Understanding and Implementing Commutability

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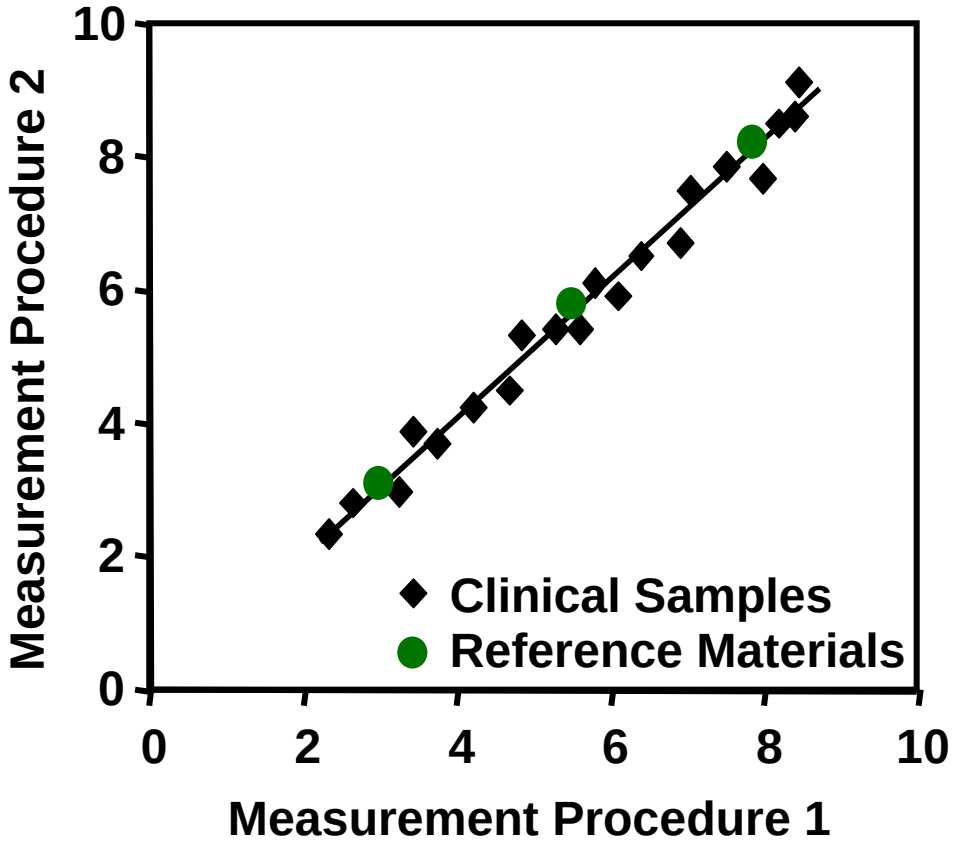
Commutability

Property of a reference material **such that the same amount of measurand in the reference material and in patients' samples produces the same measurement response in different measuring systems.**

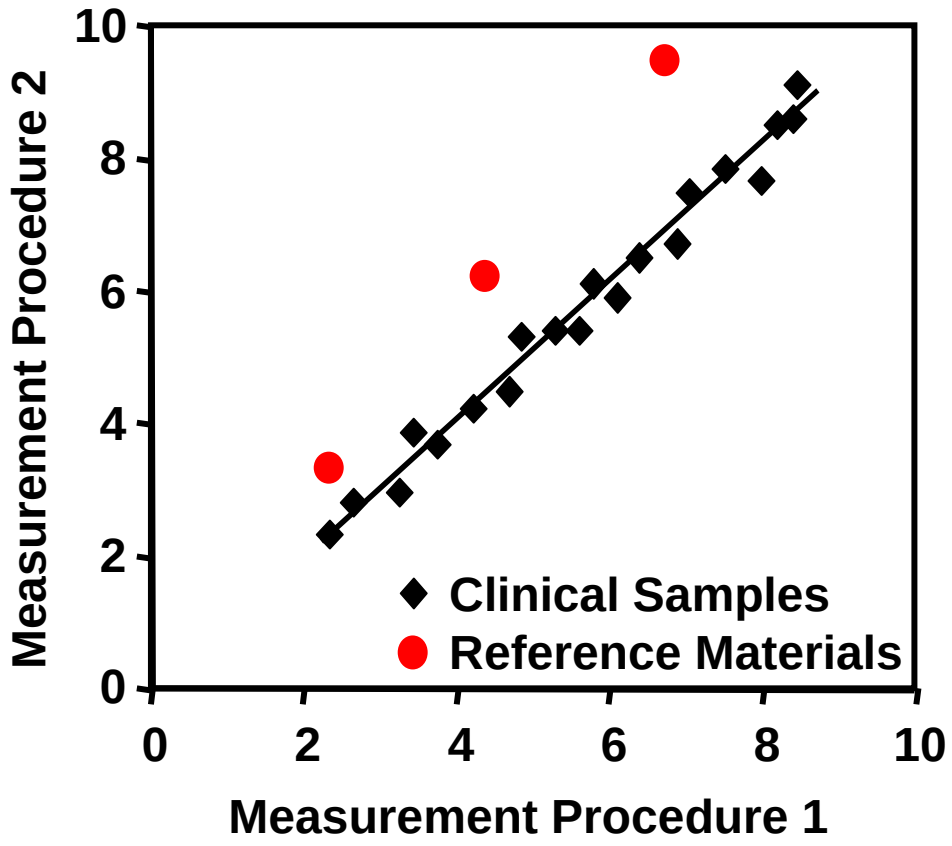
i.e. acceptable closeness of agreement between the results for the reference material and the patients' samples from two (or more) measuring systems.

Commutable



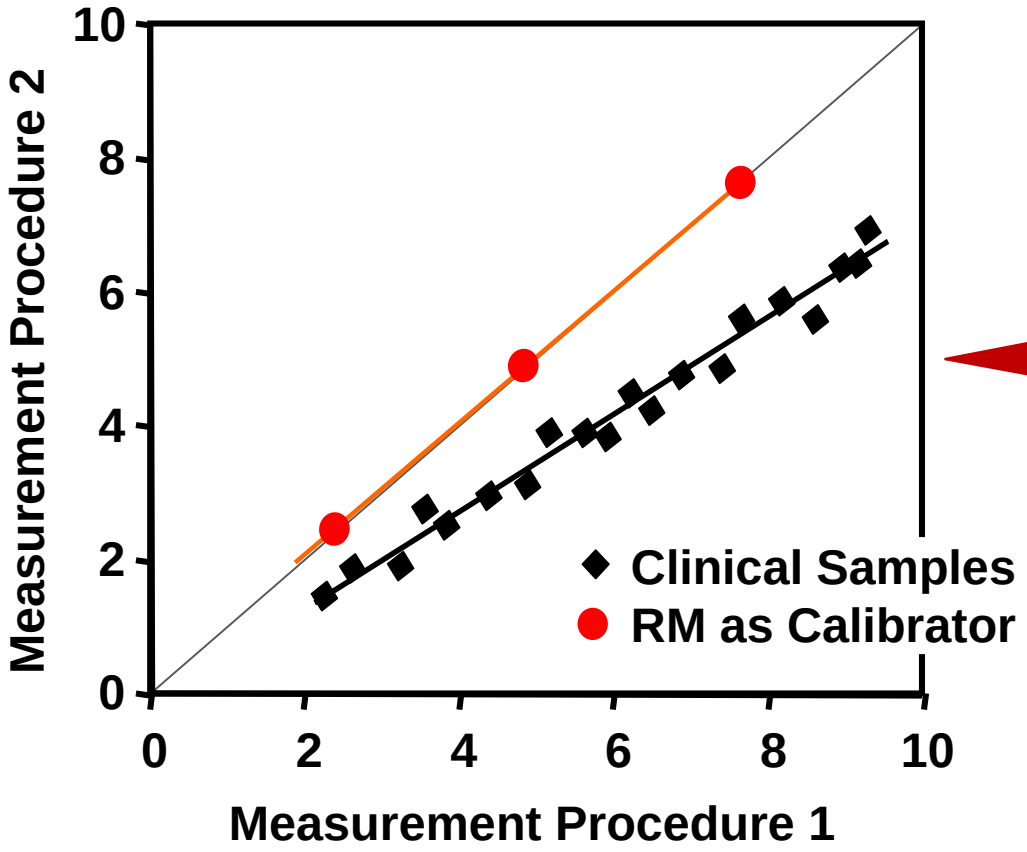
RM and CS results have the same relationship between measurement procedures

Non-Commutable



RM and CS results have a different relationship between measurement procedures

Non-Commutable Calibrator



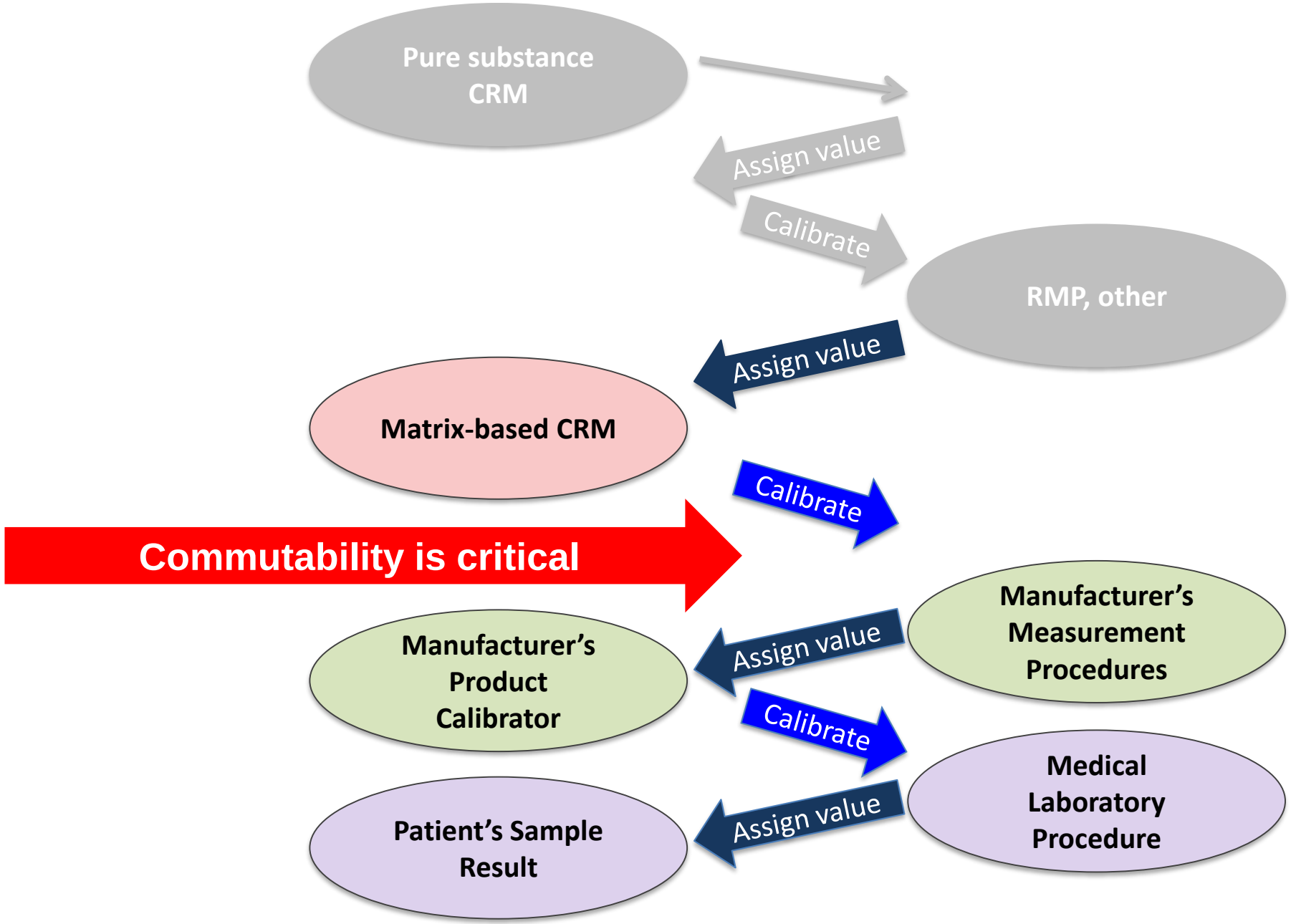
causes clinical sample results to be different

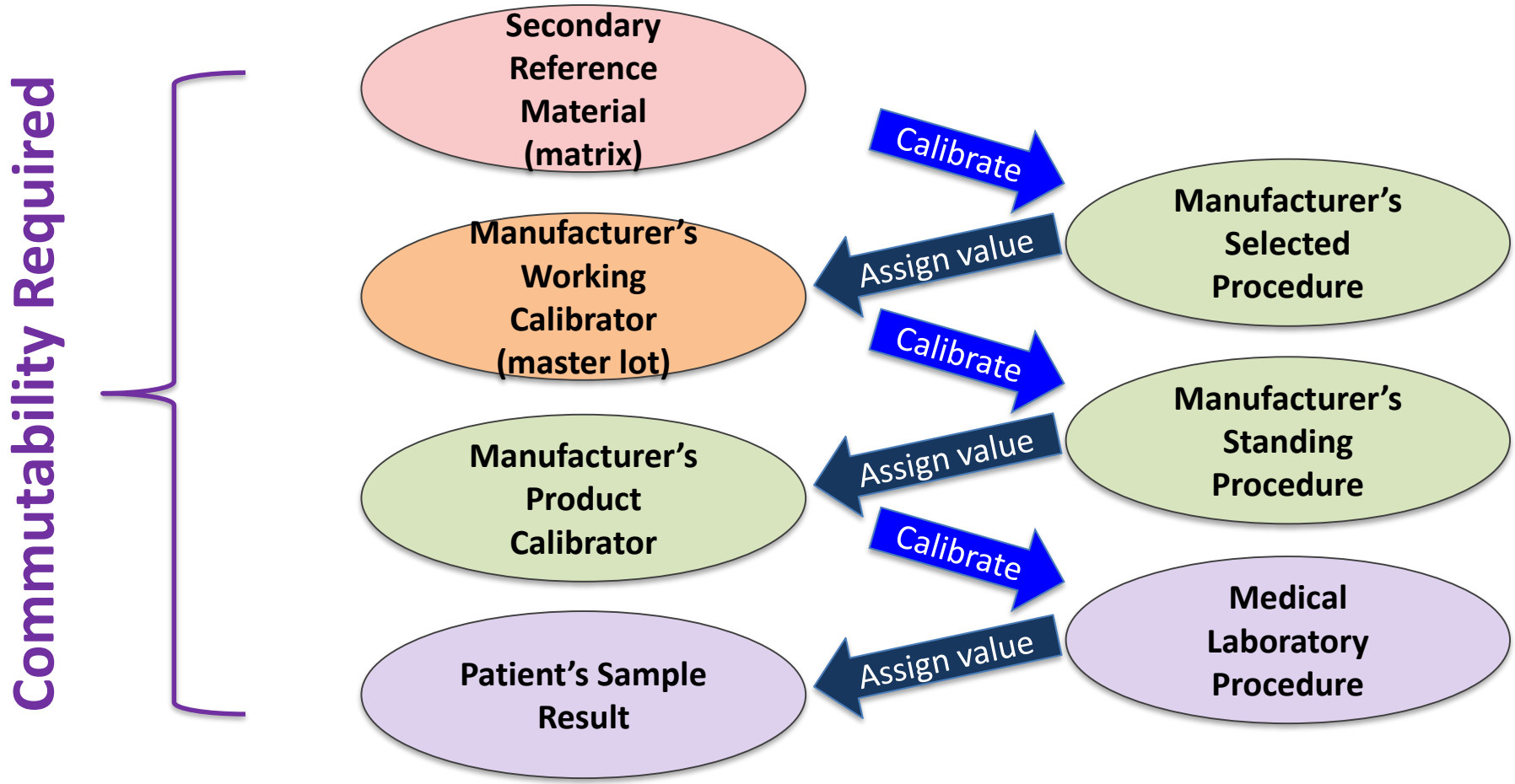
Why would anyone use a non-commutable calibrator?

