

Referring Whole Genome Sequencing (WGS) for a Rare Disease

Clinician's How-To Guide

Table of Contents

A. WGS Checklist.....	2
B. WGS Pathways	2
C. Eligibility for WGS.....	4
D. Forms required:.....	5
1. The Test Order Form: must be completed by the consultant.....	5
2. The Record of Discussion - completed by the consultant or Genomic Practitioner.....	7
E. Consent Requirements:	8
1. WGS Consenting via the Genomic Practitioner.....	8
a. <i>Preliminary WGS Discussion with the Patient:</i>	8
2. WGS Consenting yourself	8
a. <i>Full Consent Conversation required:</i>	8
F. WGS Sample Form.....	Error! Bookmark not defined.
G. More resources:	12
1. Genomics Resources.....	12
2. WGS Resources.....	12

1: Check WGS eligibility

On the [National Genomic Test Directory \(PDF\)](#), check “WGS” is indicated under “Methods” in Associated Tests.

2: Complete the Test Order Form

One [Test Order form](#) per family

3: Consent and complete the Record of Discussion form(s)

After consenting the patient, complete a [Record of Discussion](#) for each individual in the family being tested (+ a [Consultee form](#) if patient is an adult lacking capacity)

4: Organise WGS samples

Provide the patient and family members being tested with completed [Sample Forms](#) to take with them to their local hospital/phlebotomy

5: Send the Record of Discussion forms and Test Order Form to the laboratory

Send to gos-tr.wgsnorththamesglh@nhs.net and save a copy to your records

B. WGS Pathways

There are **two** suggested pathways for WGS referrals. One is by requesting and consenting for WGS yourself, and another is by requesting via a Genomic Practitioner/Associate.

Genomic Practitioner/Associate: gos-tr.ntgenomicsassociate@nhs.net

role established to help meet the demands of genetic testing, with a specialised knowledge of WGS.

- Point of contact between consultants and the laboratory
- WGS request help – consenting, forms, sample collection, sample chasing
- Track WGS activation and dispatch

Non-WGS genetic testing, clinical details, decisions on clinical urgency and feeding back clinical information/WGS results to patients are **NOT** part of the role.

Key:

Referring Consultant

Genomic Practitioner

Eligibility for Mainstream Genetic Testing

- ☐ Make sure patient fulfils [NGTD criteria \(page 4\)](#)
- ☐ Determine whether this is a singleton WGS (only the patient to be tested) or trio WGS (patient and both parents to be tested)

Note: For other family combinations (i.e patient + siblings), please check with laboratory

Patient Appointment

- ☐ Discuss family history
- ☐ Go through brief consent discussion to make sure the patient is happy with the genetic referral
- ☐ Complete [Test Order form \(page 5 and 6\)](#)

NO

? Requesting via Genomic Practitioner

YES

Patient Appointment [cont.]

- ☐ Go through entire consent discussion
- ☐ Complete [Record of Discussion \(page 7\)](#) - can be virtually completed or with the patient face-to-face) (+ [Consultee form](#) if adult lacking capacity)
- ☐ Provide [Patient Information Leaflets](#) and [video](#) link
- ☐ Provide [Sample Form\(s\) \(page 11\)](#) to all family members being tested
- ☐ Save forms to Electronic Patient Record

Following the Appointment

- ☐ Send Record of Discussion form(s) and Test Order form to goss-tr.wgsnorththamesglh@nhs.net
- ☐ Confirm with laboratory that all samples have arrived and the test has been activated

- ☐ Send Test Order Form to Genomic Practitioner (goss-tr.ntgenomicsassociate@nhs.net)

Genomic Practitioner Appointment

- ☐ Go through consent discussion
- ☐ Complete [Record of Discussion](#) (+ [Consultee form](#) if adult lacking capacity)
- ☐ Provide [Patient Information Leaflets](#) and [video](#) link
- ☐ Provide [Sample Form\(s\)](#) to all family members being tested (if not done by consultant)
- ☐ Send forms to department pathway coordinator to save to Electronic Patient Record

Following the Appointment

- ☐ Send Record of Discussion form(s) and Test Order form to goss-tr.wgsnorththamesglh@nhs.net
- ☐ Confirm with laboratory that all samples have arrived, and the test has been activated

C. Eligibility for WGS

Patient eligibility for WGS clinical indications can be found on the [NHS England » National genomic test directory](#). If you need to determine which genes/panels are included in a clinical indication, please visit [PanelApp](#).

