# Evaluation of new genetic tests for NHS services
# Report to UKGTN Clinical & Scientific Advisory Group - 2013

## Key messages

**60 new tests** recommended for NHS service

Of the new tests recommended **40 are expected to have less than 50 index cases per annum**

In addition to clinical genetics tests range across:
- 25 specialties
- **20 Clinical Reference Groups**

Total additional **funding for the UK is £651,722** of which:
- £609,072 is required for prescribed specialised services
- £42,650 is required for highly specialised services

## Context

Criteria for evaluation by UKGTN: *new genetic tests for NHS service that are provided by UKGTN member laboratories for patients and/or family members seen in clinical genetics with rare conditions.*

The burden of rare diseases was recognised in the Chief Medical Officer report 2009 stating that rare diseases when considered collectively are common and that "*a diagnosis of a rare disease has a huge impact, not just on the individual but also on their family. People with rare diseases are estimated to cost the NHS over £1 million annually in each English health region. There are potential efficiencies in treatment if repetition of tests is avoided every time the patient sees another consultant*."

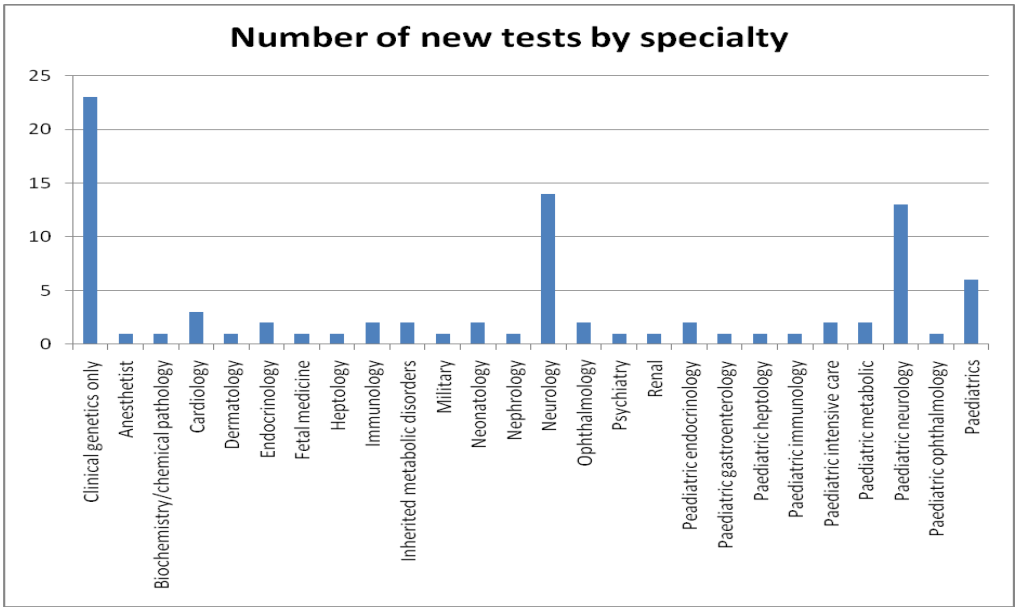
More recently the update to the Strategy for UK Life Sciences (2012) championed genetic testing "*The UK has led the world in genetic and genomic science, and the Government is determined to provide a supportive environment, to ensure that the UK remains at the forefront of new innovations in this field, capitalising on this leadership for the benefit of UK patients, the NHS, and the UK economy*."

A UK Strategy for Rare Diseases is currently being prepared by all four countries for publication by December 2013 to put the patient first to ensure that no-one is left behind simply because of their condition. The strategy will drive forward understanding of rare disease and work to increase the prospects of finding effective and sustainable treatments and therapies. The recommendations contained in this paper to introduce new genetic tests would not be evaluated by NICE as they fall outside the selection criteria due to their rarity.

