

EuroGentest

Genetic testing in Europe -
A network for test development,
harmonization, validation and
standardization of services

FP6 2005-2009

www.EuroGentest.org



Jean- Jacques Cassiman
Catholic University of Leuven, Belgium

The most popular genetic tests

- Cystic Fibrosis
- Hemochromatosis
- Fragile X mental retardation
- Factor V leiden
- BRCA 1 & 2



Potential impact of genetic tests on European health budget

30 million potential ? customers

- 500 – 4000 molecular tests/ million citizens/ year
- 4000 – 10.000 cytogenetic tests/ million citizens/ year

200 – 2000 € per test

900.000 – 28.000.000 €/ million citizens/ year



Issues to start from

- More than **1,000 laboratories/centers** in different settings
- More than **1,000 rare diseases** can be tested
- Lack of **centralized and uniform information** about services
- Limited networking
- Lack of harmonized and standardized PT/EQA
- Lack of reference materials
- Limited number of ISO 15189 **accredited labs**
- Limited analytical and clinical validation of tests
- Diverse regulatory environments
- Insufficient **counselling**/lack of harmonized approach

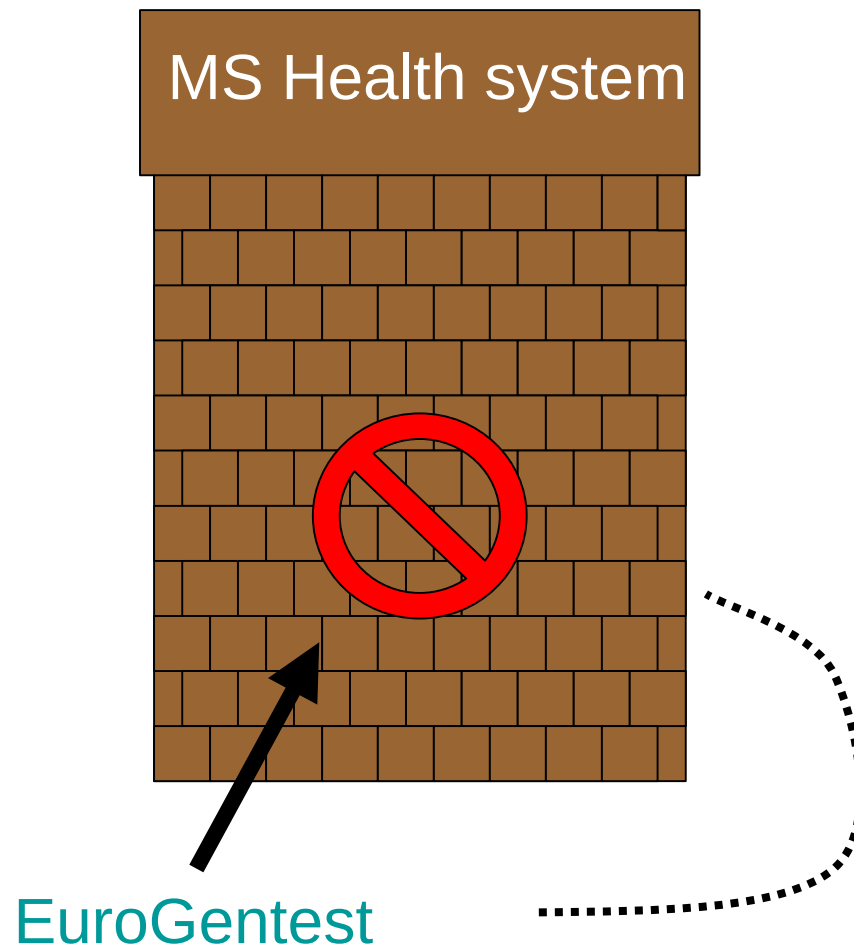
Unacceptable number of laboratory errors!!!!



IPTS report 2003

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Genetic problems are universal!



