


Introduction to Quality Management Systems

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Agenda

- **Assessing Quality in a PGD laboratory**
- **Quality standards and accreditation**
- **Quality Management Systems**

Quality ?

sportive, capacity of engine, design, tinted windows

reliable

pain control

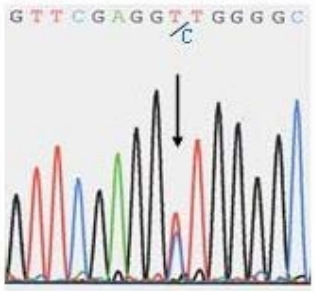
Preimplantation genetic diagnosis

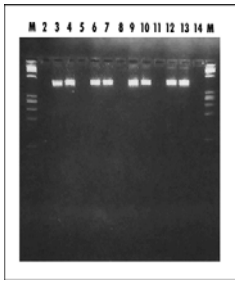
- Genetic testing of embryos, to assist couples with high risk of transmitting a severe genetic disease
- The **result** of the analysis is expected to be **correct, reliable and in time**

Assessing Quality PGD laboratory

Embryo biopsy

DNA





Genotype Analysis

Interpretation & Report

EMQN RETINOBLASTOMA PILOT EQA SCHEME-2001.
LABORATORY CODE: 3

CASE 1

Retinoblastoma Mutation Screening Report

Peter Schmid

Results

Name	Date of Birth	Status	Mutation Found	Risk on Data
Peter Schmid	01/03/01	bilateral retinoblastoma	1482delG	-

Comments

Peter Schmid was diagnosed with bilateral retinoblastoma. A peripheral blood DNA sample from him was reviewed by SSCP/heteroduplex analysis for mutations in the retinoblastoma gene, *RB1*. A novel shift was observed in the amplimer for exon 14. Direct sequencing (in both orientations) identified this as a deletion of nucleotide 1482. 1482delG results in a frameshift in exon 14 which is predicted to lead to the formation of a stop codon in the mRNA and premature termination of the retinoblastoma protein. This result provides a molecular confirmation of Retinoblastoma. Testing for 1482delG may be offered to other members of Peter's family.

Signed: Checked:

Worksheet no: 01/3017
No. of genotypes: 6

pre- / post-counselling

Assessing Quality PGD laboratory

Monday, 8 July, 2002, 12:39 GMT 13:39 UK

IVF under the microscope

IVF remains controversial

In vitro fertilisation (IVF) was pioneered in the UK in the 1970s. With thousands of test tube babies now being born every year, what is the state of the technique in its birthplace?

Almost 24 years after Louise Brown became the first so-called test tube baby, the in vitro fertilisation (IVF) techniques that brought her into the world have run into trouble.

A white mother has given birth to black twins, following a laboratory mix-up. Though the first mistake of its kind to come to light - and then, worryingly, only because of the skin-colour discrepancy - the rules which govern the fertilisation of eggs outside the womb are again under scrutiny.