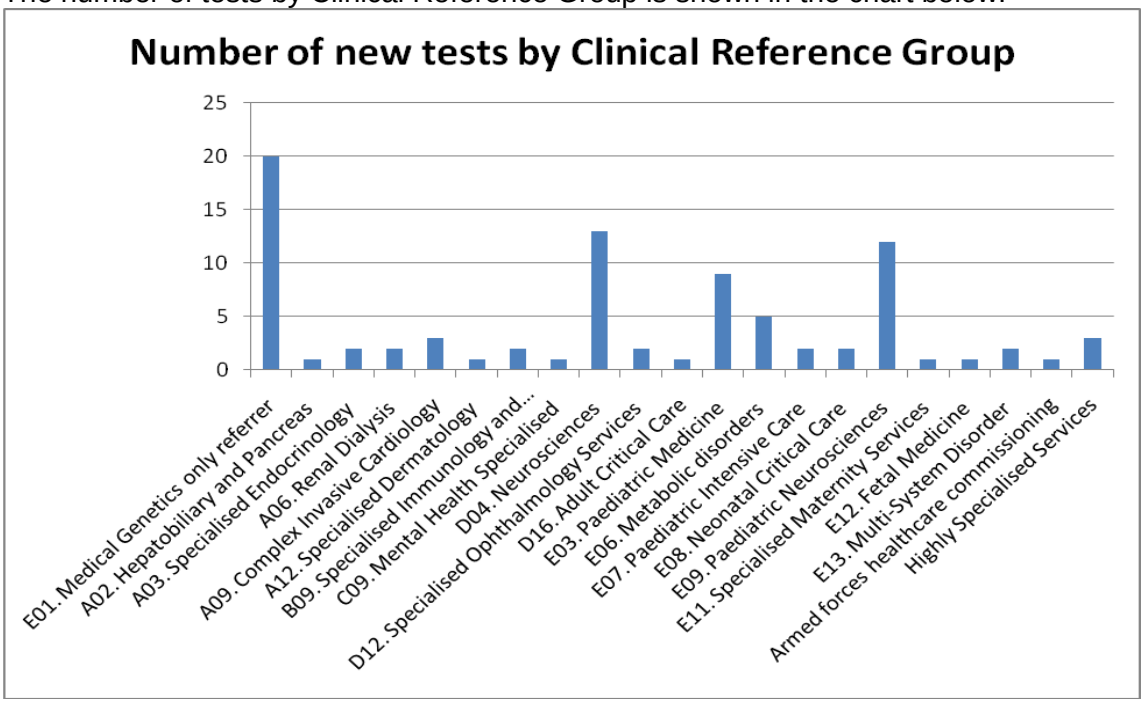
## Recommendations for new genetic tests for 2014/15

The UKGTN Genetic Test Evaluation Working Group, in the period October 2012 to August 2013:
- **evaluated 73** gene dossiers
- **recommends 60** new tests of which:
- **53** are **prescribed services** and **7** are within **Highly Specialised Services**
- **18** were evaluated through the very rare disease process (less than 20 index cases a year and less than £5000 annual costs for index cases)
- **12** are new panel tests that use Next Generation Sequencing

The number of new tests by specialty are indicated in the chart below. It would be appropriate for Clinical Geneticists to request all the new tests but 23 have clinical geneticists as the only referrer.




Based on the types of referrers for each test and the nature of each disorder it is expected that the new tests would fall within 20 prescribed specialised services in additional to medical genetics. The number of tests by Clinical Reference Group is shown in the chart below.




UKGTN is mindful of the evaluation criteria for the Clinical Priorities Advisory Group (CPAG) and gene test evaluations align to these as demonstrated:

**Does it work?**
The UKGTN has established an evidence based framework for the evaluation of genetic tests. The framework is based on the ACCE methodology which has been validated internationally.

For each genetic test application, the analytical validity, clinical validity and clinical utility of the test are evaluated. Test validation and performance data are required. In addition details of the testing pathway and its impact on the clinical pathway in terms of morbidity and mortality are provided. This includes both positive and negative consequences on the care of the patient and their families. The cost impact is described and alternative testing strategies are considered.