Major aims of the NoE

- Harmonization and quality improvement of genetic services
- Defining the European dimensions which are compatible with and complementary to National approaches

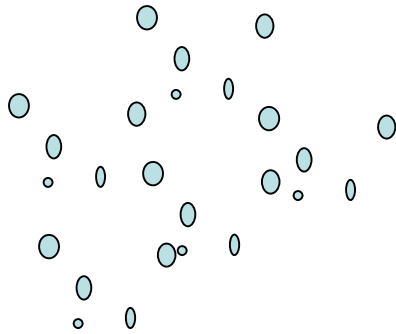
FOUR major domains of activities

- Quality of the laboratories
- Quality of the Clinical aspects of the services
- Translation of Technologies into diagnostic practice
- Educational aspects



Present

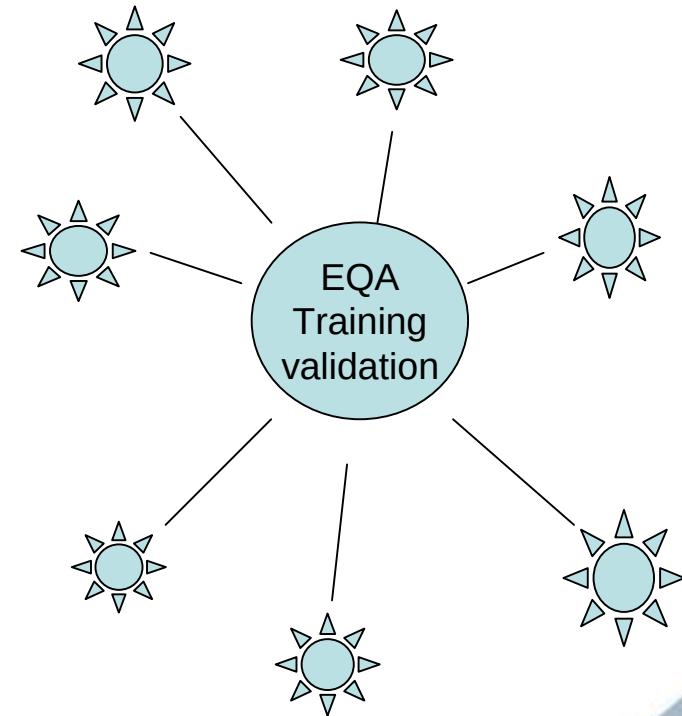
individual facilities



Future

Virtual Institute:

Structured Network of expert
and peripheral centers



Highly variable quality
Individual rules and procedures

Common goals for quality, criteria, training
Centralized information for all
EQA provision
Validation of new technologies



