Good laboratory medicine requires:

- Total error of measurement is small enough that a result reflects a patient's biological condition

- Comparable results that are independent of
  - where and when a test was performed
  - the measurement procedure used

Financial disclosures: none

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- Comparable results that are independent of
  - where and when a test was performed
  - the measurement procedure used

Why do we need comparable results

If different measurements give different results for the same patient sample:

- ⇨ Clinical practice guidelines become less useful
- ⇨ **Patients may receive incorrect treatment**
- ⇨ Laboratory results in EHRs are less useful

How to achieve comparable results

- Calibration of all measurement procedures is traceable to a common reference system
- All measurement procedures measure the same quantity

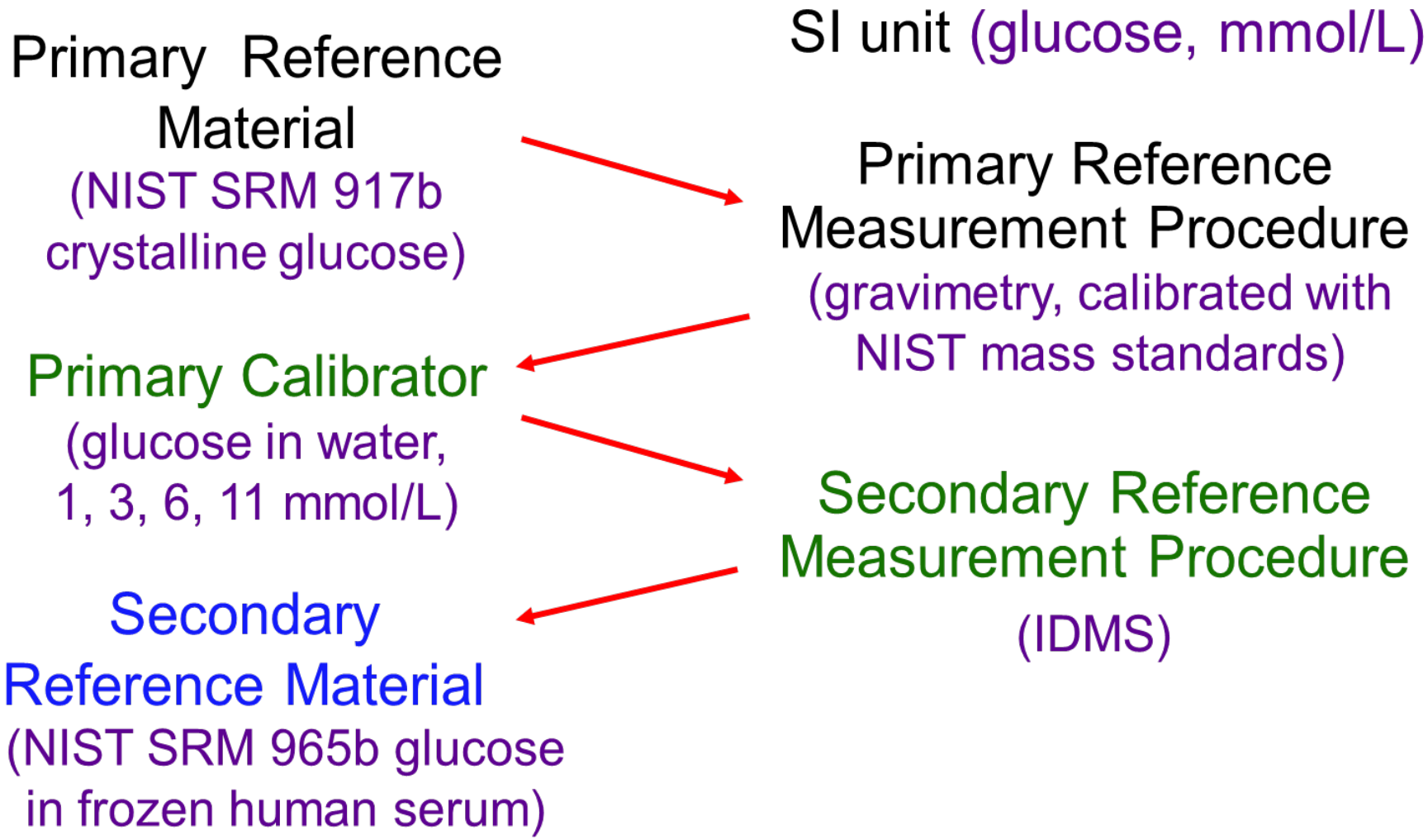
ISO 17511:2003

In vitro diagnostic medical devices -Measurement of quantities in biological samples - **Metrological traceability of values assigned to calibrators and control materials** (under revision)

