2, TPM3, TRPV4, TSEN54, UBA1, VAMP1, VIPAS39, VPS33B, ZC4H2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Antenatally detected joint contractures of more than two *different* joints OR Born with joint contractures of more than two *different* joints.
- All cases should have DM1 testing before panel testing.
- **Exclusion:** Isolated talipes. Finger contractures/camptodactyly with no other joint contractures

Please consider alternative appropriate panels in children with definite cognitive involvement, particularly those where arthrogryposis is mild or additional clinical features are present.

REQUESTING SPECIALTIES

- Clinical Genetics

CADASIL

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger	Whole gene screen	SNVs, indels	*NOTCH3*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Mid-adult onset of recurrent ischemic stroke
- Cognitive decline progressing to dementia
- A history of migraine with aura
- Diffuse white matter lesions and subcortical infarcts on neuroimaging

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

CAPILLARY MALFORMATIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*RASA1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Capillary malformations are the hallmark of capillary malformation-arteriovenous malformation (CM-AVM) syndrome.
- CV-AVM should be suspected in an individual with
    - CM, generally multifocal, small, composed of dilated capillaries, localised on face and limbs
    - AVMs in soft tissue, bone and brain and may be associated with overgrowth
    - Parkes Weber syndrome phenotype

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology
- Neurology

COGNITIVE CONDITIONS
(incl. ALS, FRONTOTEMPORAL DEMENTIA, MOTOR NEURONE DISEASE)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	Targeted screen	Repeat-primed PCR	Hexanucleotide repeat expansion	*c9ORF72*	28
Edinburgh	NGS	Whole gene screen	SNVs, indels	*ALS2, ANG, ANXA11, APP, CHMP2B, CSF1R, DCTN1, FIG4, FUS, GRN, ITM2B, MAPT, NEK1, OPTN, PFN1, PRNP, PSEN1, PSEN2, SETX, SOD1, SQSTM1, TARDBP, TBK1, UBQLN2, VAPB, VCP*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Young onset or familial neurodegeneration starting in adulthood with a likely monogenic cause, including:
    - 1. Unexplained dementia
        - a. Age at onset <55 years where acquired causes (e.g. stroke, tumour) have been excluded, OR
        - b. Family history of dementia of the same type in a first / second degree relative
- Amyotrophic lateral sclerosis (ALS) with or without frontotemporal dementia
    - a. Evidence of lower motor neuron (LMN) degeneration by clinical, electrophysiologic or neuropathologic examination, AND
    - b. Evidence of upper motor neuron (UMN) degeneration by clinical examination, AND c. Progressive course, AND
    - d. Age of onset

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

CORTICAL BRAIN MALFORMATIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ACTB, ACTG1, ADGRG1 (GPR56), AKT3, ARFGEF2, ARX, ASPM, B3GALNT2, CASK, CCND2, DAG1, DCX, DYNC1H1, EMX2,FKRP, FKTN, FLNA, GPSM2, GRIN1, ISPD, KATNB1, KIF1BP (KIAA1279), KIF2A, KIF5C, LAMA2, LAMB1, LAMC3, LARGE1 (LARGE), MACF1, MTOR, NDE1, NEDD4L, OCLN, PAFAH1B1, PEX1, PEX10, PEX11B, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PIK3CA, PIK3R2, POMGNT1 (GTDC2), POMGNT2, POMT1, POMT2, RELN, RTTN, SMO, TMEM5 (now called RXYLT1), TUBA1A, TUBB, TUBB2A, TUBB2B, TUBB3, TUBG1, VLDLR, WDR6*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Cortical brain malformation with features suggestive of a monogenic cause

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

CREUTZFELD-JAKOB DISEASE (CJD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	PCR	Repeat-primed PCR	Octapeptide repeat expansion	*PRN*	28
Edinburgh	Sanger	Whole gene screen	SNVs, indels	*PRN*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of CJD

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

DEMENTIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	PCR	Targeted screen	Hexanucleotide repeat expansion	*c9ORF72*	28
Dundee	NGS	Whole gene screen	SNVs, indels	*APP, CHMP2B, CSF1R, DNAJC5,DNMT1,EPM2A, GRN, ITM2B, MAPT, NHLRC1, NOTCH3, PSEN1, PSEN2, PRNP, TBK1, TARDBP, TYROBP, UBQLN2, VCP*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Unexplained dementia with:
  - Age at onset <55 years where acquired causes (e.g. stroke, tumour) have been excluded, OR
  - Family history of dementia of the same type in a first / second degree relative

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

DENTATORUBRAL PALLIODOLUYSIAN ATROPHY (DRPLA)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	PCR & TP-PCR	Targeted screen	Triplet repeat expansion	*ATN1*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of DRPLA

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

DYSTONIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ACTB, AFG3L2, ANO3, APTX, ATM, ATP1A2, ATP7B, C19orf12, CACNA1A, CHMP2B, CP, CSF1R, CYP27A1, DCAF17, FBXO7, FTL, GFAP, GNAL, HPCA, LYST, NKX2-1, PANK2, PDE10A, PDGFB, PDGFRB, PNKD, PRKRA, PRNP, PRRT2, RNF216, SGCE, SLC19A3, SLC20A2, SLC2A1, SPR, TBK1, THAP1, TIMM8A, TOR1A, TUBB4A, WDR45*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Unexplained dystonia, chorea or related movement disorder with onset in adulthood with a likely monogenic cause
- Overlapping indications: Parkinson's Disease

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

EPILEPSY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Microarray	Whole genome screen	CNV	Whole genome	28
Glasgow	NGS	Whole gene screen	SNVs, indels	*ADSL, AFG3L2, AGAT, ALDH7A1, ARHGEF9, ARX, ATP1A2, ATP1A3, CACNA1A, CASK, CDKL5, CHD2, CHRNA2, CHRNA4, CHRNB2, CLCN4, CLN3, CLN5, CLN6, CLN8, CRH, CSTB, CTSD, DCX, DEPDC5, DNAJC5, DNM1, DOCK7, DYNC1H1, EEF1A2, EFHC1, EPM2A, FLNA, FOXG1, GABRA1, GABRG2, GABRB3, GABRD, GABRG2, GAMT, GLRA1, GLRB, GNAO1, GOSR2, GPHN, GRIN1, GRIN2A, GRIN2B, HCN1, KCNA1, KCNA2, KCNB1, KCNC1, KCNJ10, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCTD7, LGI1, LIS1, MECP2, MEF2C, MFSD8, MOCS1, MOCS2, NEU1, NHLRC1, PCDH19, PIGA, PIK3R2, PLCB1, PNKP, PNPO, POLG, PPT1, PRICKLE1, PRICKLE2, PRRT2, RELN, SCARB2, SCN1A, SCN1B, SCN2A, SCN3A, SCN8A, SCN9A, SLC2A1, SLC6A1, SLC6A5, SLC6A8, SLC9A6, SLC12A5, SLC25A22, SPTAN1, SRPX2, STX1B, STXBP1, SUOX, SYNGAP1, TBC1D24*	56 or 112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Unexplained epilepsy with clinical suspicion of a monogenic cause.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology
- Paediatrics

EPISODIC ATAXIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger	Whole gene screen	SNVs, indels	*KCNA1, CACNA1A*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Paroxysmal attacks of ataxia and vertigo and/or nausea

