# Guidance document for the completion of the WGS Rare Disease Trio referral form and Record of Discussion

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## Contents

Objectives: Patient access to the national WGS service is now available through the Genomic Laboratory Hub network. The following indications are eligible and this document aims to support clinicians with the referral and research consenting process.

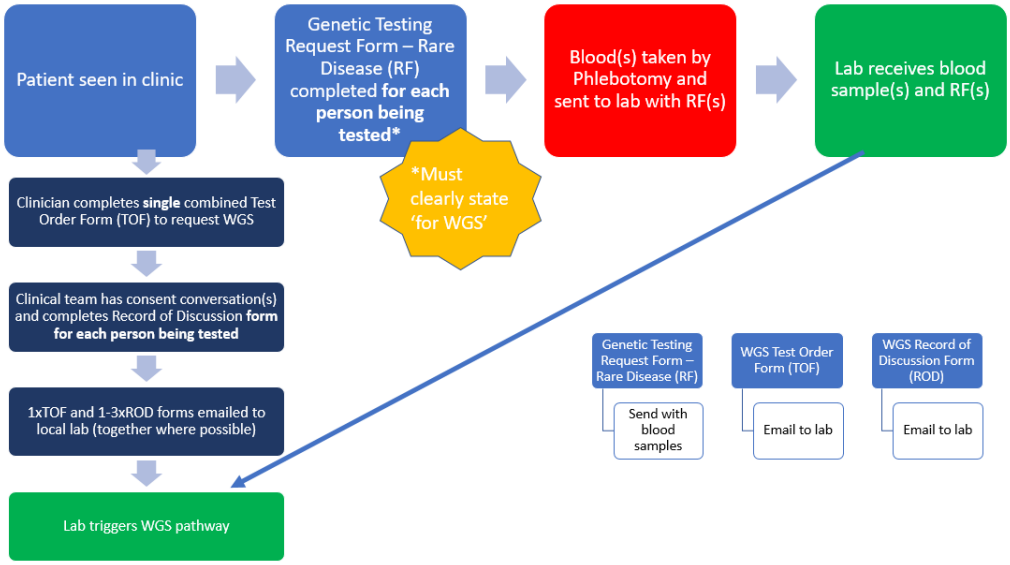
## WGS Rare Disease Indications

For eligibility criteria and sample requirements please see
Whole Genome Sequencing Documentation - NHS Yorkshire and North East Genomics Medicine Service (ney-genomics.org.uk)

| Speciality Group | Test code | Clinical Indication |
|---|---|---|
| Endocrinology | R143.4 | Neonatal diabetes |
| Metabolic | R98.2 | Likely inborn error of metabolism - targeted testing not possible |
| Musculoskeletal | R104.3 | Skeletal dysplasia |
| Musculoskeletal | R100.3 | Rare syndromic craniosynostosis or isolated multisuture synostosis |
| Neurology | R54.3 | Hereditary ataxia with onset in adulthood |
| Neurology | R55.4 | Hereditary ataxia with onset in childhood |
| Neurology | R59.3 | Early onset or syndromic epilepsy |
| Neurology | R61.4 | Childhood onset hereditary spastic paraplegia |
| Neurology | R83.2 | Arthrogryposis |
| Neurology | R381.2 | Other rare neuromuscular disorders |
| Neurology | R84.4 | Cerebellar anomalies |
| Neurology | R85.2 | Holoprosencephaly (not chromosomal) |
| Neurology | R86.3 | Hydrocephalus |
| Neurology | R87.3 | Cerebral malformation |
| Neurology | R88.3 | Severe microcephaly |
| Neurology | R109.3 | Childhood onset leukodystrophy |
| Neurology | R56.3 | Adult onset movement disorder WGS |
| Neurology | R57.5 | Movement disorders - childhood onset WGS |
| Neurology | R58.4 | Neurodegenerative disorders - adult onset WGS |
| Neurology | R60.3 | Hereditary spastic paraplegia - adult onset WGS |
| Neurology | R62.2 | White matter disorders - adult onset WGS |
| Neurology | R78.4 | Hereditary neuropathy WGS |
| Renal | R193.4 | Cystic renal disease |
| Renal | R257.2 | End-stage renal disease - childhood onset WGS |
| Core | R29 | Intellectual disability |
| Core | R27 | Congenital malformation and dysmorphism syndromes |
| Core | R69.5 | Hypotonic infant with a likely central cause |
| Core | R89 | Ultra-rare and atypical monogenic disorders |
| Cardiology | R135.2 | Paediatric or syndromic cardiomyopathy WGS |
| Opthalmology | R31.3 | Cataracts WGS |
| Opthalmology | R32.2 | Retinal disorders WGS |
| Opthalmology | R33.3 | Retinal disorders WGS |

| | | |
|---|---|---|
| Opthalmology | R34.3 | Retinal disorders WGS |
| Opthalmology | R35.3 | Retinal disorders WGS |
| Opthalmology | R36.2 | Structural eye disease WGS |
| Immunology | R15.4 | Primary immunodeficiency WGS |

## Whole Genome Sequencing Referral Process Flow




## Instructions for Completing the WGS Sequencing Referral Process

The WGS test ordering process is different from the standard request process used to access genomic testing. The preferred analytical pathway requires samples form the patient and their parents, this is trio genome analysis. In the case of adult patients it may not be possible to get samples from the family trio, in this case a singleton sample from the patient alone can be used. A family trio can be managed on one WGS Rare Disease Referral Form.

