An ISO standard for traceability to a harmonization protocol

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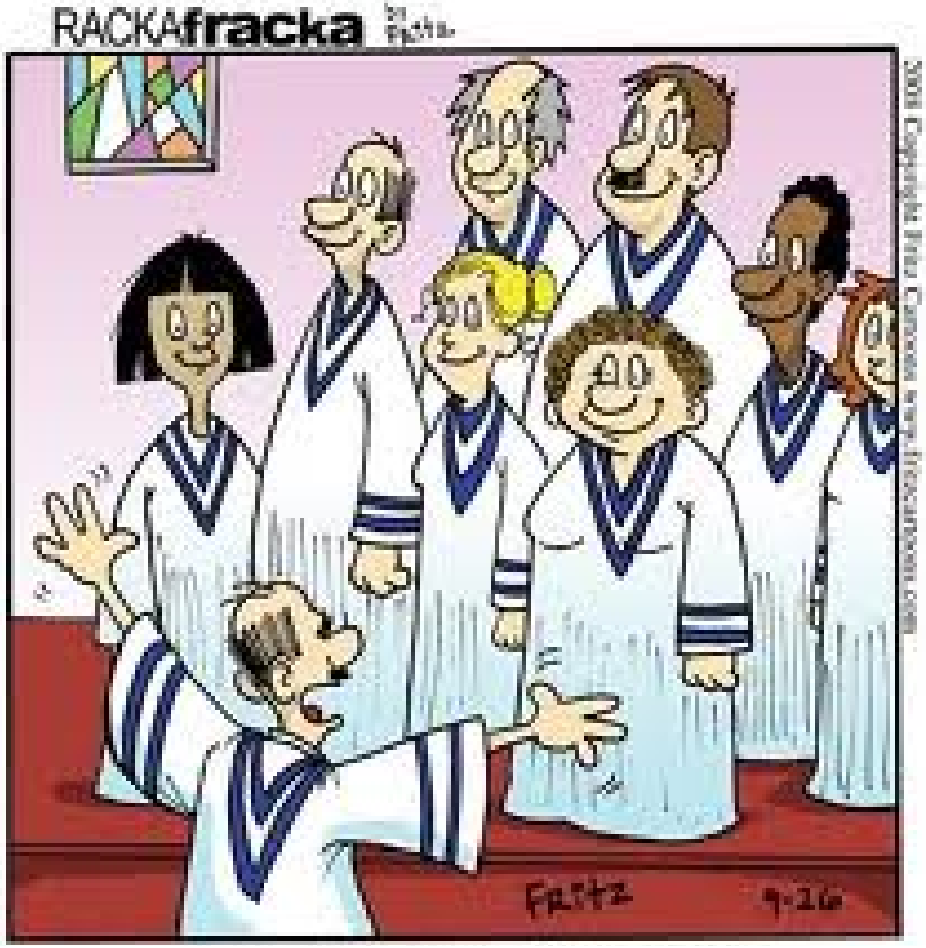
The goal:

Equivalent results, within clinically meaningful limits, among different measurement procedures for the same laboratory test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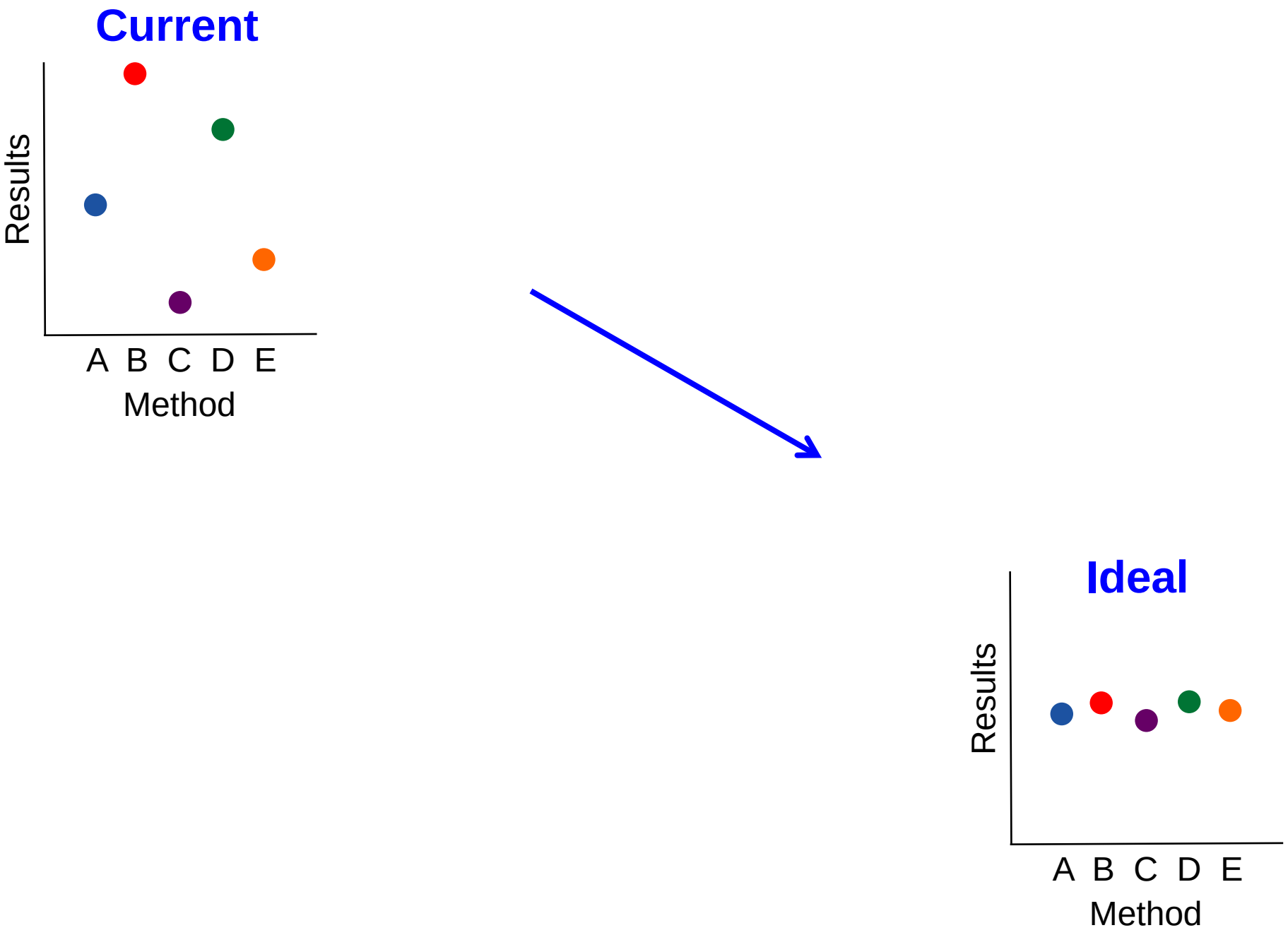
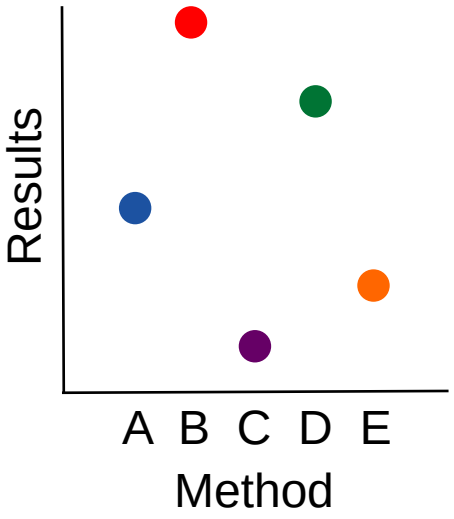
Harmonization principles