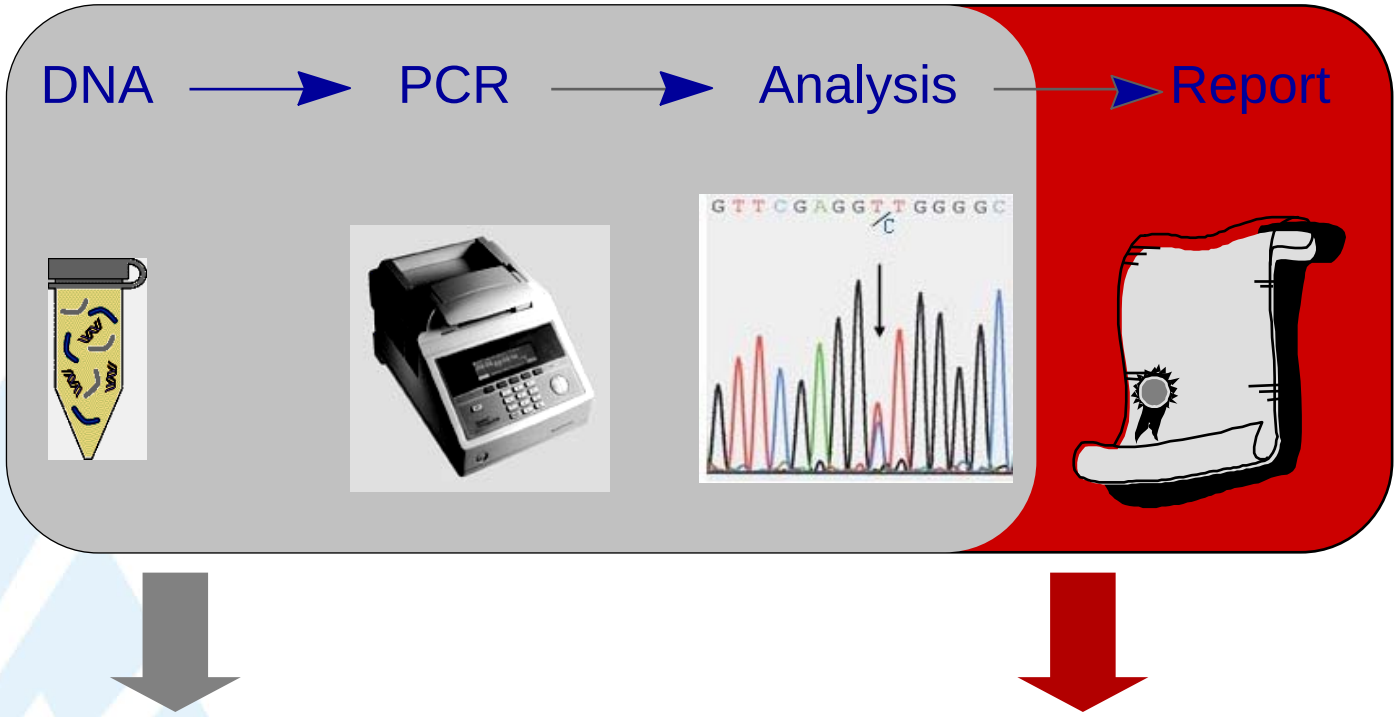
BBC NEWS

Juli 2002

A white mother has given birth to black twins, following a laboratory mix-up.

Assessing Quality PGD laboratory

External Quality Assessment scheme



1/ Evaluation of the practical analysis
accurate **genotyping**

2/ Evaluation of the data **interpretation** (written reports)

→ Clinical significance of the detected mutations

→ Residual risk if appropriate

→ Recommendations for genetic counseling, prenatal diagnosis, …

Assessing Quality PGD laboratory

ORIGINAL PAPER

Evaluation of *CFTR* gene mutation testing methods in 136 diagnostic laboratories: report of a large European external quality assessment

Table 3 Schematic overview of the results of the quality control trial

			Allele A		*Allele B*		*Total sample*	
			Testing labs[a] *n*	*Correct assignment n*	*Testing labs*[a] *n*	*Correct assignment n*	*Both alleles correctly assigned n*	*Not incorrectly assigned*[b] *n*
Sample	*Allele A*	*Allele B*	*(% of total)*	*(% of testing labs)*	*(% of total)*	*(% of testing labs*[a]*)*	*(% of testing labs*[a]*)*	*(% of all labs)*
CF96–1	dF508	N1303K	136 (100)	136 (100)	122 (90)	120 (98)	120 (98)	134 (99)
CF96–2	dI507	wild	119 (87)	101 (85)	136 (100)	131 (96)	96 (81)	113 (83)
CF96–3	dF508	G551D	136 (100)	136 (100)	127 (93)	123 (97)	123 (97)	131 (96)
CF96–4	dF508	621+1 GtoT	136 (100)	135 (99)	62 (46)	54 (87)	53 (85)	129 (95)
CF96–5	R553X	wild	123 (90)	119 (93)	136 (100)	134 (99)	117 (95)	130 (96)
CF96–6	1717–1 GtoA	wild	106 (78)	101 (92)	136 (100)	133 (98)	98 (92)	129 (95)

[a]'Testing labs': the labs that effectively tested for the particular mutation.
[b]'Not incorrectly assigned': the mutation(s) in the sample were correctly detected, or the laboratory did not test for this mutation and assigned it as wild type.