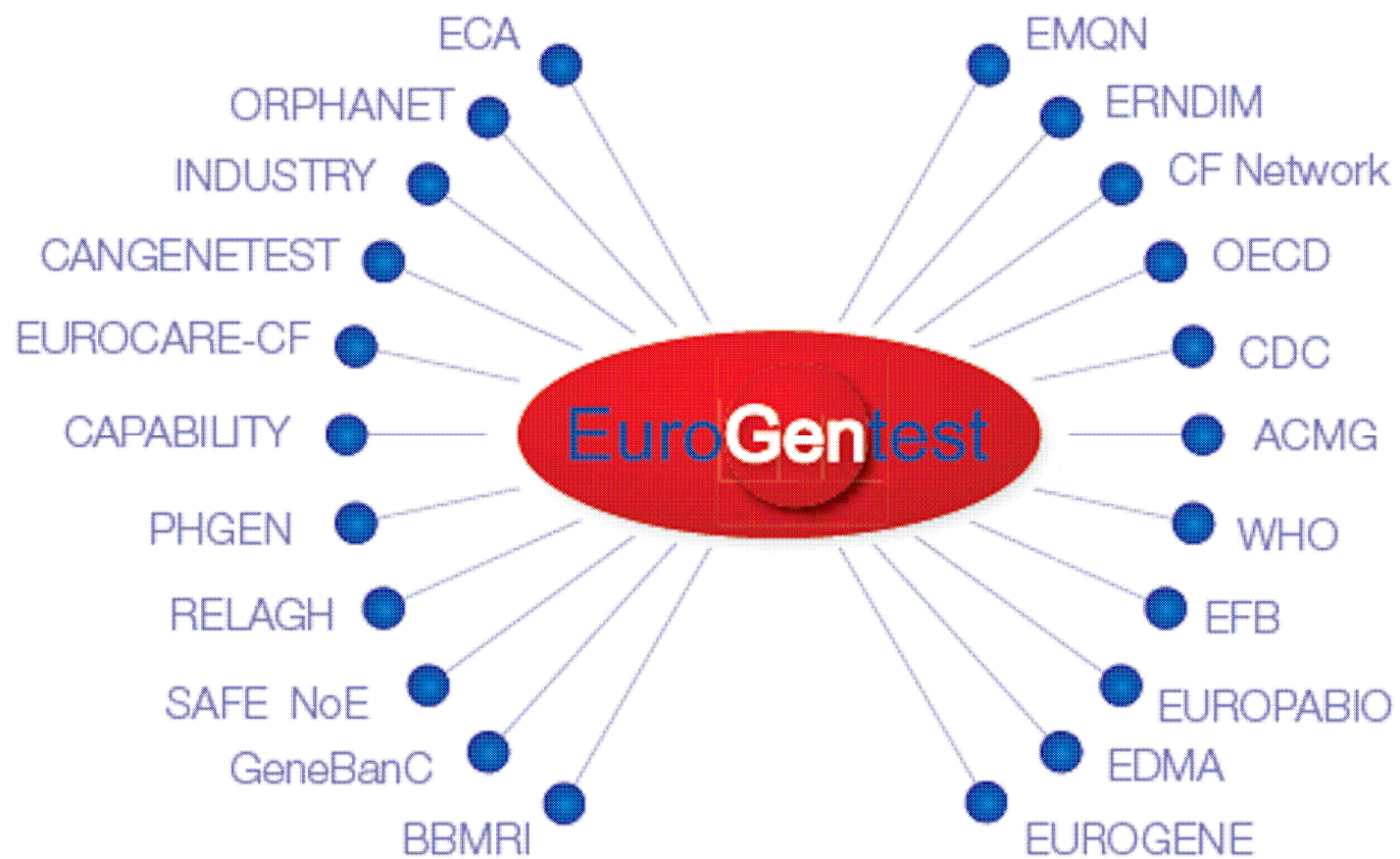
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The ACCE model

- **Analytical validity:** accuracy of test identifying biomarker
- **Clinical validity:** relationship between biomarker and clinical status
- **Clinical utility:** likelihood that test will lead to improved outcome
- **Ethical, legal and societal implications**



Creating a network of networks



Procedure for the development and follow-up of documents, guidelines etc

Survey – expert meeting

Patient organizations – Expert groups

Draft of leaflets, guidelines

Validation by the community

(Translation)