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

EPISODIC MOVEMENT, MIGRAINE & EPILEPTIC DISORDERS (BRAIN CHANNELOPATHIES)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ADCY5, ATP1A2, ATP1A3, ATP7B, CACNA1A, CACNB4, GLRA1, GLRB, KCNA1, KCNJ2, KCNMA1, KCNQ2, KCNQ3, PNKD, PRRT2, SCN1A, SCN8A, SLC1A3, SLC2A1, SLC6A5, SPR*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Unexplained clinical phenotype associated with a brain channelopathy and likely to have a monogenic cause

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

FAMILIAL CEREBRAL CAVERNOUS MALFORMATIONS (CCM)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*KRIT1, CCM2, CCM3*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals with multiple CCMs, or one CCM and at least one other family member with one or more CCMs

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

FAMILIAL HEMIPLEGIC MIGRAINE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*ATP1A2, CACNA1A, PRRT2, SCN1A, SLC2A1*	56
Family member testing					14
Proforma required?		NO			

REFERRAL CRITERIA

- Migraine with aura characterized by the presence of a motor weakness during the aura
- Family history of migraines with aura

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

FRAGILE X TREMOR ATAXIA SYNDROME (FXTAS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Edinburgh Glasgow	PCR & TP-PCR	Targeted screen	Triplet repeat expansion	*FMR1*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Hereditary ataxia with onset in adulthood

REQUESTING SPECIALTIES

- Neurology
- Clinical Genetics

FRIEDRICH ATAXIA (FRDA)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	PCR & TP-PCR	Targeted screen	Triplet repeat expansion	*FXN*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of FRDA

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

HEREDITARY ATAXIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	PCR & TP-PCR	Targeted screen	Triplet repeat expansions	*SCA1, SCA2, SCA3, SCA6, SCA7, SCA8, SCA17, FRDA, FMR1, FRDA*	28
Edinburgh*	NGS	Whole gene screen	SNVs, indels	*BCB7, ABCD1, AFG3L2, ALS2, ANO10, APTX, ATL1, ATM, ATP1A3, ATP7B, BSCL2, CACNA1A, CACNA1G, CAPN1, COQ8A, CYP27A1, CYP7B1, DDHD2, FA2H, FGF14, FTL, FXN, GBA2, GCH1, GRID2, HSPD1, ITPR1, KCNA1, KCNC3, KCND3, KIF1A, KIF5A, L1CAM, NIPA1, PDYN, PLP1, PNPLA6, POLG, PRKCG, PRNP, PRRT2, REEP1, RTN2, SACS, SETX, SIL1, SLC1A3, SLC2A1, SPART, SPAST, SPG11, SPG21, SPG7, SPTBN2, STUB1, SYNE1, TGM6, TMEM240, TTBK2, TTPA, TWNK, UBAP1, VPS13D, WASHC5, ZFYVE26*	112
Glasgow*	NGS	Whole gene screen	SNVs, indels	*AAAS, ABCB7, ABHD12, AFG3L2, AMPD2, ANO10, AP1S2, APTX, ARSA, ATCAY, ATM, ATP1A3, CA8, CACNA1A, CACNA1G, CAMTA1, CASK, CHMP1A, CLN6, COQ8A, COX20, CP, CWF19L1, CYP27A1, CYP2U1, DARS2, DDHD2, DNAJC5, DNMT1, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, ELOVL4, EPM2A, EXOSC3, FGF14, FLVCR1, FOLR1, FXN, GBA2, GJC2, GOSR2, GRID2, GRM1, HEXA, HEXB, ITPR1, KCNA1, KCNC3, KCND3, KCNJ10, KIF1C, MARS2, MMACHC, MRE11A, MTTP, NHLRC1, NPC1, NPC2, OPHN1, PAX6, PDYN, PEX16, PLA2G6, PMPCA, PNKP, PNPLA6, POLG, POLR3A, PRKCG, PRNP, PRRT2, RARS2, RNF170, RNF216, SACS, SAR1B, SEPSECS, SETX, SIL1, SLC1A3, SLC2A1, SLC9A6, SNX14, SPG7, SPTBN2, SRD5A3, STUB1, SYNE1, TGM6, TMEM240, TPP1, TSEN2, TSEN54, TTBK2, TTC19, TTPA, TUBB4A, TWNK, VLDLR, VRK1, WDR73, WDR81, WFS1, WWOX*	112
Family member testing		as indicated above			14
Proforma required?		NO			

*For patients referred from East of Scotland, testing performed in Edinburgh
*For patients referred from West of Scotland, testing performed in Glasgow

REFERRAL CRITERIA

- Targeted screen:
  - Unexplained ataxia with onset in adulthood including where differential diagnosis encompasses STR loci
- NGS panels:
  - Exclusion of metabolic, neoplastic, alcohol, and drug-related causes
  - Normal/routine neurological bloods, and vitamin E testing
  - Negative spinocerebellar ataxia repeat expansion panel, including FXTAS and FRDA
  - MRI neuroimaging normal, or isolated cerebellar atrophy
  - Family history of ataxia, or young age of onset (<50)

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurolology

HEREDITARY MOTOR AND SENSORY NEUROPATHY (HMSN) / CHARCOT MARIE TOOTH (CMT)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole Gene screen	SNVs, indels Exon level CNV*	*PMP22*, MPZ, GJB1, MFN2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical suggestive of a hereditary neuropathy – distal muscle weakness and atrophy, clawing of hands, pes cavus

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

HEREDITARY NEUROPATHY WITH LIABILITY TO PRESSURE PALSIES (HLPP / HNPP)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen	Sanger MLPA	Whole Gene screen	SNVs, indels Exon level CNV	*PMP22*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical suggestive of a hereditary neuropathy - periodic episodes of numbness and palsies following nerve compression or trauma

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

HEREDITARY SPASTIC PARAPLEGIA (HSP)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh*	NGS MLPA	Whole gene screen	SNVs, indels CNV**	*ABCB7, ABCD1, AFG3L2, ALS2, ANO10, APTX, ATL1**, ATM, ATP1A3, ATP7B, BSCL2, CACNA1A, CACNA1G, CAPN1, COQ8A, CYP27A1, CYP7B1, DDHD2, FA2H, FGF14, FTL, FXN, GBA2, GCH1, GRID2, HSPD1, ITPR1, KCNA1, KCNC3, KCND3, KIF1A, KIF5A, L1CAM, NIPA1, PDYN, PLP1, PNPLA6, POLG, PRKCG, PRNP, PRRT2, REEP1**, RTN2, SACS, SETX, SIL1, SLC1A3, SLC2A1, SPART, SPAST**, SPG11, SPG21, SPG7**, SPTBN2, STUB1, SYNE1, TGM6, TMEM240, TTBK2, TTPA, TWNK, UBAP1, VPS13D, WASHC5 and ZFYVE26*	112
Glasgow*	NGS MLPA	Whole gene screen	SNVs, indels, CNV**	*ABCD1, ADAR, AFG3L2, AIMP1, ALDH18A1, ALS2, AP4B1, AP4E1, AP4M1, AP4S1, ARG1, ATP13A2, ATL1**, BSCL2, B4GALNT1, C12orf65, C19orf12, CAPN1, CYP27A1, CYP2U1, CYP7B1, DDHD1, DDHD2, ERLIN1, ERLIN2, FA2H, FARS2, GBA2, GJC2, HACE1, HSPD1, KIAA0196 (WASHC5), KIDINS220, KIF1A, KIF5A, L1CAM, NIPA1, NT5C2, OPA3, PLP1, PNPLA6, POLR3A, REEP1, RTN2, SACS, SERAC1, SLC16A2, SLC1A4, SLC25A46, SLC2A1, SLC33A1, SPAST**,SPG7, SPG11, SPG20 (SPART), SPG21, TUBB4A, WDR45B, ZEB2ZFYVE26, ZFYVE27*	112
Family member testing		as indicated above			14
Proforma required?		YES	Edinburgh only – HSP referral proforma (see centre website)		

