SCHEDULE 2 – THE SERVICES

A. Service Specifications

Service Specification No.	**E01/Sb**
Service	**NHS Genomic Laboratory Services**
Commissioner Lead	
Provider Lead	
Period	
Date of Review	

1. Population Needs

1.1 National/local context and evidence base

The reconfiguration of Genetic Laboratory service provision in England is supporting the creation of a world class resource in the use of genomics and genetic technologies within the NHS, and the provision of high quality, equitable and cost effective services across the pipeline from sample acquisition, to data analysis, validation and clinical interpretation, with support for patients and families. This will be critical in ensuring that genomic information and genetic testing is integrated across the NHS together with clinical genomic services to improve the prevention and diagnosis of disease and to support treatment decisions by identifying the right targeted therapies in order to maximise efficacy and outcomes and to reduce adverse effects.

The service specification builds on the recommendations of the Human Genomics Strategy Group (HGSG) 2012 report *'Building on our Inheritance; Genomic technology in healthcare'.* This report recognised the need to consolidate existing resources in order to deliver genetic laboratory services for the future, and to address the wider genomic agenda inclusive of bioinformatics and data sharing.

The landscape has altered significantly since the announcement of the 100,000 Genomes Project, which, when completed in 2017, will have been instrumental in helping define the legacy requirements for sustainable delivery of Genomic Medicine in the NHS.

To enable the potential of genomics to benefit all patient populations in England requires a systematic and comprehensive approach with a laboratory service infrastructure that is flexible enough to deliver an increasing number of high quality and comprehensive diagnostic genomic tests with good access and turnaround times.

2. Outcomes

2.1 NHS Outcomes Framework Domains & Indicators

Domain 1	**Preventing people from dying prematurely**	√
Domain 2	**Enhancing quality of life for people with long-term conditions**	√
Domain 3	**Helping people to recover from episodes of ill-health or following injury**	√
Domain 4	**Ensuring people have a positive experience of care**	√
Domain 5	**Treating and caring for people in safe environment and protecting them from avoidable harm**	√

The development of genomic medicine in the NHS will lead to improvements across all domains of the NHS Outcomes Framework (Appendix 2) and significant improvements in the ability to diagnose, treat and prevent disease and to provide high quality personalised care for all. It will support the UK Strategy for Rare Diseases and the impact will affect all ages as the interaction between genetic factors and environmental modifiers is understood better thus improving diagnostic services for patients more generally.

There will be a measurable and defined impact on all domains in the NHS Outcomes Framework through:

- earlier diagnosis and prediction and prevention of disease based on the complete functional genomic pathway from genomics (DNA) to metabolomics (products and biomarkers)
- personalised monitoring of treatment response and changes in clinical status through the use of rapid point of care molecular testing and/or companion diagnostics as part of long term condition management and/or associated with episodes of ill health
- equitable and timely access to functional genomic testing and reporting provided over 7 days of the week to optimise the patient experience within the clinical care pathway encompassing for example the relevant commitments set out the UK Rare Disease Plan
- safe and effective targeted treatment based on the genomic profile with minimised side effects as part of the overall move towards stratified and precision medicine.

3. Scope

3.1 Aims and objectives of service

This specification is focused on the genomic laboratory services falling within the direct commissioning responsibilities of NHS England. It aims to:

- continue to drive economies of scale and cost improvement
- reduce the variation that arises from differences in access to approved genetic, genomic and molecular pathology testing (used in conjunction with published clinical commissioning policies)
- maximise utilisation of technology and expertise for bioinformatics, validation and clinical

interpretation
- optimise emerging techniques such as exome sequencing, array technology and whole genome sequencing in wider clinical contexts to reduce costs and improve outcomes
- maximise workforce expertise and enable the development of specialist training centres for genomics for the specialist and non-specialist workforce including in bioinformatics and reduce variation associated with differences in clinical practice and knowledge
- enable the introduction at scale and pace of powerful new technologies to replace existing genetic testing strategies
- drive improved quality through collation and sharing of data for patient benefit by standardisation of and participation in minimum agreed datasets, repertoires and testing methods and external quality assessment and benchmarking
- provide a comprehensive and co-ordinated service and network for rare and inherited disorders working with clinical geneticists and the referring clinical specialities
- establish a virtual national network linking local molecular pathology laboratories/hubs to specialist genomic/ genetic technologies, knowledge, skills and expertise linking with clinical expertise to confirm the diagnosis
- capitalise and build upon the output of the 100K Genomes Project and its legacy
- support coordination and strengthening of genomic NHS service delivery, research, academia and industry partnership and the adoption of genomic technologies at scale and pace.