1. The goal for closeness of agreement among results is based on suitability for use in medical decisions

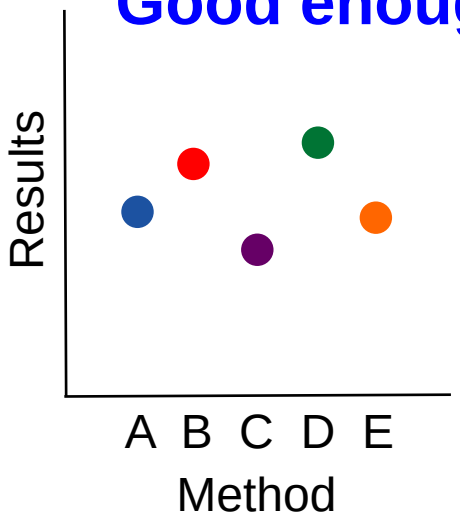
2. An improvement in agreement can reduce the risk for patient harm – even if the goal is not met


Current
Results
A B C D E
Method
Ideal
Results
A B C D E
Method

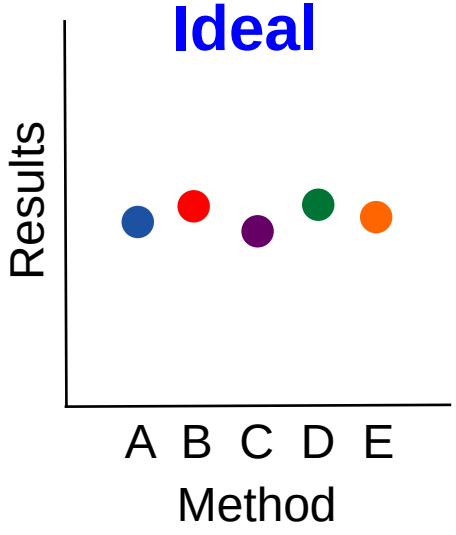
Current



Good enough ?



