The role of metrological traceability in external quality assessment schemes and calibration laboratories

Results of a survey conducted by the EMN-TLM

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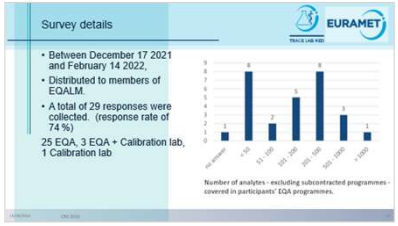
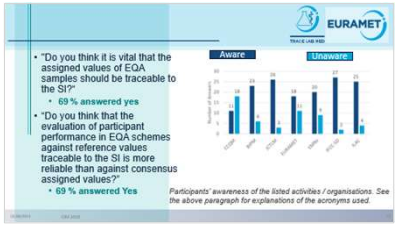
Outline

- What is the EMN-TLM
- Overview of the survey
- Current knowledge of metrology landscape and infrastructure
- Role of CRMs and RMPs in EQA





Recommendations

1. **Standardisation Platform:**
2. **Prioritising Standardisation:**
3. **Strategic Research on Priority Measurands:**
4. **Training Programs on Measurement Uncertainty:**
5. **Enhanced Support for Reference Materials and Procedures:**
6. **Streamline Commutability Studies:**
7. **Digital Transformation Awareness:**

Summary

- In 2024: 13 NMIs/DIs &
  4 Partners from 10 Countries (& JRC)
- Extensive review of stakeholders needs :
  EQA providers & IVD manufacturers
- Close collaboration with calibration laboratories
- EMN as an efficient collaborative platform for research activities

TRACE LAB MED

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The **18NET02 TraceLabMed & 23IND02 COMET** projects have received *funding* from the EMPIR programme co-financed by the Participating States and from the European Union.

Role of the European Metrology Networks

- The EMNs will analyse the European and global metrology needs and address these needs in a coordinated manner. EMN members will then **formulate common metrology strategies** including aspects such as **research, infrastructure, knowledge transfer and services**. The members will be committed to contributing to the EMN, helping to establish **sustainable structures** that are **strategically planned** from the outset.

  By providing a single point of contact for information, underpinning regulation and standardisation, promoting best practice and establishing a comprehensive, longer-term infrastructure, the EMNs **aim to create and disseminate knowledge, gain international leadership and recognition, and build collaboration across the measurement science community.**

- Advanced Manufacturing
- Climate and Ocean Observation
- Energy Gases
- **Laboratory Medicine**
- Mathmet
- Pollution Monitoring
- Quantum Technologies
- Radiation Protection
- Safe and Sustainable Food
- Smart Electricity Grids
- Smart Specialisation in Northern Europe

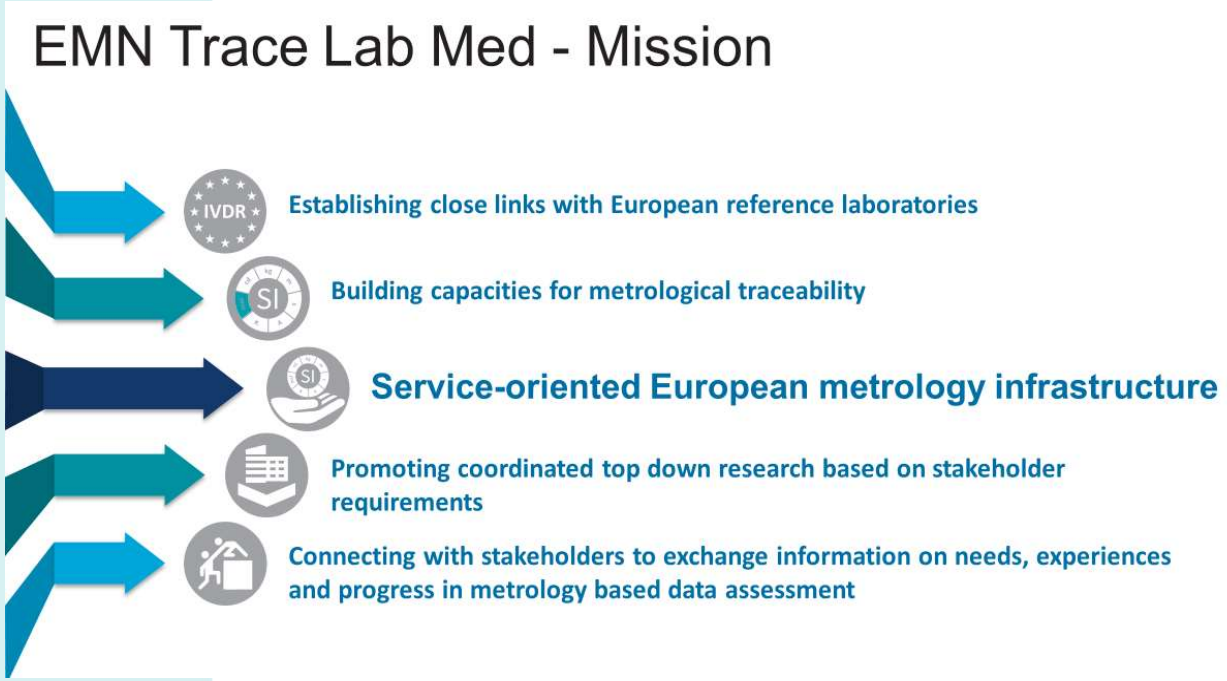
Rational for EMN-TLM

- High percentage of laboratory tests currently used are neither harmonized (comparable) nor standardized (SI-traceable).
- The IVDR defines stricter requirements for metrological traceability than the former EU directive : in addition to establishing results metrological traceability, need to verify the performance of IVD tests and the suitability of measurement uncertainties, as stated in ISO 17511:2020
- Some (but not all) EQA schemes provide insights to perform post-market surveillance but the workload cannot be covered by single NMI/DIs
- Strong collaboration needed between NMIs and stakeholders : EQA Providers, IVD manufacturers, international organizations, calibration labs