* For patients referred from East of Scotland, testing performed in Edinburgh

* For patients referred from West of Scotland, testing performed in Glasgow

REFERRAL CRITERIA

- Exclusion of metabolic, neoplastic, alcohol, and drug-related causes
- Normal/routine neurological bloods, and vitamin E testing
- Negative spinocerebellar ataxia repeat expansion panel, including FXTAS and FA testing
- MRI neuroimaging normal, or isolated cerebellar atrophy
- Family history of ataxia, or young age of onset (<50)

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

HOLOPROSENCEPHALY DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*CDON, DHCR7, DISP1, FGF8, FGFR1, GLI2, PTCH1, SHH, SIX3, TGIF1, ZIC2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Liveborn individual with unexplained holoprosencephaly in whom a chromosomal cause has been excluded by microarray or equivalent

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

HUNTINGTON DISEASE (HD)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	TPPCR	Targeted screen	Triplet repeat expansion	*HTT*	14 Prenatal 3
Edinburgh	Linkage	Targeted Screen	Exclusion testing	*HTT*	14 Prenatal 3
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of Huntington disease
- Exclusion testing – only where confirmed diagnosis of Huntington disease in the family.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology (in consultation with Clinical Genetics)

LESCH-NYHAN SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger MLPA	Whole Gene screen	SNVs, indels Exon level CNV	*HPRT1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Hyperuricaemia
- Psychomotor delay
- Mild to moderate intellectual disability
- Self-injurious behavior

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

LEUKOENCEPHALOPATHY WITH VANISHING WHITE MATTER

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*EIF2B1, EIF2B2, EIF2B4, EIF2B5, EIF2B3*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals with unexplained leukodystrophy on neuroimaging with onset in adulthood

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

NEURODEGENERATION WITH BRAIN IRON ACCUMULATION (NBIA)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*ATP13A2, C19ORF12, COASY, CP, DCAF17, FA2H, FTL, FUCA1, KIF1A, KMT2B, MECR, PANK2, PLA2G6, PSEN1, SCP2, SLC39A14, SQSTM1, TRIM32, UBTF, VPS13A, WDR45*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Suspected clinical diagnosis in patients with hallmark findings of NBIA, or further assessment of patients with clinical diagnosis of idiopathic NBIA who have had mutations ruled out in other genes.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

NEUROFIBROMATOSIS TYPE 1 (NF1)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels Exon level CNV	*NF1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical diagnosis of NF1, as defined below, AND molecular diagnosis is required for management of the proband or for reproductive planning
- Diagnosis requires two of:
    - At least 6 café au lait macules (at least 0.5cm in a child and 1.5cm in an adult)
    - At least 2 subcutaneous or cutaneous neurofibromas
    - Plexiform neurofibroma
    - Optic glioma
    - At least 2 Lisch nodules
    - Bony dysplasia (sphenoid wing, long bone bowing, pseudarthrosis)
    - Family history of NF1

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

PAIN DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ATL1, ATL3, ELP1, GLA, KIF1A, NGF, NTRK1, PRNP, RAB7A, RETREG1, SCN10A, SCN11A, SCN9A, SEPT9, SPTLC1, SPTLC2, TRPA1, TTR, WNK1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- This includes the disorders:
  - Congenital insensitivity to pain
  - Inherited erythromelalgia
  - Paroxysmal extreme pain disorder
  - Small fibre neuropathy
  - Familial episodic pain syndromes
  - Hereditary sensory and autonomic neuropathies
  - Forms of Hereditary sensory neuropathy with prominent sensory loss
- Individuals with a disorder of pain perception, including insensitivity to pain or increased pain perception that is likely to be monogenic in aetiology

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

PARKINSON'S DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels, Exon level CNV	*ATP13A2, ATP1A3, DCTN1, DNAJC13, DNAJC6, FBXO7, FTL, GBA, GCH1, GRN, LRRK2, MAPT, PARK7 (DJ-1), PINK1, PLA2G6, PRKN (Parkin), RAB39B, SLC30A10, SNCA, SPG11, SYNJ1, TH, VPS35* CNV in *SNCA, PARK2, PINK1, PARK7, ATP13A2, LRRK2, GCH1 and UCHL1*	112
Family member testing		as indicated above			14
Proforma required?		YES	Parkinson's Disease proforma		

REFERRAL CRITERIA

- Parkinson's disease or complex Parkinsonism
  - Age at onset <50 years, OR
  - First degree relative affected at <50 years, OR
  - Complex features such as spasticity, gaze palsy, early dementia, early bulbar failure, dyspraxia, ataxia, postural hypotension, cortical sensory loss, brain iron accumulation on MRI brain

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

PELIZAEUS-MERZBACHER DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV (*PLP1*)	*PLP1, GJC2(GJA12)*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with clinical or imaging features suggestive of a *PLP1* disorder
- Pathogenic variants in *GJC2* are associated with Pelizaeus-Merzbacher-like disease, an autosomal recessive disorder.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

PERIODIC PARALYSIS, HYPERKALAEMIC

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs	*SCN4A* (p.Leu689Ile, p.Ile693Thr, p.Thr704Met and p.Met1592Val)	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Hyperkalemia (serum potassium concentration >5 mmol/L) or an increase of serum potassium concentration of at least 1.5 mmol/L during an attack of weakness and/or provoking/worsening of an attack by oral potassium intake
- Normal serum potassium between attacks
- Onset before age 20 years.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

PERIODIC PARALYSIS, HYPOKALAEMIC

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs	*CACNA1S* (codons 528, 897, 1239) *SCN4A* (codons 669, 672)	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Two or more attacks of muscle weakness with documented serum potassium <3.5 mmol/L
  OR
- One attack of muscle weakness and one attack of weakness in one relative with documented serum potassium <3.5 mmol/L
  OR
- Three or more of the following six clinical/laboratory features:
  - Onset in the first or second decade
  - Duration of attack (muscle weakness involving ⩾1 limbs) longer than two hours
  - The presence of triggers (previous carbohydrate rich meal, symptom onset during rest after exercise, stress)
  - Improvement in symptoms with potassium intake
  - A family history of the condition or genetically confirmed skeletal calcium or sodium channel mutation
  - Positive long exercise test

  AND
- Exclusion of other causes of hypokalemia (renal, adrenal, thyroid dysfunction; renal tubular acidosis; diuretic and laxative abuse)