Eur J Hum Gen 1998, 6, 165-175

Assessing Quality PGD laboratory

CF EQA scheme

Participating molecular (genetic) diagnostic laboratories

1996: n=136 2010 : n >220

Participants from 34 different countries (including US, Australia)

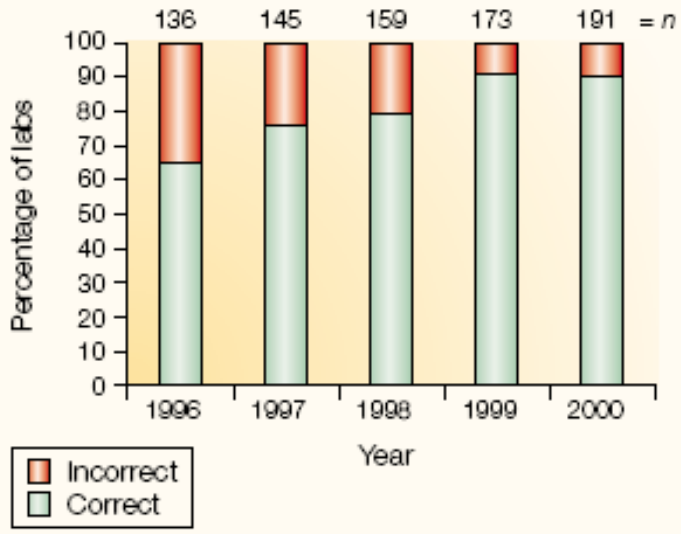


Figure 2 | **Incorrect genotypes in the European EQA scheme for cystic fibrosis.** The graph shows a progressive reduction in the percentage of laboratories making errors (red) during the five years of European external quality assessment (EQA) schemes for cystic fibrosis. Numbers across the top indicate the total number of participating laboratories (*n*).

Dequeker et al. , Nature Reviews Genetics, 2001, 2, 717-723

Assessing Quality PGD laboratory

ARTICLE

Provision and quality assurance of preimplantation genetic diagnosis in Europe

Anniek Corveleyn[1,12], Michael A Morris[2,12], Elisabeth Dequeker[1,12], Karen Sermon[3], James Lawford Davies[4,5], Guillermo Antiñolo[6,7], Andreas Schmutzler[8], Jiri Vanecek[9], Nick Nagels[1], Eleni Zika[10], Francesc Palau[6,11] and Dolores Ibarreta*[,10]

Table 3 Quality management systems

	All	*IVF clinics (n = 44)*	*IVF laboratories (n = 44)*	*Genetics laboratories (n = 53)*
Quality manager	55%	52% (23)	70% (31)	43% (23)
Accreditation	17%	7% (3)	20% (9)	23% (12)
Certification	17%	27% (12)	9% (4)	15% (8)
Accreditation and/or certification[a]	33%	34% (15)	30% (13)	34% (18)

Providers were asked to indicate if they had a designated quality manager, and if accreditation and/or certification had been obtained or was underway (the latter values are combined under accreditation, certification and accreditation and/or certification). The number of answers in each category appears in parentheses.
[a]Some centres replied positively to both accreditation and certification.