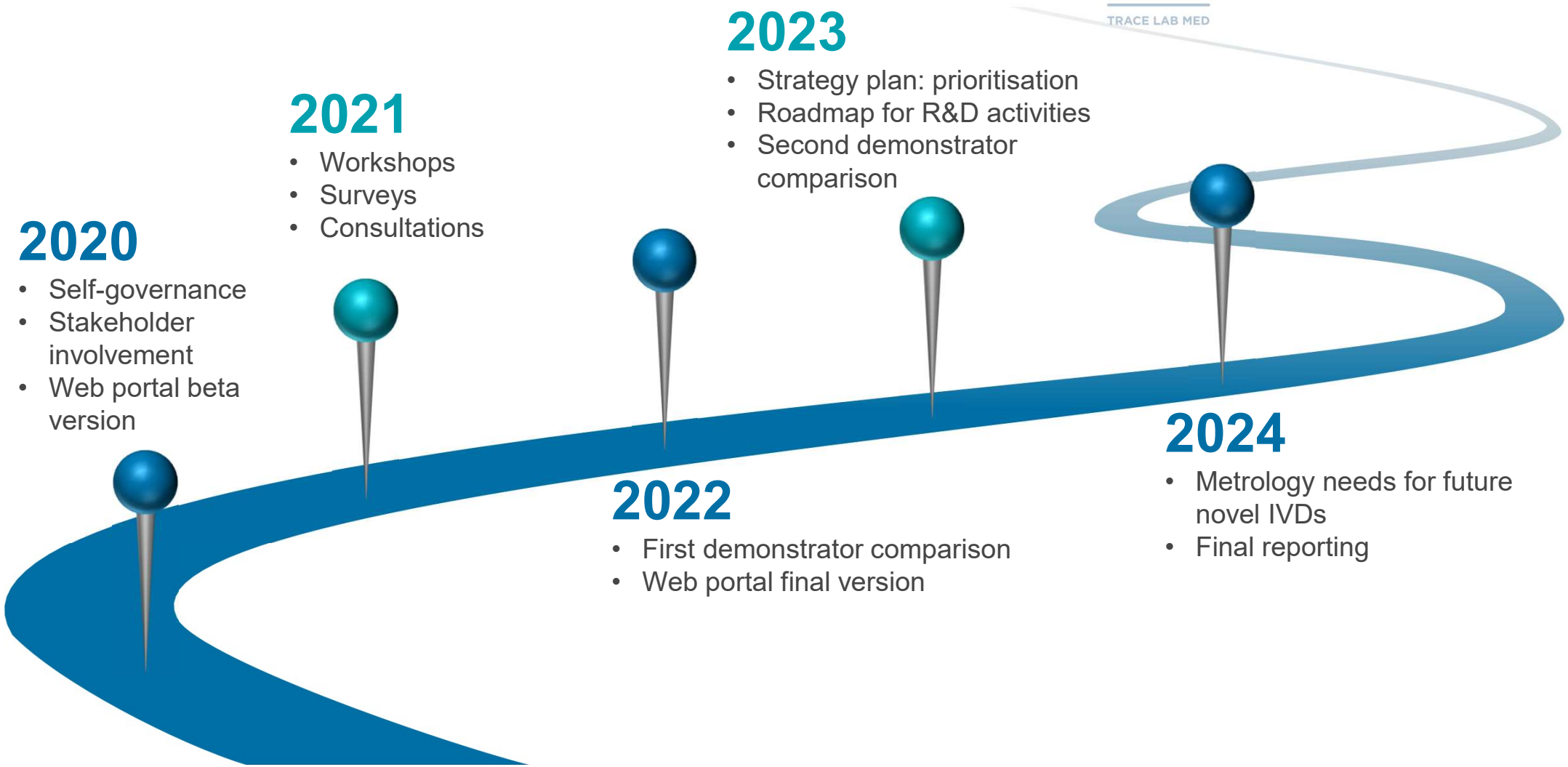
Networking: EMN TraceLabMed

EMN-Traceability in Laboratory Medicine

- The European Metrology Network (EMN) for Laboratory Medicine brings together European National Metrology Institutes, Designated Institutes and partners from medicine and industry to **<u>support the application of metrology</u>**, the science of measurement, **<u>to *in vitro* diagnostics</u>** tests.



EMN Trace Lab Med - Activities



2020

- Self-governance
- Stakeholder involvement
- Web portal beta version

2021

- Workshops
- Surveys
- Consultations

2022

- First demonstrator comparison
- Web portal final version

2023

- Strategy plan: prioritisation
- Roadmap for R&D activities
- Second demonstrator comparison

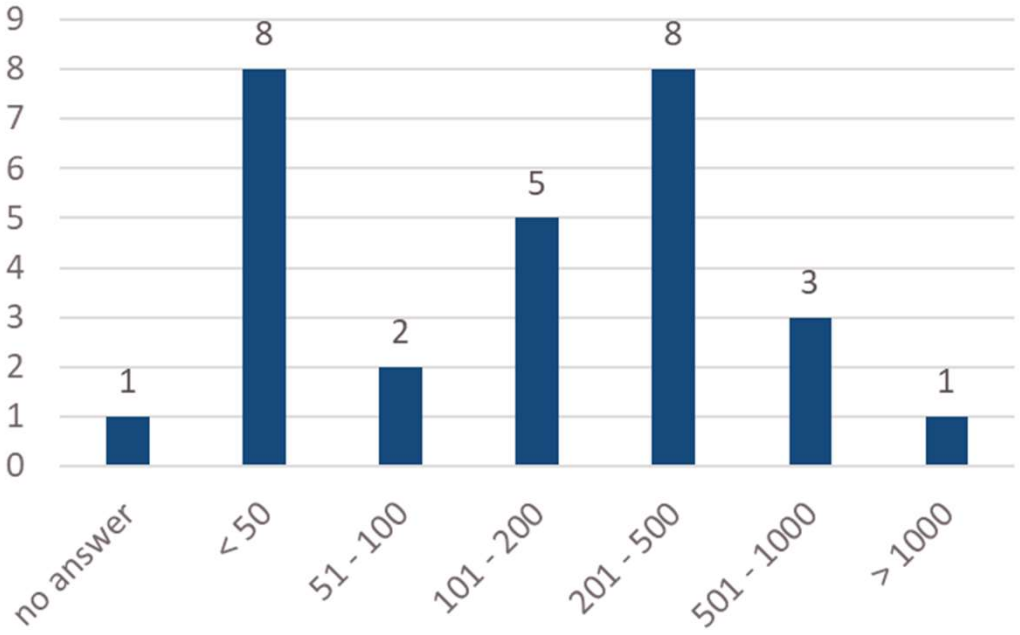
2024

- Metrology needs for future novel IVDs
- Final reporting

Survey details

- Between December 17 2021 and February 14 2022,
- Distributed to members of EQALM.
- A total of 29 responses were collected. (response rate of 74 %)

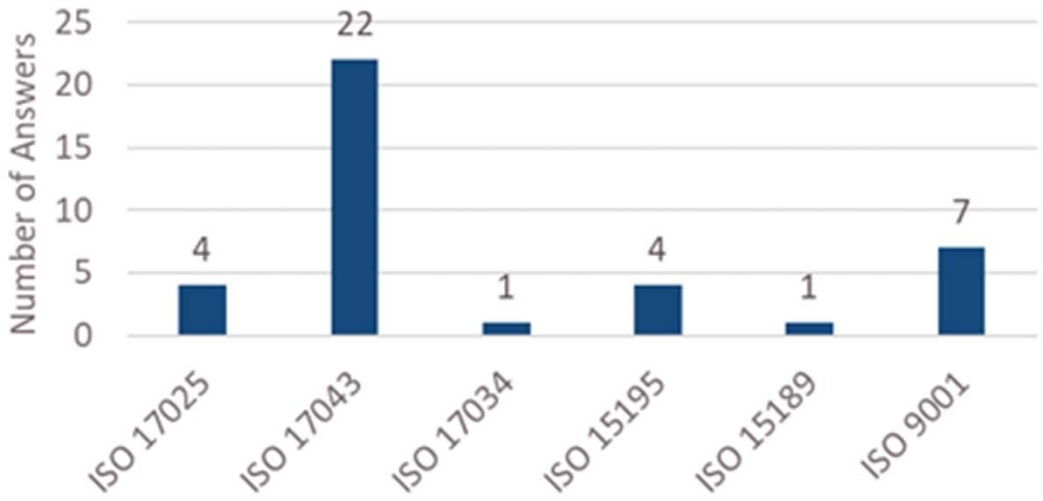
25 EQA, 3 EQA + Calibration lab,
1 Calibration lab