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

PERIPHERAL NEUROPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*AARS, ATL1, ATP7A, BICD2, BSCL2, CCT5, DCTN1, DNM2, DNMT1, DYNC1H1, EGR2, FAM134B, FGD4, FIG4, GARS, GDAP1, HINT1, HSPB1, HSPB3, HSPB8, IGHMBP2, IKBKAP, INF2, KIF1A, LITAF, LMNA, LRSAM1, MARS, MTMR2, NDRG1, NEFL, NGF, NTRK1, PLEKHG5, PRPS1, PRX, RAB7A, REEP1, SBF2, SCN9A, SETX, SH3TC2, SLC52A1, SLC52A2, SLC52A3, SORD, SPTLC1, SPTLC2, TRPV4, VCP, WNK1, YARS*	112
Family member testing		as indicated above			14
Proforma required?		YES	Peripheral neuropathy proforma (see centre website)		

REFERRAL CRITERIA

- Firm clinical diagnosis of CMT
- Length dependent neuropathy on neurophysiology
- No pathogenic variant on first tier CMT testing (performed in Aberdeen)

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology approved by Clinical Genetics

PORENCEPHALY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*COL4A1, COL4A2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with clinical features consistent with the condition

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

RETT (& RETT-LIKE) SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*MECP2, CDKL5*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that include:
  - Rapid developmental regression in infancy
  - Seizures
  - Severe intellectual disability
  - Stereotypic hand movements
  - Deceleration of head growth

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

RHABDOMYOLOSIS & METABOLIC MYOPATHIES

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*ACADVL, AGL, ALDOA, ANO5, CACNA1S, CAPN3, CAV3, CPT2, DMD, DYSF, ENO3, ETFA, ETFB, ETFDH, FKRP, GAA, GBE1, GMPPB, GYG1, GYS1, HADHA, HADHB, ISCU, LDHA, LPIN1, PFKM, PGAM2, PGK1, PGM1, PHKA1, PNPLA2, PYGM, RBCK1, RYR1, SLC22A5, TANGO2*	112
Family member testing		as indicated above			14
Proforma required?		NO			

This panel is intended for patients with isolated skeletal muscle symptoms. Patients with multisystem disease may be more appropriately tested on alternative panels

REFERRAL CRITERIA

Single episode rhabdomyolysis

- ALL MUST FULFIL 2 essential criteria:
  - CK documented >10,000IU/L associated with muscle pain
  - Mitochondrial myopathy/PEO considered and excluded where appropriate
- IN ADDITION PATIENTS AGED >10 years must fulfil at least one of the following three criteria:
  - No environmental cause AND Accustomed exercise (NOT too much, too fast, too soon)
  - High risk features- exercise intolerance preceding rhabdo +/OR weakness on examination >4mths after event +/OR family history documented rhabdo +/OR biochemistry classical of VLCAD, MADD, or CPT2 +/OR cardiomyopathy
  - K>500 IU/L >6 months after rhabdo episode

Recurrent rhabdomyolysis

- All must fulfil 3 essential criteria:
  - CK documented >10,000IU/L associated with muscle pain on at least one occasion
  - At least one further episode of acute muscle pain associated with documented CK rise or pigmenturia
  - Mitochondrial myopathy/PEO considered and excluded where appropriate

Other criteria for rhabdo panel testing

- Clinical suspicion metabolic myopathy AND any of
  - Moderate to profound XS lipid or glycogen on biopsy
  - Cores/minicores on biopsy
- Muscle MRI characteristic of RYR1

REQUESTING SPECIALTIES

- Clinical Genetics
- Metabolic
- Neurology

SPINAL MUSCULAR ATROPHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	MLPA	Targeted screen	CNV	*SMN1*	28
Glasgow	NGS	Whole gene screen	SNVs, indels	*AARS, ASAH1, ATP7A, BICD2, BSCL2, CHCHD10, DCTN1, DNAJB2, DYNC1H1, EXOSC3, EXOSC8, FBXO38, FIG4, GARS, HEXA, HSPB1, HSPB3, HSPB8, IGHMBP2, LAS1L, MATR3, MFN2, PLEKHG5, REEP1, SCO2, SETX, SIGMAR1, SLC52A2, SLC52A3, SLC5A7, SOD1, SYT2, TRPV4, UBA1, VAPB, VCP, VRK1*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Targeted screen
  - Neonates or infants with unexplained hypotonia where the clinical picture is suggestive of a central cause, i.e. particularly where the baby is not alert, but lethargic or sleepy (part of hypotonic infant screen)
  - clinical features point to a peripheral cause, i.e. particularly where the baby is alert and responsive and the floppiness appears static over a period of days
  - Carrier testing for partners of confirmed *SMN1* carriers.
- Whole gene screen
  - dHMN/SMA clinical phenotype AND
  - Compatible neurophysiology (not required in infants) AND
  - 5q linked SMA excluded (not required in infants)

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

SPINOCEREBELLAR ATAXIA 17 (SCA17)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	PCR & TP-PCR	Targeted screen	Triplet repeat expansion	*TBP*, *AR*	28
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features that indicate a likely diagnosis of SCA17

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

TORSION DYSTONIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee	PCR	Targeted screen	Deletion	*DYT1* (c.907_909del) Gene known as *TOR1A*	28
Proforma required?		NO			

REFERRAL CRITERIA

- DYT1 early-onset isolated dystonia should be suspected in individuals with
  - Onset of dystonia before the age of 26
  - Isolated dystonia with no other abnormalities on neurologic examination, normal routine neuroimaging, no known cause of acquired dystonia
  - Family history of early onset dystonia
  - Factors specific to DYT1 early onset isolated dystonia e.g. Ashkanazi Jewish ancestry, 2 or more affected limbs.

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology

TUBEROUS SCLEROSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*TSC1, TSC2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Clinical features suggestive of tuberous sclerosis requiring molecular testing
- Testing should be typically be targeted at those with one or more major features or two or more minor features:
    - Major features:
        - Hypomelanotic macules (at least 3 of at least 5 mm in diameter)
        - Angiofibromas (at least three) or fibrous cephalic plaque
        - Ungual fibromas (at least two)
        - Shagreen patch
        - Multiple retinal hamartomas
        - Cortical dysplasias characteristic of tuberous sclerosis such as tubers and cerebral white matter radial migration lines
        - Subependymal nodules
        - Subependymal giant cell astrocytoma
        - Cardiac rhabdomyomas
        - Lymphangioleiomyomatosis (LAM)
        - Angiomyolipomas (at least two)
    - Minor features:
        - Confetti skin lesions
        - Dental enamel pits (>3)
        - Intraoral fibromas (at least two)
        - Retinal achromic patch
        - Multiple renal cysts
        - Non- renal hamartomas

REQUESTING SPECIALTIES

- Clinical Genetics
- Neurology
- Nephrology
- Fetal medicine
- Respiratory medicine

RENAL

ALPORT SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	NGS	Whole gene screen	SNVs, indels	*COL4A3*, *COL4A4*, *COL4A5*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Histological evidence following electron microscopy on renal biopsy of EITHER Alport syndrome (thickening and splitting of glomerular basement membrane +/- electron lucent areas) OR thin basement membrane disease (TBMD), OR
- Clinical features of Alport syndrome (high tone sensorineural hearing loss or characteristic ophthalmic signs such as perimacular flecks or anterior lenticonus)
- Haematuria / proteinuria

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

BARTTER SYNDROME & GITELMAN SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels Exon level CNV (*CLCNKB*) if appropriate	*BSND*, *CLCNKB*, *KCNJ1*, *SLC12A1*, *SLC12A3*	56
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with either condition.

