

EQA and its „Abilities“

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ApplicAbility

AvailAbility

SuitAbility

CommunitAbility

StAbility

AcceptAbility

TracAbility

CapAbility

VariAbility

ReliAbility

ComparAbility

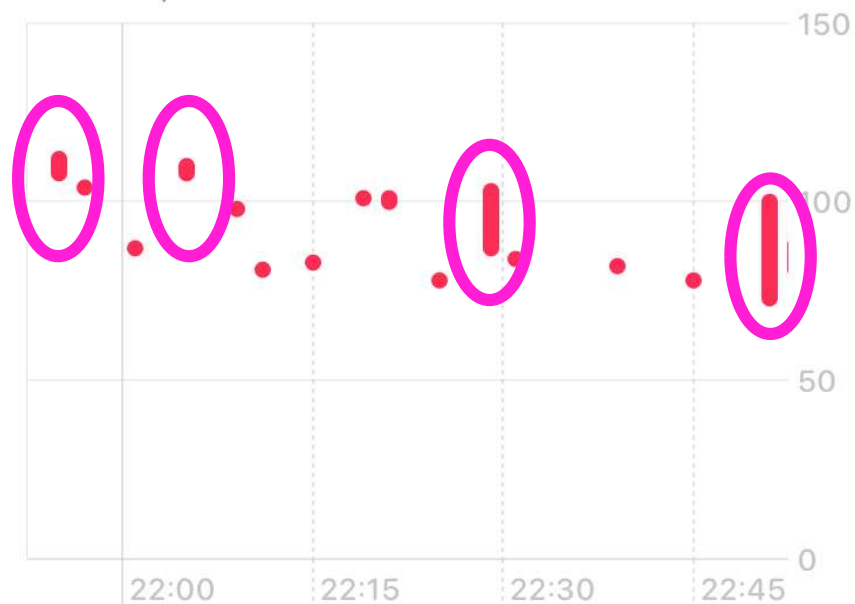


EQALM Symposium, Vienna, Austria, October 16-18, 2024

Vienna, October 16, 2024

73–112 BPM

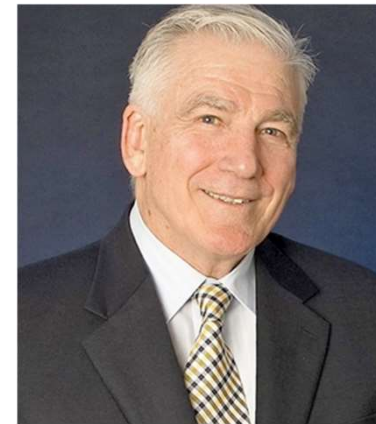
Gestern, 21:52–22:52 Uhr



Reliability of Results



The **reliability** of clinical laboratory results is dependent on precision and trueness where trueness is of particular importance for the **comparability** of results between laboratories and clinical centers necessary for the use of internationally agreed clinical protocols and common reference intervals and decision limits.



Howard Morris

Clinical Biochemistry 42 (2009) 241–245

Decisions based on laboratory diagnostics

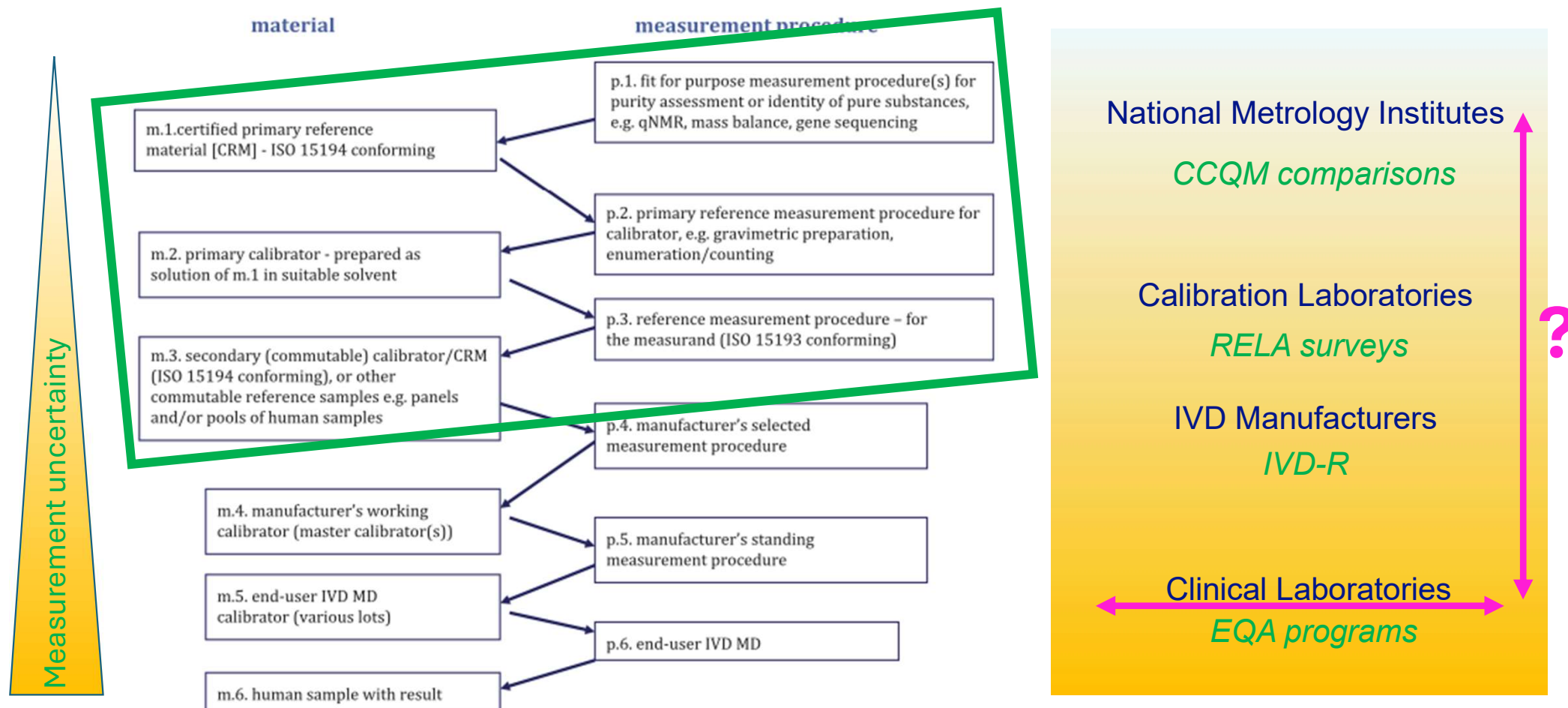
Results of medical laboratories are important for:

- Diagnosis
- Risk assessment
- Choice of treatment
- Success control

It is the responsibility of the laboratory to provide **accurate results** considering **precision and trueness**.

EQA is a powerful educational tool to **monitor quality independently** and to identify poor performing laboratories and test systems.

