NHS
North Thames
Genomic Medicine Service

Referring Whole Genome Sequencing (WGS) for Cancer

Clinician's How-To Guide

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A. WGS Checklist

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Step 1: Check WGS eligibility

On the National Genomic Test Directory, check "WGS" is indicated under "Technology"

Check patient meets 'Exhausted all Standard of Care' eligibility criteria

Step 2: Complete the Test Order Form

Complete the Test Order form and the Cancer WGS Eligibility Form

Step 3: Complete the Record of Discussion form

After consenting the patient, complete a Record of Discussion (+ a *Consultee form* if an adult lacking capacity)

Step 4: Organise WGS samples

Store a tumour and germline sample. If needed, provide the patient with completed Sample Form to take with them to their local hospital/phlebotomy for their germline sample

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

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

B. WGS Pathways

There are **two** suggested pathways for WGS referrals. One is by requesting WGS yourself, and another is by going through 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)
- ◯ Make sure patient meets the 'Exhausted all Standard of Care (ESOC)' eligibility criteria (page 8)

Patient Appointment

- ◯ Discuss family history
- ◯ Go through brief consent discussion to make sure the patient is happy with the genetic referral
- ◯ Complete the Test Order form (page 6) with input from pathology and the Eligibility form (page 8).

? Requesting via Genomic Practitioner

NO

Patient Appointment [cont.]

- ◯ Go through entire consent discussion
- ◯ Complete Record of Discussion (*page 7*) page can be virtually completed or with the patient face-to-face) (+ *Consultee form* if adult lacking capacity)
- ◯ Provide Patient Information Leaflets and video link
- ◯ Arrange for tumour sample to be stored
- ◯ Provide Sample Form(s) (page 12) for germline sample collection
- ◯ Save forms to Electronic Patient Record

Following the Appointment

- ◯ Send Record of Discussion form, Eligibility Form and Test Order form to gos-tr.pmu@nhs.net
- ◯ Confirm with laboratory that all samples have arrived and the test has been activated

Laboratory will not follow up on missing samples/incomplete referrals

YES

- ◯ Arrange for tumour sample to be stored
- ◯ Send Test Order Form and Eligibility Form to Genomic Practitioner (gos-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 Blood Test Request Form for germline sample (if not arranged before)
- ◯ Send forms to department pathway coordinator to save to Electronic Patient Record

Following the Appointment

- ◯ Send Record of Discussion form, Eligibility Form and Test Order form to gos-tr.pmu@nhs.net
- ◯ Confirm with laboratory that all samples have arrived, and the test has been activated

C. Eligibility for WGS

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Patient eligibility for WGS clinical indications can be found on the NHS England » National genomic test directory. On the spreadsheet, check "WGS" is indicated under "Technology". If you need to determine which genes/panels are included in a clinical indication, please visit PanelApp.

