NHS

UK Genetic Testing Network

The UK Genetic Testing Network and the Evaluation of Genetic Tests for National Health Service Provision

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"Implementation of array comparative genomic hybridisation into NHS genetics services"

Royal College of Pathologists

London, 8 July 2009

Outline

- UKGTN organisation
- Gene Dossier evaluation process
- Key questions for a test using array comparative genomic hybridisation

UK Genetic Testing Network

- Established in 2002 as a collaborative network of NHS molecular genetic laboratories.
- Objective is to provide high quality and equitable services for patients and their families who require genetic advice, diagnosis and management.
- Core functions include
  - » Quality assurance of laboratory services
  - » Evaluation of new genetic tests
  - » Establish robust arrangements for commissioning of services

31 NHS laboratories are members of the network (May 09).

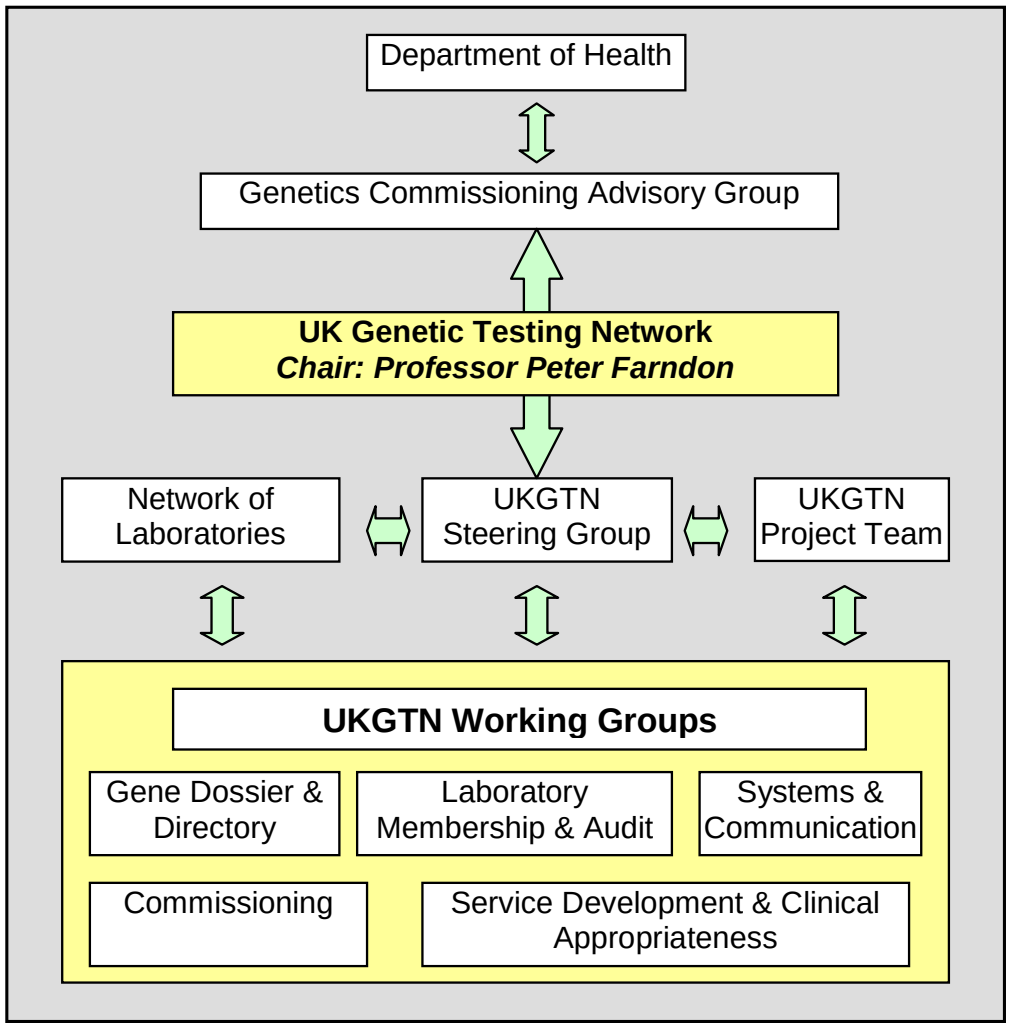
Laboratories need to be accredited with Clinical Pathology Accreditation Ltd or the UK Accreditation Service (UKAS).

The UKGTN Steering group is a subgroup of and accountable to the national Genetics Commissioning Advisory Group (GenCAG).

UKGTN Project Team includes

- Project Director
- Service Development Manager
- Communications Specialist
- 3 Specialist Advisors (Scientific, Clinical and Public Health)

UKGTN Organisation



- Genetic test is defined “as a test for an inherited disorder where nucleic acid is the analyte”.