Traceability of Results



Objectives of JCTLM



<http://www.jctlm.org>

The JCTLM was created as a worldwide platform in 2002 through a Declaration of Cooperation between the BIPM, IFCC and ILAC.

- to **promote** and give guidance on internationally recognized and accepted equivalence of measurements in Laboratory Medicine and **traceability** to appropriate measurement standards
- to set up the **JCTLM Database** listing available higher-order reference materials, measurement methods/procedures and services to be used in calibration hierarchies for value assigning **calibrators and trueness control materials** for quantities measured by **in vitro diagnostic medical devices**.

JCTLM Database

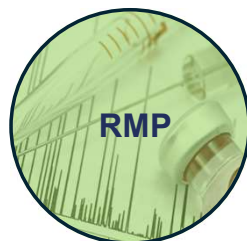


The JCTLM Database consists of:



290 Materials **238** Methods **285** Services

<http://www.jctlm.org>



Each entry has undergone **independent review** and found to be compliant with the criteria in documentary standards developed by ISO TC 212 WG2 (Reference Measurement Systems), with **reference measurements services listed for accredited calibration laboratories**.

creatinine

SEARCH

RESET

Refine results

TYPE

- ☐ Reference material (20)
- ☐ Reference method (8)
- ☐ Reference service (12)

SELECT ALL OPTIONS

ANALYTE CATEGORY

ANALYTE NAME

MATRIX CATEGORY

COUNTRY

MEASUREMENT PRINCIPLE / TECHNIQUE

40 Results

EXPORT



PDF

EXPORT



XLS

DETAILED VIEW

→ Select all results

✓ creatinine in creatinine crystalline material

National Metrology Institute of Japan →(NMIJ) - Japan
NMIJ CRM 6005-a, Creatinine

✓ creatinine in Blood serum, Blood plasma, Calibration solution

Reference Institute for Bioanalysis, Calibration Laboratory I →(SPMD-RfB) - Germany

✓ creatinine in Urine, Calibration solution

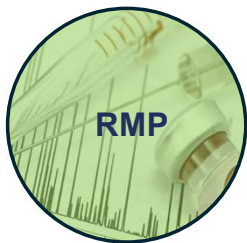
Reference Institute for Bioanalysis, Calibration Laboratory I →(SPMD-RfB) - Germany

✓ creatinine in Blood serum, Calibration solution

Laboratoire National de Métrologie et d'Essais →(LNE) - France

✓ creatinine in Blood serum, Blood plasma

Each pillar is of importance



Reference Measurement Procedures

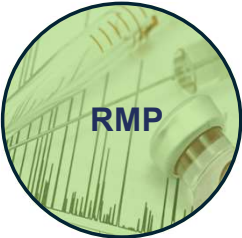


Certified Reference Materials



Calibration Services

Each pillar is of importance



Reference Measurement Procedures

- High specificity, low measurement uncertainty
- First be aware of the measurand, then develop



Certified Reference Materials

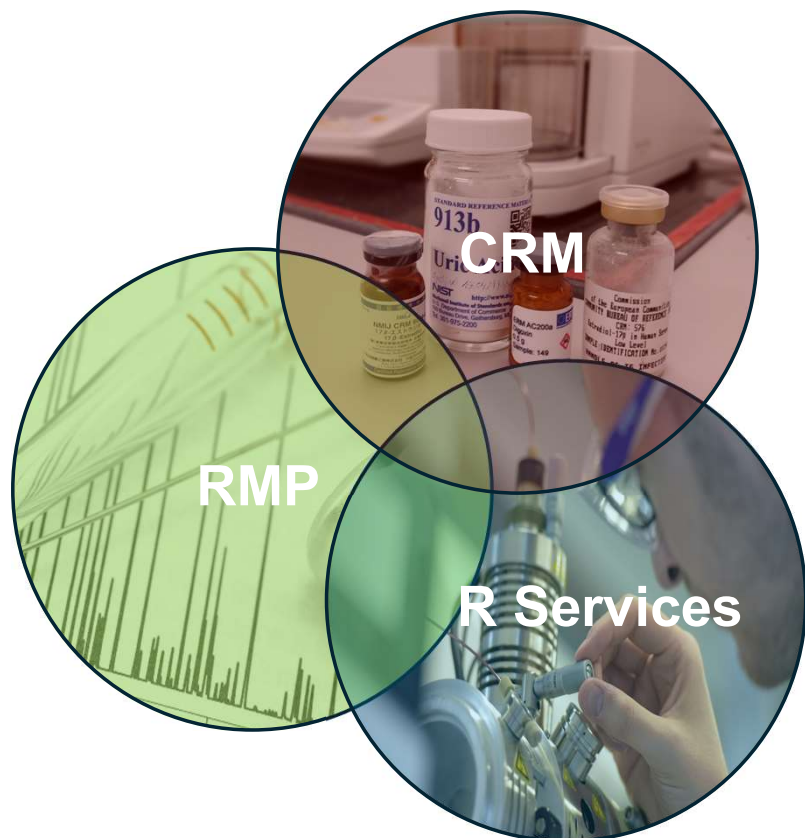
- Top of the hierarchy – we should treat them that way
- New strategies in production can fix bottlenecks



Calibration Services

- Developement and validation is time-consuming and expensive
- To achieve satisfactory results you need well trained professionals with routine praxis

Triad of Reference Systems



Reference systems are the fundament for establishing traceability for a certain measurand.

In the interlaboratory comparison “RELA”, the results of a laboratory display the combination of a reference material, a reference method and a reference service.

The tasks for the future are

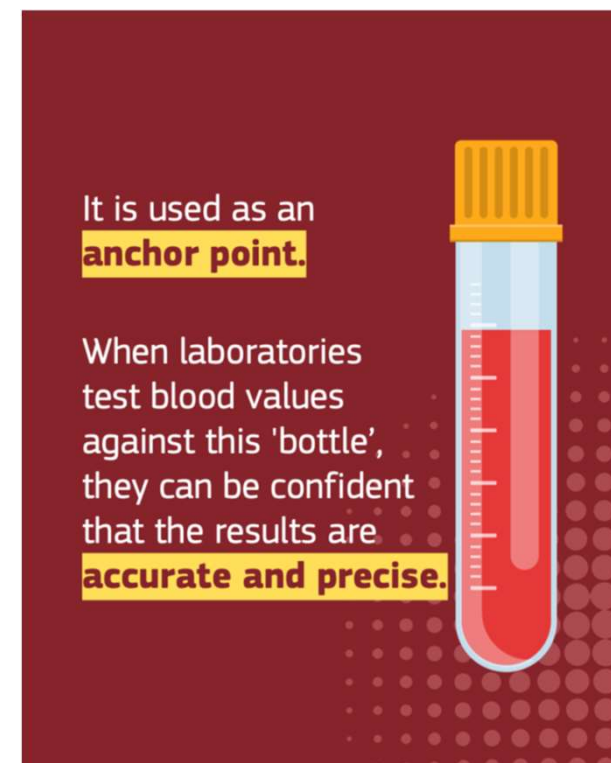
- to **extend** the number of CRM, RMP, and RMS for further measurands,
- to **preserve** current entries of the JCTLM DB.