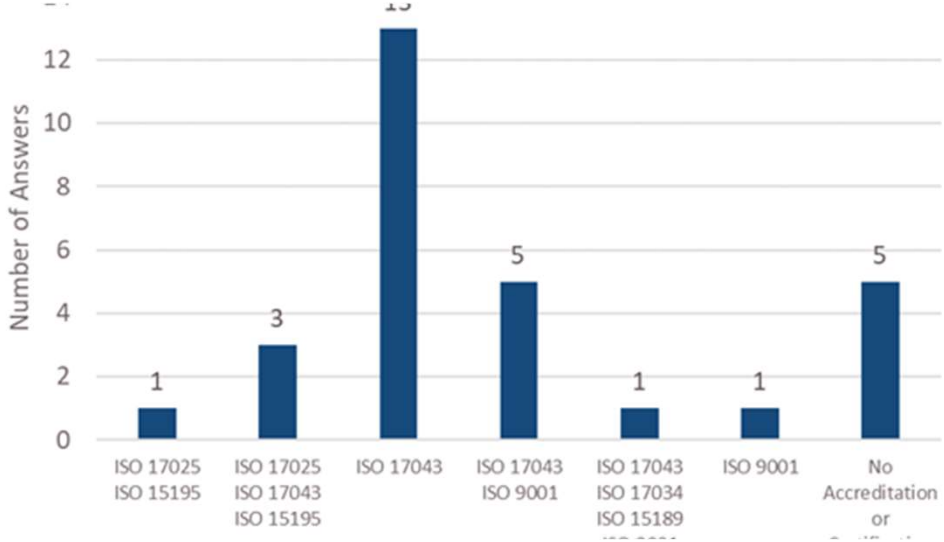


Number of analytes - excluding subcontracted programmes - covered in participants' EQA programmes.

Quality infrastructures of responding participants

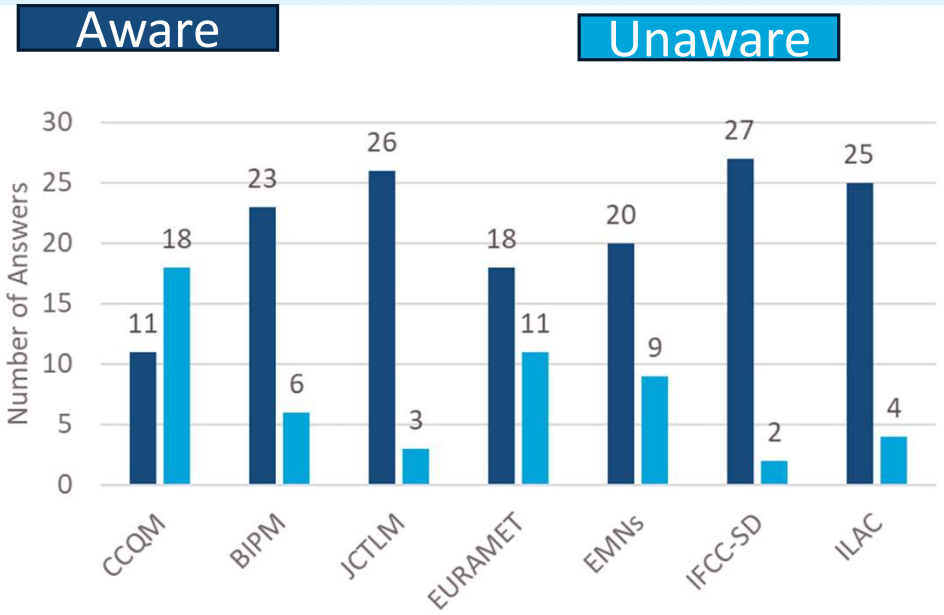
- Respondents were asked about their accreditation or certification in relation to the following standards:
  - ISO 17025: Testing and calibration laboratories
  - ISO 17043: Conformity assessment - General requirements for proficiency testing
  - ISO 17034: Competence of reference material producers
  - ISO 15195: Calibration laboratories using reference measurement procedures in laboratory medicine
  - ISO 9001: Quality management systems requirements





Reported Combinations of ISO standards.

- "Do you think it is vital that the assigned values of EQA samples should be traceable to the SI?“
  - **69 % answered yes**
- “Do you think that the evaluation of participant performance in EQA schemes against reference values traceable to the SI is more reliable than against consensus assigned values?”
  - **69 % answered Yes**



Participants’ awareness of the listed activities / organisations. See the above paragraph for explanations of the acronyms used.

Traceability to the SI (reasons for “no” answers)

1.Commutable Samples and Practical Value:

Traceability to the SI is vital, if commutability can be assured. Without commutability, assigned values traceable to the SI might lack practical significance. The importance of traceability also depends on whether it's feasible or possible to achieve within a given context.

2.Common Reference Materials or Procedures:

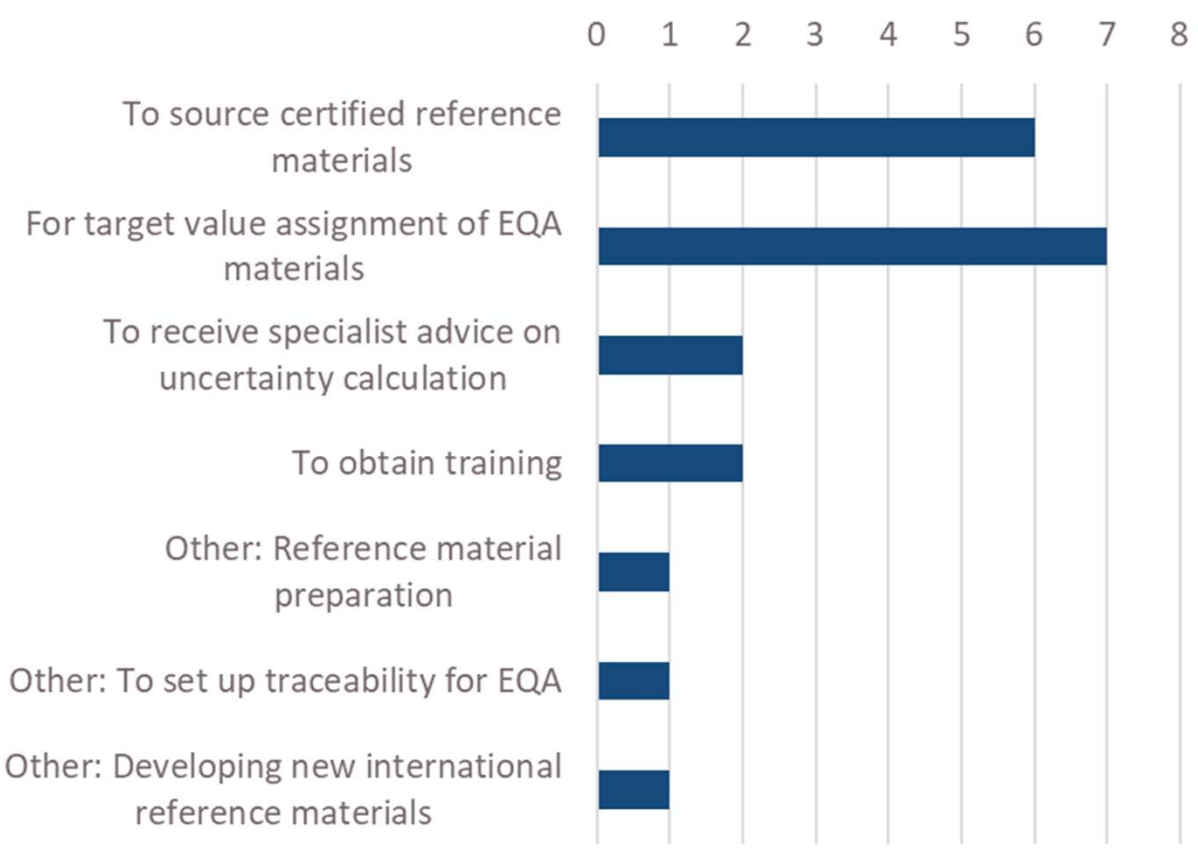
While direct traceability to the SI is ideal, in cases where it's not feasible, results should be traceable to a common reference material or procedure.