Document

.xls

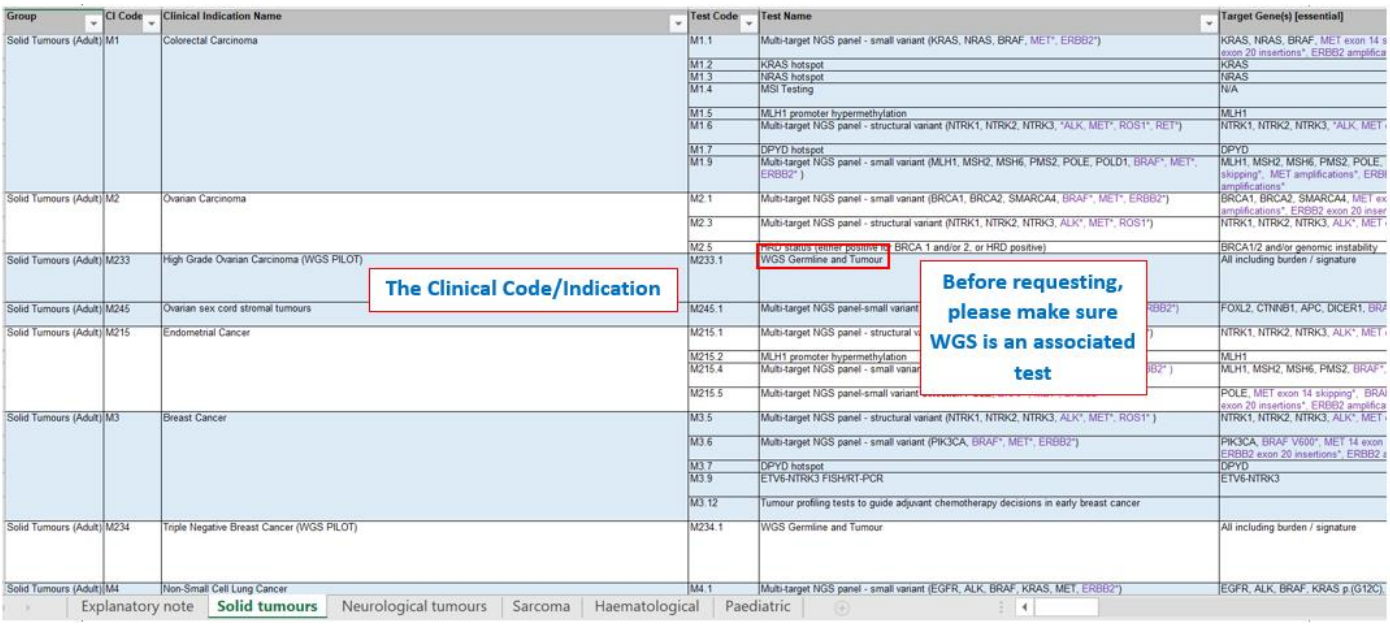
National genomic test directory for cancer

Microsoft Excel 507 KB

Summary

The national genomic test directory for cancer specifies the genomic tests commissioned by the NHS in England for cancer, the technology by which they are available, and the patients who will be eligible to access to a test.

Version 11 published January 2025.



Patient eligibility for WGS also depends upon their having received Standard of Care genetic testing. A Pro Forma document must be submitted along with the referral which outlines this eligibility criteria (page 8).

D. Sample Requirements

1. Tumour sample
   All cancer WGS tests require a somatic (tumour) sample.
   - Solid tumours
     - Formalin fixed paraffin embedded (FFPE) samples cannot be submitted WGS due to the poor data quality.
     - A suitable amount of fresh tissue is required to extract a minimum of 2ug of tumour DNA, preferably at a concentration of 50ug/ul in a volume of 115ul. Quantity of extracted DNA from a solid tumour is variable, but the following sample quantities are usually adequate to achieve 2ug:
       - 5mm x 5mm x 2mm of tumour tissues
       - 15mm x 2mm needle core biopsy

    - Invasive malignant nuclei must account for at least 30% of the nuclei present in the tissue sample submitted for WGS. Additionally, the sample should have less than 20% necrosis by area. An assessment of tumour cellularity should be included in the Test Order Form.
    - DNA extraction is usually performed on the entire sample received by the pathologist, so this should be considered if the sample is required for any other future use. Any remaining DNA may be stored.
    - Further details can be found in the sample handling guidance here.
- Haematological tumours
    - Suitable tumour material for leukaemia are bone marrow aspirate or peripheral blood samples containing at least 20% blasts morphologically.
    - Other bodily fluids can be used if proven to be infiltrated with AML/ALL, provided DNA quality and quantity metrics are met.
    - Further details can be found here.

2. Germline sample
   Most cancer WGS tests require a germline sample for paired germline and tumour testing. Acceptable germline samples are as follows:
   - Peripheral blood EDTA – Preferred for germline DNA, suitable for all solid tumours.
   - Skin biopsy – Suitable for all liquid tumours
   - Fibroblasts – DNA extracted from fibroblast culture may be submitted for individuals who have undergone a bone marrow transplantation.
   - Saliva – In exceptional circumstances saliva samples may be used. These are suitable for all solid tumours, and liquid tumours at a point where circulating myeloid cells have been removed from peripheral blood.
   - Further details can be found in the sample handling guidance here.