3.2 Service description/care pathway

The model of future provision reflects an evolution of the proposal outlined in the HGSG report (2012) and recognises a tiered approach:
Genomics England Sequencing Centre (GESC) – Genomics England is currently responsible for contracting for sequencing to support the 100,000 genome programme and this will potentially provide an accessible resource for WGS for diagnostic discovery for NHS patients.

Genomics Central Laboratory Hubs (GCLH) – these are the focus of this specialised commissioning specification. They are being configured around the concept of 'routine diagnostic clinical sequencing' and complex genome analysis supporting the full range of molecular and cytogenetic technologies as well as the validation and clinical interpretation of genomic data at the level of the whole genome, resulting in the consolidation of existing specialist genetic laboratories into state of the art, high throughput laboratories for the NHS. These GCLHs will be aligned to Biomedical Research Centres, Biomedical Research Units, Academic Health Science Centres (BRC/BRU/AHSC) and Networks (AHSNs) and/or have clear links with centres of internationally recognised academic excellence in genomics and translational medicine. Some GCLHs will undertake highly specialised testing on behalf of NHS England and possibly the UK on the basis of their current and recognised expertise in the area (i.e. not all GCLHs will undertake all tests routinely commissioned).

The GCLHs will from a strategic network with other GCLHs against which they will be benchmarked and be expected to share data, intelligence and expertise. They will be part of a group of central laboratories which will form the core of an NHS Genomics Laboratory Service where the working relationship must include a working protocol to cover the sharing of resilience measures between sites and regular structured communication.

Genomics Local Laboratory Hubs (GLLH) – these will emerge from and be formed with existing molecular pathology laboratories. They will be focused around the local planning and provision of rapid testing for clinical utility across a broad range of Pathology specialties and where appropriate other clinical specialties, and where there is likely to be a need to combine the results of different tests for integrated diagnostic reporting and for effective local management and treatment of patients. They will work closely with and be supported by the GCLHs through a managed network and the dissemination and sharing of knowledge, expertise, technology and data.

3.3 Genomics Central Laboratory Hubs

GCLHs will provide genetic and genomic testing for patients with, or at risk of, rare and inherited disorders, sporadic genetic disorders, acquired disorders (e.g. cancer) and stratified medicine as outlined in section 3.5 below and will:

- interpret variants identified through genomic sequencing (genome or exome) and provide analysis and interpretation of complex gene rearrangements
- develop quality assurance for genomic data used for clinical diagnosis (throughout the data analysis pipeline)
- validate new genomic diagnostic tests and technologies

3.4 Population covered

Based on ONS, National Population Census 2013 for England is 53,865,800. It is expected that each Genomic Central Laboratory Hub will serve a significant geographical area and population base.

3.5 Any acceptance and exclusion criteria and thresholds

The scope will include genetics/genomics services that focus on the following specific areas noting that this list is indicative and will evolve:

Inherited disorders - both rare, (defined as those affecting fewer than 1 in 2,000 individuals) and complex. These are conditions where a mutation(s)/rearrangement of the DNA is sufficient to cause the disease. These include Haematological disorders such as haemoglobinopathies, sudden cardiac death and inherited metabolic disorders. There are also children with rare diseases where the diagnosis is unclear (approximately 40,000 to 50,000 patients per year) and where appropriate genomic screening and data collection would significantly improve outcomes.
Sporadic genetic disorders: These disorders result from genetic changes that occur without any family history or genetic defects in the parents. They include sporadic findings from prenatal diagnosis, both invasive and non-invasive (NIPT-free foetal DNA analysis), and other postnatal rare and complex diseases.
Acquired disorders: These are disorders where an individual has acquired mutations in a gene or group of genes during their life. Such mutations are not inherited from a parent, but occur either randomly or due to environmental exposure. These include most cancers, including haematological cancers.
Stratified/Personalised or Precision Medicine for all conditions: Disorders that are stratified by detailed genomic profiling (rather than genetic marker expression which is usually performed locally) for treatment. Stratified medicine refers to the targeting of treatments, including pharmacological and non-pharmacological interventions, according to the biological (genetic) or risk characteristics shared by subgroups of patients.

For clarity the list above should be taken to include:

- microsatellite instability testing for mismatch repair defects (not IHC)
- the molecular testing elements within the pathways of the current antenatal and neonatal screening programmes e.g. haemoglobinopathies, MCADD and CF.

Bedside point of care testing (POCT) is expected to develop rapidly over the next few years as the benefits of personalised medicine are realised, so that POCT will also increasingly rely

on molecular technologies validated in the GCLHs.