The assessment is performed by a multi-disciplinary expert group including clinicians and scientists. The group regularly requests additional data and information as part of its assessment to confirm the performance and benefits of the test under review. In order for a test to be supported, clear and sufficient evidence of the clinical benefits for patients and their families has to be provided.

In order to ensure the appropriate use of evaluated genetic tests and to guide clinicians in their diagnostic decision making, testing criteria are produced based on the evidence presented in the application. The criteria define the suitable target population and provide guidance on which clinical specialists are able to refer for the genetic test.

The majority of the genetic tests evaluated are low volume and for a significant proportion of applications are for rare diseases. The evidence threshold will therefore vary depending on the population and NHS impact of a proposed genetic test.

All the evidence considered in a genetic test application that has been approved is made publicly available on the UKGTN website.

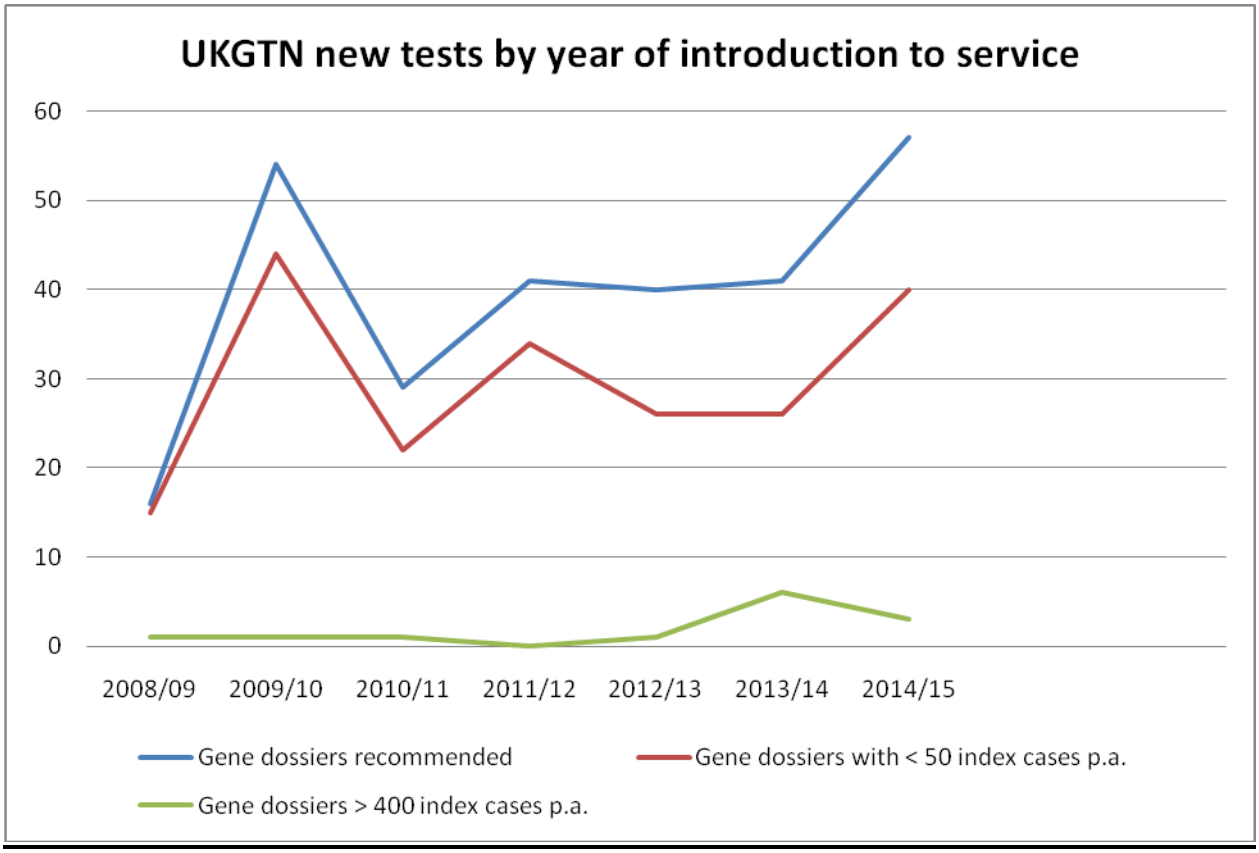
**Does it add value to society?**
Genomic research stimulates the introduction of genetic tests into clinical practice. When a body of evidence has developed for the involvement of a gene in the cause of a specific disorder, diagnostic laboratories will consider developing and validating a test for clinical use. This is often encouraged by an existing research or clinical interest in the disorder within the local Regional Genetic Centre ensuring a focus of expertise. This process will culminate in the submission of a gene dossier to UKGTN.