However, it is not possible to use  one form for Phlebotomy for the family group and so it is necessary to fill out a standard DNA request form for each member of the trio.

- When seeing a family in clinic who may be eligible for WGS testing, please complete a **Genetic Testing Request Form - Rare Disease** for **each individual** family member
- Clearly mark these forms with "FOR WGS" in the Test section
- The **Genetic Testing Request Form - Rare Disease** is to be used for Phlebotomy
- The WGS indication will enable to laboratories to signpost the sample through the correct processing route

Please use local forms. A copy of the NE&Y GLH **referral form** can be found here: [Microsoft Word - GLH_rare_Disease_final2.docx (ney-genomics.org.uk)]

A WGS Rare Disease Trio form then needs to be completed – **one for each family** (trio, duo or singleton). A copy of the form can be found by clicking here: https://ney-genomics.org.uk/wp-content/uploads/2021/07/WGS-RD-Trio-referral-form.pdf.

- This form can be completed outside of the clinic session
- All fields need to be completed – this can be done by hand or using demographic stickers, however it is advised that the form is completed electronically as this will enable auto-population of fields in other parts of the form
- The document is a pdf and can be completed electronically by clicking on the Fill and Sign icon in the right had pane

- Test Directory Clinical Indication & code (reason for testing)
  A drop-down list is provided where the clinical indication and R code can be selected. At present the number of clinical indications for which you can request WGS is limited to those in the drop-down list.
  The National Rare Disease Genomic Test Directory can be found here: https://www.england.nhs.uk/publication/national-genomic-test-directories/

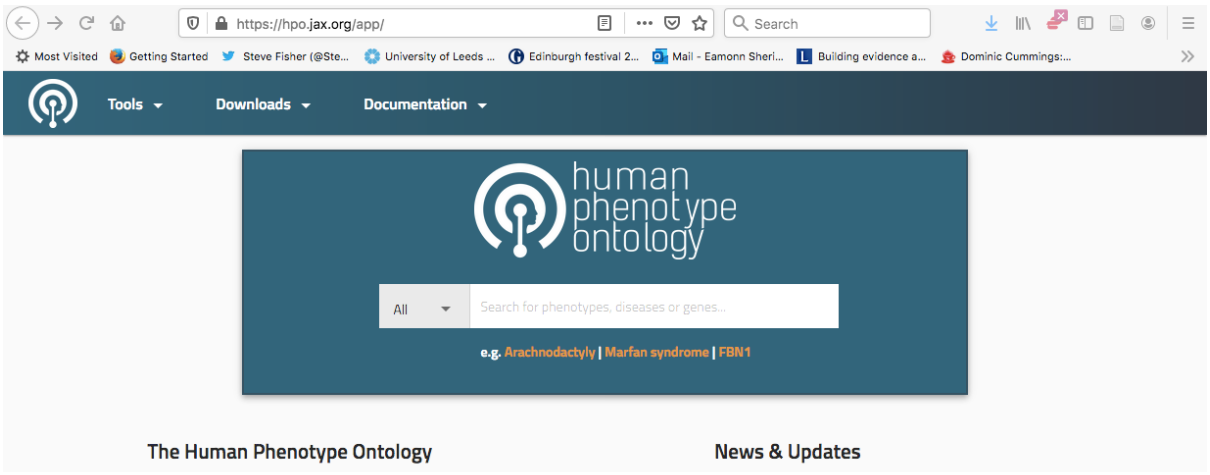
- In addition to the primary indication you can may also choose secondary indications by stating a virtual panel in the Additional Panel box. Virtual panel information can be found in PanelApp.
  https://nhsgms-panelapp.genomicsengland.co.uk/panels

  The additional panels can be found by clicking in the search box and inputting GMS Rare Disease Virtual, this will bring up a list of panels which can be chosen in addition to the primary panels

- If sending a trio or duo complete the family member to be tested section.
  Electronic entry will auto-populate the samples being sent to GLH extraction lab section
  The section on Sample volume/comments etc do not need to be completed.

- Record of discussion form. Please see next section for details. **This must be completed, or the sample will be extracted only and not sent for analysis.**
- Page 2 of the WGS Rare Disease Trio referral form concerns the collection of phenotypic information. This can be provided either through the addition of HPO terms, OR selection from the phenotypes listed in the tables provided.