1. **Regulations require metrological traceability to higher order references**
    - **e.g. EU Directive 98/79/EC in 1998**
    - **No specification regarding suitable for use**

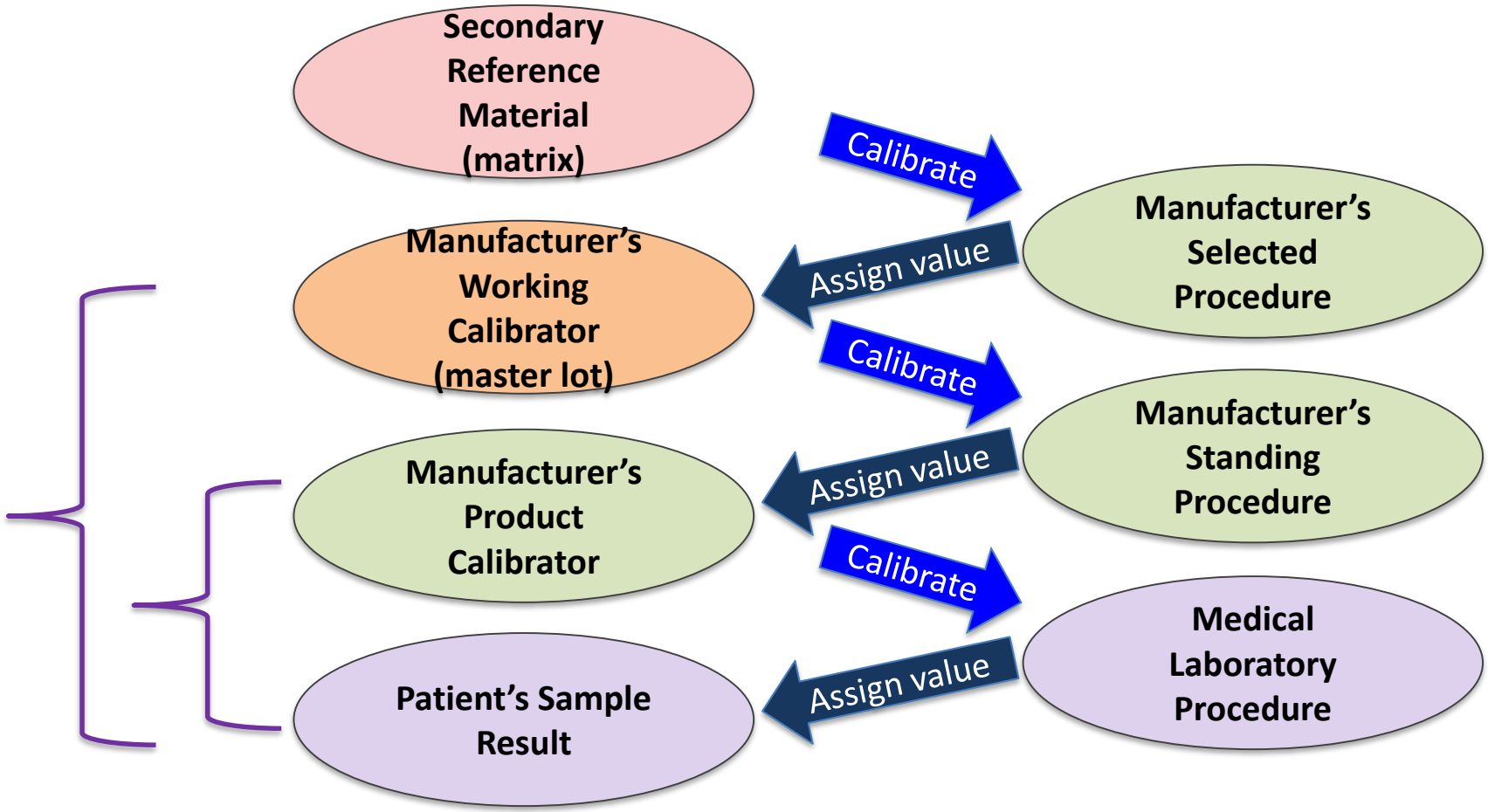
Why would anyone use a non-commutable calibrator?

2. Some matrix-based CRMs are non-commutable
    - Intended use is not always clear in the certificate
    - Many CRMs were never assessed for commutability
    - JCTLM lists matrix-based CRMs of unknown commutability
    - WHO operates independently


Pure substance CRM
Assign value
Calibrate
RMP, other
Assign value
Matrix-based CRM
Calibrate
Commutability is critical
Manufacturer's Measurement Procedures
Assign value
Manufacturer's Product Calibrator
Calibrate
Medical Laboratory Procedure
Assign value
Patient's Sample Result


Commutability Required
Secondary Reference Material (matrix)
Manufacturer's Working Calibrator (master lot)
Manufacturer's Product Calibrator
Patient's Sample Result
Calibrate
Assign value
Calibrate
Assign value
Calibrate
Assign value
Manufacturer's Selected Procedure
Manufacturer's Standing Procedure
Medical Laboratory Procedure

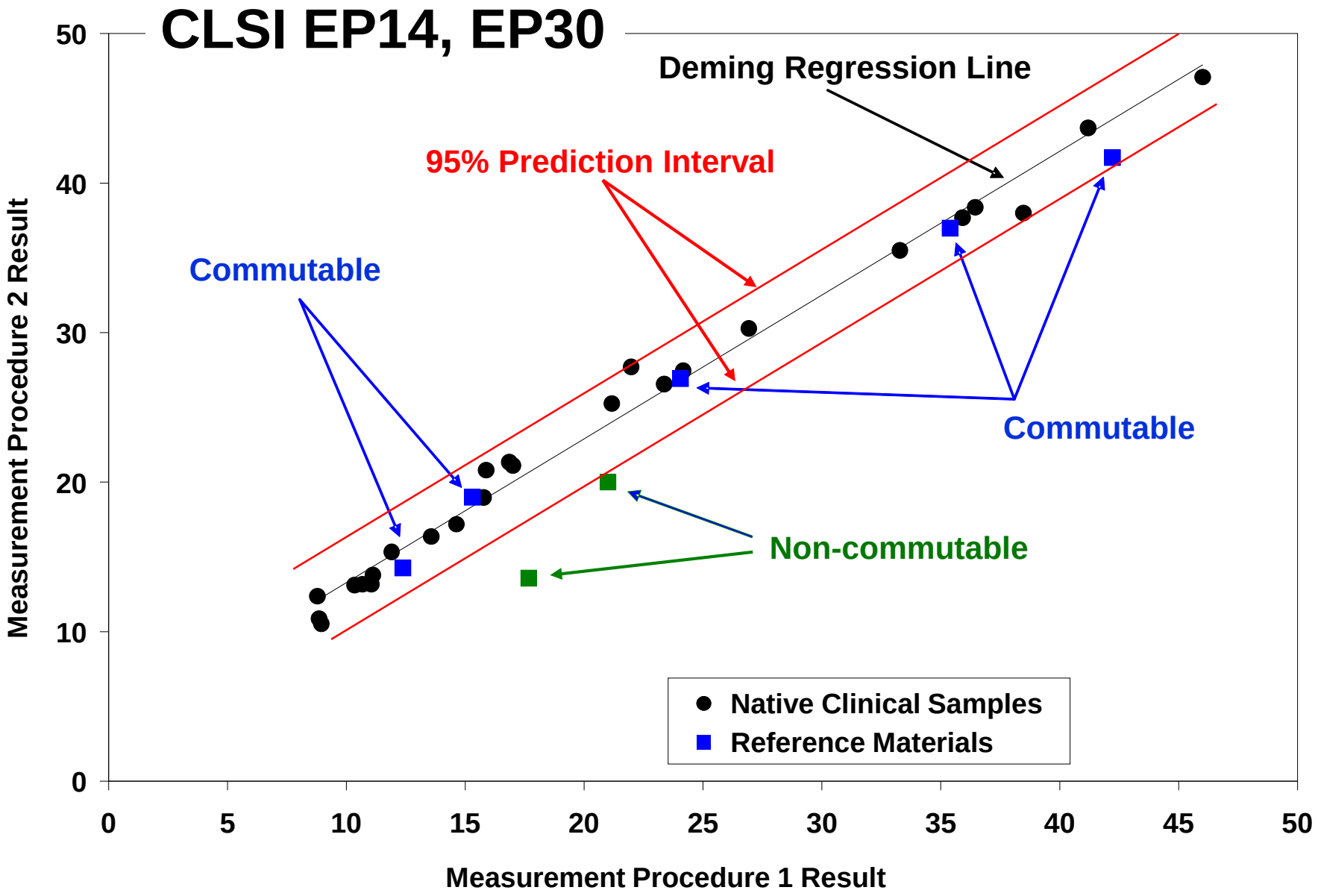
Commutability NOT REQUIRED



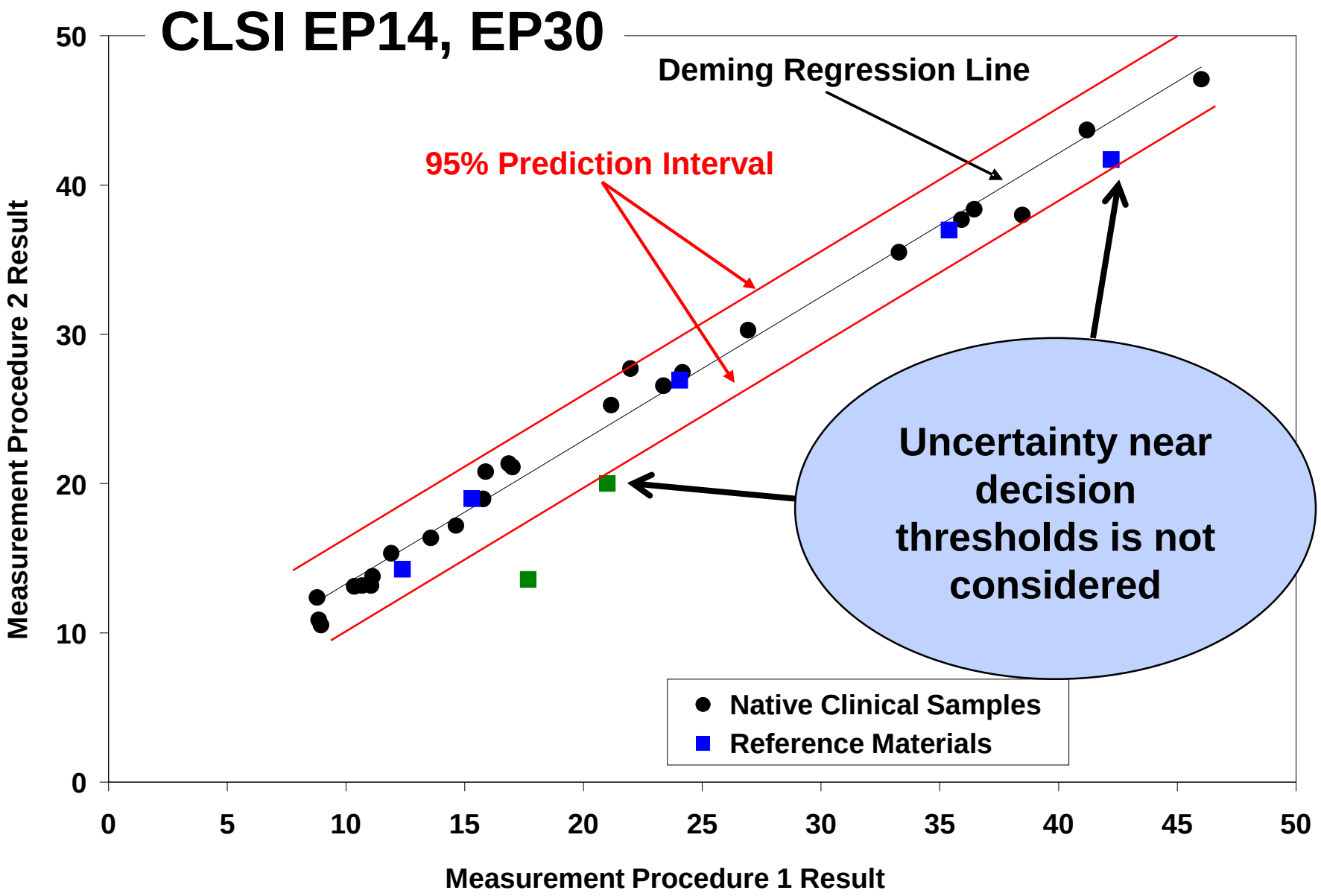
Commutability is important for:

Matrix-based CRMs used as calibrators

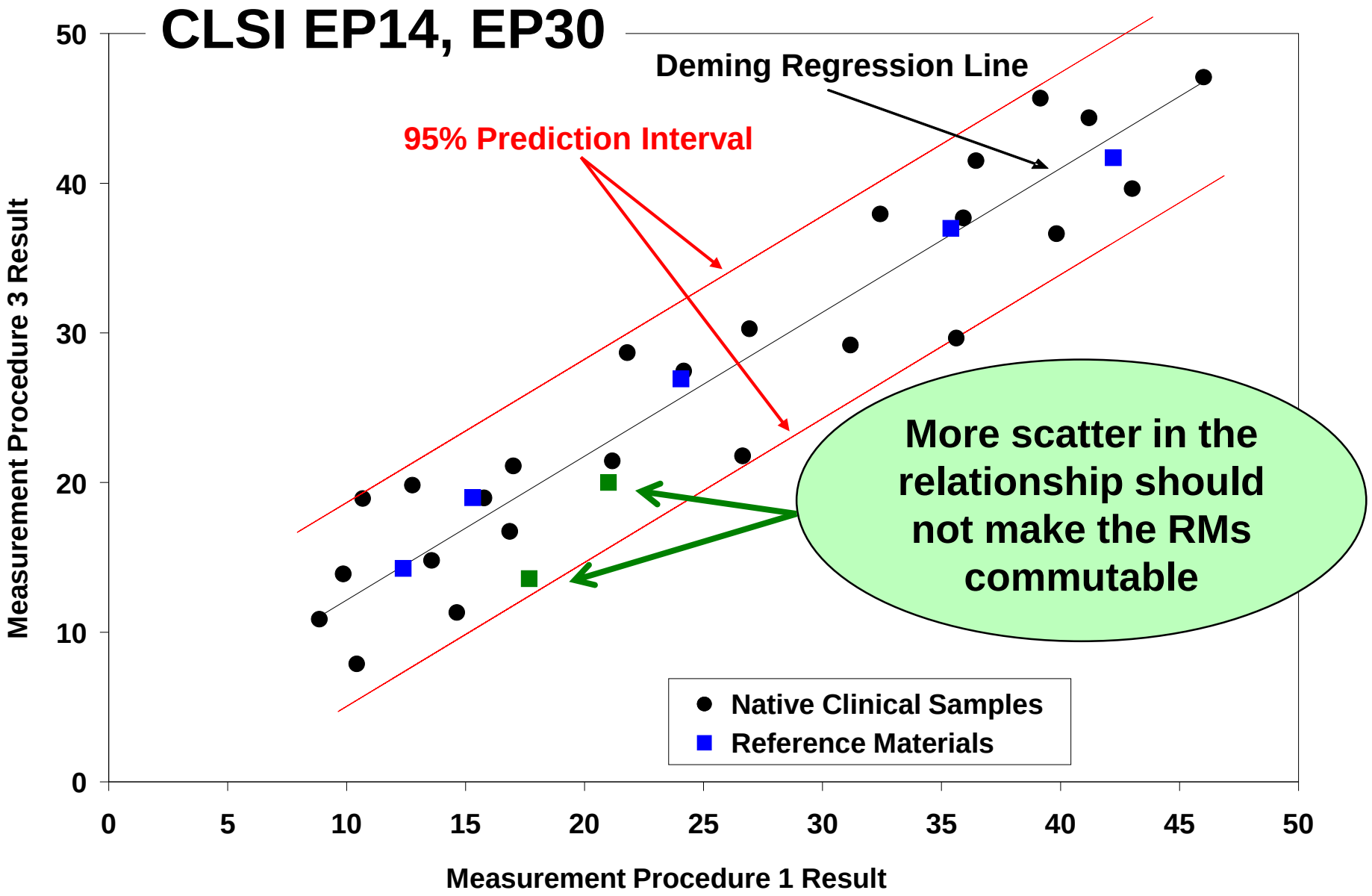
EQA materials used to assess harmonization/standardization



Adapted from CLSI EP30-A (used with permission)

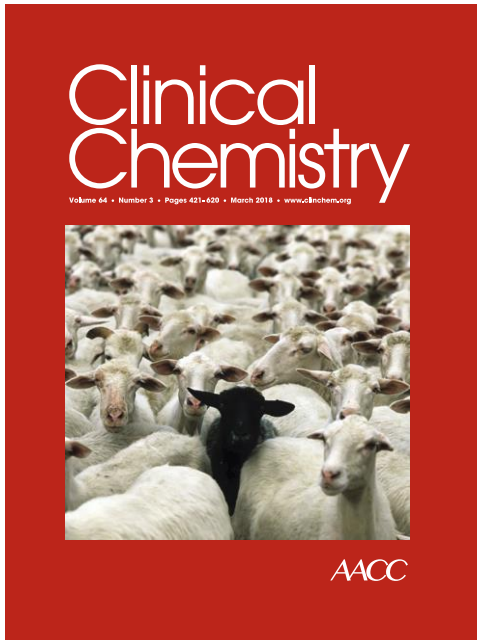


Adapted from CLSI EP30-A (used with permission)



Modified from CLSI EP30-A (used with permission)

IFCC Working Group on Commutability



Recommendations for assessing commutability:

Part 1: general experimental design; *Clin Chem* 2018;64:447-54

Part 2: using the difference in bias between a reference material and clinical samples; *Clin Chem* 2018;64:455-64

Part 3: using the calibration effectiveness of a reference material; *Clin Chem* 2018;64:465-74

Part 1: general experimental design

Measurement procedures must be qualified for inclusion in a commutability assessment

1. **Adequate calibration model over the measuring interval**
   - **Good correlation between measurement procedures for clinical samples**
2. **Adequate selectivity for the measurand**
   - **Small error component from sample specific influences**
3. **Adequate precision**

→ **Measurement procedure improvement may be a prerequisite for inclusion in a commutability assessment**

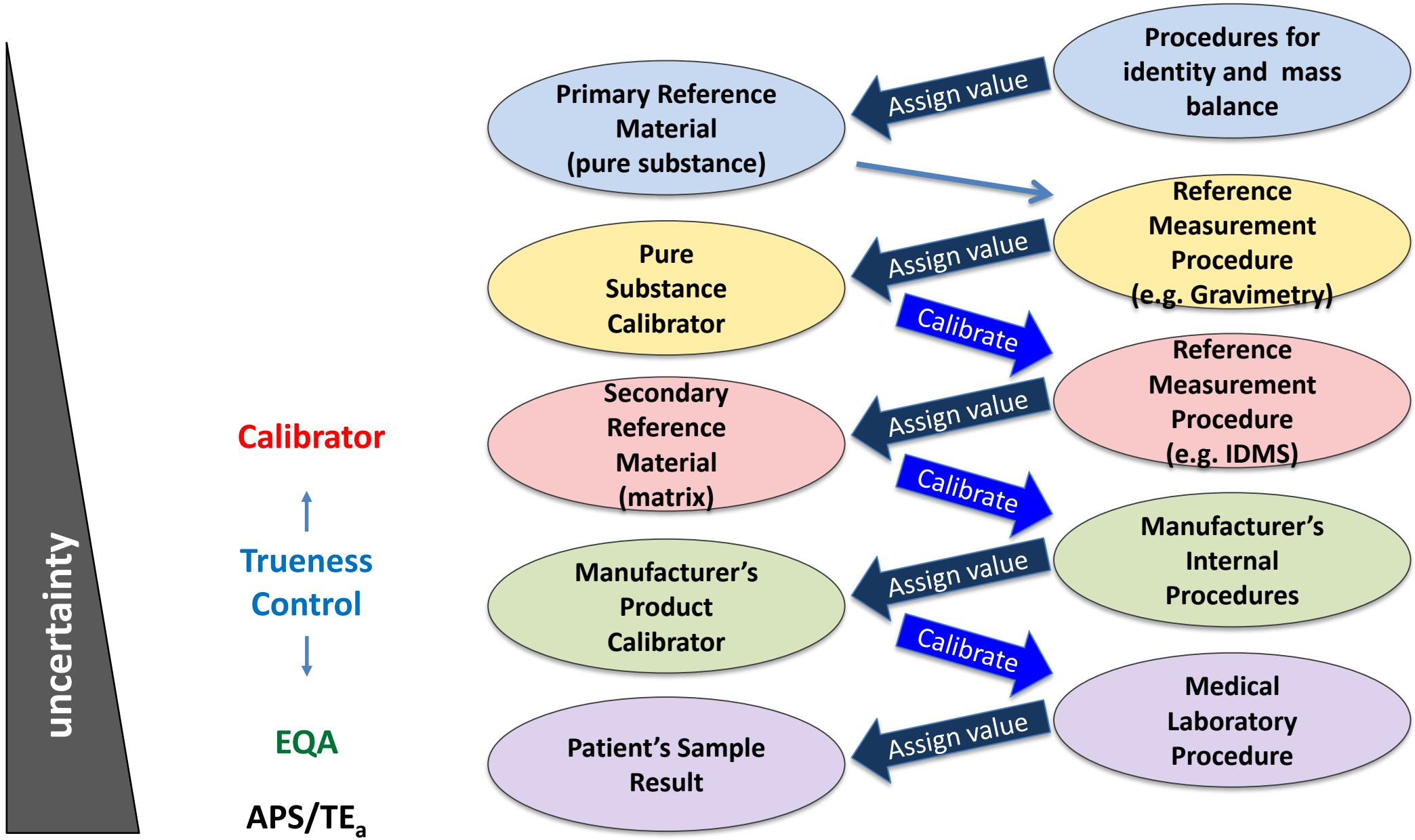
Clinical samples must be qualified as suitable for use in a commutability assessment

1. **Should not contain unusual interfering substances or analyte forms that will influence most measurement procedures**
2. **Must cover the concentrations of the RM(s)**
3. **Individual samples are preferred**
4. **Pooled samples may be needed to meet volume requirements – pooling must be validated**
5. **Preparation and storage conditions must be validated**

Criterion for commutability is based on medical use requirements

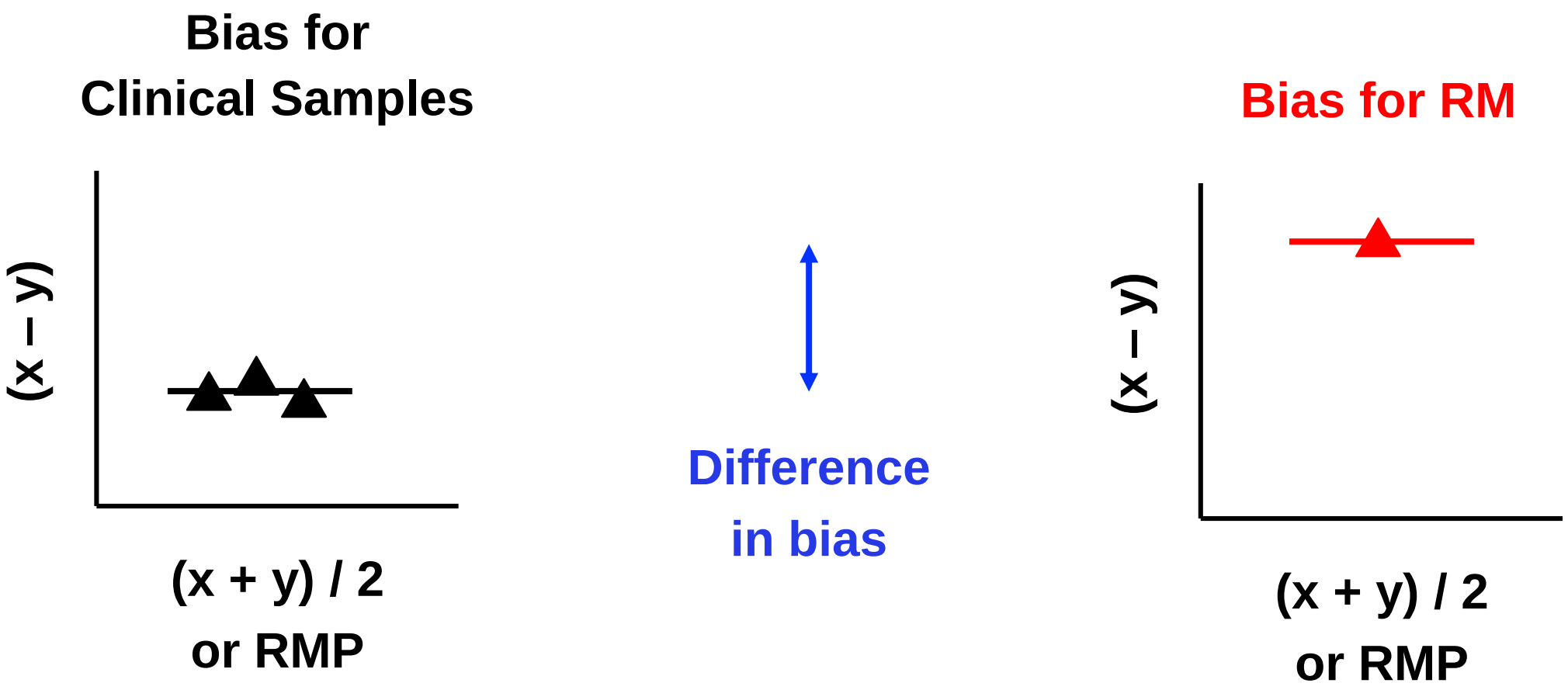
Criterion is the same for all measurement procedures in the commutability assessment

Criterion is a fraction of the uncertainty required for a reference material's intended use related to the analytical performance specification for patient sample results

