North East and Yorkshire Genomics

Guidance document for the completion of the WGS Cancer Test Order Form and Record of Discussion for HaemOnc Patients

North East and Yorkshire GLH

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Contents:

Overview:

Patient access to the national whole genome sequencing (WGS) service is now available through the Genomic Laboratory Hub (GLH) network. This document aims to support clinicians with the referral and consenting process.

- Turn-around-times (TATs) for the WGS test pathway are around 12 weeks. Therefore, standard of care (SOC) genomic testing should be prioritised and WGS only requested in addition to the SOC testing.
- WGS testing requires matched tumour (usually bone marrow or peripheral blood) and germline samples (usually skin biopsy or remission marrow samples) alongside a completed Record of Discussion (ROD) form.
- At the point of diagnosis, the testing can be discussed with the patient. Samples can be extracted and held pending further discussion and consent, but the extraction must be within 72 hours of the sample being taken.

HaemOnc WGS Indications:

HaemOnc WGS indications are available to be viewed on the National Cancer Test Directory (https://www.england.nhs.uk/publication/national-genomic-test-directories/), but are detailed for simplicity below. NHSE have also produced a sample requirements document.

Where patients may not directly benefit from this testing (for example those patients whose management is purely palliative, or where the patient dies soon after diagnosis) submitting samples may not be appropriate.

All patients (adult & paediatric):

All patients (adult and paediatric) with acute leukaemia are eligible. More specifically this table shows the eligible disease groups including their test code:

Disease Group	Test Code	Further Eligibility Criteria
AML	M80.1	
AL Other	M89.1	Includes undifferentiated acute leukaemia, leukaemia of ambiguous lineage and leukaemia of mixed lineage
BPDCN	M90.1	Blastic plasmacytoid dendritic cell neoplasm
ALL	M91.1	

Paediatric patients:

Paediatric patients (≤25 years old) with most HaemOnc disease groups are eligible for WGS. See table below for eligible disease groups including their test code:

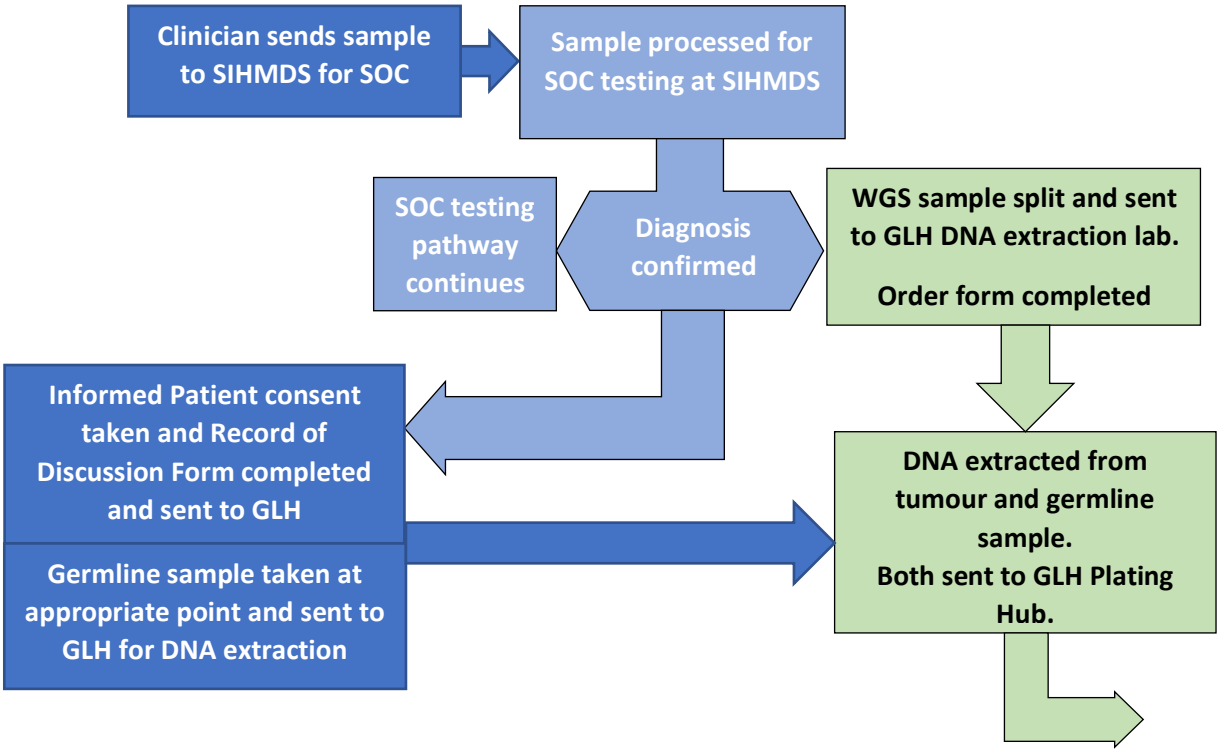
Disease Group	Test Code	Disease Group	Test Code
MDS	M82.6	**High Grade lymphoma**	M99.8
AA	M83.4	**Primary Mediastinal B Cell Lymphoma**	M100.4
CML	M84.11	**ALK Positive Large B Cell Lymphoma**	M101.4
MPN	M85.13	**Malt-Lymphoma**	M107.7
Mastocytosis	M86.3	**Paediatric Follicular Lymphoma**	M110.2
JMML	M88.2	**T Cell Non-Hodgkin Lymphoma**	M111.5
MDS/MPN	M224.4	**ALK Negative Anaplastic Large Cell Lymphoma (Inc Cutaneous Subtypes)**	M112.5
Lymphoma	M93.3	**ALK Positive Anaplastic Large Cell Lymphoma**	M182.3
B-cell Non-Hodgkin lymphoma	M95.7	**NK Cell/Gamma-Delta T Cell Lymphoma**	M115.2
Burkitt	M96.7	**Hepatosplenic T Cell Lymphoma**	M116.3
Burkitt like	M97.2	**Histiocytosis**	M117.16
Large B Cell Like Lymphoma with IRF4 Rearrangement	M98.2		

Patients with a HaemOnc disease who have exhausted all standard of care (SOC) testing or treatment:

This group of patients was added in February 2022 and allows a clinical assessment to be made and submission from this group of patients where WGS may add true clinical utility.

Whole Genome Sequencing HaemOnc Referral Process Flow – Overview:

The expectation is that patients will be highlighted for WGS through close communication with the SIHMDS's at the point of diagnosis.



Sample Requirements:

For optimal, high quality sequencing DNA from both a tumour sample and a germline sample are required.

AML

Tumour:

Peripheral blood (PB) or bone marrow aspirate (BMA) in EDTA with ≥20% blasts
This can be any blast percentage if an AML defining genetic abnormality is present
CSF/Ascitic fluid/Pleural fluid is permissible if infiltrated with ≥20% blasts, and when PB/BMA are not available
Please include the white cell count (WCC) of the sample sent on the referral form

Germline:

Skin biopsy (punch biopsy 4mm^3) for direct DNA extraction from fibroblasts
Skin biopsy (punch biopsy 4mm^3) for DNA extraction from cultured fibroblasts
Saliva, 5 days post treatment (two doses of anthracycline (or equivalent)), collected into a specialised saliva sample collection kit.
PB or BMA when appropriate genetic MRD marker (*NPM1, RUNX1::RUNX1T1*) is <0.1%

ALL

Tumour:

Peripheral blood (PB) or bone marrow aspirate (BMA) in EDTA with ≥30% blasts

CSF/Ascitic fluid/Pleural fluid is permissible if infiltrated with ≥30% blasts, and when PB/BMA are not available

Please include the white cell count (WCC) of the sample sent on the referral form

Germline:

Skin biopsy (punch biopsy 4mm^3) for direct DNA extraction from fibroblasts

Skin biopsy (punch biopsy 4mm^3) for DNA extraction from cultured fibroblasts

Saliva, 5 days post treatment (two doses of anthracycline (or equivalent)), collected into a specialised saliva sample collection kit.

