NHS
Central & South
Genomic Laboratory Hub

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Dear Colleague,

You may recently have received a letter from the C&S GLH detailing the urgent need for clinicians to assist in managing the current demand for genomic investigations to provide a sustainable and efficient service. We have now received further instructions from the NHSE Genomics Unit that we need to apply with immediate effect (NHS Genomic Medicine Service guidance to support demand management of genomic tests, June 2025; National Genomic Test Directory v8.1 July 2025). We have summarised steps we need to take to implement this guidance that may impact on clinical testing pathways in this letter. Please be assured that in addition to the measures outlined here, the GLH team is working hard behind the scenes to reduce costs of individual tests and to find every possible cost efficiency.

We have developed an area on our website which is dedicated to providing you with the relevant information on genomic testing updates, so please make sure to check this as it will be updated regularly.

The guidance from NHSE includes the following:

1) "*The primary test for rare disease clinical indications with a test method of whole genome sequencing (WGS) is WGS, and not microarray. WGS based testing is more comprehensive and able to detect almost every type of genomic variant that a microarray can detect and has a higher sensitivity for the majority of variant types. Microarray testing should not be performed instead of WGS and should only be performed prior to/in addition to WGS where there is scientific and clinical utility to do so. Test requests should only be accepted after discussion with the NHS GLH medical leadership and with agreement from the NHS GLH Operational Director*"

Following from this, the GLH will no longer accept any request for array CGH/SNP array for any test indication in the National Genomic Test Directory (NGTD) where WGS is available. This explicitly includes all individuals with who are eligible for R377 (Intellectual disability-microarray only). These patients should now be offered testing by WGS as the first line test. Where parental samples are available the test request should be made as a duo or trio of the proband and available parent(s). Microarray testing should not be requested instead of WGS and should only be requested as a first line investigation where there is scientific and clinical utility to do so, following discussion with the GLH e.g. strong clinical suspicion of chromosomal conditions like Williams syndrome, 22q11 deletion.

When requesting WGS, clinicians should ensure that detailed clinical information including all the applicable HPO terms are included. All the relevant NGTD panels must be requested as part of the primary investigation. This will increase the diagnostic yield of the test and helps to get a diagnosis promptly.

Please request the R27 (Paediatric disorders) panel instead of the R29 (Intellectual Disability) panel for all developmental delay/ intellectual disability referrals as R27 is a super panel which covers the R29 panel genes and other relevant genes. Where R29 is requested, the GLH will

convert this to R27 unless specifically stated on the test order form that there is a sound clinical reason not to do so.

All requests for R54 (Hereditary Ataxia with adult onset), R56 (Adult onset dystonia, chorea or related movement disorder), R58 (Early onset neurodegenerative disorder) and R60 (adult onset hereditary spastic paraplegia) will have all of these panels applied as a "neurology super panel, R54/R56/R58/R60", again unless it is stated on the test order form that there is a sound clinical reason not to do so.

Re-analysis of existing WGS data is extremely time consuming and the laboratory receive a very large number of WGS re-analysis requests (R387). This work could be avoided by comprehensive panel selection at the outset. We will now be strictly following published national reanalysis guidelines which can be found here and requests will only be actioned if they meet published eligibility criteria in the NGTD which can be found here.

Requests for WGS re-analysis must be made by completion of the appropriate request form which can be found here with a clear description of clinical utility and reasons why the patient/family are eligible for re-analysis. It is therefore in you and your patient's interest to include all relevant panels at the outset.

2) "*Test request forms should stipulate that the test requestor must provide detailed information on how the patient/family meet the eligibility criteria for the test indication that is being requested.*"

New genetic laboratory request forms that include space to prompt for these details will be issued by the genetic laboratories in C&S region soon. Please use them as soon as they are available to provide the required information. In the interim please add this information to the existing forms. When this information is not provided or is not clear from the referral information, the testing will not proceed. The sample will be stored, and you will be contacted to provide additional information.

A significant emphasis in the recent communication from NHSE relates to "clinical utility" of genetic tests and the following statement have been added to the NGTD (v8.1, July2025)

3) "*The NGTD sets out test eligibility criteria to provide guidance on which patients may benefit from genomic testing. Tests should only be requested where there is clear evidence that a result is highly likely to change clinical management of the patient or their family. Management includes determining clinical investigations; and/or therapeutic/treatment decisions or strategies; and/or enrolling in nationally approved surveillance programme; and/or informing and supporting reproductive choices*"

The demand management guidance document we have received also says:

4) *"Considering the clinical utility for every genomic test request/result, and how that will impact patient care, will enable best use of resources to achieve the greatest benefits to patients who need it. Not testing in situations with limited or no clinical utility will ensure patients and families who will benefit from genomic testing have equitable*

access to it within a clinically relevant timeframe (i.e., early enough to inform key clinical decisions that modify outcome).

Assessing clinical utility of course rests with the clinician making the test request. We are asking you to work with us to manage the very challenging circumstances the GLH laboratories across England now find themselves in.

An additional area of increased referral activity is the referral of babies born after abnormal screening tests in pregnancy e.g. increased Trisomy 21 risk, who have no discernible abnormal phenotype after birth. It is important we very carefully consider the clinical need and utility of testing a phenotypically normal baby. Similarly, we are seeing increasing numbers of test requests for siblings of children with de novo genetic variants in the absence of a phenotype in the sibling. Again, we must urge you to consider the utility of testing in these circumstances.

The GLH will adhere to the NGTD criteria when there is discordance between national or international guidelines with the NGTD criteria (NHS Genomic Medicine Service guidance to support demand management of genomic tests, June 2025)

These changes will take effect from the Monday 4th August 2025

We appreciate that clinicians may find some of these changes challenging but the GLH, GMSA and regional Clinical Genetics Units will always aim to offer appropriate advice and support. Additional information about ordering WGS can be found on the Central and South GMS website. The GMSA will be organising further training and education opportunities to support these changes to genomic testing pathways. The dates and times of these sessions will be communicated out from the GMSA.

The full test directory can be found here. You can contact your local genomics laboratory or Regional Clinical Genetics Unit for advice here.

Yours sincerely,

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