R59 Early onset or syndromic epilepsy

The Clinical Code/Indication

Testing Criteria

Unexplained epilepsy with clinical suspicion of a monogenic cause including:

1. Onset under 2 years, OR
2. Clinical features suggestive of specific genetic epilepsy, for example Dravet syndrome, OR
3. Additional clinical features: intellectual disability, autism spectrum disorder, structural abnormality (e.g. dysmorphism, congenital malformation), unexplained cognitive/memory decline

Testing may occasionally be appropriate where age of onset is between 2 and 3 years and following clinical agreement by a specialist MDT.

Overlapping indications

- R110 Segmental overgrowth disorders – Deep sequencing test should be used where megalencephaly is present to allow detection of somatic mosaic variants
- R14 Acutely unwell children with likely monogenic disorder should be used in acutely unwell children with epilepsy

NOTE: If a metabolic disorder is suspected, testing should be carried out either using R89 or R98 or under an alternative metabolic-related clinical indication

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.

Where in Pathway

At presentation

Requesting Specialties

- Clinical Genetics
- Metabolic Medicine
- Neurology

Check whether you are eligible for requesting this test

Specialist Service Group

- Neurology

Associated Tests

It is not a requirement to perform microarray testing in addition to WGS but microarray testing can be performed where appropriate

Code	Name	Optimal Family Structure	Scope(s)	Target Type	Target Name	Method
R59.2	Genomewide Microarray	Singleton	Genomewide CNVs	Genomewide	Genomewide	Microarray
R59.3	Epilepsy - early onset or syndromic WGS (phase 1)	Trio or singleton	Exon level CNVs, Small variants, STRs	Panel of genes or loci	Genetic epilepsy syndromes (402)	WGS

If trio is indicated, include parents if available

Make sure WGS is an associated test

Proband first name	Proband last name	Date of birth (dd/mm/yyyy)	NHS number
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* **Mandatory**

HPO terms are important for the analysis and interpretation of WGS data.
Please enter valid HPO terms present in the proband/family members being tested
HPO terms can be copied from the lists below

Follow the link for a complete list of HPO terms

Terms must be ticked as present or absent in all family members being tested.

HPO Terms - Please ensure those given match those available at https://hpo.jax.org/spp/	Proband Name DOB		Parent 1 Name DOB		Parent 2 Name DOB	
	Present	Absent	Present	Absent	Present	Absent
e.g. Epilepsy *	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Intellectual disability, developmental and metabolic Intellectual disability - mild Intellectual disability - moderate Intellectual disability - profound Intellectual disability - severe Autistic behaviour Global developmental delay Delayed fine motor development Delayed gross motor development Delayed speech and language development Generalized hypotonia Feeding difficulties Failure to thrive Abnormal facial shape Abnormality of metabolism/homeostasis Microcephaly Macrocephaly Tall stature	Neurology Muscular dystrophy Myopathy Myotonia Fatigable weakness Peripheral neuropathy Distal arthropropoisis Arthropropoisis multiplex congenita Cognitive impairment Parkinsonism Spasticity Chorea Dystonia Ataxia Cerebellar atrophy Cerebellar hypoplasia Dandy-Walker malformation Olivopontocerebellar hypoplasia Diffuse white matter abnormalities Focal white matter lesions Leukoencephalopathy Cortical dysplasia Heterotopia Lissencephaly Pachygyria Polymicrogyria Schizencephaly Holoprosencephaly Hydrocephalus Neurodegeneration Dementia	Cardiology Hypertrophic cardiomyopathy Dilated cardiomyopathy Cardiomyopathy Eye Disorders Cataract Retinal dystrophy Macular dystrophy Microphthalmia Anophthalmia Coloboma Developmental glaucoma Aniridia Abnormal anterior eye segment morphology Nystagmus
Craniosynostosis Biconal synostosis Unicoronal synostosis Metopic synostosis Sagittal craniosynostosis Lambdoidal craniosynostosis Multiple suture craniosynostosis	Epilepsy Seizures Generalized seizures Focal seizures Epileptic spasms Infantile encephalopathy Atonic seizures Generalized myoclonic seizures Generalized tonic seizures Generalized tonic-clonic seizures EEG with focal epileptiform discharges EEG with generalized epileptiform discharges Multifocal epileptiform discharges	Immune Disorders Immunodeficiency Abnormal lymphocyte morphology Abnormal lymphocyte physiology Abnormal lymphocyte count Abnormality of neutrophils Abnormality of humoral immunity Abnormal inflammatory response Abnormality of complement system
Skeletal dysplasia Disproportionate short stature Proportionate short stature Short stature Skeletal dysplasia		
Diabetes Neonatal insulin-dependent diabetes mellitus Transient neonatal diabetes mellitus		
Renal Multiple renal cysts Nephronophthisis Hepatic cysts Enlarged kidney Renal insufficiency		