3. Tumour first testing
   - In some cases, tumour first testing can be carried out which only requires a tumour sample initially.
   - This pathway aims to provide fast analysis of clinically relevant variants. It is only available for haematological tumours.
   - It is recommended that a matching germline sample is submitted once available to ensure optimal analysis.

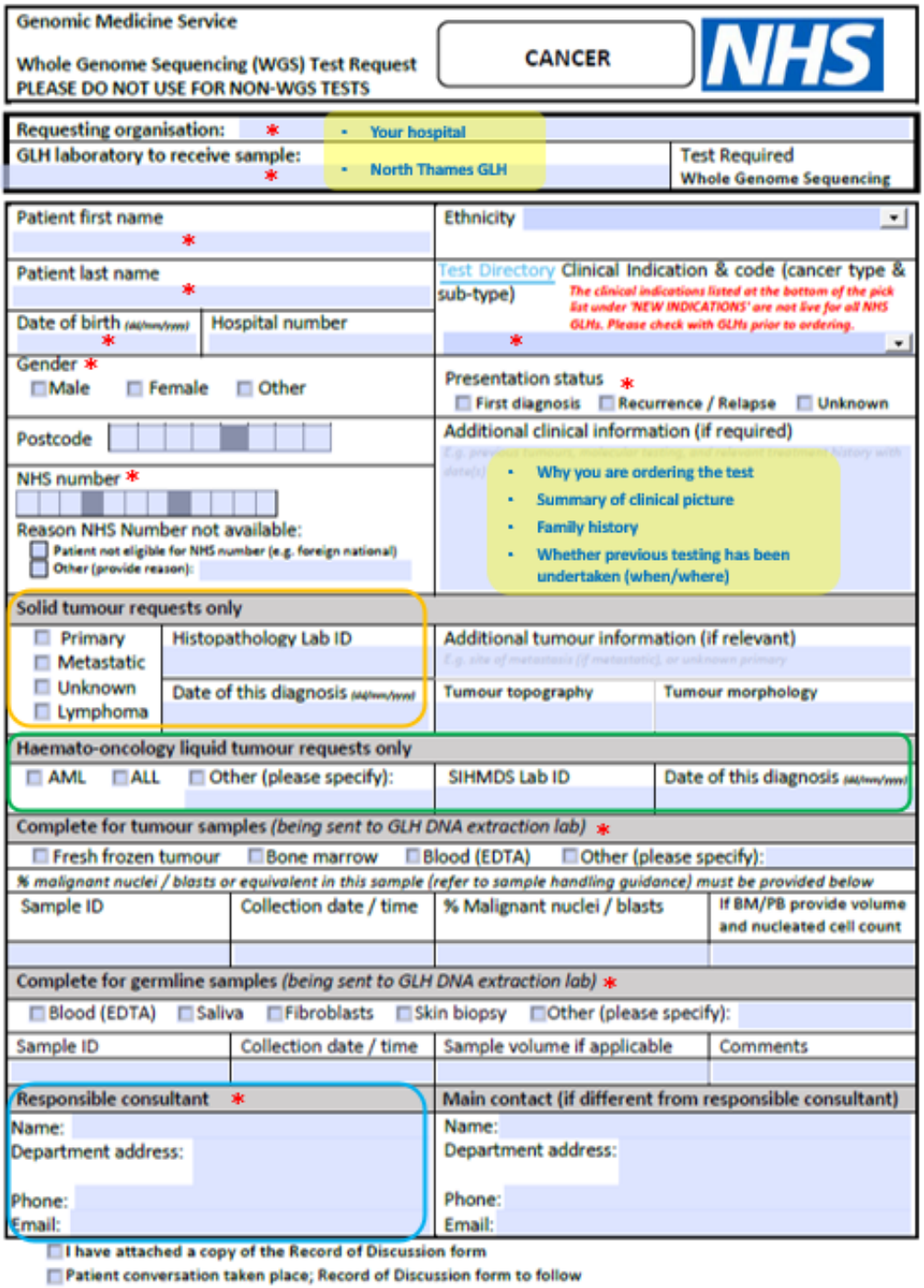
E. Forms required:

Three forms should be sent **electronically** to the NT GLH (gos-tr.pmu@nhs.net):
The Test Order Form, the Eligibility Form and the Record of Discussion.