European Journal of Human Genetics

Eur J Hum Gen 2008, 16, 290-299

Agenda

- Assessing Quality in a PGD laboratory
- **Quality standards and accreditation**
- Quality Management Systems

Quality Standards and accreditation

ISO 9001
Quality Management systems - Requirements

ISO/IEC 17025
General requirements for the competence of testing and calibration laboratories

ISO/IEC 15189
Medical laboratories – Particular requirements for quality and competence

www.iso.org

Quality Standards and accreditation

International Organization for Standardization - ISO

ISO 15189 international accreditation standard for medical laboratories

1/ Quality management system (QMS)

- Procedures and quality manual
- Document control
- Non-conformities, corrective and preventive actions
- Internal audits and management review

2/ Technical competence

- Continuous training of personnel
- Calibration and maintenance of equipment
- Validation procedures
- Internal and external quality control


INTERNATIONAL STANDARD

ISO 15189

Second edition
2007-04-15

Medical laboratories — Particular requirements for quality and competence

Laboratoires d'analyses de biologie médicale — Exigences particulières concernant la qualité et la compétence

Reference number
ISO 15189:2007(E)

© ISO 2007

www.iso.org

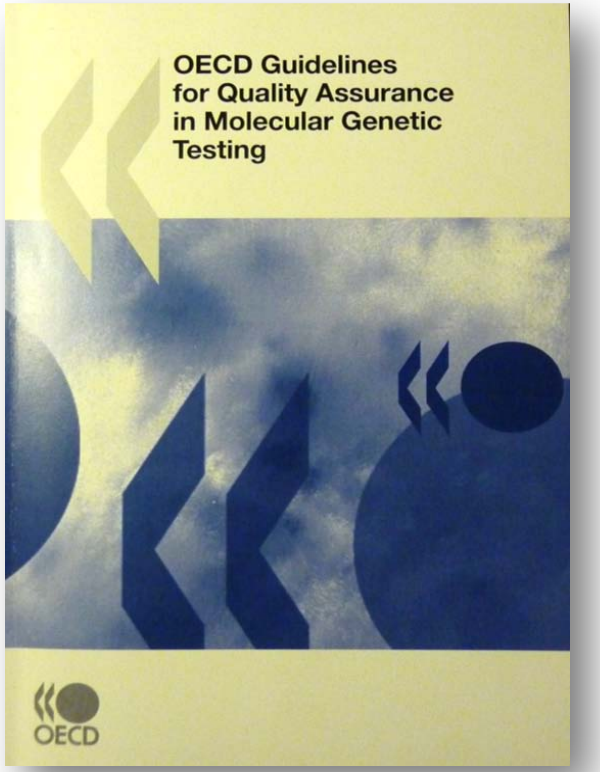
Quality Standards and accreditation

Organisation for Economic Co-operation and Development - OECD

OECD guidelines for quality assurance in molecular genetic testing (MGT), 2007

Directrices de la OECD para la gestión de la calidad de los estudios genéticos moleculares

- Quality assurance and accreditation
- External Quality Assessment (EQA) schemes
- Result reporting
- Training for laboratory personnel



www.oecd.org

Quality Standards and accreditation

ISO 15189

ISO 17025

ISO 9001

Quality Standards and accreditation

certification

accreditation

Quality Standards and accreditation

Certification

Procedure by which **a third party** gives written assurance that a product, process or service **conforms to specific requirements**

ISO 9000, 2000 Quality management systems – fundamentals and vocabulary

Example : Courier company
DHL deliver a package in 5 days
TNT deliver a package in 2 days

Process Management = requirements for quality management system
e.g. ISO 9001

Quality Standards and accreditation

Accreditation

A procedure by which **an authoritive body** gives formal recognition that a body or person is **competent** to carry out specific tasks

ISO 9000, 2000 Quality management systems – fundamentals and vocabulary

Quality Management = requirements for quality management systems + technical & analytical competence requirements

e.g.,ISO 17025 and ISO 15189

Quality Standards and accreditation

Example : Difference between accreditation and certification

Example	Certification	Accreditation
Fragile X syndrome	Simple PCR-based technique to detect normal alleles of the *FMR1* gene. Diagnosis can be excluded in males.	Comprehensive protocol based on PCR and/or Southern blotting to detect and size normal alleles, premutations and full mutations. Diagnosis and carrier status can be confirmed or excluded
Karyotyping	QF-PCR or interphase FISH can identify common aneuploidies.	Comprehensive protocol of karyotyping complemented with QF-PCR, FISH and/or microarray analysis can identify the great majority of numerical and structural anomalies.

