



Traceability in laboratory medicine: why is it important?

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On behalf of the Joint Committee for Traceability in Laboratory Medicine

Outline

- Background
- Traceability in laboratory medicine
- JCTLM
- Example
- Relevance to EQALM



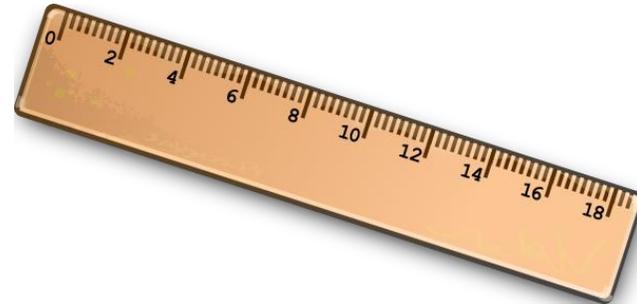
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Everyday examples of traceable measurements

Weight (mass)



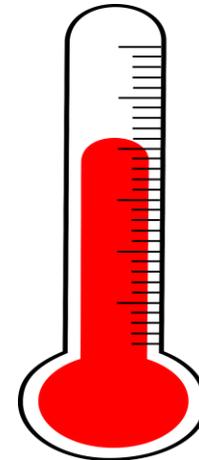
Length



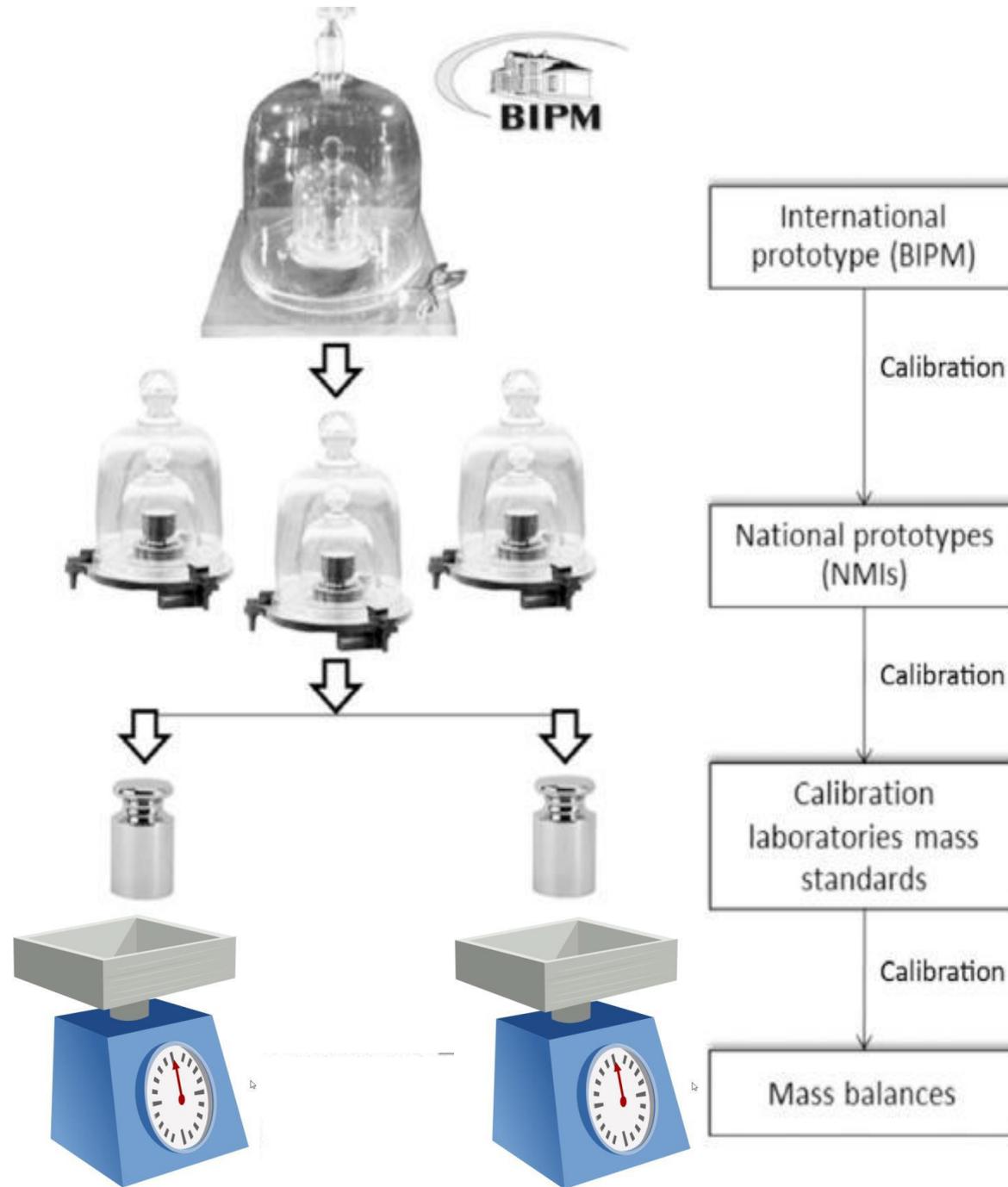
Time



Temperature



“The Kilogram” BIPM, Paris



**Traceable
results are
comparable**

Local weights and measures: Falkirk, Scotland



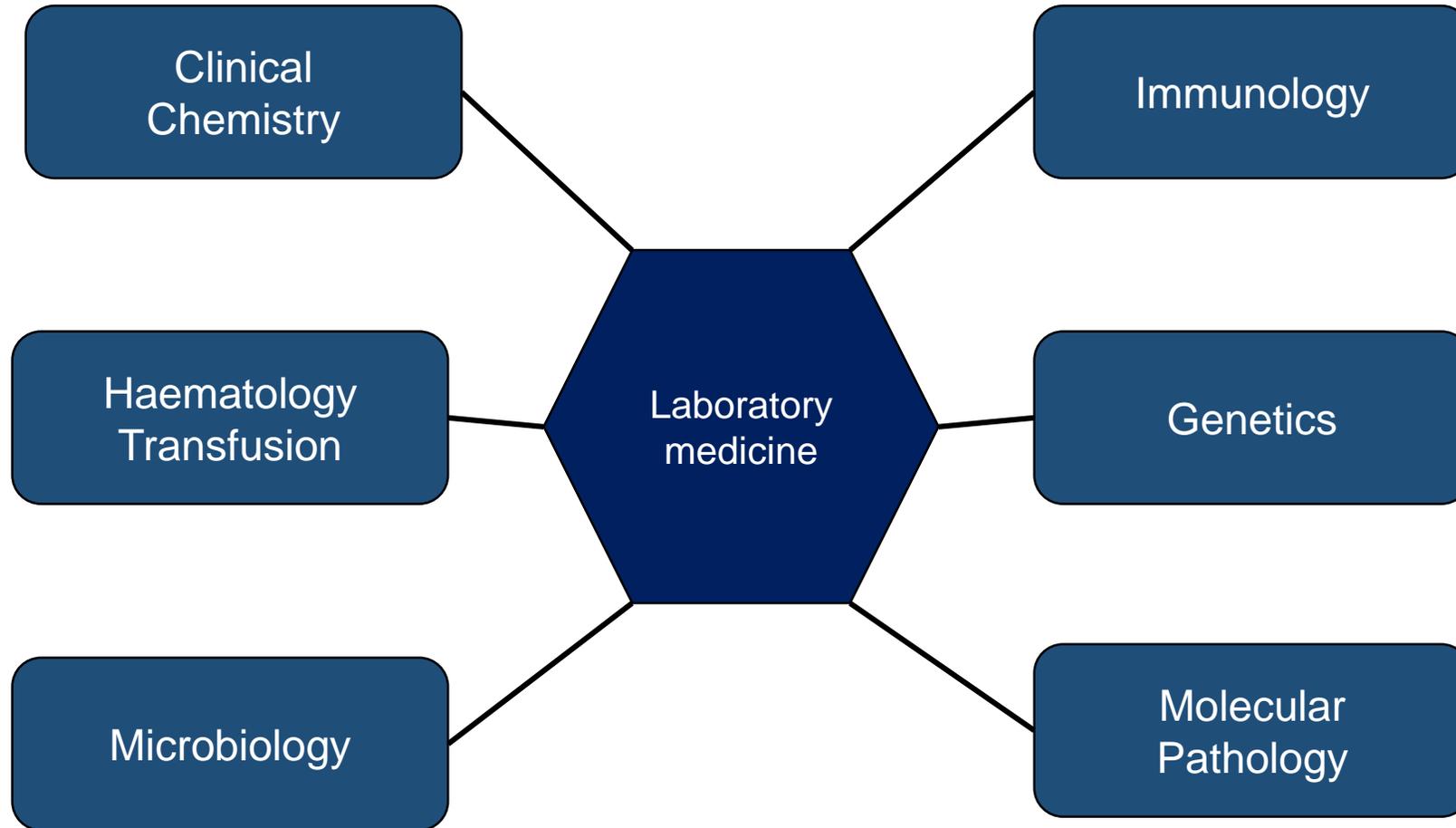
Systeme Internationale (SI) units