Once a test is approved and included in the UKGTN directory, provision of the service will increase the body of data available to clinical and research laboratories. However to ensure the maximum benefit is gained from the clinical testing, anonymised data on the mutations and associated phenotypes found in patient samples must be submitted to appropriate, secure databases. Such databases consolidate and extend knowledge of the disease mechanisms for the benefit of patients and in turn contribute to the clinical effectiveness and safety of the test.

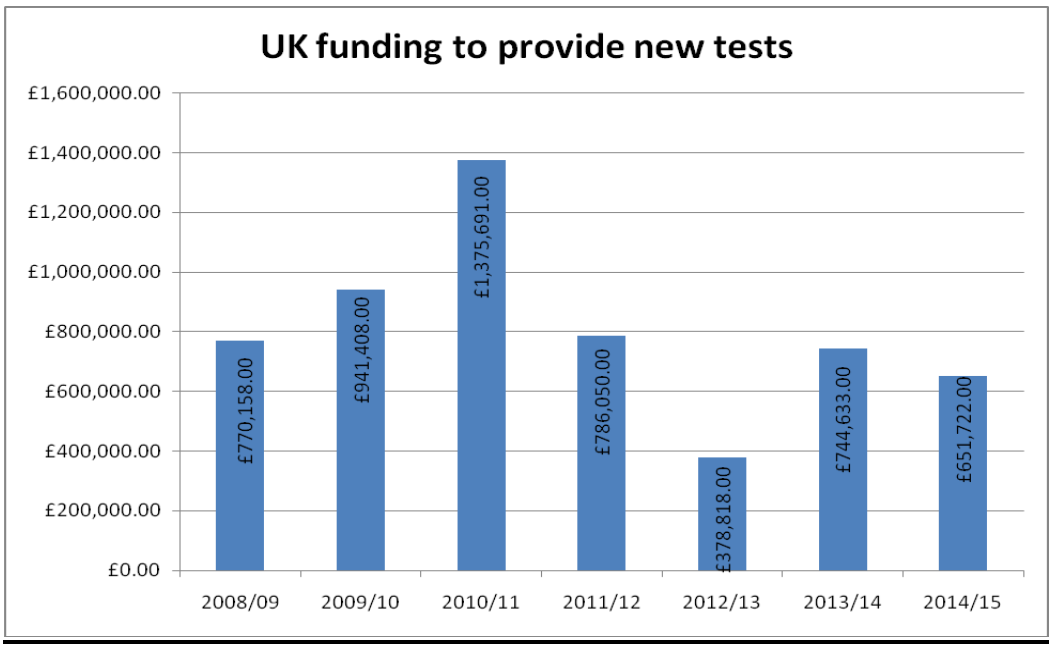
**Is it reasonable cost to the public?**
In many cases the availability of a genetic test removes the need for other tests/procedures in the diagnostic pathway. This is demonstrated in the gene test evaluations by considering the clinical utility of testing. It is important that new genetic tests that have utility are incorporated into the relevant specialties diagnostic pathways as the savings will usually be in specialties other than clinical genetics. Details of the utility of each test and the potential savings in the diagnostic pathway are considered for each evaluation.

**Is it the best way of delivering the service?**
New genetic tests will usually allow for some cost savings in the diagnostic pathway and/or savings in regular monitoring of individuals that no longer require follow up e.g. at risk family members of Sudden Cardiac Death found not to have the familial mutation. The evaluations that are submitted provide case examples both pre and post availability of genetic test to highlight the benefits in patient care, outcomes and costs. New tests that are approved for service are audited two years after service to determine the actual activity and costs against the estimates in the gene dossiers. The distribution of genetic testing is reviewed by the UKGTN in reports that provide genetic testing rates by geographical regions based on healthcare organisation boundaries.