Blood samples (1xEDTA tube) must be sent with the NT GLH Blood Test Request Form (see page 12).

1. The Test Order Form: completed by the consultant

This form should be completed with input from pathology to provide an estimate of tumour cellularity %. It is important this is provided as the minimum that should be accepted is 30%. The tumour assessment should be completed before sending the form to the Genomic Practitioner/Associate if using this pathway.



Genomic Medicine Service

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

CANCER

NHS

* Mandatory

Requesting organisation: *
- Your hospital

GLH laboratory to receive sample: *
- North Thames GLH

Test Required: Whole Genome Sequencing

Patient first name *

Patient 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 (provide reason):

Ethnicity

Test Directory Clinical Indication & code (cancer type & sub-type) *
The clinical indications listed at the bottom of the pick list under 'NEW INDICATIONS' are not live for all NHS GLHs. Please check with GLHs prior to ordering.

Presentation status *
☐ First diagnosis ☐ Recurrence / Relapse ☐ Unknown

Additional clinical information (if required)
- Why you are ordering the test
- Summary of clinical picture
- Family history
- Whether previous testing has been undertaken (when/where)

Check on the National Genomic Test Directory whether you are eligible for requesting this test

Solid tumour requests only
☐ Primary ☐ Metastatic ☐ Unknown ☐ Lymphoma
Histopathology Lab ID
Date of this diagnosis (dd/mm/yyyy)
Additional tumour information (if relevant)
Tumour topography
Tumour morphology

Mandatory to complete for Solid Tumours

Haemato-oncology liquid tumour requests only
☐ AML ☐ ALL ☐ Other (please specify):
SIHMDS Lab ID
Date of this diagnosis (dd/mm/yyyy)

Mandatory to complete for Liquid Tumours

Complete for tumour samples *(being sent to GLH DNA extraction lab)* *
☐ Fresh frozen tumour ☐ Bone marrow ☐ Blood (EDTA) ☐ Other (please specify):
% malignant nuclei / blasts or equivalent in this sample (refer to sample handling guidance) must be provided below

Sample ID	Collection date / time	% Malignant nuclei / blasts	If BM/PB provide volume and nucleated cell count

Complete for germline samples *(being sent to GLH DNA extraction lab)* *
☐ Blood (EDTA) ☐ Saliva ☐ Fibroblasts ☐ Skin biopsy ☐ Other (please specify):