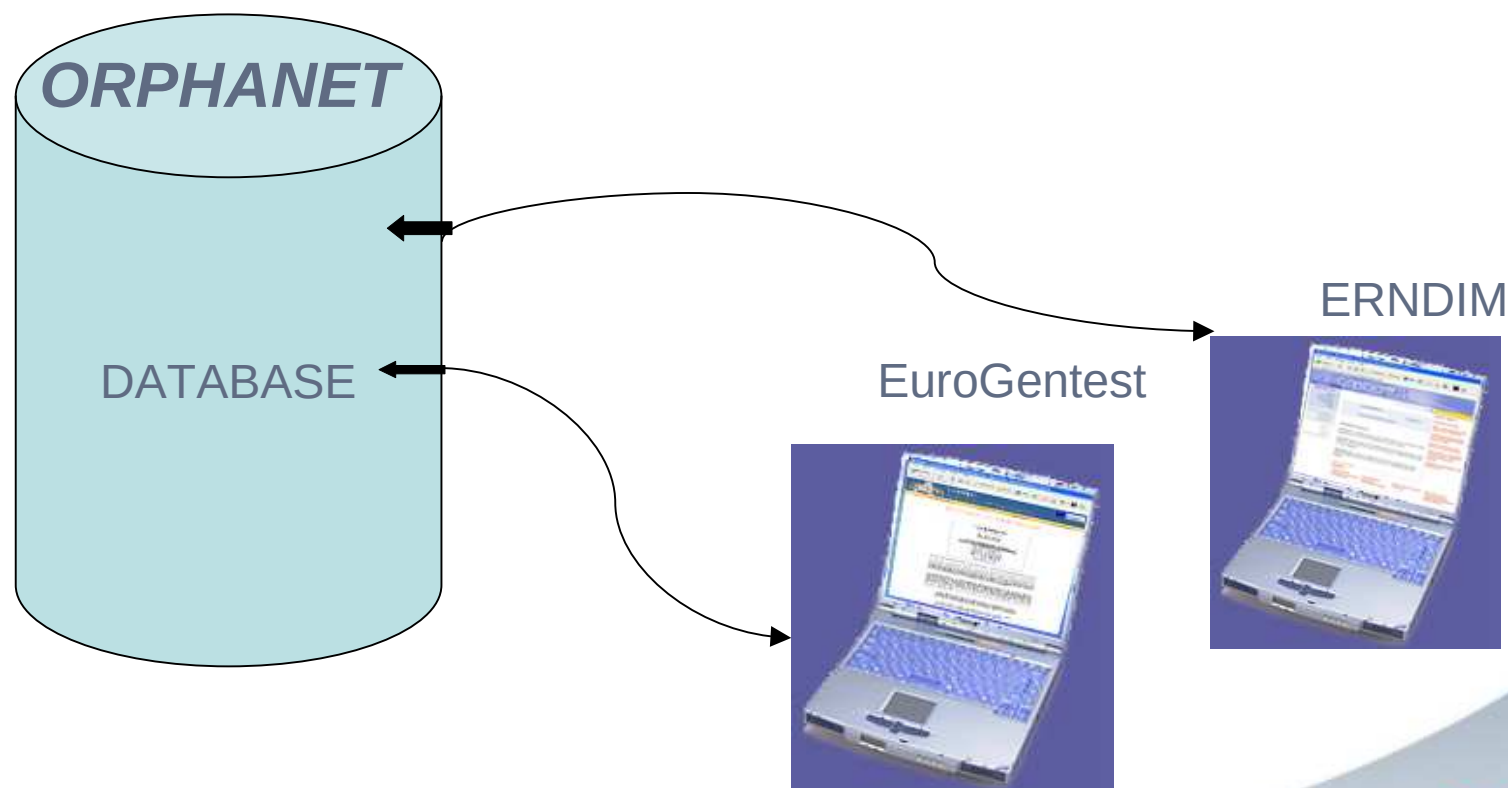
Distribution to Member States
Roadshows



A comprehensive European database of labs and tests

Biochemistry
Cytogenetics
Molecular

- Operated by Orphanet in collaboration with EuroGenTest
- Cross referenced with SwissProt, OMIM and Medline
- Used daily by 25,000 users from 160 countries



Quality Assurance Database (from 2007)

- Access via www.orpha.net and www.eurogentest.org

UNIT 1 : QUALITY MANAGEMENT AND ACCREDITATION / CERTIFICATION OF GENETIC TESTING

SIMPLE SEARCH **SEARCH**

FILTERS

Filter

Country City

Laboratory/Institution Professional

EQA provider Accreditation body

Accredited ☐ Certified ☐ EQA participating ☐

CLINICAL LABORATORIES **SEARCH**

Page: 1 Sort on: Accredited 0 - 14 of 4 Labs - 20 labs/page

A	C	E	Country	City	Laboratory	Institution	Labdirector
■	●	▲	SWITZERLAND				
■	●	▲	SWITZERLAND				
■	●	▲	SWITZERLAND				
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Certification ISO 2001

