NHS
South East
Genomic Laboratory Hub

How to Order Whole Genome Sequencing (WGS) for Rare Disease

Before ordering

- Check patient is eligible for WGS and select clinical indication using
  - National Genomic Test Directory https://www.england.nhs.uk/wp-content/uploads/2018/08/rare-and-inherited-disease-eligibility-criteria-v5-april-2023.pdf
  - Test Selection Tool https://test-selection-private.genomics.nhs.uk/test-selection/
- Check optimal family structure
  - Where indicated in the test directory, it is preferable to test as a trio with the parents of the proband as this improves the diagnostic rate and accuracy of WGS.
  - **Singleton referrals where the proband is under 16, will be paused until Records of Discussion and samples are obtained from the parents, unless a reason is provided otherwise. Contact our team for further resources and support.**
- If the test directory does not indicate the method of testing is WGS, please use a non-WGS consent form which can be found using the link below:
  - https://southeastgenomics.nhs.uk/glh/forms/

Completing a WGS referral for Rare Disease

WGS referrals can only be processed once the South East GLH laboratory has received all of the following:

1. **Record of Discussion Form**
   One form per family member
   - Ensure 'patient category' and 'test type' are completed
   - Clinician must ensure they have signed and dated the ROD
   - If consent is recorded remotely, ensure that 'remote consent' is ticked
   - If consent is recorded in person, ensure that the patient has signed and dated
   - Patient information sheets are located here: Information for Patients – South East Genomics Laboratory Hub

2. **Test Order Form**
   One form per family (proband + family members)
   - Form to be completed in full.
   - The TOF must include the Family structure and Test Directory clinical indication & code, these can be selected using the National Genomic Test Directory https://www.england.nhs.uk/publication/national-genomic-test-directories/ and the NHS Genomic Medicine Service (GMS) Signed Off Panels Resource https://nhsgms-panelapp.genomicsengland.co.uk
   - The TOF must include HPO terms using the specific terminology from Human Phenotype Ontology (jax.org)
   - Singletons (proband only) and duos (proband and one parent) can be accepted. The use of a trio (proband and both parents) for WGS testing provides a more efficient and higher quality analysis and a trio should always be referred where possible.

3. **Blood sample**
   To send a blood sample to our laboratory, please complete a blood sample order form. Samples should be stored in EDTA and sent to our South East GLH:

   South East GLH
   Genetics Specimen Reception
   5th floor Tower Wing
   Guy's Hospital
   London
   SE1 9RT

South East
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Completed Test Order forms and Record of Discussion forms can be e-mailed, once completed by clinicians, to the WGS pathway coordinators at gst-tr.wgs@nhs.net to prevent delays. **Please send one referral per email.**