Sample ID	Collection date / time	Sample volume if applicable	Comments

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

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

WGS Reports will be issued to the clinicians named here

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

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

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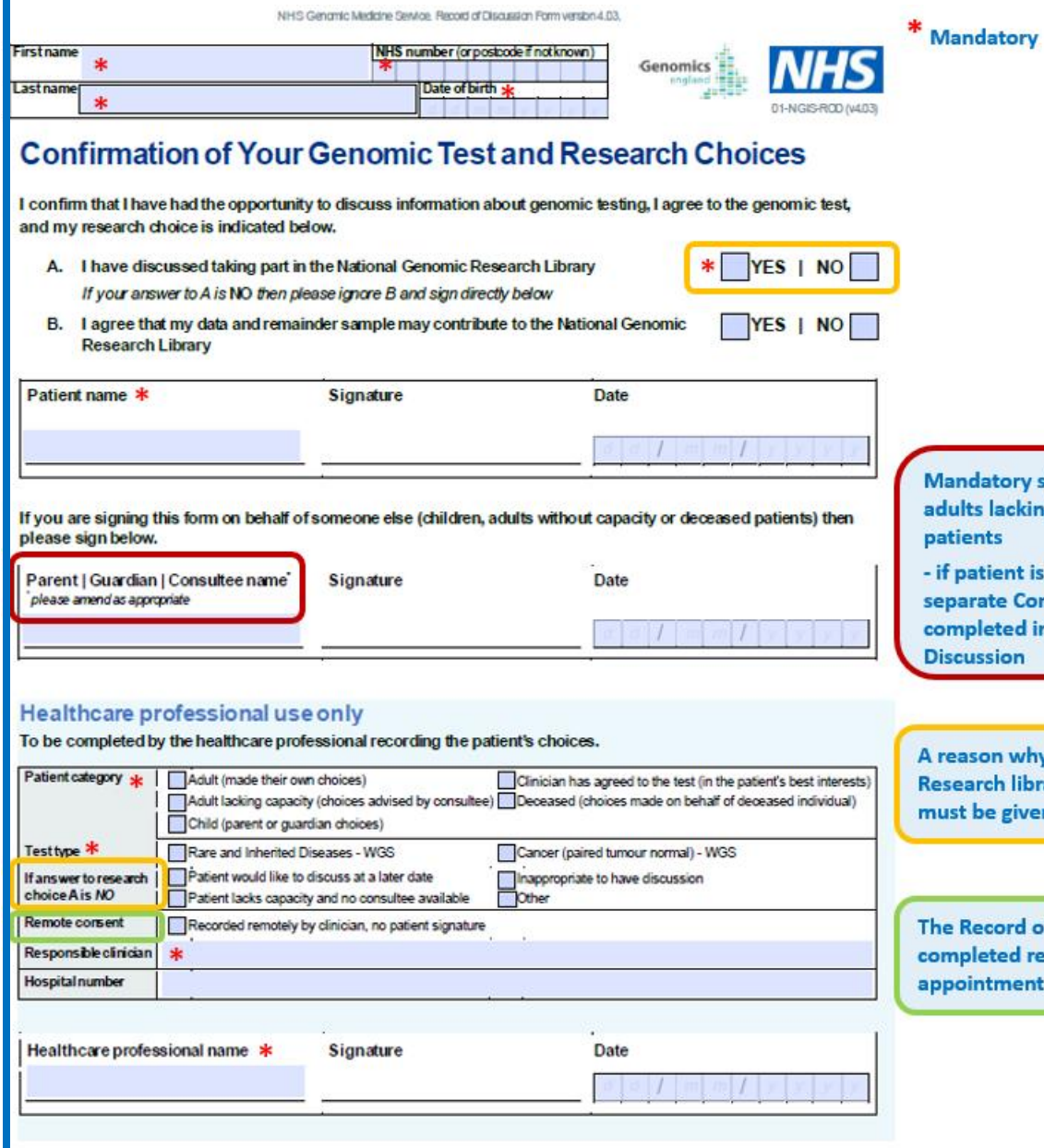
Page 3 (pictured) of the document to be completed after a full consent conversation – a summary of the conversation is listed on Page 1 and 2 (not pictured). Can be completed remotely (i.e. consent appointment over the phone/virtual). Information on what to include in the consent conversation is detailed (page 9-11).

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-ROD (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
		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

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

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

3. The Cancer WGS Eligibility Form: completed by the consultant.

The following Pro Forma must be completed to demonstrate if the patient meets the 'Exhausted all Standard of Care (ESOC)' eligibility criteria.

As stated in the form, paediatric and TYA patients, as well as CNS Tumours, can be referred without the completion of this Pro Forma.

NHS
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Genomic Laboratory Hub

Pro forma for Cases to be submitted for Cancer Whole-Genome Sequencing (WGS) under the Acute leukaemia / 'exhausted all Standard of care (ESOC)' pipelines.

Genomic testing is commissioned by NHS England with the patients eligible to access a test specified in the national genomic test directory (NHS England » National genomic test directory).

