

UK Genetic Testing Network

National Institutes for Health, USA

Request for Information (RFI) on the National Institutes for Health Plan to Develop the Genetic Testing Registry

Submission by: UK Genetic Testing Network (UKGTN) Project Team
UKGTN Programme Director: Jacquie Westwood

Project Team:

Clinical Advisor:	Dr Shehla Mohammed (Consultant Geneticist and Head of Service Guys & St Thomas' Hospital)
Scientific Advisor: Molecular	Su Stenhouse (Head of Laboratory, South West Scotland Regional Genetics Centre, Glasgow)
Scientific Advisor: Cytogenetics	Val Davison (Head of Laboratory, Birmingham Regional Genetics Centre)
Public Health Advisor	Dr Mark Kroese (Consultant Public Health, Peterborough PCT)
Communications Specialist	Dr Jacqui Hoyle
Service Development Manager	Jane Deller
Business & Corporate Support Officer	Tarita Turtiainen

Contact: UKGTN, c/o National Specialised Commissioning Group, NHS London, 2nd Floor Southside, 105 Victoria Street, London, SW1E 6QT
Tel: 020 7932 3969, email: UKGTN.Enquiries@london.nhs.uk

The United Kingdom Genetic Testing Network: Background

The UKGTN Steering Group was established in 2002 and is part of the National Specialised Commissioning Team in NHS London. It is a collaborative group of NHS laboratory scientists, clinical geneticists, genetics commissioners and patient representatives and the Steering Group is Chaired by Professor Peter Farndon. It aims to promote the provision of high quality equitable genetic testing services for NHS patients across the UK. This involves evaluating new tests and recommending to specialised services commissioners (procurers of genetic services for patients in the NHS) those appropriate for service. There are 50 member laboratories from regional genetics and other specialist laboratories. A small project team and four working groups carry out the work on behalf of the Steering Group. The working group members are nominated representatives from healthcare professionals and patient representatives from across the UK.

The UKGTN has an internationally recognised process (commonly referred to as the "Gene Dossier process") to evaluate new genetic tests (within its scope) being proposed for NHS service nationally from its member laboratories. Tests that pass the UKGTN evaluation process are recommended to commissioners for funding. A Directory¹ is produced annually listing all the tests that have been through this process and the associated testing criteria to promote appropriate referrals. Currently there are 487 diseases on Directory which equates to 659 tests (i.e. disease/gene pairs). The Genetic Alliance UK (formerly the Genetic Interest Group) reports that patients have recognised the increased availability of genetic tests because of the UKGTN system. Different approaches are used internationally², but the UK is seen as a world leader.

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1. *The Directory of genetic tests that have been evaluated and are available from UKGTN member laboratories is available from the UKGTN website at www.ukgtn.nhs.uk*
 2. *The evaluation of clinical validity and clinical utility of genetic tests (September 2007), authors Dr Mark Kroese, UKGTN Public Health advisor; Dr Rob Elles, Director NGRL Manchester; Dr Ron Zimmern, Executive Director PHG Foundation.*

UK Genetic Testing Network

Question 1: Are there any types of genetic tests that should not be included in the GTR?

It is suggested that the tests listed on the GTR should have proven validity and utility. We note that the purpose of the GTR differs to the purpose of the UKGTN Directory. Therefore it may be helpful to differentiate between the tests in research and tests established and in full service.

The UK Genetic Testing Network (UKGTN) has a Directory of tests (<http://www.ukgtn.nhs.uk/gtn/Information/Services/Genetic+Testing+Directory>) and an online database (<http://www.ukgtn.nhs.uk/gtn/Search>) showing which member laboratories are providing the tests listed. Tests listed are those that have been evaluated for analytical and clinical validity and clinical utility and recommended to NHS commissioners for funding. The UKGTN currently limits the types of tests that it evaluates to those that would be ordered for patients in the NHS from clinical genetics specialties i.e. generally genetic tests for rare inherited single gene disorders.

Question 2: What the potential uses of the GTR for researchers, patients/consumers, health care providers, clinical laboratory professionals, payers, genetic testing entities/data submitters, policy makers, and electronic health records?

The potential uses of a GTR for all types of stakeholder listed in the question are many. However the usefulness of the GTR to each group will depend on the detail of the information provided and the background information available.

The UKGTN provides information for service users and commissioners on the price of testing in the NHS and the estimated turn round times via the online database. The evidence base for making recommendations is contained in the gene dossier form (see question 3). All service users, commissioners, researchers and consumers may find the information contained in the gene dossiers useful. The gene dossiers that are approved are available for download from the online database by searching the alphabetical disease list.

Question 3: What data elements are critical to include for use by stakeholders listed in question two above?

The UKGTN believe that the critical information required is the information elements in the gene dossier form (<http://www.ukgtn.nhs.uk/gtn/Information/Services/Gene+Dossiers/Forms>). A "Gene Dossier" form is submitted by laboratories to a UKGTN evaluation panel for consideration for NHS service. Each new test that is listed on the database and Directory has been evaluated through this UKGTN process (termed the Gene Dossier process) in order to establish if there is validity and utility.

