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NHS North West
NHS Genomic Laboratory Hub

9th January 2025

USER COMMUNICATION: CHANGES TO THE NHS ENGLAND COMMISSIONED RARE AND INHERITED DISEASE NATIONAL GENOMIC TESTING DIRECTORY

Dear colleagues,

We would like to inform you of some changes that have been made in a new publication of the Rare and Inherited Disease National Genomic Test Directory on 2nd January 2025 (version 7.1).

For convenience, the main changes have been summarised by speciality in the Appendix overleaf. Please note, only the main non-cancer changes are included here and we advise referring to the Test Directory (link above) for the complete details of eligibility criteria.

Final ratification of changes to the test directory were received from NHSE on the 8th January 2025. To enable transition to the new specification, any referrals received by the North West Genomic Laboratory hub (NW GLH) before 3rd February 2025 will continue to be processed in accordance with the previous National Genomic Test Directory (version 7). From Monday 3rd February 2025 the changes will be implemented. Testing will not be initiated for samples received after this date, which no longer meet the version 7.1 eligibility criteria or where the relevant tests are no longer available. DNA will be stored and a banking report will be sent to the referring clinician, as appropriate.

To minimise the chance of delays in testing please provide clear patient details and clinical information on the test request form and include the appropriate Test Directory indication code(s). Please also include a contact telephone number or email so we can contact you if there are any queries.

Any WGS requests require completion of a mandatory Test Order Form (TOF) and Record of Discussion (RoD) form (a RoD form is needed per individual). The TOF and RoD forms should be sent to mft.nwglhdnalab@nhs.net.

For clinicians that have access to the Manchester HIVE test ordering system, please note that the testing options are not yet linked to the live genomics test directory and may be out of date.

For any queries about these test directory changes or questions about genomic testing please contact the laboratory at mft.genomics@nhs.net. Useful links are included in the appendix.

Yours faithfully,

S. Barton

Stephanie Barton, NW GLH Rare Disease Scientific Lead (Consultant Clinical Scientist)

APPENDIX

Cardiology

- R454-Mavacamten for treating symptomatic obstructive HCM has been added as a new clinical indication

- R137 Congenital heart disease microarray – exclusion criteria added. Not indicated for common CHD (eg VSD) or non-syndromic CHD.
  *R27 also not indicated for isolated CHD, even if there is familial recurrence

- R131 Hypertrophic cardiomyopathy - if atypical or syndromic features, R135 may be more appropriate but must fulfil R135 criteria in the NGTD

Neurology

- Chromosomal microarray testing has been removed from the following neurology indications, and testing will be delivered solely by whole genome sequencing (WGS) analysis:

  R59.2 Early onset or syndromic epilepsy
  R69.3 Hypotonic infant
  R83.2 Arthrogryposis
  R84.2 Cerebellar anomalies
  R86.2 Hydrocephalus
  R87.2 Cerebral malformation
  R88.2 Severe microcephaly

- R56 Adult onset dystonia, chorea or related movement disorder

  Eligibility criteria updated to
  1.Unexplained isolated dystonia, chorea or related movement disorder with onset before age of 30, or familial
  2.Unexplained complex dystonia, chorea or related movement disorder with onset before age of 45, or familial
  3.HD-like (regardless of age or dystonia type), following a negative R68 HD test

- R58 Adult onset neurodegenerative disorder

  Testing criteria has been updated for dementia referrals:
  Unexplained dementia where acquired cause excluded AND
  - Age of onset less than 55 years
  - 1st or 2nd degree relative with MND
  - Neurological condition where cognitive impairment is part of a wider phenotype of a likely monogenic disorder
  - Family history suggestive of a monogenic disorder (onset below 65 years of age)

- R28 Congenital malformation and dysmorphism syndromes – microarray only
  The testing criteria has been amended to state that clinical features should be highly suggestive of a chromosomal cause and that, where possible, the specific chromosomal disorder suspected should be included on the request form (although this is not mandatory). Clinicians are being encouraged to consider broader testing at the outset.