NHS England have changed the eligibility criteria for Cancer WGS referrals. This criterion only applies to adults over the age of 26 and excludes CNS Tumours.

To accept submissions for solid and haematological tumour cases under the new criteria, we require the completion of the details below in addition to the information provided via the ROD and TOF. Please note that incomplete or lacking forms will delay the submission of these cases and that the lab will not actively chase missing information.

Paediatric and TYA patients, as well as CNS Tumours, can be referred without the completion of this pro forma.

1. **Disease entity/Pathway (i.e. AML, ALL, ESOC):**

2. **G-banding/karyotype:**

3. **DNA NGS:**

4. **RNA Fusion NGS:**

5. **Specific question/Issue to be address by WGS:**

Please contact gos-tr.pmu@nhs.net with queries on how to submit/organisational queries. Please get in touch with dortewren@nhs.net to discuss eligibility in further detail for specific cases.

F. 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 patient and fill the Record of Discussion form.

a. Preliminary WGS Discussion with the Patient:

1. What WGS is – reading through all the DNA from the germline and tumour sample and analysing specific areas (virtual panels) – NOT gene agnostic
2. Germline sample required as well as tumour sample - discuss options for both.
3. Managing expectations - Turnaround time from the point that all samples/consent forms have arrived at the laboratory
    a. 12 weeks (routine tests) *(as of August 2024)*
4. 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 from the tumour sample and healthy sample and analysing specific areas (virtual panels) to find the changes in the tumour DNA as well as possible germline risk genes.
2. Sample required from both tumour and healthy cells.
3. Turnaround time from the point that all samples have arrived at the laboratory.
    a. 12 weeks (routine tests) *(as of August 2024)*
4. Somatic Findings
    a. Provide information about tumour type, how it developed and how it may behave
    b. Possibly influence treatment options and clinical trial eligibility
    c. May not provide further information than standard of care testing
5. Germline findings
    a. Provide information about any heritable risk contributing to development of this tumour
    b. Identify risk of developing other tumour types in the future

c. Could be relevant to other family members

6. Family Implications
    a. Germline results have 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 germline pathogenic variant is found (it is helpful to start early conversations about this rather than only after the results are available)
7. 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 individua or family members
    d. This result may change over time as this can be re-analysed in future
8. 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 different cancers 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
9. DNA storage
    a. The samples 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
10. 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