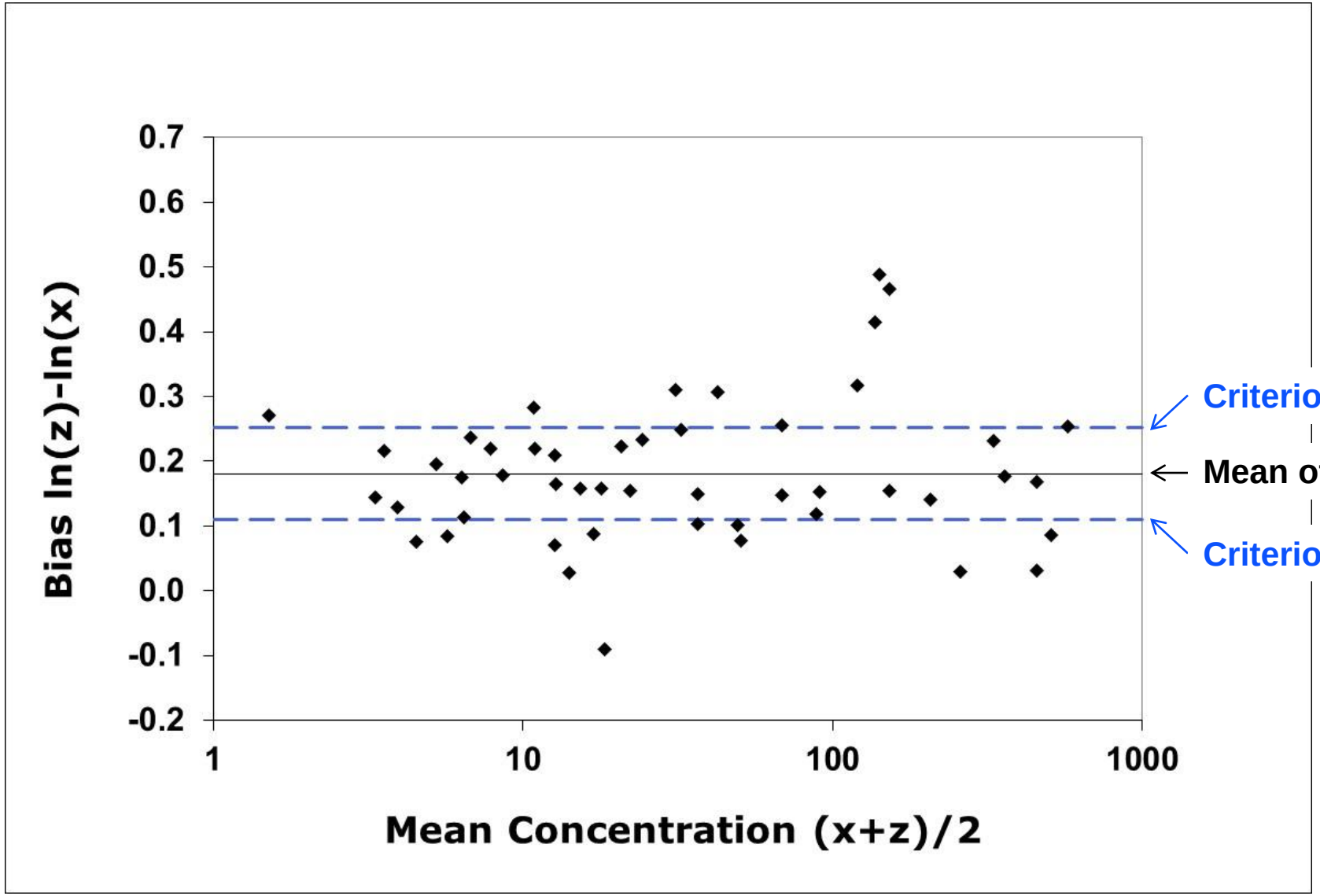


Part 2: assessment by difference in bias

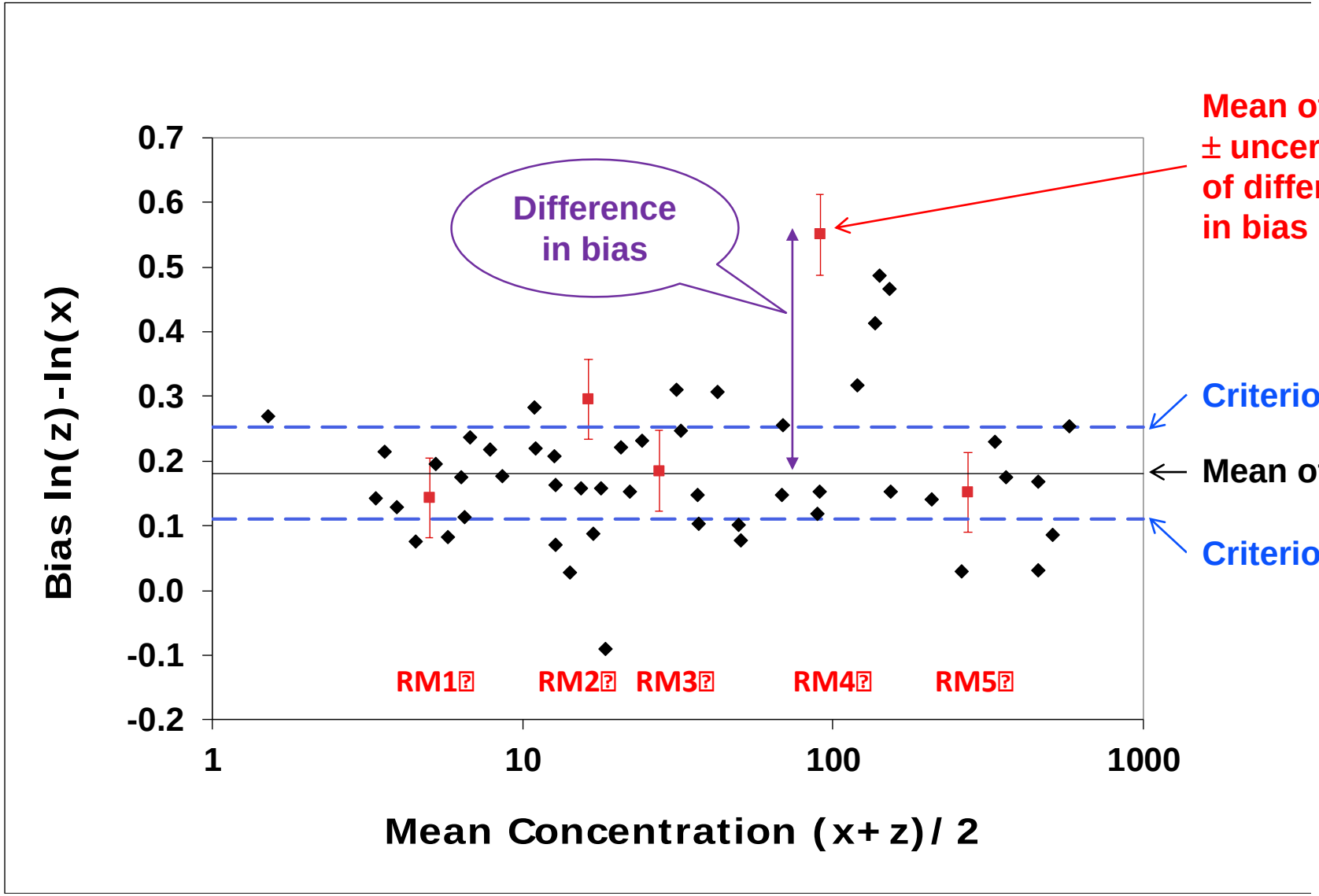
Difference in Bias



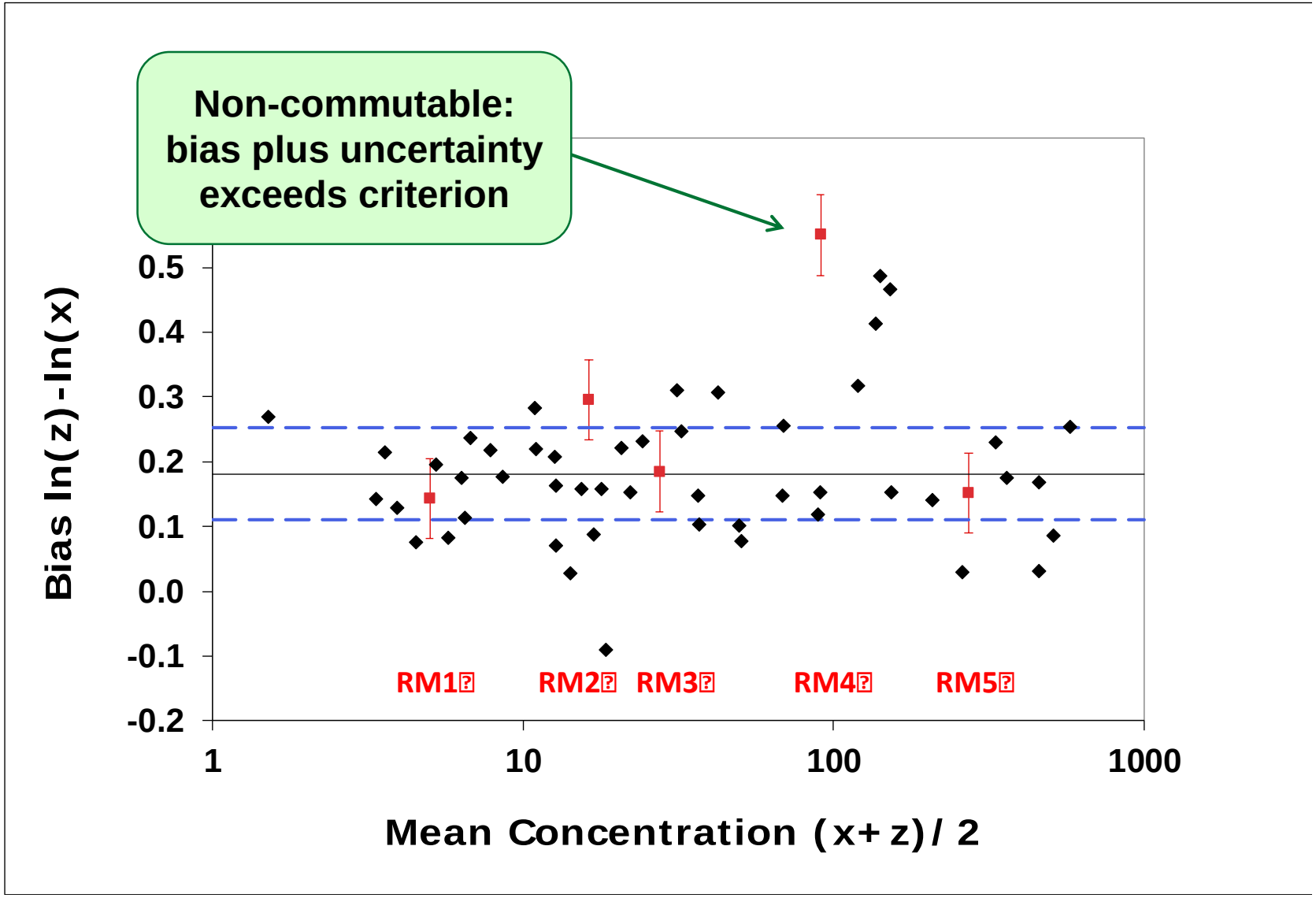
Difference in bias vs. fixed criterion



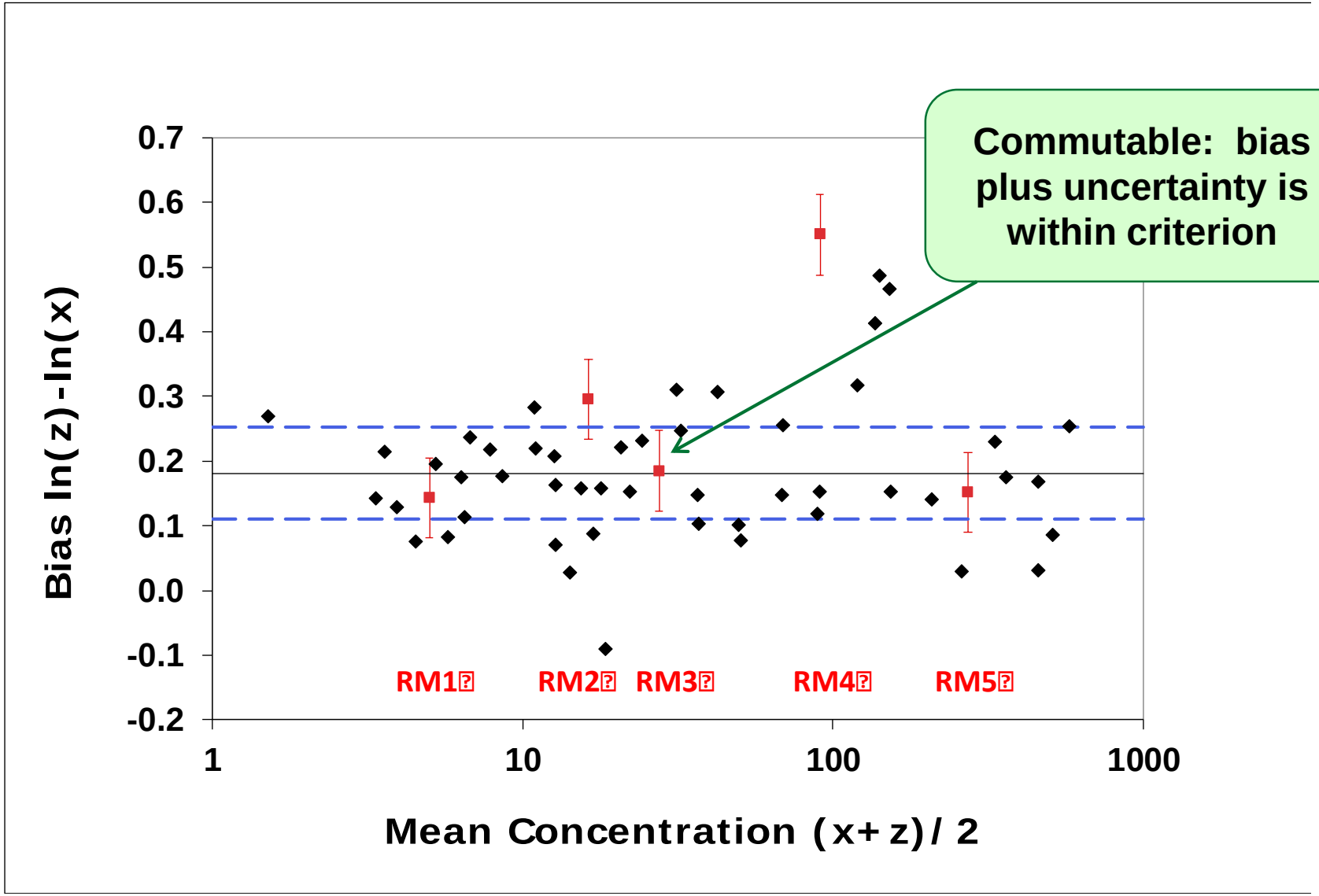
Difference in bias vs. fixed criterion



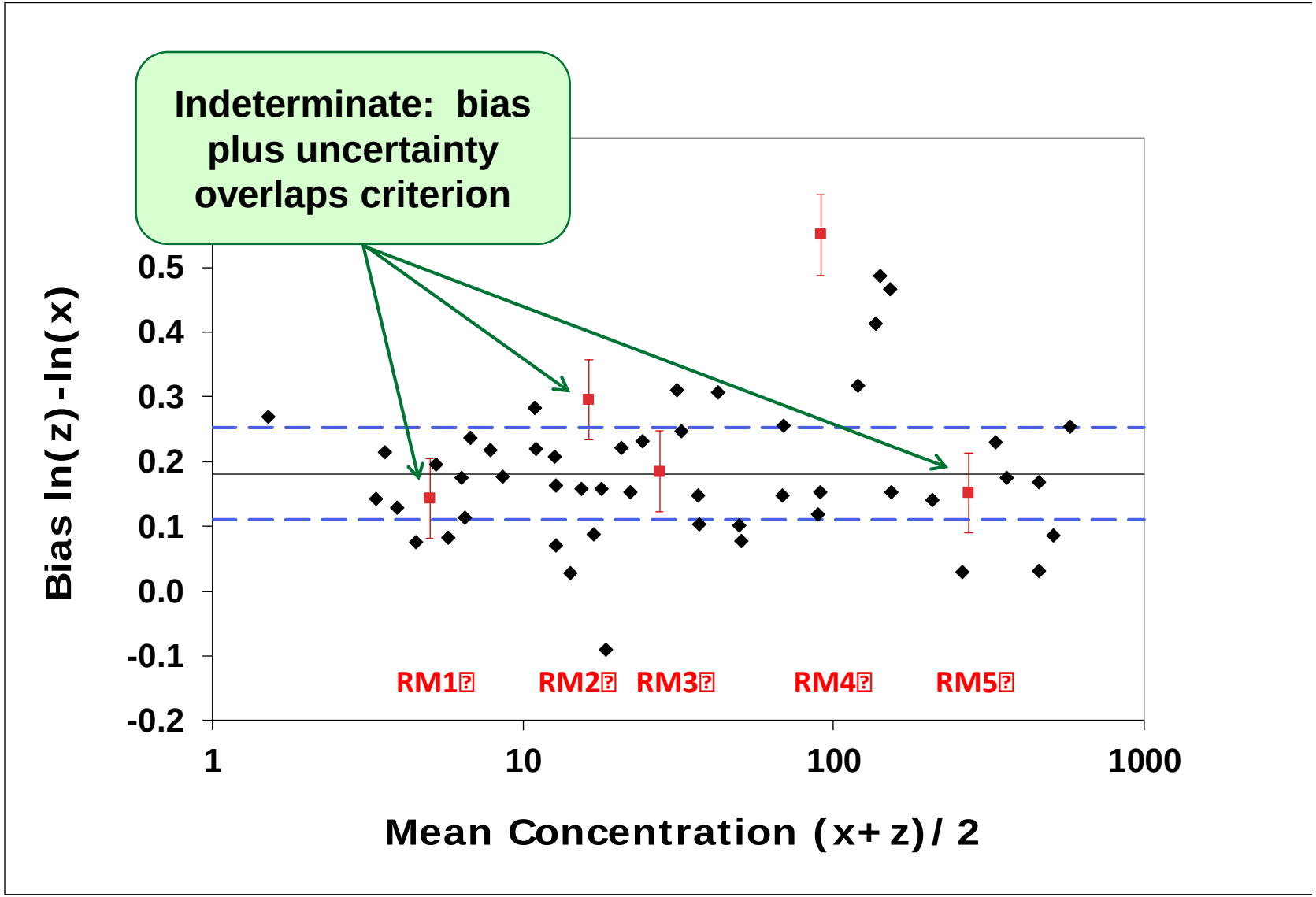
Difference in bias vs. fixed criterion



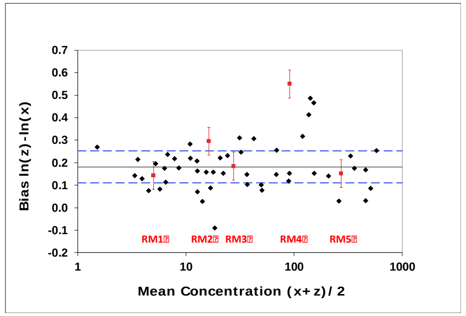
Difference in bias vs. fixed criterion

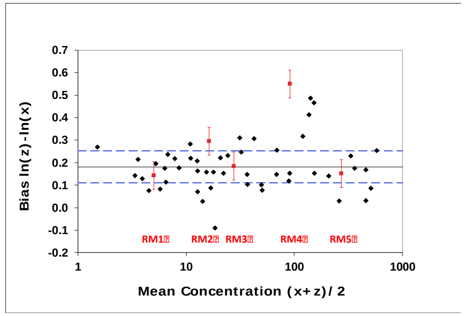


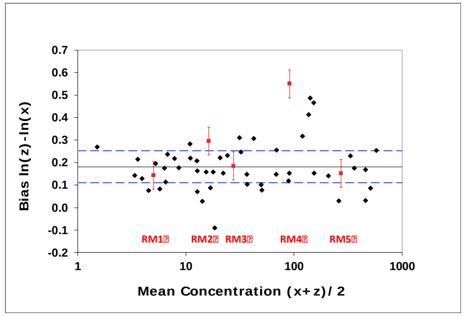
Difference in bias vs. fixed criterion

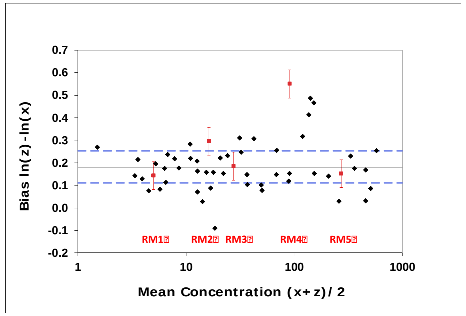


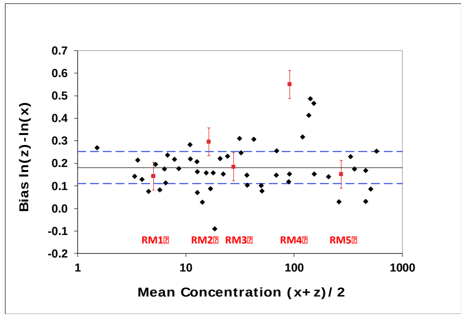
Evaluate all combinations of pairs of measurement procedures