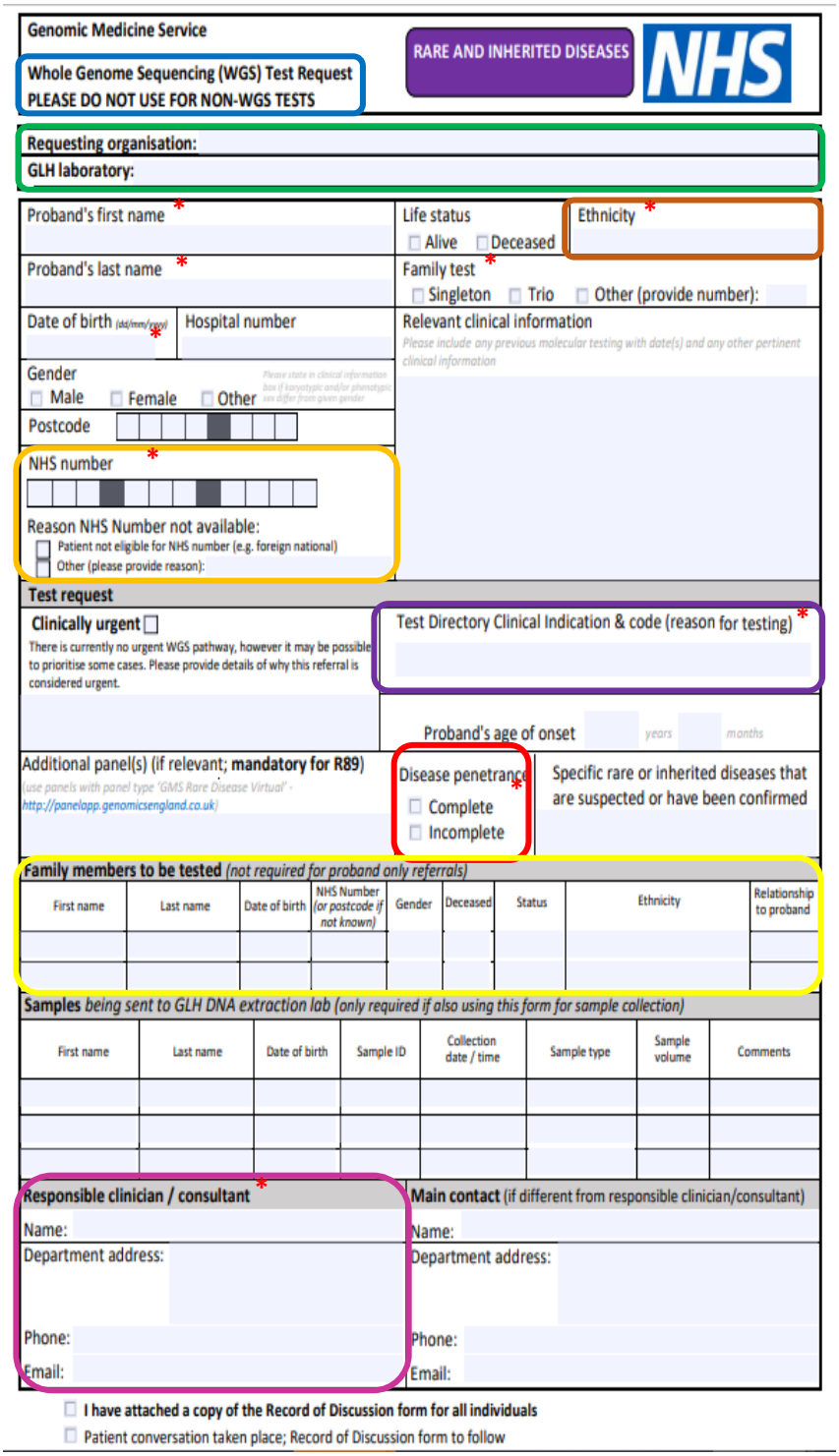
WGS forms can be downloaded here on our website: RD Whole Genome Sequencing – South East Genomics

These forms are for WGS testing only; if non-WGS testing, that isn't present on the additional panels, is required in addition to WGS please complete a separate standard genetics laboratory referral form.

Forms are shown below with guidance on all of the different sections which require completion.

Test Order Form (page 1)

Sections with an * must be completed



Genomic Medicine Service

Whole Genome Sequencing (WGS) Test Request
PLEASE DO NOT USE FOR NON-WGS TESTS

RARE AND INHERITED DISEASES

NHS

Requesting organisation:
GLH laboratory:

Proband's first name *
Proband's last name *
Date of birth (dd/mm/yyyy) *
Hospital number
Gender
Male Female Other
Postcode
NHS number *
Reason NHS Number not available:
Patient not eligible for NHS number (e.g. foreign national)
Other (please provide reason):

Life status
Alive Deceased
Family test *
Singleton Trio Other (provide number):
Relevant clinical information
Please include any previous molecular testing with date(s) and any other pertinent clinical information

Ethnicity *

Test request

Clinically urgent
There is currently no urgent WGS pathway, however it may be possible to prioritise some cases. Please provide details of why this referral is considered urgent.

Test Directory Clinical Indication & code (reason for testing) *

Proband's age of onset years months

Additional panel(s) (if relevant; **mandatory for R89**)
(use panels with panel type 'GMS Rare Disease Virtual' - http://panelapp.genomicsengland.co.uk)

Disease penetrance *
Complete
Incomplete

Specific rare or inherited diseases that are suspected or have been confirmed

Family members to be tested *(not required for proband only referrals)*

First name	Last name	Date of birth	NHS Number (or postcode if not known)	Gender	Deceased	Status	Ethnicity	Relationship to proband

Samples *being sent to GLH DNA extraction lab (only required if also using this form for sample collection)*

First name	Last name	Date of birth	Sample ID	Collection date / time	Sample type	Sample volume	Comments

Responsible clinician / consultant *
Name:
Department address:
Phone:
Email:

Main contact (if different from responsible clinician/consultant)
Name:
Department address:
Phone:
Email:

I have attached a copy of the Record of Discussion form for all individuals
Patient conversation taken place; Record of Discussion form to follow

Please complete the TOF **electronically** and send to gst-tr.wgs@nhs.net to reduce discrepancies and delays in testing.
Completion of patient details electronically will auto-populate relevant sections of the TOF.