RMP: The listed methods are published and available.

RMS: the number of potential laboratories providing services is continuously growing.

CRM: The stock of reference materials is limited.

Importance of CRM



All efforts shall be sustainable



- IVDR requests traceability, life cycle management and continuous evaluation of the products



- JCTLM database summarizes and visualizes the pillars and is updated regularly



- Resources, especially CRMs, should be handled with care



- Valuable work of scientific groups of national and international societies is a starting point for standardization, the outcome has to be strategically continued in follow-up projects.



→ The aim is not a proof of concept, but actually establish reference systems to provide traceability permanently and successfully

Sustainability of CRM



Substance	RM	Listed in JCTLM database?	Actually available?	Comments
Cholesterol	NIST 911c		Yes	Expires 2024. Will there be a new lot?
	CRM 6001-a	Yes	Yes	Long delivery time, short shelf life (1 year)
	LNE CRM Bio 101a		Unclear	Waiting for answer to purchase request
Creatinine	NIST 914b	Not anymore	Yes	Why is it not listed anymore?
	CRM 6005-a	Yes	Yes	Long delivery time, short shelf life (1 year), not yet tested,
	LNE CRM Bio 101a	Yes	Unclear	Waiting for answer to purchase request
Trioleine (total glycerides)				Long delivery time, short shelf life (1 year). Ordered from Wako, but listed as "unavailable" on NMIIJ website, oil(!) --
	CRM 6009-a	Yes	Unclear	> Why is tripalmitin (solid) not used anymore?
	DRE-C14036700	No	Yes	Complies with 17034
	LNE CRM Bio 101a	Yes	Unclear	Waiting for answer to purchase request
Uric acid	NIST 913b	Not anymore	Yes	Expires 2024. Will there be a new lot?
	CRM 6008-a	Yes	Yes	Long delivery time, short shelf life (1 year), not yet tested
	SRM 1950	No	Yes	Substitute for NIST 909c
	HRM-3007A	Yes	Unclear	
Urea	NIST 912	Not anymore	Yes	Why is it not listed anymore?
	CRM 6006-a	Yes	Yes	Long delivery time, short shelf life (1 year), not yet tested
	NIST 909c	Not anymore	Yes	Expires 2025. Will there be a new lot?
	HRM-3007A	Yes	Unclear	
17-β-Estradiol	NMIJ CRM 6004-a	Yes	Yes	Long delivery time, short shelf life (1 year)
	DRE-C13213100	No	Yes	Complies with 17034
	BCR-576, -577, -578	Yes	Yes	

May 2023

Sustainability of CRM



Substance	RM	Listed in JCTLM database?	Actually available?	Comments
Estriol	FOR0130.00	No	Yes	No material listed.
	GBW(E)091048 - 52	Yes	No	All levels out of stock
17-Hydroxyprogesterone	S041	Yes	Yes	Long delivery time
	DRE-C14241000	No	Yes	Not listed. Tested: Complies with NMIA material.
Progesterone	NMIJ CRM 6003-a	Yes	Yes	Long delivery time, short shelf life (1 year)
	ERM-DA347, BCR-348R	Yes	Yes	
Testosterone	M914c	Yes	Yes	Very small sales unit!
	CRM 6002-a	No	Yes	Not listed.
	ERM-DA345a, -346a	Yes	Yes	
T4	IRMM-468	Yes	Yes	
T3	IRMM-469	Not anymore	No	Leftovers at lab, Cerilliant not yet tested
	CERT-074	No	Yes	Not yet tested
Digitoxin		No		No material listed. Complies with ISO 17034.
Digoxin	ERM-AC200	Yes	Yes	
	ERM-DA200a, ERM-DA201a	Yes	Yes	
HbA1c	LNE HbA1c 401, -402, -403	Yes	Unclear	3 concentrations listed; Waiting for answer to purchase request
Aldosterone	A9477	No	(Yes)	Characterized by Currenta via qNMR, necessary for every lot, only small production scale
	6402-a nd -b	Not anymore	No	Out of stock. Will there be a new lot?
Cortisol	NIST 921a	Not anymore	Yes	Why not listed anymore?
	NMIJ CRM 6007-a	Yes	Yes	Long delivery time, short shelf life (1 year)
	ERM-DA451/IFCC	Yes	Yes	
	ERM-DA192, -193	Yes	Yes	

May 2023

Availability of CRM – Bad News



Email of a supplier of CRMs, September 27, 2024

*... We have received information from the manufacturer that the item ERM-DA193 (**Cortisol**) is no longer available.*

Therefore, we had to cancel this item from your order.

*We have also received information about Nist-911c (**Cholesterol**).*

This is currently available with a short expiration date of December 31, 2024. New production is not currently planned. ...

The decision of CRM manufacturers is the result of economical resource planning.

Availability of CRM – Good News?

Tripalmitin from NIST available again, BUT ...



1) only because CDC put pressure on this!