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

CYSTINURIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*SLC3A1*, *SLC7A9*	56
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition.

REQUESTING SPECIALTIESS

- Clinical Genetics
- Nephrology

NEPHROCALCINOSIS OR NEPHROLITHIASIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AGXT, APRT, ATP6V0A4, ATP6V1B1, BSND, CA2, CASR, CLCN5, CLCNKB, CLDN16, CLDN19, CYP24A1, FAM20A, GRHPR, HOGA1, HPRT1, KCNJ1, OCRL, PHEX, SLC12A1, SLC22A12, SLC2A9, SLC34A1, SLC34A3, SLC3A1, SLC4A1, SLC7A9, SLC9A3R1, STRADA, XDH*	112
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Nephrocalcinosis or nephrolithiasis where acquired causes have been excluded

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

POLYCYSTIC KIDNEY DISEASE, AUTOSOMAL DOMINANT

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels Exon level CNV	*PKD1, PKD2*	56
Dundee	NGS	Whole gene screen	SNVs, indels	*AGT, ALG8, ALG9, ANKS6, CEP164, CEP83, COL4A1, DNAJB11, DZIP1L, GANAB, HNF1B, INVS, LRP5, MAPKBP1, NPHP1, NPHP3, NPHP4, PKD1, PKD2, PKHD1, PRKCSH, REN, SEC61B, SEC61A1, SEC63, TMEM67, TSC1, TSC2, TTC21B, UMOD, VHL, WDR19*	112
Family member testing		as indicated above			14
Proforma required?		Yes	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- For Autosomal Dominant Polycystic Kidney Disease: Individuals with a suspected or established diagnosis of Autosomal Dominant Polycystic Kidney Disease based on renal imaging.
    - Initial analysis of *PKD1* and *PKD2* then further analysis of the full cystic kidney panel if appropriate.
- The full cystic kidney disease full panel is recommended for individuals that meet the following criteria:
    - Patients with non-syndromic cystic renal disease (excluding acquired cystic disease due to chronic or end stage kidney disease) which is EITHER
    - Clinically not characteristic of ADPKD and underlying diagnosis is required for management purposes, OR
    - Clinically symptomatic disease presenting before the age of 18, OR
    - Clinical diagnosis of ADPKD where a genetic diagnosis is required to influence management

REQUESTING SPECIALTIES

- Clinical Genetics
- Fetal Medicine
- Nephrology
- Paediatrics

POLYCYSTIC KIDNEY DISEASE, AUTOSOMAL RECESSIVE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*PKHD1*	56
Family member testing		as indicated above			14
Proforma required?		Yes	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Individuals with a suspected or established diagnosis of Autosomal Recessive Polycystic Kidney Disease based on renal imaging or pathology.
- Onset is typically prenatal, in infancy or early childhood/young adulthood

REQUESTING SPECIALTIES

- Clinical Genetics
- Fetal Medicine
- Nephrology
- Paediatrics

POLYCYSTIC LIVER DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AGT, ALG8, ALG9, ANKS6, CEP164, CEP83, COL4A1, DNAJB11, DZIP1L, GANAB, HNF1B, INVS, LRP5, MAPKBP1, NPHP1, NPHP3, NPHP4, PKD1, PKD2, PKHD1, PRKCSH, REN, SEC61B, SEC61A1, SEC63, TMEM67, TSC1, TSC2, TTC21B, UMOD, VHL, WDR19*	112
Family member testing		as indicated above			14
Proforma required?		Yes	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Individuals with a suspected or established diagnosis of Polycystic Liver Disease based on imaging or pathology.

REQUESTING SPECIALTIES

- Clinical Genetics
- Fetal Medicine
- Nephrology
- Paediatrics

PRIMARY HYPEROXALURIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AGXT, GPHPR, HOGA1*	56
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with clinical and biochemical features consistent with the condition.
- Overlapping conditions: Nephrocalcinosis or nephrolithiasis

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

PSEUDOHYPOALDOSTERONISM TYPE 1

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*NR3C2, SCNN1A, SCNN1B, SCNN1G*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with clinical and biochemical features consistent with the condition.

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics

RENAL CILIOPATHY

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels, Exon level CNV where appropriate	*AHI1, ALMS1, ANKS6, ARL13B, ARL6, B9D2, BBS1, BBS10, BBS12, BBS2, BBS4, BBS5, BBS7, BBS9, C2CD3, C5orf42 (CPLANE1), CC2D2A, CEP164, CEP290, CEP41, CEP83, CRB2, CSPP1, DDX59, DHCR7, DYNC2H1, HNF1B, HYLS1,ICK, IFT122, IFT43, INVS, IQCB1, KIF7, LZTFL1, MKKS, MKS1, NEK8, NPHP1, NPHP3, NPHP4, OFD1, PKD1, PKD2, PKHD1 PMM2, RPGRIP1L, SDCCAG8 , TCTN1, TCTN2, TCTN3, TMEM138, TMEM216, TMEM231, TMEM237, TMEM67, TRAF3IP1, TTC21B, TTC8 , WDPCP, WDR19, WDR35, WDR60*	112
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Individuals with a suspected clinical diagnosis associated with the above genes

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

RENAL TUBULOPATHIES, RENAL TUBULAR ACIDOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AP2S1, AQP2, ATP1A1, ATP6V0A4, ATP6V1B1, AVPR2, BSND, CA2, CASR, CLCNKB, CLDN16, CLDN19, CTNS, CUL3, CYP24A1, FAH, GATM, GNA11, HNF1B, KCNJ1, KCNJ10, KLHL3, NR3C2, REN, SCNN1A, SCNN1B, SCNN1G, SLC12A1, SLC12A3, SLC22A12, SLC2A9, SLC4A1, SLC4A4, SLC5A2, TRPM6, UMOD, WNK4*	112
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Patients with a primary renal tubulopathy presenting as one of the following conditions:
  - Hypokalaemic alkalosis with normal or low blood pressure (e.g. Bartter/Gitelman syndromes), OR
  - Hypokalaemic alkalosis with elevated blood pressure (e.g. Liddle syndrome), OR
  - Hyperkalaemic acidosis with low/normal BP (PHA type 1), OR
  - Hyperkalaemic acidosis with elevated BP (PHA type 2), OR
  - Hypokalaemic acidosis (pRTA and renal Fanconi syndromes), OR
  - Hypomagnesaemia, OR
  - Nephrogenic diabetes insipidus, OR
  - Other rare types of renal tubulopathy seen in an expert center
- Overlapping conditions: Nephrogenic diabetes insipidus, Bartter/Gitelman syndromes and Nephrocalcinosis or nephrolithiasis

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

STEROID RESISTANT NEPHROTIC SYNDROME (SRNS) AND PROTEINURIC RENAL DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ACTN4, ARHGDIA, CLCN5, COL4A3, COL4A4, COL4A5, COQ2, COQ6, COQ8B, CRB2, CUBN, DLC1,, EMP2, FAT1, INF2, ITGA3, ITSN1, LAMB2, LMX1B, MAGI2, MYH9, MYO1E, NPHS1, NPHS2, NUP107, OCRL, PAX2, PDSS2, PLCE1, PODXL, SCARB2, SMARCAL1, TNS1, TP53RK, TRPC6,, WDR73, WT1*	112
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Steroid-resistant nephrotic syndrome presenting at any age, OR
- Proteinuria with a histological picture of focal segmental glomerulosclerosis (FSGS) or diffuse mesangial sclerosis (DMS) on biopsy, with no identifiable cause, where a transplant or immunosuppression is planned