**Evaluation Trend 2008/09 to 2014/15**



## Funding requirements trend 2008/09 to 2014/15




## Funding for new genetic tests for NHS service from 2014/15

Estimated funding required for clinical genetics separately from the funding requirements for specialties outside of clinical genetics has been calculated based on expected activity for testing from the genetics specialty and expected activity from mainstream specialties.

For the whole of the UK for clinical genetics activity only: **£422,526**;
For the whole of the UK for specialties activity EXCLUDING clinical genetics: **£186,546.**

The UK figures above exclude additional funding for tests that are part of **Highly Specialised Services (HSS)**. All HSS funding is for activity for the whole of the **UK** and amounts to **£42,650** although it is recognised that activity from the devolved countries may not be part of a HSS contract.

Funding for England and the Devolved Countries for all specialties and for clinical genetics only (excluding HSS) is shown in table 1.

**Table 1**. Estimated costs for new UKGTN recommended testing services for all UK countries for all specialties and for clinical genetics only

| Country | POPULATION | FUNDING (excludes HSS previously NSCT/NCG) | |
|---|---|---|---|
| | | All specialties (including clinical genetics) | Clinical Genetics only |
| **England** | 53,107,169 | £512,311 | £355,401 |
| **Wales** | 3,006,430 | £29,002 | £20,120 |
| **Scotland** | 5,200,000 | £50,163 | £34,799 |
| **Northern Ireland** | 1,824,000 | £17,596 | £12,206 |

The total estimated costs for new UKGTN recommended tests for England for the clinical genetics specialty only are listed by Area Team in Table 2. The costs across all specialties (including clinical genetics) are listed in Table 3.

**Table 2**. Estimated costs for new UKGTN recommended testing services for Clinical Genetics specialty for England.

| Country & Region (England) | POPULATION | FUNDING |
|---|---|---|
| **England** | 53,107,169 | £355,401 |
| North | 15,086,775 | £100,963 |
| Midlands and East | 16,117,771 | £107,862 |
| London | 8,204,407 | £54,905 |
| South | 13,698,216 | £91,670 |

| Region | Area Team | POPULATION | FUNDING |
|---|---|---|---|
| North | Cheshire, Warrington and Wirral | 1,222,808 | £8,183 |
| | Durham, Darlington and Tees | 1,176,022 | £7,870 |
| | Greater Manchester | 2,718,544 | £18,193 |
| | Lancashire | 1,461,295 | £9,779 |
| | Merseyside | 1,186,655 | £7,941 |
| | Cumbria, Northumberland, Tyne and Wear | 1,926,321 | £12,891 |
| | North Yorkshire and The Humber Area Team | 1,661,577 | £11,120 |
| | South Yorkshire and Bassetlaw Area Team | 1,456,808 | £9,749 |
| | West Yorkshire Area Team | 2,276,745 | £15,236 |
| Mids & East | Arden, Herefordshire and Worcestershire | 1,613,645 | £10,799 |
| | Birmingham and the Black Country | 2,422,818 | £16,214 |
| | Derbyshire and Nottinghamshire | 1,964,165 | £13,144 |
| | East Anglia | 2,430,414 | £16,265 |
| | Essex | 1,729,141 | £11,572 |
| | Hertfordshire and the South Midlands | 2,652,229 | £17,749 |
| | Leicestershire and Lincolnshire | 1,733,155 | £11,599 |
| | Shropshire and Staffordshire | 1,572,204 | £10,521 |
| London | **London** | 8,204,407 | £54,905 |
| South | Bath, Gloucestershire, Swindon and Wiltshire | 1,463,090 | £9,791 |
| | Bristol, North Somerset, Somerset and South Gloucestershire | 1,426,163 | £9,544 |
| | Devon, Cornwall and Isles of Scilly | 1,671,475 | £11,186 |
| | Kent and Medway | 1,731,351 | £11,586 |
| | Surrey and Sussex | 2,691,451 | £18,012 |
| | Thames Valley | 2,025,120 | £13,552 |
| | Wessex | 2,689,566 | £17,999 |

