North East and Yorkshire Genomics

Guidance document for the completion of the WGS Solid Tumour referral form and Record of Discussion

North East and Yorkshire GLH

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Contents

Overview: Patient access to the national WGS service is now available through the Genomic Laboratory Hub network. Phase 1 and 2 cancer indications are eligible and this document aims to support clinicians with the referral and research consenting process.

- Turn-round-times for the WGS test pathway are around 6 weeks, so "routine/ standard of care" (SOC) tumour genomic assessments should still be continued at present
- WGS testing requires receipt of adequate matched samples of fresh/fresh frozen tumour tissue and whole blood for germline assessment, together with a completed Test Order Form (TOF) and Record of Discussion (ROD) form before the WGS test can be submitted for analysis.
- Tumour sampling and decision to undertake WGS testing can be at the diagnostic or therapeutic stages of the patient pathway
- Blood sampling and the Record of Discussion for germline assessment may be best undertaken after it is confirmed by Cellular Pathology that there is sufficient fresh tissue to undertake WGS testing
- Blood sampling and the Record of Discussion may be undertaken before tumour sampling (within the month) but WGS will not proceed until after it is confirmed by Cellular Pathology that there is sufficient fresh tissue to undertake WGS testing followed by completion of the Test Order Form.
- Sampling and discussion with the patient may need to take place before a definitive tumour diagnosis is confirmed and both may need to be undertaken on a "presumptive" diagnosis

Solid Tumour WGS Indications

Solid tumour WGS diagnostic indications are listed on the National Cancer Test Directory for cancer (https://www.england.nhs.uk/publication/national-genomic-test-directories/).

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

Sarcomas - All patients (adult & paediatric):

All patients (adult and paediatric) with sarcomas are eligible. These include cases where specialist sarcoma pathology review indicates that molecular assessment will aid diagnosis or management, and/or those cases deemed eligible at the discretion of the histopathologist. As WGS is a part of the normal diagnostic repertoire in these patients it is recommended that clinicians base decisions on whether to submit samples on similar criteria to those they use for submission of other diagnostic tests

Disease Group	Test Code	Disease Group	Test Code
Alveolar Rhabdomyosarcoma	M42.4	Sclerosing Epithelioid Fibrosarcoma	M76.2
Alveolar Soft Part Sarcoma	M43.2	Synovial Sarcoma	M77.2
Angiomatoid Fibrous Histiocytoma	M45.3	Undifferentiated Round Cell Sarcoma of Infancy	M78.2
Chondrosarcoma Conventional Central	M46.2	Well Differentiated/Dedifferentiated Liposarcoma	M79.2
Chondroblastoma	M47.2	Bone Forming Soft Tissue Tumour Differential	M196.3
Clear Cell Sarcoma of Soft Tissue	M48.2	Round Cell Sarcoma of Soft Tissue Differential	M197.10
CNS Ewing Sarcoma Family Tumour With CIC Alteration	M49.2	Vascular Soft Tissue Tumour Differential	M198.4
Dermatofibrosarcoma Protuberans	M50.2	Spindle Cell Soft Tissue Tumour Differential	M199.12
Desmoplastic Small Round Cell Tumour	M52.2	Myxoid Soft Tissue Tumour Differential	M200.7
Endometrial Stromal Sarcoma	M53.4	Adipocytic Soft Tissue Tumour Differential	M201.3
Ewing Like Sarcoma/PNET	M55.3	Epithelioid Soft Tissue Tumour Differential	M202.6
Ewing Sarcoma of Bone	M56.2	Uterine Sarcomas (Inc Endometrial)	M203.5
Ewing-Like Soft-Tissue Sarcoma	M57.3	Undifferentiated tumour	M204.1
Extraskeletal Myxoid Chondrosarcoma	M58.2	Cartilage Forming Bone Tumour Differential	M205.7
Giant Cell Tumour of Bone	M60.2	Bone Forming Bone Tumour Differential	M206.7
High-Grade Neuroepithelial Tumour-BCOR Group	M61.3	Osteoclast-Rich Bone Tumour Differential	M207.6
Infantile Fibrosarcoma	M62.2	Round Cell Sarcoma of Bone Differential	M208.6
Inflammatory Myofibroblastic Tumour	M63.4	Vascular Tumour of Bone Differential	M209.4
Low Grade Fibromyxoid Sarcoma	M64.2	Spindle Cell Tumour of Bone Differential	M210.5
Mesenchymal Chondrosarcoma	M65.2	Fibro-Osseous Tumour of Bone Differential	M211.3
Myoepithelial Tumours of Soft Tissue	M66.2	Undifferentiated Round Cell Sarcoma of Infancy	M78.2
Myxoid/Round Cell Liposarcoma	M67.2	Well Differentiated/Dedifferentiated Liposarcoma	M79.2
Myxoinflammatory Fibroblastic Sarcoma	M68.2	Bone Forming Soft Tissue Tumour Differential	M196.3
Osteosarcoma	M70.2	Round Cell Sarcoma of Soft Tissue Differential	M197.10
Phosphaturic Mesenchymal Tumour	M71.2	Vascular Soft Tissue Tumour Differential	M198.4
Primitive Mesenchymal Myxoid Tumour of Infancy	M72.3	Spindle Cell Soft Tissue Tumour Differential	M199.12
Pseudomyogenic Haemangioendothelioma	M73.2	Undifferentiated Round Cell Sarcoma of Infancy	M78.2
Radiation Induced Angiosarcoma	M74.2	Well Differentiated/Dedifferentiated Liposarcoma	M79.2
Round Cell Sarcoma Nos	M75.3		