Mass	kilogram	kg
Length	metre	m
Time	second	s
Electric current	Ampere	A
Temperature	Kelvin	K
Amount of substance	mole	mol
Luminosity	candela	cd

SI units underpin our scientific, manufacturing & technological civilisation

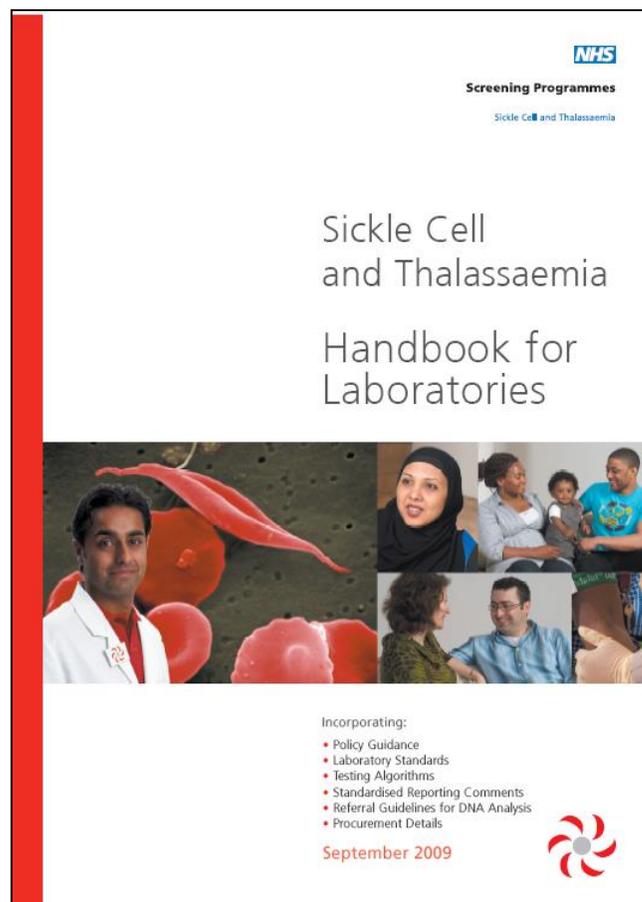
So what about laboratory medicine?



Patients assume and expect that all methods will give the same result for a single test!

HbA2 and clinical practice guidelines

Many clinical practice guidelines exist for thalassaemia that link diagnosis to target HbA2 levels.



For example UK NHS sickle cell and thalassaemia screening programme:

“A national recommended cut-off for HbA2 of 3.5% has been set as the action point in the diagnosis of carriers of beta thalassaemia.”

