NHS
Central & South
Genomic Laboratory Hub

November 2021

To all users of the Genomic Medicine Service for Rare Disease indications

Re: Whole Genome Sequencing (WGS) for Phase 2 clinical indications in the National Genomic Test Directory (NGTD)

The Central and South Genomic Laboratory Hub (GLH) has successfully introduced Whole Genome Sequencing (WGS) for NHSE Phase 1 clinical indications. To develop the service, the GLH will now deliver NHSE phase 2 clinical indications as per the National Genomic Test Directory - https://www.england.nhs.uk/publication/national-genomic-test-directories/

We have also listed the Phase 2 WGS Clinical indications at the end of this letter.

We will ask that you submit the test request, appropriate paperwork and samples according to NHSE Whole Genome Sequencing requirements. The regional Clinical Genetics services have been undertaking a program of engagement for WGS roll-out. If you need further support, please get in touch with your local clinical genetics service directly.

An FAQ and Guide document for the Genomic Medicine Service and Whole Genome Sequencing is available here https://bwc.nhs.uk/whole-genome-services-rare-disease-cs-glh. Please read through this document and the website page before contacting the laboratory for further information.

Any blood samples received for Phase 2 indications from 1st January 2022 will have DNA extracted and banked until the required WGS paperwork has been received. Currently available "panel tests" for these clinical indications will no longer be offered from that date.

Points to note:-

- The initial target turnaround time for WGS sequencing and reporting is **12 weeks** from receipt of **all** required samples and paperwork at the Central and South GLH, however as this service is developed and expanded this turnaround time may not be achieved immediately for all clinical indications.
- WGS in this context is the *technology* used to sequence the genetic code, not the analysis method. The analysis currently relies on bioinformatic application of the gene panel(s) linked to the clinical indication; hence this is **not** an 'agnostic' trio genome.
- **This is not a "rapid" service**. If an urgent result is required, the South West GLH is commissioned to provide the rapid Whole Exome Sequencing service for the indication R14 – *"Acutely unwell children with a likely monogenic disorder"*. R21 – "*Fetal anomalies with a likely genetic cause"* requiring rapid testing is commissioned separately through the Central and South GLH. If a "rapid" or urgent result is required for phase 2 WGS clinical indications the Central and South GLH laboratory will aim to provide a trio based whole exome sequence analysis. This will be on an individual patient basis and will require prior discussion with senior laboratory scientists or the rare disease medical team of the GLH.
- For the majority of paediatric WGS clinical indications in the NGTD, it is expected that the referring clinician will submit a **trio of parents and proband**. We understand will not always be possible and testing can still be offered for the child alone or with one parent.

- For adult-onset conditions we appreciate that a trio or duo may not be possible. However, in many instances a trio submission will provide the most complete data analysis and better test outcomes for your patients. We hope that the provision of the Genomic Practitioner/Associate network will encourage submission of informative family members when possible.

If you require further information or training in how to order the test and arrange consent for Whole Genome Sequencing, please get in touch with your regional genetics service in either Birmingham, Oxford or Southampton. Please also see the attached FAQ document.

For specific WGS-related questions such as choice of panel, please contact bwc.centralsouthGLH@nhs.net

Please do not hesitate to contact us if you have any questions about this expansion of WGS provision.

Yours sincerely,

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Phase 1 Rare Disease Clinical Indications for Whole Genome Sequencing
(Available from 15/05/2021)

Clinical indication (CI) Code	CI Name	CI Test Type Code
R27	Congenital malformation and dysmorphism syndromes - microarray and sequencing	R27.3
R29	Intellectual disability – microarray, fragile X and sequencing	R29.4
R69	Hypotonic infant	R69.5
R143	Neonatal diabetes	R143.4
R98	Likely inborn error of metabolism - targeted testing not possible	R98.2
R104	Skeletal dysplasia	R104.3
R100	Rare syndromic craniosynostosis or isolated multisuture synostosis	R100.3
R54	Hereditary ataxia with onset in adulthood	R54.3
R55	Hereditary ataxia with onset in childhood	R55.4
R59	Early onset or syndromic epilepsy	R59.3
R61	Childhood onset hereditary spastic paraplegia	R61.4
R83	Arthrogryposis	R83.3
R381	Other rare neuromuscular disorders	R381.2
R84	Cerebellar anomalies	R84.4
R85	Holoprosencephaly - NOT chromosomal	R85.2
R86	Hydrocephalus	R86.3
R87	Cerebral malformation	R87.3

R88	Severe microcephaly	R88.3
R109	Childhood onset leukodystrophy	R109.3
R193	Cystic renal disease	R193.4
R89	Ultra-rare and atypical monogenic disorders	R89.3

Phase 2 Rare Disease Clinical Indications for Whole Genome Sequencing
(Available from 01/11/2021)

Clinical indication (CI) Code	CI Name	CI Test Type Code
R135	Paediatric or syndromic cardiomyopathy	R135.2
R31	Bilateral congenital or childhood onset cataracts	R31.3
R32	Retinal disorders	R32.2
R33	Possible X-linked retinitis pigmentosa	R33.3
R34	Sorsby retinal dystrophy	R34.3
R35	Doyne retinal dystrophy	R35.3
R36	Structural eye disease	R36.2
R15	Primary immunodeficiency	R15.4
R56	Adult onset dystonia, chorea or related movement disorder	R56.3
R57	Childhood onset dystonia, chorea or related movement disorder	R57.5
R58	Adult onset neurodegenerative disorder	R58.4
R60	Adult onset hereditary spastic paraplegia	R60.3
R62	Adult onset leukodystrophy	R62.2
R78	Hereditary neuropathy or pain disorder , NOT PMP22 copy number	R78.4
R257	Unexplained paediatric onset end-stage renal disease	R257.2