**Table 3**. Estimated costs for new UKGTN recommended testing services across all specialties (including clinical genetics) for England.

| Country & Region (England) | POPULATION | FUNDING |
|---|---|---|
| **England** | 53,107,169 | £512,311 |
| North | 15,086,775 | £145,538 |
| Midlands and East | 16,117,771 | £155,484 |
| London | 8,204,407 | £79,146 |
| South | 13,698,216 | £132,143 |

| Region | Area Team | POPULATION | FUNDING |
|---|---|---|---|
| North | Cheshire, Warrington and Wirral | 1,222,808 | £11,796 |
| | Durham, Darlington and Tees | 1,176,022 | £11,345 |
| | Greater Manchester | 2,718,544 | £26,225 |
| | Lancashire | 1,461,295 | £14,097 |
| | Merseyside | 1,186,655 | £11,447 |
| | Cumbria, Northumberland, Tyne and Wear | 1,926,321 | £18,583 |
| | North Yorkshire and The Humber Area Team | 1,661,577 | £16,029 |
| | South Yorkshire and Bassetlaw Area Team | 1,456,808 | £14,053 |
| | West Yorkshire Area Team | 2,276,745 | £21,963 |
| Mids & East | Arden, Herefordshire and Worcestershire | 1,613,645 | £15,566 |
| | Birmingham and the Black Country | 2,422,818 | £23,372 |
| | Derbyshire and Nottinghamshire | 1,964,165 | £18,948 |
| | East Anglia | 2,430,414 | £23,446 |
| | Essex | 1,729,141 | £16,681 |
| | Hertfordshire and the South Midlands | 2,652,229 | £25,585 |
| | Leicestershire and Lincolnshire | 1,733,155 | £16,719 |
| | Shropshire and Staffordshire | 1,572,204 | £15,167 |
| London | **London** | 8,204,407 | £79,146 |
| South | Bath, Gloucestershire, Swindon and Wiltshire | 1,463,090 | £14,114 |
| | Bristol, North Somerset, Somerset and South Gloucestershire | 1,426,163 | £13,758 |
| | Devon, Cornwall and Isles of Scilly | 1,671,475 | £16,124 |
| | Kent and Medway | 1,731,351 | £16,702 |
| | Surrey and Sussex | 2,691,451 | £25,964 |
| | Thames Valley | 2,025,120 | £19,536 |
| | Wessex | 2,689,566 | £25,946 |

Costs have not been provided for testing for those laboratories that have requested to be an additional provider as the resource is already available for these tests.

Services will be commissioned from 1st April 2014. The new test service information will be available from the website http://ukgtn.nhs.uk/find-a-test/.

## Background

The Gene Dossier provides a standardised format for the evaluation of the key information about a genetic test. A UKGTN multidisciplinary Working Group performs the evaluation of these applications and one of its key objectives is to confirm the clinical utility of a proposed genetic test. In annex B, the Working Group has included brief details about the clinical impact of each genetic test and the clinical consequences of not providing the test for NHS patients. Tests recommended for funding through NHS England prescribed services arrangements that have potential cost savings in the diagnostic care pathway and in many cases prevent unnecessary investigations for a proportion of the patients tested and are indicated in the cost columns.

Every Gene Dossier submitted has to include *Testing Criteria* for the test. The UKGTN developed the concept of *Testing Criteria* as part of the Gene Dossier application process. *Testing Criteria* defines the appropriateness of a genetic test referral, and it is intended that the test is only carried out in accordance with the criteria set out in the Gene Dossier and approved by the UKGTN Clinical and Scientific Advisory Group. *Testing Criteria* should include only those data that are specified within the Gene Dossier, and should not be confused with any other information that a provider laboratory may wish to have for research or any other reasons. The additional benefit of these criteria is that they can inform clinicians' decisions about which investigations are suitable for their patients. A summary of the Genetic Test Evaluation process is provided below.

