NHS
South East
Genomic Laboratory Hub

Whole Genome Sequencing

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What Test?

- National Genomic Test Directory
  - https://southeastgenomics.nhs.uk/glh/#national-test-directory
- Testing method
  - WGS / Non-WGS – paperwork is different
- Optimal Family Structure
  - Singleton / Trio (trio is preferred)
- Test Selector
  - https://test-selection-private.genomics.nhs.uk/test-selection/
- PanelApp
  - For when you are interested in specific genes
  - https://nhsgms-panelapp.genomicsengland.co.uk/
- Epilepsy
  - R59 – WGS and Microarray
  - SCN1A
  - Dravet

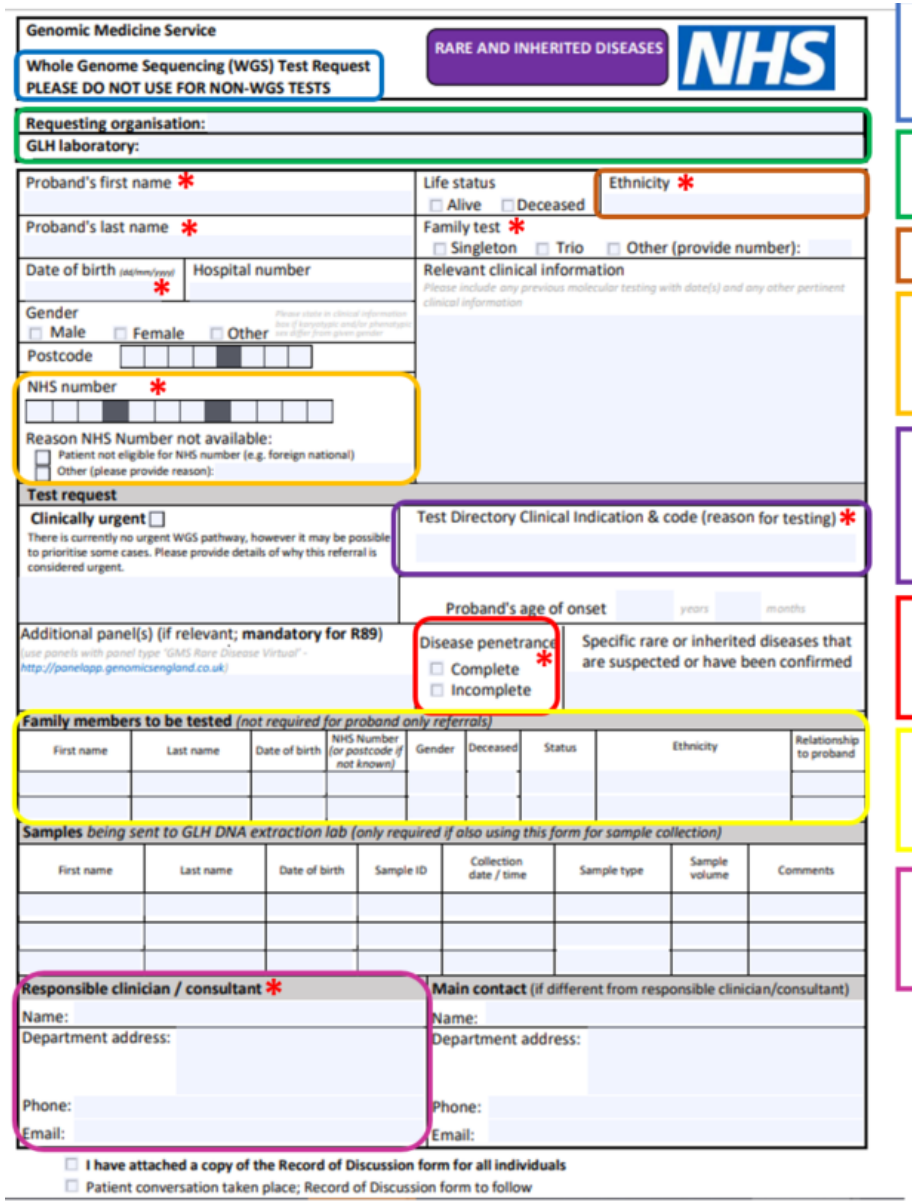
WGS: What do you need?