The scope of the service specification will exclude:
Infectious diseases, e.g. molecular sequencing of pathogens, the provision of which will be led by Public Health England, which is currently developing its own Genomic Strategy. However it is recognised that molecular technological advances will drive rapid point of care diagnostics in infection.
Tissue typing, for which the demand is determined by factors such as the location of transplant units and will continue to be commissioned through Specialised Blood Transfusion and Transplantation Services.
Histopathology and cytopathology not using genomic technologies e.g. immunochemistry, or using routine molecular pathology testing such as HER2 and ALK, as their provision is integrated with current histological examination.
Newborn screening, as much of this testing at present is biochemical and performed on Tandem Mass Spectrometers rather than using genetic/genomic technologies.
Biochemical antenatal screening and other screening programmes (although non-invasive prenatal testing will be included in the scope).
Immunological tests that are not for single gene disorders e.g. rheumatoid factors (genetic/genomic-based tests for primary immunodeficiency, lymphoid and myeloid malignancies will be included in the scope).

3.6 Interdependencies with other services/providers

The strategic network of Central Laboratory Hubs is not expected to test for every rare disorder but to access specialist expertise appropriately and minimise the unnecessary duplication of service provision. GCLHs will:

- form a managed network with GLLHs, across the associated geographical area; but specialist areas of clinical interest may lead to more distant working partnerships which will need to be declared at the procurement process
- must be able to demonstrate translation of research into clinical practice, working with research and clinical staff to achieve this. They will focus on the interface between translational research and service innovation in genetics/genomics and will be aligned to established academic centres of excellence in the field
- demonstrate their experience of teaching and training. Working with Health Education England, they will have a lead role in teaching and training the new and existing healthcare workforce (including academic capacity building) to make best use, for the NHS, of the expertise in genomic technology and its application for patient benefit.

4. Applicable Service Standards

4.1 Applicable national standards e.g. NICE

Work within agreed and published NHS England Clinical Commissioning policies and policy statements, which set out funded treatment thresholds and eligibility

Use standardised test, gene and mutation nomenclature in accordance with current professional guidelines, HGVS recommendations, UKGTN listings and future National Laboratory Medicine Catalogue entries as required in the UK Strategy for Rare Diseases.

Follow applicable NICE guidance for specific clinical conditions e.g. for genetic testing of cancer and for diagnostic services when available.

Be compliant with European requirements including OECD Guidelines for Quality Assurance

in Molecular Genetic testing (2007) and the In Vitro Diagnostic Medical Devices Directive.

Use of commercial automated DNA extractors and the measurement of the DNA success rates and report on failure rates where these apply.

Meet the requirements set out in the NHSE Pathology Quality Assurance Review .

All Statutory Regulated healthcare scientists with the Health & Care Professions Council must have the necessary training, qualifications, experience and competence to perform their roles and undertake relevant continuing professional development or further registration requirements as appropriate to the level of staff. Those staff not subject to statutory regulation must be working towards accredited voluntary registration arrangements with the Academy for Healthcare Science and demonstrate that they undergone appropriate education and training for the role being performed.

Providers must be compliant with NHS England guidance on Information Governance.

4.2 Applicable standards set out in Guidance and/or issued by a competent body (e.g. Royal Colleges)

Compliant with the relevant Best Practice Guidelines of the Association for Clinical Genetic Science/ British Society for Genomic Medicine, the Royal College of Pathology and applicable guidelines from other Royal Colleges.

4.3 Applicable local standards

GCLHs will:

- provide information to commissioners about the use and activity levels of their service, by User and by responsible commissioner, and the performance of their services against key outcomes to be agreed with Commissioners
- fulfil the membership criteria for UKGTN (or any future successor arrangements) and participate in annual benchmarking of their services against other providers by submitting data to UKGTN. This will include activity and workload data, EQA performance data, Patient Safety data and efficiency data
- participate in the UK NEQAS scheme
- have responsibility for ensuring that all sites including those working in partnership arrangements are appropriate and equipped to support the delivery of genetic and genomic diagnostic services in accordance with the requirements specified by the commissioners
- be responsible for the transport of sample to their sites; and for the security and integrity issues involved in the transportation, handling and storage of clinical laboratory samples. These must meet CPA/UKAS ISO 15189 requirements
- be responsible for the security of, and access to, electronic data. All requesting clinicians should be notified of results within an agreed time frame (pertinent to the test). All anonymised data should be transferred to nominated data repositories in a timely manner.

Transitional risks must be identified and managed so that services to patients are not destabilised during any service re-provision activities and provide an infrastructure available that is flexible enough to deliver an increasing number of high quality diagnostic genomic tests.