Ideal



Harmonization principles

3. Any process to achieve agreement in results is acceptable

Perfect is the Enemy of Good

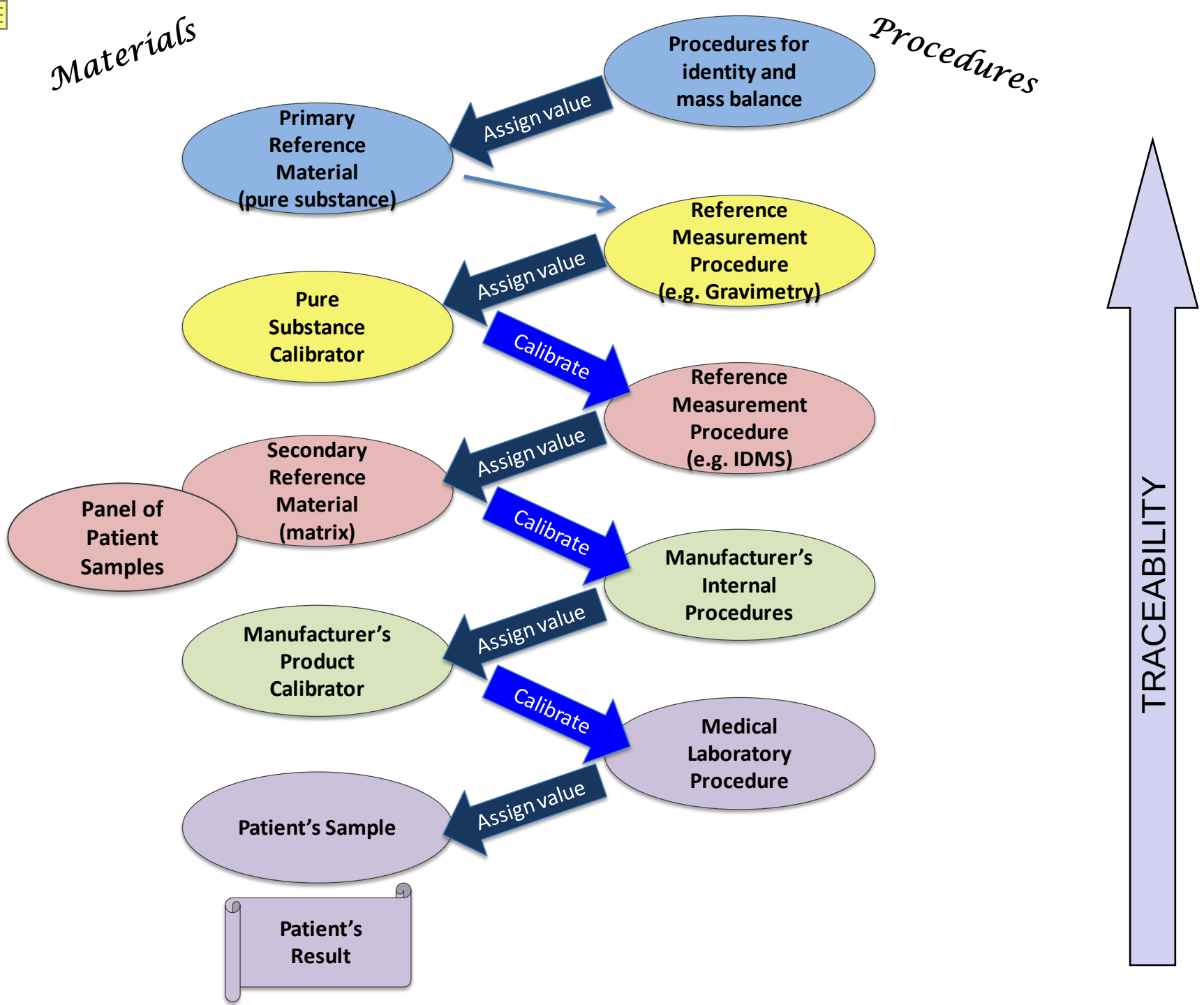
ISO 17511:2003

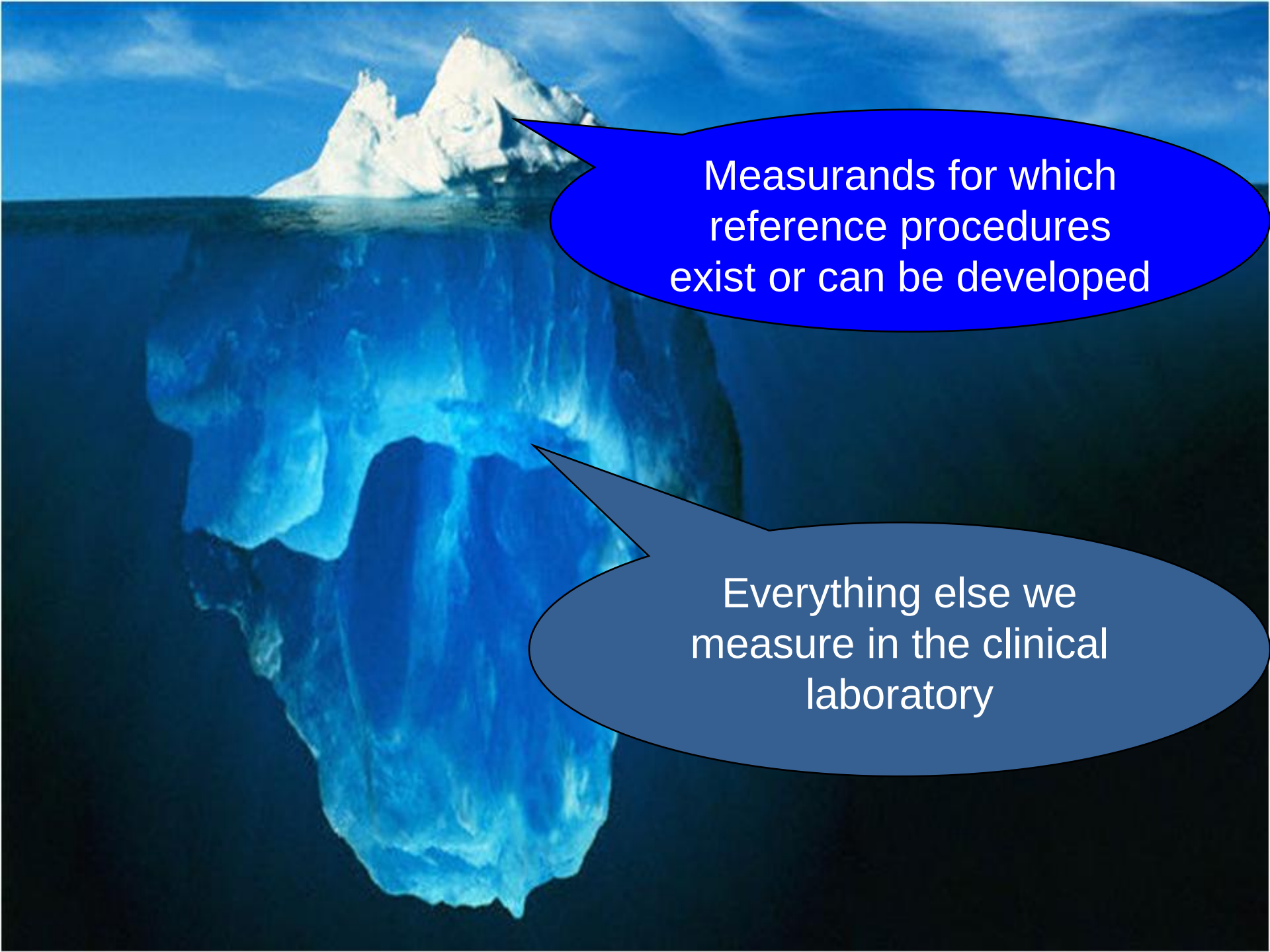
Metrological traceability of values assigned to calibrators and control materials