Paperwork emailed to gst-tr.wgs@nhs.net

- For any patient who is having Whole Genome Sequencing:
- Sample
  - 2x EDTA sent to:
  - Genetics Laboratories, 5th Floor, Tower Wing, Guy's Hospital, Great Maze Pond, London, SE1 9RT
  - http://www.viapath.co.uk/sites/default/files/upload/MF-G-RequestForm_2.pdf
- Test Order Form
  - One per family
  - With the R code, familial structure and HPO terms
  - https://southeastgenomics.nhs.uk/wp-content/uploads/2021/04/GMS-Test-Order-Form-Rare-Disease-Trio-Pilot-Apr-2021.pdf
- Record of Discussion
  - One per person
  - https://www.england.nhs.uk/wp-content/uploads/2021/09/nhs-genomic-medicine-service-record-of-discussion-form.pdf

Test Order Form (TOF)

One per family



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

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

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.**

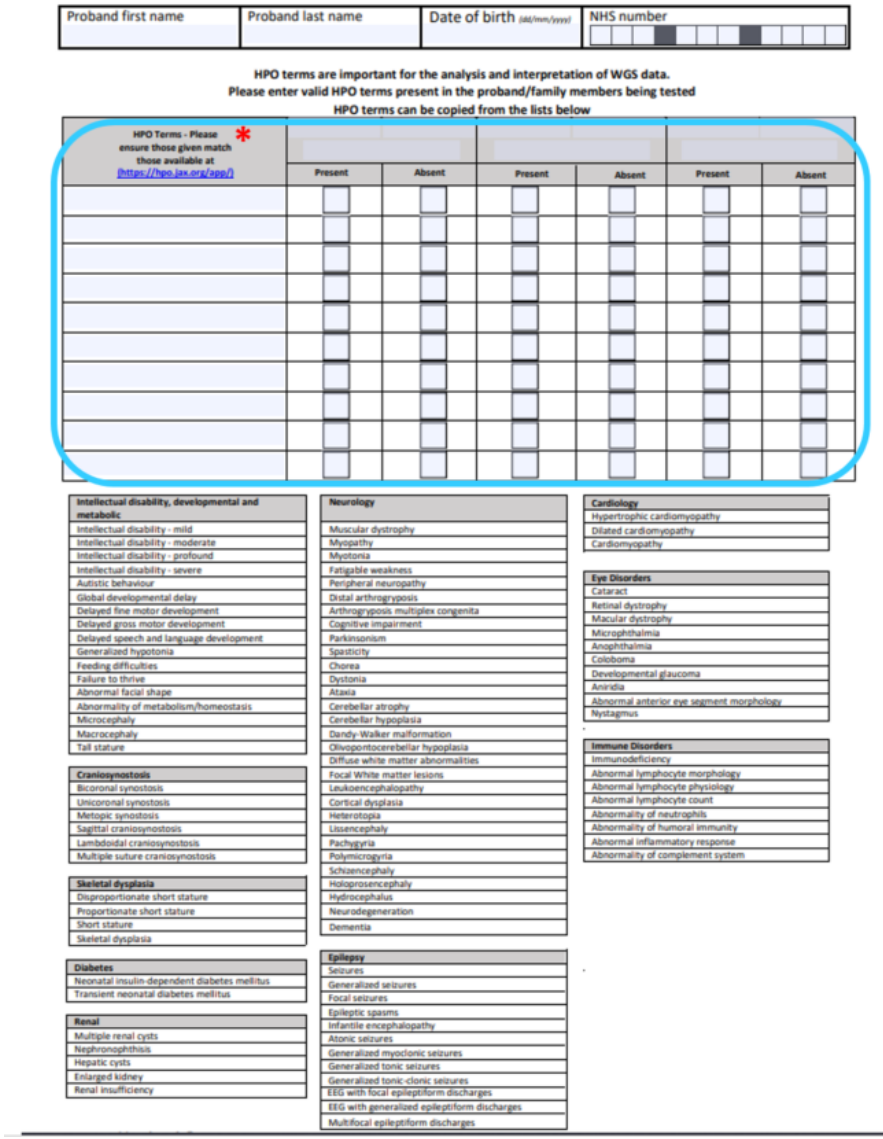
Disease penetrance options alter variant filtering so it is important to select the most appropriate and applicable option.