E Dequeker (in press 2009) Quality Management Systems and Accreditation In: Kristofferson U, Schmidtke J, Cassiman JJ (ed) Quality Issues in Clinical Genetic Services. Springer Press Heidelberg/New York

Quality Standards and accreditation

Austria

Denmark

Italy

The Netherlands

Belgium

Croatia

Estonia

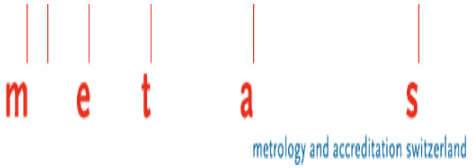
Portugal

U.K.

Czech Republic

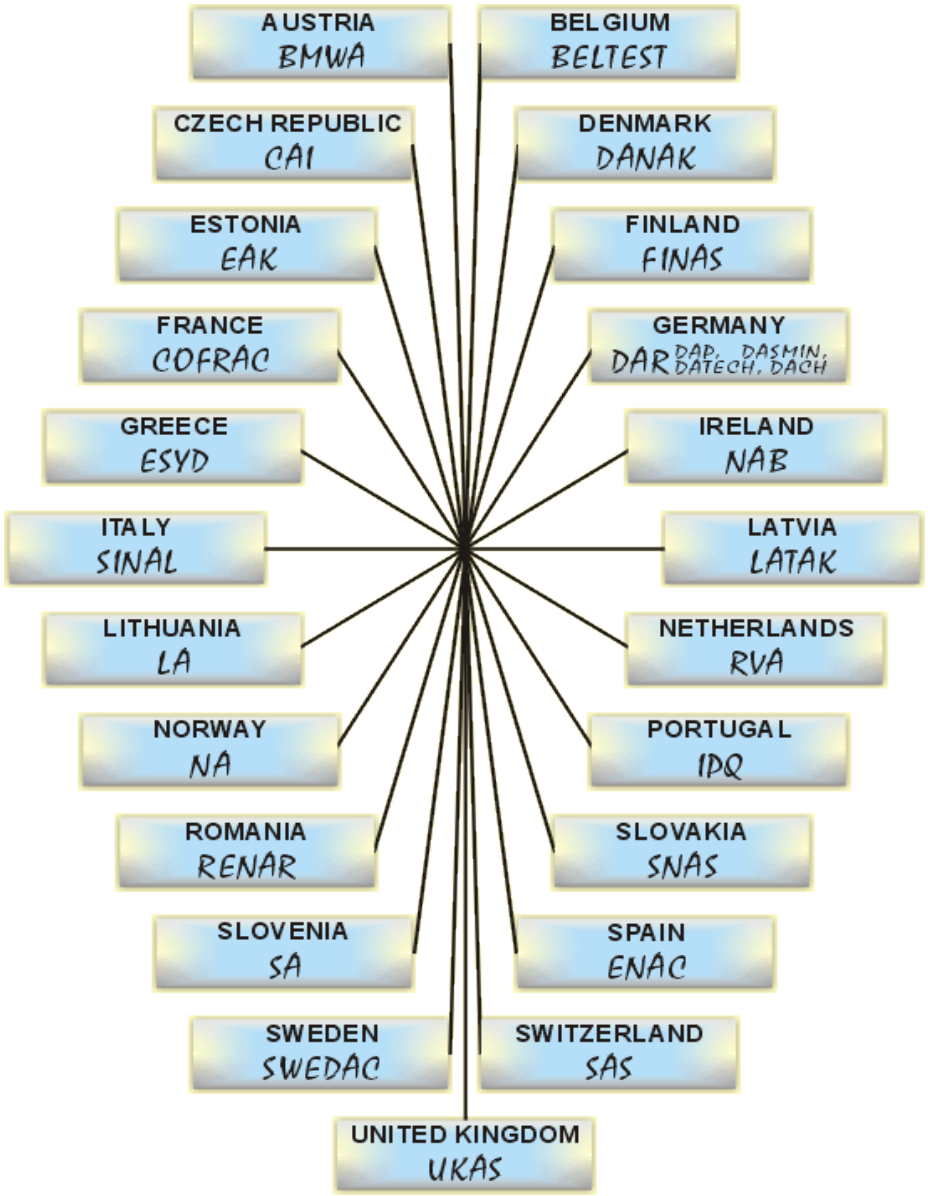
Finland

Spain



Switzerland

Quality Standards and accreditation

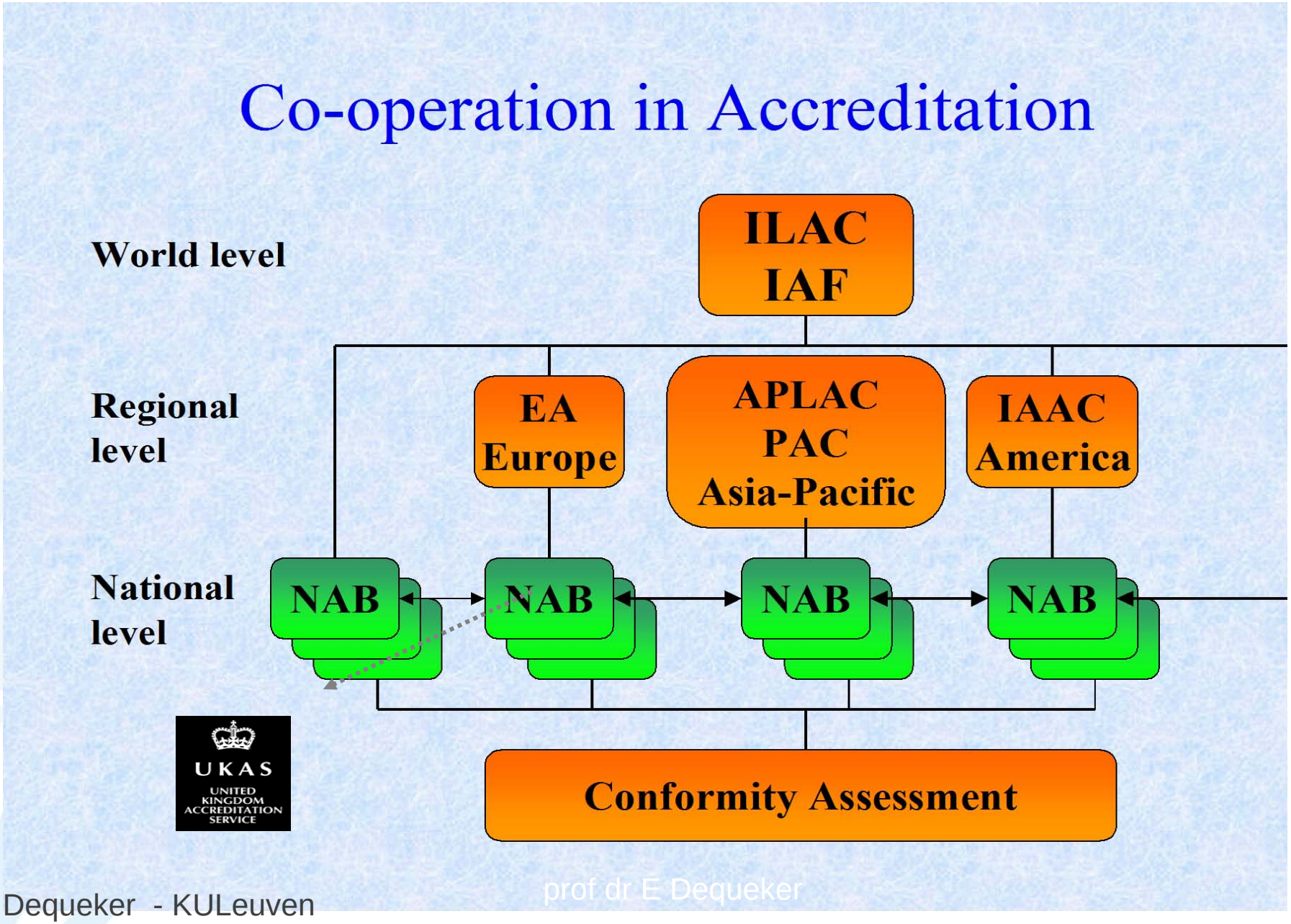
MLA - 

Signatories

European co-operation for Accreditation

www.european-accreditation.org

Quality Standards and accreditation



prof dr E Dequeker

Preimplantation genetic diagnosis

- Genetic testing of embryos, to assist couples with high risk of transmitting a severe genetic disease
- The **result** of the analysis is expected to be **correct, reliable and in time**

Quality Standards and accreditation

Why accreditation?

- **Benefit through better processes and quality of results** (QM process + technical and analytical process)
- Accreditation is a good way to **demonstrate competence**
- Accreditation is a **tool** world-wide to **recognize laboratories**
- In some countries accreditation is mandatory or will be mandatory in the future
- More and more international pressure, attention to quality assurance and accreditation (see OECD guideline for Molecular Genetic Testing laboratories June 2007)

Agenda

- Assessing Quality in a PGD laboratory