Accreditation ISO 15189

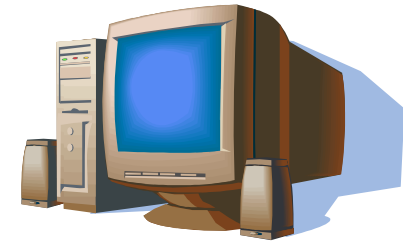
Forms under development



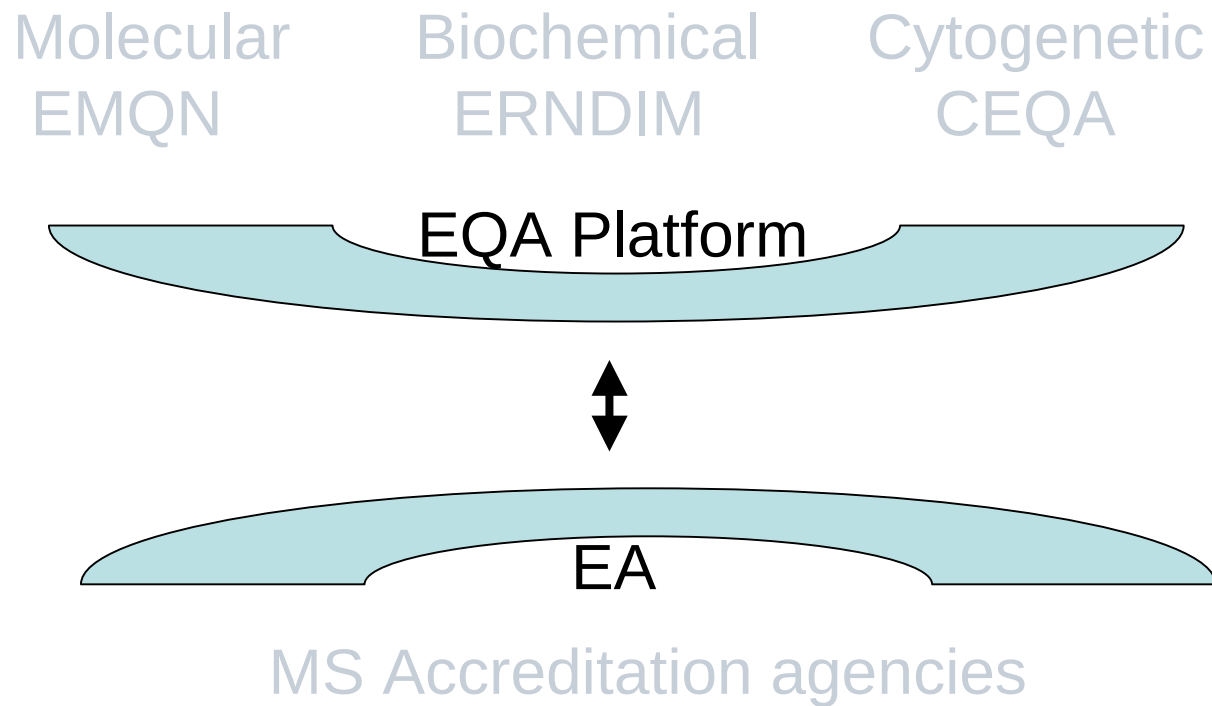
Cytogenetics EQA - CEQA



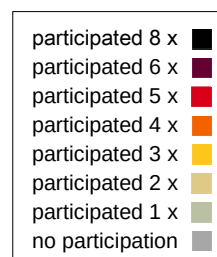
- **On-line EQA – feasibility and viability demonstrated**
 - Feasibility initially tested on UK NEQAS participants
 - Two pilots and then extended to routine EQAs
 - Subsequent improvements to the website
 - Administrative interface improved
 - Library of FISH images/EQA cases being created
- **First pilot European on-line EQA for Cytogenetics, CEQA**
 - 25 countries registered, one postnatal and prenatal EQA case
 - European assessors/experts meeting
 - Summary report prepared - now with assessors for validation
 - EQA templates/registration documents revised for incorporation onto the line management system



Common Platform for European EQAs



Expert workshops and training:



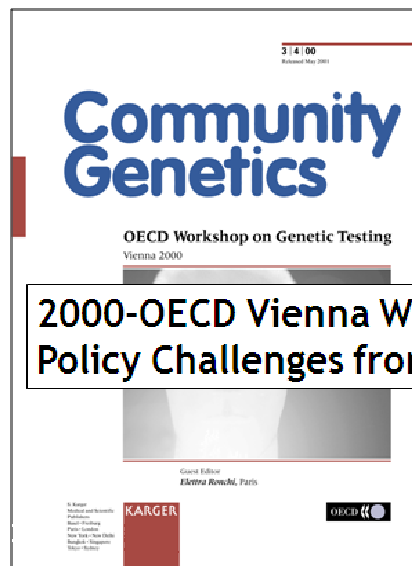
9 workshops organized

- 27 different countries participated
(Europe: 24, North-America: 1, South-America: 1, Australia: 1)
- 86 different institutes participated
- 156 different participants, 29 of them participated more than once

