ISO 21151 Harmonization Protocol

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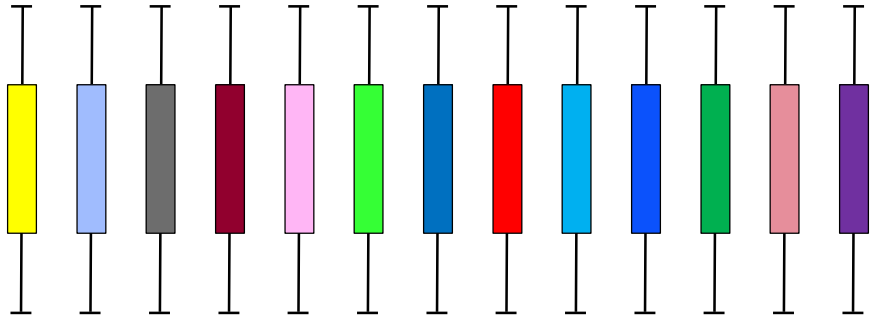
Harmonization

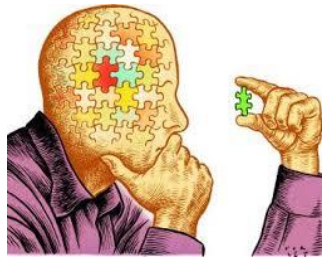
One of the most important challenges in laboratory medicine

What is harmonization

Equivalent results among different measurement procedures for the same laboratory test



Clinical decisions need equivalent results from different measurement procedures



- Equivalent does not mean identical
- Equivalent means within an allowable error consistent with an acceptable risk of harm from decisions based on a lab test result

How to achieve equivalent results

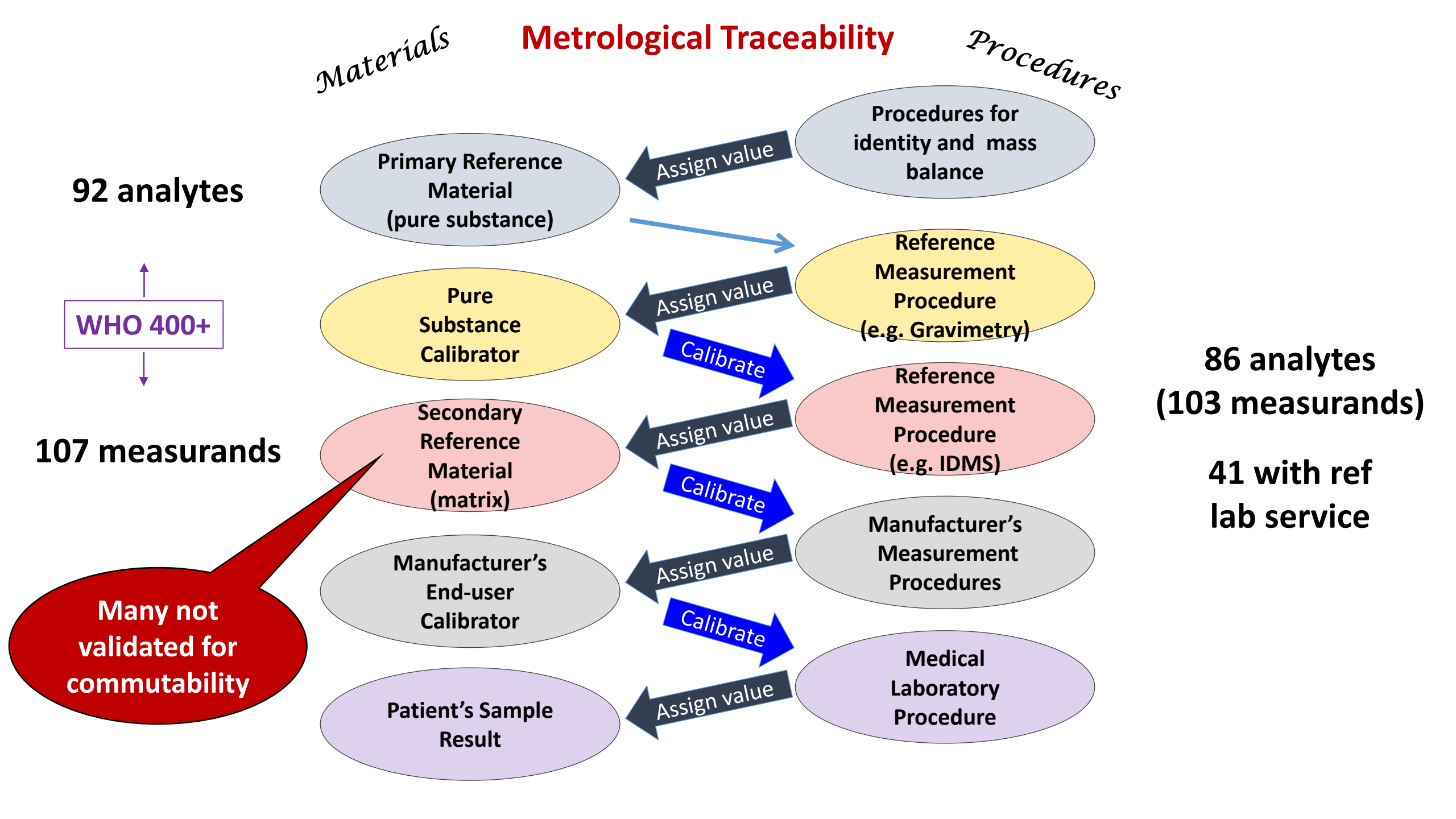
1. **Calibration of all measurement procedures is traceable to a common reference system**