PB or BMA when appropriate genetic MRD marker (*IGH/TCR, BCR::ABL1*) is <0.1%

Paediatric cases

Tumour:

Peripheral blood (PB) or bone marrow aspirate (BMA) in EDTA with ≥30% blasts

Tumour tissue biopsy with ≥30% tumour burden (this may be calculated using the non-lymphoid cell count or other method depending on the disease group)

Germline:

Skin biopsy (punch biopsy 4mm^3) for direct DNA extraction from fibroblasts

Skin biopsy (punch biopsy 4mm^3) for DNA extraction from cultured fibroblasts

Saliva, 5 days post treatment (two doses of anthracycline (or equivalent)), collected into a specialised saliva sample collection kit.

PB or BMA when appropriate genetic MRD marker is <0.1%

TINC – Tumour in Normal Contamination:

HaemOnc germline samples are prone to being contaminated with tumour DNA. Tumour DNA can be seen at low levels in remission blood or bone marrow samples, saliva samples and in skin biopsies. Whilst we can ensure this is kept to a minimum, the WGS results highlights the level of TINC and where this is seen to be high an additional bioinformatics pipeline can be employed to aid the analysis process. Although this can provide a more accurate analysis in some ways, it also creates complexity in the numbers of variants returned and difficulty in knowing whether the variants are germline or somatic. This process will be managed by the scientists in the laboratory.

Instructions for Completing the WGS HaemOnc Tumour Request:

The HaemOnc tumour sample (usually bone marrow or blood) will need to have an accompanying paper copy of the GMS WGS Test Order Form (TOF) for Cancer (v1.16). This can be completed by the patients consultant or a member of the SIHMDS/genomics lab where the sample maybe undergoing SOC testing.

The Record of Discussion (ROD) form can be sent at this stage or with the germline sample. The sample will be extracted and stored but cannot be sent until the full set of samples (at a suitable quality) and the paperwork (TOF and ROD) are available.

Instructions for Completing the WGS HaemOnc Germline Request:

The HaemOnc germline sample will need to have an accompanying paper copy of the GMS WGS Test Order Form for Cancer (v1.16). This is usually completed at the time the sample is taken. The germline samples should be clearly marked for whole genome sequencing (WGS).

The Record of Discussion (ROD) form is usually completed at this stage as signatures from the patient (or patient's parents) are required.

Instructions for Completing the Record of Discussion Form (ROD):

A record of discussion (ROD) form is required for each referral and indicates that the patient (or family) has consented for the WGS test. This can be completed electronically or by hand, by the consultant / registrar / specialist nurse. The form can be found at the address below

https://ney-genomics.thumbdevelopment.online/wp-content/uploads/2021/07/WGS-Record-of-Discussion-form.pdf

The form covers consent for the genomic testing and covers research consent for the data to be used as part of the national genomic research library (NGRL). The statements provided in each of the record of discussion sections must be discussed with each patient / relevant family member.

Summary and Contacts:

Referral for HaemOnc WGS testing requires two samples; tumour and germline. Both samples require a test order (TOF) form, although this can be the same form if sent together. A record of discussion (ROD) form is also required.

The samples and documentation can be sent to your local SIHMDS using your usual transport arrangements or can be emailed if preferred. Enter the patient NHS number and WGS request in the subject field

Leeds HMDS Laboratory hmds.lth@nhs.net
Sheffield Diagnostic Genetic Laboratory sheffield.diagnosticgenetics@nhs.net
Newcastle Genetic Laboratory nuth.dna@nhs.net

Samples cannot be submitted for WGS testing and analysis until both tumour and germline samples with an appropriate referral 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)