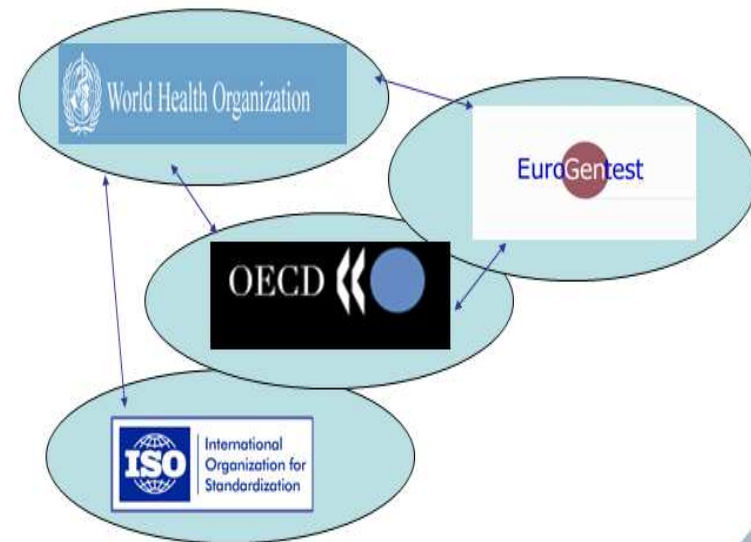
<http://www.eurogentest.org/unit1/workshops.xhtml>



OECD Guidelines for Quality Assurance in Genetic Testing



**2000-OECD Vienna Workshop:
Policy Challenges from the New Genetics**

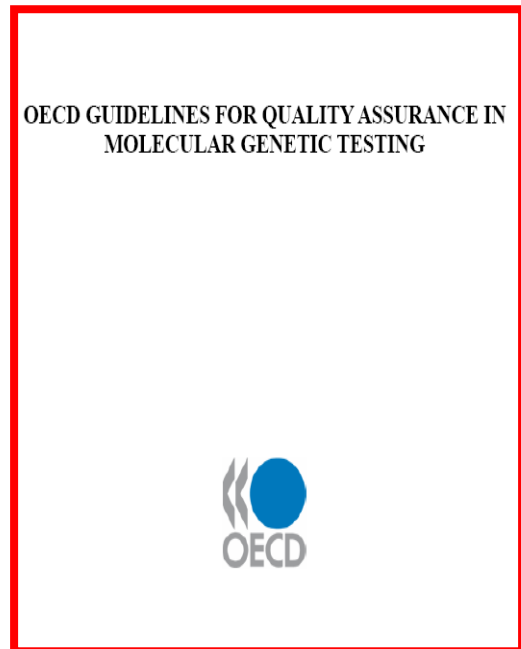


OECD Guidelines

- Guidelines are relevant to OECD and non-OECD countries
- Countries need to implement what they approved.
- Implement the Best Practice in your laboratory
- Spread the quality message!
- EuroGentest is available to help!
 - Workshops
 - Documentation
 - Validation
 - Advice
 - EQA

www.EuroGentest.org

[www. OECD.org/biotechnology](http://www.OECD.org/biotechnology)



Research and emerging technologies

Aim:

- To support and to guide the implementation of new technologies into diagnostic application.
- Set up a rigorous test evaluation program, with Beta testing in accredited laboratories, on selected clinical samples, to ease introduction of new technologies into the European diagnostic laboratories.

DNA extraction methods, MLPA, Conformation Sensitive Capillary Electrophoresis, High Resolution Melting Curve Analysis, Pyrophosphorolysis-Activated Polymerization

Long term goal:

Constitute a Network of Excellent laboratories (NoE) and SME's for Beta testing of new technologies following established procedures.