- Vague regarding focus on patient results

ISO 17511:201x revision

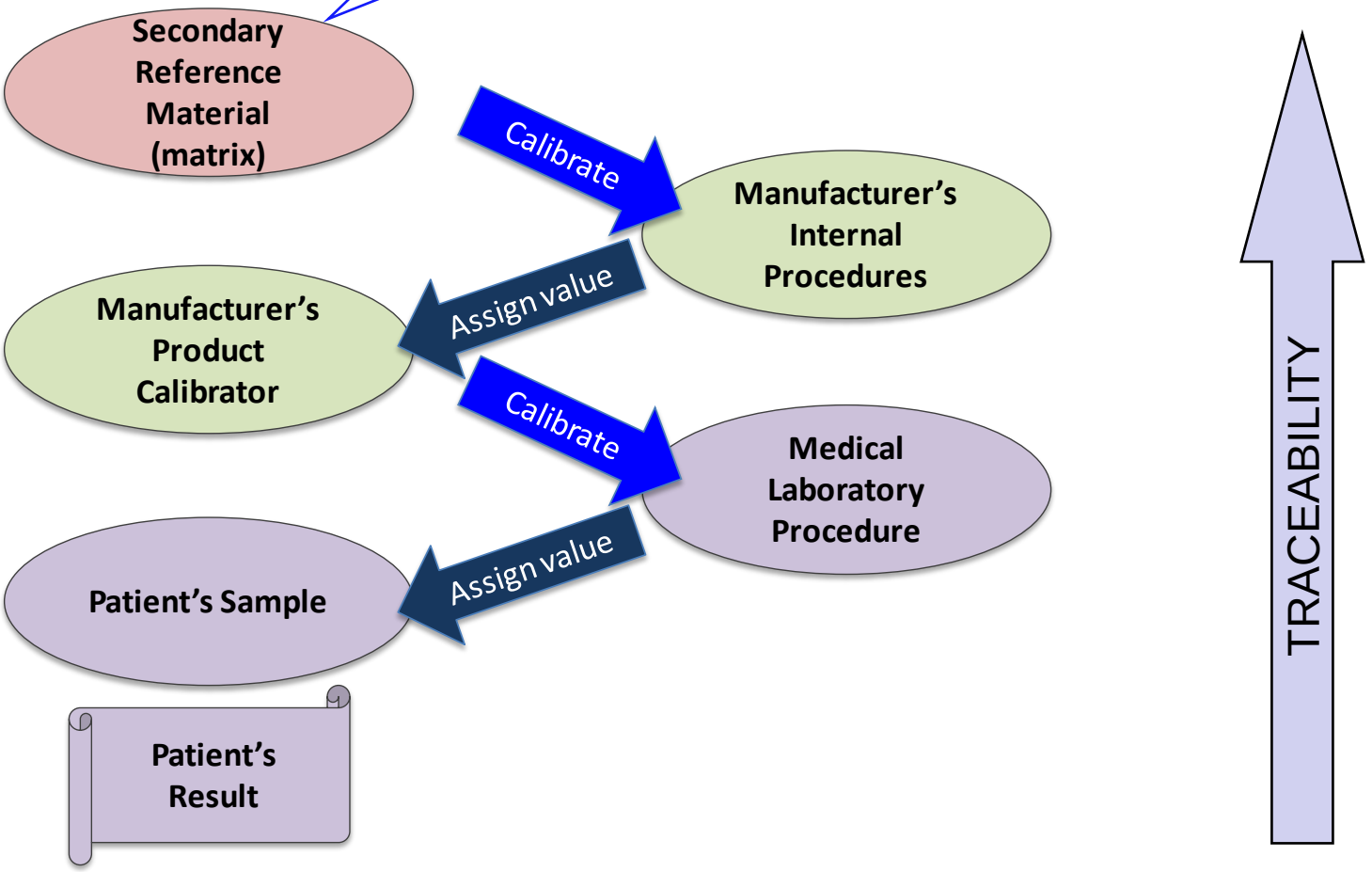
Establishing metrological traceability of values assigned to calibrators, trueness control materials and **human samples**


Materials
Procedures
Procedures for identity and mass balance
Assign value
Primary Reference Material (pure substance)
Reference Measurement Procedure (e.g. Gravimetry)
Assign value
Pure Substance Calibrator
Calibrate
Reference Measurement Procedure (e.g. IDMS)
Assign value
Secondary Reference Material (matrix)
Panel of Patient Samples
Calibrate
Manufacturer's Internal Procedures
Assign value
Manufacturer's Product Calibrator
Calibrate
Medical Laboratory Procedure
Assign value
Patient's Sample
Patient's Result
TRACEABILITY

