CLINICAL AND LABORATORY STANDARDS INSTITUTE®

1st Edition

EP36

Harmonization of Symbology and Equations

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This report provides a standardized symbology for use throughout CLSI documents. Use of these standardized symbols is expected to be of great benefit to the CLSI readership, volunteers participating in CLSI committees, and the scientific community in general.

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Harmonization of Symbology and Equations

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Abstract

Clinical and Laboratory Standards Institute document EP36—*Harmonization of Symbology and Equations* provides readers with a list of the most common statistical symbols and formulas to describe testing procedures and statistical analyses. The purpose is to provide a standardized symbology for use in CLSI documents that will benefit the CLSI readership as well as the volunteers participating on CLSI committees. Symbols are based on International Organization for Standardization guidelines and the most recent CLSI documents. They are grouped in different categories related to performance evaluation testing. CLSI document development committees and working groups are expected to adhere to these symbols unless there are strong arguments for deviating from these recommendations.

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Foreword

The CLSI documents use statistical symbols and formulas to describe testing procedures and statistical analyses. Most of these symbols represent mainstream statistical and *in vitro* diagnostic concepts and definitions. However, the symbols used in different CLSI documents are sometimes not harmonized.

The purpose of this document is to provide a standardized symbology for use throughout CLSI documents. This will be a great benefit to the CLSI readership, volunteers participating in CLSI committees, and the scientific community in general.

The International Organization for Standardization documents as well as the terminology, symbols, and equations used in all of the CLSI Evaluation Protocols (EP) documents were considered in the development of this report. Symbols were grouped based on the evaluation approach they applied.

Key Words

Equations, evaluation protocols, operations, parameters, symbol

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Harmonization of Symbology and Equations

Chapter 1: Introduction

This chapter includes:

- Document scope and applicable exclusions
- "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions
- Abbreviations and acronyms used in the document
- Listing of documents consulted in the creation of this report

1.1 Scope

The purpose of this document is to provide recommendations on harmonized symbols and notations that describe concepts, procedures, and test approaches used in statistical equations and models within CLSI documents.

The intended users of this document are CLSI volunteers and staff involved in developing standards, guidelines, and related products. It is intended that future CLSI documents will converge to a more standardized symbolism and notation by taking into account the recommendations made in this document. This document is not intended to cover all mathematical symbols and operations nor all statistical procedures used or referenced in CLSI documents.

1.2 Terminology

1.2.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization wherever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in the United States, Europe, and elsewhere; that these differences are reflected in CLSI, International Organization for Standardization (ISO), and European Committee for Standardization (CEN) documents; and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. In light of this, CLSI's consensus process focuses on harmonization of terms to facilitate the global application of standards and guidelines.

1.2.2 Abbreviations and Acronyms

NOTE: The abbreviations and acronyms for symbols and equations that are the subject of this report are included in Chapter 2.

AMI	analytical measuring interval
CEN	Comité Européen de Normalisation (European Committee for Standardization)
EP	evaluation protocols
ISO	International Organization for Standardization
JCGM	Joint Committee for Guides in Metrology

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LoD	limit of detection
LLQ	lower limit of quantitation
LoQ	limit of quantitation
RI	reportable interval
ULQ	upper limit of quantitation
VIM	*Vocabulaire International de Métrologie (International Vocabulary of Metrology – Basic and General Concepts and Associated Terms)*

1.3 Documents Consulted

Table 1 includes the CLSI EP, ISO, and Joint Committee for Guides in Metrology (JCGM) guidelines that were considered in the development of this document.

Table 1. Standards and Guidelines Used in the Development of This Document

Document Code	Document Title
CLSI EP05[1]	*Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition* (2014)
CLSI EP06[2]	*Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline* (2003)
CLSI EP09[3]	*Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition* (2013)
CLSI EP14[4]	*Evaluation of Commutability of Processed Samples; Approved Guideline—Third Edition* (2014)
CLSI EP15[5]	*User Verification of Precision and Estimation of Bias; Approved Guideline—Third Edition* (2014)
CLSI EP17[6]	*Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition* (2012)
CLSI EP24[7]	*Assessment of the Diagnostic Accuracy of Laboratory Tests Using Receiver Operating Characteristic Curves; Approved Guideline—Second Edition* (2011)
CLSI EP25[8]	*Evaluation of Stability of* In Vitro *Diagnostic Reagents; Approved Guideline* (2009)
CLSI EP26[9]	*User Evaluation of Between-Reagent Lot Variation; Approved Guideline* (2013)
CLSI EP28[10]	*Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition* (2010)
CLSI EP29[11]	*Expression of Measurement Uncertainty in Laboratory Medicine; Approved Guideline* (2012)
ISO 3534-1[12]	*Statistics – Vocabulary and symbols – Part 1: General statistical terms and terms used in probability* (2006)
ISO 5725-2[13]	*Accuracy (trueness and precision) of measurement methods and results – Part 2: Basic method for the determination of repeatability and reproducibility of a standard measurement method* (1994)
ISO 11843-1[14]	*Capability of detection – Part 1: Terms and definitions* (1997)
ISO 11843-2[15]	*Capability of detection – Part 2: Methodology in the linear calibration case* (2000)
ISO 11843-3[16]	*Capability of detection – Part 3: Methodology for determination of the critical value for the response variable when no calibration data are used* (2003)
ISO 11843-4[17]	*Capability of detection – Part 4: Methodology for comparing the minimum detectable value with a given value* (2003)
ISO 21748[18]	*Guidance for the use of repeatability, reproducibility and trueness estimates in measurement uncertainty estimation* (2010)
ISO 80000-1[19]	*Quantities and units – Part 1: General* (2009)