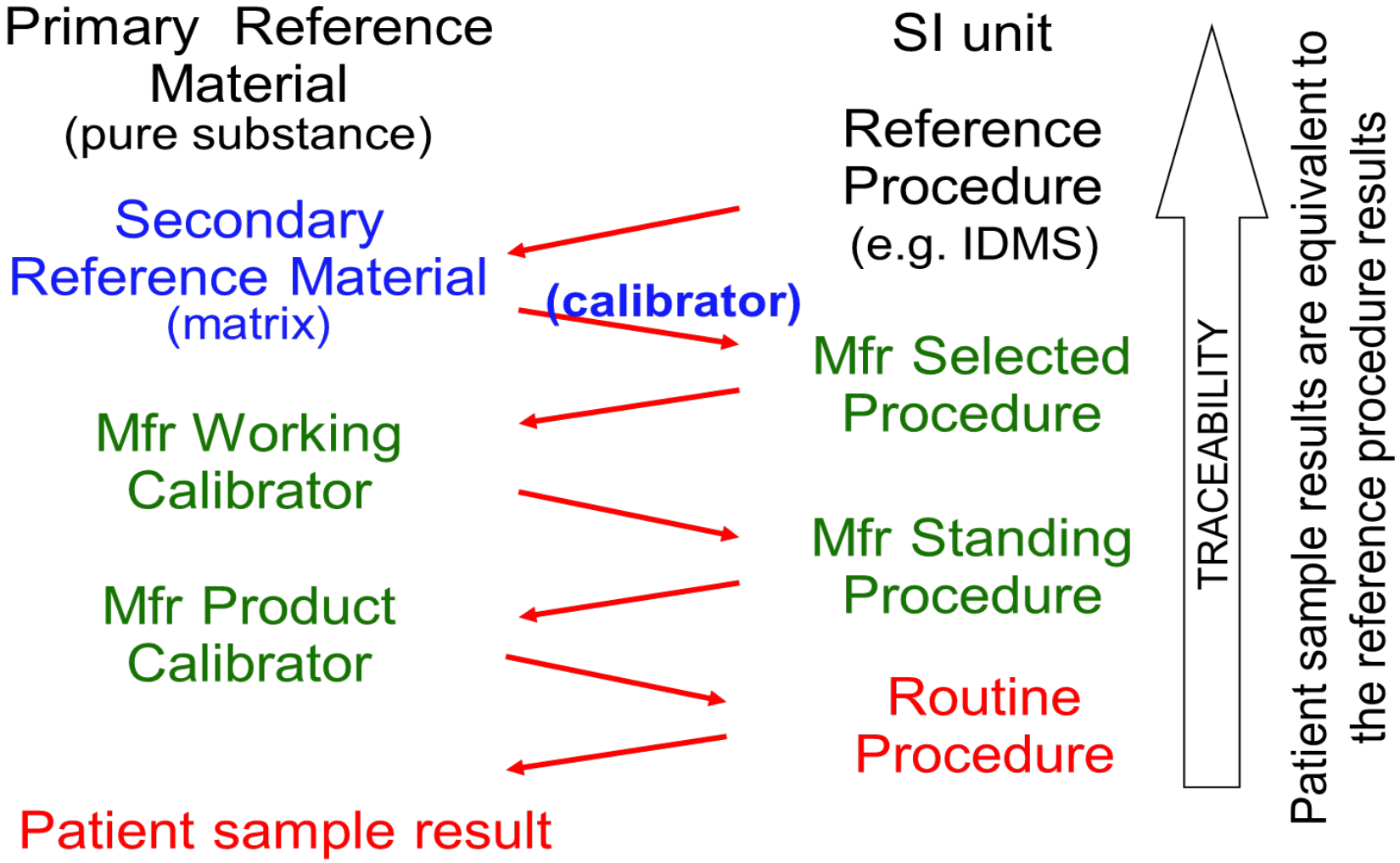
- **CLSI: implementation guideline**
  - X5R (2006) and C29 (in preparation)

Traceability (based on ISO 17511)