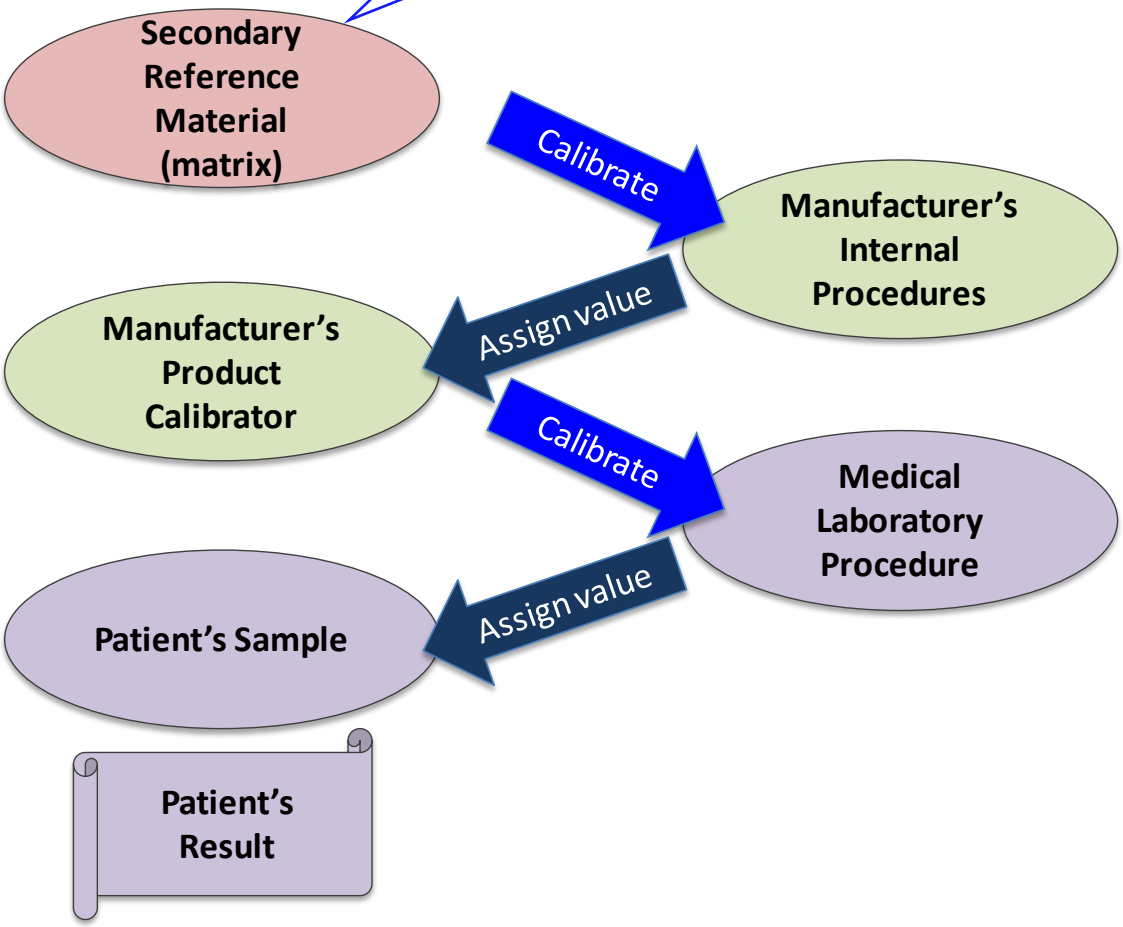

Measurands for which reference procedures exist or can be developed
Everything else we measure in the clinical laboratory

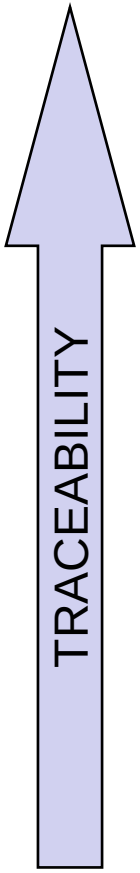
What happens when there is no reference measurement procedure