Human Phenotype Ontology (HPO) terms are a standardised vocabulary of phenotypic abnormalities which are important for the analysis and interpretation of WGS data.

Please complete accurately for each family member being tested (present/absent boxes ticked).

A complete list can be found at [Human Phenotype Ontology \(jax.org\)](https://hpo.jax.org/).

Follow this [link](#) for more information on how to use HPO terms in a clinical context.

HPO terms are very important for increasing the chances of finding a potential diagnosis via the panel agnostic exomiser variant prioritisation analysis that is carried out if the panel-tiering analysis is negative. If choosing HPO terms is done properly, this would also reduce the need for further analysis.

2. The Record of Discussion - completed by the consultant or Genomic Practitioner

Page 3 (pictured) of the document to be completed after a full consent conversation – a summary of the conversation is listed on Page 1 and 2 (not pictured). This can be completed remotely (i.e. consent appointment over the phone/virtual). Information on what to include in the consent conversation is detailed page 8-10.

For adults lacking capacity, please also complete the [Consultee form](#).

NHS Genomic Medicine Service, Record of Discussion Form version 4.03.

First name *	NHS number (or postcode if not known) *
Last name *	Date of birth *

Genomics
england
NHS
01-NGIS-RCD (v4.03)

* **Mandatory**

Confirmation of Your Genomic Test and Research Choices

I confirm that I have had the opportunity to discuss information about genomic testing, I agree to the genomic test, and my research choice is indicated below.

A. I have discussed taking part in the National Genomic Research Library

* ☐ YES | ☐ NO

If your answer to A is NO then please ignore B and sign directly below

B. I agree that my data and remainder sample may contribute to the National Genomic Research Library

☐ YES | ☐ NO

Patient name *	Signature	Date

If you are signing this form on behalf of someone else (children, adults without capacity or deceased patients) then please sign below.

Parent Guardian Consultee name* please amend as appropriate	Signature	Date

Mandatory signature for children, adults lacking capacity or deceased patients

- if patient is an adult lacking capacity, a separate Consultee form must be completed in addition to the Record of Discussion

Healthcare professional use only

To be completed by the healthcare professional recording the patient's choices.

Patient category *	<input type="checkbox"/> Adult (made their own choices)	<input type="checkbox"/> Clinician has agreed to the test (in the patient's best interests)
	<input type="checkbox"/> Adult lacking capacity (choices advised by consultee)	<input type="checkbox"/> Deceased (choices made on behalf of deceased individual)
	<input type="checkbox"/> Child (parent or guardian choices)	
Test type *	<input type="checkbox"/> Rare and Inherited Diseases - WGS	<input type="checkbox"/> Cancer (paired tumour normal) - WGS
	<input type="checkbox"/> Patient would like to discuss at a later date	<input type="checkbox"/> Inappropriate to have discussion
	<input type="checkbox"/> Patient lacks capacity and no consultee available	<input type="checkbox"/> Other
Remote consent	<input type="checkbox"/> Recorded remotely by clinician, no patient signature	
Responsible clinician *		
Hospital number		