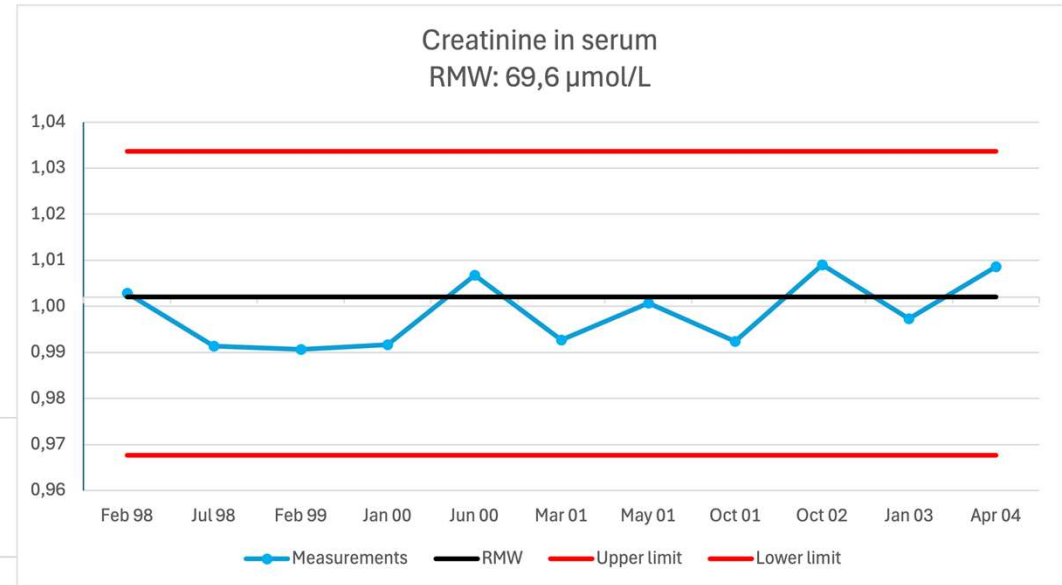
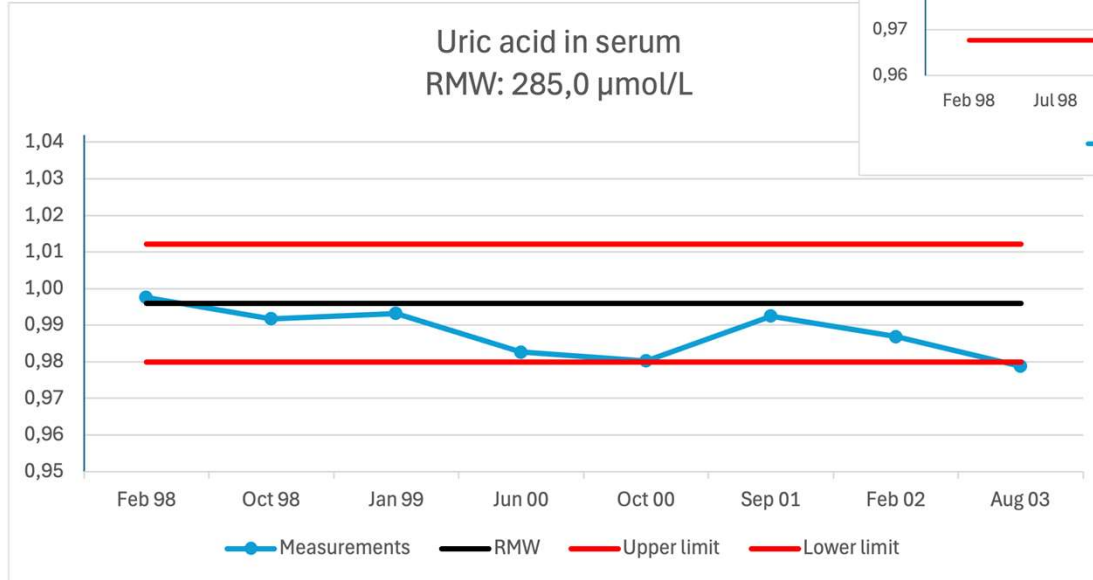
2) you can currently only order it from NIST itself and the distributors in Europe have not been informed at all



New approaches must be developed to maintain CRMs as anchors of traceability.

Controll Material 799 00

- Liquid, frozen serum
- RMV assigned for creatinine, urea, and uric acid
- Used as control material in alternation with NIST SRM 909



- Produced by
Adam Uldall, DEKS
1998

Communicate, prioritize, collaborate



- The list of those who create or use CRM is long:

National Metrology Institutes

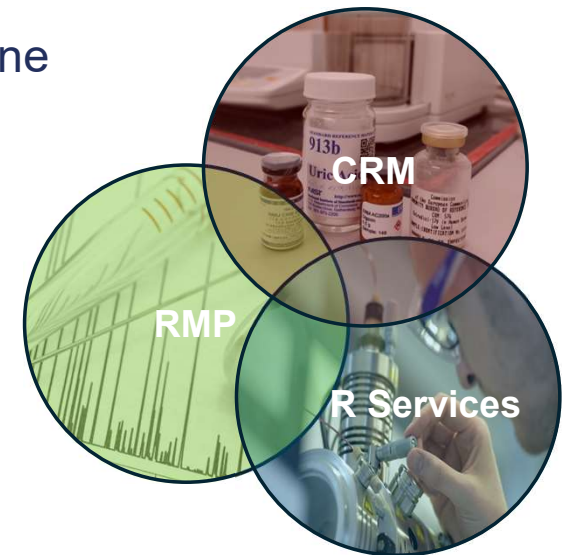
Scientific Societies of Clinical Chemistry and Laboratory Medicine

Suppliers of Certified Reference Materials

Calibration Laboratories (also of EQA Organizers)

IVD Industry

- Selection of projects should be done with respect to medical needs and state of art
- Avoid any redundancy
- Limitations should be addressed (selectivity, measurement uncertainty, analytical performance, ...)
- Distinguish when the use of primary CRM, secondary CRM, or certified materials makes sense

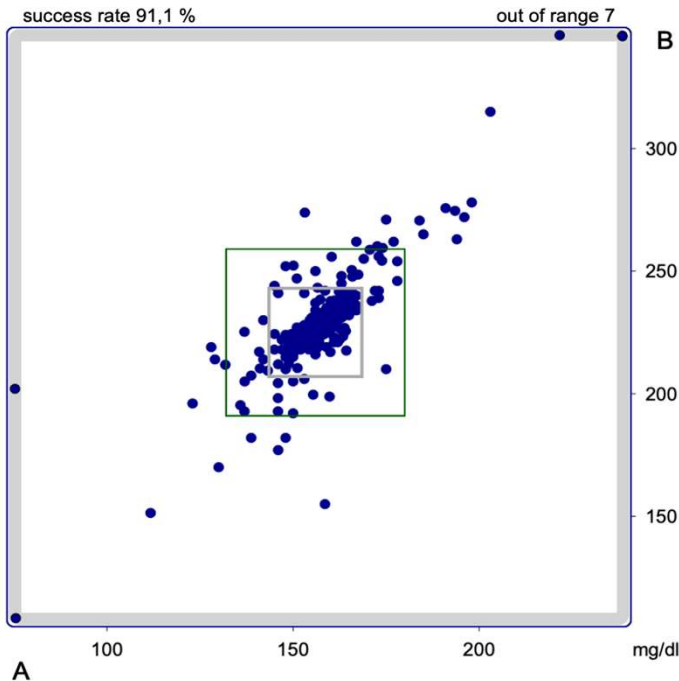


Commutability

- The major role of EQA is to display and improve laboratory performance. Beside standardisation and implementation of traceability the quest for commutable samples shapes the value of EQA.
- Commutability implies that results for a reference material had the same mathematical relationship between methods that was observed for native clinical samples measured by those methods.
- Similar to the "true value", the request for "the commutable material" is always an approximation, even when considering only one measurement value, it is always a multifactorial situation.

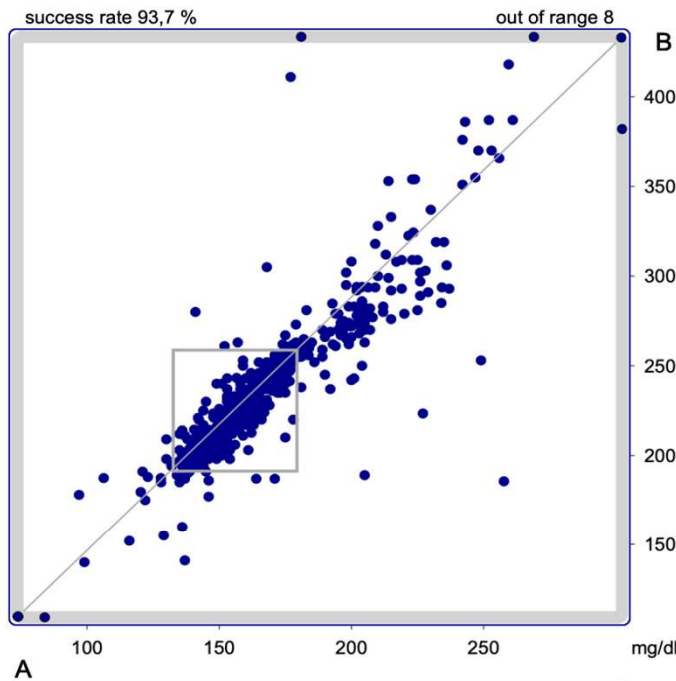
Glucose – Wet Chemistry vs. POCT

Analyte **Glucose**
Method all methods



No of participants	339		
sample/unit	A	mg/dl	B
mean	157		228
standard deviation	9.89		16.0
coefficient of variation	6.30		7.04