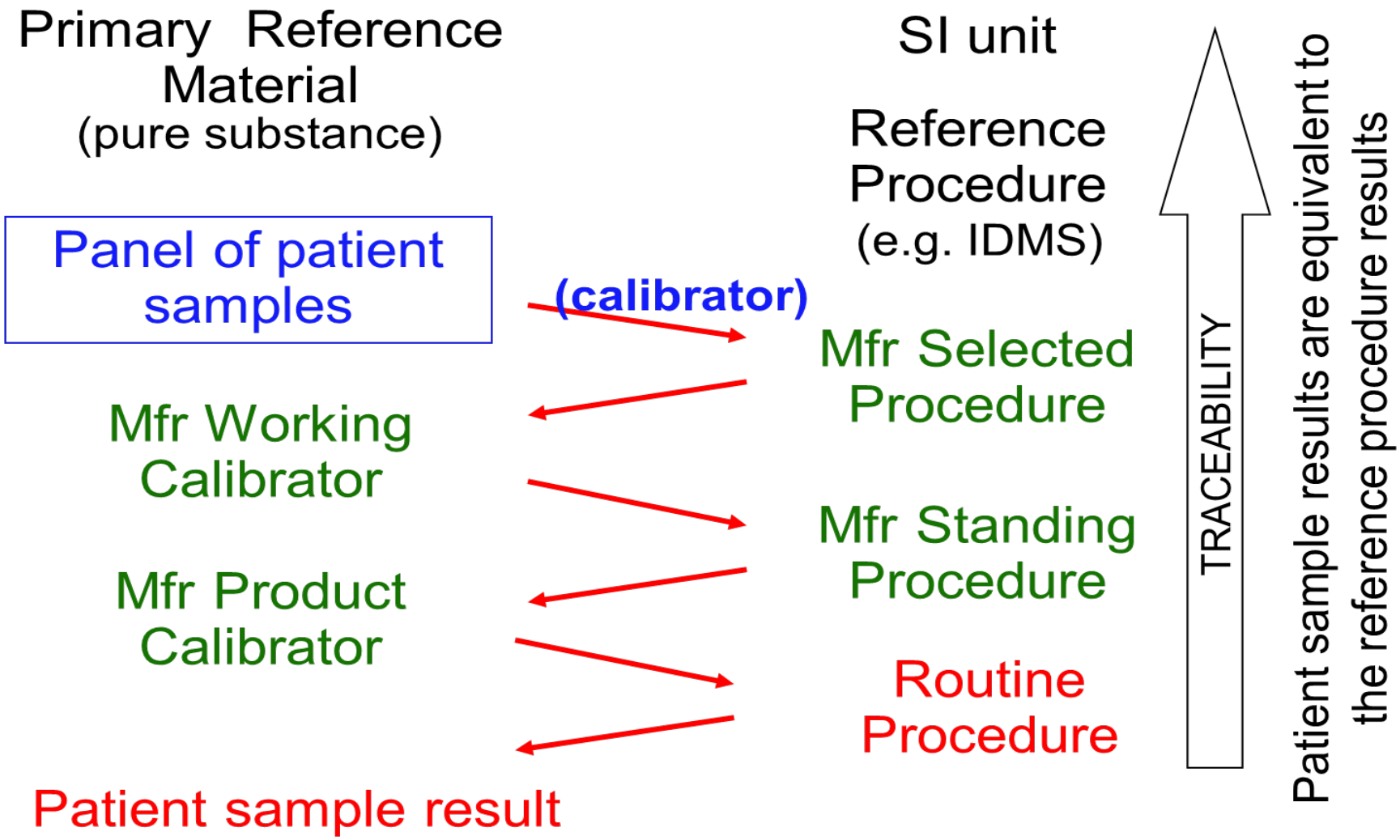
A reference system



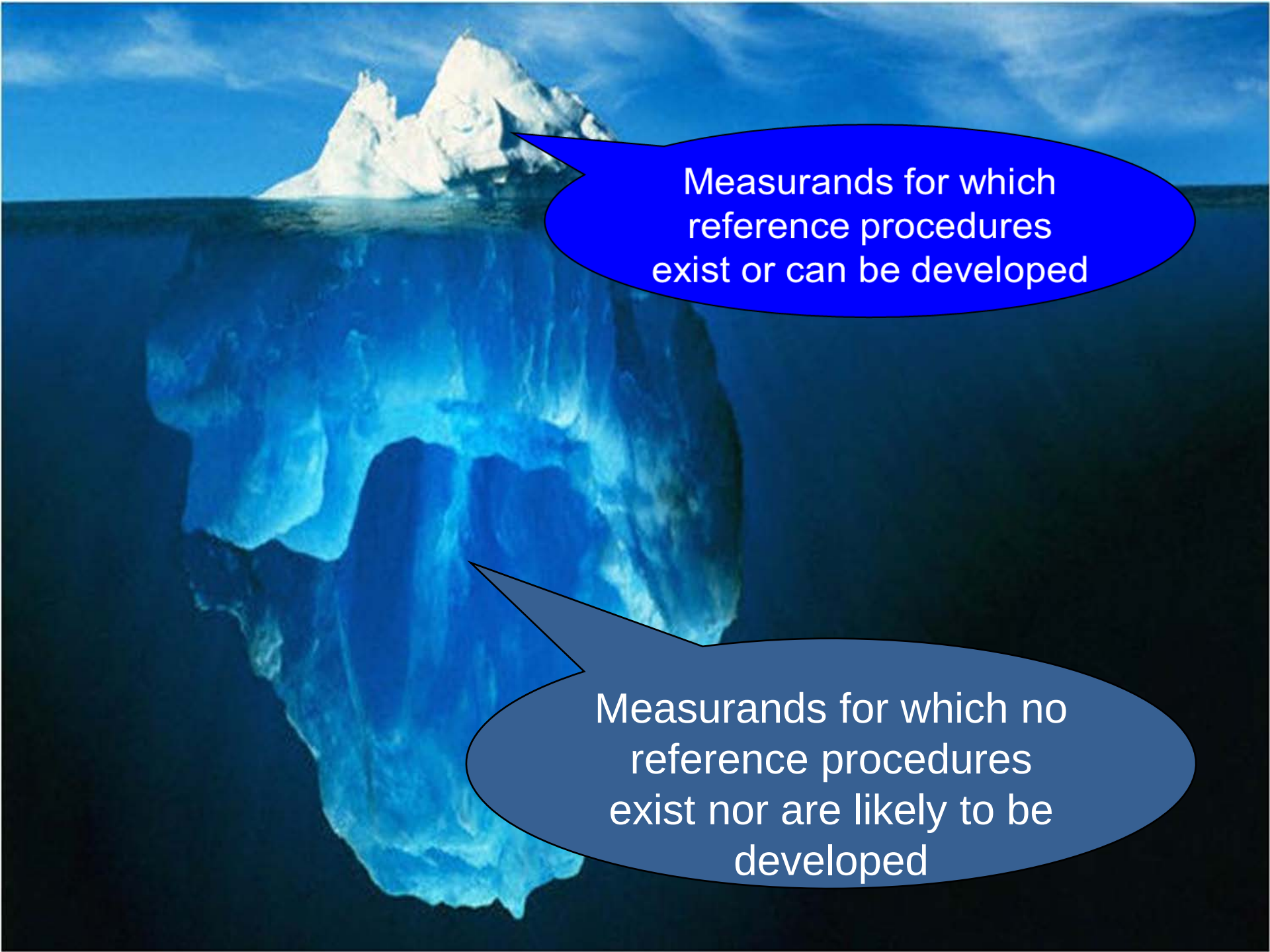
Traceability (based on ISO 17511)



Traceability (based on ISO 17511)