G. WGS Sample Form

NHS
North Thames
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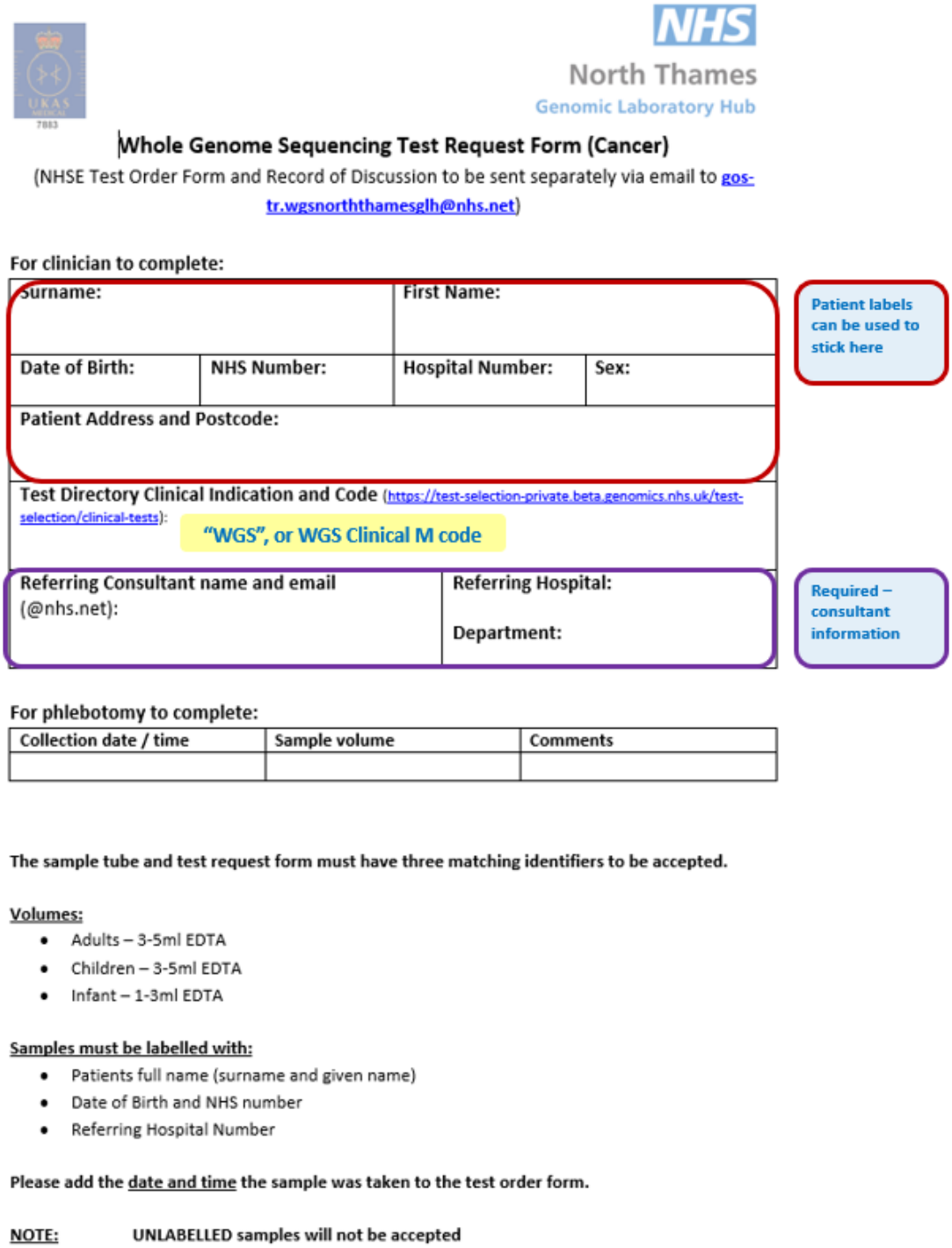
A completed NT GLH Sample Form with patient details **must** be attached to the labelled blood tube (1x EDTA) for WGS germline samples.

If the patient is unable to provide a blood test, 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, for the saliva and form to reach the laboratory for extraction:

SIHMDS, North Thames GLH
Specimen Reception, Level 5 Barclay House, 37 Queen Square,
London WC1N 3BH

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.



NHS
North Thames
Genomic Laboratory Hub

Whole Genome Sequencing Test Request Form (Cancer)

(NHSE Test Order Form and Record of Discussion to be sent separately via email to gos-tr.wgsnorththamesglh@nhs.net)

For clinician to complete:

Surname:		First Name:	
Date of Birth:	NHS Number:	Hospital Number:	Sex:
Patient Address and Postcode:			
Test Directory Clinical Indication and Code (https://test-selection-private.beta.genomics.nhs.uk/test-selection/clinical-tests): "WGS", or WGS Clinical M code			
Referring Consultant name and email (@nhs.net):		Referring Hospital: Department:	

Patient labels can be used to stick here

Required – consultant information

For phlebotomy to complete:

Collection date / time	Sample volume	Comments

The sample tube and test request form must have three matching identifiers to be accepted.

Volumes:

- Adults – 3-5ml EDTA
- Children – 3-5ml EDTA
- Infant – 1-3ml EDTA

Samples must be labelled with:

- Patients full name (surname and given name)
- Date of Birth and NHS number
- Referring Hospital Number

Please add the date and time the sample was taken to the test order form.

NOTE: **UNLABELLED samples will not be accepted**

H. More resources:

NHS North Thames Genomic Medicine Service

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-cancer-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)
Cancer Test Order Forms and Clinician Packs (scroll to Cancer (solid tumour and haematological malignancy) – 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.