Analyte **Glucose POCT**
Method all methods



No of participants	784		
sample/unit	A	mg/dl	B
mean	166		237
standard deviation	23.6		33.8
coefficient of variation	14.2		14.3

Material: freeze dried human serum

RMV as target value:

- 15% → acceptable
- 8% → limited acceptable
- POCT → RMV not applicable

Requirements to the EQA samples

- RMV assigned
- Commutable
- Guarantee for stability during EQA period

Patricia Kaiser*, Udo Kramer, Hannah Rosenthal, Christian Genz, Nathalie Weiss, Ingo Schellenberg and Michael Spannagl

New concept for control material in glucose point-of-care-testing for external quality assessment schemes

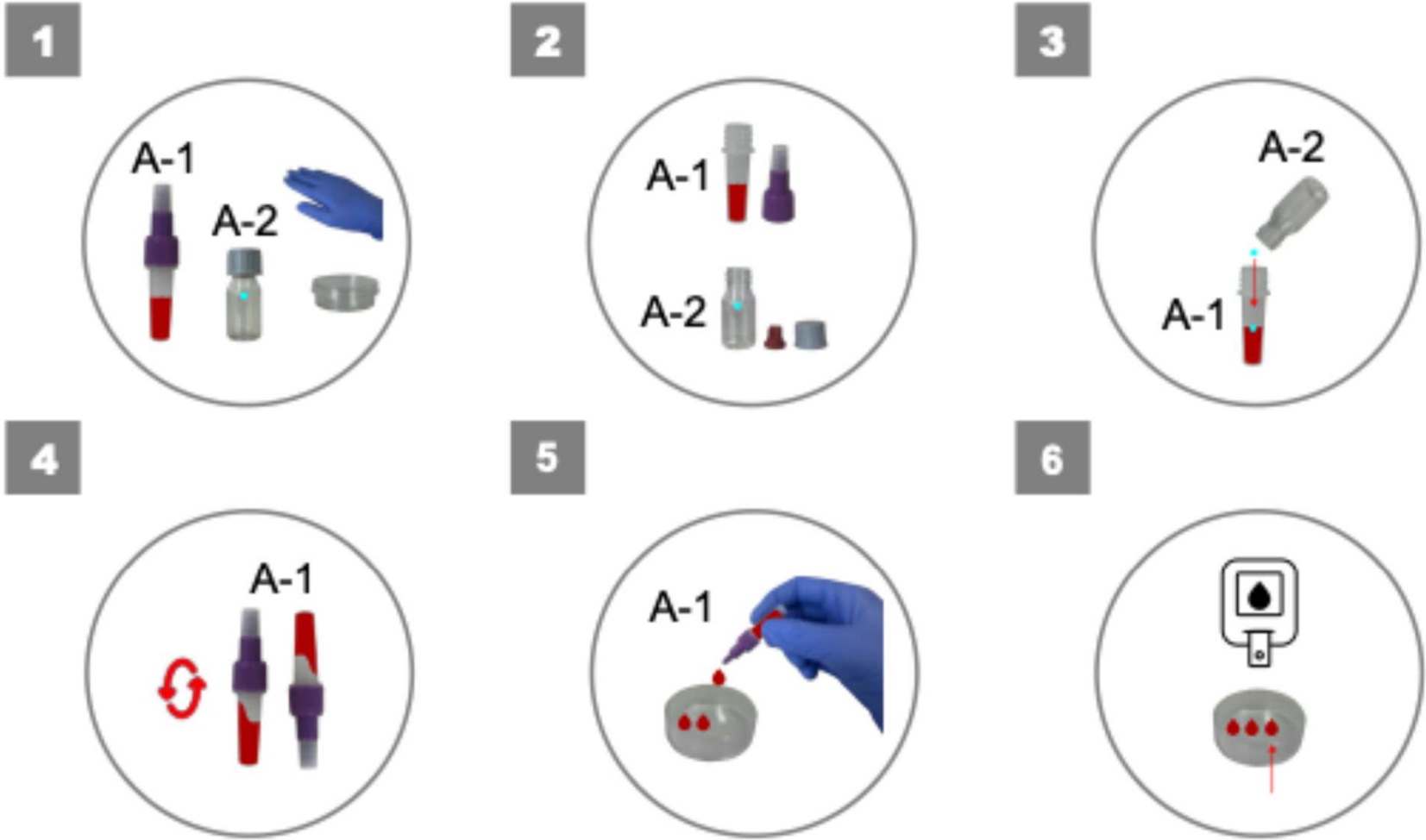
<https://doi.org/10.1515/ccim-2024-0822>

Received July 17, 2024; accepted September 10, 2024;
published online September 24, 2024