A reason why the National Genomic Research library has not been discussed must be given (i.e. if A is ticked as NO)

The Record of Discussion form can be completed remotely if the patient appointment is virtual/over the phone

Healthcare professional name *	Signature	Date

E. Consent Requirements:

1. WGS Consenting via the Genomic Practitioner

It is important to note that the consultant **ultimately has responsibility for patient consent**. Therefore, it is essential that you make sure the patient is happy to proceed with the genetic testing before referring them. The Genomic Practitioner would then speak to the patients and all family members to be tested and fill the Record of Discussion form.

a. Consultant Preliminary Discussion with the Patient:

1. What WGS is – reading through all the DNA and analysing specific areas (virtual panels) – NOT gene agnostic
2. Managing expectations - Turnaround time from the point that all blood samples/consent forms have arrived at the laboratory
 - a. 12 months (routine tests) *(as of August 2024)*
 - b. 12 weeks (urgent tests) *(as of August 2024)*
3. Understanding that the patient will be contacted by a Genomic Practitioner

The Genomic Practitioner will discuss the National Genomic Research Library with the patient.

If possible, please provide [Patient Information Leaflets](#) and the WGS [video](#) link

2. WGS Consenting yourself

a. Full Consent Conversation required:

	Individuals aged 16+ years with capacity	Children (less than 16 years)	Adults without capacity	Individuals who are deceased
Clinical test	RoD reviewed with each individual	RoD reviewed with parent/guardian	RoD reviewed with person acting in best interests of the patient	RoD reviewed with appropriate relative

1. What WGS is – reading through all the DNA and analysing specific areas (virtual panels)
2. Small blood sample required for each family member
3. Turnaround time from the point that all blood samples have arrived at the laboratory
 - a. 12 months (routine tests) *(as of August 2024)*
 - b. 12 weeks (urgent tests) *(as of August 2024)*
4. Family Implications
 - a. Implications on other family members or future pregnancies
 - b. Opportunities for relatives to have access to screening, predictive genetic testing and/or information about reproductive choices based on these results or family history
 - c. Importance of sharing results with family members if a pathogenic variant is found (it is helpful to start early conversations about this rather than only after the results are available)
5. Uncertainty

- a. Results may find a variant of uncertain/unknown significance (VUS) = a genetic change that may affect the way the gene is working, but there is not enough evidence available to confirm this as a disease-causing or likely disease-causing variant.
- b. May require a referral for further genetic testing via Clinical Genetics Service
- c. Variants of uncertain significance should not be used to make clinical decisions for the individual or family members
- d. This result may change over time as this can be re-analysed in future

6. Unexpected Information/ Incidental Findings

- a. Pathogenic variants may be identified that are unrelated to the reason for the genetics referral, and may indicate an underlying predisposition to a different phenotype (e.g. risk of further cancer or diagnosis with other possible health problems)
- b. These are not routinely looked for and they are rare to come across as the laboratory focuses analysis on virtual panels relevant to the genetic referral
- c. The results will NOT inform all health conditions – currently, there are no additional looked-for findings, however these may still be found by chance
- d. Misattributed parentage is another example of incidental findings

7. DNA storage

- a. The blood sample will be sent to the laboratory and DNA will be extracted
- b. This DNA will continue to be stored (approximately 30 years) unless the patient requests this to be destroyed
- c. This DNA can be accessed by other laboratories within the NHS Genomic Medicine Service
- d. The DNA will not be used for further genetic testing without consent – however, this may be used as a control sample for testing other family members
- e. DNA is not always of sufficient quality and another sample may be required to complete testing

8. Data storage

- a. Data includes patient's health and genomic information, which can be securely access on an ongoing basis by NHS healthcare professionals
- b. Data is stored behind various NHS firewalls
- c. National (identifiable) and international (non-identifiable) comparison of data for greater understanding of significance of any results may be required
- d. Germline variants may be shared for relatives to access testing (limited identifiers to process the test) but medical information will not be shared with relatives
- e. Genomic data may be re-analysed in future as new evidence can occasionally change results
- f. The report will be available on the patient's clinical record

b. [The National Genomic Research Library \(Genomics England\)](#)