Traceability is established to a reference material



- Value assignment
- Commutability



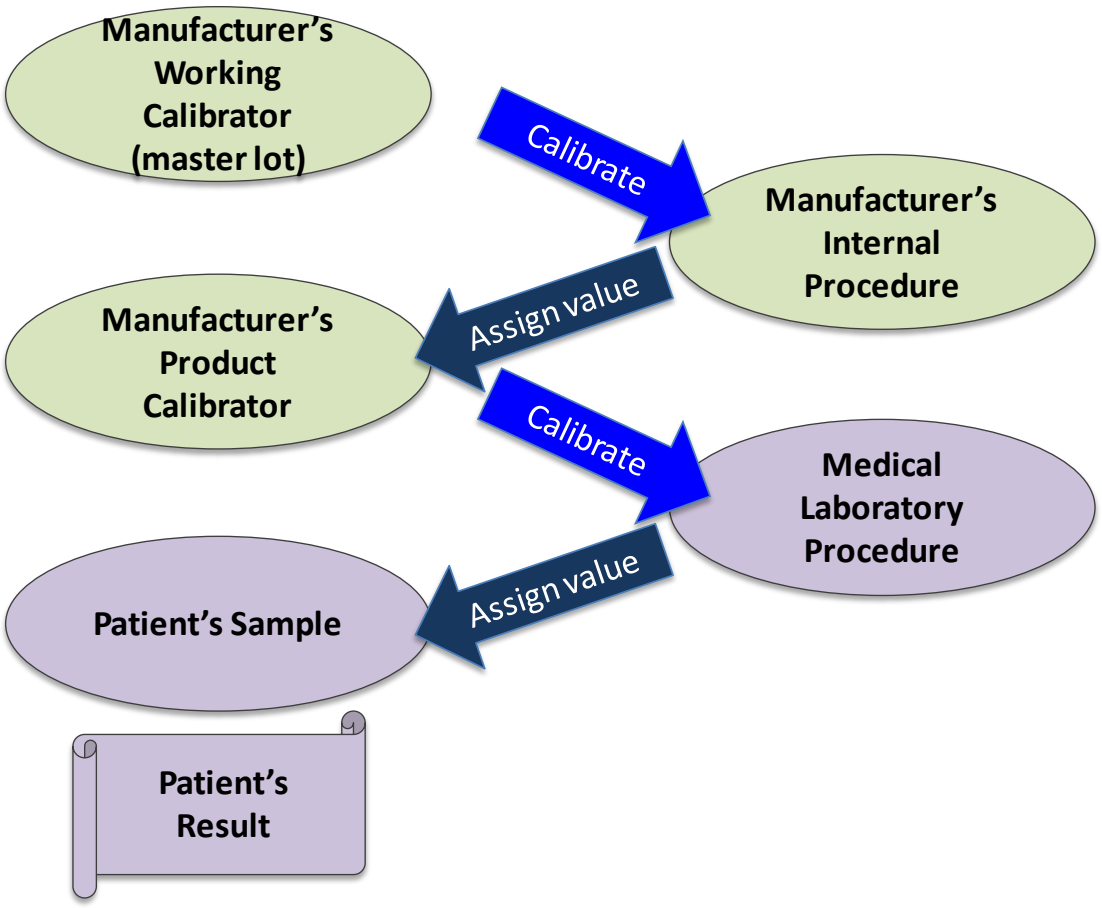


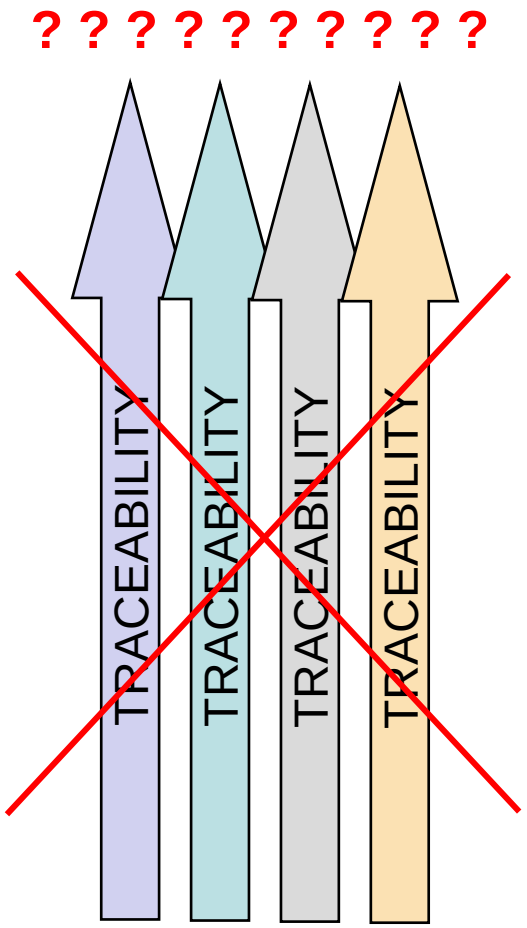
What happens when there is both:

- no reference measurement procedure
- no certified reference material or international conventional reference material

Traceability is established to to a material selected for a measurement procedure

No coordination among producers (IVD or LDT)