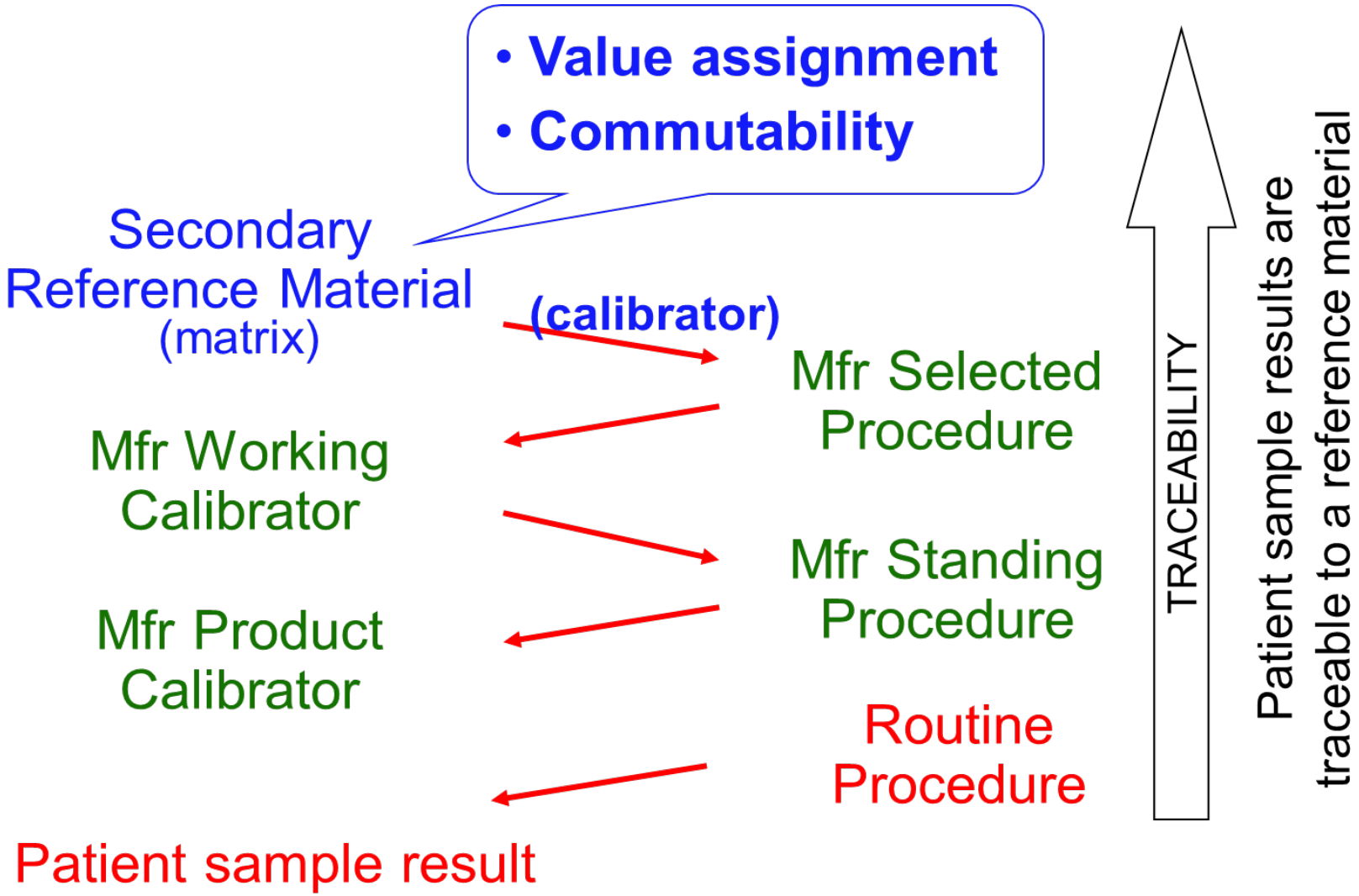


Measurands for which reference procedures exist or can be developed

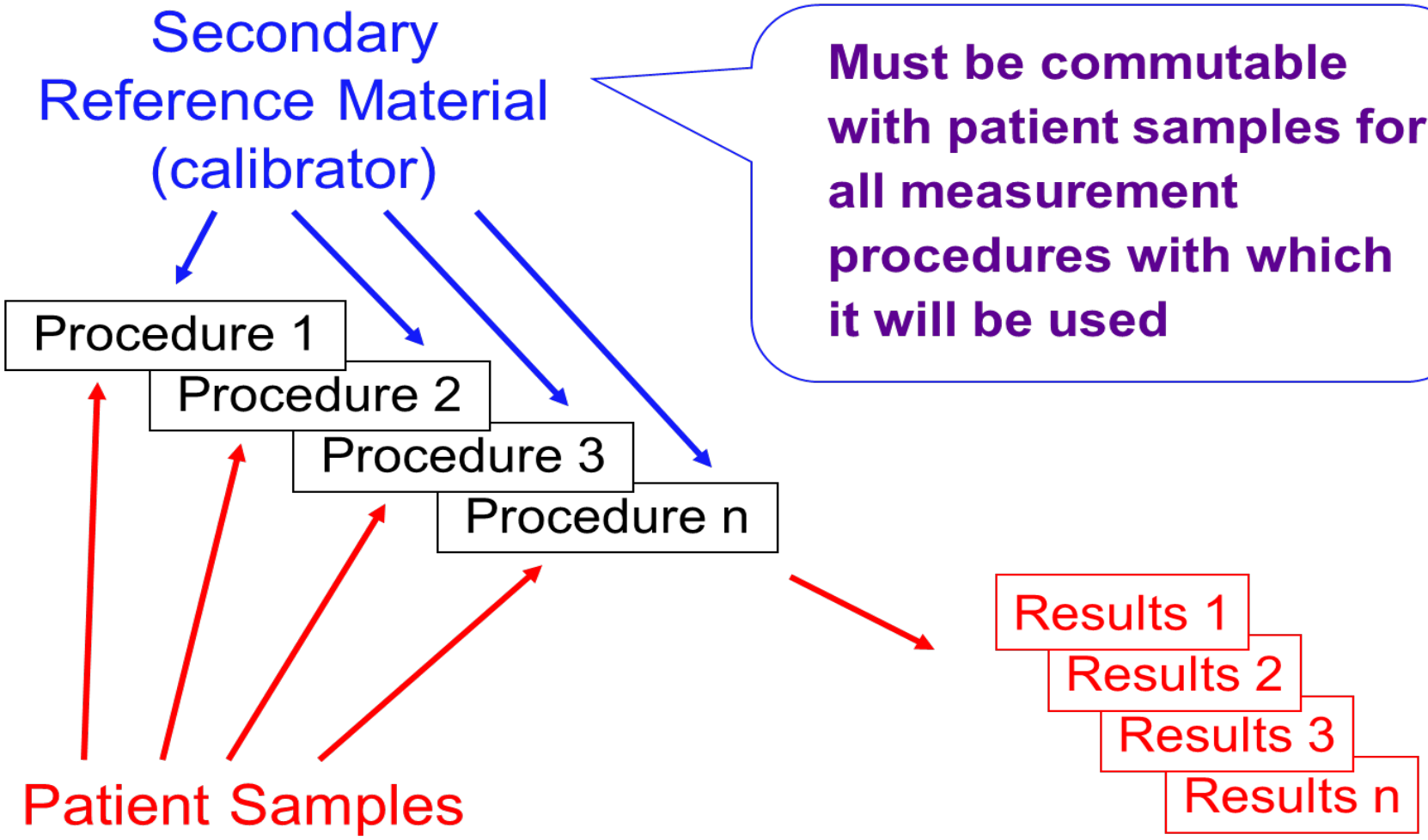

Measurands for which reference procedures exist or can be developed
Measurands for which no reference procedures exist nor are likely to be developed

What happens when there is no reference measurement procedure

Traceability (based on ISO 17511)

