"Why is quality important”

Prof Dr Els Dequeker
EQA scheme coordinator since 1996
Quality Manager at the University of Leuven

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Quality of care and medical laboratory testing

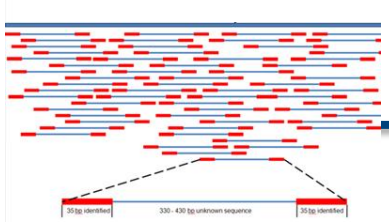
Expectations :

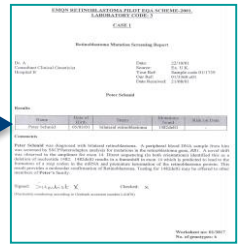
As physician / patient / family we expect

- a correct test results, in an appropriate time
- and a correct interpretation for further decisions

Quality of care and medical laboratory testing

Quality *: "the degree to which a set of inherent characteristics fulfils requirements". (ISO definition)*





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Tools to assure quality of care and laboratory testing

Quality Management System

External Quality Assessment

- Requirements in some European countries
- Hospital and laboratory accreditation
- More and more evidence that obtaining/ holding an accreditation is a step forward

ISO 15189 - a test .... for the *purpose of providing information for the diagnosis, management, prevention and treatment of disease in, or assement of the health of human beings*, ...

- Pre-examination
- Examination
- Post-examination

Quality management system


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

Quality Standards and accreditation / certificaton

- ISO 15189
- ISO 17025
- ISO 17020
- ISO 9001
- (CPA, CCKL)
- ...

L 218/30 EN Official Journal of the European Union 13.8.2008

REGULATION (EC) No 765/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 9 July 2008

setting out the requirements for accreditation and market surveillance relating to the marketing of products and repealing Regulation (EEC) No 339/93

one recognized accreditation body in **each country** that assesses laboratories against an international agreed standard

CCKL part of RvA since 2008

AB accredited according EN ISO/IEC 17011

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Who is working in a diagnostic laboratory?

Is your laboratory accredited for ISO 15189 ?

yes

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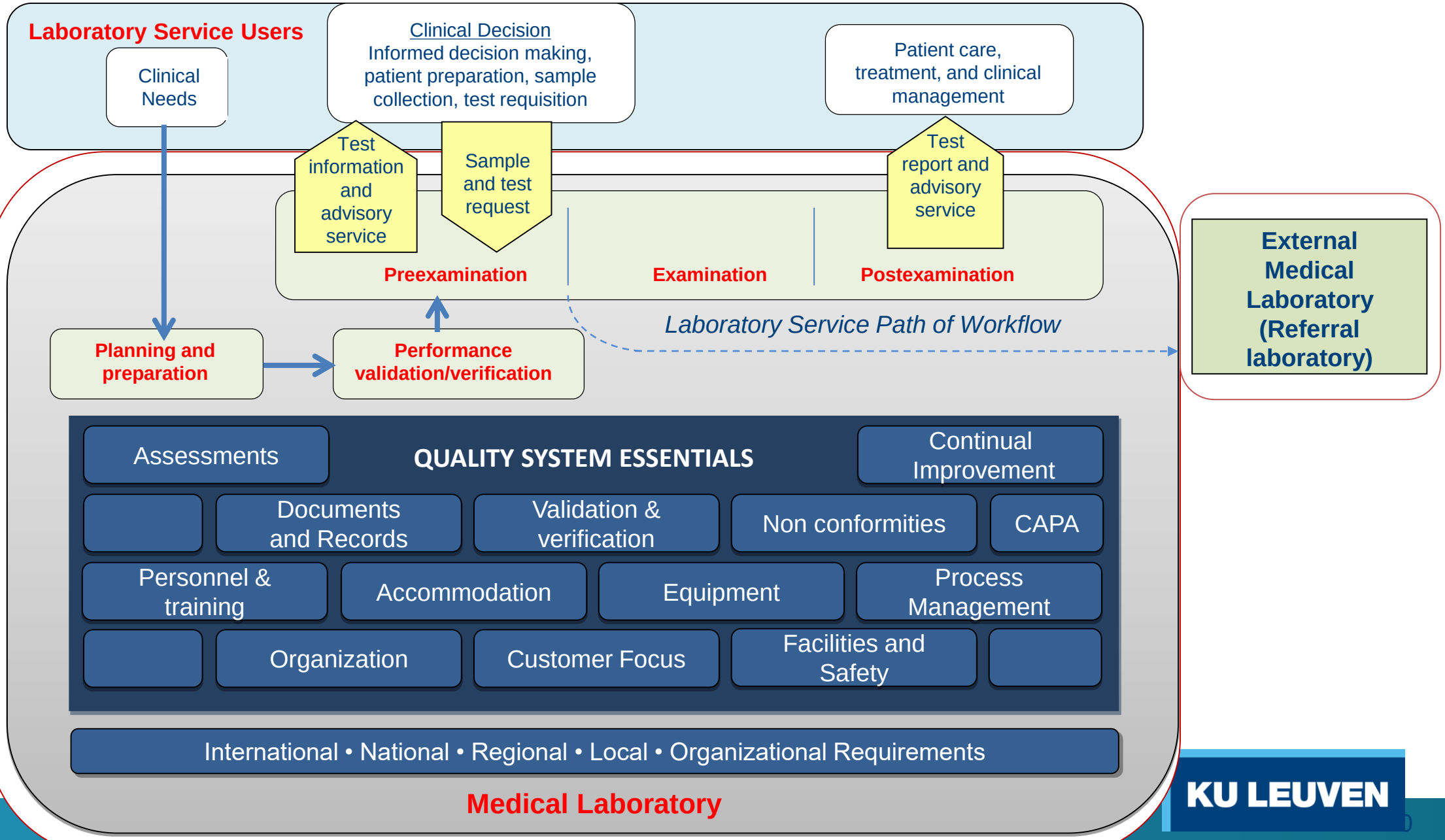
Your laboratory is accrediteted – Great !