3.Field-Specific Challenges:

Certain fields, may lack the necessary RMPs and CRMs needed. Hematology covers many qualitative measurands, not amenable to SI traceability.

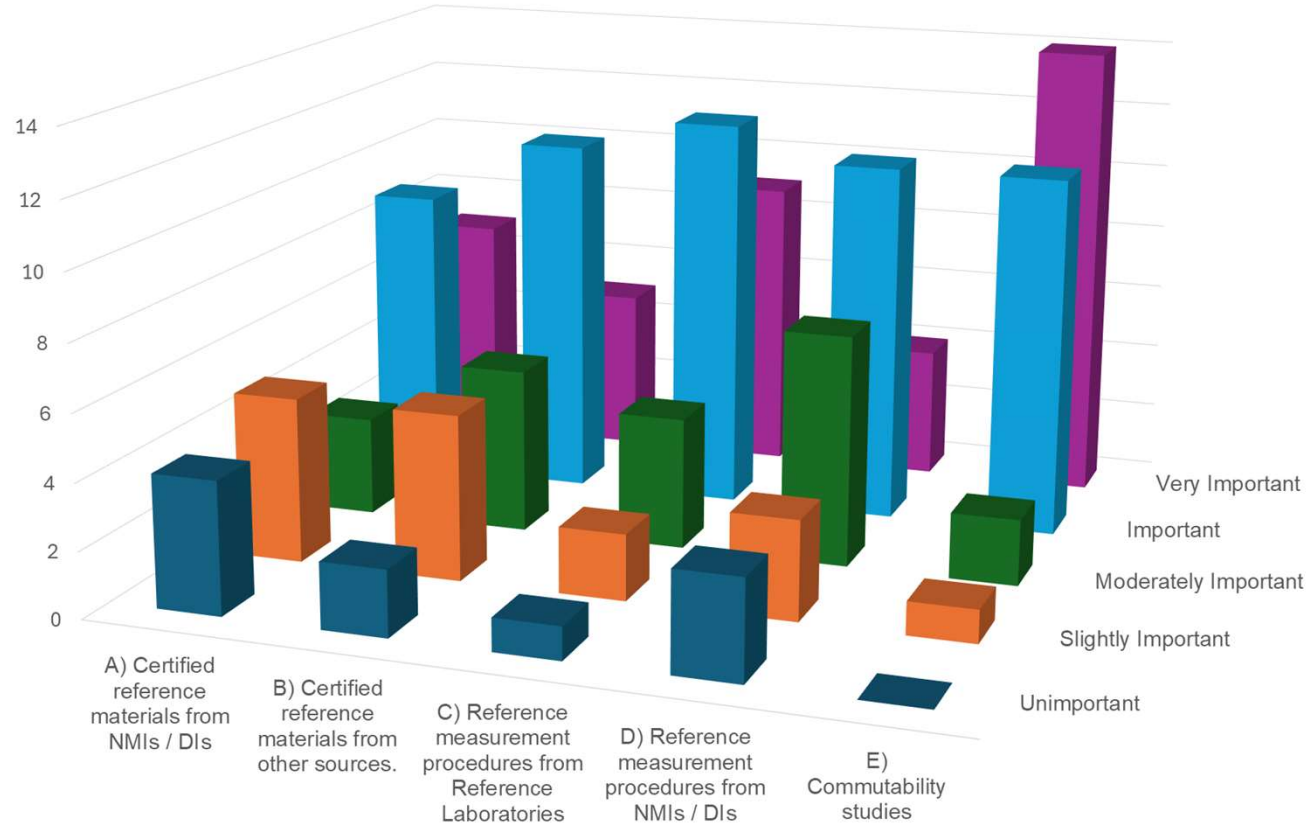
Current NMI/EQA interactions

- The prevalent collaboration focus of EQA providers with NMIs and DIs centres around ensuring traceable EQA schemes.
  - value assignment of EQA materials
  - sourcing of appropriate reference materials



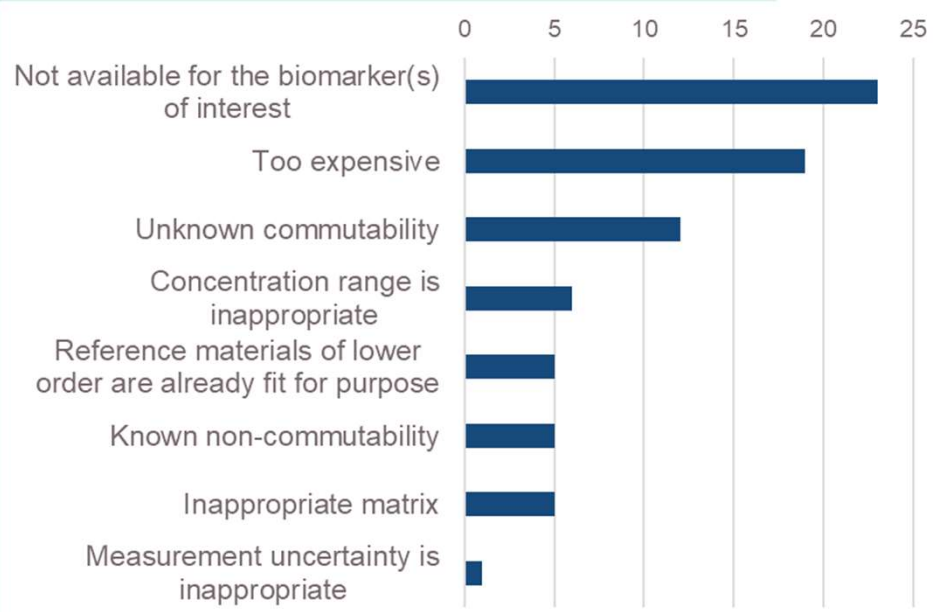
Nature of collaboration between EQA providers and NMIs/DIs