For WGS testing only- if non-WGS testing is required in addition to WGS please use separate standard referral form.

Requesting organisation: **Your hospital**
GLH laboratory to receive sample: **South East GLH**

Ethnicity required to be entered for patient to improve equity of access to genetic testing

Important to include an NHS number as required for the WGS pipeline. If no NHS number is available a reason will need to be provided.

This should be the main clinical indication (R code) which can be found in the National Test Directory. Only record **ONE** in this box and must be a **WGS eligible clinical indication.** Additional panels can be requested using the 'Additional panels' box

Disease penetrance options alter variant filtering so it is important to select the most appropriate and applicable option**. If unknown: Select incomplete**

It is important to detail the clinical status of family members as this can affect the filtering of variants based on expected inheritance. **If status of parent(s) is unknown: Select unaffected**

Add your details: Name department address and email. This will ensure the results get sent back to you.

Test Order Form (page 2)

Sections with an * must be completed

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

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

HPO Terms - Please ensure those given match those available at (https://hpo.jax.org/app/) *						
	Present	Absent	Present	Absent	Present	Absent

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

Craniosynostosis
Bicoronal synostosis
Unicoronal synostosis
Metopic synostosis
Sagittal craniosynostosis
Lambdoidal craniosynostosis
Multiple suture craniosynostosis

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

Neurology
Muscular dystrophy
Myopathy
Myotonia
Fatigable weakness
Peripheral neuropathy
Distal arthrogryposis
Arthrogryposis 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

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

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

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

Select as many specific HPO terms as possible, relevant to your patient and parents.
The more accurate the HPO terms, the more accurate the analysis and interpretation of the results.

Add HPO terms that apply to patient and tick whether these are present in proband and parents who were referred. HPO terms can be found on: Human Phenotype Ontology (jax.org)

a. We need AT LEAST ONE HPO term to be filled out – please do not leave this section blank
b. Do not abbreviate HPO terms; please write them out in full.
c. Please do not use nonstandard descriptions of HPO terms; please check on the HPO database that the HPO term you wish to record is listed.
d. There are some transcription errors of HPO terms. We should be able to pick up on most of these, but please be careful to ensure the HPO term is exactly as it appears on the database.
e. There are 10 allocated slots for HPO terms, as well as a section for additional HPO terms. Please fill in the 10 slots first before moving onto the additional section. If you need to fill in this section, please record whether the HPO term is present or absent
f. For unaffected parents, it is not necessary to record 'absent' HPO terms unless they have specifically been tested for that phenotype.

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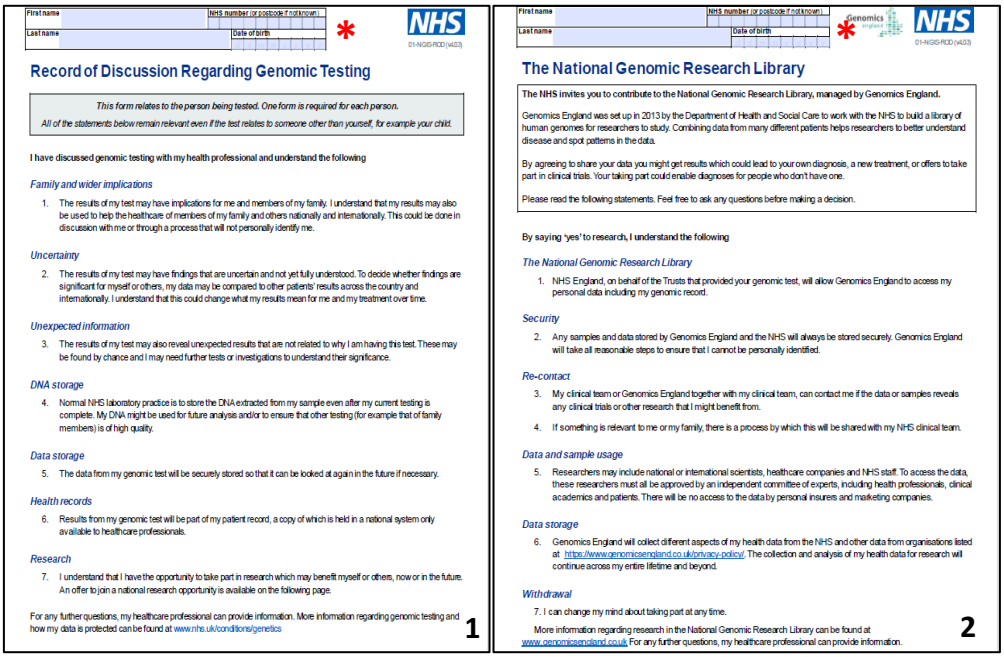
Record of Discussion form consent form (pages 1-3)