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

TUBULOINTERSTITIAL KIDNEY DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ANKS6, CEP164, CEP83, GATM, HNF1B, INVS, MUC1, NPHP1, NPHP3, NPHP4, REN, TMEM67, TTC21B, UMO, WDR19*	112
Family member testing		as indicated above			14
Proforma required?		YES	Renal Genetics Proforma (see centre website)		

REFERRAL CRITERIA

- Previously known as hyperuricemic nephropathy, familial juvenile, type 1 & 2 and only UMOD and REN tested. Includes both dominant and recessive TKD.
- Renal impairment caused by tubulointerstitial fibrosis with no glomerular lesion, with no identifiable cause, often associated with medullary cysts, hyperuricaemia or gout, AND
- A first degree relative with TKD or unexplained end-stage renal disease

- Testing note: the majority of pathogenic variants in the MUC1 gene are within a Variable Nucleotide Tandem Repeat (VNTR) region, these are not detectable by this method

REQUESTING SPECIALTIES

- Clinical Genetics
- Nephrology

RESPIRATORY

ASTHMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNV	*ADRB2* p.(Gly16Arg)	28
Proforma required?		NO			

REFERRAL CRITERIA

- Asthma patient who may be using or about to be prescribed long acting B2 agonist therapy.
- Some evidence to suggest that homozygotes for arginine at codon 16 (*ADRB2* p.(Arg16Arg)) may not benefit from long acting B2 agonist therapy

REQUESTING SPECIALTIES

- Clinical Genetics
- Respiratory

CYSTIC FIBROSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Aberdeen Dundee Edinburgh Glasgow	ARMS	Targeted screen	SNVs, indels	Common mutations	28 Prenatal 3
Glasgow	ARMS	Targeted screen	SNVs, indels	CFTR newborn screening (p.508del, p.G542*, p.G551D, c.469+1G>T common mutations)	7
Edinburgh	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*CFTR*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Test in an individual clinically likely to be affected with cystic fibrosis:
- Child with clinical suspicion of CF (e.g. recurrent chest infections, failure to thrive, fat malabsorption, neonatal history of meconium ileus), AND
    - A not normal sweat test performed in a recognised experienced test centre/laboratory (i.e. sweat chloride >40mM with sufficient sweat obtained; >30mM in infants), OR
    - An additional urgent prenatal situation for the parents or for a close relative, but urgent sweat testing not accessible
- Adult with CT-proven bronchiectasis, AND
    - A not normal sweat test performed in a recognised experienced test centre/laboratory (i.e. sweat chloride >40mM with sufficient sweat obtained), OR
    - Chronic suppurative chest infection with colonisation by Pseudomonas and Staph aureus, OR
    - Additional exocrine pancreatic dysfunction
- Idiopathic chronic pancreatitis with exocrine dysfunction (fat malabsorption) with other obvious and acquired causes excluded, AND
    - A not normal sweat test performed in a recognised experienced test centre/laboratory (i.e. sweat chloride >40mM with sufficient sweat obtained), OR
    - Sweat testing not practical, and all other causes excluded
- Male infertility associated with obstructive azoospermia, AND
    - CBAVD (or isolated CUAVD) diagnosed from expert clinical examination, OR
    - CBAVD identified at incidental herniotomy
- Fetal echogenic bowel as bright as bone on 2nd trimester scan, AND
    - Both parents not available for carrier testing [if both parents are available, Cystic fibrosis carrier testing should be used instead of an invasive prenatal test], AND
    - Isolated anomaly or <2 other common fetal markers, AND
    - Other more common causes excluded (e.g. IUGR, placental failure, earlier bleeding, infection, raised aneuploidy markers)

REQUESTING SPECIALTIES

- Clinical Genetics
- GP
- Obstetrics
- Paediatrics
- Respiratory

HEREDITARY HAEMORRHAGIC TELANGIECTASIA, PRIMARY PULMONARY HYPERTENSION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Edinburgh	HHT-NGS	Whole gene screen	SNVs, indels, CNV**	*ACVRL1***, *ENG***, *EPHB4*, *GDF2*, *RASA1*, *SMAD4***	56
Edinburgh	PPH-NGS	Whole gene screen	SNVs, indels, CNV**	*ACVRL1***, *ATP13A3*, *BMPR2***, *CAV1*, *GDF2*, *EIF2AK4*, *ENG***, *KCNK3*, *SMAD9*, *SOX17*, *TBX4*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- HHT: Test where any THREE of the following criteria are met:
  - 1. Epistaxis: spontaneous, recurrent nose bleeds
  - 2. Telangiectases: multiple, at characteristic sites (lips, oral cavity, fingers, nose)
  - 3. Visceral lesions such as gastrointestinal telangiectasia (with or without bleeding), pulmonary arteriovenous malformation (AVM), hepatic AVM, cerebral AVMs, spinal AVM
  - 4. Family history: a first degree relative with HHT according to these criteria (as above) or an autosomal dominant family history of nosebleeds or first degree relative with cerebral AVM / cerebral haemorrhage / pulmonary or hepatic AVM.

- Alternatively, test where any ONE of the following criteria are met:
  - A) Personal history of at least one pulmonary AVM*
  - B) Personal history of two or more AVMs at one or more characteristic sites (pulmonary*, cerebral, hepatic or spinal)
  - C) Personal history of at least one AVM and severe epistaxis or characteristic telangiectasia or family history
  - D) Personal history of telangiectasia, and refractory or severe epistaxis (e.g. requiring recurrent transfusions)

* *Pulmonary AVM only if confirmed by cross sectional imaging (usually thoracic CT scan), and/or later therapeutic angiography/surgery. Do not diagnose if only supported by a positive right-to-left shunt study ("bubble echo") or chest x-ray

- Clinical features that indicate a likely diagnosis of PPH.

REQUESTING SPECIALTIES

- Clinical Genetics
- Respiratory

PRIMARY CILIARY DYSKINESIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*ARMC4, C21ORF59, CCDC39, CCDC40, CCDC65, CCDC103, CCDC114, CCDC151, CCNO, DNAAF1, DNAAF2, DNAAF3, DNAAF5, DNAH5, DNAH11, DNAI1, DNAI2, DNAL1, DRC1, DYX1C1, GAS8, LRRC6, MCIDAS, RPGR, RSPH1, RSPH4A, RSPH9, SPAG1, ZMYND10*	112
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Neonate - at least one of the following:
  - Situs inversus plus lower airway or nasal symptoms
  - Persistent respiratory distress where other causes have been excluded
  - Persistent rhinorrhoea and cough distress where other causes have been excluded
  - Sibling with PCD
- Childhood – at least one of the following:
  - Persistent lifelong wet cough (cystic fibrosis excluded)
  - Unexplained bronchiectasis (cystic fibrosis excluded)
  - Serious otitis media in association with recurrent lower and upper airway symptoms
- Adults
  - Symptoms as above since, often associated with infertility or subfertility

