Updating the National Genomic Test Directory

Guidance for Applications to amend the Test Directory

NHS England and NHS Improvement

Updating the National Genomic Test Directory

Guidance for Applications to amend the Test Evaluation

Version number: 1

First published: December 2020

Updated: N/A

Prepared by: Lauren Marks, Genomics Policy and Strategy Manager, Genomics Unit

Classification: OFFICIAL

This information can be made available in alternative formats, such as easy read or large print, and may be available in alternative languages, upon request. Please contact ENGLAND.genomics@nhs.net

Contents

1. Introduction

The NHS Genomic Medicine Service (GMS) was established in October 2018 with the aim of providing consistent and equitable care to the country's 55 million population.

A central feature of the NHS GMS is the National Genomic Test Directory (Test Directory), which identifies the full range of genomic tests – from whole genome sequencing (WGS) to tests for single genes and molecular markers – that are commissioned by the NHS in England. The Test Directory sets out the technology by which tests are available and the patients who will be eligible to access a test. The NHS Genomic Laboratory Hubs (GLHs) are responsible for delivering the testing outlined in the Test Directory.

The Test Directory was first published in October 2018. To develop the Test Directory, NHS England and NHS Improvement established two expert groups – one for rare and inherited disorders and one for cancer. The groups brought together clinicians, scientists, health economists, policy experts, public representatives and patient organisations. The Test Directory builds on the evaluation work undertaken by the UK Genetic Testing Network and through a detailed process combining national and international evaluation approaches, emerging evidence, findings from research and the 100,000 Genomes Project and an analysis of current NHS testing activity.

The contents, structure and format of the Test Directory is copyrighted by NHS England and NHS Improvement and therefore the content is owned, controlled and maintained by NHS England and NHS Improvement. The Test Directory may only be amended pursuant to the robust and evidence-based test evaluation process managed by NHS England and NHS Improvement.

The Test Directory will be updated on an annual basis following the process outlined in the document "Updating the National Genomic Test Directory" and is supported by this guidance document. The annual update to the Test Directory will provide stability and clarity for the NHS GMS in implementing genomic testing and will be linked to the appropriate annual funding and commissioning processes.

2. The Process

2.1 Overview & Aims of the Process

NHS England and NHS Improvement, supported by the Genomics Clinical Reference Group (CRG) and genomic test evaluation working groups, will review and update the Test Directory on an annual basis following a robust and evidence-based process. Through this process NHS England and NHS Improvement will continue to consider the potential costs and benefits of expanding or altering the genomic testing which it commissions, ensuring that this testing is available for all patients for whom it would be of clinical benefit.

The main aims of the process are:

- To systematically review all available genomic testing by condition to inform the definitive repertoire of tests commissioned by the NHS in England and ensure that the best outcomes for patients at the best value is achieved;
- To support ongoing evaluation of new tests and technologies to enable access to the most effective and affordable technology now and in the future, including replacing tests where appropriate; and
- To assess clinical utility of genomic tests and to understand the implications of the genomic testing on the end to end patient pathway.

There are two possible routes by which the Test Directory may be updated:

- **An update linked to a policy decision,** such as medicine approvals by the National Institute for Health and Care Excellence (NICE), where a genomic test forms part of the access criteria for a drug. These updates may be made in-year as required.
- **Updates following the receipt and assessment of an application to amend the Test Directory.** Any proposed amendments to the Test Directory which are not mandated by a policy decision will go through the evaluation process to ensure that NHS commissioning of genomic tests in England is supported by the most up-to-date scientific, clinical and economic evidence.

2.2 Test Evaluation Working Groups

To provide clinical and scientific support to the process, NHS England and NHS Improvement has convened three test evaluation working groups reporting into the Genomics CRG in the following areas;

- Rare and inherited disease
- Cancer
- Pharmacogenomics

Membership of the genomic test evaluation working groups includes scientists, clinicians, health economists, and patient and public representatives.

2.3 Applications to the Test Evaluation Process

Applications to the test evaluation process may seek to:

- Add new clinical indications to the Test Directory;
- Amend existing clinical indications in the Test Directory, including the eligibility criteria, requesting specialities, constituent tests, test targets or technologies for existing clinical indications;
- Amend the content of gene panels;

- Decommission a test where it is obsolete or no longer supported by the clinical scientific or economic evidence;
- Move a clinical indication to whole genome sequencing (once this technology becomes more widely available).