Sections with an * must be completed



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

NHS 01-NGIS-ROD (v4.03)

Record of Discussion Regarding Genomic Testing

This form relates to the person being tested. One form is required for each person.
All of the statements below remain relevant even if the test relates to someone other than yourself, for example your child.

I have discussed genomic testing with my health professional and understand the following

Family and wider implications

1. The results of my test may have implications for me and members of my family. I understand that my results may also be used to help the healthcare of members of my family and others nationally and internationally. This could be done in discussion with me or through a process that will not personally identify me.

Uncertainty

2. The results of my test may have findings that are uncertain and not yet fully understood. To decide whether findings are significant for myself or others, my data may be compared to other patients' results across the country and internationally. I understand that this could change what my results mean for me and my treatment over time.

Unexpected information

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

DNA storage

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

Data storage

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

Health records

6. Results from my genomic test will be part of my patient record, a copy of which is held in a national system only available to healthcare professionals.

Research

7. I understand that I have the opportunity to take part in research which may benefit myself or others, now or in the future. An offer to join a national research opportunity is available on the following page.

For any further questions, my healthcare professional can provide information. More information regarding genomic testing and how my data is protected can be found at www.nhs.uk/conditions/genetics

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

Genomics England | NHS 01-NGIS-ROD (v4.03)

The National Genomic Research Library

The NHS invites you to contribute to the National Genomic Research Library, managed by Genomics England.

Genomics England was set up in 2013 by the Department of Health and Social Care to work with the NHS to build a library of human genomes for researchers to study. Combining data from many different patients helps researchers to better understand disease and spot patterns in the data.

By agreeing to share your data you might get results which could lead to your own diagnosis, a new treatment, or offers to take part in clinical trials. Your taking part could enable diagnoses for people who don't have one.

Please read the following statements. Feel free to ask any questions before making a decision.

By saying 'yes' to research, I understand the following

The National Genomic Research Library

1. NHS England, on behalf of the Trusts that provided your genomic test, will allow Genomics England to access my personal data including my genomic record.

Security

2. Any samples and data stored by Genomics England and the NHS will always be stored securely. Genomics England will take all reasonable steps to ensure that I cannot be personally identified.

Re-contact

3. My clinical team or Genomics England together with my clinical team, can contact me if the data or samples reveals any clinical trials or other research that I might benefit from.

4. If something is relevant to me or my family, there is a process by which this will be shared with my NHS clinical team.

Data and sample usage

5. Researchers may include national or international scientists, healthcare companies and NHS staff. To access the data, these researchers must all be approved by an independent committee of experts, including health professionals, clinical academics and patients. There will be no access to the data by personal insurers and marketing companies.