REQUESTING SPECIALTIES

- Clinical Genetics
- Paediatrics
- Respiratory Medicine

SURFACTANT METABOLISM DYSFUNCTION

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Glasgow	NGS	Whole gene screen	SNVs, indels	*ABCA3, NKX2-1, SFTPB, SFTPC*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Neonatal respiratory insufficiency of disproportionate severity for advanced gestation, with clinical and X-ray features consistent with pulmonary surfactant deficiency AND no other obvious cause for respiratory distress e.g. no difficult delivery, no infection, not premature

REQUESTING SPECIALTIES

- Clinical Genetics
- Intensivists

SKIN

ACRAL PEELING SKIN SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*TGM5*	56
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
  - Painless peeling of the epidermis
  - Itchy and red skin
  - Blisters

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

AUTOSOMAL RECESSIVE CONGENITAL ICHTHYOSIS (ARCI)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ABCA12, ALDH3A2, ALOX12B, ALOXE3, CERS3, CYP4F22, NIPAL4, PNPLA1, SLC27A4, ST14, STS, SULT2B1, TGM*	56
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition
  - Born with collodion membrane
  - Thick, hyperkeratotic skin
  - The later development of at least one of the following:
    - classic lamellar ichthyosis (LI)
    - (nonbullous) congenital ichthyosiform erythroderma (CIE)
    - intermediate forms with some features of both LI and CIE, or nonLI/nonCIE form with mild hyperkeratosis
  - Excludes Harlequin ichthyosis

REQUESTING SPECIALTIES

- Dermatology
- Clinical Genetics

BIRT-HOGG-DUBE SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*FLCN*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Individuals with either:
  - five or more facial or truncal papules with at least one histologically confirmed fibrofolliculoma
- or two of:
  - early-onset [age <50 years] or multifocal/bilateral renal cell cancer
  - renal cell cancer with mixed chromophobe/oncocytic histology
  - multiple lung cysts with or without spontaneous pneumothorax
  - first degree relative with BHDS

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology
- Respiratory

BULLOUS CONGENITAL ICHTHYOSIFORM ERYTHRODERMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*KRT1, KRT10*	56
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Also known as Epidermolytic hyperkeratosis (EHK) or Epidermolytic ichthyosis (EI)
- Any individual with a clinical presentation consistent with the condition:
    - Hyperkeratotic scaliness
    - Severe blistering
    - Hyperproliferation in the basal cells
    - Thickened, granular layer of the epidermis
    - Skin biopsy recommended if mosaic form suspected (epidermolytic epidermal naevus)

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

ECTODERMAL DYSPLASIA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*APCDD1, CDH3, CDSN, DSG4, EDA, EDAR, EDARADD, GJB2, GJB6, GRHL2, HLA-DRA, HOXC13, HR, IKBKG, KRT14, KRT71, KRT74, KRT81, KRT83, KRT85, LIPH, LPAR6, MBTPS2, MSX1, NECTIN1, NECTIN4, NFKB2, NFKBIA, PKP1, PORCN, RSPO4, SNRPE, TP63, TSPEAR, WNT10A*	112
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical diagnosis of ectodermal dysplasia with one or more of the following:
  - abnormality of hair (hypotrichosis, sparse hair, sparse/missing eyebrows)
  - abnormality of teeth (hypodontia, conical incisors)
  - abnormality of skin (hypohidrosis, episodes of hyperthermia)
- Includes Hypohidrotic X-linked Ectodermal Dysplasia (XHED), Anhidrotic (autosomal dominant and recessive) Ectodermal Dysplasia, Odontoonychodermal Dysplasia (OODD), Clouston's disease, Witkop syndrome, and Ectrodactyly, Ectodermal Dysplasia and Cleft Lip/Palate syndrome (EEC_3)

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

EPIDERMOLYSIS BULLOSA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*KRT5*, *KRT14*	56
Dundee	NGS	Whole gene screen	SNVs, indels	*COL17A1*, *COL7A1*, *DSP*, *DST*, *EXPH5*, *FERMT1*, *ITGA3*, *ITGA6*, *ITGB4*, *JUP*, *KRT14*, *KRT5*, *LAMA3*, *LAMB3*, *LAMC2*, *PKP1*, *PLEC*, *TGM5*	112
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Includes common types of Epidermolysis bullosa simplex (EBS): localized (EBS-loc, previously known as Weber-Cockayne type), generalized intermediate (EBS-gen intermed, previously known as Koebner type), motteled (EBS-MP) and generalized severe (EBS-gen sev, previously known as Dowling-Meara type)
    - Sanger sequencing for *KRT5* and *KRT14* for EBS
    - Dowling-Degos Syndrome – Sanger sequencing for *KRT5*
    - Naegeli-Franceschetti-Jadassohn Syndrome – Sanger sequencing for *KRT14* exon 1
    - NGS test for other rarer forms of EB
- Genetically heterogeneous disorder of skin fragility, manifested by blistering and/or erosions with little or no trauma

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

EPIDERMOLYTIC PALMOPLANTAR KERATODERMA (EPPK)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*KRT1, KRT9*	56
Family member testing		as indicated above			14
Proforma required?		YES	Skin Disorders Proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
  - Yellow and diffuse thickening of the skin on the palms and soles (palmoplantar keratoderma)
  - Erythema
  - Localised epidermolytic hyperkeratosis
  - Onset in infancy

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

FERGUSON-SMITH DISEASE

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*TGFBR1*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
    - Squamous cell carcinomas or keratoacanthoma which heal spontaneously leaving pitted scars

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

FOCAL PALMOPLANTAR KERATODERMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	*KRT6C (ex1&7), KRT16 (ex1,6,7,8)*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
    - Focal palmoplantar hyperkeratosis
    - Palmoplantar keratoderma
    - Autosomal dominant

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

GLOMUVENOUS MALFORMATIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Targeted screen	SNVs, indels	*GLMN* (exons 2, 3, 6, 8, 12, 13)	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- A clinical diagnosis of glomuvenous malformations (GVM) based on the International Society for the Study of Vascular Anomalies (ISSVA) classification
- Two or more combined malformations consisting of capillary and venous malformations found in one lesion

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

HAIR DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*APCDD1, ATP7A, CDH3, CDSN, DSC3, DSG4, EDAR, ERCC2, GJB2, GJB6, HOXC13, HR, JUP, KRT71, KRT74, KRT81, KRT83, KRT85, KRT86, LIPH, LPAR6, MBTPS2, RIPK4, SNRPE, SPINK5, VDR*	112
Family member testing		as indicated above			14
Proforma required?		YES	Skin Disorders Proforma (see centre website)		

REFERRAL CRITERIA

- Includes Hypotrichosis Simplex, Marine Unna Hypotrichosis, Familial Woolly Hair (WFH), Hypotrichosis with Juvenile Macular Dystrophy, Netherton Syndrome, Monilethrix, Clouston Syndrome, Menkes Syndrome, Hypohidrotic Ectodermal Dysplasia (HED), Trichothiodystrophy (TTD), Ectodermal Dysplasia-9 (ECTD9), Alopecia Universalis Congenita (ALUNC), Naxos Syndrome, CHAND Syndrome, and Atrichia with papular lesions (APL).
- Individuals with a hair disorder with a likely monogenic cause