2.4 Amending NHS GMS Virtual Gene Panels

NHS England and NHS Improvement will undertake a quarterly review and update of NHS GMS virtual gene panel content. Proposed amendments to the content of NHS GMS virtual gene panels should be submitted as evidence reviews via the Genomics England PanelApp platform: https://panelapp.genomicsengland.co.uk. The dates of the quarterly reviews will be published on the NHS England and NHS Improvement genomics website each year here: https://www.england.nhs.uk/genomics/the-national-genomic-test-directory/

This process does not apply to any NHS GMS panels which are not virtual (e.g. wet lab panels). Any amendments to NHS GMS panels which are not virtual should be submitted via the relevant application form as per the annual process (see sections 2.3 and 3).

2.5 Fast Track Process

A fast track process for applications to amend the Test Directory is provided to support amendments that may be identified as requiring implementation more urgently than through the annual update to the Test Directory, if the amendment meets one of the following criteria:

- An error is identified that needs to be corrected to ensure correct delivery of testing
- An urgent change is needed to benefit patients with limited financial impact
- An urgent change is needed to benefit operational implementation in the GMS with limited financial impact
- Newly emerged guidance or clinical policy mandates the amendment
- An urgent change is needed as a result of the COVID-19 response.

For further guidance on the completion and submission of applications, please see section 3.

2.6 Evaluation & Approval of Proposed Amendments

The Genomics Unit will carry out initial review of all applications and will request further information or clarifications where necessary. The application will then be allocated to the relevant genomic test evaluation working group where a full review will be carried out by members with appropriate expertise to determine the clinical and scientific basis for the proposed amendment. If the working group supports the proposed amendment at this stage, they will proceed to impact assessment.

An impact assessment will be carried out in collaboration with the NHS Genomic Laboratory Hubs (GLHs) to consider the operational, workforce and financial implications of implementing the proposed amendment to the Test Directory. Evidence reviews and impact assessments will take place between April and September each year.

Where a proposed amendment is identified to have a significant impact on patients, early engagement will be carried out with relevant patient groups to ensure that their views are taken into consideration in advance of recommendations being produced.

Based on the evidence review, impact assessment and early patient engagement, the test evaluation working group will make recommendations to the Genomics CRG on whether to support the proposed amendment.

The proposed amendments will be collated by NHS England and NHS Improvement and a formal decision through the appropriate governance will be made on the level of patient and public consultation which will be required to support prioritisation. Where amendments are limited to technical updates, a formal consultation may not be required. However, where the proposed amendments are likely to have a significant impact on patients, NHS England and NHS Improvement may consider a 30, 60, or 90-day public consultation.

The Genomics CRG will receive the outputs from any public consultation, along with the recommendations from the test evaluation working groups and will prioritise the proposals to develop recommendations on how the budget for updating the Test Directory should be spent. An equalities and health inequalities impact assessment will be carried out for the prioritised amendments to the Test Directory and published annually with the updated Test Directory. The Genomics CRG will make recommendations to the Genomics Programme Board in November each year.

For accepted proposed amendments further implementation details will also be established, for example, finalising gene panel content, allocating specialist testing delivery, finalising panel slicing approaches etc. Submitters of applications may be re-contacted to support with this phase.

2.7 Publication & Implementation of the Test Directory

Following approval by the Genomics Programme Board, NHS England and NHS Improvement will publish the updated Test Directory in December each year. The updated Test Directory will be linked to the NHS GLH Planning Guidance to support implementation. The updated Test Directory will be fully implemented by April each year.

3. Completion & Submission of Applications

The submission of applications to update the Test Directory is open to any individual or organisation, and stakeholders are not required to sign up to a stakeholder list prior to being able to submit an application. Applications are not required to be affiliated to an NHS GMS organisation (e.g. GLH or GMS Alliance), however each application form provides an opportunity to identify whether the application is supported by other organisations or is being co-submitted in partnership with another individual or organisation. Applications can be submitted by individuals, on behalf of an organisation, or as a collaborative application from a group of individuals, organisations or groups.