The Role of CRMs in EQA

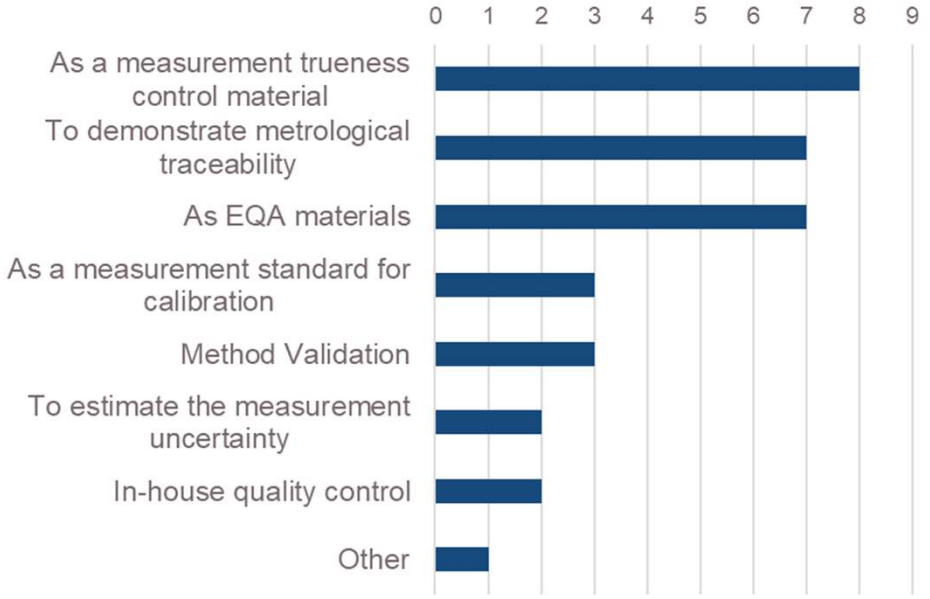


The Role of CRMs in EQA

- What are the barriers in using CRMs

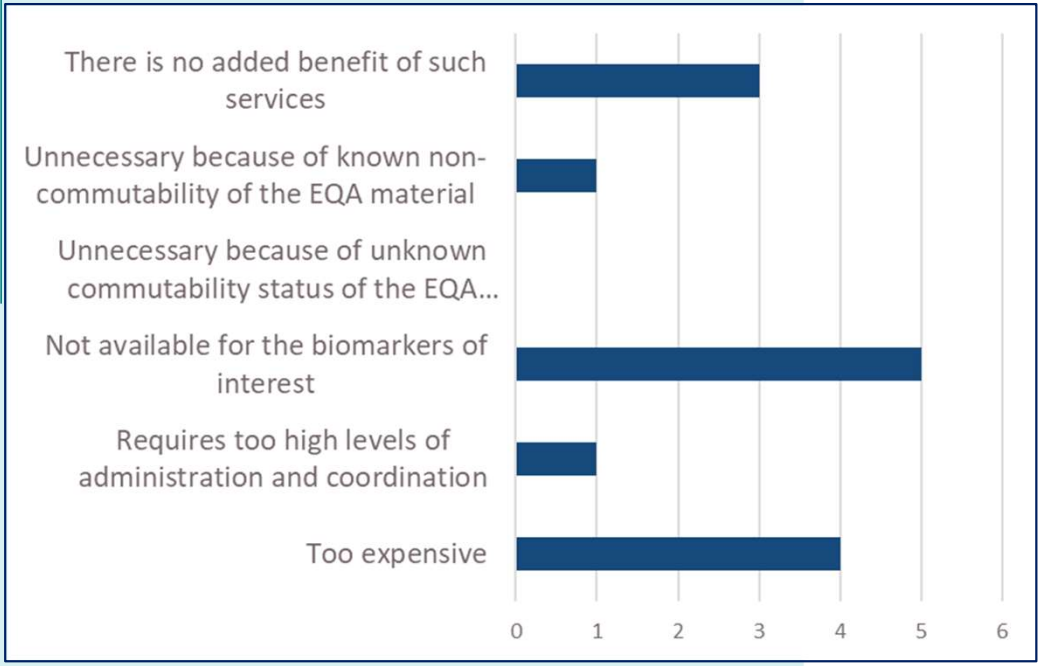


For what are CRMs used

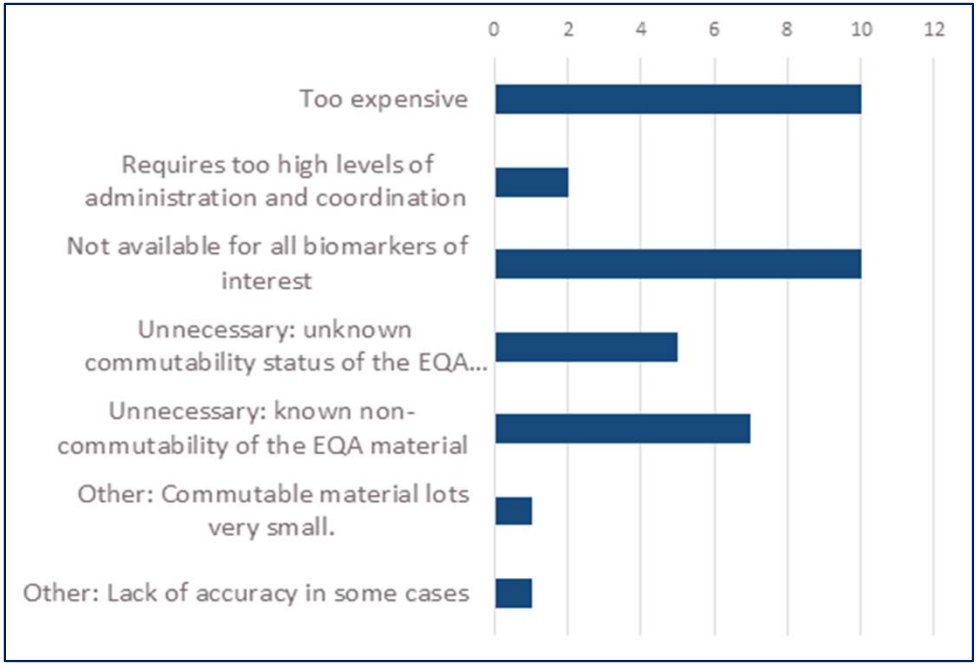


The Role of RM services in EQA

9 declared that they do not use reference measurement services

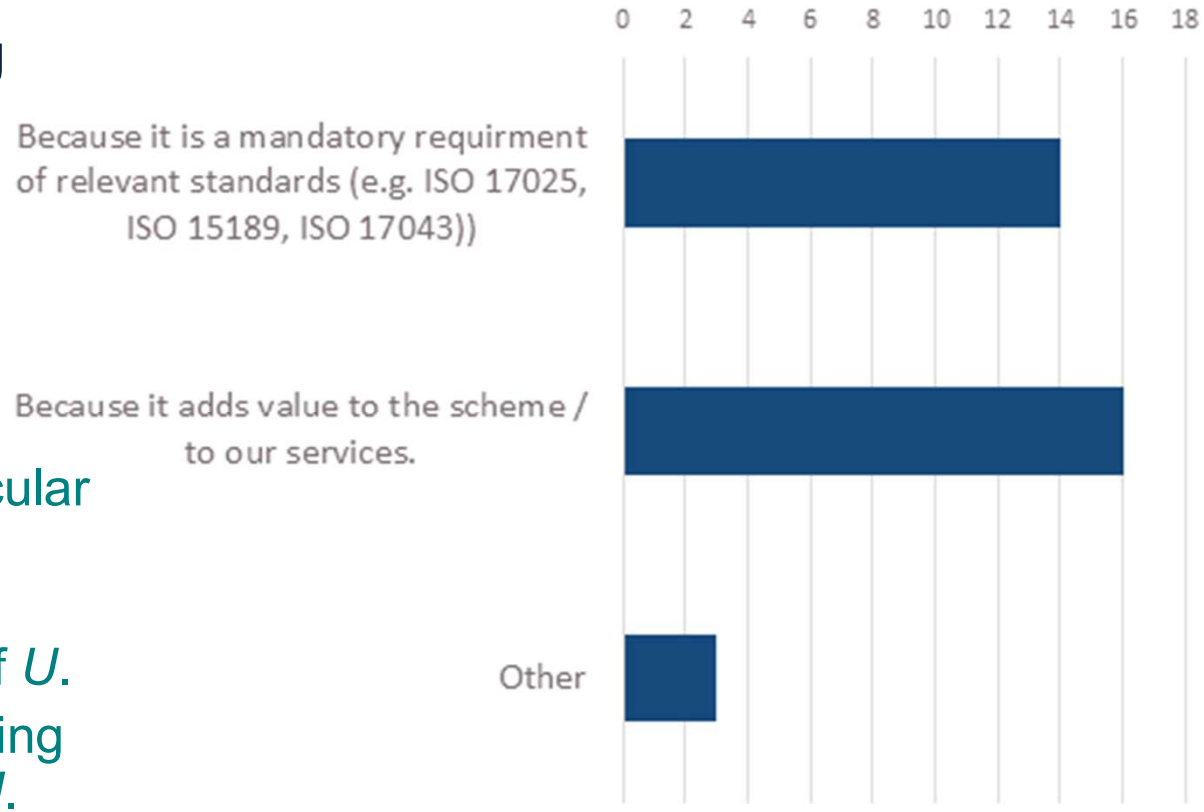


12 respondents answering that they use reference measurement services



Measurement Uncertatinty

- Reasons given for not calculating measurement uncertainty
  - General absence of participant requests.
  - A lack of necessity in their schemes.
  - Inapplicability to qualitative measurands in the field of molecular genetics
  - Use of predefined uncert. target intervals instead of calculation of *U*.
  - Inability to assess bias as a limiting factor in the ability to calculate *U*.



