CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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# CLSI EP30™

## Characterization and Qualification of Commutable Reference Materials for Laboratory Medicine



CLSI EP30 provides information to help material manufacturers in the production and characterization of commutable reference materials.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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# Characterization and Qualification of Commutable Reference Materials for Laboratory Medicine

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## Abstract

Clinical and Laboratory Standards Institute EP30—*Characterization and Qualification of Commutable Reference Materials for Laboratory Medicine* provides guidance on characterizing and qualifying the fitness for use of commutable reference material (RM) as either a common calibrator or a trueness control for multiple measurement procedures.

This guideline covers RM qualification requirements, characterization of homogeneity and stability, the assignment of quantity values, and determining RM value uncertainties. Three approaches for assessing commutability of RM are provided along with worked examples. Recommendations are made on how to report the results of the RM qualification process.

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# Foreword

Reference materials (RMs) are an important requisite for ensuring reliable laboratory measurements and appropriate patient care. To ensure that an RM is suitable for its intended purpose, its characteristics need to be assessed in a defined manner, taking all relevant aspects into consideration. This guideline provides information to help RM manufacturers in the production and characterization of commutable RMs. Guidance on characterization requirements for RM related to the definition of the measurand, the intended use of the material, and other material specifications is provided. Information is included on study designs; data evaluation; assigning quantity values; and assessing measurement uncertainty, homogeneity, and stability. This guideline provides recommendations on how to perform a commutability assessment and what information to report in a certificate that accompanies an RM.

## Overview of Changes

This guideline replaces CLSI EP30-A, published in 2010. Several changes were made in this edition, including:

- Updating to align with the latest revision of ISO 17511[1]
- Changing content to align commutability assessment techniques with the latest revision of CLSI EP14[2] and with recommendations by the International Federation of Clinical Chemistry and Laboratory Medicine working group on commutability in metrological traceability
- Updating content on characterization of stability to align with the latest revision of CLSI EP25[3]

**NOTE:** The content of this guideline is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

**KEY WORDS**

**commutability**
**homogeneity assessment**
**measurement quantification**
**measurement uncertainty**
**metrological traceability**
**reference material**
**stability assessment**

# Chapter 1

# Introduction

# Characterization and Qualification of Commutable Reference Materials for Laboratory Medicine

## 1 Introduction

CLSI EP30 provides information to assist reference material (RM) manufacturers in the production and characterization of commutable RMs and users of these RMs, such as *in vitro* diagnostic (IVD) manufacturers and medical laboratories, in assessing the applicability of RMs for a specific measurement procedure (MP) or clinical application.

### 1.1 Scope

This guideline provides recommendations for the material characterization, assessment of commutability, and assignment of measurand concentration values to commutable RMs that are used at the higher levels of the calibration hierarchy. These RMs are created with the intent of promoting the generation of equivalent results for a measurand across multiple end-user MPs. Commutable RMs include:

- Secondary certified reference materials (CRMs)
- International conventional calibrators

The commutable RMs covered in this guideline are all at position m.3 in the calibration hierarchies shown in Figures 1A, 1B, and 1C. The designations "m" for material and "p" for procedure are as used in ISO 17511 to designate sequential positions in calibration hierarchies.[1] The m.3 designation is used for a commutable CRM or a commutable international conventional calibrator, which are the focus of this guideline. Similarly, a p.3 designation is used to describe the reference measurement procedure (RMP) used to assign the value of m.3, and a primary calibrator (m.2) designation can be used to describe the next higher-level calibration material in the calibration hierarchy, when applicable.

Commutable RMs with a certified assigned value and associated uncertainty can be used as controls for trueness assessment of measuring systems. Commutable RMs without a certified assigned value can be used to assess equivalence of measuring system results, for example in an external quality assessment or proficiency testing program, but such applications are not in scope for this guideline. Also not in scope are MP manufacturer-specific working or end-user calibrators.

This guideline does not apply to qualitative examinations whose purpose is to provide only nominal or ordinal results. In addition, laboratories should refer to CLSI EP25[3] for establishing and verifying the shelf life and in-use stability for reagent kits, calibrators, and control products.

## Appendix C. (Continued)

Using these assumptions, the RM CIs add ($\sqrt{(2.87^2 / 2)} = 2.03$) to the delta distance of the RM point to the regression fit. Therefore, with an acceptance criterion of 5.0, any RM (x,y) point that is greater than (2.97 = 5.0 – 2.03) delta distance away from the regression line will have a CI that is greater than a 5.0 delta distance from the regression line.

The resultant absolute value delta decision limits for RM (x,y) points are:

< 5.0 – 2.03 = 2.97: C

> 5.0 + 2.03 = 7.03: NC, else

< 5.0: I1

> 5.0: I2

Performing the calculations and comparisons for the data in Figure C1 gives the following results:

**Table C1. Comparison of RM Deltas With Commutability Criteria for the MPJ to MPA Plot**

| RM | Orthogonal Delta | Category |
|---|---|---|
| RMA | 0.044 | C |
| RMB | 0.570 | C |
| RMC | 1.942 | C |
| RMD | 1.889 | C |
| RME | 0.488 | C |
| RMF | 3.926 | I1 |
| RMG | 0.513 | C |

Abbreviations: C, commutable; I, indeterminate; MP[X], measurement procedure [X]; RM[X], reference material [X].

The "I1" RM point to the left of the line fit is RMF. The categorizations can be added up over both MPs and RMs shown in Tables C2 and C3, respectively.

**Table C2. Comparison Between MPs of Commutability Category Across All RMs**

| MP | C | I1 | I2 | NC | Total |
|---|---|---|---|---|---|
| MPA | 56 | 6 | 1 | 0 | 63 |
| MPB | 55 | 5 | 1 | 2 | 63 |
| MPC | 54 | 8 | 1 | 0 | 63 |
| MPD | 54 | 5 | 3 | 1 | 63 |
| MPE | 56 | 5 | 2 | 0 | 63 |
| MPF | 58 | 5 | 0 | 0 | 63 |
| MPG | 57 | 6 | 0 | 0 | 63 |
| MPH | 39 | 21 | 3 | 0 | 63 |
| MPI | 51 | 11 | 0 | 1 | 63 |
| MPJ | 56 | 6 | 1 | 0 | 63 |

Abbreviations: C, commutable; I, indeterminate; MP[X], measurement procedure [X]; NC, noncommutable; RM, reference material.

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