- R377 Intellectual disability - microarray only
  The criteria has been amended to clarify that R377 microarray is not a requirement prior to testing both R27 Paediatric disorders and R29 Intellectual disability

Paediatrics

- R53 Fragile X
  This indication has been removed from the TD due to low diagnostic yield nationally. Testing is available as part of R27 Paediatric disorders or R29 Intellectual disability

- Chromosomal microarray testing has been removed from the following indications, and testing will be delivered solely by whole genome sequencing (WGS) analysis:

  R59.2 Early onset or syndromic epilepsy
  R88.2 Severe microcephaly
  R69.3 Hypotonic infant

- R69 Hypotonic Infant

  The R69.5 WGS test includes multiple sub-panels but does NOT include the following conditions, which must be requested separately, if required:
  R72 Myotonic dystrophy
  R70 SMA
  R48 Prader Willi syndrome

  For acutely unwell neonates with hypotonia, R14 Acutely unwell children with a likely monogenic disorder may be more appropriate.
  Please note, R28.1 Congenital malformation and dysmorphism syndromes microarray testing should be undertaken in parallel with R14 testing where clinically indicated, and in advance of R14 where the cause is highly likely to be chromosomal. R14 also doesn't include R72, R70 and R48 as part of the test.

- R27 Paediatric disorders

  The following eligible referring specialties have been added for this indication:
  Paediatrics
  Paediatric neurology
  Community paediatrics

  The eligibility testing criteria for R27 has also been amended to:

- Congenital malformations and/or dysmorphism **highly** suggestive of an underlying monogenic disorder where targeted genetic testing is not possible.
- Unexplained moderate/severe/profound global developmental delay or unexplained moderate/severe/profound intellectual disability, and where clinical features are highly suggestive of an underlying monogenic disorder requiring sequencing and targeted genetic testing is not possible.
- Craniofacial dysmorphism in combination with additional issues with health or development suggestive of a single genomic explanation, e.g. intellectual disability, congenital malformation, organ dysfunction.
- Syndromic overgrowth or overgrowth in combination with intellectual disability or developmental delay.
- Adults with congenital malformation and dysmorphism syndromes, however the clinical utility of testing should be made clear on the request form e.g. to inform a clinical management decision or reproductive choice.
- Fetus from a demised/non-continued pregnancy, with multiple major structural abnormalities detected on fetal ultrasound or post-mortem examination and where a monogenic malformation disorder is considered highly likely

- R28 Congenital malformation and dysmorphism syndromes – microarray only
  The testing criteria has been amended to state that clinical features should be highly suggestive of a chromosomal cause and that, where possible, the specific chromosomal disorder suspected should be included on the request form (although this is not mandatory). Clinicians are being encouraged to consider broader testing at the outset.

- R137 Congenital heart disease microarray – exclusion criteria added. Not indicated for common CHD (eg VSD) or non-syndromic CHD.
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Community paediatrics

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  This indication has been removed from the TD due to low diagnostic yield nationally. Testing is available as part of R27 Paediatric disorders or R29 Intellectual disability

- R69 Hypotonic Infant

  Chromosomal microarray testing has been removed from the R69.3 Hypotonic infant indication. Testing will be delivered solely by whole genome sequencing (WGS) analysis.

  The R69.5 WGS test includes multiple sub-panels but does NOT include the following conditions, which must be requested separately, if required:
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- Fetus from a demised/non-continued pregnancy, with multiple major structural abnormalities detected on fetal ultrasound or post-mortem examination and where a monogenic malformation disorder is considered highly likely.

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Endocrinology and Gynaecology

- R146 Differences in sex development
  Karyotyping is no longer needed for this prior to this indication and therefore only an EDTA sample is required (not lithium heparin) to confirm XX or XY (via R26).

Fetal medicine

- R137 Congenital heart disease microarray – exclusion criteria added. Not indicated for common CHD (eg VSD) or non-syndromic CHD.
  *R27 also not indicated for isolated CHD, even if there is familial recurrence

- R297 Possible structural chromosomal rearrangement – karyotype or Targeted Chromosome Analysis

  Updated Clinical Indication name to include Targeted Chromosome Analysis and amended criteria for recurrent miscarriage to:

  Recurrent miscarriage (defined as three or more miscarriages):

  • where testing of the pregnancy loss has not been possible due to an unsuitable/failed sample eg. no fetal material/MCC/fixed in formalin, and no previous losses have been successfully tested and reported

  Note that although parental karyotype analysis is available following a failed test, this is of limited utility and the most informative pathway is to test any subsequent pregnancy loss

  • with five or more pregnancy losses where none of the previous losses has been successfully tested and reported eg. biochemical pregnancies, no products available for testing

Useful Links:

National Genomic Test Directory and eligibility criteria
https://www.england.nhs.uk/publication/national-genomic-test-directories/

Rare disease Test request forms
https://mft.nhs.uk/nwglh/documents/test-request-forms/

WGS forms and information
https://mft.nhs.uk/nwglh/test-information/rare-disease/whole-genome-sequencing/.

Genomic Education Programme - Genomic notes for clinicians
https://www.genomicseducation.hee.nhs.uk/about-us/genotes-genomic-notes-for-clinicians/