It is important to detail the clinical status of family members as this can affect the filtering of variants based on expected inheritance.

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

Test Order Form (TOF)

One per family



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

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. Do not abbreviate HPO terms; please write them out in full.
b. 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.
c. 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.
d. 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
e. For unaffected parents, it is not necessary to record 'absent' HPO terms unless they have specifically been tested for that phenotype.
f. We need AT LEAST ONE HPO term to be filled out – please do not leave this section blank

- https://hpo.jax.org/app/

Record of Discussion (ROD)

One per person

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

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.

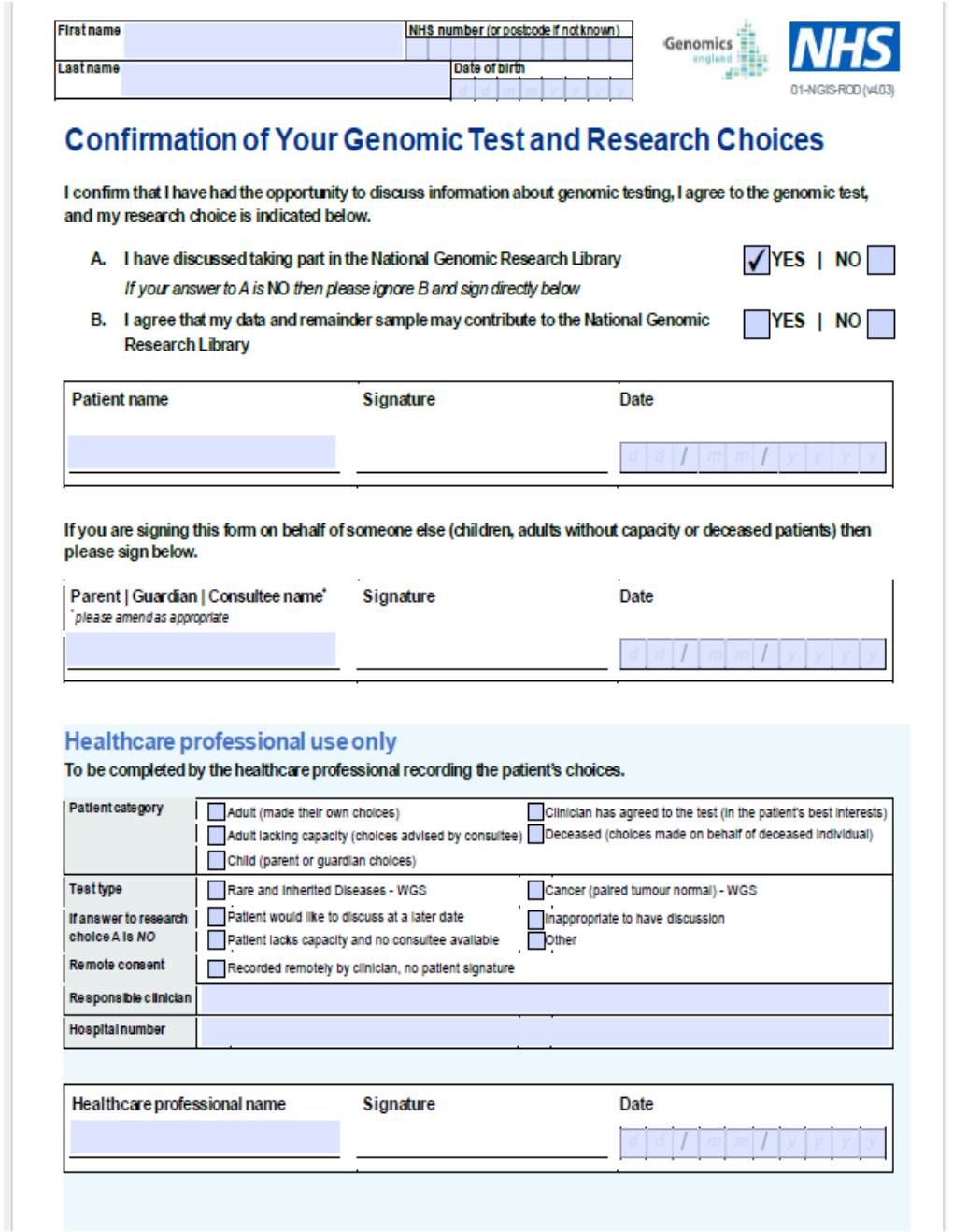
Withdrawal

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.

Record of Discussion (ROD)

One per person



First name		NHS number (or postcode if not known)	
Last name		Date of birth	d d / m m / y y y y

Genomics england

NHS

01-NGIS-RCD (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

National Genomic Research Library (NGRL)

- Optional research offered to patients who are having WGS
- Database of de-identified genomic data, health data and samples
- Approved researchers can access the data
- Aim is to improve the diagnostic potential of genomic information
- Patients may or may not benefit
- Patients may be contacted