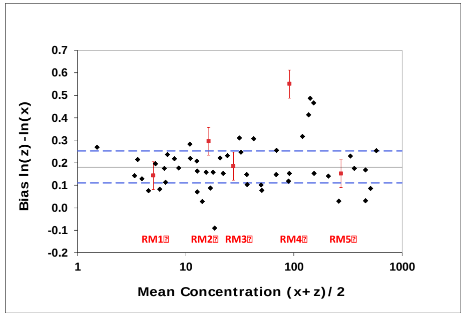


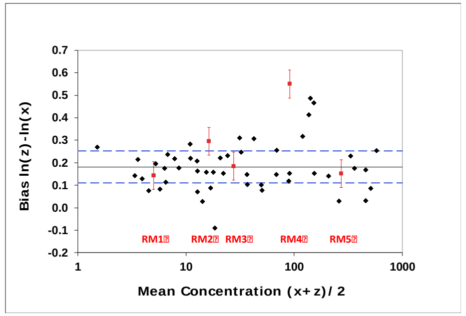


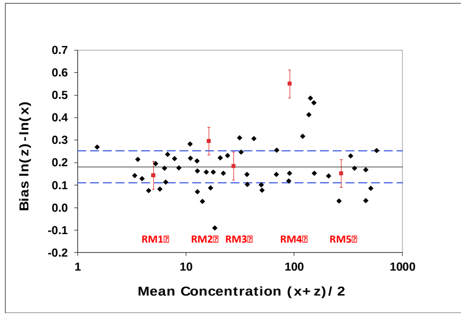


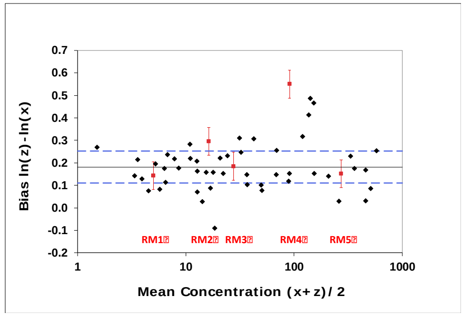


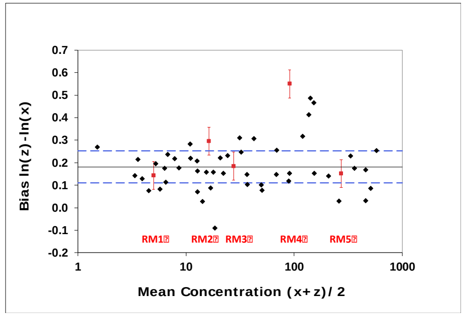




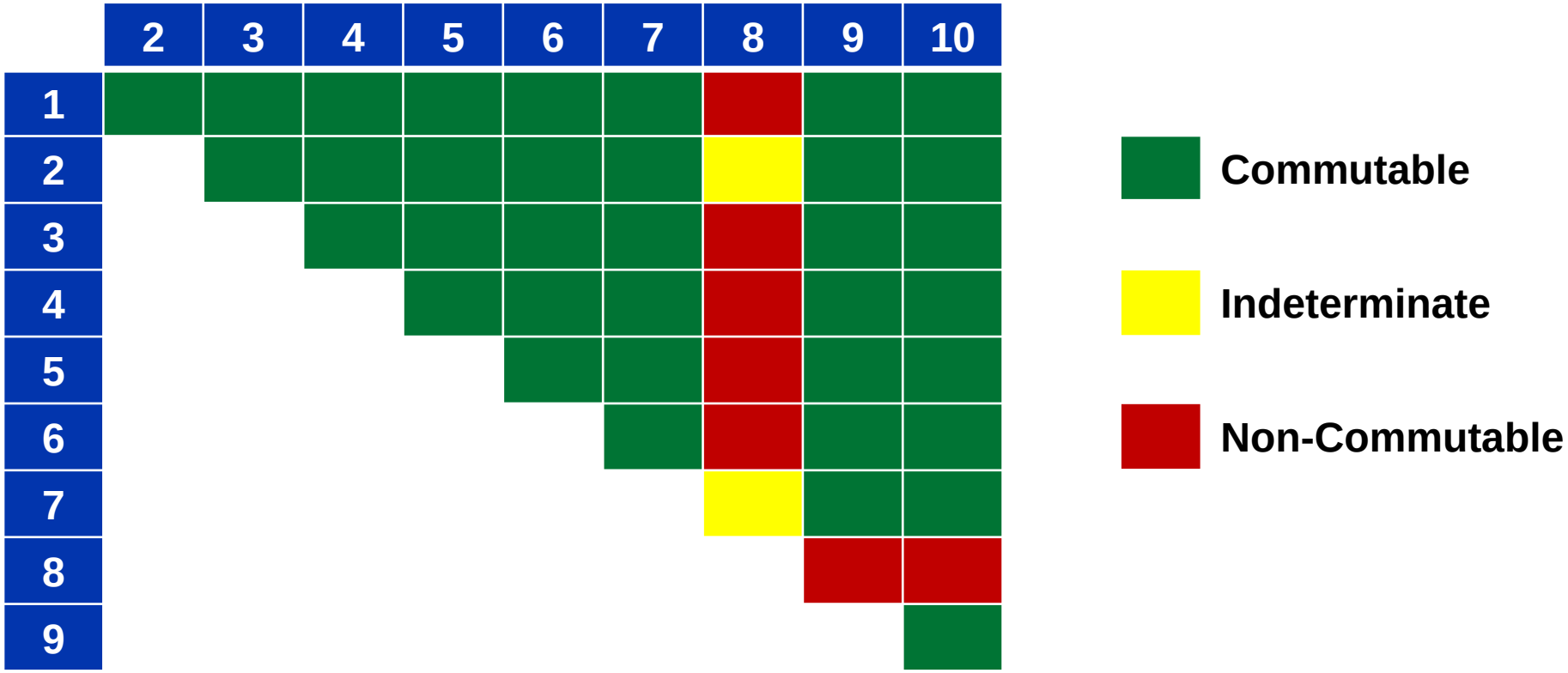




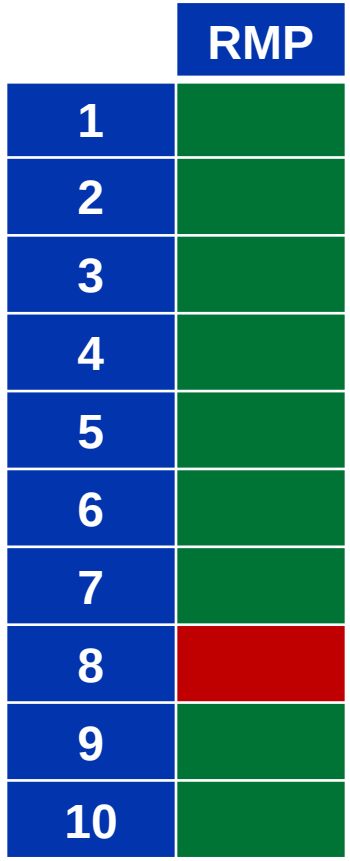


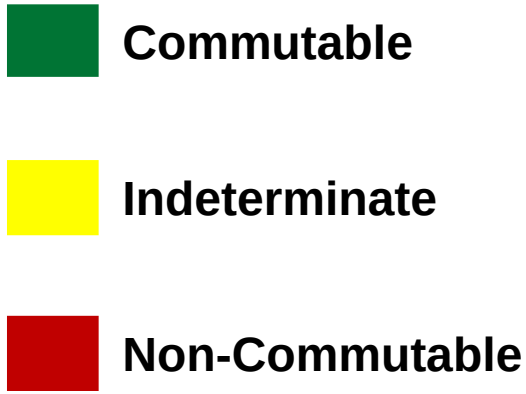


Conclusion for all combinations of pairs of measurement procedures



Simpler experiment when a RMP is available

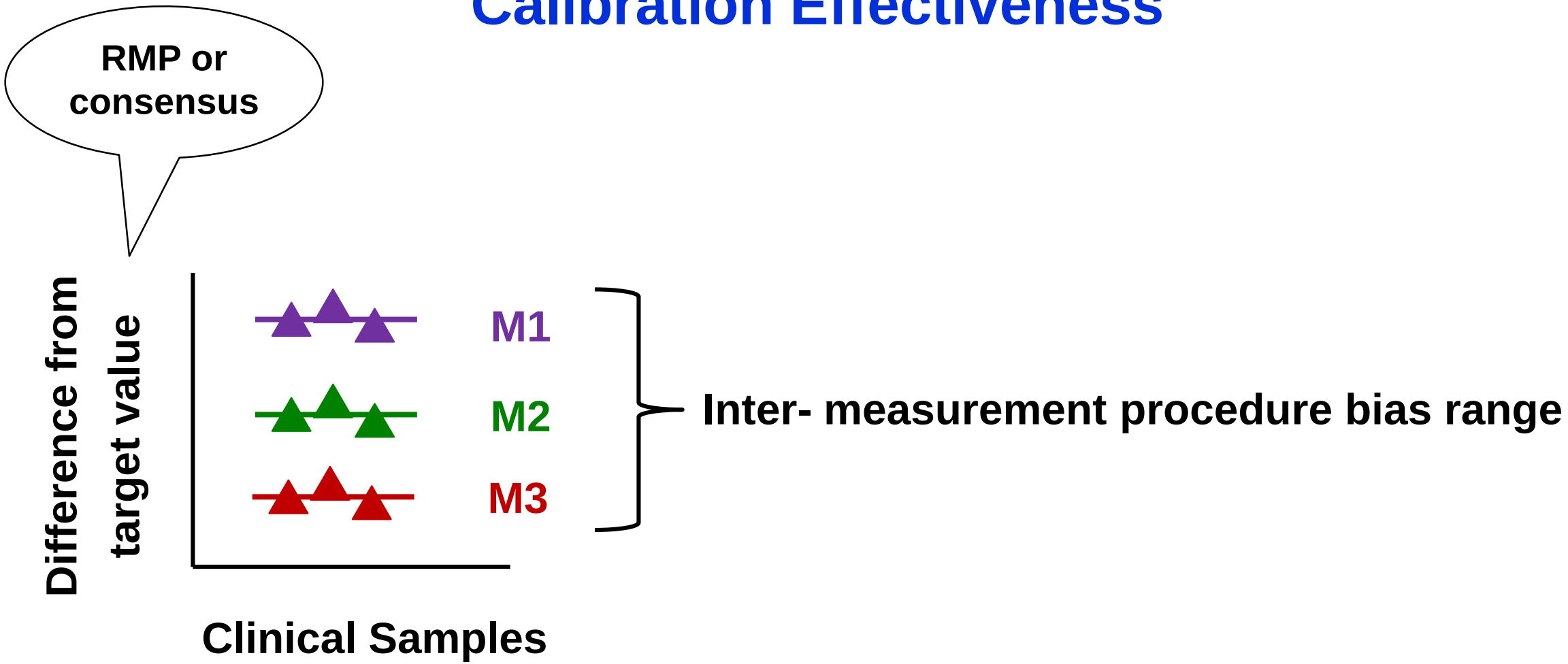




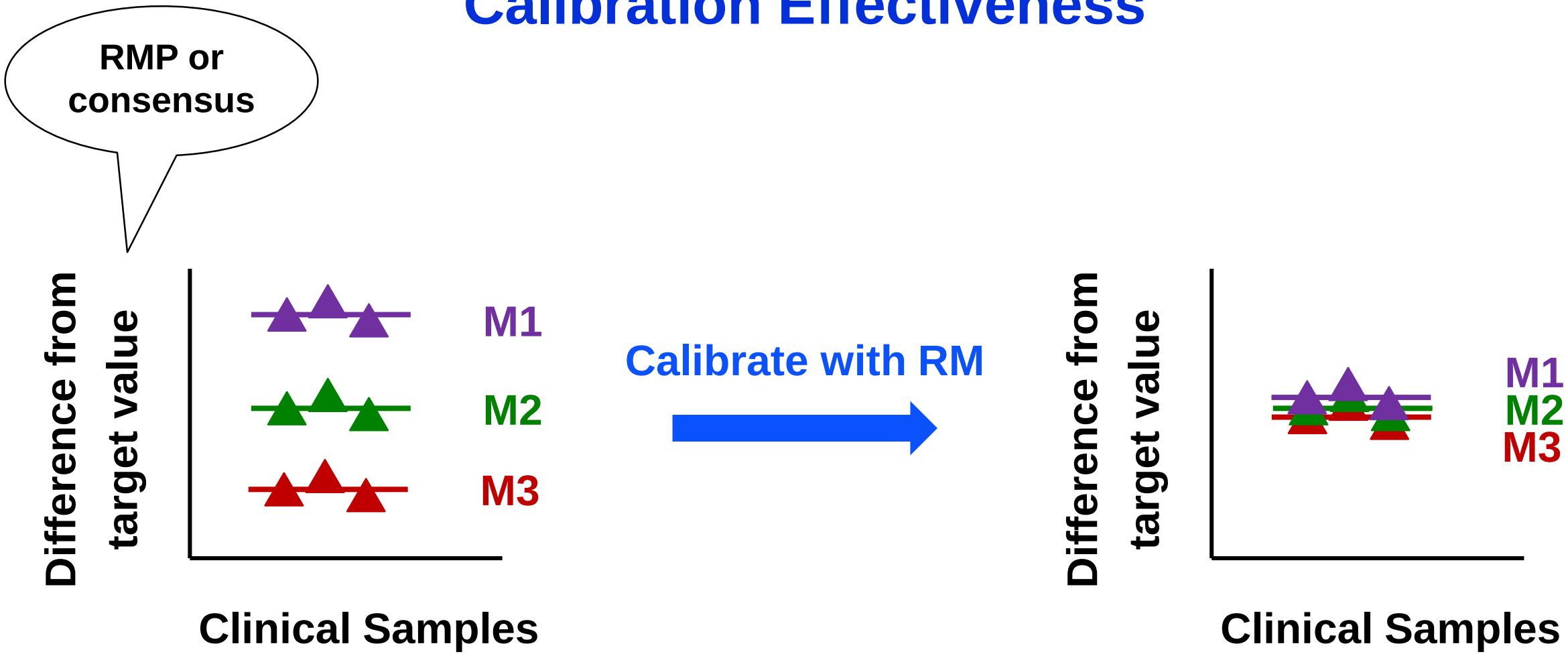
Part 3: assessment by calibration effectiveness