	Individuals aged 16+ years with capacity	Children (less than 16 years)	Adults without capacity	Individuals who are deceased
NGRL	The research choice is captured within the RoD. There is an additional 'Participation in the NGRL' form to note the individual's choice if this was not made at the time when the clinical test was discussed.			
	No additional forms	OPTIONAL assent form signed by child	MANDATORY form signed by consultee	No additional forms

For adults lacking capacity, a [Consultee form](#) is also required (will be completed by the Genomic Practitioner if using this pathway).

1. What it is - a comprehensive database that enables approved researchers to access *de-identified* genomic data, health data and samples
2. Research participation is an opt in process (they can choose to take part)
3. Who can access – national and international scientists, researchers, and healthcare companies
4. Data accessed
 - a. The Data is de-identified (pseudonymised) – each patient record is given a unique identification number instead of name, DOB and contact details
 - b. The data available included data about the sample, the raw data of the sample analysis, the patient clinical data (information about their condition that was submitted when ordering WGS) and secondary clinical data from NHS and GP records
5. Patients may be re-contacted for years to come by GE or clinical team
 - a. Certain approved staff within Genomics England will be able to see both identified and de-identified patient data to inform patients about any diagnosis found or to access a clinical trial
 - b. They will NOT be contacted for marketing purposes
6. They can withdraw from research and data sharing at any time
 - a. Partial withdrawal: the patient is happy for their data to continue to be stored but they do not wish to be contacted by Genomics England
 - b. Full withdrawal: all data will no longer be included in any future data releases for further research access

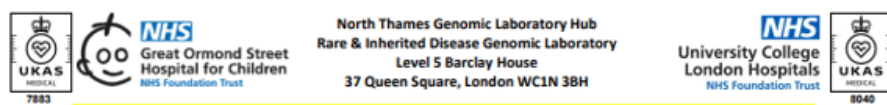
F. Sample Form

A completed NT GLH [Sample Form](#) with patient details **must** be attached to the labelled blood tube (1x EDTA) for WGS. A printed copy of the typed (not handwritten) [Test Order Form](#) can also be sent with labelled blood tubes.

From November 2025, the laboratory has implemented a “WGS Incomplete Referrals” Pathway – e-mails will be sent to consultants when a WGS sample is received as a reminder to send Record of Discussions and Test Order Forms. If these forms are not received by the laboratory, WGS will not be activated. Sample forms with “DNA for storage” will also be accepted.

If the patient is unable to provide a blood sample, a saliva kit can also be accepted. In this case, please provide the patient with a completed [Sample Form](#), a saliva kit (e.g. OG-600 or OG-500 kits) and a pre-paid envelope with the GLH address:

North Thames GLH, Rare & Inherited Disease Genomic Laboratory
Specimen Reception, Level 5 Barclay House, 37 Queen Square,
London WC1N 3BH



Please note that forms received with missing information (patient/referrer/test eligibility/utility) will not be tested.

*** Mandatory**

I. Patient Details (Use FOUR patient identifiers*)		II. Referring Clinician Details (All MANDATORY *)	
SURNAME*: *	FIRST NAME*: *	Referring Consultant (Please provide full name)*: *	
DATE OF BIRTH*: *	Sex at Birth*: *	NHS.net email (for queries)*: *	
NHS Number* (Mandatory)*: *	Hospital No/ Your Ref:	Department*: *	
Ethnicity:	GOSH Family ID (If known):	Hospital (No initials, please provide full name/address)*: *	
Patient Address & Postcode:		Referring Clinician: I have discussed genomic testing with this patient and have retained a record of discussion (see page 2). Consent is not required for DNA storage.	
GP Name & Address:			

Consanguineous: ☐ Yes ☐ No

Please select **ONE** option for report and provide details:

<input type="checkbox"/> Email (NHS.net email):	
<input type="checkbox"/> Outreach Portal Submitter ID:	
<input type="checkbox"/> Post:	

