NHS
North West
NHS Genomic Laboratory Hub

Requesting Whole Genome Sequencing Through The North West Genomic Laboratory Hub

Frequently Asked Questions

When will requests for WGS go live?

WGS is being phased in at different times for different specialties and clinical indications.

Phase 1 went live in the North West at the beginning of 2021.

Phase 2 is going live from autumn 2021.

A list of Phase 1 and 2 indications and their "go-live" dates are given below:

Phase	R Code	Clinical Indication	Date request can be accepted from
1	R89	Ultra-rare and atypical monogenic disorders	April 21
1	R27	Congenital malformation and dysmorphism syndromes	April 21
1	R29	Intellectual disability	April 21
1	R69	Hypotonic infant with a likely central cause	April 21
1	R104	Skeletal dysplasia	April 21
1	R100	Rare syndromic craniosynostosis/isolated multisuture syn.	April 21
1	R143	Neonatal diabetes unexplained after panel test	April 21
1	R98	Likely inborn error of metabolism	May 21
1	R54	Hereditary ataxia, adult onset	August 21
1	R55	Hereditary ataxia, childhood onset	August 21
1	R59	Early onset or syndromic epilepsy	August 21
1	R61	Childhood onset hereditary spastic paraplegia	August 21
1	R83	Arthrogryposis/distal arthrogryposis	April 21
1	R381	Other rare neuromuscular disorders - myopathy	April 21
1	R84	Cerebellar abnormalities	April 21
1	R85	Holoprosencephaly, not chromosomal	April 21
1	R86	Hydrocephalus	April 21
1	R87	Cerebral malformation/cortical dysplasia	April 21
1	R88	Severe microcephaly	April 21
1	R109	Childhood onset leukodystrophy	April 21
1	R193	Cystic renal disease, multiple renal cysts	April 21
2	R135	Paediatric or syndromic cardiomyopathy	25th October 2021
2	R31	Bilateral congenital/childhood onset cataracts	4th January 2022
2	R32	Retinal disorders	4th January 2022
2	R33	Possible X-linked retinitis pigmentosa	4th January 2022
2	R34	Sorsby retinal dystrophy	4th January 2022
2	R35	Doyne retinal dystrophy	4th January 2022
2	R36	Structural eye disease	4th January 2022
2	R15	Primary immunodeficiency	22nd November 2021
2	R56	Adult onset dystonia, chorea, movement disorder	4th October 2021

2	R57	Childhood onset dystonia, chorea or related movement disorder	4th October 2021
2	R58	Adult onset neurodegenerative disorder	4th October 2021
2	R60	Adult onset hereditary spastic paraplegia	4th October 2021
2	R62	Adult onset leukodystrophy	4th October 2021
2	R78	Hereditary neuropathy/pain disorder, not PMP22 copy no.	4th October 2021
2	R257	Unexplained paediatric onset end stage renal disease	25th October 2021

For more information on who will be able to request WGS for these indications and which patients are eligible, see the National Genomic Test Directory

Where can I find more information on consenting for WGS?

Many clinicians will have been used to consenting for gene panel tests and the issues are really not that different. As with panel tests you need to cover possible outcomes including unexpected findings, data storage, implications for family members, how results will be fed back, timeframe etc. In addition the WGS consent form, called the Record of Discussion form requires you to discuss with the patient participation in the National Genomics Research Library. Information about the latter is given in the WGS information leaflets and on the RoD form. If you need supplementary information in participation in genomic research a rather longer document on genomic research is also available on the NWGLH website.

Health Education England have written a competency framework for consenting a patient to genomic testing. It can be found here: https://www.genomicseducation.hee.nhs.uk/competency-frameworks/consent-a-competency-framework/

There is also a short online course which covers an introduction to offering genomic tests here: https://www.genomicseducation.hee.nhs.uk/education/online-courses/facilitating-genomic-testing-introduction-to-offering-genomic-tests/

HEE have also produced some useful factsheets about requesting WGS which cover consent issues. These are concise A4 sheets which cover all the basic areas you need to go over when having the consent conversation. The rare disease factsheet can be accessed here: https://www.genomicseducation.hee.nhs.uk/wp-content/uploads/2019/11/Guide-to-requesting-WGS-RD-Nov-20.pdf

Within the GLH we have some limited resources for training clinicians in the areas of consent for WGS. These are mainly through engagement sessions which we have been organising with each specialty. In some circumstances it may be possible to offer some local training if sufficient numbers of staff will attend. Please ask us.

How do I know which WGS test to request?

WGS can be requested at present only for the clinical indications given in the Table above. If you need a test for another indication it may still be being offered as a panel or single gene. Consult the National Genomic Test Directory for a list of all the possible NHS tests you can order and criteria for

eligibility which your patient must fulfil. https://www.england.nhs.uk/wp-content/uploads/2018/08/Rare-and-Inherited-Disease-Eligibility-Criteria-November-2020-21.pdf

What will the WGS test actually test for?

Although the patient's whole genome will be sequenced, not all of the genes will be analysed. The test will only look at genes on the accepted gene panel for the clinical indication you have requested. You can find out which genes are on e.g. the Arthrogryposis (R83) panel by looking at the panelapp site. https://nhsgms-panelapp.genomicsengland.co.uk/

In addition to analysing all the approved (green) genes on the panel, the clinical scientist will look at the top three genomic variants in the patient's sequence which have been prioritised based on the closest phenotypic match to your patient i.e . match their symptoms most closely.