Impact of IVDR

- **Increased Interest Among IVD Manufacturers in EQA Data for Post-Market Surveillance:** Thirteen EQA providers anticipate a surge in interest from *in vitro diagnostic* manufacturers who aim to utilize EQA data as a crucial component of their post-market surveillance systems.
- **Increased Interest in Traceable and Commutable EQA Schemes:** Fourteen EQA providers expect a growing interest in traceable and commutable EQA schemes.
- **Other Responses:**
  - One EQA provider expressed uncertainty, stating they do not know what to expect regarding the impact.
  - Another respondent expected the emergence of EQA for in-house methods, indicating that some providers may adapt to new demands for quality assurance in laboratory-developed tests

EMN Trace Lab Med - Aims

TRACE LAB MED

Support for EU reference laboratories

Metrological traceability for *in vitro* diagnostics

Service-oriented European metrology infrastructure

Coordinated top-down research

Capacity building & knowledge transfer

EMN Trace Lab Med

TRACE LAB MED

13 NMIs/DIs
9 Countries + JRC
4 Partner Laboratories

IVDR

EU IVDR (2017/746):
Demand for **metrological Traceability**

ISO

International Standards for medical Laboratories:
Demand for **metrological Traceability**

EU citizens: Metrological traceability
for **patient safety** & public confidence

EMPIR
EURAMET
The EMPIR initiative is co-funded by the European Union's Horizon 2020 research and innovation programme and the EMPIR Participating States

Objectives

1) **To develop a plan for a joint sustainable European metrology infrastructure for traceability in laboratory medicine**
   Targets: Establish self-governance of the EMN, stakeholder mapping, stakeholder communications plan, development of EMN web portal.

2) **To develop a coherent strategy plan […] to implement sustainable services for delivering metrological traceability as required by the IVDR**
   Targets: EMN as single access point, NMI/DI service database, EMN-coordinated approach for sharing the workload among NMIs/DIs, demonstration exercises.

Objectives

3) **To develop a joint strategy with EQA providers and reference laboratories to identify and prioritise measurands for which SI traceability is required.**
   Targets: Inventory of existing priority lists vs standardized procedures and ref. materials; establish a priority list of measurands in cooperation with EQA providers, national medical associations → roadmap for R&D activities (SRA); plan for uptake and exploitation of research results.

4) **To set up a roadmap addressing the further development of the EMN […] once the key tasks are addressed and after the core services have been implemented.**
   Targets: Expanding the EMN; support for other NMIs/DIs in building their capacities.

PTB Engineering for Health

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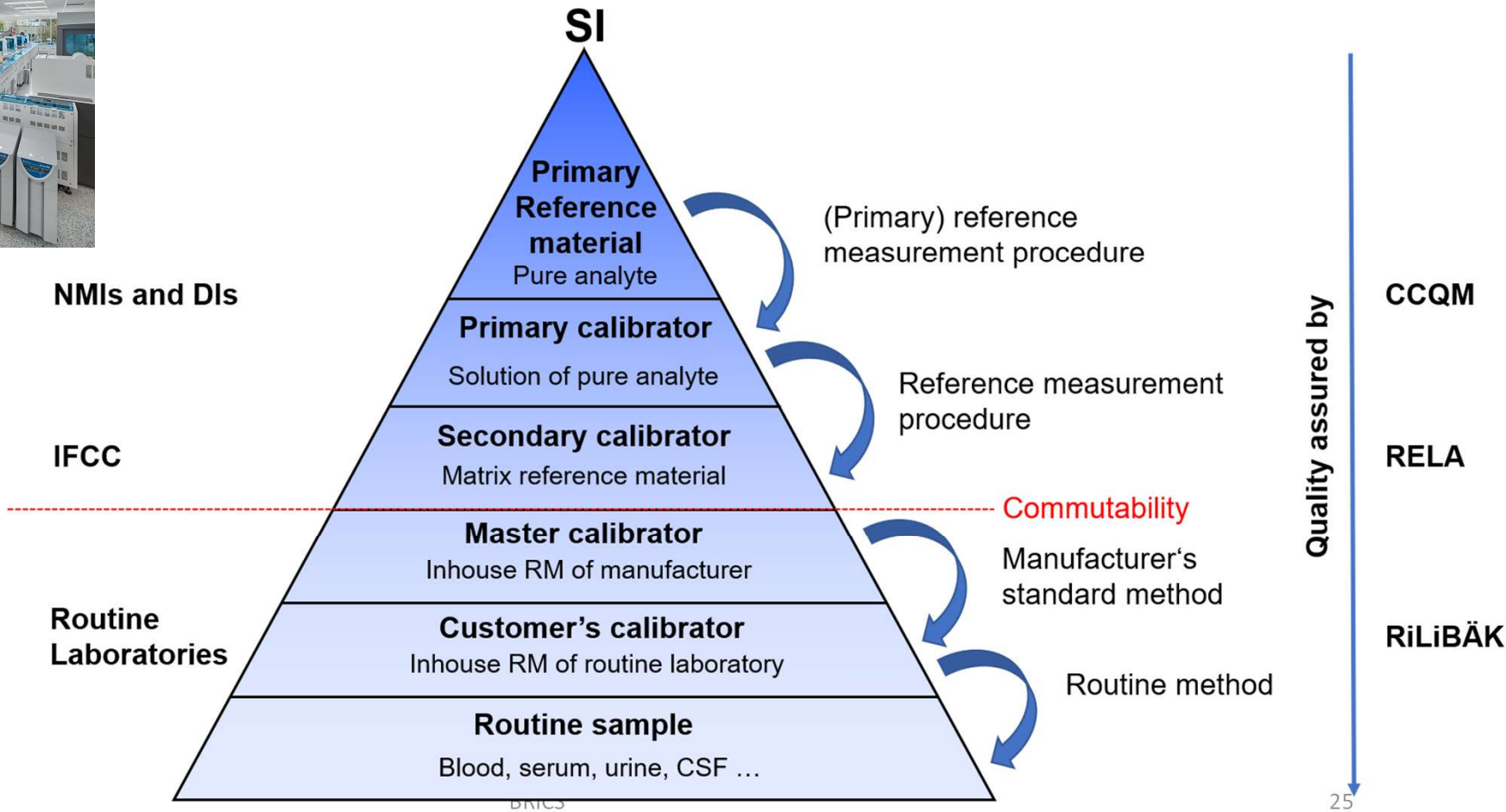
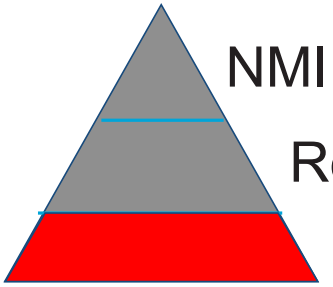