3.1 Application Forms

Any proposed amendment or addition to the Test Directory must be submitted via the relevant application form. Application forms are downloadable from the NHS England and NHS Improvement genomics website here: https://www.england.nhs.uk/genomics/the-national-genomic-test-directory/

The application forms available are;

- **Test Evaluation Application - Amendment to Existing Clinical Indication.** This application form should be used for any amendments to existing clinical indications in the Test Directory, including;

  Test name
  Testing criteria
  Where in the pathway testing occurs
  Requesting specialities
  Optimal family structure
  Test method
  Test technology
  Test scope (type of variants being tested for)
  Test targets (gene(s)/panel(s) being tested for including panel content)
  Addition or removal of any constituent tests

- **Test Evaluation Application – New Clinical Indication.** This application form should be used for proposing new clinical indications to be added to the Test Directory.

For any applications being submitted under the fast track criteria (see section 2.3), the accompanying fast track coversheet must be downloaded and completed in full in addition to the relevant application form.

3.2 Completion of Application Forms

Each application form contains an instructions tab to support the completion of the application. Application forms must be completed in full detail. Applications with insufficient information will be returned for the provision of further information. Where there are difficulties in fully completing any sections or there are any questions on the level of detail that can be provided for any sections, or for any further support with this process, please contact the Genomics Unit on ENGLAND.testevaluation@nhs.net.

The mandatory fields to be completed by the submitter are highlighted in yellow. Non-mandatory fields are highlighted in blue and also specified using e.g. "if known", "if relevant" etc.

The application forms contain a combination of free text fields and drop-down lists. Free text fields should be completed in full detail. The relevant option should be selected from any drop-down lists. Additional instructions for each field are provided where relevant.

Appropriate evidence for the proposed amendment should be provided, based on the available evidence base and context of each application. Examples of the types of evidence that could be provided to support applications include (but not limited or mandated to):

- recommendations of national or international organisations and professional bodies
- published academic papers including published outcomes of clinical and randomised control trials
- data from online repositories of genomic variants
- cost effectiveness analyses
- international evidence (not limited to evidence generated within the UK).

Where it is asked to provide the potential benefit to patients of the proposed amendment, consideration should be given to all aspects of patient benefit, including but not limited to):

- ability to receive a diagnosis
- benefit to clinical management
- benefit to patient health and physical wellbeing
- quality of life
- socioeconomic wellbeing
- mental wellbeing
- implications for family
- social implications.

3.2.1 Amendment to Existing Clinical Indication

General guidance for the completion of the application form for an amendment to an existing clinical indication is provided in the table below. Where prompted on the application form, references to relevant research should be provided.

Form Section	Guidance
Admin details	Provide the full details of; • the individual submitting the application • any co-submitters involved in developing the application • any support for the proposal from other organisations • if known, details of any previous instanced of the proposal having been evaluated through the test evaluation process.
About the current clinical indication & proposed change	Provide the details of; • the current clinical indication you are proposing to amend • the element(s) of the current clinical indication you are proposing to amend • why the change is necessary, including evidence to support • the proposed change • impacts of the proposed change, including benefits to patients.
Test targets	For proposed additions of test targets, please provide for each target; • gene name • target region (if relevant) • mode of inheritance • phenotypes associated with the gene/region • mode of pathogenicity (if known) • penetrance (if known) • supporting evidence for the information provided • note if the change may be potentially applicable to other clinical indication or NHS GMS gene panels • note if you would like to propose a recommended slicing approach for any of the proposed targets provided*

Form Section	Guidance
	*Some NHS GMS gene panels may be best analysed in “slices” of genes based on phenotypic information. Laboratories may use slicing information to prioritise interpretation of genetic variants associated with the phenotypic information and clinical suspicion.
Patient perspective	Provide any supporting evidence (if available) on the patient perspective of the proposed change.
Additional information	Provide any additional information relevant to the application not already covered in previous sections.

3.2.2 New Clinical Indications

General guidance for the completion of the application form for a new clinical indication is provided in the table below. Where prompted on the application form, references to relevant research should be provided.