2. **All measurement procedures measure the same quantity (the same molecule)**

Standardization:

equivalent results are achieved by metrological traceability to a fit-for-purpose higher order reference system

Metrological Traceability



Situation in 2019:

1. **Higher order reference systems for ~100 measurands**

2. **Metrological traceability to some non-commutable CRMs**

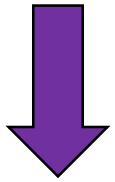
3. **How can we improve this situation?**

International Organization for Standardization

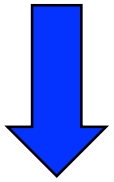
FDIS 17511:2019 ***Requirements for establishing metrological traceability of values assigned to calibrators, trueness control materials and human samples***

- ✓ **includes a harmonization protocol as one approach to achieve metrological traceability**

2010: AACC Workshop on issues in harmonization



2013: ICHCLR formed



NWIP to ISO TC 212

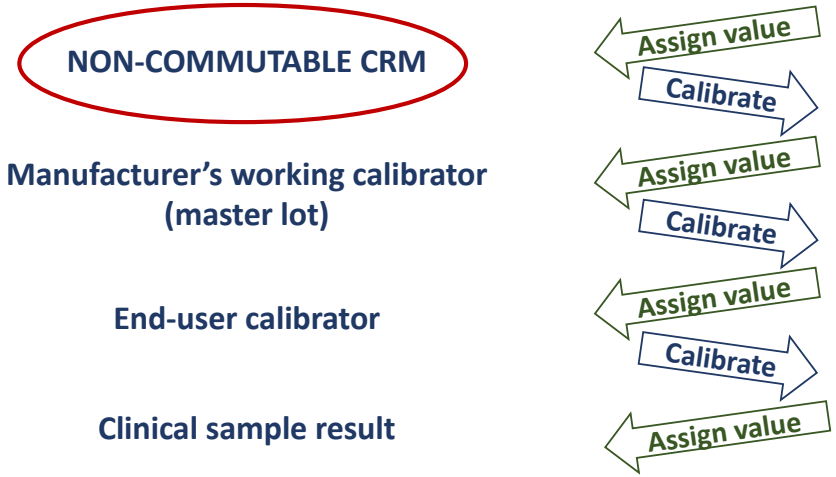
2020: ISO 21151