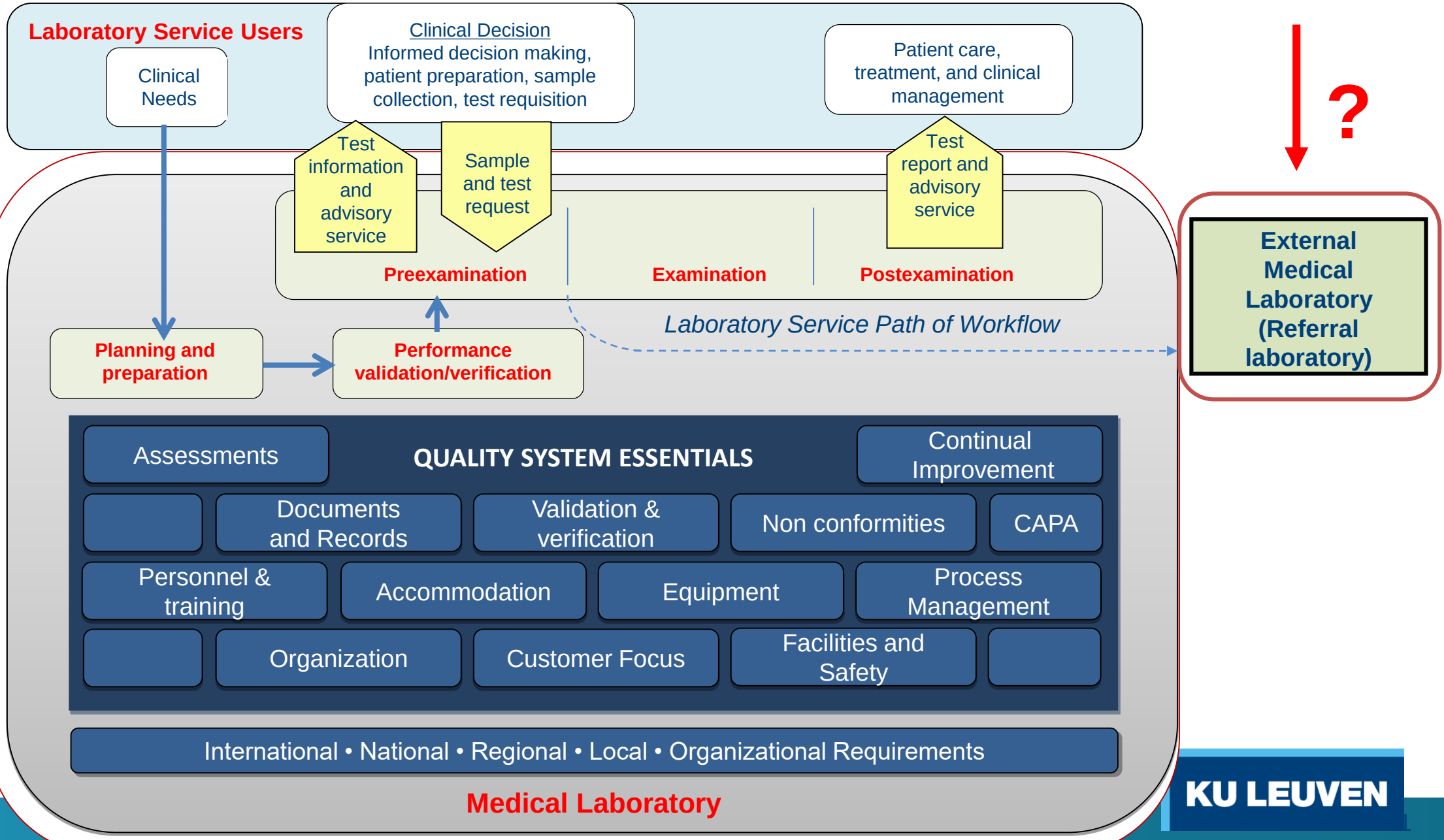
Is ct DNA analysis included in the scope of accreditation?