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

ICHTHYOSIS & ERYTHROKERATODERMA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*AAGAB, ABCA12, ALOX12B, ALOXE3, AQP5, CARD14, CAST, CERS3, CLDN1, CYP4F22, DSC2, DSG1, DSP, ENPP1, FLG, GJA1, GJB2, GJB3, GJB4, GJB6, JUP, KDSR, KRT1, KRT10, KRT14, KRT16, KRT17, KRT2, KRT6A, KRT6B, KRT6C, KRT9, LOR, MSMO1, NIPAL4, PIGL, PNPLA1, RSPO1, RHBDF2, SERPINB7, SLC27A4, SLURP1, SMARCAD1, SNAP29, SPINK5, ST14, STS, SULT2B1, TAT, TGM1, TRPV3*	112
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Clinical presentation with at least two of the following features:
  - born with collodion membrane
  - erythroderma
  - dark plate-like scales or fine white scaling
  - ectropium/eclabium
  - hyperkeratosis
- First line testing for punctuate PPK is Sanger sequencing of *AAGAB*; proceeding to the full panel if negative.
- For ARCI referrals, ARCI panel will be applied in the first instance; proceeding to the full panel if negative and appropriate.

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

ICHTHYOSIS VULGARIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	*FLG* (p.Arg501*; c.2282_2285delCAGT, p.Arg2447*; p.Ser3247*)	28
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition
  - Early onset (usually before 1 year old)
  - Mild ichthyosis/xerosis
  - Keratosis pilaris
  - Hyperlinear pals and soles
  - Atopic eczema

REQUESTING SPECIALTIES

- Dermatology
- Clinical Genetics

LEGIUS SYNDROME

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*SPRED1*	56
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
  - Five or more café au lait macules which are bilaterally distributed
  - Axillary or inguinal freckling
  - No other NF1-related criteria

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

MULTIPLE CUTANEOUS AND MUCOSAL VENOUS MALFORMATIONS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	*TIE2* exon 15, exon 17	28
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
  - Small, multifocal cutaneous and/or mucosal bluish-purple vascular malformations
  - Early onset (mostly at birth)
  - Slow blood flow on Doppler ultrasound
  - Elevated D-dimer concentration

REQUESTING SPECIALTIES

- Dermatology
- Clinical Genetics

PACHYONYCHIA CONGENITA

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	*KT6A* (ex1&7) *KRT6B* (ex1&7) *KRT6C* (ex1&7) *KRT16* (ex1,6,7&8) *KRT17* (ex1,6&7)	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
  - Plantar keratoderma including callus with underlying blisters
  - Plantar pain
  - Hypertrophic nail dystrophy, often present within the first few months of life
  - Oral leukokeratosis

REQUESTING SPECIALTIES

- Dermatology
- Clinical Genetics

PALMOPLANTAR KERATODERMAS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Targeted screen	SNVs, indels	*KRT1, KRT5, KRT9, KRT10*	56
Dundee	NGS	Whole gene screen	SNVs, indels	*AAGAB, ABCA12, ABHD5, ADAM17, ALDH3A2, ALOX12B, ALOXE3, AP1S1, AQP5, ARSE, CAST, CDSN, CERS3, CLDN1, CSTA, CTSC, CYP4F22, DSC2, DSC3, DSG1, DSG4, DSP, EBP, ELOVL4, ENPP1, FLG, GJA1, GJB2, JUP, KANK2, KDSR, KRT1, KRT10, KRT2, KRT6C*, KRT9, LIPN, MBTPS2, MVK, LOR, NIPAL4, NSDHL, PEX7, PHYH, PKP1, PNPLA1, POMP, RHBDF2, RSPO1, SERPINB7, SLC27A4, SLURP1, SNAP29, SPINK5, ST14, STK11, STS, SULT2B1, TGM1, TRPV3, VPS33B*	112
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Initial testing by Sanger sequencing for KRT1 and KRT9 (epidermolytic PPK), KRT6c and KRT16 (focal PPK), and KRT6a/b/c, KRT16 and KRT17 (PC) before proceeding to full panel.
- Any individual with a clinical diagnosis of one of the following:
  - Diffuse palmoplantar keratoderma
  - Focal keratoderma with or without nail involvement
  - Pachyonychia congenital phenotype
  - Punctate keratoderma
  - Striate keratoderma with woolly hair
  - Keratoderma with deafness
  - Unusual/unique rare keratodermas occurring alone or as part of syndromes
  - Erythrokeratoderma

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

RARE GENETICS INFLAMMATORY SKIN DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ABCC6, ADA2, ADAMTS2, AGPAT2, AIRE, ANTXR2, ATP6V0A2, ATP7A, ATP7B, CARD11, CARD14, CARD9, COL1A1, COL1A2, COL3A1, COL4A3, COL4A4, COL4A5, COL5A1, COL5A2, CSTA, CYBB, DCLRE1C, DOCK8, EFEMP2, EGFR, ELN, FBLN5, FDPS, FGF23, FLG, FLT4, FMO3, FOXC2, GALNT3, GGCX, GJA1, GJB3, IKBKG, IL1RN, GJB4, IL36RN, KIT, KRT1, KRT10, LYST, MVD, NCSTN, NLRP1, NLRP3, NOD2, NSDHL, OSMR, PSEN1, PSENEN, RAG1, RAG2, SAMHD1, SH3PXD2B, SLC39A4, STAT3, TMEM173, TREX1*	112
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical diagnosis of a rare inflammatory skin disorder of a likely germline genetic cause
    - Includes autoinflammatory disease (e.g. early onset urticaria, recurrent febrile erythemas), infantile pustular psoriasis, likely genetic forms of pityriasis rubra pilaris

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology
- Rheumatology

SUPERFICIAL EPIDERMOLYTIC ICHTHYOSIS (SEI)
(previously known as ICHTHYOSIS BULLOSA of SIEMENS)

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger	Whole gene screen	SNVs, indels	*KRT2*	56
Family member testing		as indicated above			14
Proforma required?		NO			

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
- Erythroderma, widespread blistering, hyperkeratosis with onset at birth

REQUESTING SPECIALTIES

- Dermatology
- Clinical Genetics

VASCULAR SKIN DISORDERS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	NGS	Whole gene screen	SNVs, indels	*ACVRL1, ADAMTS13, ALAS2, ATM, ATR, CCBE1, ENG, EPHB4, F12, FECH, FLT4, FOXC2, GLMN, KRIT1, PIK3CA, PIK3R2, PTEN, RASA1, SCN9A, SMAD4, SOX18, TEK, TMEM173*	112
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a vascular skin disorder with a likely germline genetic cause

REQUESTING SPECIALTIES

- Clinical Genetics
- Dermatology

X-LINKED ICHTHYOSIS

AVAILABLE TESTING

Centre	Method	Scope and range of test		Targets	TAT
Dundee	Sanger MLPA	Whole gene screen	SNVs, indels Exon level CNV	*STS*	56
Family member testing		as indicated above			14
Proforma required?		YES	Skin disorders proforma (see centre website)		

REFERRAL CRITERIA

- Any individual with a clinical presentation consistent with the condition:
  - Steroid sulfatase (STS) enzyme deficiency
  - Dry skin
  - Hyperkeratosis
  - Hypohidrosis
  - Ichthyosis

REQUESTING SPECIALTIES

- Dermatology
- Clinical Genetics