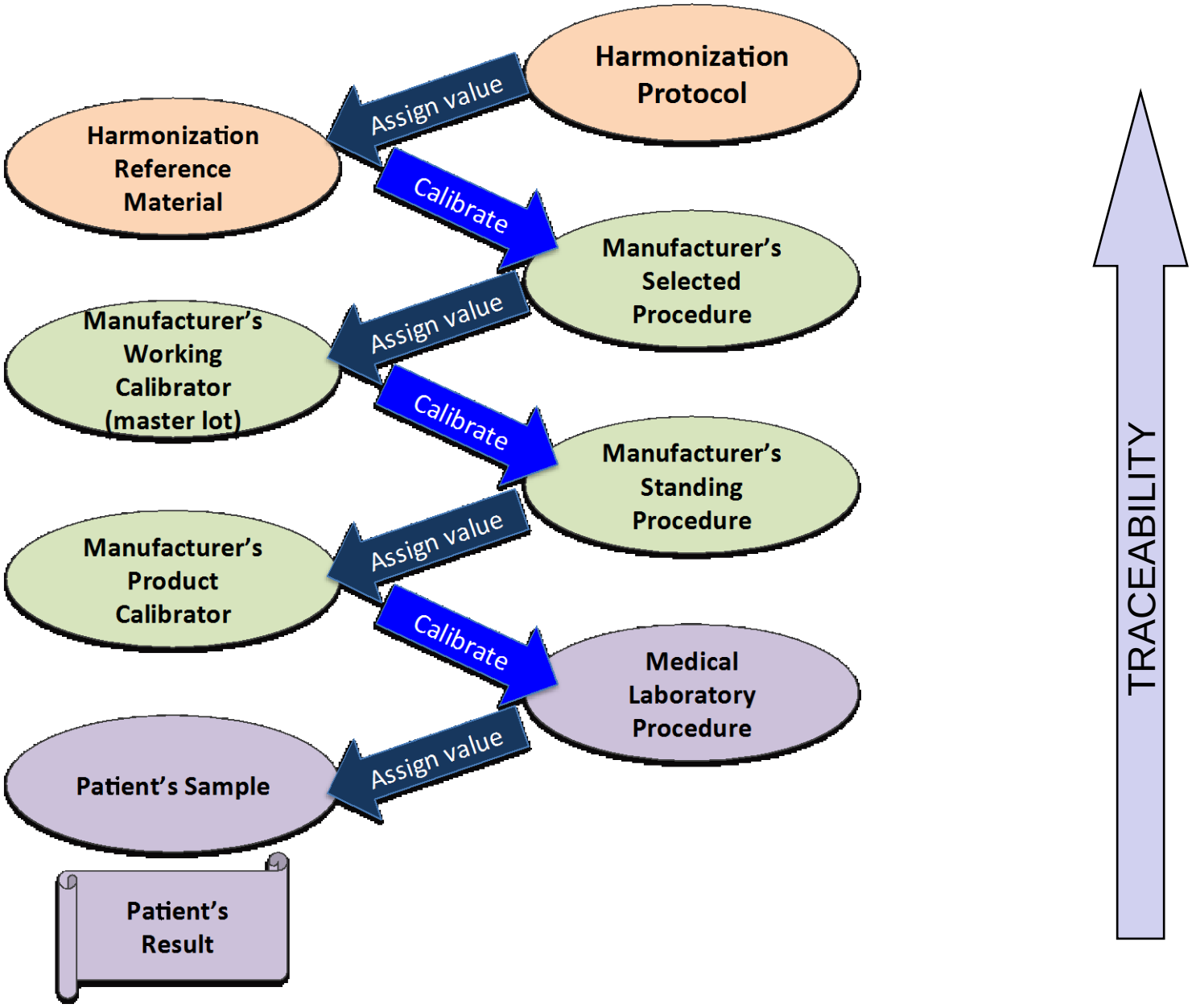
ISO Standards

- 17511:2003, Calibration Traceability
- 18153:2003, Traceability for Enzymes
- 15193:2009, Reference Measurement Procedures
- 15194:2009, Certified Reference Materials
- 15195:2003, Reference Measurement Laboratories

JCTLM lists reference materials, reference measurement procedures and reference laboratories that conform to the ISO Standards

ISO TC 212 WG2

Revision of the traceability standard 17511 is expected to include traceability to a harmonization protocol


Harmonization Protocol
Assign value
Harmonization Reference Material
Calibrate
Manufacturer's Selected Procedure
Assign value
Manufacturer's Working Calibrator (master lot)
Calibrate
Manufacturer's Standing Procedure
Assign value
Manufacturer's Product Calibrator
Calibrate
Medical Laboratory Procedure
Assign value
Patient's Sample
Patient's Result
TRACEABILITY

ISO 20089, NWIP: A new standard to support JCTLM listing of harmonization protocols

Requirements for international harmonization protocols intended to establish metrological traceability of values assigned to product (end user) calibrators and patient samples