- Patients can withdraw at any time
- https://www.youtube.com/watch?v=oPfZxoevYGI
- https://www.genomicseducation.hee.nhs.uk/supporting-the-nhs-genomic-medicine-service/national-genomic-research-library-information-for-clinicians/

Sample and Result Process

- Blood sample sent to Guy's Laboratories, where DNA is extracted
- DNA sent to Birmingham for processing and plating
- Plate sent to Cambridge for sequencing
- Sequence is returned to GSTT (usually) for analysis
- Analysis takes around 6 months
- Reports emailed to clinician on TOF
- **Whole process is around 12-14 months**

Resources

- Required Paperwork:
  - Test Order Form https://bit.ly/41YUVvI
  - Record of Discussion https://bit.ly/3NGLY5I
- Patient Information Sheets:
  - WGS PIS https://bit.ly/3HyOvLu
  - Research PIS https://bit.ly/3LS0101
- Useful websites:
  - SE GLH guidance on filling out forms https://bit.ly/3LAfqbg
  - Clinician Guide to Consenting https://bit.ly/4227mXM
  - Future Learn Course https://bit.ly/40XCg1Z
  - National Genomic Test Directory https://bit.ly/3VtnFKp
  - HPO terms https://hpo.jax.org/app/
  - Test Selector https://bit.ly/42g6heu
  - PanelApp https://nhsgms-panelapp.genomicsengland.co.uk/
  - NGRL Information https://bit.ly/3Vuwswo

Contacts

- Clinical Queries
  - Dragana Josifova Dragana.Josifova@gstt.nhs.uk
  - Deborah Ruddy Deborah.Ruddy@gstt.nhs.uk
- Nursing Queries
  - Mark Mencias Mark.Menciaso@stgeorges.nhs.uk
- Consenting training
  - Genomic Practitioners: gst-tr.hellogenomics@nhs.net
- WGS referral email
  - gst-tr.wgs@nhs.net
- General Genetic Queries
  - gst-tr.southeastglh@nhs.net
  - gst-tr.viapathgeneticsadmin@nhs.net