Current HbA2 EQA performance

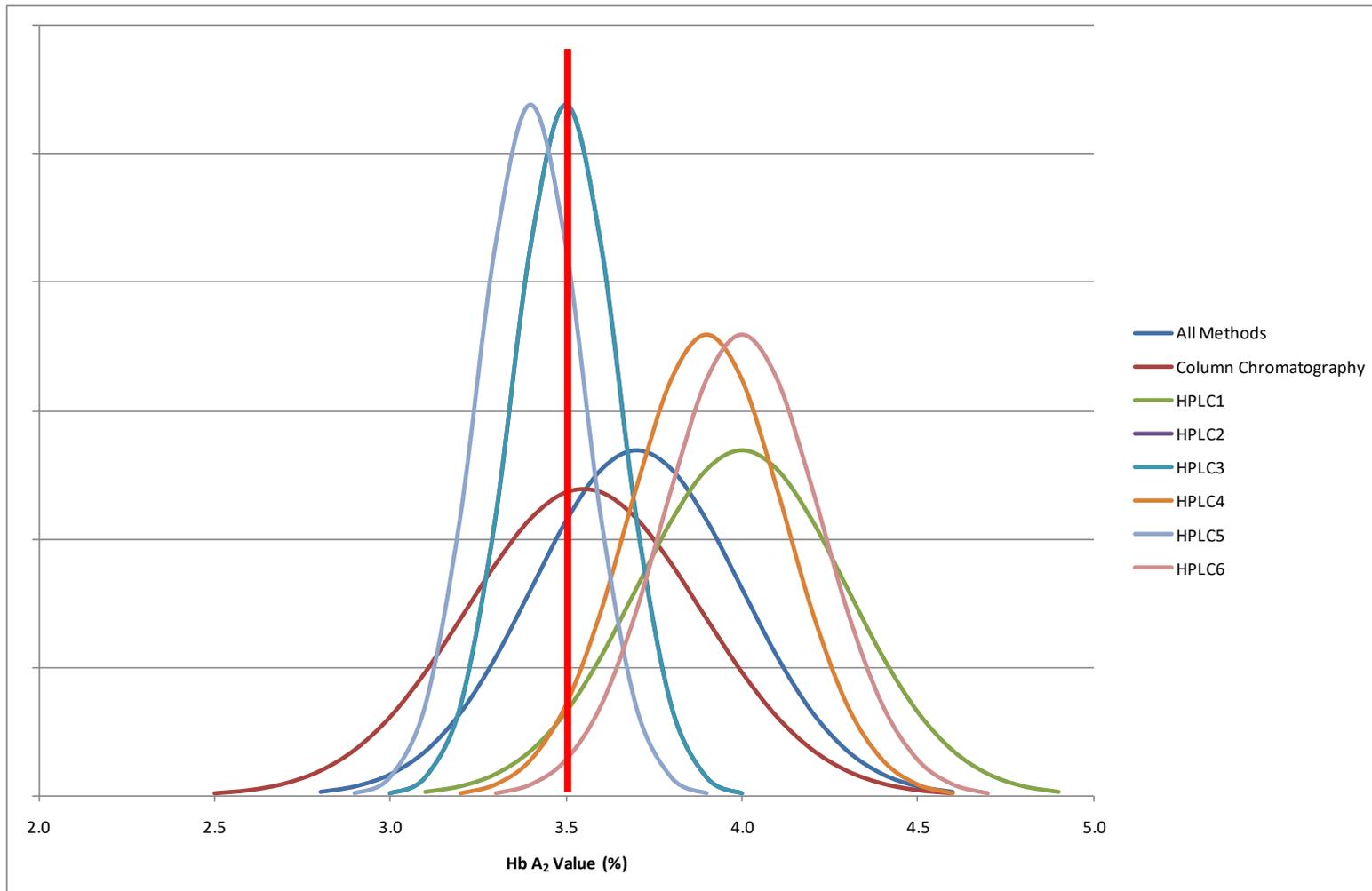
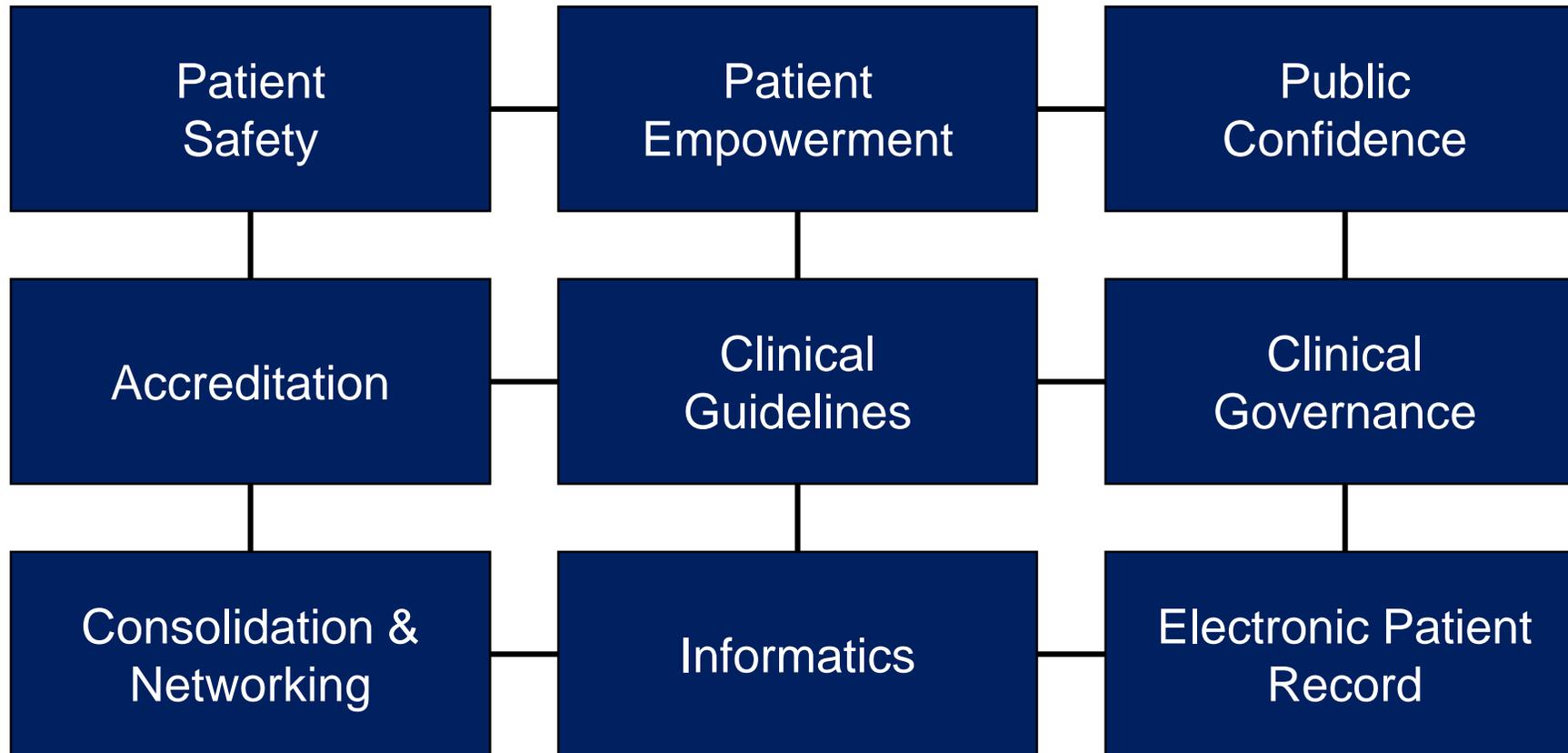
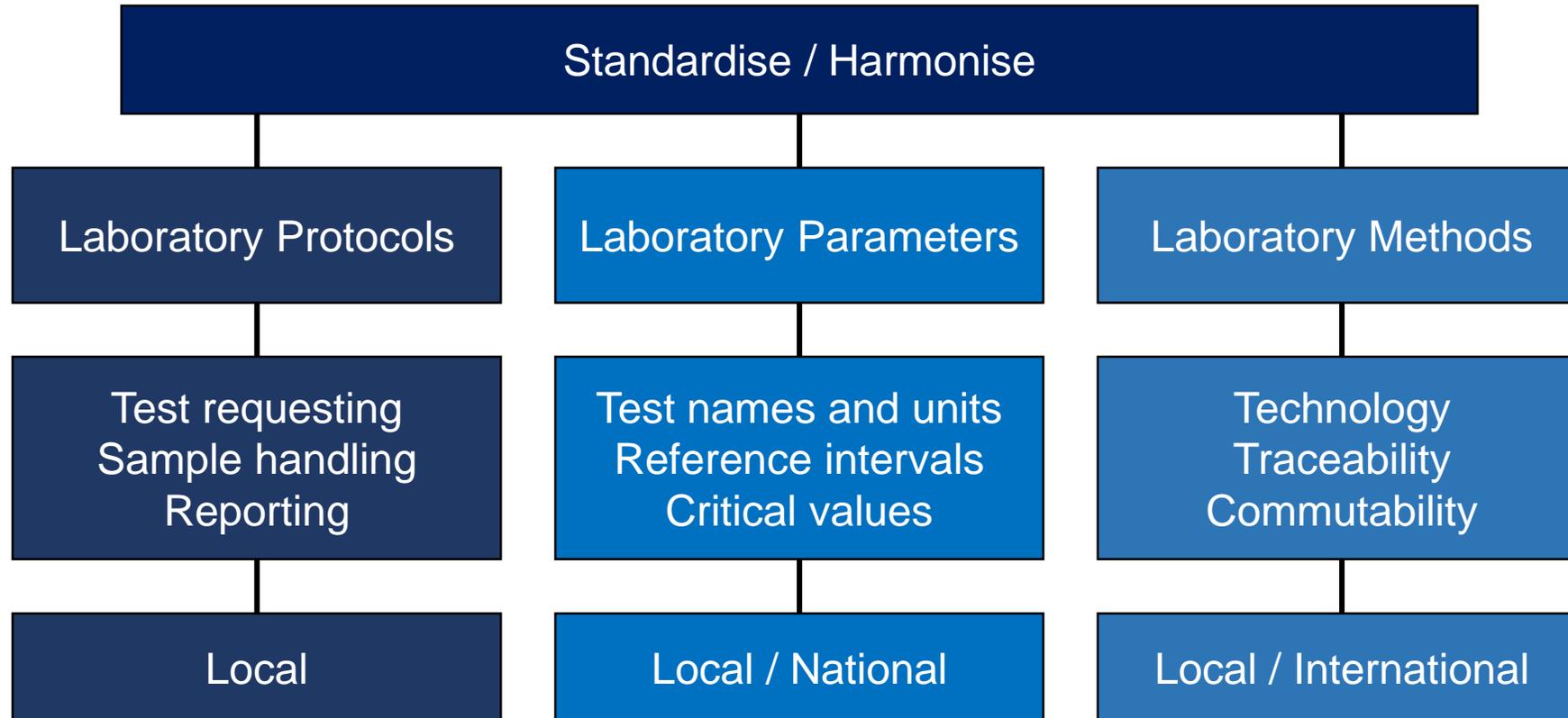