Finally, the analysis software does highlight genomic variants which are novel and likely to be disease causing if you have submitted a trio. This is why there may be a small risk of finding an additional/unexpected variant in a gene which is not on the panel you requested, so it's important to counsel patients regarding this possibility.

When do I need to send a trio rather than a single sample?

Analysis of the many genomic variants identified on WGS is much easier, and more likely to be fruitful if you send samples from a patient and both parents rather than a single sample, as it enables us to see what might be "normal" for that family. It's therefore especially helpful if the parents are clearly unaffected with the condition that affects the child. In these cases, if parents are available it's better to consent and send samples from them.

There are of course many circumstances where parents are not available and so a single sample can be sent. You might also want to send a single sample where you have a very good idea of the clinical diagnosis and are mainly interested in a single gene or group of genes.

When sending familial samples, it's important to make it clear on the second page of the test request form whether the parents have any of the clinical features, as this affects the way the data is interpreted. If you are not sure whether the parent has the same condition as the child, or may show mild signs, remember to tick the box showing penetrance as incomplete on the test request form, so that during the analysis, variants which a child shares with a parent are not ignored.

Where do I find more information on phenotyping and HPO terms?

The phenotype of the patient refers to their actual clinical characteristics. These need to be listed on the request form, using accepted Human Phenotype Ontology Terms. A short list of the most commonly used terms is given at the bottom of the request form so you can use any of these. If you want to use additional terms, you can check on the HPO website https://hpo.jax.org/app/ whether the term you are using is an accepted HPO term, or get ideas as to the best term to use. Some specialties are compiling their own lists of frequently used terms. The website gives further information about the phenotype ontology.

For paediatric developmental disorders, the American Journal of Medical Genetics produced a series of articles on HPO typing. See: Elements of morphology: general terms for congenital anomalies. Hennekam RC, Biesecker LG, Allanson JE, Hall JG, Opitz JM, Temple IK, Carey JC; Elements of Morphology Consortium. Am J Med Genet A. 2013 Nov;161A(11):2726-33

Accurate and full phenotyping is really important when requesting WGS. Some variants which come up for consideration in the analysis could possibly be discarded if they do not fit with any of the phenotypic features. The Exomiser programme which picks out the three best clinical matches for your patient (see above) also relies on full and accurate phenotyping. To enhance this, some specialties use a specific proforma. Please assist by completing this if there is one.

What should I tell patients who are asking who can see their data?

All the data will be kept securely and confidentially in an NHS database. Only authorised personnel will be able to have access to this. Not all NHS staff will be able to see your data, only those who need to be able to see it for analysis and to feed your results back to you. The data will, however, form part of your medical record.

If you consent for your data to be part of the National Genomic Research Library, then others outside the NHS, mostly researchers but possibly healthcare companies such as pharmaceutical companies will be able to look at your genomic sequence. They will not use your name or personal identifiers but will see your list of symptoms. If someone wants to look at your data e.g. for research, then they have to be approved by a special data access committee which includes lay members. Your data cannot be accessed by insurance companies or by marketing companies.

You have a choice as to whether to make your data available to the genomic library or not. It might mean that there is a better chance of finding an answer for your condition and it will also further knowledge on what we understand by the "normal" genome sequence. It could also help with drug development in the future. However, it's impossible for us to tell you exactly who would have access to this data in the future. Usually, if anything was identified in the data it would be fed back via the doctor who organised your WGS test, rather than you being contacted by a researcher directly.

There is a separate information leaflet about genomic research that you could ask to look at.

Can I request to have more than one panel analysed?

Yes you can, as long as your primary clinical indication falls within the Phase 1 and Phase 2 indications listed in the table. Then, if your patient has other symptoms, too, you can add one of the panels which are listed as genomic virtual panels on panelapp e.g Hearing loss panel. You will need to find the R number associated with that panel.

How many WGS test request can I send?

The numbers we can send off from the NWGLH will be limited to begin with as we test the safety and efficiency of our systems. For example, we will be able to handle approximately 10 requests per week for the neurology and the ophthalmology indications when these start. We will inform you if there is a build up of samples in the system, and numbers will increase as time goes on. Currently, as we all get used to requesting the tests, there should be capacity for the number of tests we are receiving.

How long will it take to get results?

Ideally, we would like to get results back to you within an 84 day turn around time. Some WGS results are currently coming through within this time frame but some are taking a little longer. We are still being cautious with patients in giving them a time-frame but are mentioning 4-6 months. Over the next year or so, as the pipelines for testing mature we will have a better indication of what our turn around times are likely to be.

Where can I get the necessary request forms from?

You can download these from our North West GLH website https://mft.nhs.uk/nwglh/ under documents and forms and then WGS forms. For each request you will need:

a) WGS patient information leaflet standard/easy read /both to give to patient
b) A Record of Discussion form for each family member
c) A single test request form for the family, details of the whole trio can be entered, or of a duo if sending one parent.
d) If you are obtaining a fresh blood sample for the WGS test (which is preferable to using an old stored one) use our new WGS blood test request form

Which lab shall I send the request to?

You should e-mail the request form and the scanned, signed, RoD forms to the Manchester lab on mft.nwglhdnalab@nhs.net

The blood samples, if sent on the form above will come to the lab directly. DNA needs to be extracted in the Manchester laboratory

If I have a problem during the requesting process, who shall I contact?

In the first instance, contact the lab on mft.nwglhdnalab.nhs.net . They will try to answer your query or pass you on to someone who can help.

October 29th 2021