Standardization and Harmonization in Laboratory Medicine

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Acknowledgements:

- IFCC Scientific Division Executive Committee
- Dr Greg Miller, Virginia Commonwealth University Richmond, Virginia, USA
- Australasian Association of Clinical Biochemists Harmonization Working Group

Overview:

- The lack of comparability of patient results is a major issue for laboratory medicine
- Standardization and harmonization - what are the differences?
- Why do we need commutability?
- What are the international efforts being undertaken to improve harmonization?

Why do we need comparable results?

- Clinical practice guidelines are established to provide optimal clinical treatment

- They often include the use of laboratory test results to guide clinical practice – even when the different clinical assays provide different patient results

Examples of variation of immunoassays currently used for clinical decision limits included in clinical guidelines

Analyte	Reference Level Standard	CV%	Range	
Troponin I (ng/L)	SRM	51.4	34.3	23 – 90
HbA1c (mmol/mol)	RMP	49.9	3.6	40 – 55
GH (µg/L)	IS	0.58	12.0	0.24-0.9
PTH (pmol/L)	IS	10.8	21	6.6-11.9
hCG (U/L)	IS	5.1	14.9	2.0-9.0
CA125 (kU/L)	-	71	12.7	52-103

Adapted from Sturgeon CM, Clinica Chimica Acta 2014; 432: 122-126.

Why do we need comparable results?

- Clinical practice guidelines are established to provide optimal clinical treatment
- They often include the use of laboratory test results to guide clinical practice
- If different assays provide different results for the same patient sample clinical practice guidelines become less useful; at best the patient will not receive the optimal treatment, at worst the patient may receive incorrect treatment

Terminology:

- Standardization: Results are uniform among routine clinical measurement procedures

assay traceability is established to a recognised standard reference material defined by International System of Units (SI) providing **uniform results independent of assay technique**

- Harmonization: Results are uniform among routine clinical measurement procedures

no reference measurement procedure or standard reference material exists and uniformity of results are likely to be **dependent on analytical techniques**

Traceability categories from ISO 17511

Category	Reference measurement procedure	Primary (pure substance) reference material	Secondary (value assigned) reference material	Examples
1	Yes	Yes	Possible	Electrolytes, glucose, cortisol
2	Yes	No	Possible	Enzymes
3	Yes	No	No	Hemostatic factors
4	No	No	Yes	Proteins, tumor markers HIV
5	No	No	No	Proteins, EBV, VZV

Traceability categories from ISO 17511

Standardization

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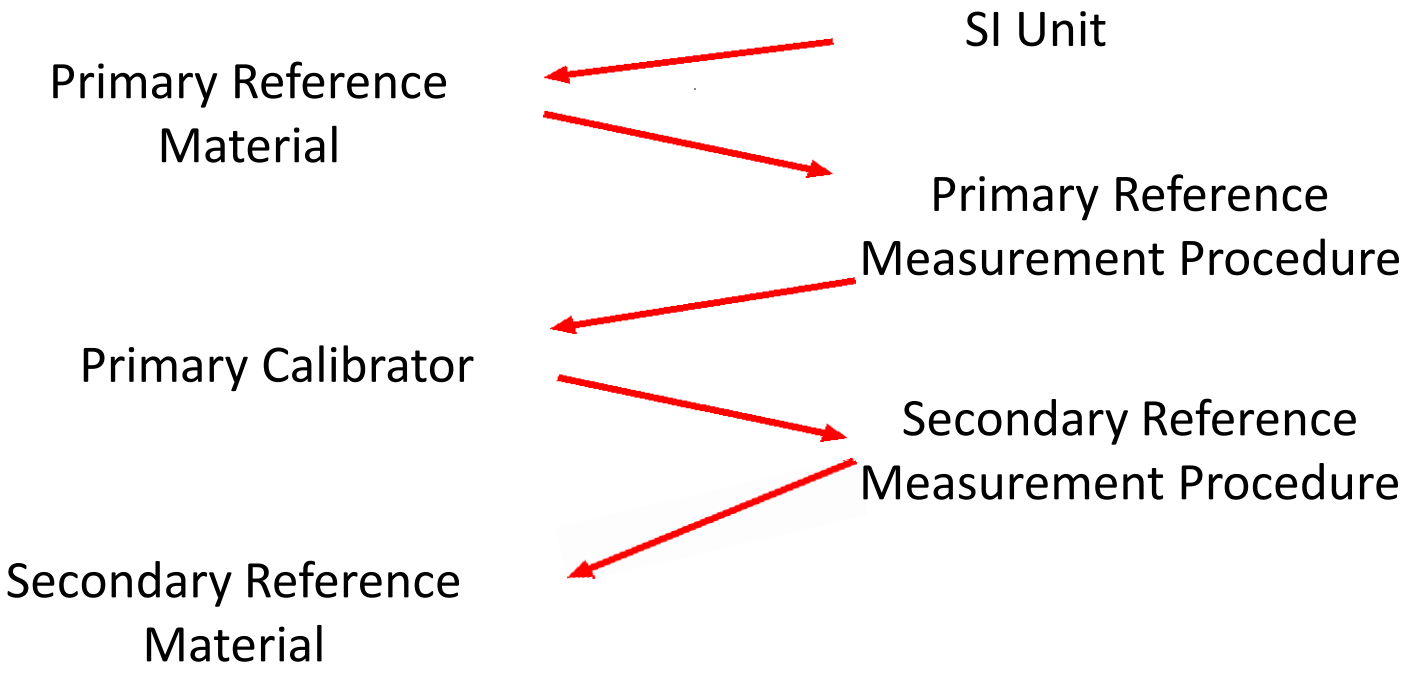
Standardization