Figure from UK NEQAS with permission

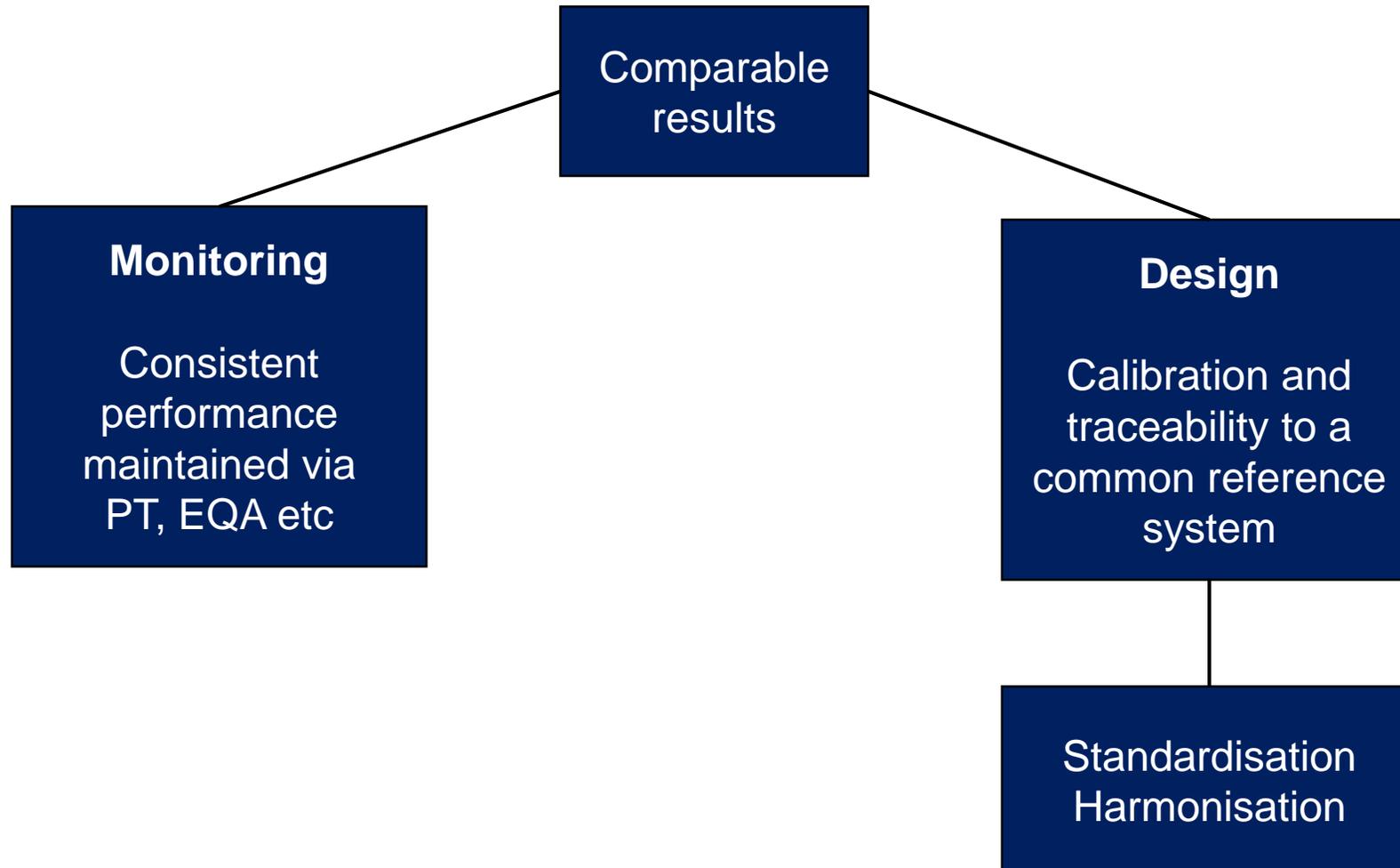
Why should different methods give the same result?



What can we standardise / harmonise in laboratory medicine?



Reducing between method variability



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What is traceability in laboratory medicine?

- Metrological traceability is the property of a measurement result, which can be related to a **reference** through a documented unbroken chain of **calibrations**, each contributing to the **measurement uncertainty**
- Traceability requires both (certified) reference materials and the reference measurement procedures (methods) in which they are used
- For structurally simple measurands (analytes) it is possible to get pure substance primary reference materials . For more complex measurands pure substance may not be available
- Primary reference measurement procedures are based on physical methods (e.g. ID-MS)

Reference materials (calibrators)

- Primary reference material (pure substance)
- Primary calibrator (SI traceable)
- Secondary calibrator
- Product calibrator