Completed gene dossiers are available from the UKGTN database and a template form is also available from the UKGTN website. All the elements that are critical are listed in this form. The development of the form is based on the ACCE framework (<http://www.cdc.gov/genomics/gtesting/ACCE/index.htm>)

A paper published in 2007 explains the experiences of the UKGTN in evaluating genetic tests (Kroese M, Zimmern R, Farndon P, Stewart F, Whittaker J. *How can genetic tests be evaluated for clinical use? Experience of the UK Genetic Testing Network*. European Journal of Human Genetics (2007) <http://www.nature.com/ejhg/journal/v15/n9/abs/5201867a.html>).

UK Genetic Testing Network

Gene Dossiers are accepted from UKGTN member laboratories only. Member laboratories have to meet specified quality criteria in order to become a UKGTN member and provide NHS services nationally (research laboratories and tests are not included). Therefore UKGTN is assured of the quality of the test provision and the GD is evaluated within this context.

- Question 4: What are the potential benefits and risks associated with facilitating public access to information about the:
- availability and accessibility of genetic tests?
 - scientific basis and validity of genetic tests?
 - utility of genetic tests?

The overall benefit is that all members of society from patient to policy maker and healthcare professional has access to information. However the presentation of information may need to differ depending on the type of user. The language used for clinical geneticists would be significantly different to that used to inform patients with no training or education in medical terminology. In the UK the information element of the UKGTN website has different sections for laboratory scientists, healthcare professionals and patient groups with different information targeted at these different groups.

Potential risks include extra burden on healthcare professionals for genetic services that may not have any clinical utility for particular groups of patients but where patients believe that there is a benefit due to misunderstanding of the information presented.

It is not clear if the GTR propose to evaluate the utility and validity of the tests uploaded or peer review the information submitted for upload.

It is unclear from the consultation if the GTR has a process or are proposing a process to quality assure the information which could be made available. In the UK there are regulation processes to ensure that the public are informed about what a test can achieve. The quality processes of UKGTN give public assurance that the tests being offered from these laboratories are reliable for the purpose of diagnoses. The UKGTN laboratory membership quality criteria ensure testing is provided within an environment that meets accreditation standards. Research laboratories are not included because they do not meet this criteria and do not provide a full clinical service.

The information provided in the gene dossiers that are available from the UKGTN website are submitted by UKGTN member laboratories that have to reach quality criteria in order to become members. The information is evaluated by an independent group including scientists, clinical geneticists, public health and commissioning.

The information would need to be continually validated to ensure that it is up to date.

UK Genetic Testing Network

Question 5: No comment

Question 6: To describe adequately and accurately a genetic test, which of the following data elements should be included in the GTR? Are there any other data elements that should be added? What information is necessary to represent adequately each data element? (list of data elements listed in the GTR).

The information required in the Gene Dossier document and the information provided on the online UKGTN database are the data elements that UKGTN believe are important.

Question 7: What types of information might be difficult for test providers to submit and why?

Test providers may find it difficult to provide epidemiological data and a sound evidence base for very rare disorders due to the small numbers affected. International studies are important in this respect.

Question 8: What are the advantages and disadvantages of collecting and providing information on the molecular basis of genetic tests, such as detailed information about what the test detects and the specific methods employed?

In the UK the advantages are in the consolidation of information which provides transparency for public and professionals.

Question 9: In addition to the data elements would it be helpful to reference other resources, and if so, which ones?

The UKGTN find it useful to reference other resources. For example from the online database there is a link for each disease to the OMIM database and for each gene to the HUGO database. There is also a link to GeneReviews for each disease. Furthermore in the links section there are links to the professional organisations, the Royal Colleges, umbrella patient support groups and other UK genetics information sites. Within the gene dossier we do request that submitters provide references for published papers where these are available.

Question 10: As the GTR is being designed, what are the important processes to consider to make the submission of data as easy as possible for the data provider?

The UKGTN would suggest a standard proforma for the information submitted to be reviewed consistently.

Question 11: Which potential benefits and risks would be most likely to affect the decisions of researchers, test developers, and manufacturers on whether to submit data to the GTR, and what factors will best encourage submission of complete and accurate data?

No comment.

Question 12: What are the most effective methods to ensure continued stakeholder input into the maintenance of the GTR?

The UKGTN experience is to ensure that all submitters of information are members of the UKGTN. Consequently UKGTN will only evaluate gene dossiers submitted by laboratories that have been through an application process. The application

UK Genetic Testing Network

process includes completion of a form which is evaluated against agreed quality criteria. Member laboratories are keen to ensure that the data that is presented for their laboratory is accurate.

Question 13: For what purpose(s) would you use the Registry to support your professional efforts?

The UKGTN could reference the Registry in the States.

Question 14: Are there any other issues that NIH should consider in the development of the GTR?

Collaboration with the UKGTN maybe mutually beneficial.