PTB

KS2/22 Creatinine in Serum



NMI

Ref lab

Clinical lab

All results

Kit 4

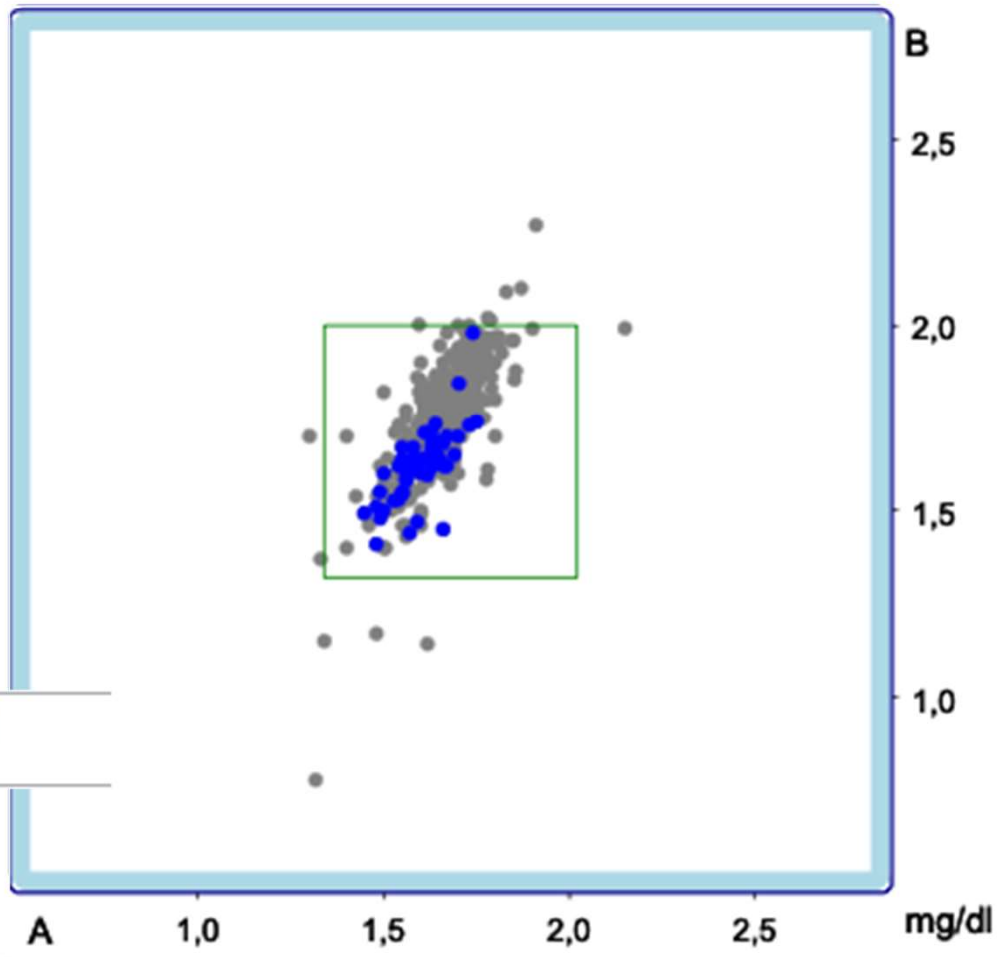
Kit 38

RfB Referenzinstitut für Bioanalytik

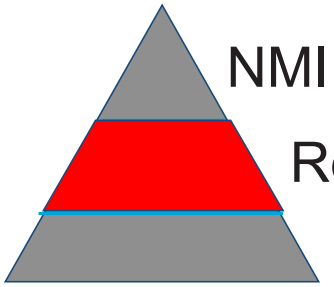
REFERENZINSTITUT FÜR BIOANALYTIK
Ringversuche - Referenzlaboratorien

56	Kreatinin	11,5 %	0,5 44	10 884	mg/dl µmol/l	20,0 %	RMW

https://www.rfb.bio

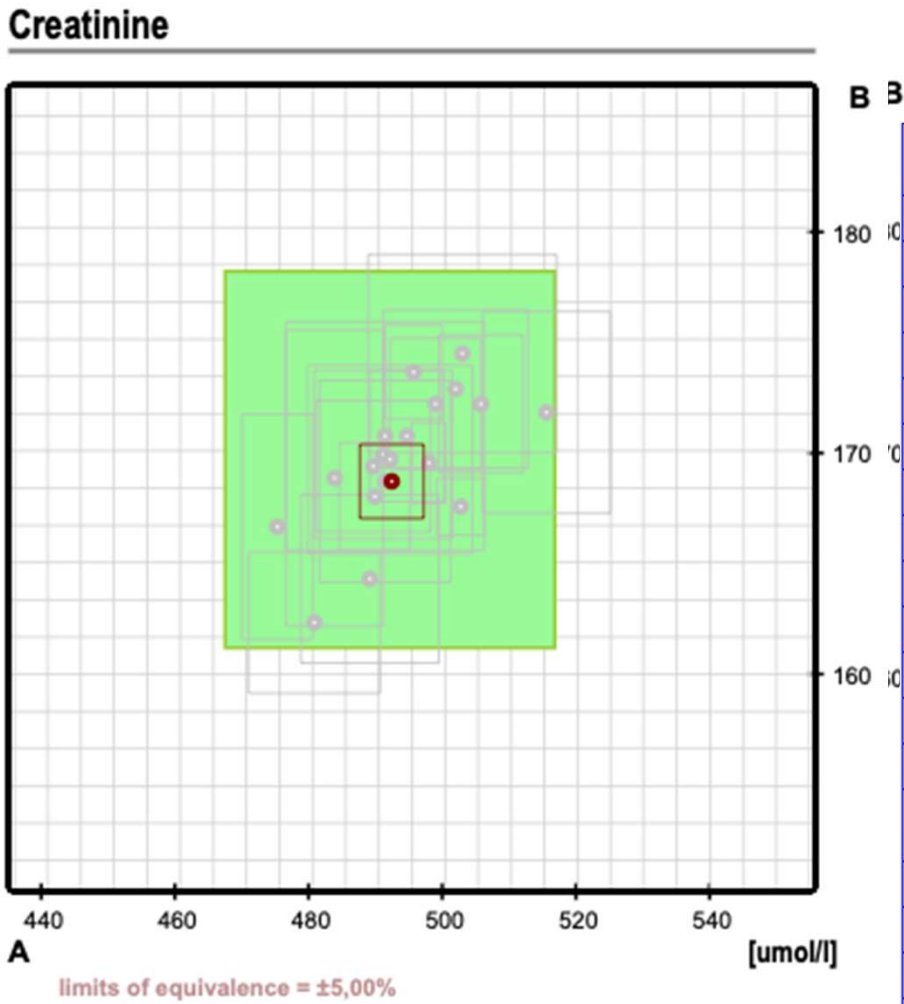


number of results		63	
rate		100%	
target value	1.68		1.66
limits	1.34 - 2.02		1.32 - 2
mean	1.602		1.626
standarddeviation	0.067		0.093
coefficient of variation	4.161		5.689