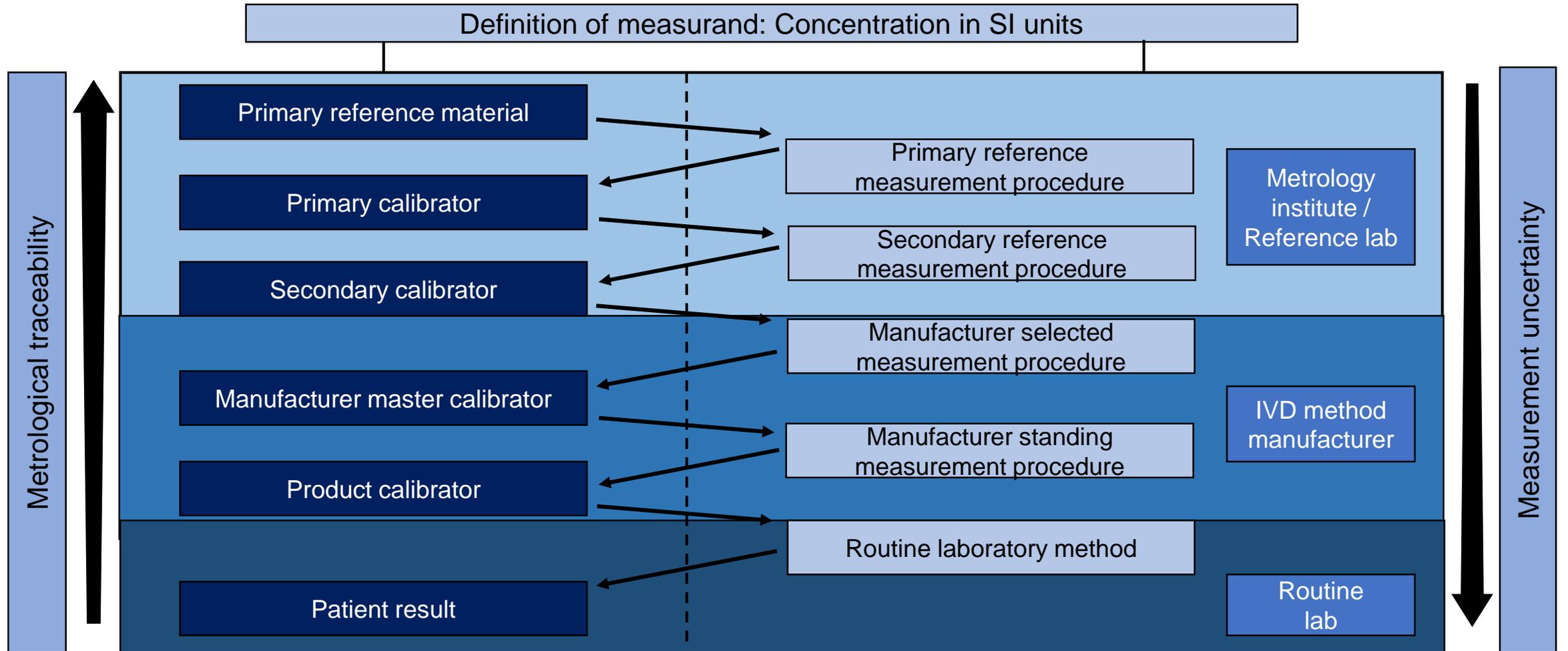


Reference measurement procedures

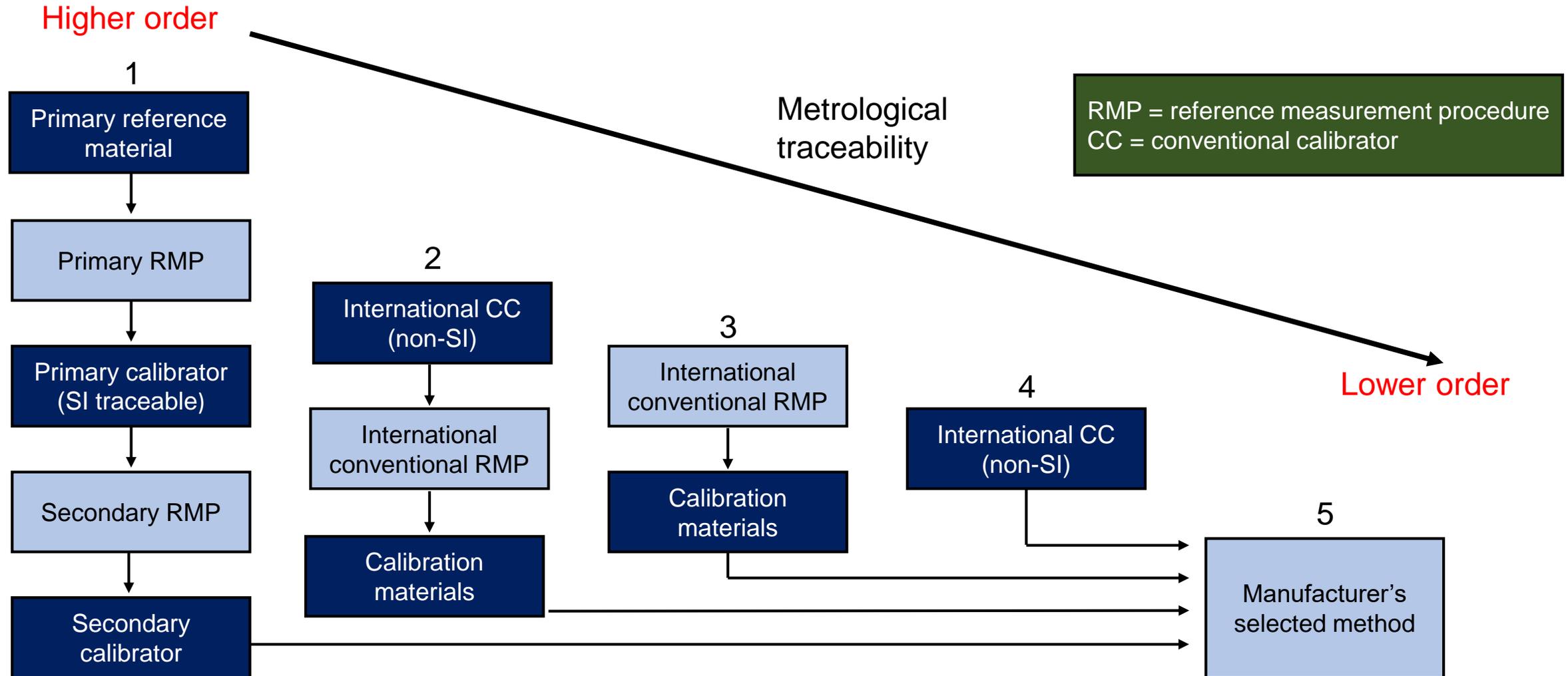
- Primary reference measurement procedure
- Secondary reference measurement procedure
- Manufacturer selected procedure
- Routine laboratory procedure

Hierarchy

The metrological traceability chain



'Higher order' materials and procedures



Requirements for traceability in laboratory medicine

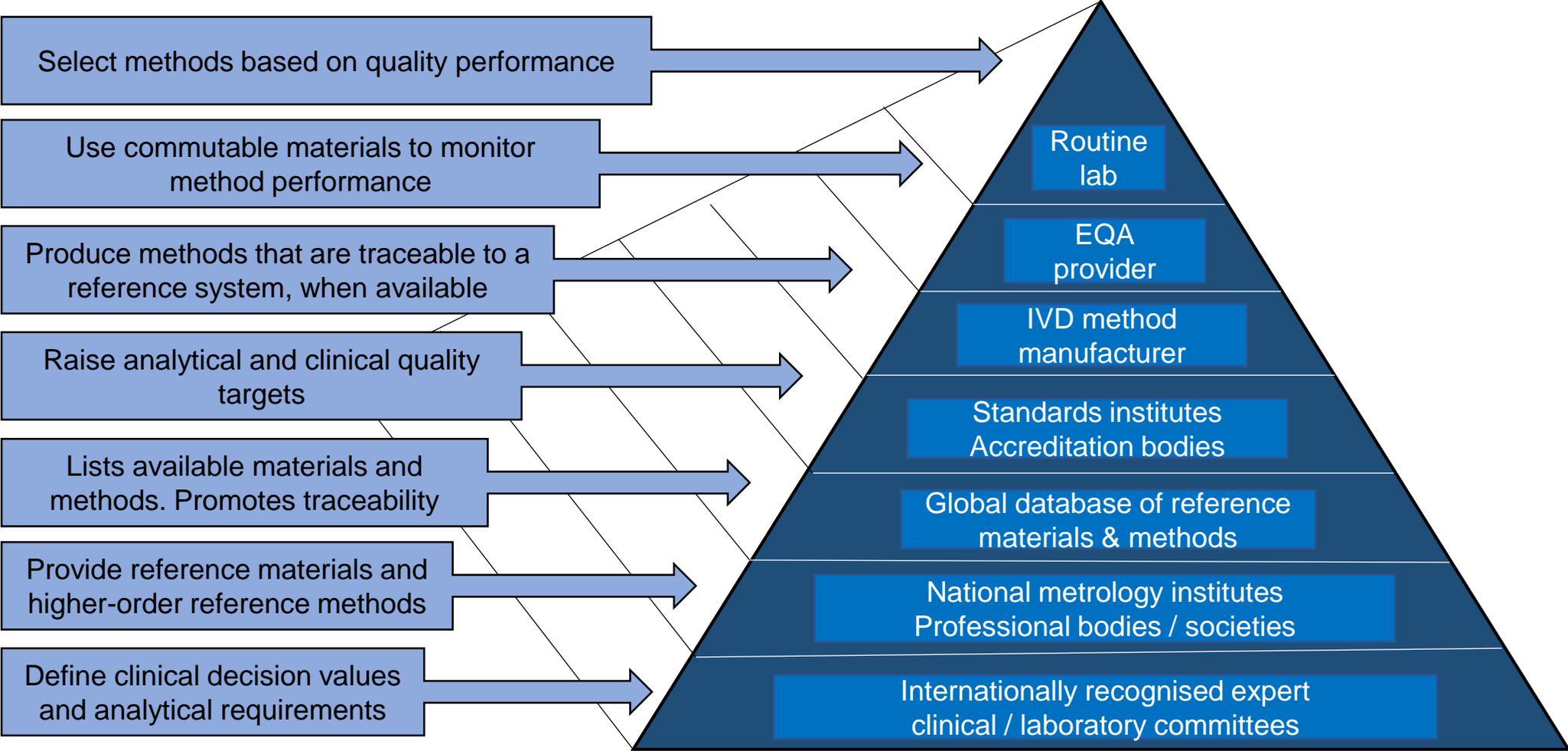
European Union In-Vitro Diagnostic Directive (IVDD): 98/79/EC

“The traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order.. ”

EU In-Vitro Diagnostic Device Regulation (IVDR): EU/2017/746

“9.3. Where the performance of devices depends on the use of calibrators and/or control materials, the metrological traceability of values assigned to calibrators and/or control materials shall be assured through suitable reference measurement procedures and/or suitable reference materials of a higher metrological order”.