yes

Laboratory Path of Workflow



Laboratory Path of Workflow



Definition of a referral laboratory

(ISO 15189: 2012 3.23) : external laboratory to which a sample is submitted for examination

Is your laboratory using a referral laboratroy for a part of the examination process for a test using liquid biopsy in lung or colon cancer?

yes

Elements of a quality management system

- Qualified personnel – continuous education
- Standard operating procedures (SOPs)
- Document control
- Equipment and accommodation
- Validation of tests / equipment
- Non conformities, corrective and preventive actions
- Internal audit, Management review
- Quality improvement projects
- Participation to external quality assessment schemes

Key message:
→ tracebility & demonstrate competence

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Qualified personnel – continuous education

- Who is qualified to do what ?
  - Functional organogram + qualification declarations
- Replacements of key functions
- Education files
- Traceability of actions

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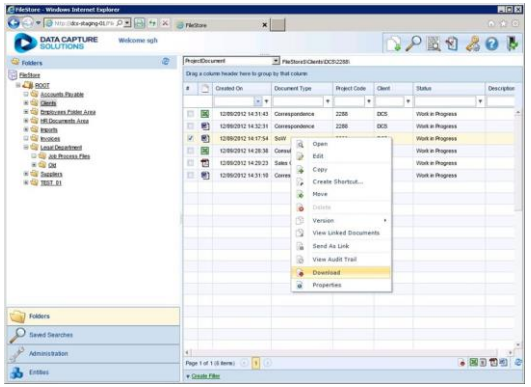
SOP’s – documentcontrol – registrations

- Which procedure is now applied? And 3 months or 1 year ago?
- Was this equipment well maintained between that period?
- Approval of procedures?
- Publication of procedures?



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Accommodation and environmental conditions

- Laboratory design suitable for the tasks carried out
  - Description of laboratory facilities
  - Preventive measures to take
  - Access control

Equipment

- Unique identification of each item of equipment
- Equipment instructions , specifications, certificates
- Validation documents
- logbooks: maintenance, problems, defects, breakdowns…
- Selection procedure with criteria for purchase
- Controlled release–initially after installation, after intervention

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Validation of tests / equipment

- Demonstrate that the test / process delivers accurate reliable results and correct interpretation of the data
- Drafting validation plan and report
- Reliable operation of a device

Validation of tests (including equipment)

VALIDATION	VERIFICATION
All new laboratory procedures before application to clinical testing	Only for procedures with specified characteristics: • IVD with CE mark or FDA approval • validated procedures implanted from an accredited expert laboratory • tests with precisely-specified requirements employing only validated techniques • sequencing of a specific target