*** only applicable for RMs used as calibrators ***

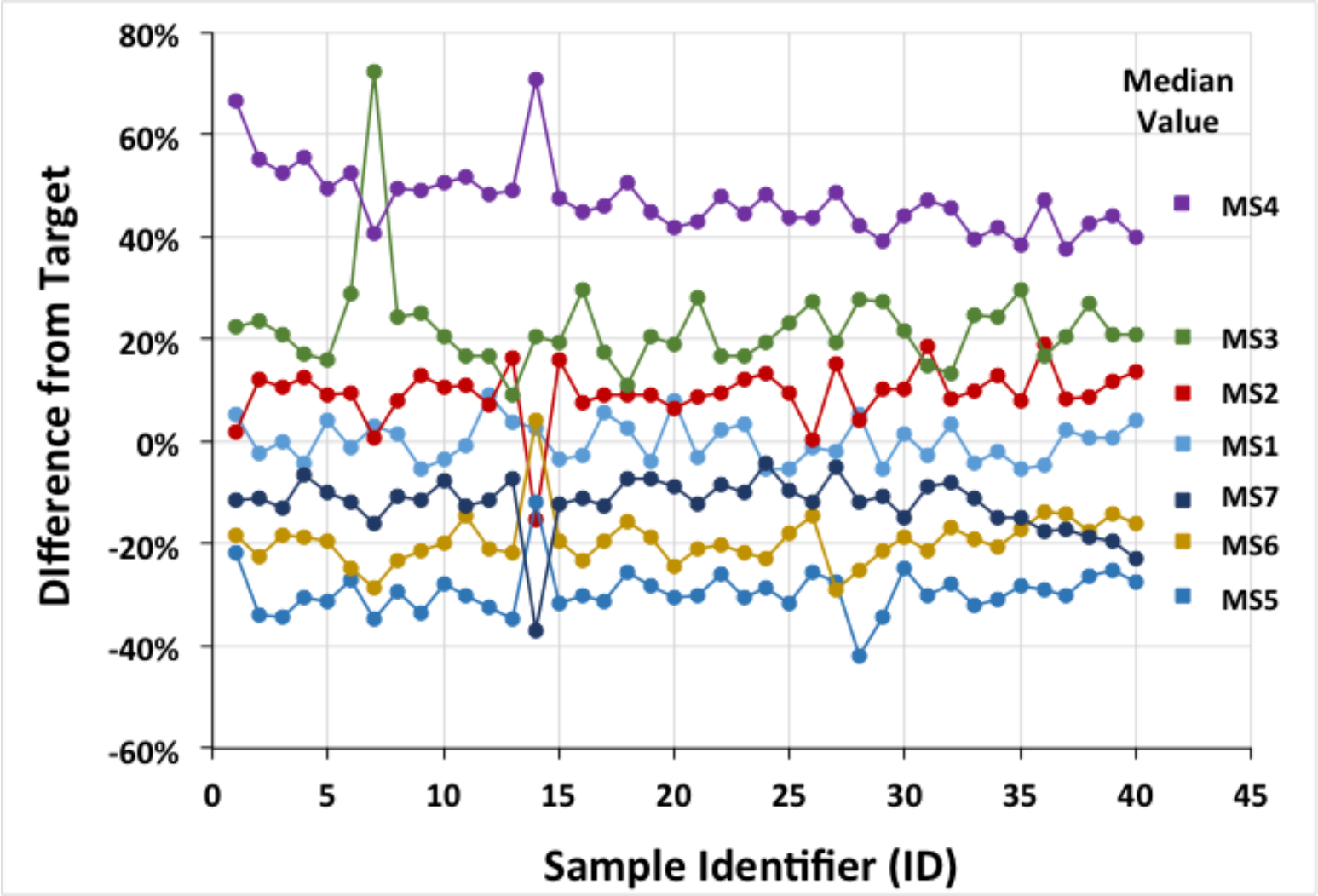
Calibration Effectiveness



Calibration Effectiveness



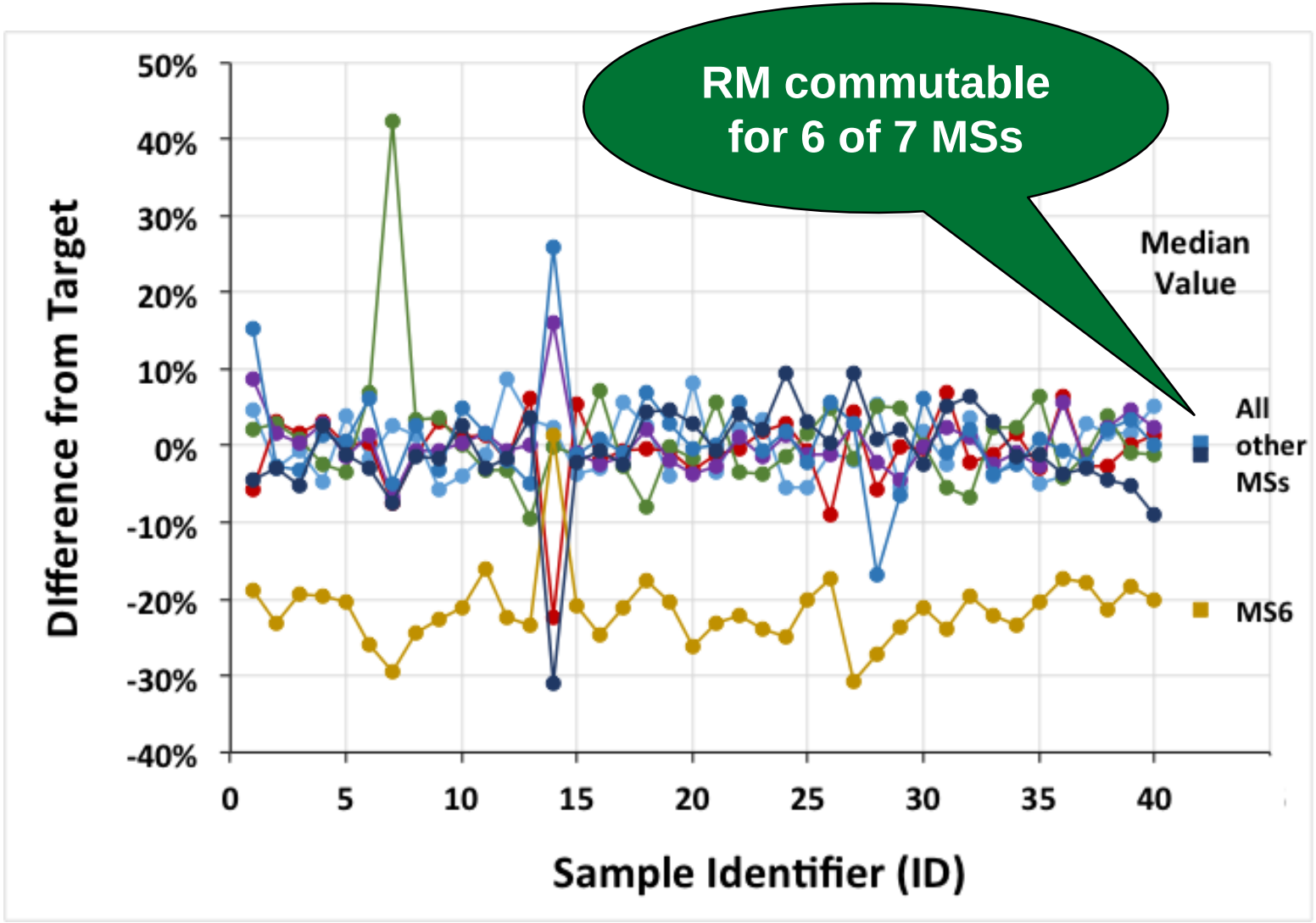
Initial status of calibration



Bias Range

Criterion

Recalibration with RM

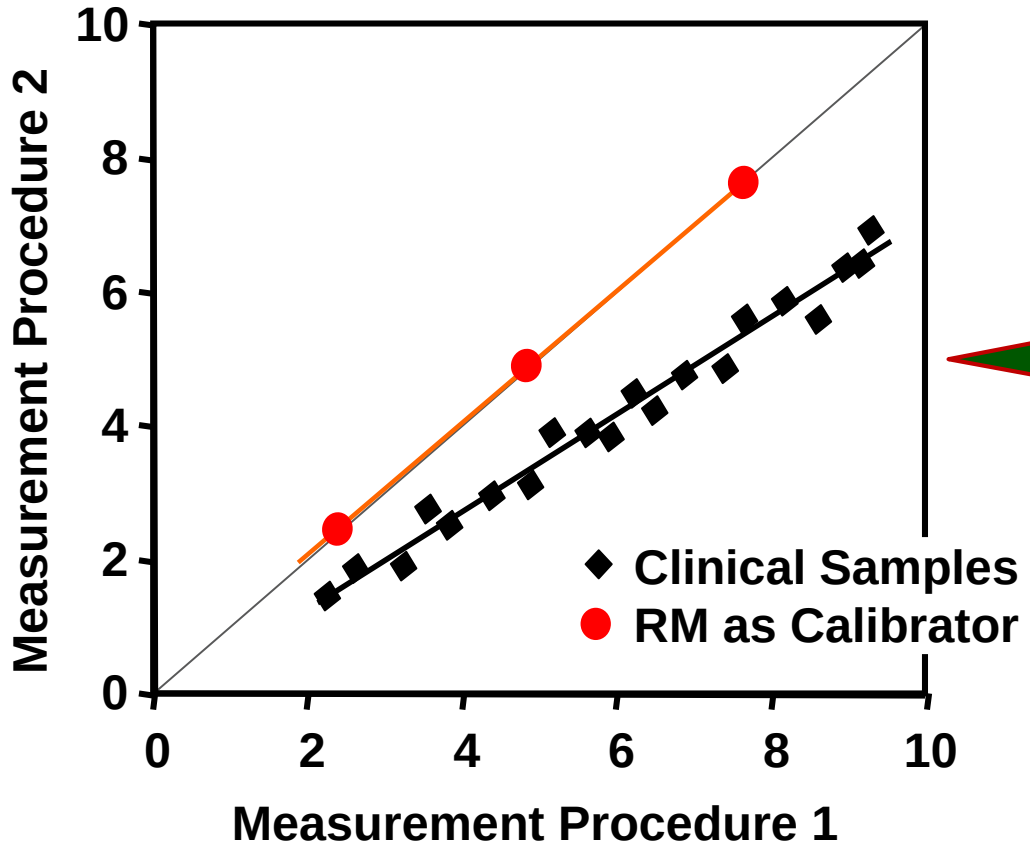


↑
Criterion
↓

Part 4: correction for non-commutability bias

Submitted for publication

Non-Commutable CRM as Calibrator



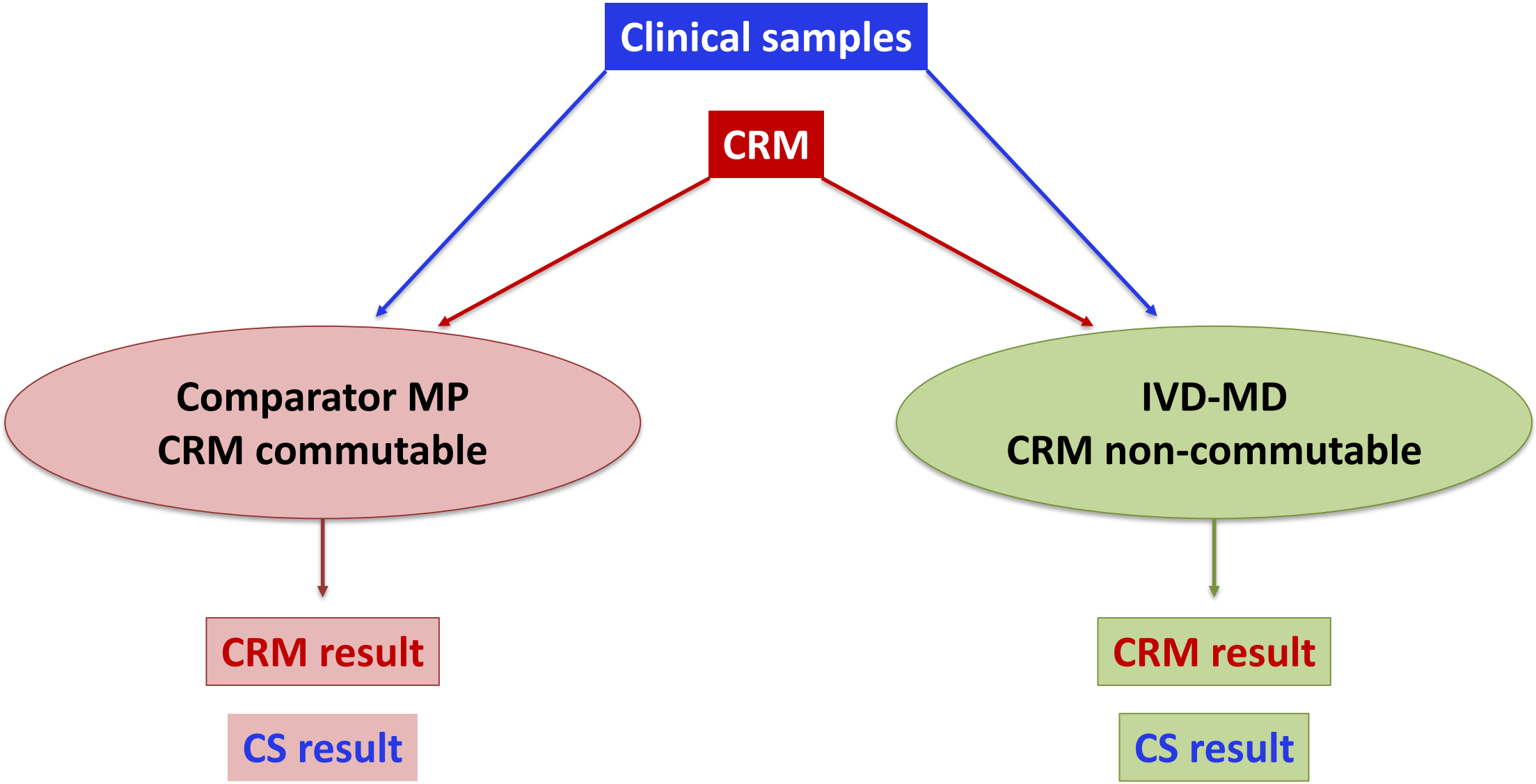
Correction in the calibration hierarchy IF the bias is stable

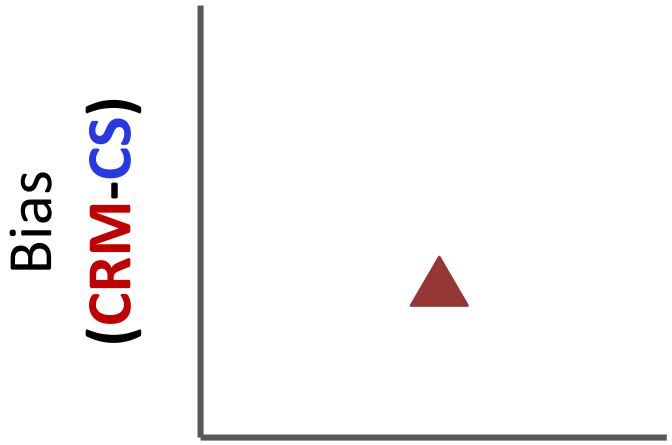
How to determine a correction for non-commutability bias

Comparator MP
CRM commutable

- **Another MP for which the CRM is commutable for use as a calibrator**
- **RMP if available**

IVD-MD
CRM non-commutable

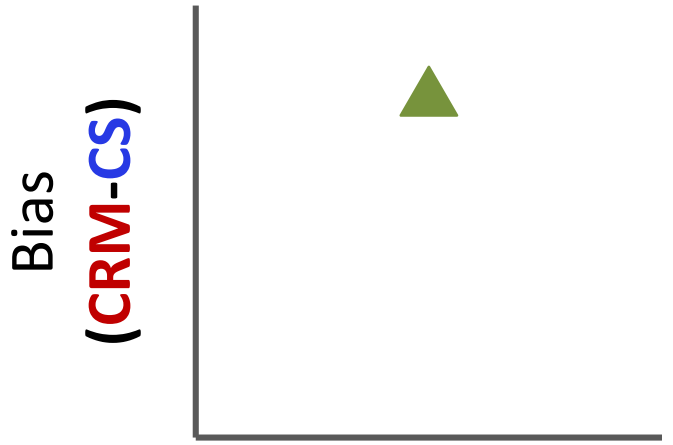

Clinical samples
CRM
Comparator MP
CRM commutable
IVD-MD
CRM non-commutable
CRM result
CS result
CRM result
CS result