Harmonization

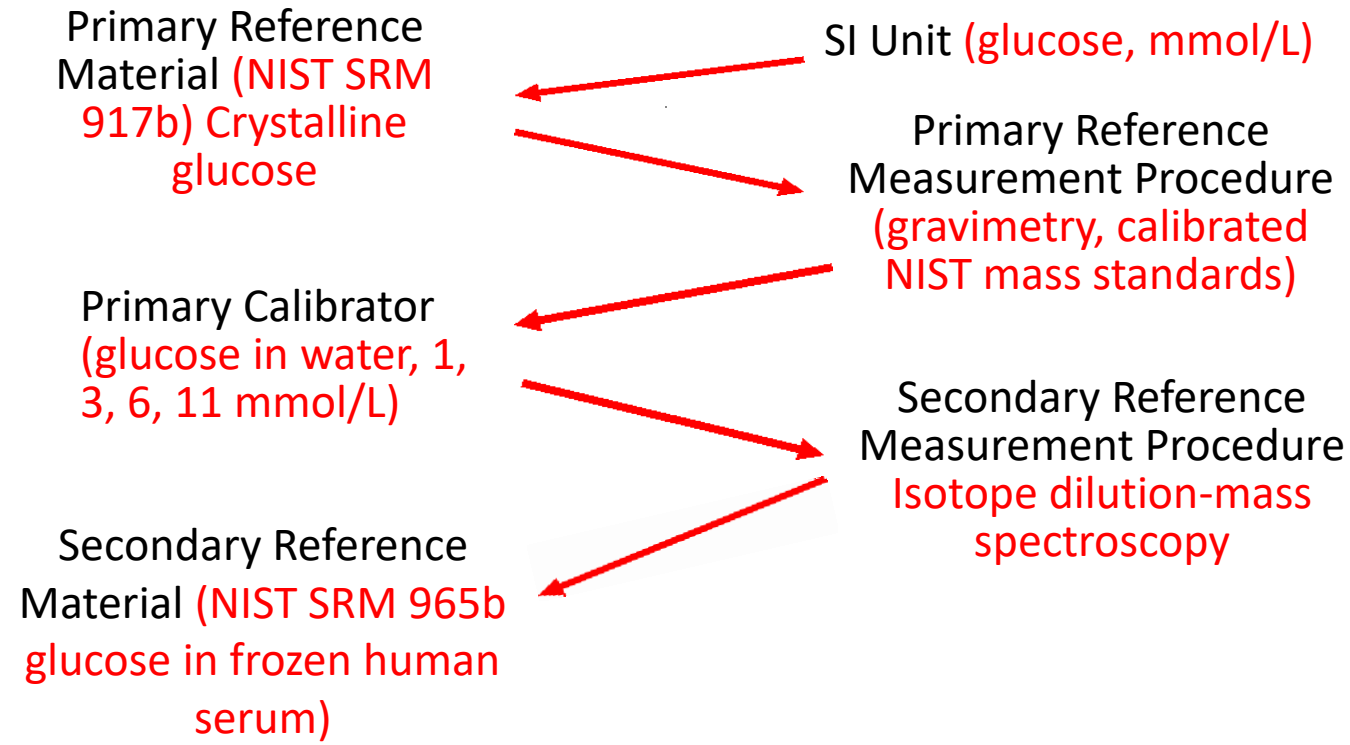
Traceability based on ISO 17511

An ideal reference system

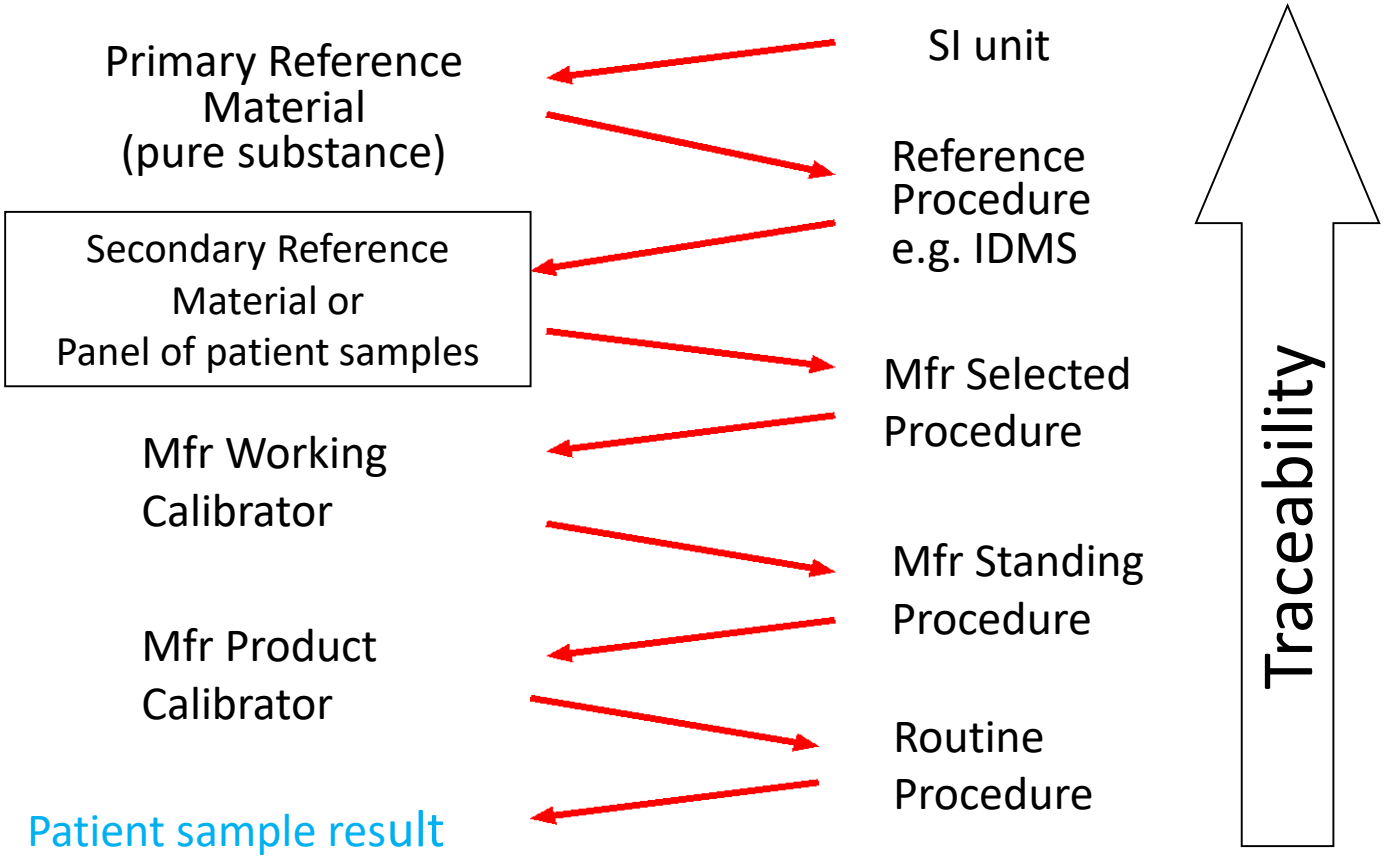


Traceability based on ISO 17511

A reference system for glucose

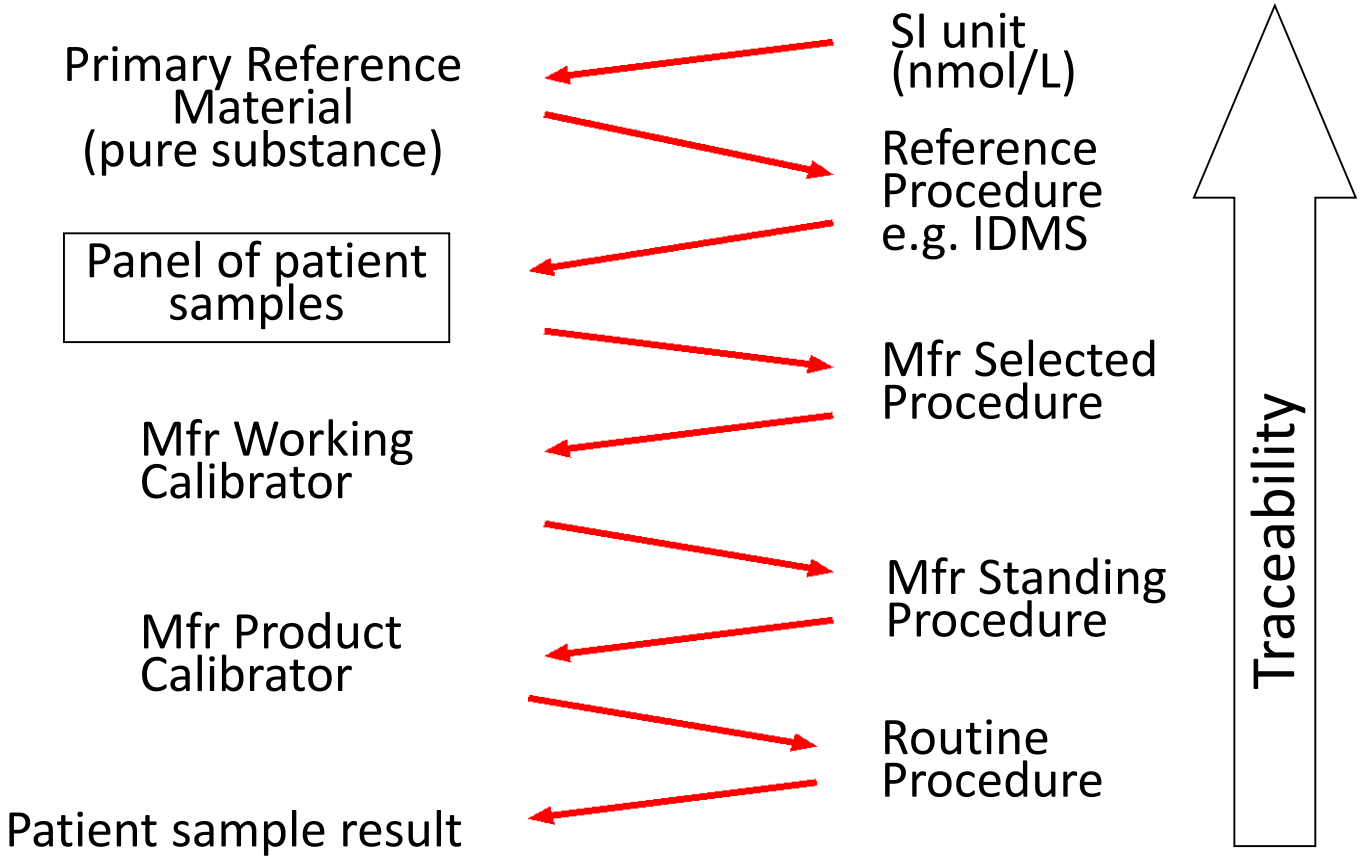


Traceability based on ISO 17511



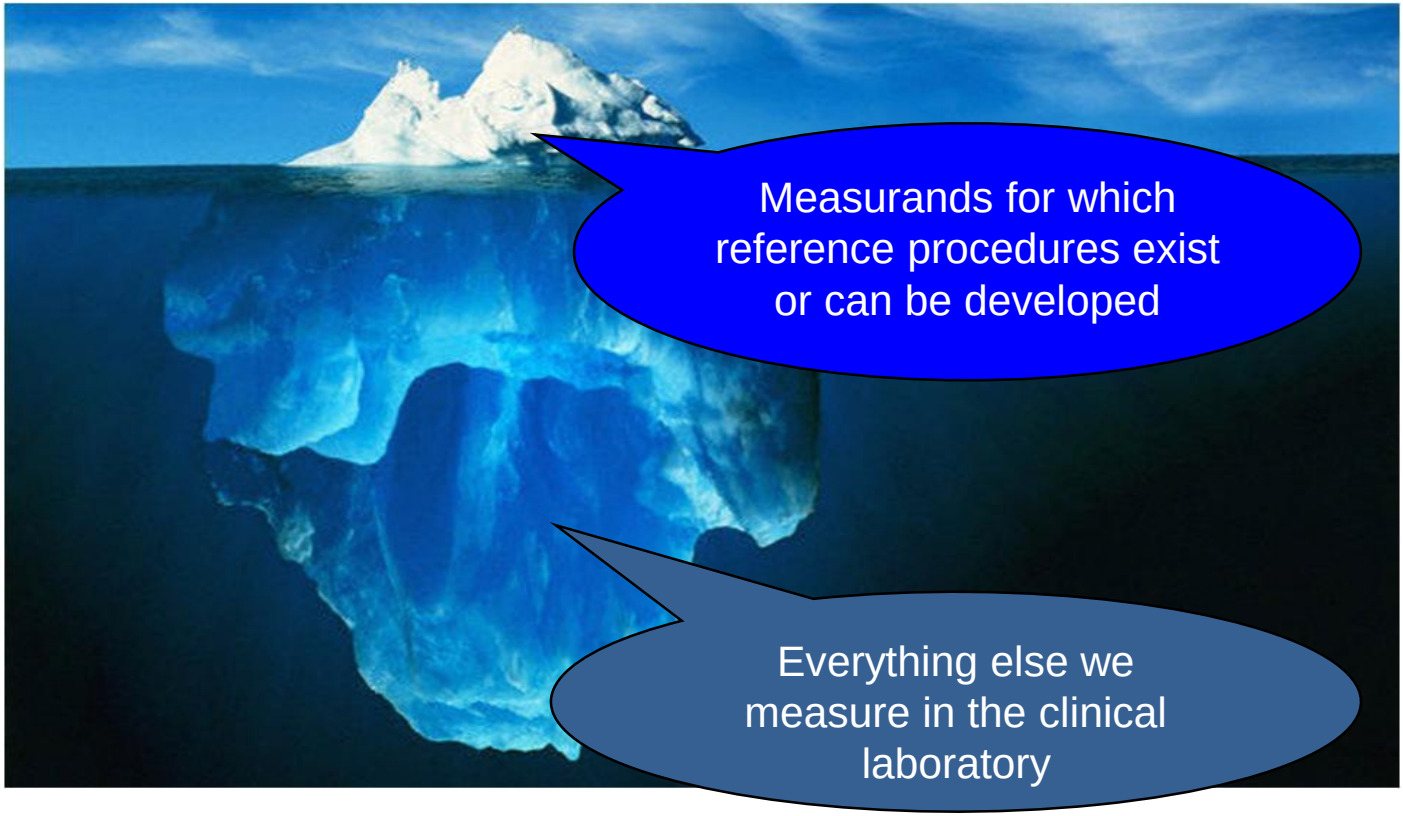
Traceability based on ISO 17511

A reference system for cortisol



www.jctlm.org

A general information portal for global standardization reference materials, reference measurement procedures and networks of accredited reference laboratories


Measurands for which reference procedures exist or can be developed
Everything else we measure in the clinical laboratory

What happens when there is no reference measurement procedure?

Traceable to an international conventional reference material (ISO1751 Category 4)

- The true value is unknown

- Since the goal of harmonization is comparable results irrespective of the measurement procedure used,

