UK NEQAS FOR MOLECULAR GENETICS

External Quality Assurance
monogenic disorders

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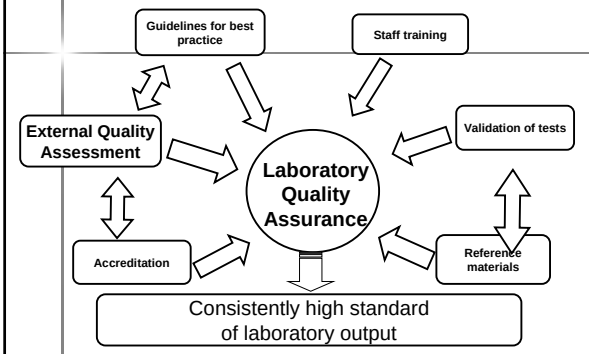
Ensuring Quality



What is External Quality Assessment?

- EQA = proficiency testing
- Procedure for assessing and maintaining the quality and standards of output from a laboratory
- Measures the error rate of the laboratory and helps to identify any underlying problems.
- The end result is improved performance and better quality control

What is the purpose of EQA?

- Mechanism to quantify the quality of output of a laboratory
  - the analytical service of the laboratory and/or
  - the interpretations provided by individual members of staff
- Raise and harmonise standards
- Education
- Ensures that patients and clinicians receive the best possible service

The laboratory's point of view

- Participate in approved EQA Schemes appropriate to the examination and interpretations provided.
- Maintain a record of results against the agreed performance criteria in EQA schemes.
  Record should be - reviewed
  - communicated to staff
  - decisions recorded, monitored and acted upon
- Participation in EQA schemes is an essential element in informing both the providers and users of the quality of the service.

The patient's point of view

- Available and accessible
- Turnaround time
- Understand the result
- Assume test is correct

Molecular Genetic Testing

- A genotype is usually only established once
- A genetic test result is important for life decisions
- A genetic test is important for the whole family

Molecular Genetic Testing

Genotyping → Interpretation → Clinical context

- UK National External Quality Assessment Services (UKNEQAS)

"helping to ensure clinical laboratory test results are accurate, reliable and comparable wherever they are produced"

- UK NEQAS for Molecular Genetics
  - Established in 1991
  - Provide EQA for Molecular Genetics
  - Self funding, non-profit making scheme

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Accredited EQA Scheme
Reference No: 051

- Clinical Pathology Accreditation (UK) Ltd
  - Full Accreditation since 2001
  - Assessment visit every 2 years
- Adhere to UK Joint Working Group on Quality Assurance conditions of participation
- Assess
  - Genotyping
  - Interpretation
  - Clerical Accuracy

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- Steering Committee comprised of
  - Senior Molecular Geneticists (UK, Ireland, Netherlands)
  - Clinical Geneticists
  - NHS and Private Sector Representatives
- Report to National Quality Assurance Advisory Panel (NQAAP) on UK participant performance against Poor Performance criteria.
- Web-based system for
  - EQA scheme registration
  - Report return submission
  - Scheme marking
  - Data manipulation
  - Publication of scores and reports
  - Record of participation and performance
  - Invoicing

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Examples of errors detected by molecular EQA schemes

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Laboratory 1

- Participated in Fragile X syndrome (FRAX) EQA
- Clinical case scenario
  - *Individual with family history of FRAX referred for molecular testing*
- DNA sample provided - carrier of a FRAX methylated full mutation
- Result submitted – NOT carrier of FRAX mutation
- Follow up - all Southern blot analysis for FRAX suspended
  - clinical cases sent on to other diagnostic lab
  - repeat samples supplied
  - methodology reviewed
  - test with extra EQA samples

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Laboratory 2

- Participated in Hereditary non-polyposis colon cancer EQA
- Clinical case scenario
  - *Patient was referred for testing of presence of familial pathogenic variant*
- DNA sample provided was a carrier of this familial variant
- Result submitted – patient did NOT carry this variant
- Follow up - lab contact immediately following all EQA reports submission
  - lab investigated their testing procedure
  - identified a sample mix-up with clinical sample
  - management informed
  - lab to show evidence of review of procedures
  - extra round of EQA

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Laboratory 3

- Participated in Molecular Rapid Aneuploidy EQA
- Clinical case scenario
  - *Patient with ultrasound abnormalities*
- DNA sample extracted from CVS provided had normal chromosome complement for chromosomes 13, 18 and 21. Fetus was female.
- Result submitted – Fetus was male
- Follow up - lab appealed against marking
  - declared it was a clerical error in transcription of results into report
  - Appeal overruled
  - Poor performance stood
  - even a transcription/clerical error can affect the quality of the output of the lab

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Laboratory 4

- Participated in Cystic fibrosis EQA
- Clinical case scenario
  - *Prenatal sample to be tested for CF*
- DNA sample extracted from CVS had two CF mutations present
- Result submitted – Fetus was a carrier of one CF mutation and therefore UNAFFECTED
- Follow up - lab contact immediately following all EQA reports submission
  - lab investigated
  - staff interpretation of results incorrect
  - staff on annual leave
  - inadequate checking procedures in place
  - service has been suspended until review of lab undertaken

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Errors detected by EQA

- Methodology based error
- Sample mix-up
- Error occurring when transferring result
- Error in interpretation of result/insufficient staffing & checking procedure

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Pilot EQA for PGD Monogenic disorders 2008

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Initial Stages

- Identified need for EQA
- CPA (UK) funding for pilot scheme (1 year)
- Collaboration with ESHRE
- Initiated PGD Molecular EQA Working Group

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Aims of Pilot EQA

- Assess all stages of the process to allow comparisons between laboratories and techniques
- Stage 1 - Ability to perform a feasibility work-up for PGD
- Stage 2 - Technical ability to perform single cell PCR
  - Interpretation and reporting of results

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2008 - Pilot EQA for Cystic fibrosis

- Identified 12 PGD labs performing CF
- Commercially available samples from CF families cell lines -
  - Independently validated samples
  - DNA samples for feasibility work-up
  - Cell lines for single cell PCR
- Pilot EQA scheme – no participation fee
- Use of UK NEQAS for Molecular Genetics website

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Outline

Stage 1 - November 2008

- Distribution of "parental" and "CF affected relative" DNA samples
- Participants required to perform feasibility work-up
- 1 month given for testing
- Submit results in format – YES PGD is possible in this lab
  - NO PGD not possible in this lab

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Outline

Stage 2 – December 2008/January 2009

- Distribution of "embryo cells" – derived from "parents" provided in Stage 1
- Participants required to perform single cell PCR
- 1 month given for testing
- Submit results - Report diagnostic result in regular reporting format
  - In addition must include information:
    i) if embryo suitable/unsuitable for transfer
    ii) if unsuitable then reason must be stated
    iii) methodology used

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Outline

Stage 3 – January/February 2009

- Assessment of reports against consensus marking criteria
- Collation of data obtained
- Publication of EQA scheme report including anonymised laboratory results and issues arising from scheme
- Feedback from Participating laboratories

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