# 100,000 Genomes Project Closure and Future of Genomic Testing

## Summary Update for Rare Disease Clinicians – December 2018

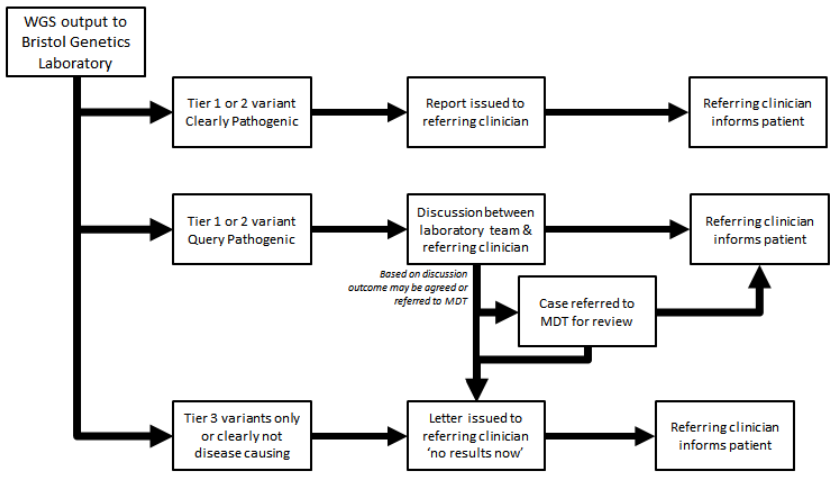
### 100,000 Genomes Project Closure & delivery:

1. The 100,000 Genomes Project closed to rare disease sample submissions in October and to supporting clinical data November 2018
2. Nationally, the 100,000 genomes samples completed sequencing on 5th December 2018. This total included 69,000 samples from rare disease patients and families
3. 2,655 people with rare diseases across the West-of-England Genomic Medicine Centre (GMC) joined the project.

### Proposed Return of Results Process for 100,000 Genomes Project patients:

1. All samples that we have collected will be sequenced at the national sequencing centre
2. The whole genome sequence is initially analysed against panels of genes selected according to the clinical data provided at enrolment (https://panelapp.genomicsengland.co.uk)
3. 172 gene panels have been developed nationally, based on current clinical knowledge of gene-disease associations. The report received by the referring clinician will highlight the panels applied to the analysis of each patient
4. Potentially causal genetic variants are initially stratified using bioinformatics approaches. There is a simple classification system (*tier 1*- very likely to be a pathogenic variant; *tier 2*- potentially a pathogenic variant; *tier 3*- uncertain significance in genes not normally linked to the phenotype of the patient)
5. The Bristol Genetics Laboratory (BGL) team review all tier 1 and 2 variants and match the results with the inheritance and family segregation data, and check that the right panel of genes has been analysed. Some variants will be discussed in more detail with clinical teams at MDT meetings
6. For each genetic result that is likely to be pathogenic and has been checked by reanalysis in the BGL, a report will be issued to the referring clinician. If there are no results that are likely to be pathogenic, then this will also be reported to referring clinicians, with emphasis that further analyses may occur in future.

**Diagram 1. Proposed pathway for managing variants from BGL to local clinicians**



*Please note:*

- *The GMC or Bristol Genetics Laboratory will not communicate genetic test results back to individual patients. We would recommend that this is the responsibility of the referring clinician*
- *At enrolment to the 100,000 Genomes Project, patients were invited to give additional consent for additional genetic analyses to look for other health related genetic changes, unrelated to their main genetic disorder. In these patients, the very small number that have relevant 'additional looked-for findings' will have an additional genetics report returned to their referring clinician.*

**Future genetic and genomic testing in the NHS**

1. From April 2019 a new national testing directory will be implemented that informs NHS clinicians about all of the genetic tests available in the NHS. This includes whole genome sequencing for some groups of rare diseases.
2. The national test directory outlines which patients are eligible for genetic testing and the testing process to follow. An excel version of the test directory can be found at: (https://www.england.nhs.uk/publication/national-genomic-test-directories/)
3. An informatics system called the "National Genomics Informatics Service" (NGIS) is being developed to help clinicians choose the right test for their patients and to give information about how to order a test and how to record the patient's consent for diagnosis and participation in research. The first release of this system will be in 2019.
4. All tests in the national test directory will be funded through new national commissioning arrangements under a standard national contract. This means that ordering a test from the national directory will not result in a direct charge to the host organisation.
5. All NHS genetic testing will be provided by one of seven nationally commissioned Genomic Laboratory Hubs (GLH). The GLH provider for hospitals in the West-of-England region is the South West Genomic Laboratory Hub, based at North Bristol Trust.
6. The transition to the new genetic testing arrangements has already begun and will continue through a transition period during 2019. **The exact timings of transition, including the timing of the new commissioning structure have not yet been finalised nationally.** Transition will be supported by the teams at our local GLHs and GMC.

For queries regarding the 100,000 Genomes Project please contact: ubh-tr.wegmc@nhs.net

For queries regarding future genetic or genomic testing please contact the Bristol Genetic Laboratory team at: nbn-tr.geneticsenquiries@nhs.net

Further support and information regarding returning of results for rare disease patients is being developed by the Genomics Education Programme and a draft of this information is available here: https://www.genomicseducation.hee.nhs.uk/news/item/473-review-our-guide-to-returning-genomic-test-results/