Who are the stakeholders in achieving traceability?



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Joint Committee for Traceability in Laboratory Medicine

Formed in 2002 to enable a global response to the IVD Directive



Intergovernmental treaty organisation for measurement standards



International NGO for professionals in laboratory medicine



International NGO for accreditation bodies

Now has 49 members from 19 countries
NMIs, EQA providers, professional bodies, IVD manufacturers



What does JCTLM do?

Maintains a global database of:

- Reference materials
- Reference methods
- Reference laboratories

www.bipm.org/jctlm

Co-ordinates the nomination and review process for database entries

www.bipm.org/jctlm



Contributes to ISO Working Groups on reference systems, which are responsible for global standards

Provides news and freely available resources on traceability in laboratory medicine:

- Webinars; publication lists

www.jctlm.org

Hosts a biennial scientific meeting

JCTLM Database : www.bipm.org/jctlm/



Bureau International des Poids et Mesures

Database of higher-order reference materials,
measurement methods/procedures and services



JCTLM Database
Laboratory medicine and *in vitro* diagnostics

> You are here : JCTLM-DB



JCTLM database: Laboratory medicine and *in vitro* diagnostics

JCTLM-DB

- ➔ [Search Form](#)
- ➔ [General information](#)
- ➔ [List of reference materials no longer listed](#)
- ➔ [Leaflet](#)
- ➔ [Contact us](#)

Highlights

- ➔ [Extension of the JCTLM-DB](#)
- ➔ [Publication of new data](#)

JCTLM

- ➔ [General information](#)

Analyte keyword search for reference materials, measurement methods/procedures and services

Type an analyte name in part or full, e.g. cholesterol

Refine search by analyte category

Refine search by matrix category

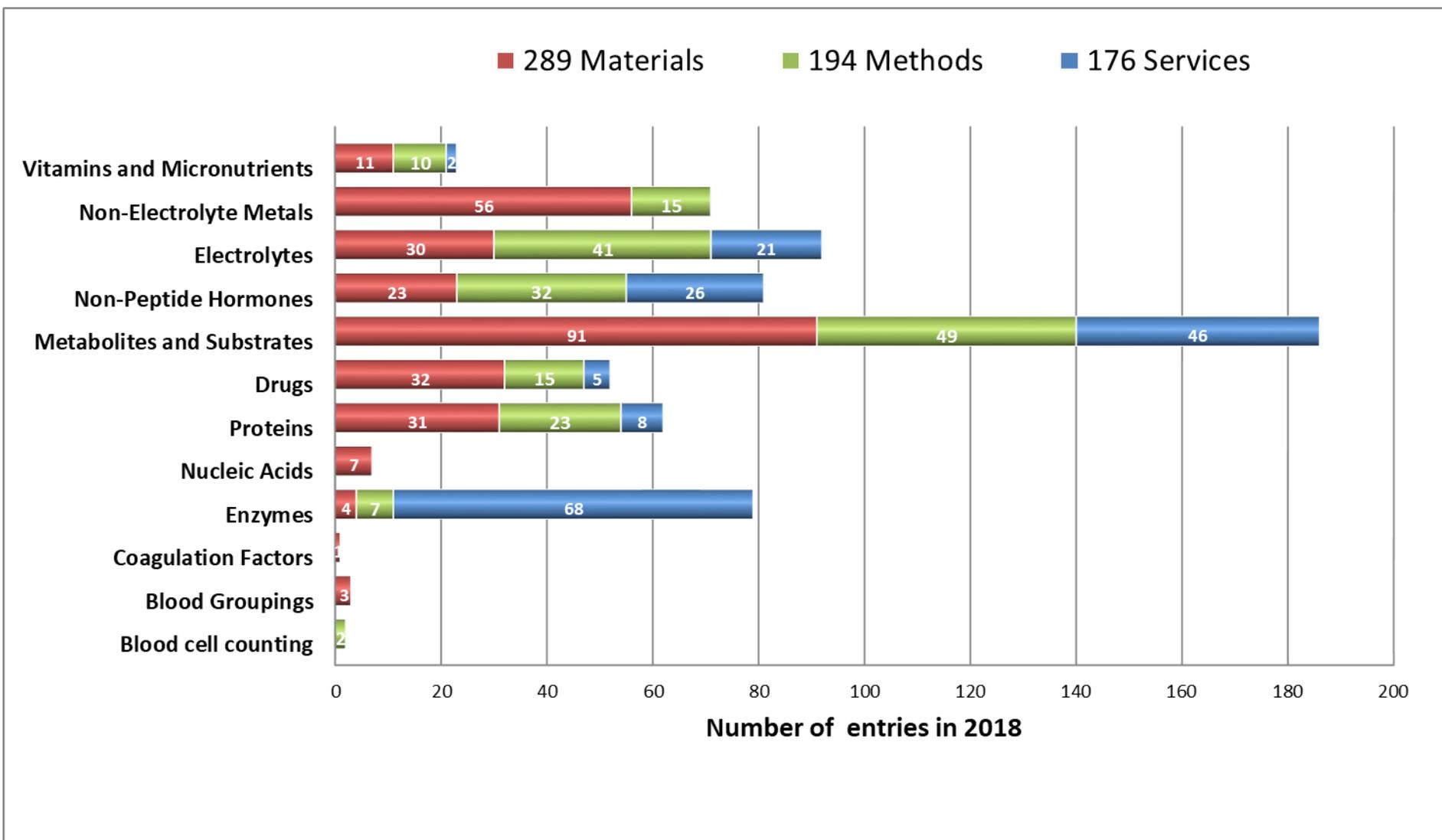
Please select your requirement :

- Higher-order reference materials
- Reference measurement methods/procedures
- Reference measurement services

Reset

Search

JCTLM database entries: October 2018



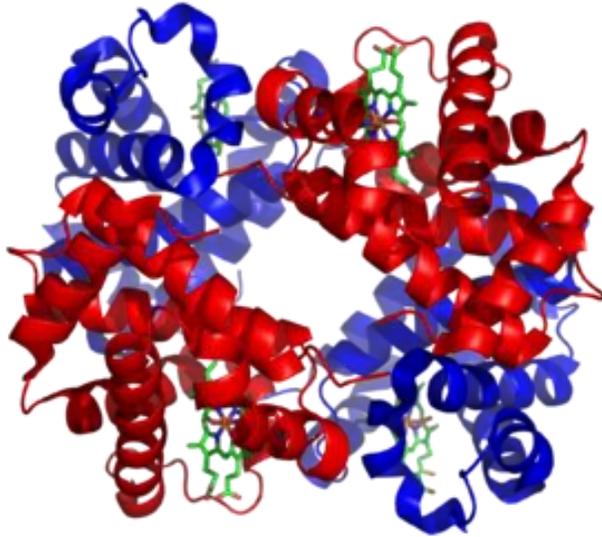
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Case study: haemoglobin A_{1c} (HbA_{1c})