## Genetic Test Evaluation Process

The Genetic Test Evaluation process (previously referred to as the Gene Dossier process) was developed by the UKGTN in 2003 as a tool to evaluate whether a proposed laboratory genetic test for a specific genetic disease is to be recommended for inclusion on the NHS Directory of Genetic Disorders/Genes for Diagnostic Testing (previously NHS Directory for Genetic Testing). Once a test is on the Directory it is recommended to be considered for funding under local commissioning arrangements. The Directory lists disease and gene combinations for which tests are available, that have been agreed as appropriate for clinical use, from member laboratories. The testing services provided and the laboratories providing them are available from the online database on the UKGTN website. The purpose of the Directory is to allow equity in access to genetic testing across the NHS. The process ensures that the decision regarding the recommendation of a test is explicit, transparent and based on evidence. The Genetic Test Evaluation documents (Gene Dossier and Additional Provider forms) and a description of the process can be found at http://ukgtn.nhs.uk/resources/genetic-test-evaluation-process/.

A gene dossier must be submitted to the UKGTN for any new genetic test that a UKGTN laboratory member wishes to provide and have listed on the NHS Directory of Genetic Disorders/Genes for Diagnostic Testing. For the UKGTN genetic test evaluation purposes, prior to April 2013, a genetic test was defined as any test for NHS service provision by a UKGTN member laboratory which required funding by specialised commissioning arrangements as supporting provision of clinical genetics services as defined in the national definition set for medical genetics services. Since April 2013, the definition of genetic testing has been expanded to include tests for any prescribed specialised service.

For diseases that are currently listed on the NHS Directory of Genetic Disorders/Genes for Diagnostic Testing or UKGTN website an additional provider form must be submitted.

It is recommended that a gene dossier is completed by the UKGTN laboratory in collaboration with clinical colleagues. The dossier is submitted by the laboratory director to the UKGTN and the UKGTN Genetic Test Evaluation Working Group (previously Gene Dossier working group) undertakes the evaluation of the dossier. The membership of this group includes professionals from clinical genetics, clinical laboratory genetics, public health, commissioning and patient groups.

The evaluation is based on agreed evaluation criteria. A template has been developed including the criteria and is part of the *Gene Dossier*. The evaluation criteria are summarised below:

(1) The seriousness of the condition
(2) The prevalence of the condition
(3) The purpose of the test – diagnosis, treatment, prognosis and management, presymptomatic testing, risk assessment
(4) The technical details of the test
(5) The context in which the test is to be used – defined population groups
(6) The characteristics of the test – the clinical sensitivity, specificity and predictive value
(7) The clinical utility of the test – how it adds to patient management and the availability of alternative diagnostic procedures
(8) Ethical, legal and social considerations
(9) The price of the test

The evaluation process includes both quantitative and qualitative information. The evaluations carried out so far have focused on molecular tests for rare genetic disorders. In many cases this results in limited test data and service information being available.

The results of the evaluation are reported to the UKGTN Clinical and Scientific Advisory Group (previously UKGTN Steering Group). Those disorders for which testing has been recommended by the working group and endorsed by the Clinical and Scientific Advisory Group are recommended to NHS commissioners for funding as NHS services and added to the NHS Directory of Genetic Disorders/Genes for Diagnostic Testing.

The Genetic Test Evaluation Working Group also reviews a number of the tests that are already on the NHS Directory of Genetic Testing in order to develop *testing criteria* for these tests. The UKGTN project team organises conferences/workshops on specific disorders (e.g. Cystic Fibrosis, Marfan and Fragile X) for scientists, clinicians and public heath consultants. Consensus *testing criteria* is produced so that all genetic laboratories are able to use them. This ensures a consistent approach to genetic test provision for these conditions throughout the UK.

The UKGTN has established a process to monitor the number of tests performed for all approved tests and will compare these figures to the predicted level of testing. If there is a significant difference then the UKGTN will investigate to establish the reasons for this.