1. Test development and assessment of utility (technical and diagnostic)
2. Define performance specifications (accuracy, limitations, control)
3. Comparison with performance specifications (EQA, IQC, audit)

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Non conformities, corrective and preventive actions

- Policies / procedures in place to identify and resolve any aspect of examinations not conforming to defined standards
- Analyse and eliminate root causes of a possible recurring problem
- Procedures in place for the release of results in the case of a nonconformity

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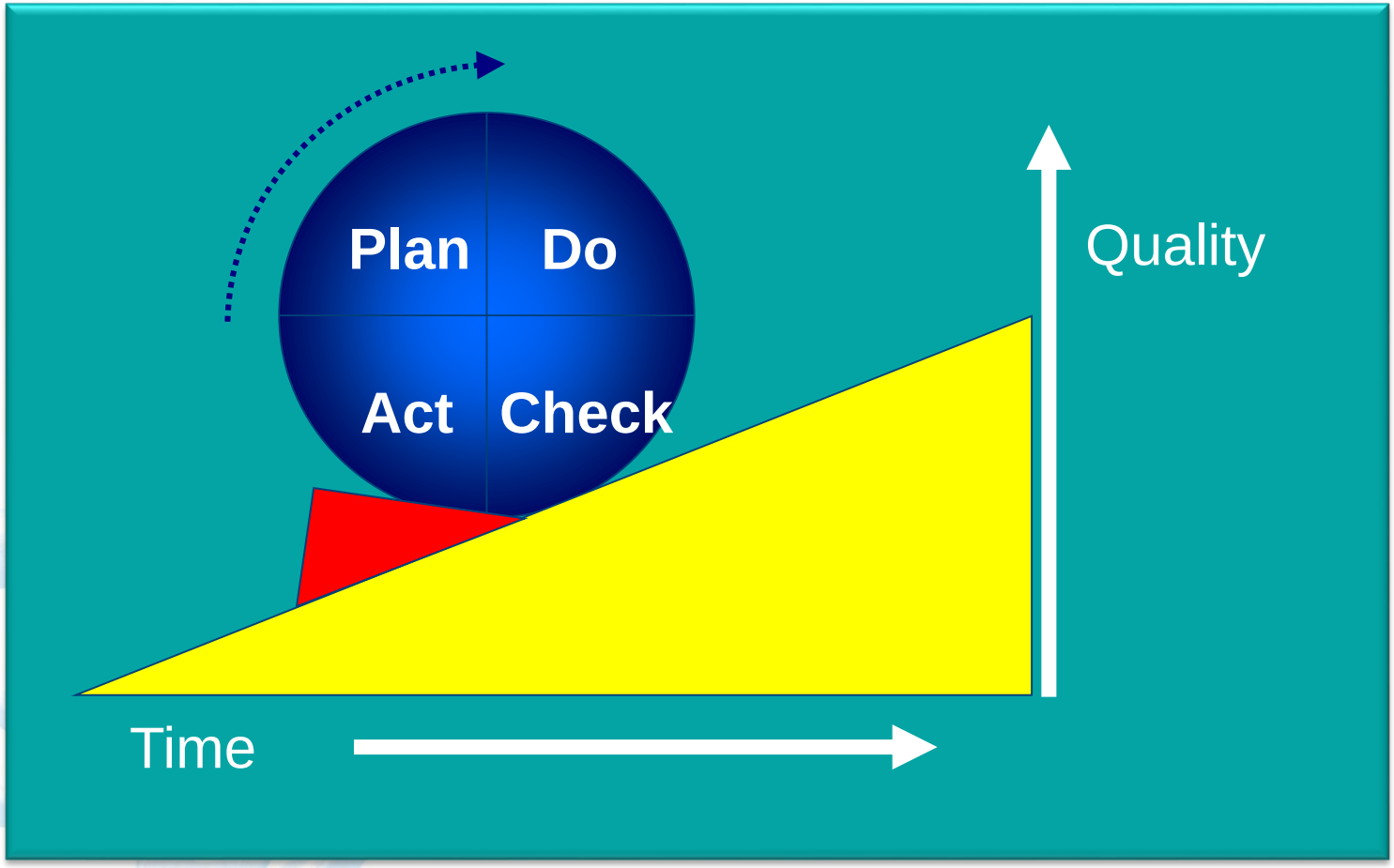
Quality improvement !