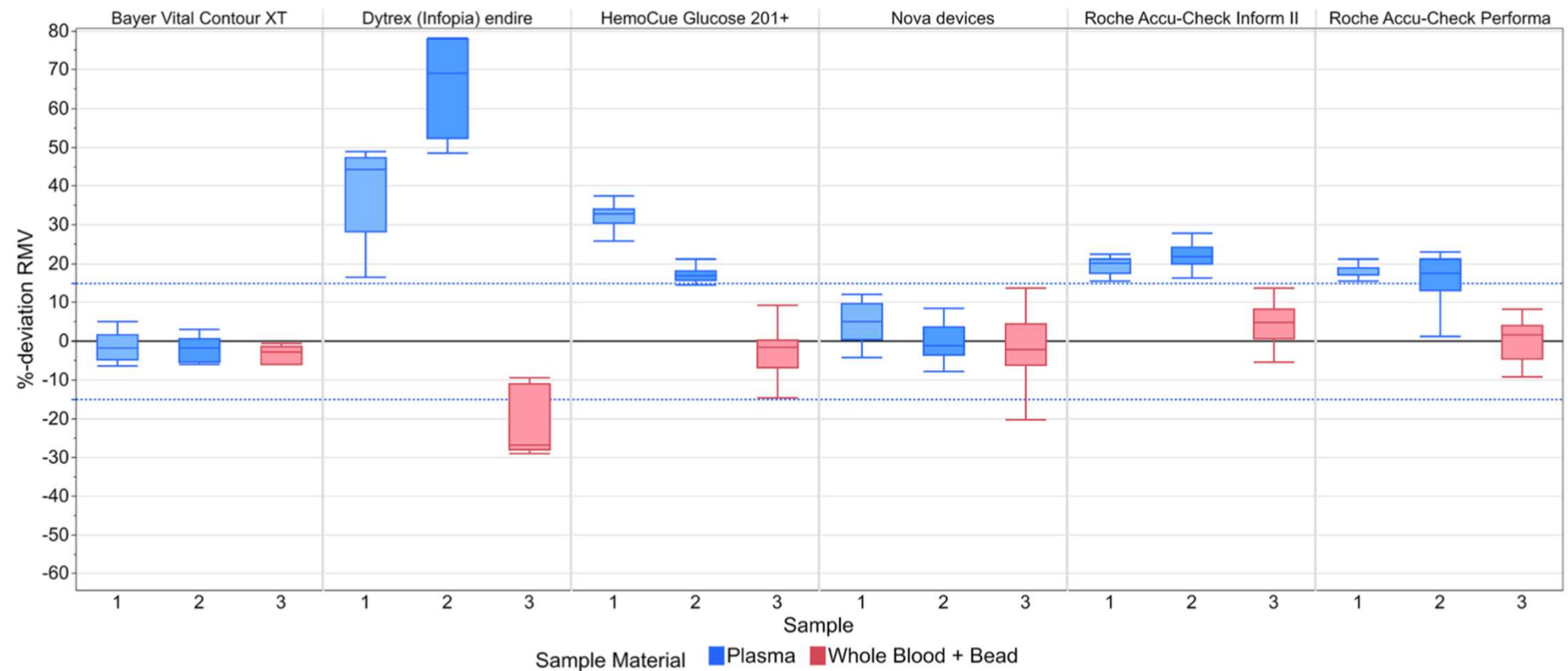
Keywords: glucose bead; glucometer; proficiency testing; reference measurement procedure; traceability; whole blood

- Handled by non-laboratory personnel without the need for laboratory equipment such as pipettes
- Two-component sample where the matrix and the analyte are kept apart until the measurement is performed

Bead Concept for POCT



Bead Concept – Results for Glucose/POCT



Kaiser, P., et al., Clin Chem Lab Med (2024), <https://doi.org/10.1515/cclm-2024-0822>

National Lighthouse Project for Glucose/POCT



- Publication is open access
- Reference system for glucose applicable
- Commutability of material
- Nationally uniform procedure under the umbrella of BÄK

RfB pilot study

- November, 13 – 15, 2024
- Two different approaches:
 - I. group receives a stabilized whole blood sample that can be used without further preparation
 - II. group receives a whole blood sample according to the bead concept

Quality Assurance for Patient Safety



WHO Global patient safety action plan states:

- **Health technologies are essential** for a functioning health system.
- **Safety, quality and performance** of in vitro diagnostics (IVDs) have to be ensured in a comprehensive and transparent approach.
- So, there is a need to improve the **availability and quality of information about health care services**.

Implementation of traceability is one important step to establish quality assurance for patient safety.

What **other options** are there through which **EQALM** can support the **implementation** of these requirements?





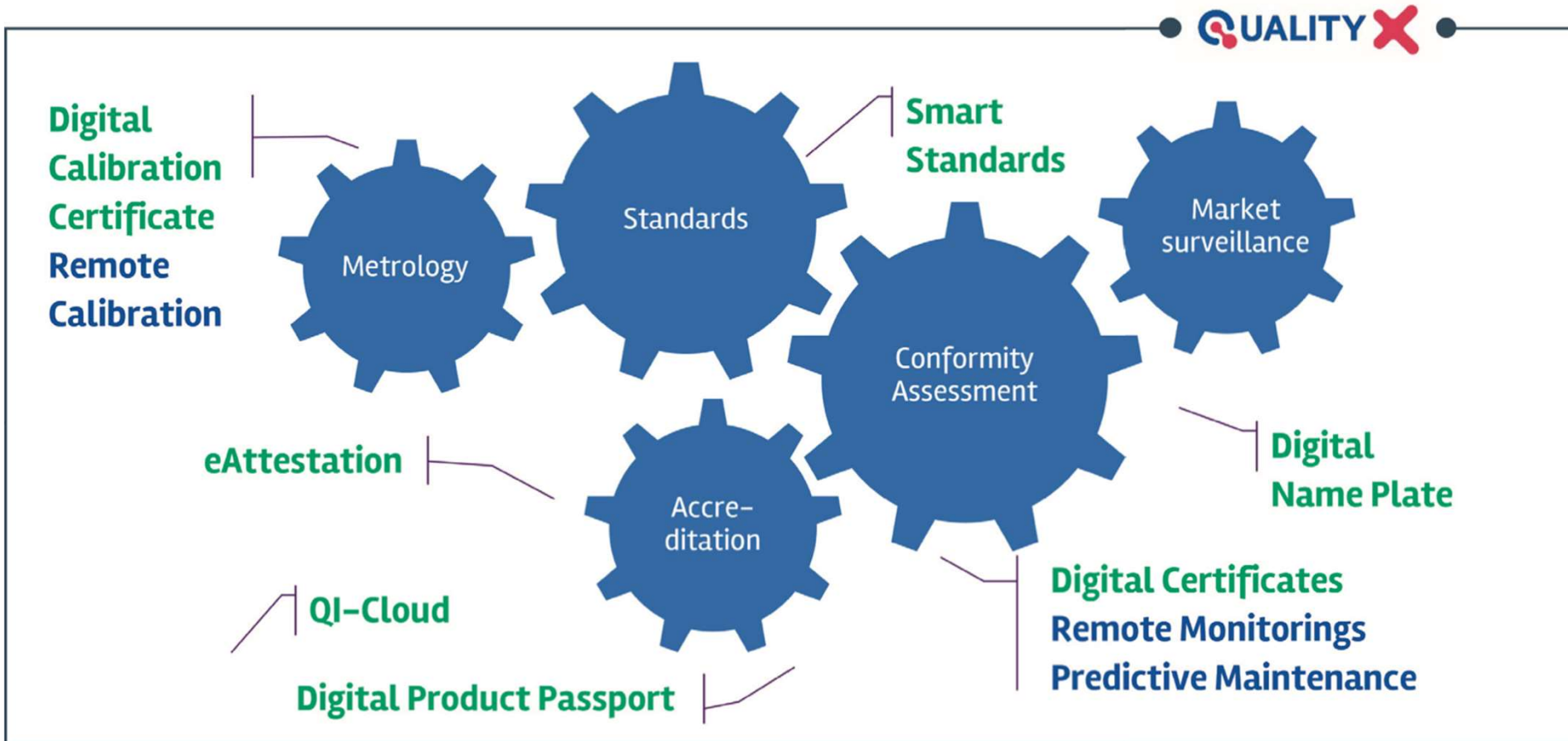
Definition of quality infrastructure:

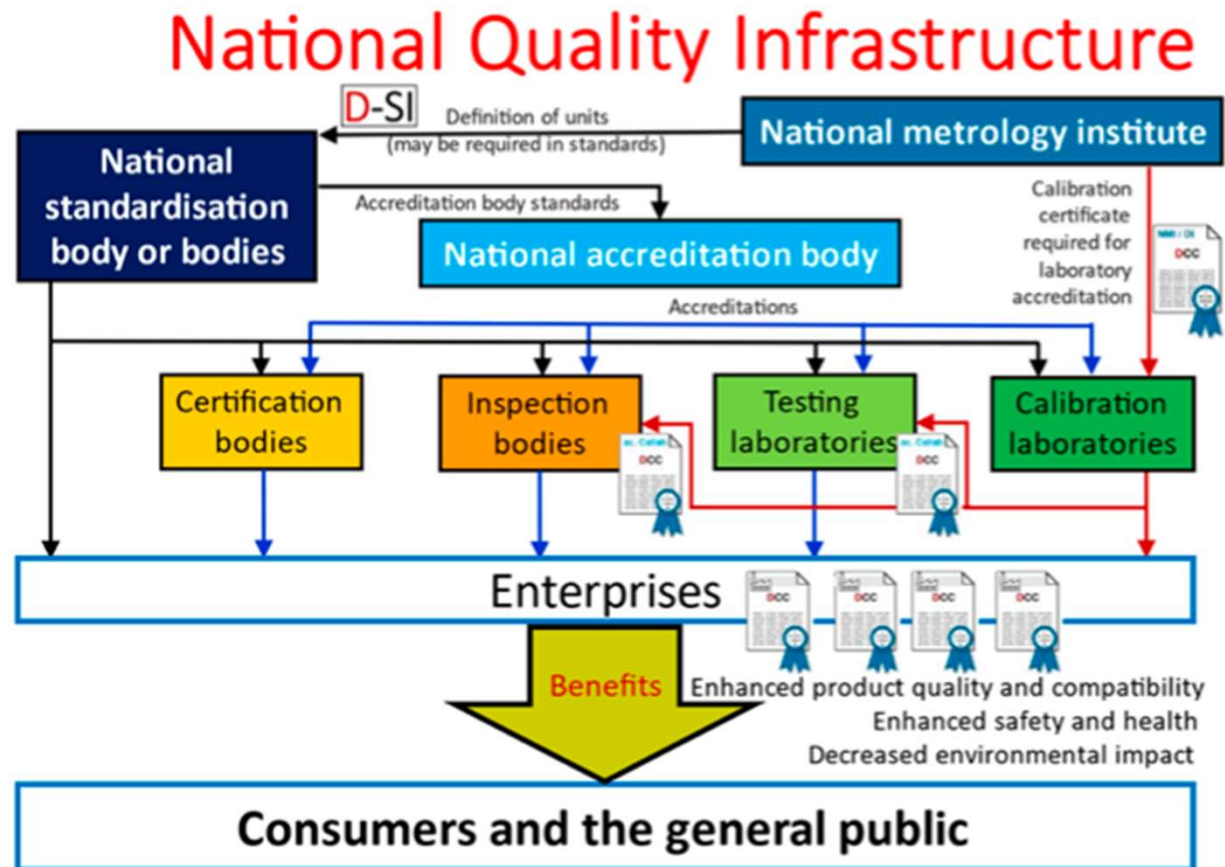
A national system for quality assurance and consumer protection.



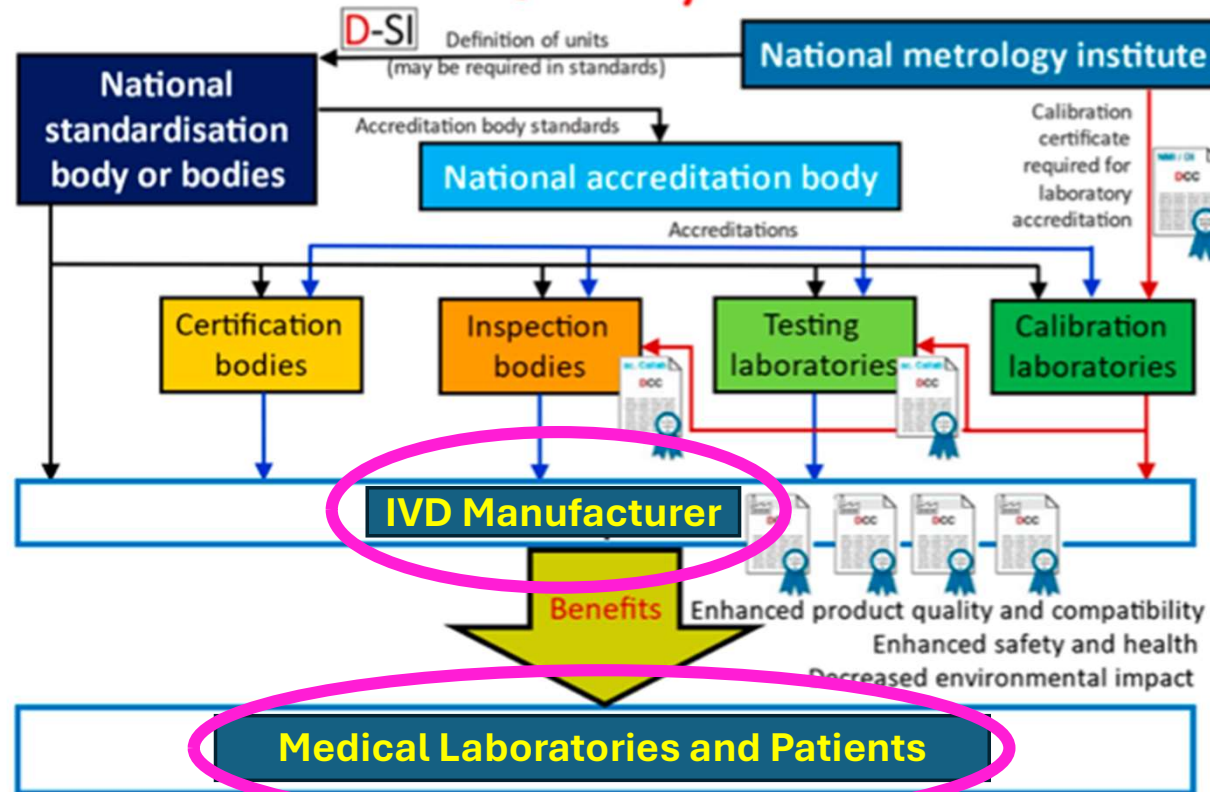
Definition of quality infrastructure in medicine:

A (inter)national system for quality assurance and patient safety.