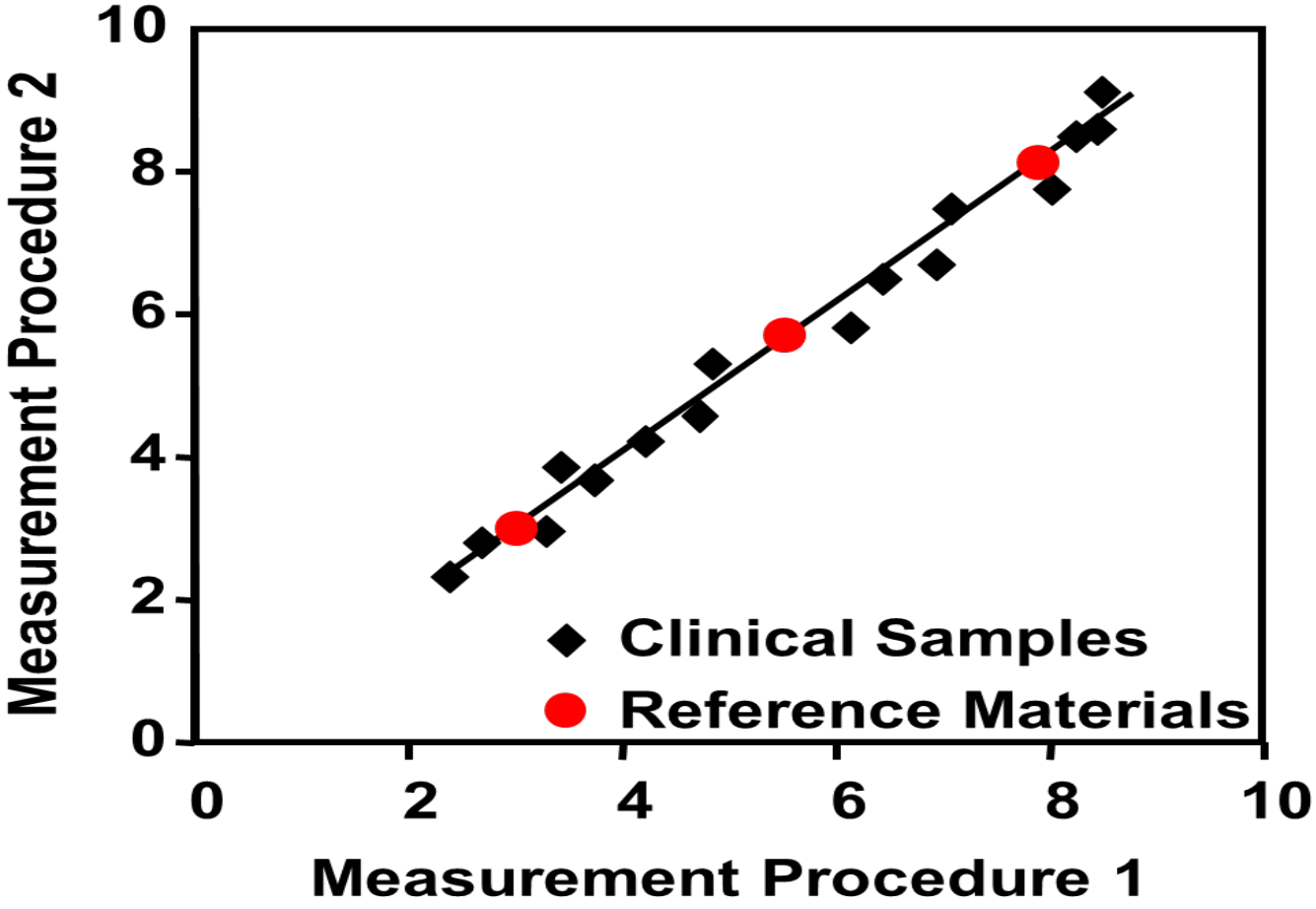


Traceability to a Reference Material

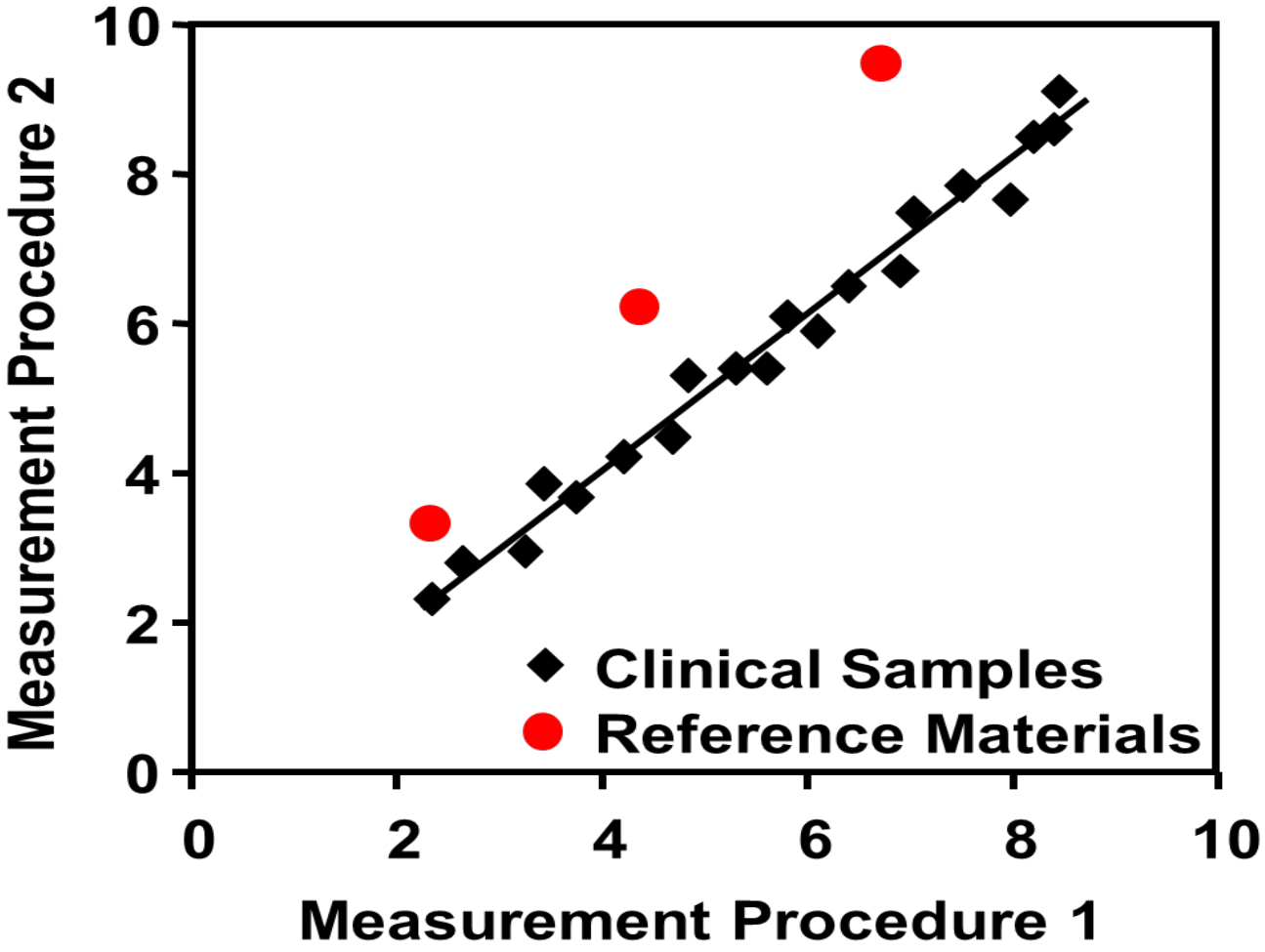


Commutable means that values measured for a calibration material and for representative clinical samples have the same relationship between two, or more, measurement procedures for the same measurand.