Form Section	Guidance
Admin details	Provide the full details of; • the individual submitting the application • any co-submitters involved in developing the application • any support for the proposal from other organisations • if known, details of any previous instances of the proposal having been evaluated through the test evaluation process.
About the clinical indication	Provide the details of; • the proposed indication, including associations to any existing clinical indications • description of the indication • proposed eligibility criteria • where in the pathway testing would occur • turnaround times • requesting specialities who would request the test.
Scope and implementation (rare disease only)	Provide the details of; • optimal family structure to be tested • test scope *(the type of variation to be detected)* • test target(s) *(genes/variants to be detected)* • suggested test method(s) • proposed delivery model in the NHS GMS • analytical validity *(ability to measure accurately and reliably the genotype of interest)* • clinical validity *(how well the test predicts the presence or absence of the phenotype, clinical condition or predisposition)* • evidence for the association of the genotype to the clinical indication • any variation between frequency of variants and associated phenotypes between ethnic groups.
Scope and implementation (cancer only)	Provide the details of; • test target(s) *(genes/variants to be detected)* • suggested test method(s) • proposed delivery model in the NHS GMS • analytical validity *(ability to measure accurately and reliably the genotype of interest)* • clinical validity *(how well the test predicts the presence or absence of the phenotype, clinical condition or predisposition)*

Form Section	Guidance
	• evidence for the association of the genotype to the clinical indication • any variation between frequency of variants and associated phenotypes between ethnic groups.
Test targets	For proposed additions of test targets, please provide for each target; • gene name • target region (if relevant) • mode of inheritance • phenotypes associated with the gene/region • mode of pathogenicity (if known) • penetrance (if known) • supporting evidence for the information provided • note if the change may be potentially applicable to other clinical indication or NHS GMS gene panels • note if you would like to propose a recommended slicing approach for any of the proposed targets provided*. *Some NHS GMS gene panels may be best analysed in "slices" of genes based on phenotypic information. Laboratories may use slicing information to prioritise interpretation of genetic variants associated with the phenotypic information and clinical suspicion.
Clinical utility	Provide the details of; • use of the test (e.g. diagnostic, prognostic) • impact on clinical management • benefit to patients • non-molecular alternatives to the proposed test and advantage of proposed test • evidence to support the clinical utility and implementation of the clinical indication • existing implementation in the NHS in England or elsewhere.
Epidemiology	Provide the details of; • prevalence and annual incidence of the clinical indication in England • estimated diagnostic yield *(percentage of people tested who will obtain a diagnosis)* • estimated therapeutic yield *(percentage of people tested who will have improved prognostication or benefit from a proposed therapy).*
Finance	Provide the details of, where known; • estimated annual number of tests • cost per test • estimated total cost of national activity • expected cost savings or investment required per year • cost effectiveness.
Legal, ethical and social issues	Provide the details of; • any changes to nationally recommended patient choice process • any issues which may arise as a result of testing for the clinical indication • unexpected or incidental findings • equitability of testing • whether testing for the clinical indication would disproportionately advantage or disadvantage any groups with protected characteristics.
Patient perspective	Provide any supporting evidence (if available) on the patient perspective of the proposed change.

Form Section	Guidance
Additional information	Provide any additional information relevant to the application not already covered in previous sections.

3.3 Submission of Application Forms

Applications for amendments to the Test Directory must be submitted to the Genomics Unit at ENGLAND.testevaluation@nhs.net. Applications can be submitted at any point in the year. Confirmation of receipt of the application and any further information will be provided within 5 working days.

Each year NHS England and NHS Improvement will publish the timelines for the annual process on the NHS England and NHS Improvement genomics website:

This will outline the defined "cut off" dates at which;

- Applications submitted prior to the date would be considered for the annual update to the Test Directory occurring within the annual cycle;
- Applications submitted after the date would be accepted but may not be able to be fully evaluated within the current annual cycle and would be progressed in line with the next available update to the Test Directory.

3.4 Resubmission of Application Forms

If an application is either;

- submitted to the process but deemed insufficient during initial triage, OR;
- evaluated through the process and is not accepted as an amendment to the Test Directory,

the Genomics Unit will contact the submitter confirming why the application was not accepted. Applications to the process can be resubmitted at any time, for example, following the provision of further information to support the evaluation of the application.

3.5 Potential Future Amendments

If you are aware of a potential amendment to the Test Directory that could be required in the future that is not in a position to be formally submitted to the process, or is reliant on an external process or policy change (for example, the submission of a NICE Technology Appraisal by industry to NICE), you can notify NHS England and NHS Improvement of this activity by using the notification form. NHS England and NHS Improvement will keep a log of all notifications and continue to monitor these in relation to potential changes required to the Test Directory, and action them as appropriate.

4. Further information

For any further information on the National Genomic Test Directory or the process, please contact ENGLAND.testevaluation@nhs.net.