- **Clinical guidelines can still be implemented**

Examples of assays traceable to a reference material

Human chorionic gonadotropin

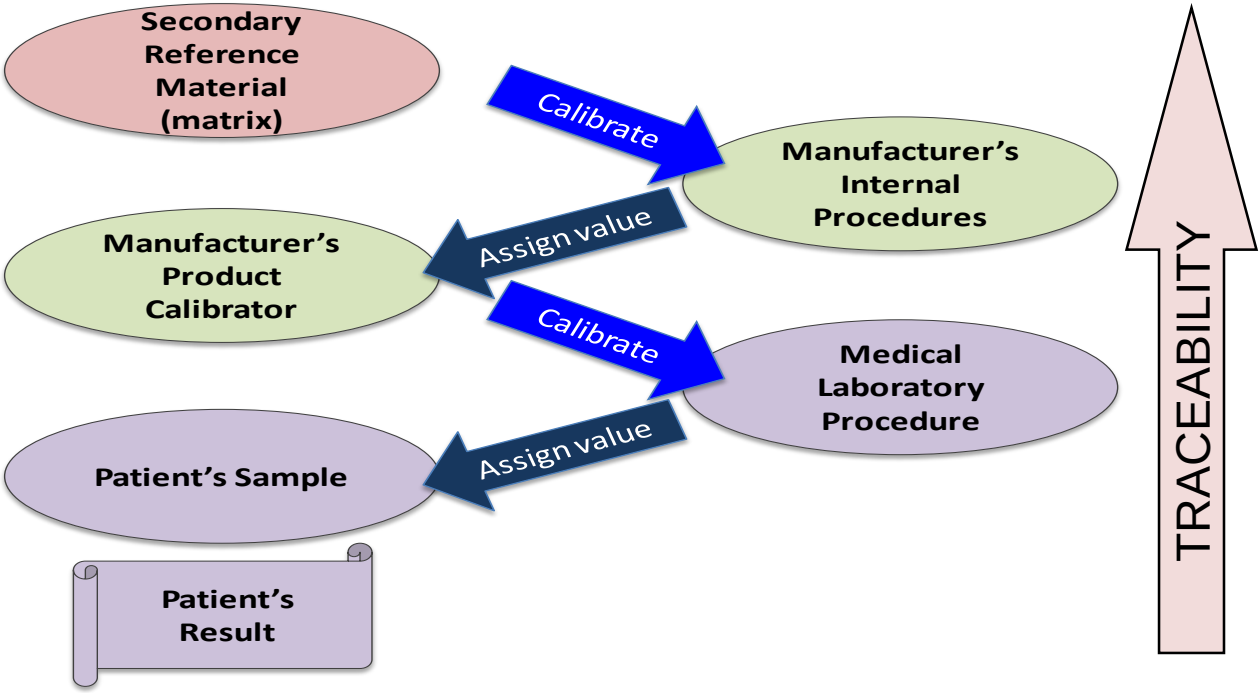
Prostate-specific antigen

Thyroid stimulating hormone

Human immunodeficiency virus

(no reference measurement procedure available)