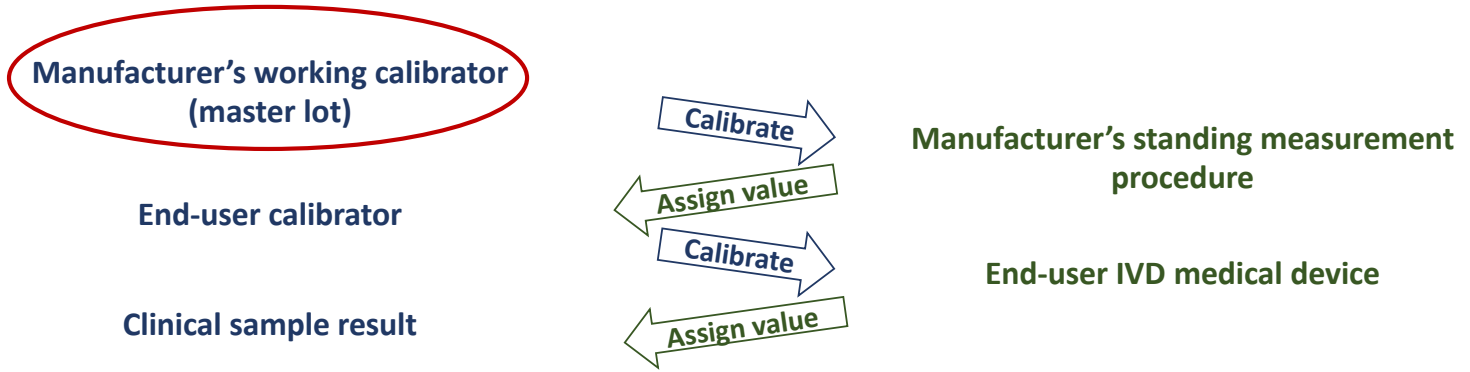
International Organization for Standardization

DIS 21151:2019 Requirements for international harmonisation protocols establishing metrological traceability of values assigned to calibrators and human samples

FDIS not required (no technical comments on DIS vote)

Replace these inadequate calibration hierarchies …





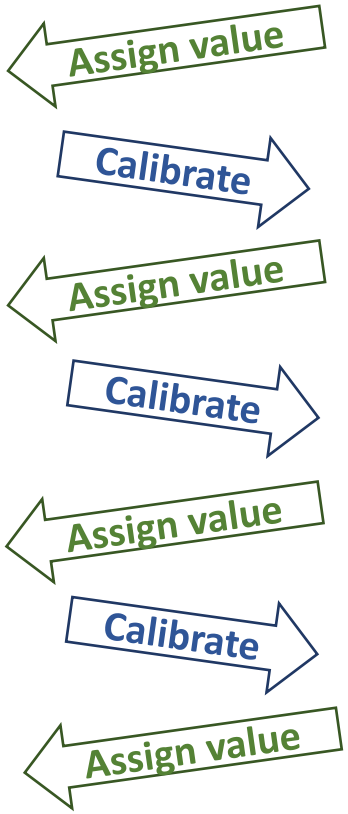
… with metrological traceability to a harmonization protocol

Harmonization reference material (e.g. a panel or pools of clinical samples)

Manufacturer's working calibrator (master lot)

End-user calibrator

Clinical sample result



International harmonization protocol for a calibration hierarchy

Manufacturer's selected measurement procedure

Manufacturer's standing measurement procedure

End-user IVD medical device

Requirements in ISO DIS 21151:2019

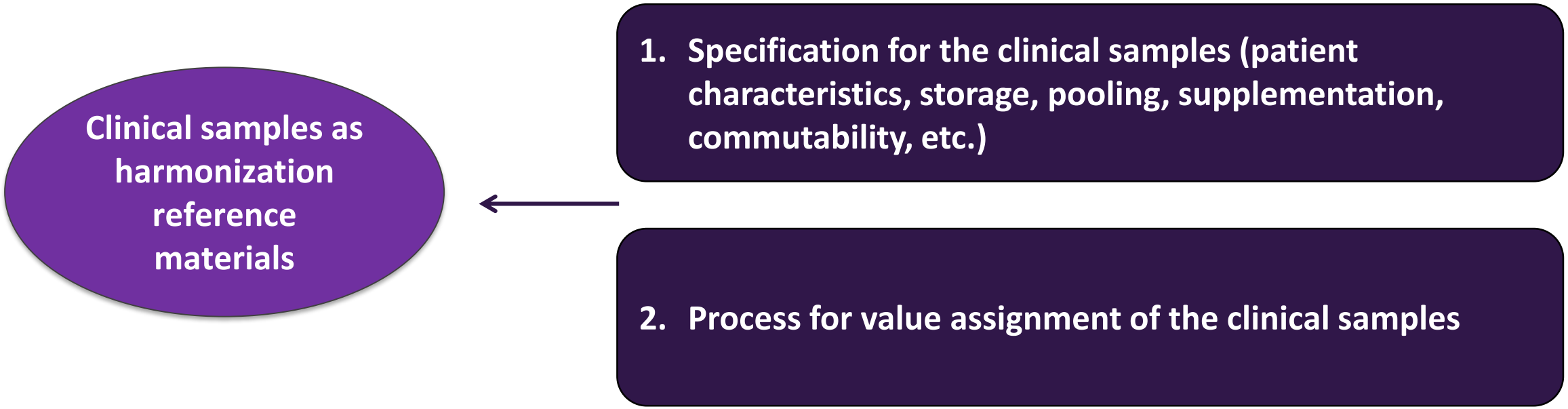
Publication of the final 17511 and 21151 standards is expected in 2020