Data storage

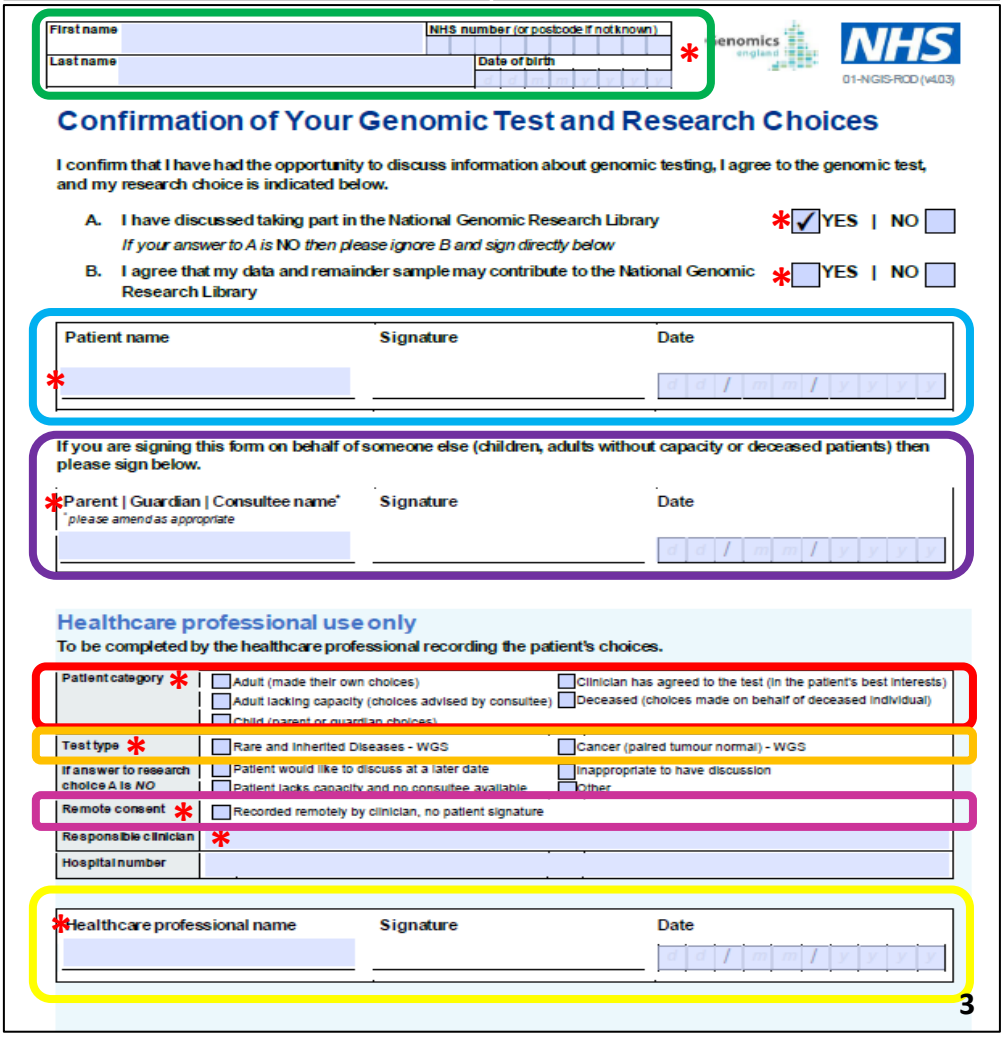
6. Genomics England will collect different aspects of my health data from the NHS and other data from organisations listed at https://www.genomicsengland.co.uk/privacy-policy/. The collection and analysis of my health data for research will continue across my entire lifetime and beyond.

Withdrawal

7. I can change my mind about taking part at any time.

More information regarding research in the National Genomic Research Library can be found at www.genomicsengland.co.uk For any further questions, my healthcare professional can provide information.

2



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

Genomics England | NHS 01-NGIS-ROD (v4.03)

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

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
		d d / m m / y y y y

Healthcare professional use only

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

Patient category *	☐ Adult (made their own choices)	☐ Clinician has agreed to the test (in the patient's best interests)
	☐ Adult lacking capacity (choices advised by consultee)	☐ Deceased (choices made on behalf of deceased individual)
	☐ Child (parent or guardian choices)	
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	☐ Inappropriate to have discussion
	☐ Patient lacks capacity and no consultee available	☐ Other
Remote consent *	☐ Recorded remotely by clinician, no patient signature	
Responsible clinician *		
Hospital number		

*Healthcare professional name	Signature	Date
		d d / m m / y y y y

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Contact gst-tr.hellogenomics@nhs.net to arrange consenting training for WGS.

Patient information sheets for WGS are located here: Information for Patients – South East Genomics Laboratory Hub

Patient name, NHS number and DOB are to be entered to the signature page. *Tip: Completion of patient details electronically will auto populate patient details for all three*

If patient has capacity to consent for themselves, they will need to sign and date here. If consent is being recorded remotely, please enter the patient's name here and indicate 'remote consent' below.

If patient does not have capacity to consent for themselves, they will need a consultee to sign and date here. If consent is being recorded remotely, please enter the consultee's name here and indicate 'remote consent' below.

Ensure the correct patient category is indicated here.

Ensure test type is highlighted here as 'Rare and Inherited Diseases-WGS'.

If consent was recorded remotely, please tick this box.

Please ensure you have signed and dated here.