Traceability can be established to a reference material such as a secondary reference material



Traceability requires commutable calibration materials

Commutable means that values measured for a calibration material and for patient clinical samples have the same relationship between two, or more, measurement procedures for the same measurand.

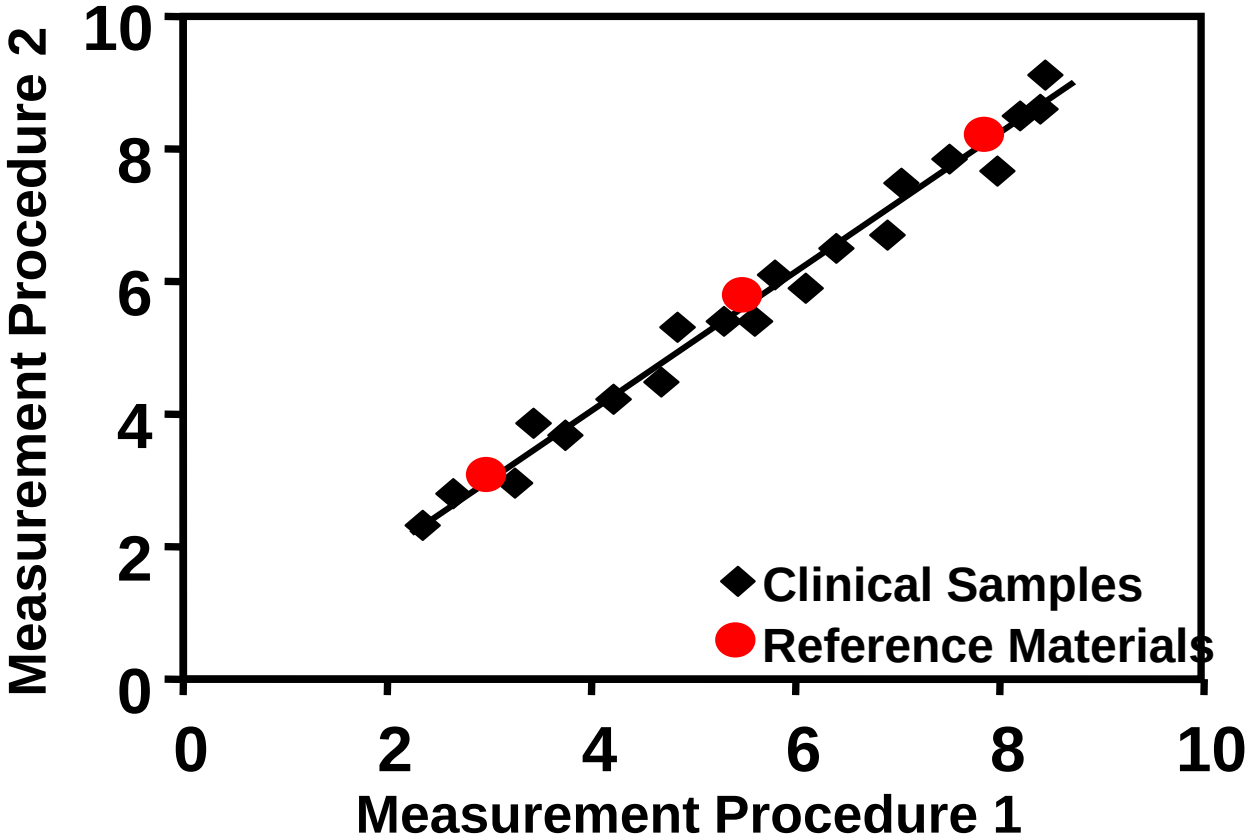
Commutability:

A reference material is commutable if it demonstrates closeness of agreement

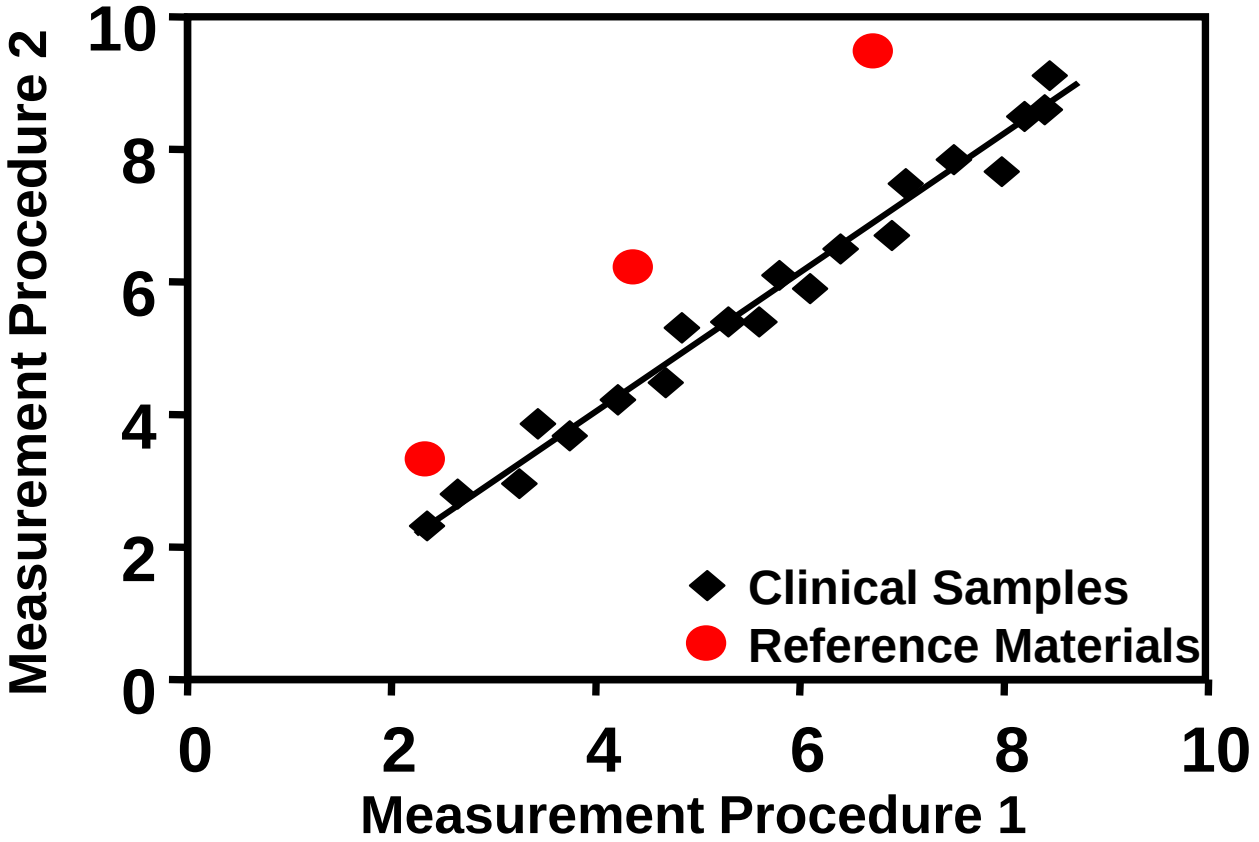
- for results obtained from two measurement procedures
- among results for clinical samples from the same two measurement procedures

(Rephrased from VIM 3: 2008)