Qualify measurement procedures for inclusion

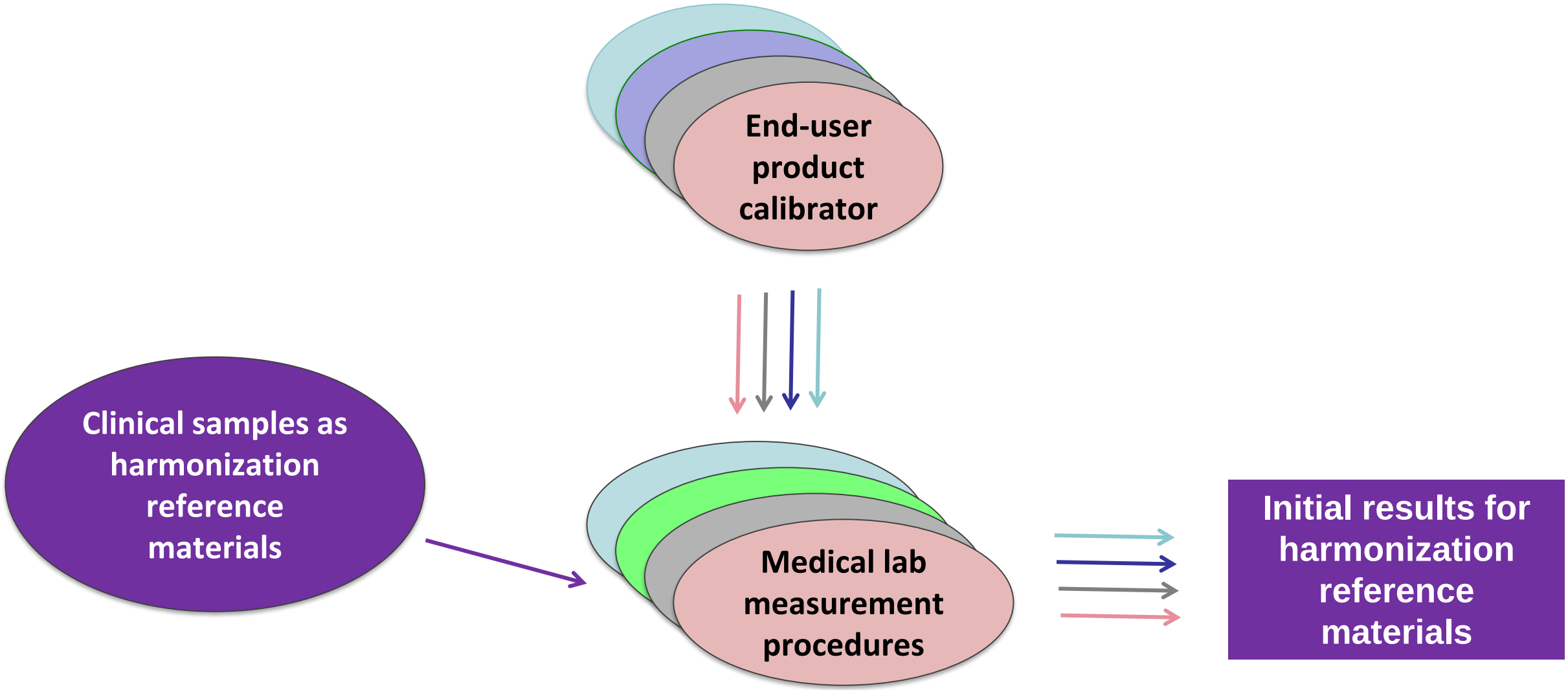
1. **Measure the same quantity (molecular form)**
   - **Correlated measurement responses**
   - **Similar specimen specific influences = similar selectivity for the measurand**