Established from major clinical trials as key analyte for long-term monitoring of diabetes

Method improvement following IFCC standardisation [Ref 1]

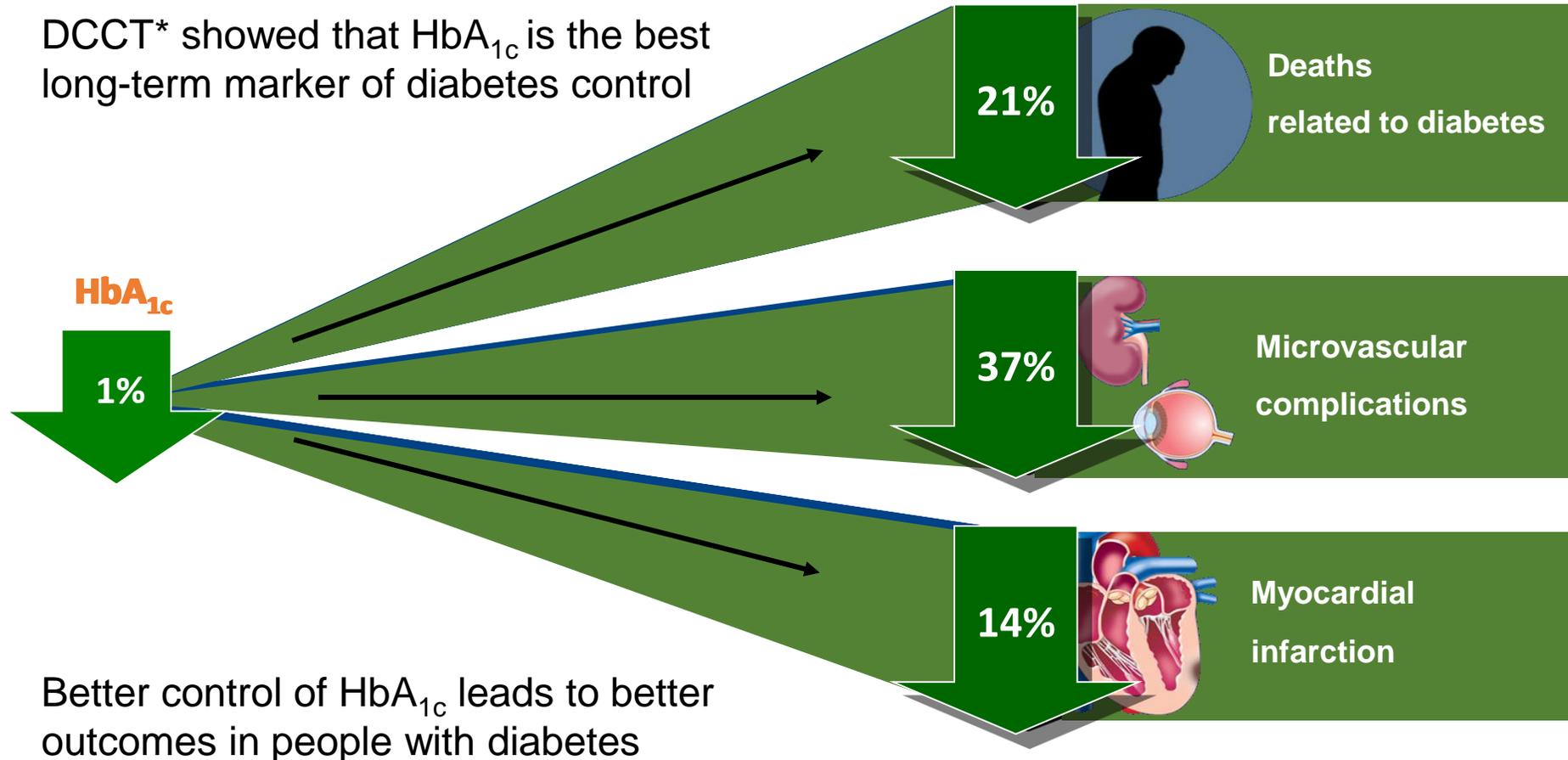
IFCC reference laboratory network established [Ref 2]

Many laboratory and POCT methods available

1. Hoelzel W *et al.* IFCC Reference System for Measurement of Hemoglobin A1c in human blood and the national standardization schemes in the United States, Japan and Sweden: a method comparison study. *Clin Chem* 2004; 50: 166-174
2. IFCC network laboratories for HbA1c www.ifcchba1c.net

Why is HbA_{1c} so important?

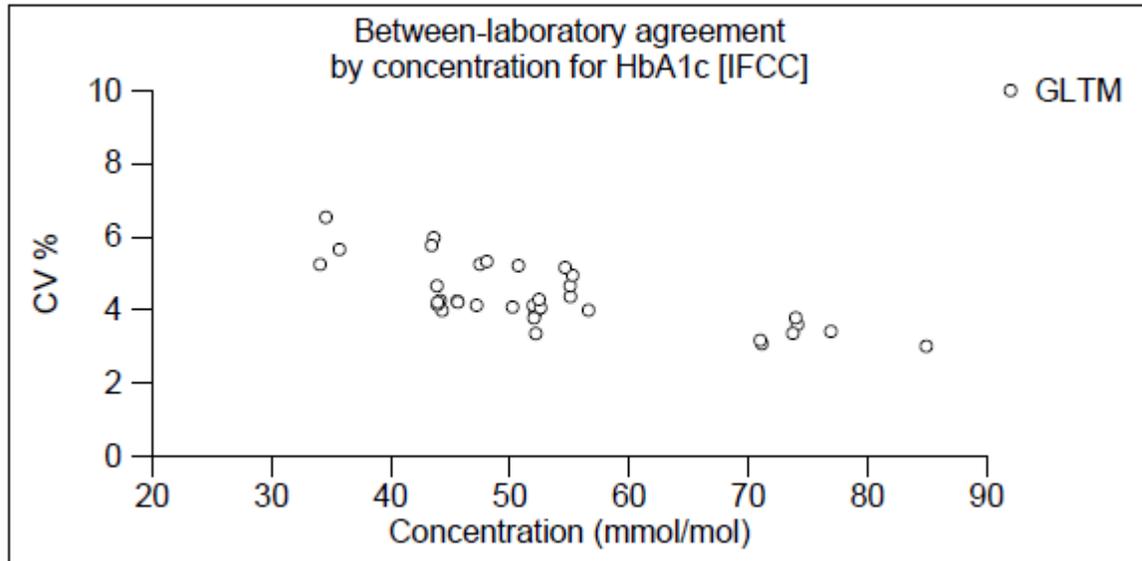
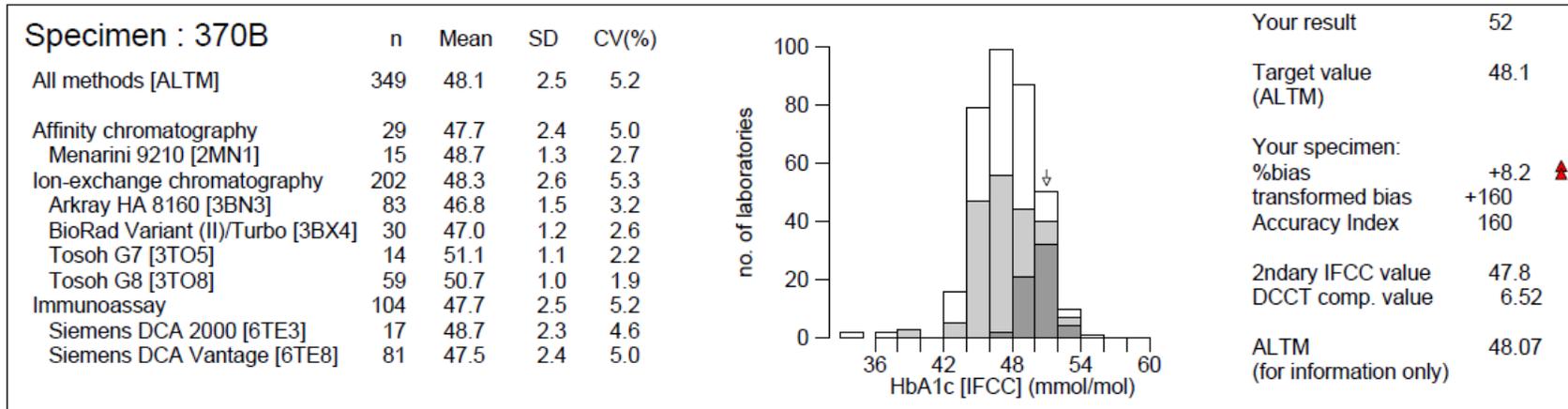
DCCT* showed that HbA_{1c} is the best long-term marker of diabetes control