Comparator MP

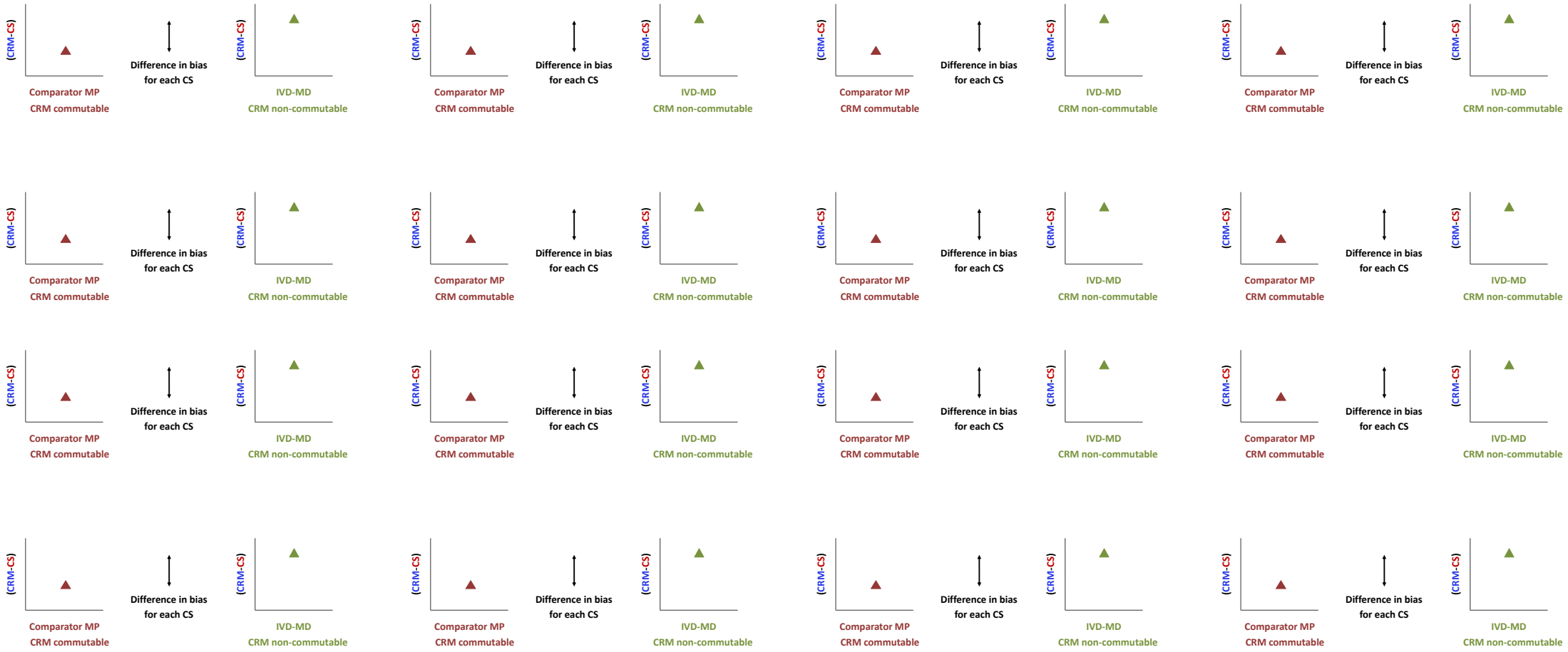
CRM commutable

Difference in bias for each CS

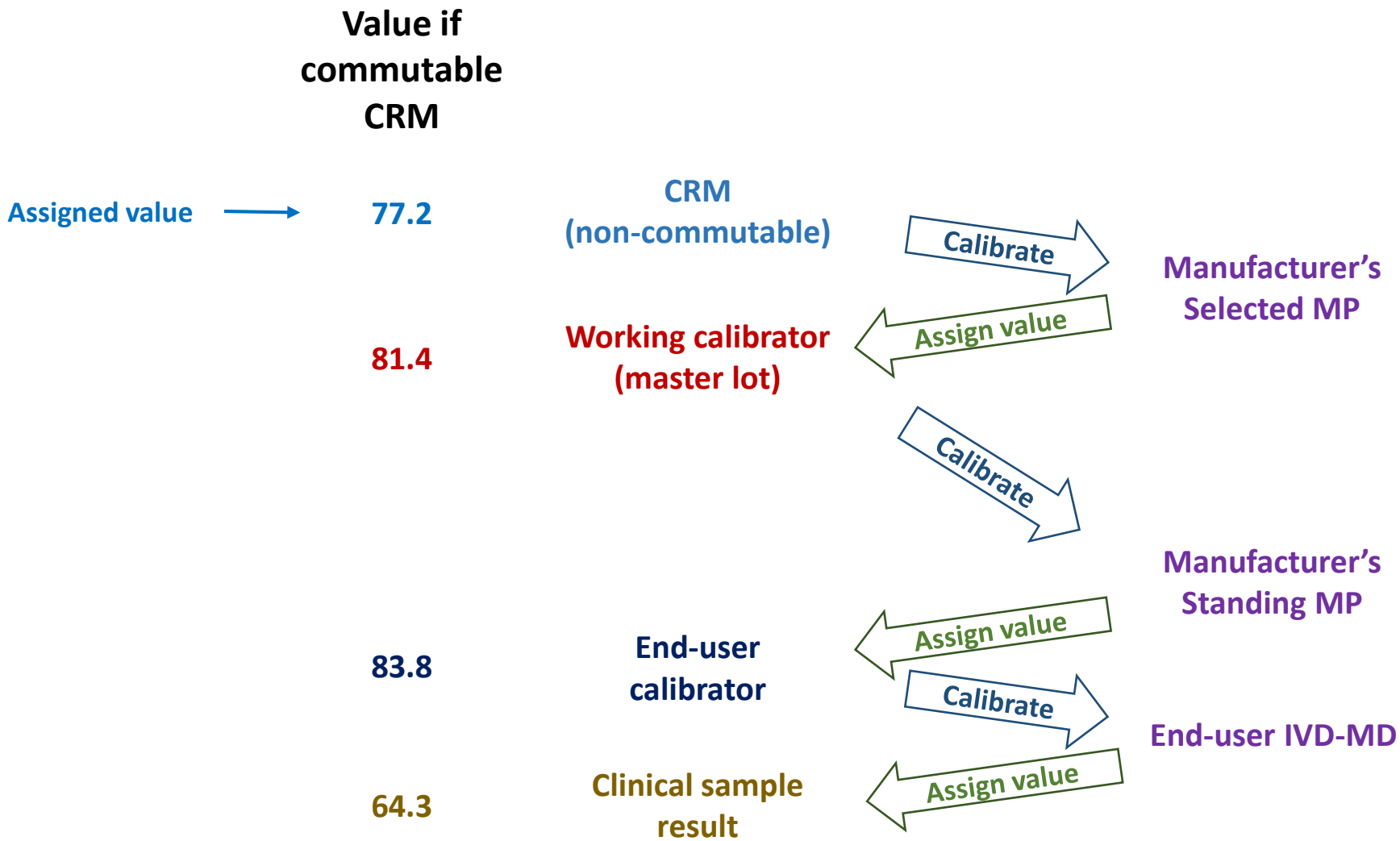


IVD-MD

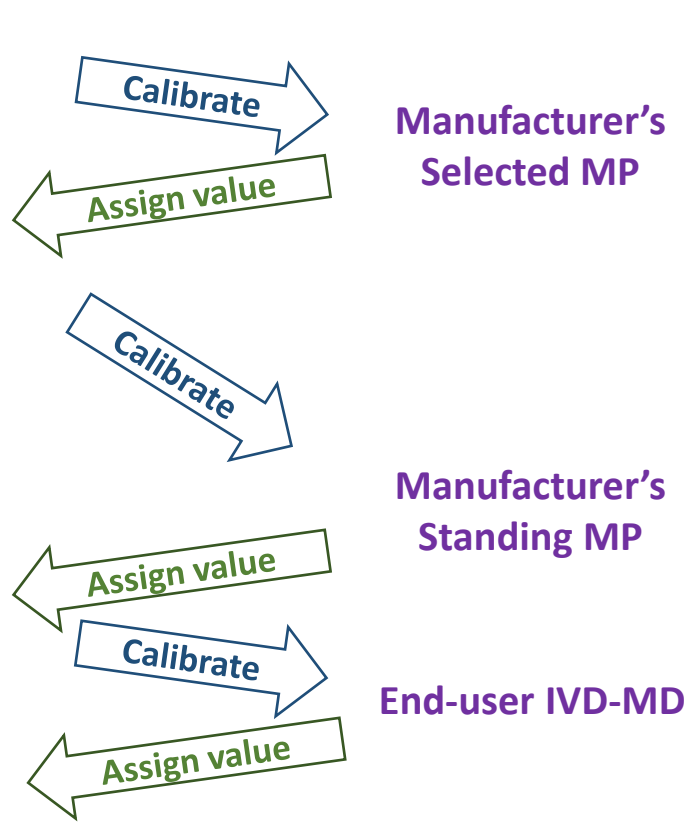
CRM non-commutable



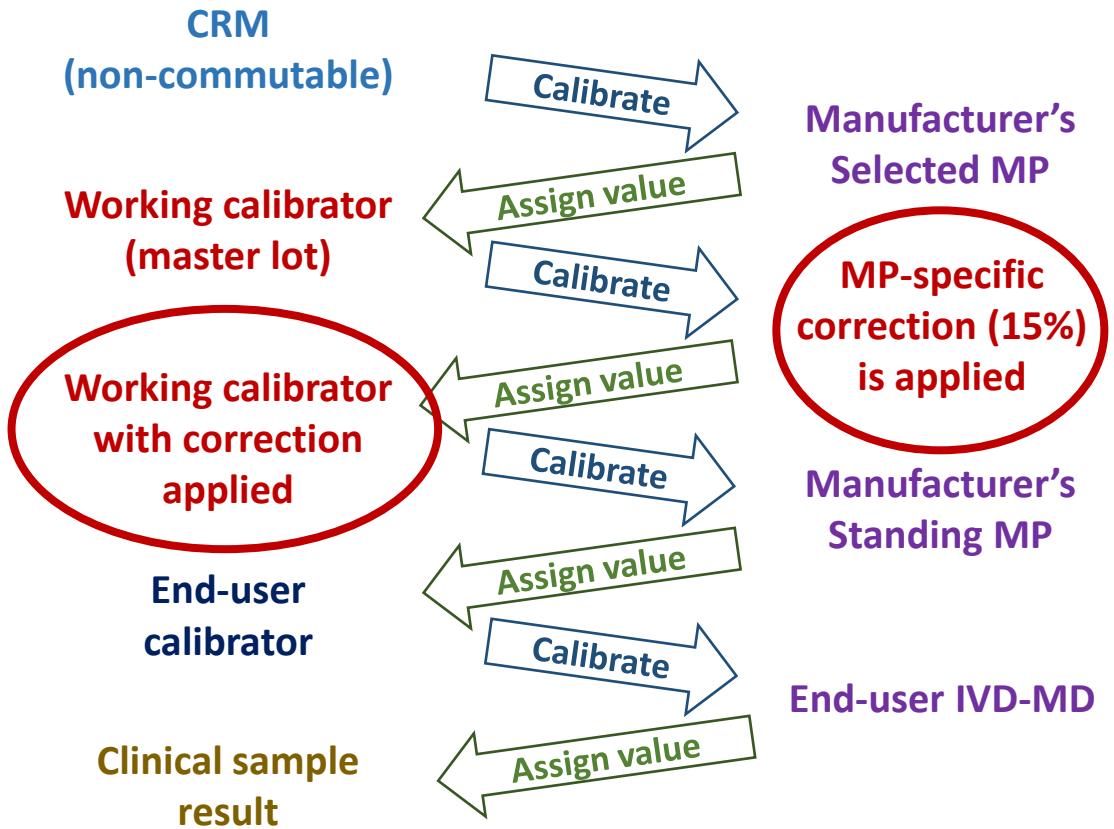
CORRECTION derived from difference in bias for all CS-CRM pairs


Value if commutable CRM
Assigned value
77.2
CRM (non-commutable)
Calibrate
Manufacturer's Selected MP
Assign value
81.4
Working calibrator (master lot)
Calibrate
Manufacturer's Standing MP
Assign value
83.8
End-user calibrator
Calibrate
End-user IVD-MD
Assign value
64.3
Clinical sample result

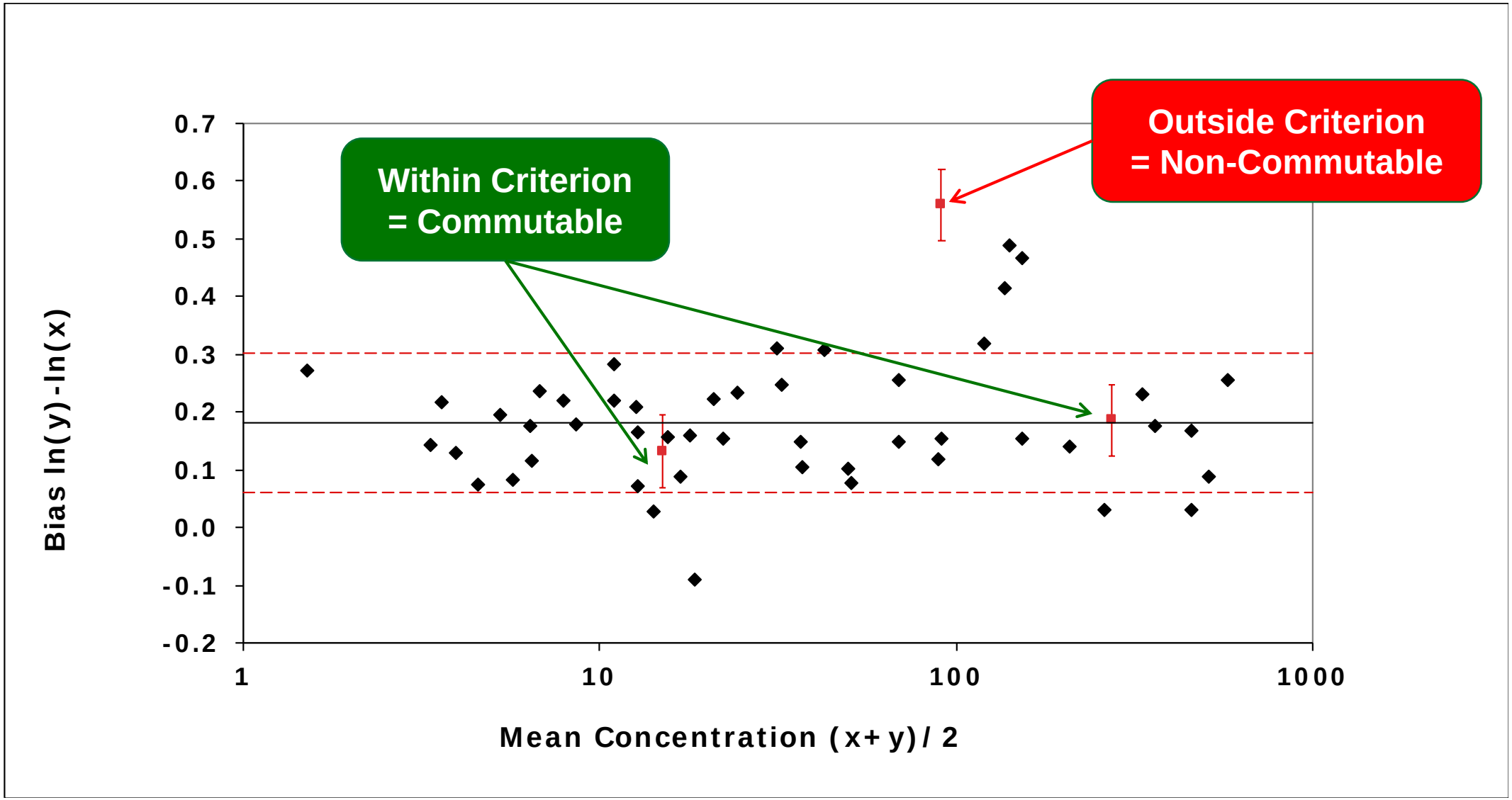
	WITHOUT CORRECTION for 15% non-commutability bias of CRM	Value if commutable CRM
Assigned value →	77.2	77.2
15% Non-commutability bias reflected in value	93.6	81.4
15% Non-commutability bias propagated in chain	96.4	83.8
15% error because of non-commutability bias	73.9	64.3



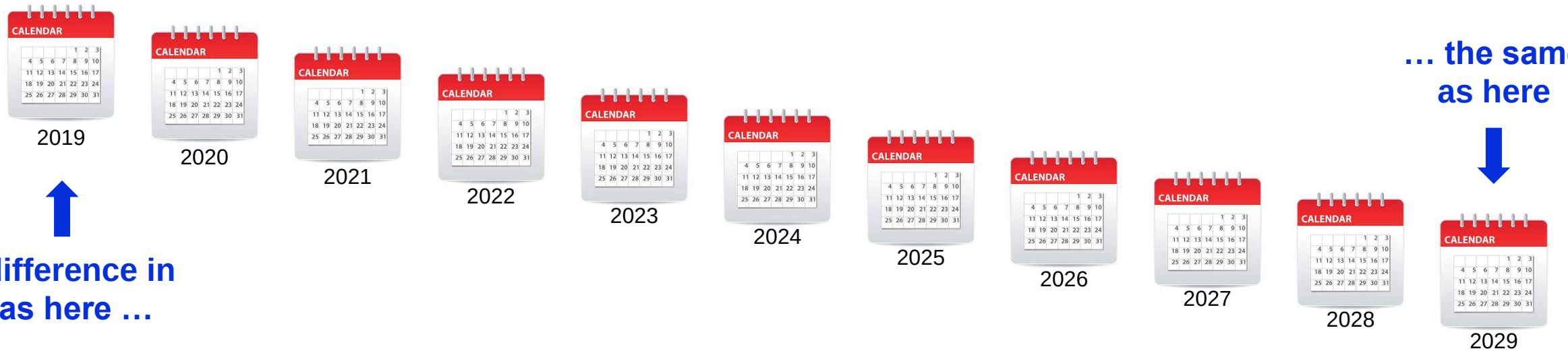
	WITH CORRECTION for 15% non-commutability bias of CRM	Value if commutable CRM
Assigned value →	77.2	77.2
15% Non-commutability bias reflected in value	93.6	81.4
(Uncertainty added)	81.4	
Non-commutability bias removed	83.8	83.8
Value traceable to CRM	64.3	64.3



Commutable is a conclusion from the difference in bias