III. Specimen Details	If high risk please specify:	Sample Type	Date / Time Collected	Collected By
High Risk Specimen? <input type="checkbox"/> Yes <input type="checkbox"/> No				

Clinical Indication Code: R	"WGS", or WGS Clinical R code	<input type="checkbox"/> Urgent <input type="checkbox"/> Routine
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THIS FORM IS FOR POSTNATAL NON-WHOLE GENOME SEQUENCING GENETIC TESTS (ALTERNATIVE FORMS LISTED OVERLEAF)

* For NHS England referrals, please refer to the National Genomic Test Directory for available tests and eligibility criteria:

<https://www.england.nhs.uk/publication/national-genomic-test-directories/>

<input type="checkbox"/> DNA storage (no testing)	EDTA	Contact lab to activate testing on stored DNA
<input type="checkbox"/> DNA based testing: <input type="checkbox"/> Diagnostic <input type="checkbox"/> Carrier <input type="checkbox"/> Predictive	EDTA	(Provide R code, eligibility details and clinical utility)

<input type="checkbox"/> Rapid type/FISH testing/Fairchild Aspermatid/obesity	EDTA / Lithium Heparin	(Provide R code, eligibility details and clinical utility)
Nijmegen		
Rapid testing (infants): <input type="checkbox"/> trisomy 13/18 <input type="checkbox"/> trisomy 21	EDTA / Lithium Heparin	<input type="checkbox"/> SRY (chromosomal sex)

IV. Reason for referral (Please give details of previous genetic investigations in the family, if any.)

(For familial/cascade/follow up testing, provide index patient name and DOB, NHS no. or index patient report.)

V. Clinical Utility — Please indicate category of Clinical Utility **AND** provide details.

- ☐ Patient management (determining therapeutic decisions and/or clinical investigations and/or surveillance programme)
- ☐ Patient, parents, or adult relative reproductive decision making
- ☐ Unaffected relatives are seeking predictive testing

Details:

VI. Eligibility — Please provide details to confirm patient meets NHSE eligibility criteria for the test(s) requested.

Details:

If 'WGS' or the WGS Clinical Code is indicated (and 'Diagnostic' ticked), the laboratory will send you a reminder to send Record of Discussion(s) and the Test Order Form.

For WGS samples, it is also possible to send sample forms as “DNA for storage” by leaving Clinical Indication Code blank and ticking:

'DNA storage (no testing)'

- Requesting clinicians will receive a notification that DNA has been stored but the laboratory will not send any reminders for missing forms

If only requesting a sample for WGS, this section is optional (as this information will be included in the Test Order Form).

If requesting other non-WGS genetic testing (e.g. microarray, WES), please include clinical information

The form is double sided (page-2 not pictured) – please make sure to print both sides as information on the back is needed for phlebotomy and the processing of samples at the laboratory.

G. More resources:

1. Genomics Resources

[What is Genomics?](#)

[Genomics 101: Genomics in Healthcare](#)

[The Genomics Era: The Future of Genetics in Medicine](#)

[RCGP Genomics Toolkit](#)

[New Conditions Factsheet \(Genomics Education Programme\)](#)

2. WGS Resources

[Guide-to-requesting-WGS-RD-Nov-20.pdf \(hee.nhs.uk\)](#)

[Requesting whole genome sequencing: information for clinicians - Genomics Education Programme \(hee.nhs.uk\)](#)
[Test order forms - North Thames GMS : North Thames GMS \(norththamesgenomics.nhs.uk\)](#)

[Whole Genome Sequencing - North Thames GMS : North Thames GMS \(norththamesgenomics.nhs.uk\)](#)

[Rare Diseases Test Order Forms and Clinician Packs](#) (scroll to Rare Disease- whole genome sequencing (WGS))

[Whole Genome Sequencing Animation – North Thames GMS](#)

[Genomic Question Time drop-in session](#) (Teams link)

- First Thursday of the month 12:30-13:00
- Passcode: aDYRNt
- Or contact us on: nt-gmsa@gosh.nhs.uk

[Whole Genome Sequencing – Genetic Test Ordering](#)

How useful did you find this how-to guide? Please let us know how we can improve.