5. Applicable quality requirements and CQUIN goals

For NHS service provision, the GCLHs must:

- be CQC diagnostic service regulated and CPA/UKAS ISO 15189 accredited (or by any replacement body) for all the services that it offers and meet MHRA and HTA regulatory

requirements

- inform commissioners of any change in accreditation or regulatory status to any part of its service and implement an action plan with timescales to achieve full compliance
- have a robust quality management system in place. All the quality standards, policies and procedures that it implements must be consistent with national, professional and regulatory guidelines and national benchmarking and EQA processes
- apply internal quality control procedures to all results prior to reporting to ensure that they are accurate and fit for purpose and validating against known datasets where clinically appropriate for example within the Genomics England Clinical Interpretation Partnership
- participate in relevant external quality assurance assessment schemes where they exist (e.g. UK and/or European National External Quality Assurance Schemes). In the absence of an appropriate external quality assurance scheme the Genomics Centralised Hub must ensure that there is appropriate assurance of the test results and reports participate in the NHSE Medical Genetics CRG quality dashboard monitoring including any relevant extension of KPIs for laboratories as a result of these developments.

5.1 Applicable quality requirements (See Schedule 4 Parts A-D) Please note that further details and specific parameters are being developed as part of the planned procurement preparation process and are therefore not yet available for this draft document. It should be noted quality requirements are largely service or technically based given this is not a patient facing service

5.2 Applicable CQUIN goals (See Schedule 4 Part E)

6. Location of Provider Premises

The Provider's Premises are located at:

7. Individual Service User Placement

N/A

8. Glossary

NHS	National Health Service
NHSE	National Health Service England
HGSG	Human Genomics Strategy Group
DNA	Deoxyribonucleic acid
UKGTN	UK Genetics Testing Network
CCG	Clinical Commissioning Groups
WES	Whole Exome Sequencing
WGS	Whole Genome Sequencing
GECIP	Genomics England Clinical Interpretation Partnership
NGS	Next Generation Sequencing
arrayCGH	Array Comparative Genomic Hybridisation
MLPA	Multi Ligation-dependent Probe Amplification
ACGS	Association for Clinical Genetic Science
QC	Quality Control
EQA	External Quality Assurance
HGSG	Human Genomics Strategy Group
GESC	Genomics England Sequencing Centre
GCLH	Genomic Central Laboratory Hubs
BRC	Biomedical Research Centres
BRU	Biomedical Research Units
AHSC	Academic Health Science Centres
AHSN	Academic Health Science Networks
GLLH	Genomics Local Laboratory Hubs
ONS	Office National Statistics
IHC	Immunohistochemistry
MCADD	Medium-chain acyl-CoA dehydrogenase deficiency
CF	Cystic Fibrosis
POCT	Point of Care Testing

HER2	Human epidermal growth factor receptor 2
ALK	Aplastic lymphoma receptor tyrosine kinase
UKAS	United Kingdom Accreditation Service
CPA	Clinical Pathology Association
HGVS	Human Genome Variation Society
OECD	Organisation for Economic Co-operation Development
NICE	National Institute for Health and Care Excellence
SNOMED	Systematised Nomenclature of Medicine
SNOMED-CT	Systematised Nomenclature of Medicine--Clinical Terms
Orphanet	The portal for rare diseases and orphan drugs
HPO	Human Phenotype Ontology
CQC	Clinical Quality Commission
MHRA	Medicines and Healthcare Products Regulatory Authority
HTA	Heath Technology Assessment
CRG	Clinical Reference Group
KPI	Key performance indicators

Appendix Two

Quality standards specific to the service using the following template:

Quality Requirement	Threshold	Method of Measurement	Consequence of breach
Domain 1: Preventing people dying prematurely			
Adhering to Required Reporting Turnaround Targets	3 days for pre-natal tests 10 days for familial mutation 40 days for panel, WES and diagnostic tests	Routine contractual reporting	As per contract terms
Domain 2: Enhancing the quality of life of people with long-term conditions			
Adhering to Required Reporting Turnaround Targets	3 days for pre-natal tests 10 days for familial mutation 40 days for panel, WES and diagnostic tests	Routine contractual reporting	As per contract terms
Domain 3: Helping people to recover from episodes of ill-health or following injury			
Adhering to Required Reporting Turnaround Targets	3 days for pre-natal tests 10 days for familial mutation 40 days for panel, WES and diagnostic tests	Routine contractual reporting	As per contract terms
Domain 4: Ensuring that people have a positive experience of care			
Patient experience	To be agreed	Submission of agreed	As per contract terms

Quality Requirement	Threshold	Method of Measurement	Consequence of breach
and satisfaction		patient experience survey	
Domain 5: Treating and caring for people in a safe environment and protecting them from avoidable harm			
DNA Extraction Rates Laboratory Errors (such as logging and categorisation review and actions taken to reduce re-occurrence)	Failure rates ≤1%	Routine contractual reporting Submission of annual report to CPA	As per contract terms