Commutable: same relationship for clinical samples and reference materials

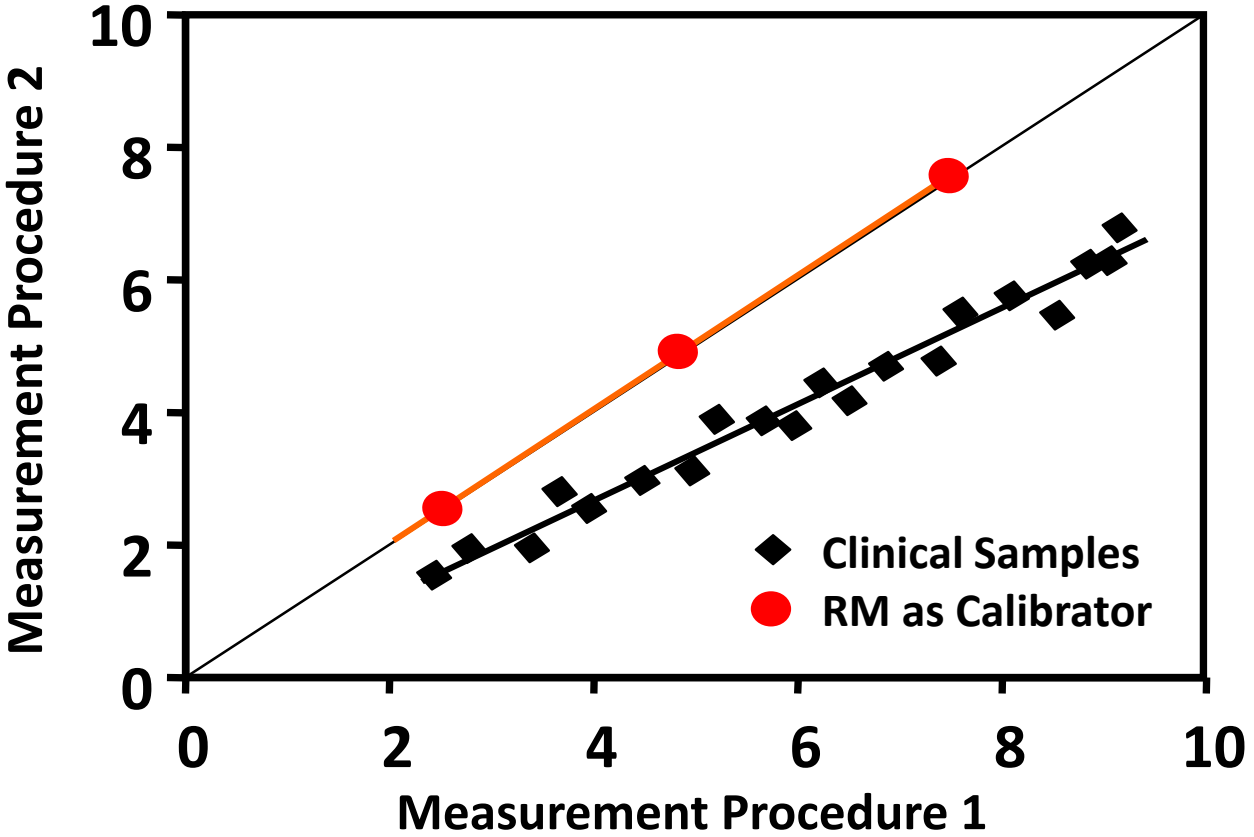


Non-commutable: different relationship for clinical samples and reference materials



Calibration with non-commutable materials

Patient results between the 2 measurement procedures are now different



IFCC Working Group on Commutability

Developing

- Operating procedures for the formal assessment of commutability
- Criteria for commutability taking into account the intended use of a reference material

What happens when there is :

- No reference measurement procedure
- No reference material

ISO1751 Category 5

Harmonization strategies are implemented

Barriers to Harmonization

Lack of a systematic process to identify and prioritize measurands

Materials are labelled as “reference materials” that have not been validated to be commutable for the intended measurement procedures

Inadequate definition of the measurand

Inadequate analytical specificity for the measurand

Lack of systematic procedures to implement harmonization, in particular:

- when there is no reference measurement procedure
- when there is no reference material

International coordination of harmonization activities (International Collaboration for Harmonization of Clinical Laboratory Results)

Develop an infrastructure to coordinate harmonization activities world wide to include:

1. Prioritization of analytes
2. Gap analysis for what needs to be done
3. Technical processes to achieve harmonization
4. Surveillance of success of harmonization

www.harmonization.net

A general information portal for global standardization / harmonization activities

Currently 96 measurands are recorded with regard to medical impact and harmonization status.

This list is the subject of a major project by ICHCLR officers.

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

STBC Société Tunisienne de Biologie Clinique

Thankyou

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