2. **Adequate performance**
   - **Precision**
   - **Proportional response over concentration**

Specify reference materials, e.g. clinical samples



Describe how to derive correction: e.g. initial results

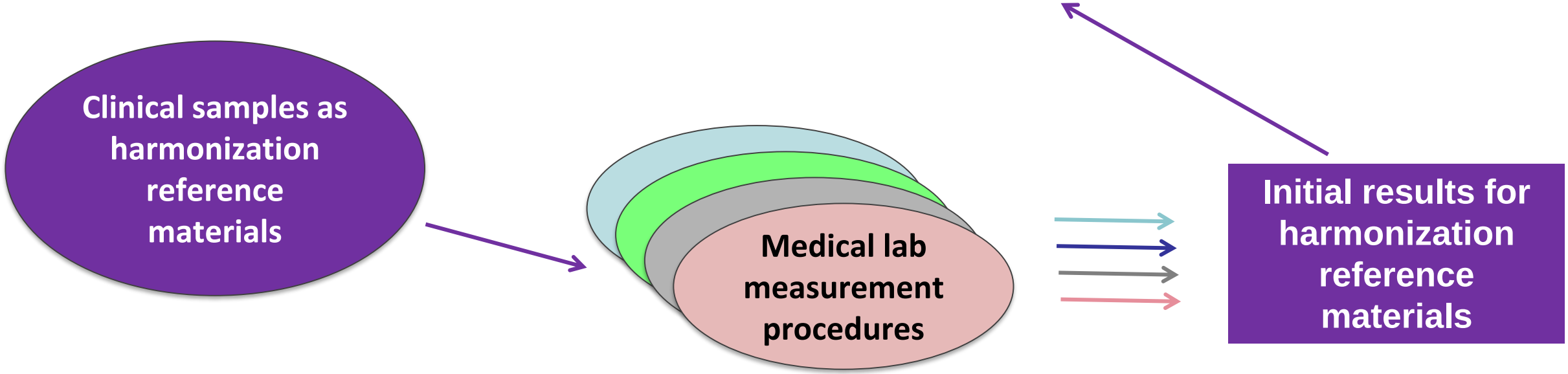


Describe how to derive the method-specific correction

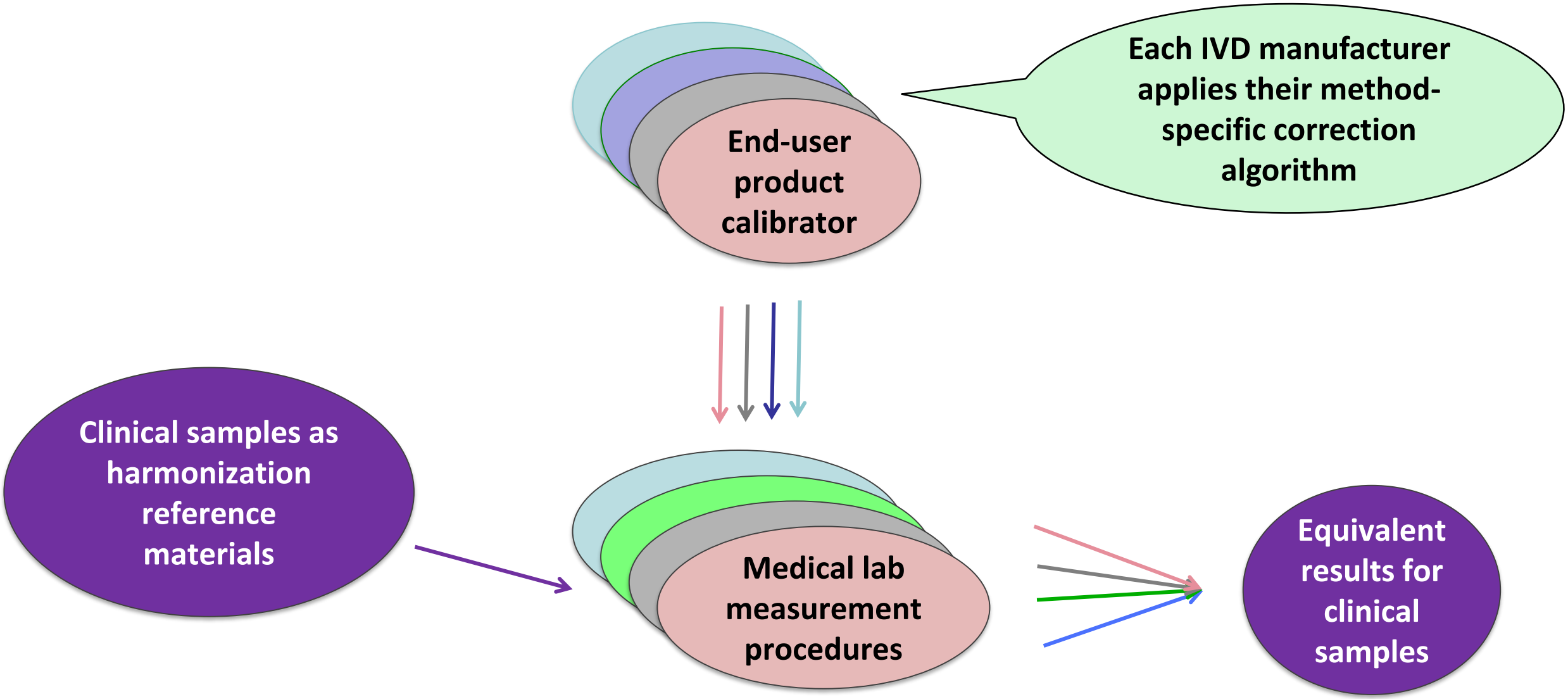
Each IVD manufacturer develops a method-specific correction algorithm to achieve equivalent results for clinical samples.

Can apply the correction to:

1. Working (master) calibrator, or
2. End-user calibrator, or
3. Clinical sample result

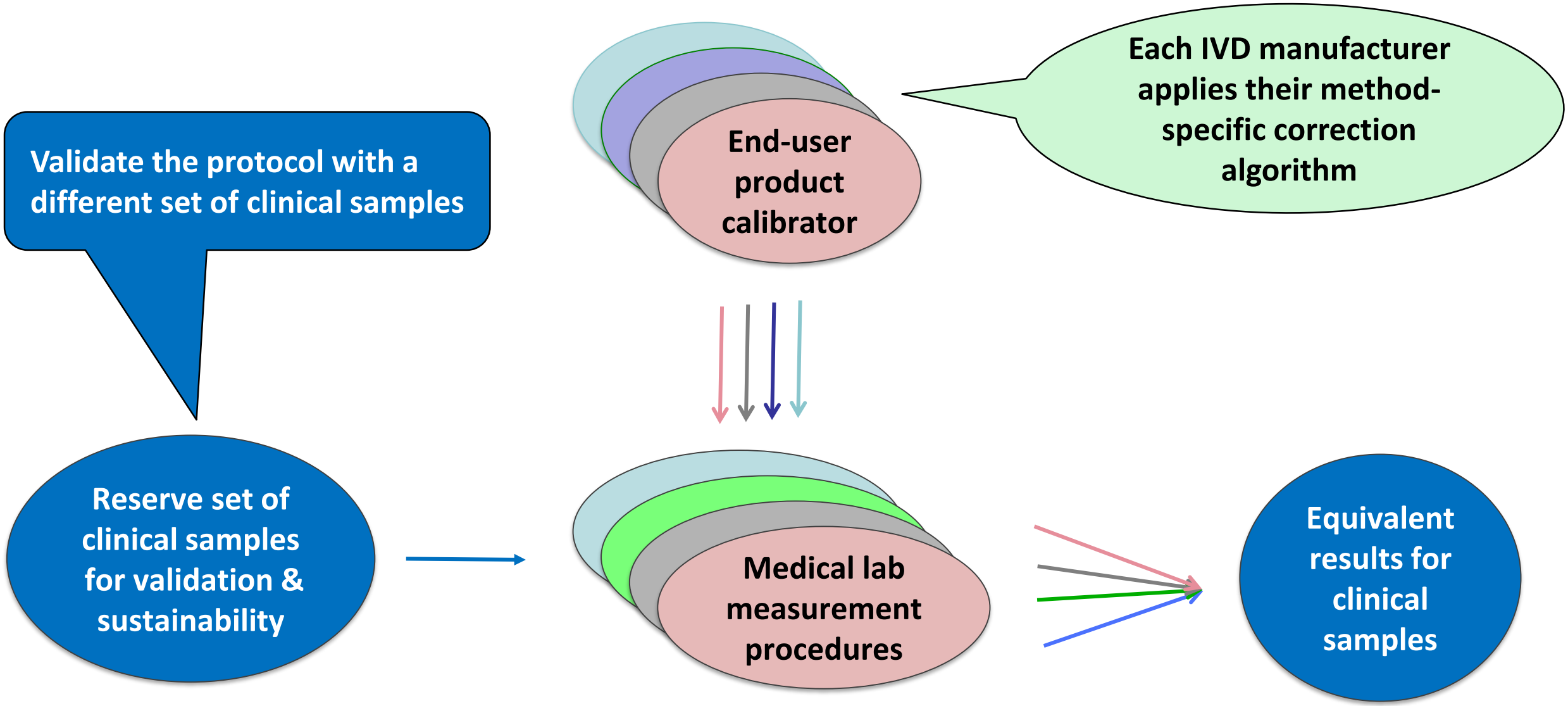


Apply the method-specific correction



Describe validation and sustainability

Validate the harmonization protocol

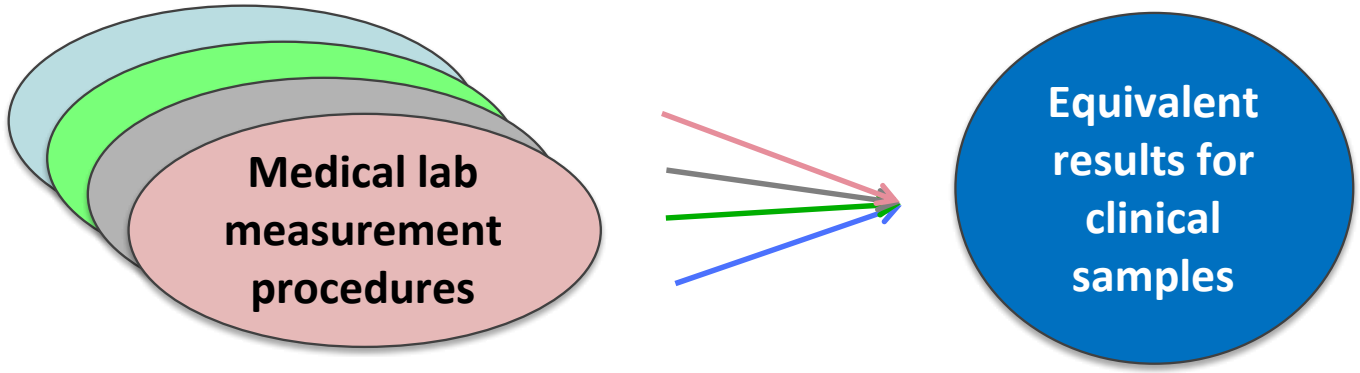


Surveillance over time (sustained validation)

1. Feedback to labs and IVD manufacturers
2. Repeat harmonization protocol if needed (reserve set)
3. Provision for harmonization of new or improved measurement procedures

Surveillance of harmonized results

- **EQA/PT** (commutable samples)
- Other scheme; e.g. patient medians



EQA data aggregation project (ICHCLR / EQALM)

- Commutable samples
- Aggregate results from global providers
- Feedback to IVD and laboratories
- Pilot from 4 EQA providers

JCTLM

Accurate results
for patient care

ISO 21151 will enable JCTLM to list harmonization protocols

Conclusions

- **Metrological traceability to higher order CRMs or RMPs is preferred.**

- **A harmonization protocol provides metrological traceability when:**
  - **higher order CRMs or RMPs do not exist,**
  - **are technically inadequate,**
  - **or are difficult to develop.**

- **JCTLM will be able to list harmonization protocols in its database**