- Quality standards and accreditation
- **Quality Management Systems**

Quality Management Systems

- Qualified personnel – continuous education
- Standard operating procedures (SOPs)
- Document control
- Equipment (maintenance and calibrated)
- Non conformities, corrective en preventive actions
- Internal audit
- Quality Manual
- Validation of tests
- Management review

Quality Management Systems

Non-conformities

Corrective actions

Preventive actions

Internal and external audit
Management review

MANAGEMENT ORGANISATION

Suppliers
Contracts
Referral laboratories
Advisory services

EXTERNAL SERVICES

Document control
Quality manual and policy
Standard operating procedures
Log books

Personnel
Training

Batch control
Reagents inventory

RESOURCES

Quality System

DOCUMENTS

Equipment and accommodation
Validation

External quality assessment
Internal quality control
Calibration

CONTINUAL IMPROVEMENT AND QUALITY ASSURANCE

TEST PROCESSES

Request

Patient

Report
Interpretationn

Patient

by S Berwouts

ISO 15189 : 2007

human reproduction REPRODUCTIVE GENETICS *Review*

Accreditation of the PGD laboratory

J.C. Harper[1,2,9], S. SenGupta[1], K. Vesela[3], A. Thornhill[4], E. Dequeker[5,6], E. Coonen[7], and M.A. Morris[6,8]

Table IV Examples of quality indicators for PGD and molecular genetics laboratories.

Technical	Management
Number of new tests deployed	Complaints (and compliments)
Number of patients/PGD cases tested	Complaint response times
Number of tests performed/outsourced	Customer satisfaction survey