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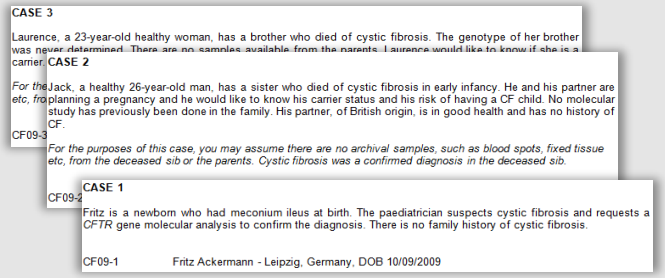
External quality assessment – EQA

EQA provider


CASE 3

Laurence, a 23-year-old healthy woman, has a brother who died of cystic fibrosis. The genotype of her brother was never determined. There are no samples available from the parents. Laurence would like to know if she is a carrier.

CASE 2

For the purposes of this case, you may assume there are no archival samples, such as blood spots, fixed tissue etc, from the deceased sib or the parents. Cystic fibrosis was a confirmed diagnosis in the deceased sib.

Jack, a healthy 26-year-old man, has a sister who died of cystic fibrosis in early infancy. He and his partner are planning a pregnancy and he would like to know his carrier status and his risk of having a CF child. No molecular study has previously been done in the family. His partner, of British origin, is in good health and has no history of CF.

CASE 1

Fritz is a newborn who had meconium ileus at birth. The paediatrician suspects cystic fibrosis and requests a *CFTR* gene molecular analysis to confirm the diagnosis. There is no family history of cystic fibrosis.

CF09-1 Fritz Ackermann - Leipzig, Germany, DOB 10/09/2009

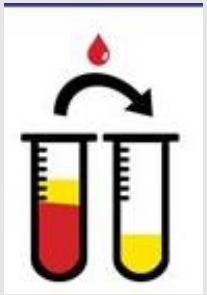
Request forms (clinical cases) + samples

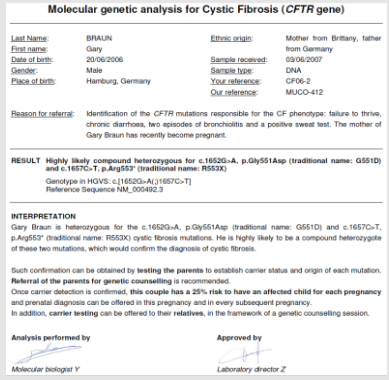
Evaluation reports

General report and individual comments

Laboratory

Test




Molecular genetic analysis for Cystic Fibrosis (*CFTR* gene)

Last Name:	BRAUN	Ethnic origin:	Mother from Brittany, father from Germany
First name:	Gary		
Date of birth:	20/06/2006	Sample received:	03/06/2007
Gender:	Male	Sample type:	DNA
Place of birth:	Hamburg, Germany	Your reference:	CF06-2
		Our reference:	MUCO-412

Reason for referral: Identification of the *CFTR* mutations responsible for the CF phenotype: failure to thrive, chronic diarrhoea, two episodes of bronchiolitis and a positive sweat test. The mother of Gary Braun has recently become pregnant.

RESULT **Highly likely compound heterozygous for c.1652G>A, p.Gly551Asp (traditional name: G551D) and c.1657C>T, p.Arg553* (traditional name: R553X)**

Genotype in HGVS: c.[1652G>A];[1657C>T]
Reference Sequence NM_000492.3

INTERPRETATION

Gary Braun is heterozygous for the c.1652G>A, p.Gly551Asp (traditional name: G551D) and c.1657C>T, p.Arg553* (traditional name: R553X) cystic fibrosis mutations. He is highly likely to be a compound heterozygote of these two mutations, which would confirm the diagnosis of cystic fibrosis.

Such confirmation can be obtained by **testing the parents** to establish carrier status and origin of each mutation.
Referral of the parents for genetic counselling is recommended.
Once carrier detection is confirmed, **this couple has a 25% risk to have an affected child for each pregnancy** and prenatal diagnosis can be offered in this pregnancy and in every subsequent pregnancy.
In addition, **carrier testing** can be offered to their **relatives**, in the framework of a genetic counselling session.