Commutable: same relationship for clinical samples and reference materials



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

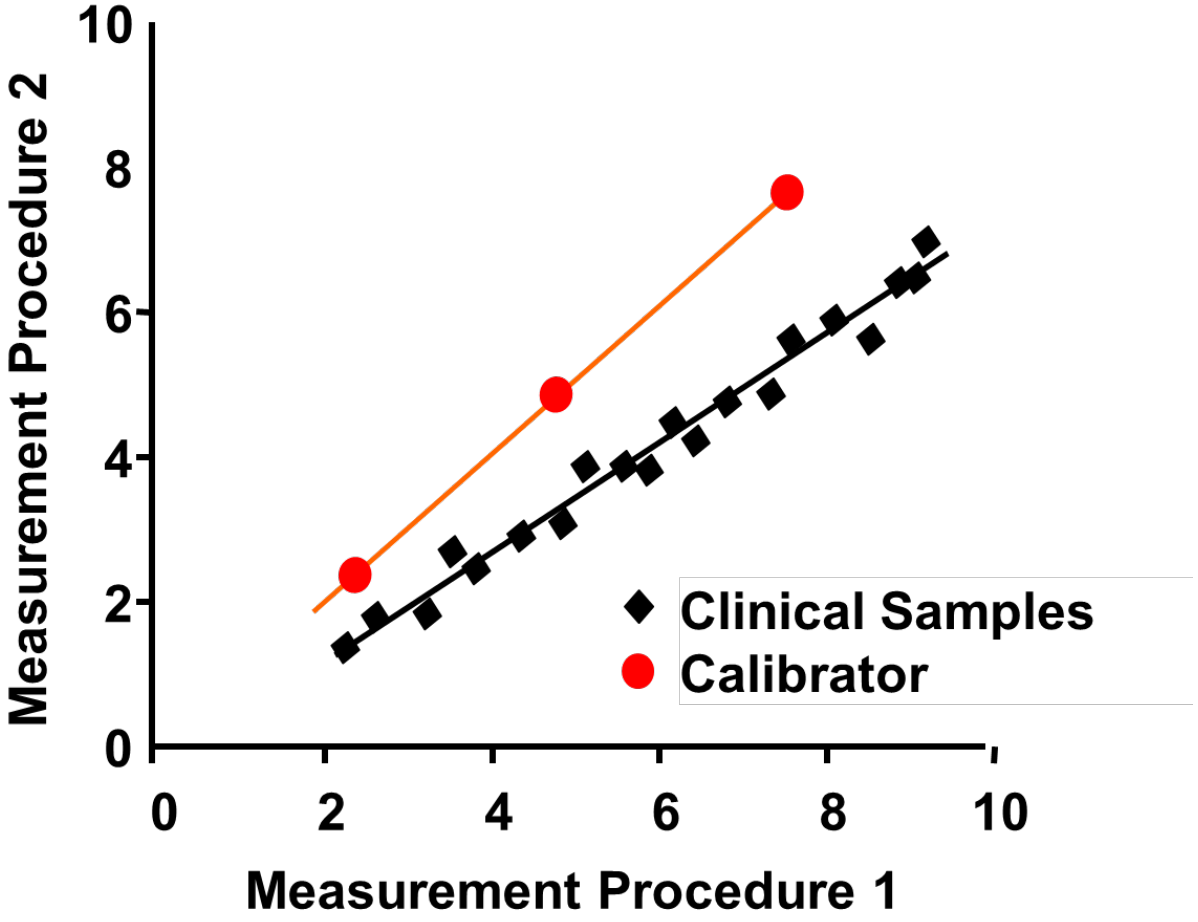


Use of a non-commutable material for calibration traceability will cause:

- Incorrect value assignment for a routine **(field) measurement procedure calibrator**
- **Incorrect results for patient samples**

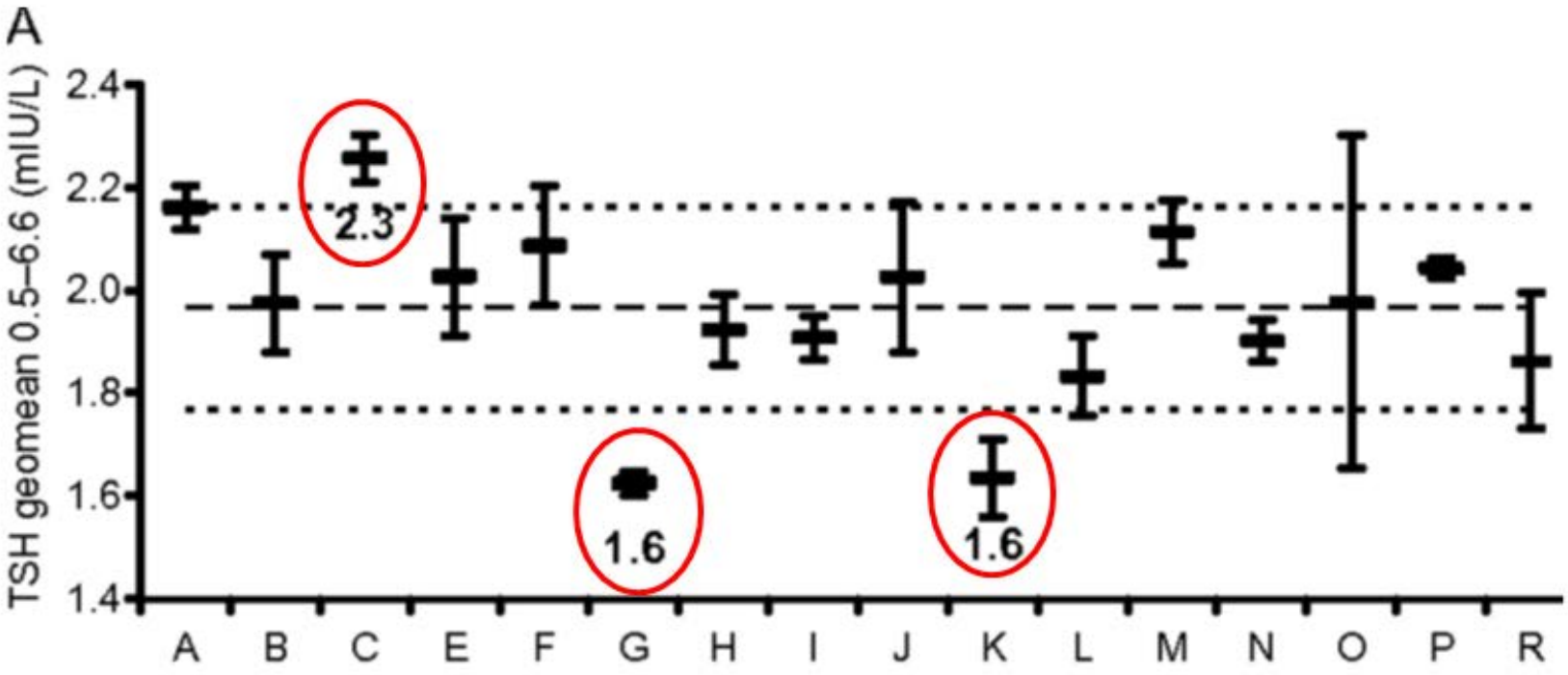
Miller, Myers, Rej. Why commutability matters. Clin Chem 2006; 52: 553-4.