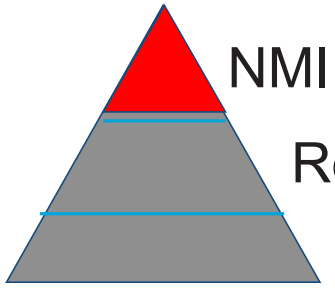
http://www.dgkl-rfb.de

RELA Results 2022

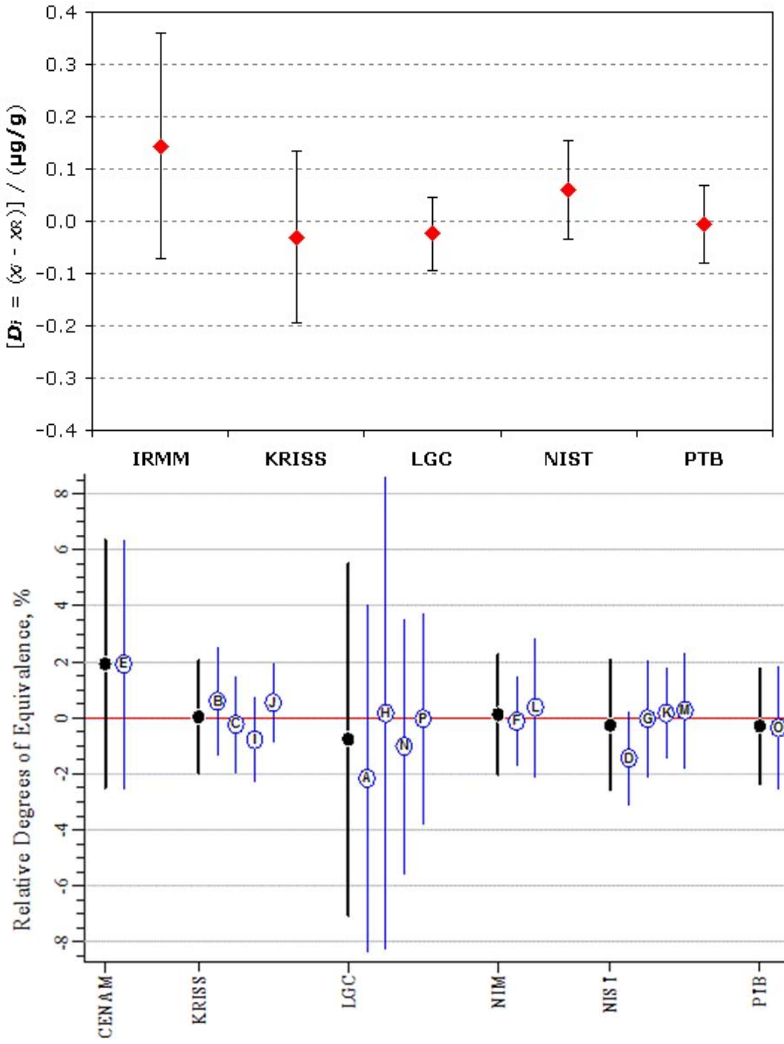


Labcode	A	e.u. A	B	e.u. B	Method
1	**489.9**	**5.3**	**168**	**2.4**	**ID/GC/MS**
12	475.3	5.39	166.7	5.13	spectrophotometry
25	**489.7**	**8.48**	**169.4**	**2.93**	**ID/GC/MS**
27	**492.4**	**4.9**	**168.7**	**1.7**	**ID/GC/MS**
51	**499**	**6.8**	**172.2**	**3**	**ID/LC/MS/MS**
54	**502.1**	**10.82**	**172.9**	**3.57**	**ID/LC/MS/MS**
61	491.5	14.8	170.8	5.2	ID/LC/MS/MS
63	491.4	9.8	168.7	4.6	spectrophotometry
87	494.8	5.6	170.8	3	spectrophotometry
98	503	14	174.5	4.5	ID/LC/MS
104	497.9	2.5	169.5	1.8	ID/LC/MS/MS
124	495.7	4.3	173.7	2.1	spectrophotometry
138	489.1	10.3	164.3	3.8	ID/LC/MS/MS
139	483.8	7.3	168.9	6.7	spectrophotometry (Doumas)
143	515.6	9.5	171.8	4.6	spectrophotometry
151	491.3	10.2	169.9	3.8	ID/LC/MS/MS
153	492.2	12.31	169.7	4.24	spectrophotometry
160	**481**	**9.9**	**162.3**	**3.2**	**spectrophotometry**
175	505.8	6.2	172.2	3.1	spectrophotometry
177	502.7	3.49	167.6	1.27	spectrophotometry

NMI activities for clinical metabolites



- **Current CCQM Key studies**
- Only 8 measurands in serum and urine
- Only 35 Priority measurands in serum from ICHCLR & Rili BÄK



Comparison of CRMs for metabolite in serum

PTB Dissemination of Traceability

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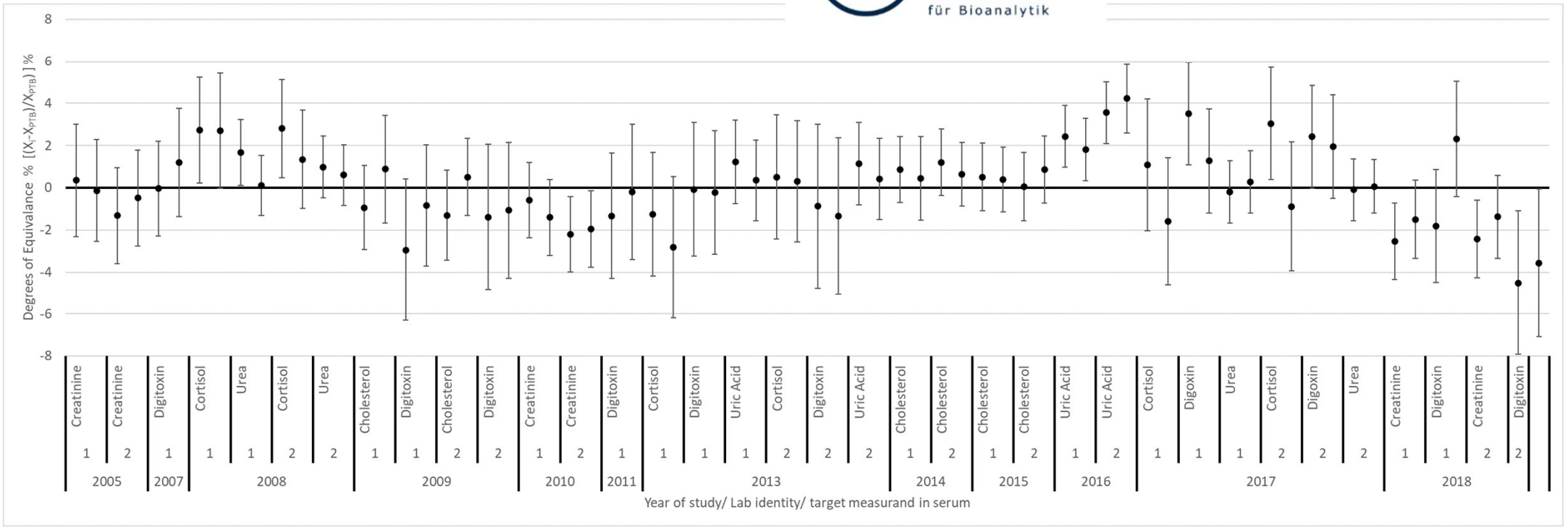
German Reference labs
v's
PTB

INSTAND

RfB Referenzinstitut für Bioanalytik



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v's
rest of world