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UNIT 5 : RESEARCH AND EMERGING TECHNOLOGIES

Nt

SIMPLE SEARCH

ADVANCED SEARCH

 (searches on all fields)

Filter

Abbreviation

Full name

Aliases

+ Legal Issues

PAGE

1

MAX RECORDS

25

RESULTS

19

NEW TECHNOLOGIES

Abbreviation	Full name	Aliases
ARMS	Amplification refractory mutation system	Allele-specific PCR (ASPCR) / PCR amplification of specific alleles (PASA)
ASO	Allele-Specific Oligonucleotide hybridization	Allele Specific Hybridization
CCM	Chemical Cleavage of Mismatch	Chemical Mismatch Cleavage, Amplification Mismatch Detection (AMD), HOT
DGGE	Denaturing Gradient Gel Electrophoresis	Constant denaturant gel-elpho (CDGE), perpendicular denaturing gradient gel-elpho
DHPLC	Denaturing High-Performance Liquid Chromatography	temperature-modulated heteroduplex analysis (TMHA)
FAMA	Fluorescence-assisted mismatch analysis	none
fiber-FISH	fiber-Fluorescence In Situ Hybridization	
FISH	Fluorescence In Situ Hybridisation	
HA	Heteroduplex analysis	Slab gel heteroduplex analysis (HDA)
Invader	Invader	Invasive cleavage
MAPH	Multiplex Amplifiable Probe Hybridisation	
MCA	Melting Curve Analysis	High-resolution melting curve analysis (HRMA), High-resolution DNA melting curve analysis
MLPA	Multiplex Ligation-dependent Probe Amplification	-
PAP	Pyrophosphorolysis-Activated Polymerization	PAP-A, BI-PAP (variant of PAP in which both primers are blocked at their 3' terminus with a ddNTP)
PCR	Polymerase Chain Reaction	Multiplex PCR (variant of PCR; using several primer pairs simultaneously amplify multiple sequences)
PTT	Protein Truncation Test	IVSP - In Vitro Synthesized Protein assay
RNAse Cl	RNAse cleavage	Non-isotopic RNAse cleavage assay (Nirca)

Clinical validity and utility of genetic testing

- Defining **clinical utility** criteria of genetic testing
- Investigating access to and utilisation of genetic services in EU
- Initiating an international collaborative network in order to promote internationally shared quality standards for clinical utility assessment
- Investigating criteria and mechanisms to maximize the output of genetic services, given limited resources
- Validate and translate the **utility guidelines** developed by the GSHG

Genetic Counselling

- Aim to improve the quality of genetic counselling

Specific Support Action to integrate partners from developing countries

“CAPABILITY Project” (2007-2009)



Clinical genetics and community genetics

- Summary of Guidelines for Genetic Counselling
- What counselling in different testing categories?
- Who is qualified to give counselling?
- What aspects of the "ideal genetic counselling" should be included in genetic counselling in real life?



What is genetic testing?

	Context			Type of testing										Phenotypes			Mut	Object							
	Medical applications			Scientific research	No medical applications	Diagnostic testing	Presymptomatic testing	Disease prediction testing	Drug response	Carrier testing	Prenatal testing	PGD	Population screening	Paternity testing	Criminal identification	Mendelian trait	Genetic predispositions	Other polymorphic traits	Sexual markers (w/ parental only)	Chromosomes	Genes/DNA	Specific gene products	Routine blood test	Physiognomy	Family history
EC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	
CoE	+	0	0	+	+	+	0	+	+	+	+	+	0	0	0	+	+	0	0	+	+	+	+	+	+
CDBI	+	+	0	+	+	+	+	+	+	+	+	+	0	0	0	+	+	0	0	+	+	+	0	+	+
IPTS	+	0	0	+	+	+	+	0	+	+	+	+	0	0	0	+	+	0	0	+	+	+	+	+	0
ESHG	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	+	+	+	+	+	+
ASHG	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	+	+	0	0	0
OECD	+	0	0	+	+	+	+	0	+	+	+	+	0	0	0	+	+	0	0	+	+	+	+	+	0
WHO	+	0	0	+	+	+	+	+	+	+	+	0	0	0	0	+	+	0	0	0	+	0	0	0	0
UNESCO	+	+	0	+	+	+	+	+	+	+	+	+	0	0	0	+	+	0	0	+	+	+	0	0	0
CDC	+	0	0	+	+	+	+	0	+	+	+	0	0	0	0	+	+	0	+	+	+	0	0	0	0
NIH	+	0	0	+	+	+	+	+	+	+	+	+	0	0	0	+	+	0	+	+	+	+	0	0	0
HGP	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	+	+	+	0	0	0
Genetic Alliance	+	+	0	+	+	+	0	+	+	+	+	+	0	0	0	+	+	0	0	+	+	+	+	0	0
NI Cancer Inst. (US)	+	0	0	+	+	+	0	0	+	+	+	0	0	0	0	+	+	0	+	0	+	0	0	0	0
NAHU	+	0	0	+	+	+	+	+	+	+	+	+	0	0	0	+	+	0	+	+	+	+	0	0	0
ACGM/ NPGCW	+	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	+	+	+	+	+	+
CAP	+	0	0	+	+	+	0	+	+	+	+	+	0	0	0	+	+	0	0	+	+	0	0	0	0
ACGT	+	+	0	+	+	+	+	+	+	+	+	+	0	0	0	+	+	0	0	+	+	+	0	+	0
Nuffield	+	+	0	+	+	+	+	+	+	+	+	+	0	0	0	+	+	0	0	+	+	+	0	+	+