Positive result rate	Meetings with IVF unit
TAT/turnaround time (including from patient DNA reception to preparatory work-up being completed)	Analytical non-conformities
External quality assessment results	Outcomes of external audits
Internal quality control (IQC) results/score (intermediate precision)	Documents revised and created
Test failures	Outcomes of internal audits
Number/level of PCR contaminations	Corrective action completion
Diagnosis per embryo/single cell	Unplanned absence (including sick leave)
Confirmation of results in untransferred embryos	Maintenance of staffing levels
Misdiagnosis per untransferred embryo/pregnancy	Maintenance of accreditation

Management requirements

Organization and QMS (ISO 15189: 4.1 and 4.2)

To achieve accreditation, the PGD laboratory needs a quality manual, quality policy, with specific measures to ensure document control, record control, sample control all of which combine to form the

Document control (ISO 15189: 4.3) and quality and technical records (ISO 15189: 4.13)

There is a considerable amount of documentation required to fulfil the standards, which can be paper-based, electronic or both. Some may

Technical requirements

Accommodation and environmental conditions (ISO 15189: 5.2)

As is the case with personnel, the accommodation and environment of the PGD laboratory must be 'adequate' for the tasks and the

Different activities in a PGD lab

Elements of ISO 15189

“Quality Management system”
ISO 15189 accreditation