Analysis performed by *Molecular biologist Y*

Approved by *Laboratory director Z*

Report (test result, interpretation)

Discussion of the results, corrective actions

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EQA scheme for ctDNA analysis

Two survey's

2015 - ESP EQA provider survey

- ***65/90 (72%) acknowledges*** the need to develop an international EQA scheme for ctDNA analysis
- discussed during the ***ESP / IQNPath meeting*** April 2015 (Naples)
- ***Decide to start with a group of voluntary people & EQA providers*** the challenge to set up an ct DNA EQA scheme

2016 - IQNPath survey prior to ctDNA pilot EQA scheme

Deans ZC *et al*.
Review of the implementation of plasma ctDNA testing: A perspective from an EQA providers survey (2017).
Submitted at Virchows Archiv.

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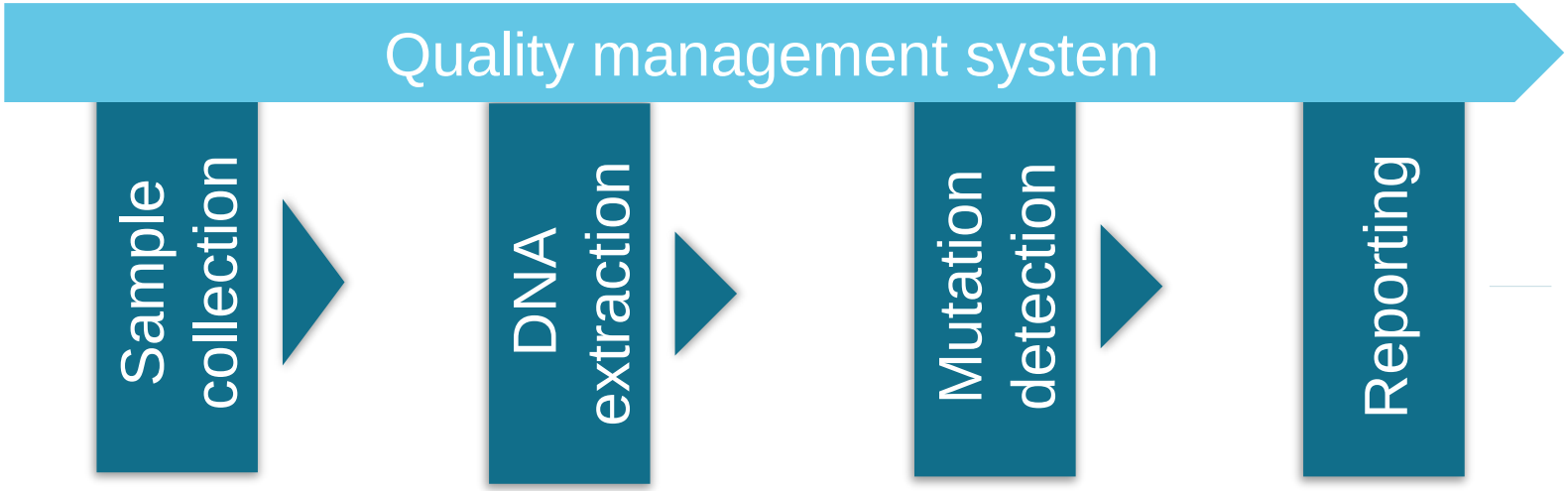
Why is quality important ?

Medical laboratories **need to participate in interlaboratory comparison** programme's (such as an external quality assessment programme or proficiency testing programme) appropriate to the examination and interpretations of examination results (ISO 15189 2012 5.6)

NOTE The laboratory should participate in interlaboratory comparison programmes that substantially fulfil the relevant requirements of ISO/IEC 17043.

Diagnostic process for ctDNA analysis



-Blood collection (amount, tubes)
-Storage conditions (period, temperature)
-Transportation

-Sample preparation
-Method
-Equipment
-DNA quantification

- Sensitivity of mutation detection method, LOD
- Content of the report

Critical steps ? Control elements in the process ? Tracebility ?

Why is quality important ?

Medical laboratories are a **key figure** today that

the right treatment for the right person

at the right time is given

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