Paediatric patients:

All malignant tumours diagnosed in paediatric patients (≤19 years old) other than some subtypes of sarcoma specifically excluded on the sarcoma testing sheet are eligible for WGS. These include cases where the neuropathologist or specialist paediatric pathology review indicates that molecular assessment will aid diagnosis or management. See table below for eligible disease groups including their test code:

Disease Group	Test Code	Disease Group	Test Code
Anaplastic Astrocytoma	M20.3	Medulloblastoma	M145.13
Diffuse Astrocytoma	M22.4	Medulloblastoma Group 3	M146.6
Embryonal Tumours with Multi-Layered Rosettes	M24.3	Medulloblastoma Group 3/4	M147.7
Ependymoma	M25.6	Medulloblastoma TP53 WT	M148.8
IDH-Wildtype Glioblastoma	M30.2	Melanotic Tumours	M149.2
Pineoblastoma	M37.2	Meningioma	M150.6
Rare Primitive Neuroectodermal Tumours Groups 2/3	M39.2	Midline Carcinoma	M151.5
Diffuse Midline Glioma	M183.5	Neuroblastoma	M152.14
Glioma	M184.2	Nodular Brain Tumour	M153.4
High Grade Glioma	M185.2	Oligoastrocytoma	M155.3
Low Grade Glioma	M186.2	Oligodendroglioma	M156.8
Glial and Glioneuronal Tumour Differential	M213.37	Thyroid Papillary Carcinoma	M157.5
Brain Tumour - No Further Morphological Classification	M189.17	Pilocytic Astrocytoma	M158.5
Embryonal Tumour Differential	M190.30	Pituitary Blastoma	M159.4
Medulloblastoma all Subtypes	M194.22	Pleomorphic Xanthoastrocytoma	M160.14
Paediatric Tumours (general)	M119.1	Pleuropulmonary Blastoma	M161.4
Atypical Teratoid/Rhabdoid Tumour	M120.16	Primitive Neuroectodermal Tumours	M162.8
Clear Cell Kidney Sarcoma	M124.9	Renal Tumours	M165.6
CNS High-Grade Neuroepithelial Tumour with MN1 Alteration	M126.2	Renal Tumour Differential	M212.14
Congenital Mesoblastic Nephroma	M127.3	Rhabdoid Tumours	M167.4
Craniopharyngioma	M195.3	Rosette-Forming Glioneuronal Tumour	M168.5
Cribriform Neuroepithelial Tumour	M130.4	Secondary Glioblastoma	M169.4
Cystic Nephroma	M131.4	SHH Medulloblastoma	M170.6
Desmoplastic Infantile Gangliogliomas	M132.12	SHH Medulloblastoma - TP53 WT	M171.7
Desmoplastic Medulloblastoma	M133.3	SHH Medulloblastoma - TP53 MUTANT	M172.6
Fibrolamellar Hepatocellular Carcinoma	M136.2	t(6;11) Translocation-Associated Renal Cell Carcinoma	M173.2
Ganglioglioma	M137.13	Testicular	M174.3
Glial Tumours	M138.2	Wilms Tumours	M178.3
Glioblastoma	M139.16	WNT Medulloblastoma	M179.8
Lung	M143.4	Xp11.2 Translocation-Associated Renal Cell Carcinoma	M180.6

These groups of patients have been added in February 2022, for now using a temporary code pending formal addition to the National Test Directory:

Teenage & Young People <25 years of age:

All malignant tumour types which are seen usually in paediatric patients (≤19 years old) are now eligible for WGS testing in patients from age groups up to 25 yrs.