- The Human Phenotype Ontology (HPO) provides a standardized vocabulary of phenotypic abnormalities encountered in human disease. Each term in the HPO describes a phenotypic abnormality.
  Follow the link below which takes you to page, the top of which looks like the image below.
  Human Phenotype Ontology (jax.org)




- Enter a search term in the search box and select from the drop down list
  Clicking on the selected phenotype will bring up a page with further information
  You can copy and paste the appropriate HPO terms into the table and indicate presence or absence for each affected family member
  Up to ten terms can be added
- Alternatively, choose from the phenotypes available on the form and tick them if they are present in the proband

It is critical that this information is entered clearly and correctly and that exact HPO terms are used. Incorrect clinical and / or family information can lead to incorrect or missed results.

| 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 |

| Neurology |
|---|
| Muscular dystrophy |
| Myopathy |
| Myotonia |
| Fatigable weakness |
| Peripheral neuropathy |
| Distal arthrogryposis |
| Arthrogryposis multiplex congenita |
| Cognitive impairment |
| Parkinsonism |
| Spasticity |
| Chorea |

That completes the WGS Rare Disease Trio request form. Once the Record of Discussion for each family member is complete, the forms can be sent together, to your local GLH laboratory.

## Instructions for Completing the Record of Discussion Form (RoD).

- A RoD form needs to be completed for **each member** of the trio, duo, or singleton case. A copy of the form can be found by clicking here: https://ney-genomics.org.uk/wp-content/uploads/2021/07/WGS-Record-of-Discussion-form.pdf
  Anyone of age 16 years and over should complete the form
- A parent can sign for a child, please indicate in appropriate box
- If signing as a Consultee, on behalf of an adult without capacity, please indicate in the appropriate box (see below).
- Instructions for the Consultee: If the Research option is selected (i.e. The answer to question B is 'Yes'), you MUST complete the Mandatory Genomic Consultee Declaration, which can be found here:
  NHS England » NHS Genomic Medicine Service genomic consultee declaration

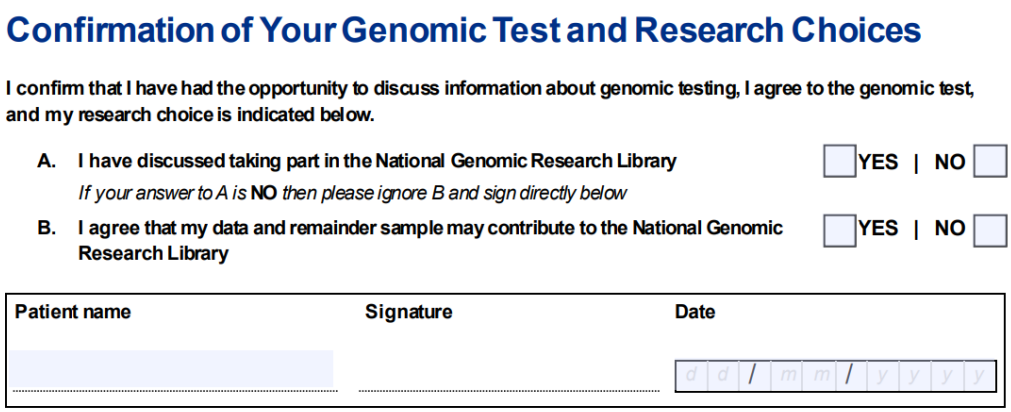
- This is an electronic form and can be completed using Fill and Sign, this will auto-populate demographic information

- The form is in four sections

    - Record of discussion regarding genomic testing
    - Record of discussion regarding the national genomic research library (NGRL)
    - Confirmation of your genomic test and research choices
    - Healthcare professional use only

The statements provided in each of the record of discussion sections must be discussed with each family member

- Confirmation of your genomic test and research choices
  **This must be completed.** If and only if, the National Genomic Research Library (NGRL) has been discussed, tick Yes to question A.
  Depending on the patient's response tick either yes or no to question B.
  If you have not discussed the (NGRL) then select No to question A and move to the patient or guardian signatures.



**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 |
|---|---|---|
| | | d d / m m / y y y y |

- Healthcare professional use only

Complete this section. Patient category must be completed in all cases.
Test Type is always Rare and Inherited Diseases - WGS.
If the answer to research choice A is No, then fill this section.
Enter your name as the responsible clinician and the local hospital number.
Once complete sign the form, you can use the signature facility in Adobe.
This is accessed by clicking on the fountain pen nib icon in the tools pane

**Healthcare professional use only**

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

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

The WGS Rare Disease referral and record of discussion process is now complete.
The full set of documentation can be emailed to your local GLH laboratory.
Enter the proband NHS number and WGS request in the subject field

Leeds Genetic Laboratory leedsth-tr.DNA@nhs.net.
Sheffield Diagnostic Genetic Laboratory sheffield.diagnosticgenetics@nhs.net
Newcastle Genetic Laboratory nuth.dna@nhs.net

**THE SAMPLES WILL NOT BE DISPATCHED FOR ANALYSIS UNTIL A COMPLETED TEST REQEUST FORM AND THE REQUISITE ROD FORMS HAVE BEEN RECEIVED IN THE LAB.**

Additional information and support tools can be found at Whole Genome Sequencing - NHS Yorkshire and North East Genomics Medicine Service (ney-genomics.org.uk)