- NHS Directory of tests – total number of diseases for which molecular tests are available - 454 (2009).

- The purpose of the Directory is to allow equity in access to genetic testing across the NHS.

- Gene Dossier was developed in 2004 to evaluate new genetic tests in order to inform decision of whether these should be funded as NHS care.

Gene Dossier process is based on

- **A nalytical validity**
- **C linical validity**
- **C linical utility**
- **E thical, legal and social**

- **Analytical validity** of a genetic test defines its ability to measure accurately and reliably the genotype of interest.
- **Clinical validity** of a genetic test defines its ability to detect or predict the presence or absence of the phenotype, clinical disease or predisposition to disease.
- **Clinical utility** of a genetic test refers to the likelihood that the test will lead to an improved outcome.
- **Ethical, legal and social implications** of a genetic test.

Gene dossier incorporates the key concept that a “genetic test” describes a test that detects.

i. a particular genetic variant (or set of variants)
ii. for a particular disease
iii. in a particular population
iv. for a particular purpose

Test is not considered in isolation but as a component of care pathway.

UKGTN does not perform health technology assessments.

Key Requirements

- Disorder and healthcare setting needs to be described.
- Purpose of testing and target population needs to be clearly defined.
- Evidence of analytical validity, clinical validity and clinical utility.
- Impact of test in care pathway for condition to be described.
- Testing algorithm to be presented.
- Cost of test.

Each Gene Dossier application requires collaboration.

Test – Disease – Population Triad

Disease – name	
OMIM number for disease	
Disease – alternative names please provide any alternative names you wish listed	
Disease – please provide a brief description of the disease characteristics	
Disease - mode of inheritance	
Gene – name	
OMIM number for gene	

Clinical utility of test in target population (Please refer to Appendix A) Please provide a description of the testing pathway.	
How will the test add to the management of the patient or alter clinical outcome?	

Gene Dossier Group Membership

- Clinical Geneticist (4)
- Laboratory Scientist (2)
- Genetic Counsellor
- Commissioner
- Public Health
- Patient Group Representative (2)
- Dept. of Health representative
- UKGTN Service Development Manager

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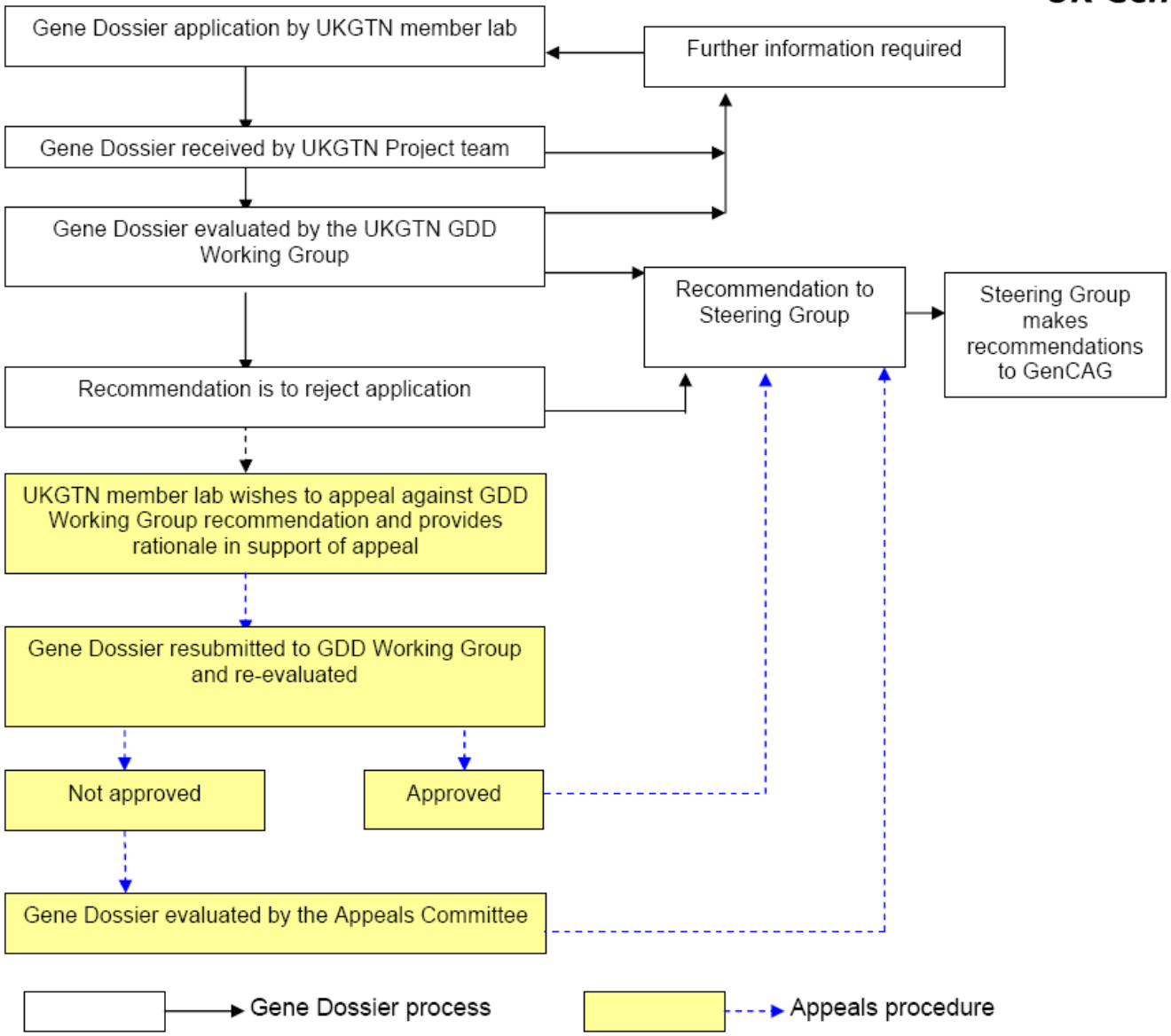