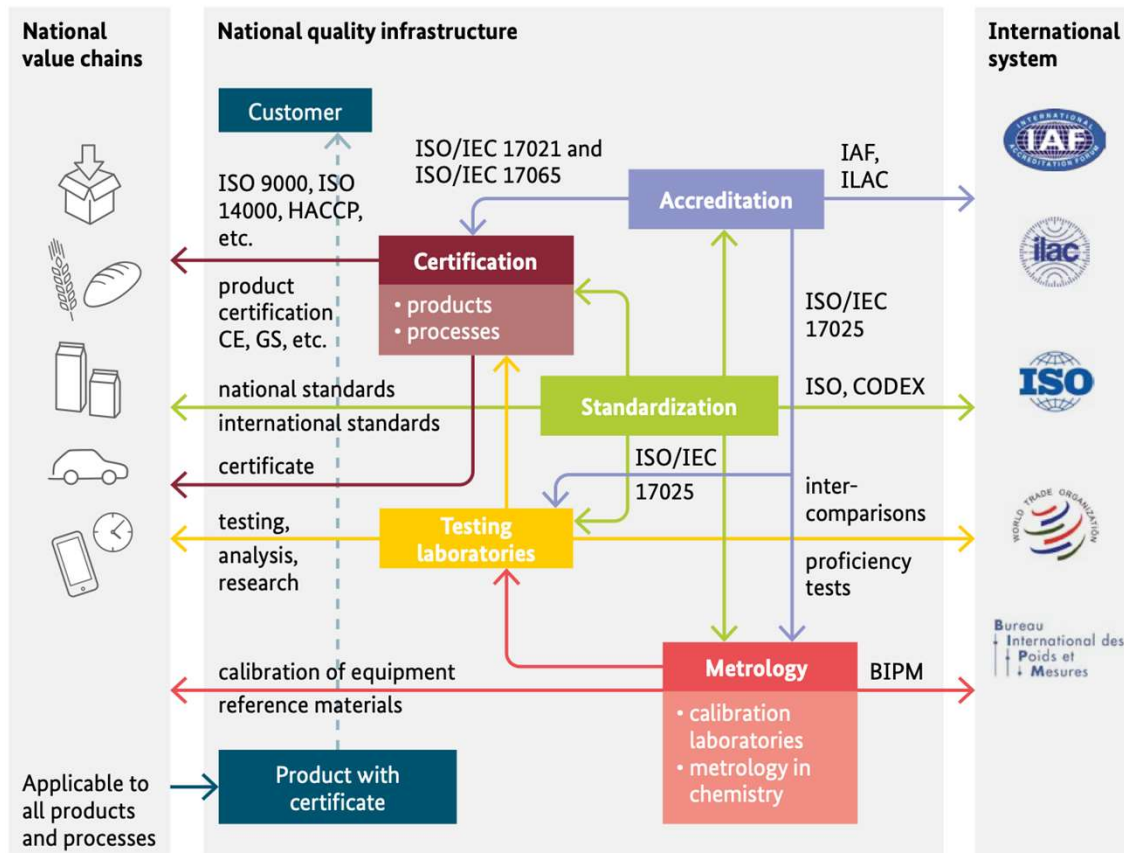




National Quality Infrastructure



Quality Infrastructure



The **definitions of measurands** in laboratory medicine are **complex** and the **results** of laboratory medicine are directly linked to the diagnostic decisions, which **have consequences for patient safety**.

→ The results and **data of EQA** providers should be taken into account when **setting up the quality infrastructure for laboratory medicine**.

Quality Infrastructure



The five technical components – standardization, metrology, testing, certification, and accreditation – comprise a **Quality Infrastructure (QI) in laboratory medicine** as in other areas. This infrastructure can be used for all products and services. It ensures that they will comply with the requirements of clients, either consumers, manufactureres or regulators.

Digital solutions of end user health services, such as medical laboratories, have to be developed and implemented to **improve the safety** of health care.

The global move from paper-based systems to **digital infrastructures enables research and innovation** in patient safety to be carried out in a timely, efficient and cost-effective manner.

The **data of EQA** is of particular value. What is of importance?

- the **quality of data**,
- the **consistency of data interpretation**.



Biomedical Alliance in Europe

- A **non-profit European organisation** that represents 35 medical societies including more than 400,000 researchers and health professionals
- Supports biomedical research
- Provides **expert advice to policy makers and regulators** on the implementation of the MDR and IVDR
- Partner in the **H2020 CORE-MD Project**, which aimed to recommend an appropriate balance between innovation, safety, and clinical effectiveness

The *in-vitro* Diagnostics Regulation 2017/746 (IVDR) aims

- to improve and to warrant quality and patient safety in laboratory diagnostics in Europe,
- to evaluate - by manufacturers - diagnostic products already in daily clinical during postmarket surveillance.

Review of IVD-R – Analysis and Recommendations



In general:

- Reform was needed, but both the MDR and IVDR have had **unintended consequences**
 - e.g. disappearing devices, absence of special pathways
- **Limited capacity** of Notified Bodies

With special focus on IVDR:

- Special issues for IVD regarding the **recognition of established EQA**

The aim is:

- To propose **practical solutions** that should be introduced to ensure that the MDR and the IVDR can **meet the needs** of the public, patients, and healthcare professionals.

External Quality Assurance (EQA) programs are a means of **monitoring analytical quality** in the diagnostic laboratory community providing an important **real-time monitoring** opportunity from the postmarket perspective.

BioMedAlliance – IVD Task Force Survey



IVD Task Force of BioMedAlliance conducts a **survey on the European EQA landscape**.

The **aim of the survey** is to create with your data two matrices:

- to visualize - for the EU area - an **EQA landscape plot** showing the degree/density of coverage by the EQA structures/organisations **for medical laboratory diagnostics** in the 27 EU countries.
- to visualize the **biomarker spectra** (supposedly available online) offered by EQA providers and to plot them to show their availability in the EU-wide coverage.

Three aspects of the survey:

1. In which countries a) within the EU and b) outside the EU EQA programmes are provided?
2. How high are the proportional subscription quotes of the services of the EQA organization among their subscribers in the EU (on a scale of 1-10)?
3. Is participation in EQA programmes required by law or accreditation requirements in the country of the EQA provider?



External quality assessment (EQA) is defined as a system for objectively checking the laboratory's performance. It is a challenge of the **effectiveness of a laboratory's quality management system** by using an external facility.

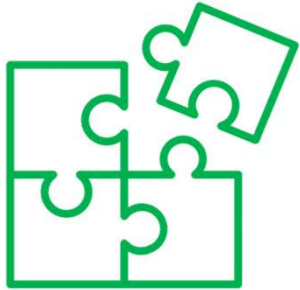


Concepts such as **reference systems, traceability and standardization** as well as the **commutability** of the materials used in EQA surveys have to be considered to ensure the reliability of the results.



Despite all the new approaches and ideas of EQA surveys, the challenge is to **maintain achieved goals**. Both new generations of test procedures and the availability of reference materials (CRM) require maintenance on a permanent basis.

Network to improve quality



The **cooperation** between laboratories, EQA providers, IVD manufacturers and regulators/legislators is crucial for quality assurance in laboratory diagnostics.



Therefore, **data, transparency and open discussions** are needed with comprehensive information on the evaluations, if applicable with findings and comments



Further **investigation** and development is necessary to improve the quality even **for new analytes** in future.



Special thanks
to the whole RfB team for their
wonderful performance day by day...
and to you for your attention!