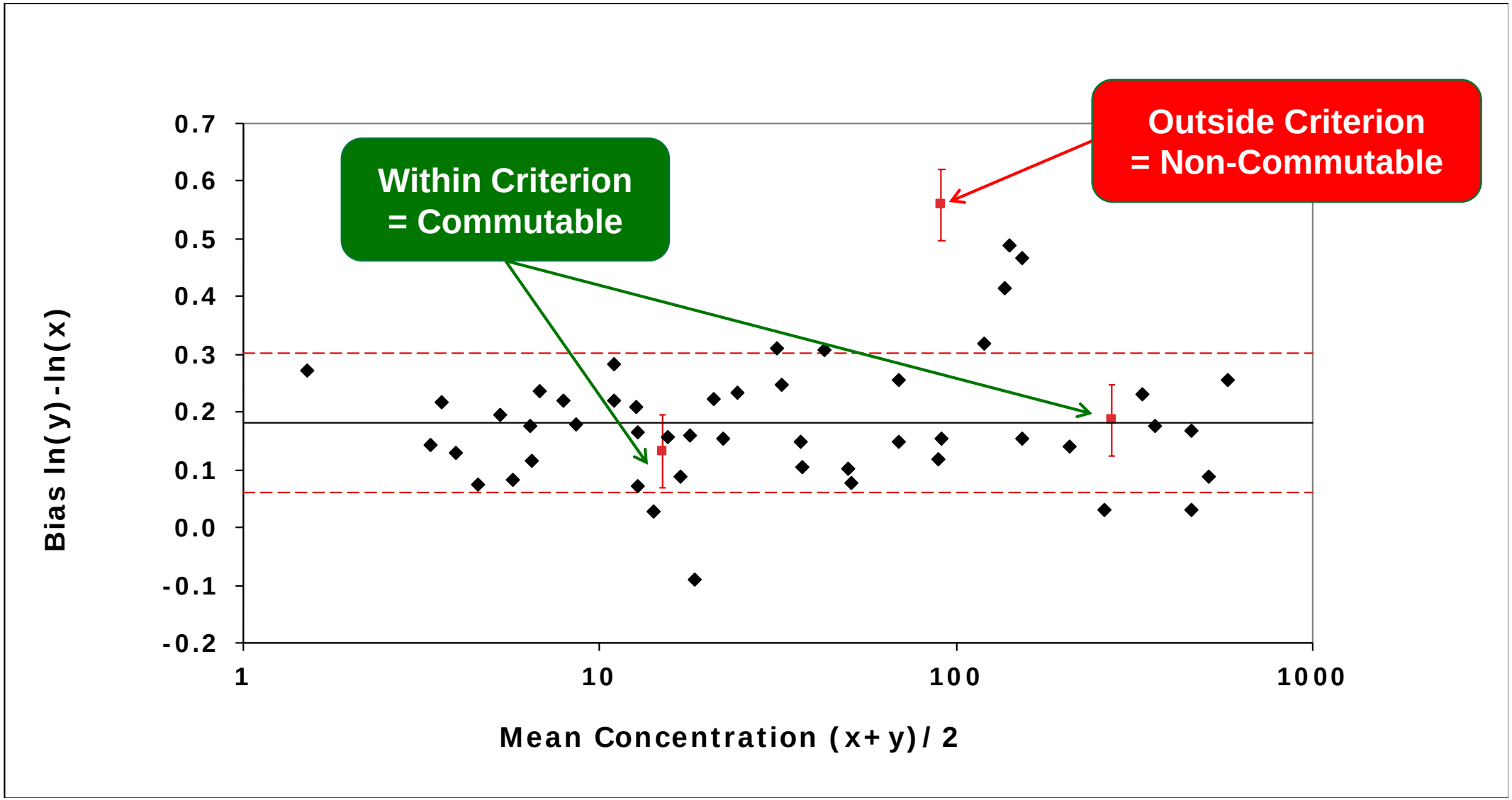
Difference in bias must be stable within acceptable uncertainty limits



Stability considerations

1. Measurand in the CRM
2. Matrix of the CRM
3. Measurement procedure
    a) Reagent lot changes
    b) Calibrator lot changes
    c) Changes in instrument performance

Stability is not related to the magnitude of the difference in bias



A change in the difference in bias over time

- **Could make a commutable decision become non-commutable**
- **Could make a non-commutable decision become commutable**
- **Could change the magnitude of a correction for non-commutability bias**

ISO/IEC 17025:2017 recommends to periodically reverify metrological traceability of the calibration hierarchy

- **reverification should include the commutability of a matrix-based CRM**
- **NOT CURRENT PRACTICE**
- **A role for surveillance schemes, EQA, other?**

Summary: Commutability

1. **Property of a matrix-based reference material**

2. **Required for matrix-based CRMs used in the calibration hierarchies of end-user measuring systems**

   ✓ **Correction for non-commutability bias of a CRM is possible**

3. **Required for EQA samples intended to access trueness or harmonization among different measuring systems**