Gene Dossier applications 2004 – 2008

Total of 153 Gene Dossier submissions

- 122 were accepted
- 13 were rejected
- 6 submissions withdrawn
- 12 submissions still under consideration

The Gene Dossier application form and process is reviewed annually.

Test criteria developed in 2005.

Test criteria reflect the important features of a test such as target population, the disease and the purpose of testing.

Can act as a useful guide for clinicians.

During 2005 - 2008, the Gene Dossier working group reviewed and approved test criteria for 124 genetic tests.

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UK Genetic Testing Network

Name of Disease/test:
Steroid Resistant Nephrotic Syndrome; NPSH2 testing

Referrals only will be accepted from one of the following:
(Please indicate with a tick which category refers to the referrer).

Referrer	Tick if this refers to you.
Paediatric Nephrologist	
Consultant Clinical Geneticist	

Minimum criteria required for testing to be appropriate as stated in the Gene Dossier:

Criteria	Tick if this patient meets criteria
Presence of nephrotic syndrome (Serum albumin < 25g/l and urine albumin > 4 mg/m2/h or urine albumin/creatinine ratio > 100 mg/mmol), that is either:	
1) resistant to treatment with steroids, or	
2) present in the first 3 months of life, or	
3) has a histological picture of FSGS on biopsy.	

If the sample does not fulfil these criteria and you still feel that testing should be performed please contact the Paediatric Nephrology Service at the Royal Manchester Children's Hospital 0161 727 2357 to discuss testing of the sample.

Issues encountered with Gene Dossier applications

- Clinical validity data for tests - challenging
- Distinction between research information and information with clinical applications
- The target population poorly defined in some applications
- Lack of information about the clinical context of testing
- Financial data difficult to obtain
- Considerable uncertainty about expected test activity
- Balance between the degree of detail on test performance necessary, the resources available to achieve this and the negative impact of not providing the test

Test using array comparative genomic hybridisation

- A UKGTN subgroup established including cytogenetic scientists.

- Gene Dossier assessed as fit for purpose for a test using aCGH.

Issues to be considered

- Test definition still required.
- Confirmed copy number variation (CNV) of no clinical significance – clinical interpretation.
- Copy number variation (CNV) of uncertain significance – clinical consequences.
- Test with potential for significant health service and/or population impact will require pilot data to confirm expected outcomes.

Scientific Validity + Test Performance = Clinical Validity

Scientific validity

Evaluation of the relationship between biomarker and disease

Test performance

Evaluation of the test performance in the clinical situation

Evidence of biomarker-disease association is necessary, but by no means sufficient, as an indicator of effective and useful test performance

Dr Ron Zimmern, PHG Foundation

Acknowledgements

UKGTN Project Team

Ms J Deller

Dr J Hoyle

Dr P Lunt

Ms S Stenhouse

Ms J Westwood

Gene Dossier and Directory Working Group

Further information

www.ukgtn.nhs.uk

Report of the UKGTN, "*Supporting genetic testing in the NHS*" 2008

Kroese M, Zimmern RL, Farndon P, Stewart F, Whittaker J. How can genetic tests be evaluated for clinical use? Experience of the UK Genetic Testing Network. *Eur J Hum Genet.* 2007;**15**:917-21