Calibration with non-commutable materials



TSH methods
All traceable to IS 94/674 (WHO)

Mean ±95% CI for 40 patient samples



Thienpont et al. Clin Chem 2010; 56: 902-911.

The Problem

Many secondary reference materials are not commutable with native clinical samples for routine clinical laboratory procedures

The Problem

Many secondary reference materials are not commutable with native clinical samples for routine clinical laboratory procedures

- Historically, commutability of reference materials was frequently not validated for use with routine clinical laboratory measurement procedures

The Problem

Many secondary reference materials are not commutable with native clinical samples for routine clinical laboratory procedures

- A manufacturer's standing procedure is frequently the same as the clinical laboratory procedure but may be calibrated with a "master lot of calibrator" that is traceable to a non-commutable reference material

The Problem

Many secondary reference materials are not co es for rou

A non-commutable calibration material breaks the traceability chain

- A is frequen same as the clinical laborat ocedure but may be calibra with a “master lot of calibra or” that is traceable to a non-commutable reference material

The Problem

Many secondary reference materials are not commutable with native clinical samples for routine clinical laboratory procedures

- Even though manufacturers show traceability, the process fails to provide equivalent results for patient samples when different measurement procedures are used


What do we do?

Must change practice to require commutability validation for reference materials intended for use with:

- Manufacturer's standing procedures
- Routine clinical laboratory procedures

A guideline is available: CLSI C53-A Characterization and Qualification of Commutable Reference Materials for Laboratory Medicine (2010)

Clinical Chemistry 57:8
1108–1117 (2011)

Special Report

Roadmap for Harmonization of Clinical Laboratory Measurement Procedures

W. Greg Miller,[1*] Gary L. Myers,[2] Mary Lou Gantzer,[3] Stephen E. Kahn,[4] E. Ralf Schönbrunner,[5] Linda M. Thienpont,[6] David M. Bunk,[7] Robert H. Christenson,[8] John H. Eckfeldt,[9] Stanley F. Lo,[10] C. Micha Nübling,[11] and Catharine M. Sturgeon[12]

Report from an *AACC* conference, October, 2010: Improving Clinical Laboratory Testing through Harmonization: An International Forum

AACC

Barriers to harmonization

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

- Inadequate understanding of the measurand – the quantity intended to be measured

- Inadequate analytical specificity for the measurand

Barriers to harmonization

- Lack of a systematic process to identify and prioritize measurands in need of harmonization

- Lack of systematic procedures to implement harmonization, in particular:

  - ⇨when there is no reference measurement procedure

  - ⇨when there is no reference material

The Roadmap

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

Focus technical work on measurands for which no reference measurement procedure exists

- Measurands in this category have been technically challenging
- There have been few effective procedures implemented for harmonization of these measurands

Cooperation

- With other organizations already working to improve standardization / harmonization
- Provide a communications portal among organizations to prioritize and coordinate standardization / harmonization activities
- Maintain an open and transparent process