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The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system (QMS) approach in the development of standards and guidelines, which facilitates project management; defines a document structure using a template; and provides a process to identify needed documents. The QMS approach applies a core set of "quality system essentials" (QSEs), basic to any organization, to all operations in any health care service's path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager's guide. The QSEs are as follows:

Organization	Personnel	Process Management	Nonconforming Event Management
Customer Focus	Purchasing and Inventory	Documents and Records	Assessments
Facilities and Safety	Equipment	Information Management	Continual Improvement

EP36 addresses the QSEs indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
					X	X EP05 EP06 EP09 EP14 EP15 EP17 EP24 EP25 EP26 EP28 EP29	X				

Path of Workflow

A path of workflow is the description of the necessary processes to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver the laboratory's services, namely quality laboratory information.

EP36 addresses the clinical laboratory path of workflow steps indicated by an "X." For a description of the other document listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Preexamination				**Examination**			**Postexamination**	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
				X	X	X EP14		

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Related CLSI Reference Materials*

EP05 **Evaluation of Precision Performance of Quantitative Measurement Procedures. 3rd ed., 2014.** This document provides guidance for evaluating the precision performance of quantitative measurement procedures. It is intended for manufacturers of quantitative measurement procedures and for laboratories that develop or modify such procedures.

EP06 **Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach. 1st ed., 2003.** This document provides guidance for characterizing the linearity of a method during a method evaluation; for checking linearity as part of routine quality assurance; and for determining and stating a manufacturer's claim for linear range.

EP09 **Measurement Procedure Comparison and Bias Estimation Using Patient Samples. 3rd ed., 2013.** This document addresses the design of measurement procedure comparison experiments using patient samples and subsequent data analysis techniques used to determine the bias between two *in vitro* diagnostic measurement procedures.

EP14 **Evaluation of Commutability of Processed Samples. 3rd ed., 2014.** This document provides guidance for evaluating the commutability of processed samples by determining if they behave differently than unprocessed patient samples when two quantitative measurement procedures are compared.

EP15 **User Verification of Precision and Estimation of Bias. 3rd ed., 2014.** This document describes the estimation of imprecision and of bias for clinical laboratory quantitative measurement procedures using a protocol that can be completed within as few as five days.

EP17 **Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures. 2nd ed., 2012.** This document provides guidance for evaluation and documentation of the detection capability of clinical laboratory measurement procedures (ie, limit of blank, detection, and quantitation), for verification of manufacturers' detection capability claims, and for the proper use and interpretation of different detection capability estimates.

EP24 **Assessment of the Diagnostic Accuracy of Laboratory Tests Using Receiver Operating Characteristic Curves. 2nd ed., 2011.** This document provides a protocol for evaluating the accuracy of a test to discriminate between two subclasses of subjects when there is some clinically relevant reason to separate them. In addition to the use of receiver operating characteristic curves and the comparison of two curves, the document emphasizes the importance of defining the question, selecting the sample group, and determining the "true" clinical state.

EP25 **Evaluation of Stability of *In Vitro* Diagnostic Reagents. 1st ed., 2009.** This document provides guidance for establishing shelf-life and in-use stability claims for *in vitro* diagnostic reagents such as reagent kits, calibrators, and control products.

EP26 **User Evaluation of Between-Reagent Lot Variation. 1st ed., 2013.** This document provides guidance for laboratories on the evaluation of a new reagent lot, including a protocol using patient samples to detect significant changes from the current lot.

EP28 **Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory. 3rd ed., 2010.** This document contains guidelines for determining reference values and reference intervals for quantitative clinical laboratory tests.

EP29 **Expression of Measurement Uncertainty in Laboratory Medicine. 1st ed., 2012.** This guideline describes a practical approach to assist clinical laboratories in developing and calculating useful estimates of measurement uncertainty, and illustrates their application in maintaining and improving the quality of measured values used inpatient care.

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