Better control of HbA_{1c} leads to better outcomes in people with diabetes

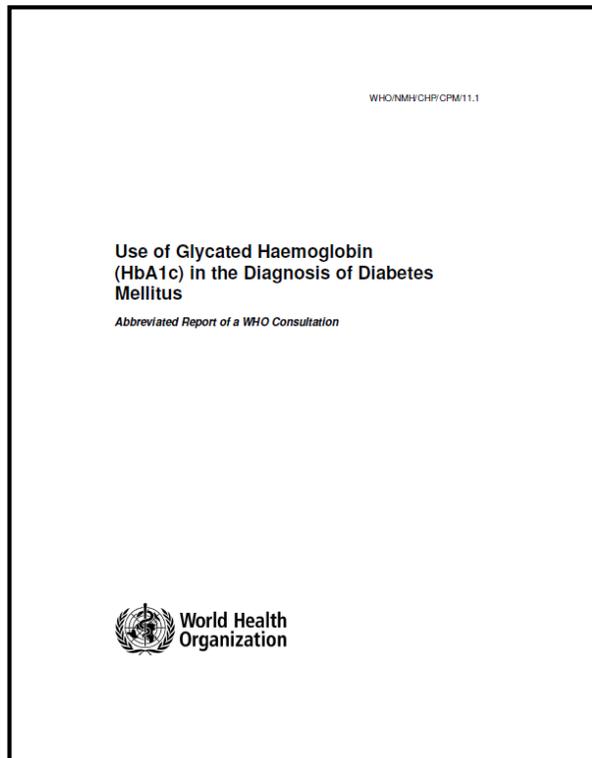
* DCCT = Diabetes Control and Complications Trial

HbA1c: typical current EQA



HbA1c as a diagnostic test for diabetes

- Many clinical practice guidelines exist that link monitoring of diabetic control to target HbA1c levels.
- WHO guidelines for HbA1c in diagnosis of diabetes



WHO Guideline 2011

“HbA1c can be used as a diagnostic test for diabetes providing that stringent quality assurance tests are in place and assays are standardised to criteria aligned to international values, and there are no conditions present which preclude its accurate measurement.

An HbA1c of 48mmol/mol (6.5%) is recommended as the cut point for diagnosing diabetes. A value of <48mmol/mol does not exclude diabetes diagnosed using glucose tests.”

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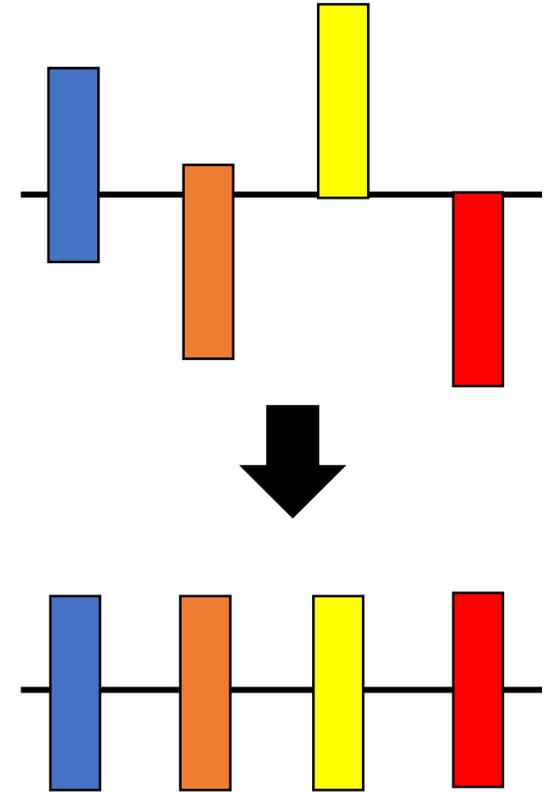
Facing the challenge



The world population of



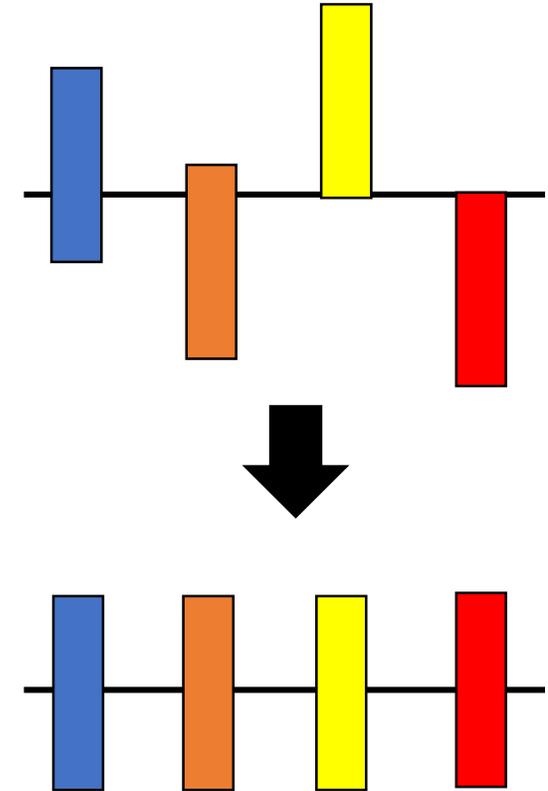
7.7 billion people



is entitled to believe that all methods will give the same result on their specimen

What can EQA achieve?

- EQA is an essential and effective tool to reduce between method variability
- In addition to its proficiency testing role EQA has an important educational role with users and IVD method manufacturers
- Wherever possible EQA specimens should perform like fresh patient specimens (commutable EQA)
- However, EQA alone may not be sufficient to harmonise patient results from different methods:
 - Different measurands
 - Different reference materials
 - Different measurement procedures (e.g. antibodies)
- EQA organisers have a vital role in highlighting analytes with high between method variability that may benefit from an international standardisation / harmonisation initiative



Possible roles for EQALM

Possible Projects

Project 1

Review clinically important analytes where EQA performance is poor and identify candidates for method harmonisation (www.harmonization.net)

Project 2

- Lead / support a project to explore relationship of EQA performance to method traceability
- Outcome
 - Review article
 - Presentation at international meeting
 - Freely available webinar

Publicity and Promotion

Working with JCTLM

- Encourage EQA organisers to include a session on TLM in their user group meetings
- Distribute news and educational material on traceability in laboratory medicine (TLM) to participants and manufacturers
- Highlight methods where performance is improving as a result of EQA leadership
- Promote www.jctlm.org to participants and manufacturers