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Ethical and Legal Issues

- P. Borry, JP. Fryns, P. Schotsmans & K. Dierickx, Attitudes towards **carrier testing in minors**: a systematic **review**, in Genetic Counseling 16 (2005) 4, p. 341-352.
- P. Borry, JP. Fryns, P. Schotsmans & K. Dierickx, **Carrier testing in minors**: a systematic review of guidelines and position papers, in European Journal of Human Genetics 14 (2006) 2, 133-138.
- P. Borry, L. Stultiens, H. Nys, JJ. Cassiman, K. Dierickx, **Presymptomatic and predictive genetic testing in minors**: a systematic review of guidelines and position papers, Clinical Genetics 70 (2006) 5, 374-81.
- P. Borry, J.P. Fryns, K. Dierickx, Predictive Genetic Testing in Children. **A clinical-ethical analysis**, in A. de Bouvet, P. Boitte, G. Aiguié, Questions éthiques en médecine prédictive, Montrouge, John Libbey and Company, 2006.



PATIENT RIGHTS IN THE EU



CZECH REPUBLIC

EUROPEAN ETHICAL - LEGAL PAPERS N° 1

EuroGentest

PATIENT RIGHTS IN THE EU



DENMARK

EUROPEAN ETHICAL - LEGAL PAPERS N° 2

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Education and patient issues

- Updated list of National **Societies** of Genetics and others relevant ones
- List of European and National **genetic courses**
- List of other **educational material** and list of relevant institutions involved in genetics education
- Network of **national contact persons** in the European countries
- 1st Workshop on “Patient and Professional Perspective of Genetic Information/Education in Europe”
- **Core competences** for geneticists and allied health professionals



Developing informative guides

What is a Genetic Test?



Information for Patients and Families

The Amniocentesis Test



Information for Patients and Families

Frequently Asked Questions



Information for Patients and Families



E-News

EuroGentest e-news

EuroGentest Harmonising genetic testing across Europe

Inspiring professionals, reassuring patients and families

What can EuroGentest offer you?

Geneticists
The opportunity to join one of the most working groups

Patients
Advocates providing valuable experience

Industry
A unique network for your new technologies

Legislators
Expert advice on ensuring the quality of your genetic actions

Patients and families
A comprehensive database of European genetic testing laboratories

Genetic testing in Europe

Facts and figures
No of testing centres in Europe - 1000

Number of conditions tested - 1000

Annual growth in testing - 10-30%

Number of people in the EU suffering from genetic diseases - 100 million

Cost to EU health sector - EUR 200 billion

Project coordinator:
Professor Jean-Jacques Cassiman

Home of EuroGentest and EuroGentest Chair
All Europe Genetics at the Center for Human Genetics in Leuven, Belgium

For more information please visit www.eurogentest.org

EuroGentest e-news

EuroGentest Harmonising genetic testing across Europe

Actions speak louder than words

Spreading the quality message
Our aim is to help all categories of genetic laboratories fully meet accreditation, certification and licencing criteria.

Already we have held several Expert Workshops on Laboratory Accreditation, which were well subscribed. This work continues in 2007 with a further two workshops and Round-table sessions at the European Society of Human Genetics on specific, quality related, topics.

Inspiring professionals, reassuring patients and families

EuroGentest is a Network of Excellence funded by the EU to promote the harmonisation and improvement of genetic testing standards. Now