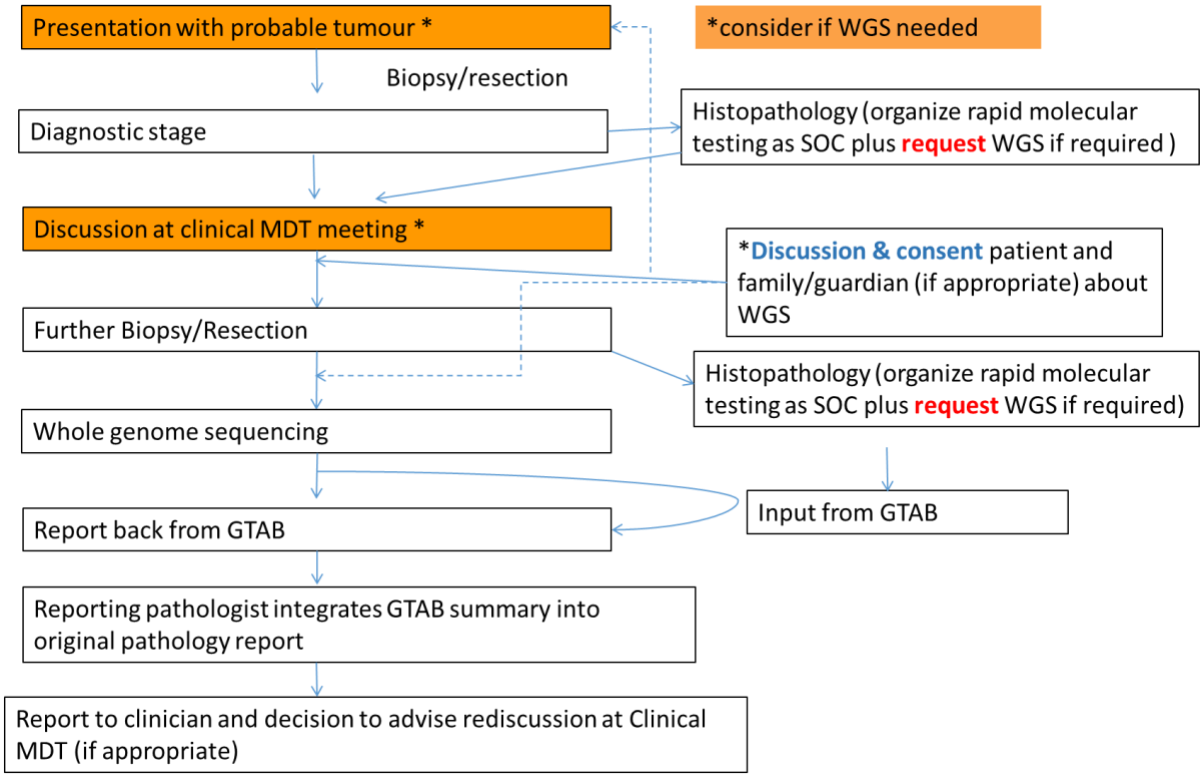
Patients with Malignant CNS Tumours:

All patients with a malignant CNS tumour are eligible for WGS testing.

Patients with Metastatic and Inoperable Solid Tumours:

All patients with metastatic or inoperable solid tumours who have exhausted all testing in standard of care approaches and/or treatment are eligible for WGS.

In case of queries about eligibility for WGS please discuss with the local GLH laboratory or Clinical Lead for Cancer/Pathology. Whole Genome Sequencing Solid Tumour Referral Process Flow - Overview



Instructions for Completing the WGS Sequencing Solid Tumour Request

The fresh/ fresh frozen tumour tissue sample will need to have an accompanying paper copy of the GMS WGS Test Order Form for Cancer (v1.16). NHS England » NHS Genomic Medicine Service test order forms. This is usually completed by the Cellular Pathologist or lab team who assessed the tumour tissue content. An indication should be ticked at the bottom of the form as to whether the sample is being requested attached with the Record of Discussion form, or whether that form will be/ has been sent on separately by the clinical team. See next section for details of the Record of Discussion form, but **please note that the sample will be extracted only and not sent on for WGS analysis until the ROD form and germline blood samples have also been received**.