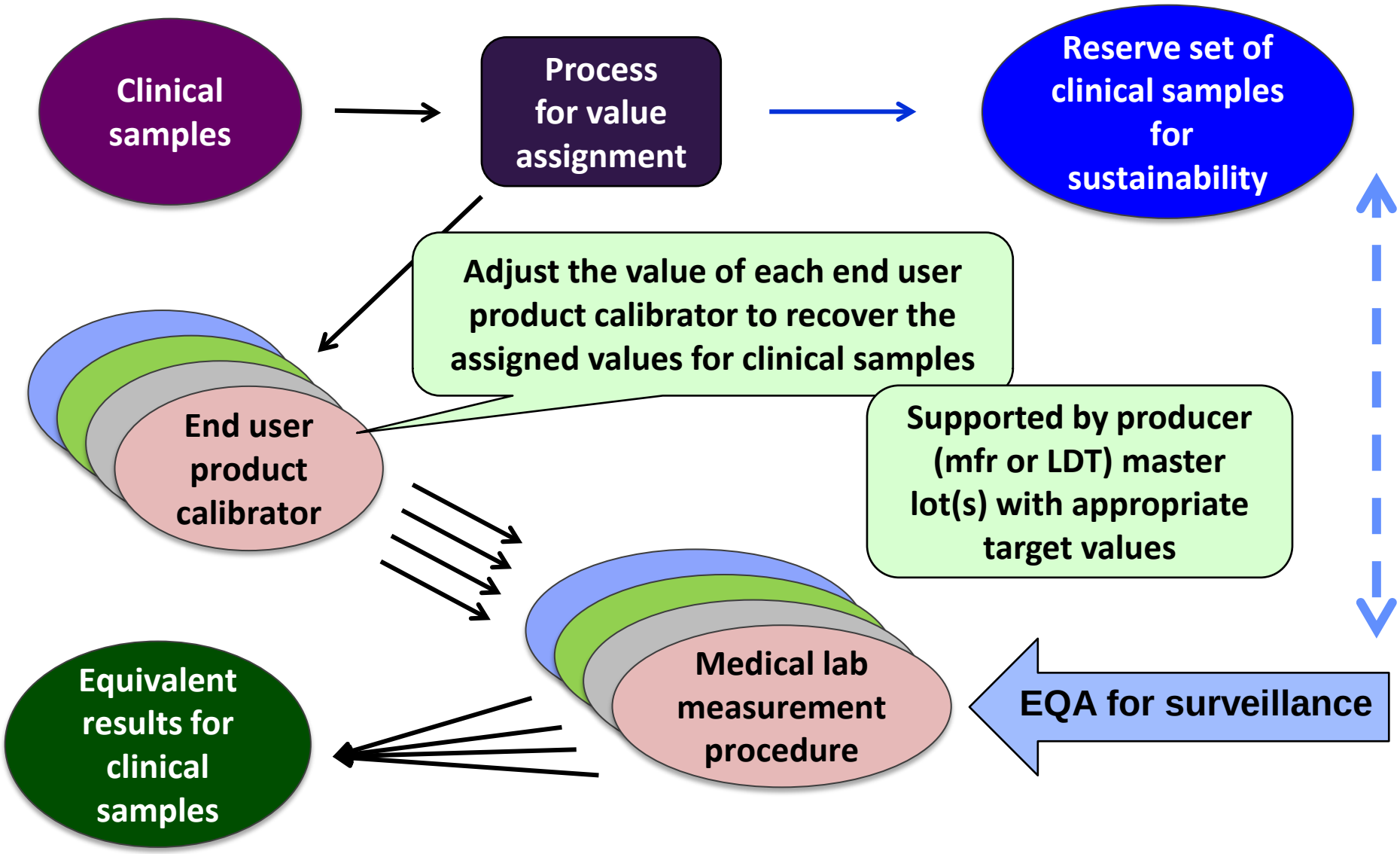
Critical components for harmonization

1. Calibration of all measurement procedures is traceable to a common reference protocol

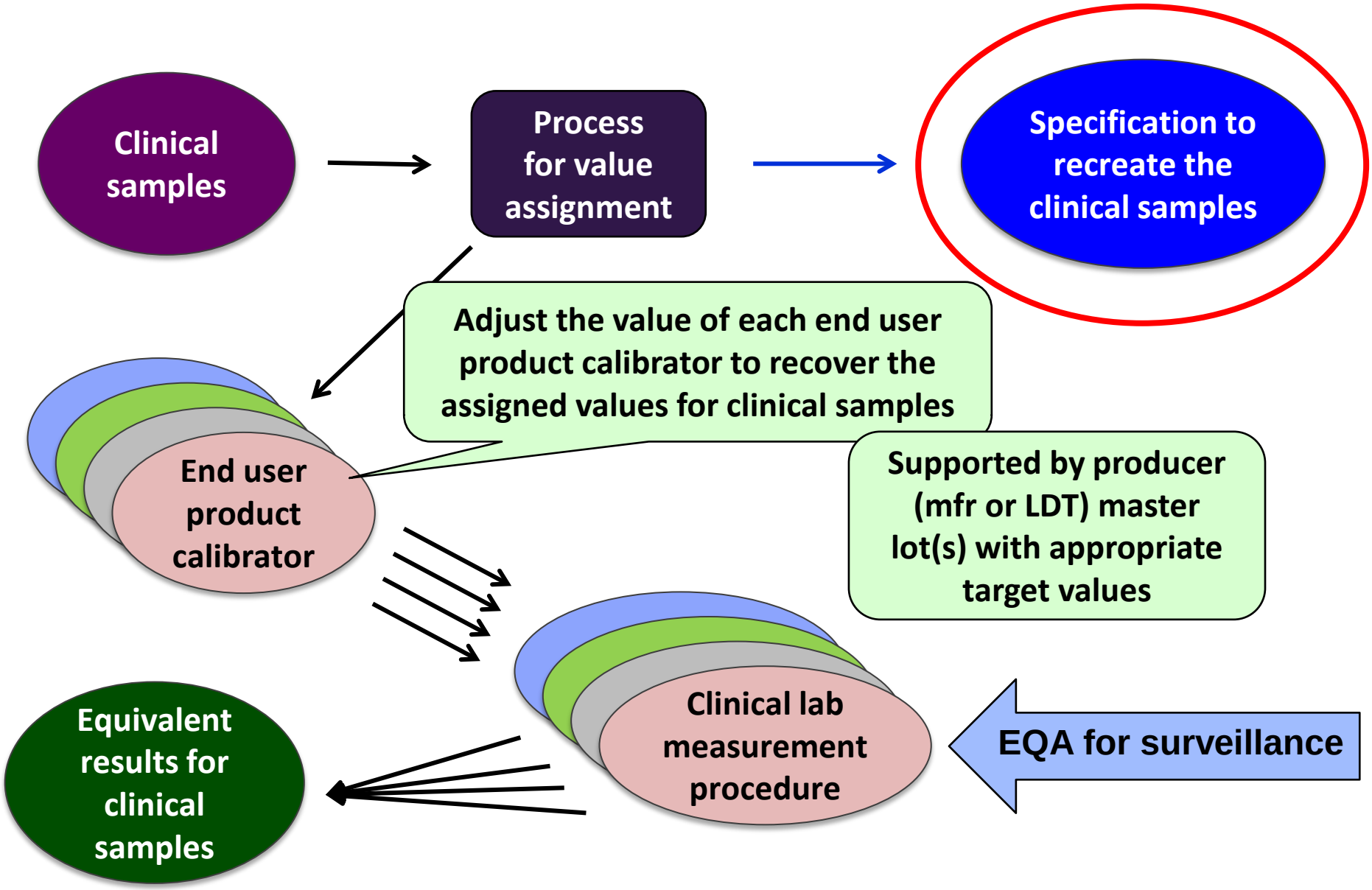
2. All measurement procedures measure the same quantity (the same molecular form)

3. Traceability can be sustained over time and location

Example 1: harmonization protocol



Example 2: harmonization protocol



A harmonization protocol has reference materials

- Suitable for use material(s)
  - Panel of individual clinical samples
  - Pool of suitable clinical samples
  - Other – supplemented …
- Commutability must be ensured
  - Influence of sample collection, handling, storage, pooling, supplementation, etc.

A harmonization protocol has reference materials

- Materials do not meet requirements for a CRM or an international conventional reference material
  - May be used over a short time for a protocol
  - Protocol specifies how to obtain/prepare the material(s)
    - Clinical characteristics for inclusion or exclusion
    - Sample collection, handling, storage, pooling, supplementation, etc.

ISO 20089 – Requirements for international harmonization protocols

1) Description of the measurand and what is actually measured
2) Acceptable agreement among measurement procedures
3) Criteria for inclusion or exclusion of measurement procedures
4) Description of the process to achieve harmonization
5) Process to add measurement procedures not included
6) Materials used (typically patient samples that meet specifications)
7) How to assign quantity values to materials
8) How to assign values to end user calibrators (product calibrators)
9) Evidence for validation of the protocol
10) Provision for sustainability of the protocol over time

Questions / Comments

Perfect is the Enemy of Good