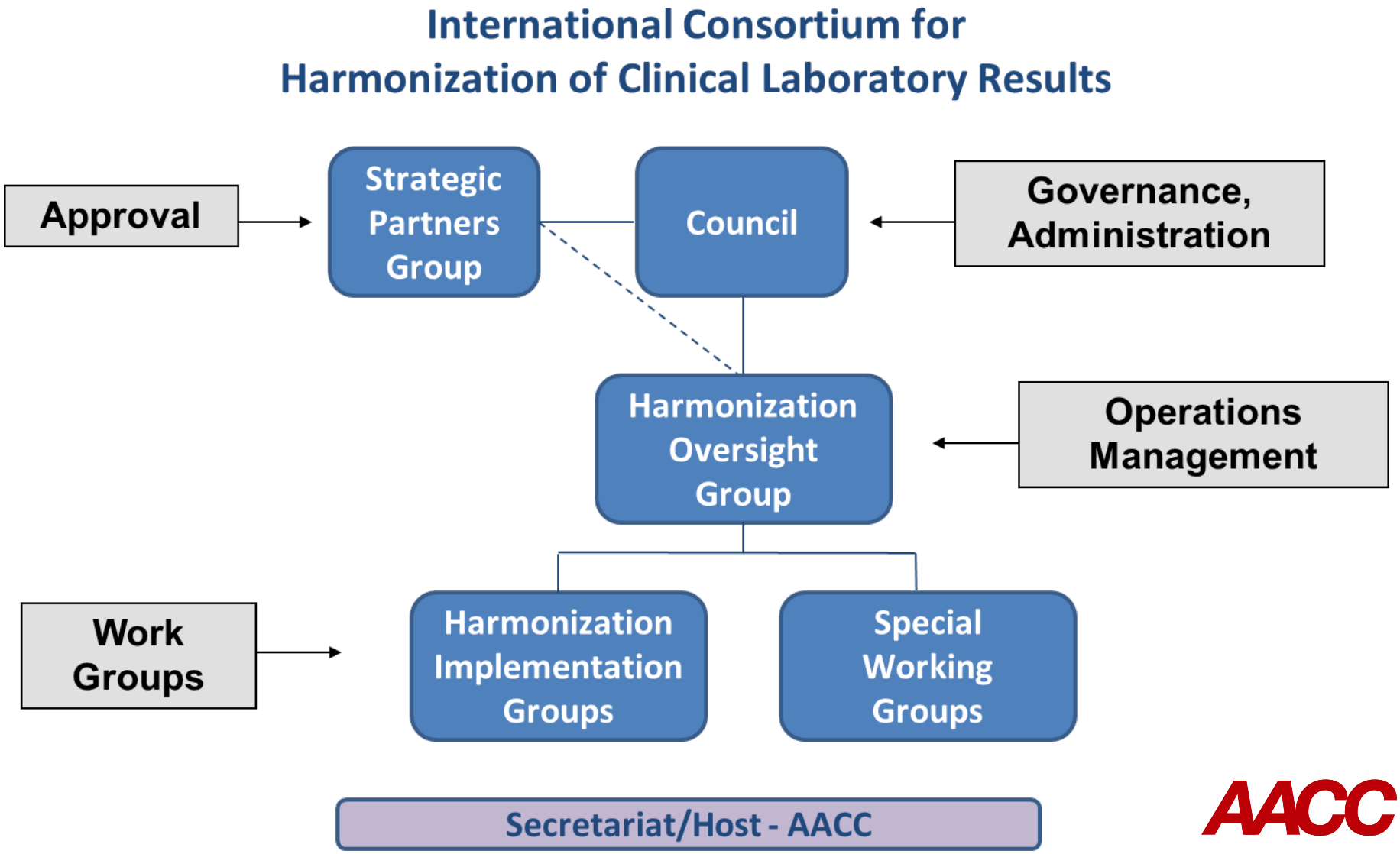
Path Forward
2011-2012

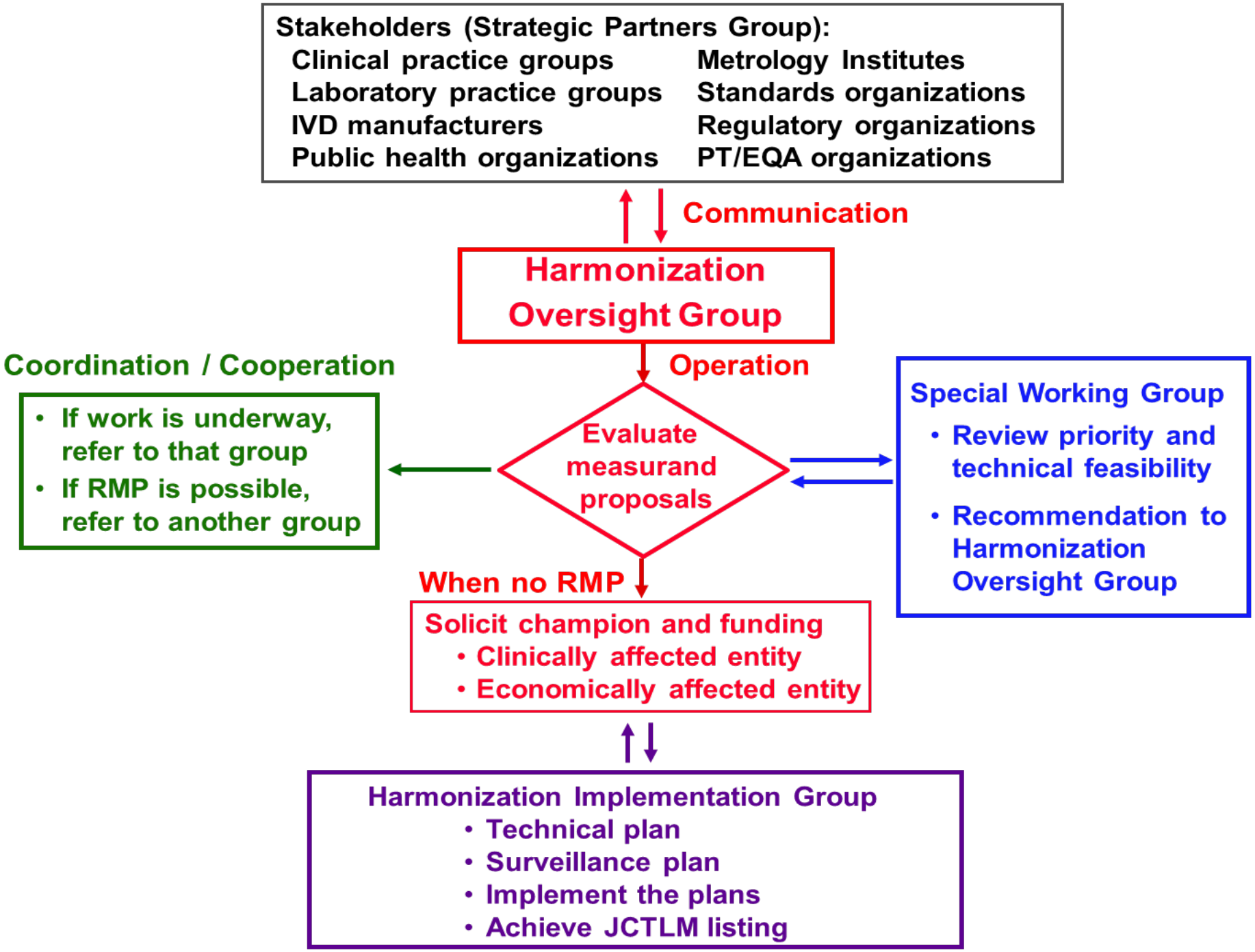
- Steering Committee
- 3 Task Forces

1. Administrative operations
2. Checklists for submission and evaluation
3. Tool box of approaches to harmonization

AACC

AN INFRASTRUCTURE FOR HARMONIZATION




Stakeholders (Strategic Partners Group):
Clinical practice groups
Laboratory practice groups
IVD manufacturers
Public health organizations
Metrology Institutes
Standards organizations
Regulatory organizations
PT/EQA organizations
Communication
Harmonization Oversight Group
Operation
Coordination / Cooperation
• If work is underway, refer to that group
• If RMP is possible, refer to another group
Evaluate measurand proposals
Special Working Group
• Review priority and technical feasibility
• Recommendation to Harmonization Oversight Group
When no RMP
Solicit champion and funding
• Clinically affected entity
• Economically affected entity
Harmonization Implementation Group
• Technical plan
• Surveillance plan
• Implement the plans
• Achieve JCTLM listing

http://www.harmonization.net

- A general information portal for global standardization / harmonization activities
  - Communication with stakeholders
  - Status reports on measurands
  - Useful technical information
  - Information on global activities
  - Links to other organizations

International Consortium for Harmonization of Clinical Laboratory Results

AACC

College of American Pathologists

SBAC
Sociedade Brasileira de Análises Clínicas

The Korean Society for Laboratory Medicine

Chinese Association for Clinical Laboratory Management