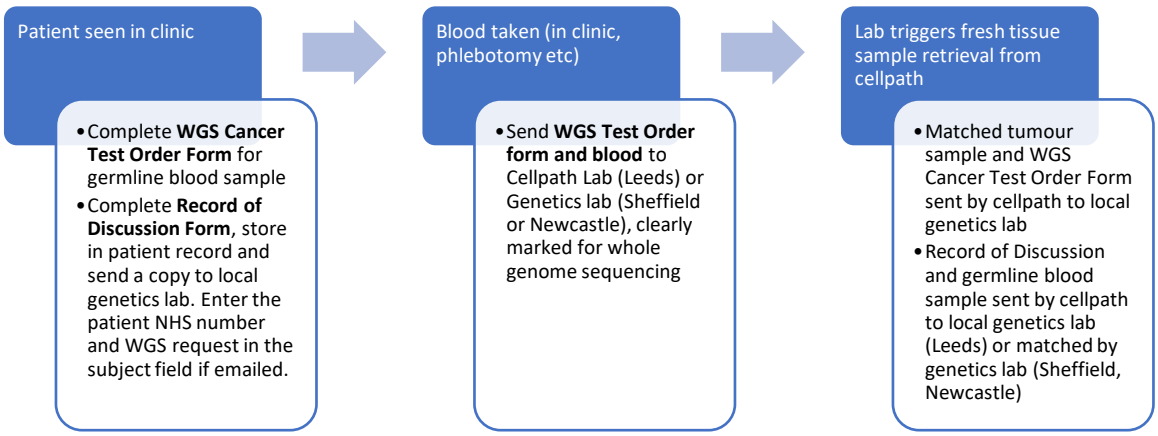
Tissue Requirements

For optimal, high quality sequencing a fresh tumour sample is required. Tumour tissue for WGS may be taken as a biopsy (e.g. core biopsy, punch biopsy) or resection surgical specimen. Tumour cells must account for at least 30% of the nucleated cells present in the tissue used for DNA extraction and also should have less than 20% necrosis by area. A minimum of 2µg of tumour DNA must be submitted for WGS at a preferred concentration of 45ng/µl in a minimum volume of 115µl. The following are examples of minimum tumour quantities which should be adequate to achieve 2µg of DNA:

- 5mm x 5mm x 2mm of tumour tissue
- 15mm x 2mm diameter needle core biopsy

In general, in cases where risk to patients is unlikely to be increased by taking more than one biopsy, then 2-3 needle cores or 1-2 standard endoscopic forceps biopsies, if feasible, are recommended. Other fresh tumour sample types may need discussion with the cellpath and/or genetic laboratories.
Frozen sections should be used to assess the tumour content of the tissue samples taken for WGS and submission to the DNA extracting laboratory. Formalin fixed tumour tissue cannot be submitted for whole genome sequencing.

Whole Genome Sequencing Record of Discussion and Germline Blood Testing Process Flow for Solid Tumour – Overview



Instructions for Completing the WGS Sequencing Germline Blood Request

The germline blood sample will also need to have an accompanying paper copy of the NHS England » NHS Genomic Medicine Service test order forms). This is usually completed in clinic and sent with the blood sample or to phlebotomy for them to undertake blood sampling. These are then sent to the Cellpath Lab (Leeds), or genetics lab (Newcastle/ Sheffield) clearly marked for whole genome sequencing.

An indication should be ticked at the bottom of the test order form as to whether the blood sample is being accompanied by the Record of Discussion form, or whether that form will be/ has been sent on separately by the clinical team. See next section for details of the Record of Discussion form, but please note that the sample will be extracted only and not sent on for analysis until that form is received.

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

- A RoD form needs to be completed for each patient. A copy of the form can be found here NHS England » NHS Genomic Medicine Service record of discussion form
- 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 and complete the Genomic Consultee Declaration that 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 patient/ relevant family member or consultee

- 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 Cancer (paired tumour normal) - 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) ☐ Adult lacking capacity (choices advised by consultee) ☐ Child (parent or guardian choices)	☐ Clinician has agreed to the test (in the patient's best interests) ☐ 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 ☐ Patient lacks capacity and no consultee available	☐ Inappropriate to have discussion ☐ Other
Remote consent	☐ Recorded remotely by clinician, no patient signature	
Responsible clinician		
Hospital number		

The WGS Solid Tumour test order and record of discussion process is now complete.
The full set of documentation can be emailed to your local GLH laboratory.
Enter the patient 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 REQUEST FORM AND THE REQUISITE ROD FORMS HAVE BEEN RECEIVED IN THE LAB AND MATCHED WITH AN ADEQUATE SAMPLE OF EXTRACTED TUMOUR DNA.

Summary and Additional Information:

Referral for Solid Tumour WGS testing requires two samples; tumour tissue and germline blood. Both samples require a WGS Cancer Test Order Form, although this can be the same form if both are sent together. A completed patient record of discussion (ROD) form is also required before WGS analysis will be performed.

The pathway for samples and documentation are via your local Leeds, Sheffield or Newcastle laboraties, as described above.

Samples cannot be submitted for WGS testing and analysis until both tumour and germline samples with completed WGS Cancer Test Order Form & a completed ROD form have been received. The sample quality & quantity also have strict eligibility criteria. The laboratory will contact you if further samples are required.

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