CLINICAL AND LABORATORY STANDARDS INSTITUTE®

4th Edition

CLSI EP05™

Evaluation of Precision of Quantitative Measurement Procedures

CLSI EP05 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.

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

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Evaluation of Precision of Quantitative Measurement Procedures

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Abstract

CLSI EP05—*Evaluation of Precision of Quantitative Measurement Procedures* provides guidance for evaluating the precision of *in vitro* diagnostic quantitative measurement experimental designs and includes recommendations for establishing precision performance. Included are guidelines for durations of testing, experimental designs, materials, data analysis, data summary, and interpretation techniques adaptable for a wide spectrum of measurands and system complexity. These guidelines are intended for manufacturers or developers of medical laboratory measurement procedures and for users to determine their own system and measurand performance characteristics. A balance is created in CLSI EP05 between complexity of design and analysis and simplicity of the evaluation procedure.

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Contents

Contents (Continued)

Foreword

Current medical laboratory literature contains numerous examples of product evaluations. For characterizing basic precision types, many of these examples use the basic concepts, designs, and analyses discussed in CLSI EP05. In special cases, more complex and customized experimental designs have been used for both published studies and regulatory purposes. However, there remains a strong need in the medical laboratory community for the basic rationales and approaches described in CLSI EP05 for assessing the precision performance characteristics of quantitative measurement procedures.

The great diversity of *in vitro* diagnostic devices currently available makes it impossible to recommend a single experimental design for all measurement procedures and associated devices. Nevertheless, requirements for materials, procedures, data analysis, and interpretation must be adaptable for the widest possible variety of measurands and instruments. In developing the standardized protocols in CLSI EP05, many recommendations for duration, inclusion of QC procedures, and methods of determining the relevant sources of variation were carefully considered. The resulting protocols represent a balance between complexity of design and data analysis, and simplicity of implementation and efficiency. CLSI EP05 was written to provide general guidance consistent with other international consensus standards.

Overview of Changes

CLSI EP05 was revised in 2025 under the Limited Revision Process and replaces CLSI EP05-A3, which was published in 2014. Several changes were made in this edition, including:

- Updating language for improved clarity
- Adding references to other updated CLSI documents
- Aligning the use of the terms “imprecision” and “precision,” using “imprecision” when referring to measures or estimates and using “precision” in other contexts
- Supplying example data in a downloadable file

KEY WORDS

analysis of variance
evaluation protocol
experimental design
imprecision
outliers
precision
precision profile
quality control
repeatability
reproducibility
variance components
within-laboratory precision

Chapter 1

Introduction

Evaluation of Precision of Quantitative Measurement Procedures

1 Introduction

CLSI EP05 focuses its discussion of single-site experimental designs to procedures suitable for establishing or validating precision performance characteristics. Accordingly, CLSI EP05 is primarily intended for manufacturers and developers. Recommendations for end-user laboratories for verifying repeatability and within-laboratory precision claims can be found in CLSI EP15.[1] The precision verification protocol in CLSI EP15[1] has been tailored for compatibility with CLSI EP05's single-site study designs.

The single-site protocol from previous editions of CLSI EP05—calling for measurements on 20 days, with 2 runs per day and 2 replicates per run for a given sample, reagent lot, etc.—is retained in this edition as a standardized experiment for use by manufacturers and developers in evaluating the repeatability and within-laboratory (within-device) precision of a measurement procedure (or "assay").

No matter how these performance characteristics are established, it is important that the assessments be verifiable and that they characterize precision over a substantial period of time and across most of the assay's stated measuring interval. The single-site experimental designs described in CLSI EP05 meet these requirements (see Chapter 3 and Appendix A). It is expected that the original "20 × 2 × 2" design will continue to serve well for the great majority of quantitative assays used in medical laboratories. However, extensive guidance was added on how to optimize this design for a given assay in light of its sources of variation and their relative magnitudes and interrelationships (see Chapter 2).

CLSI EP05 retains a second standardized experiment: a multisite protocol for repeated measurements at minimally 3 sites on 5 days. Both 3 (sites) × 5 (days) × 5 (replicates per day) and 3 (sites) × 5 (days) × 2 (runs per day) × 3 (replicates per run) implementations are described (see Chapter 4 and Appendix B). This ancillary protocol addresses site-to-site variability and estimates of reproducibility. It has been tailored for suitability in the context of validating a new assay, when such a study may be required because of the assay's character and/or to meet regulatory requirements.

Moreover, in recognition of the wide diversity of quantitative devices in use today, which differ in character and complexity, variants of the 20 × 2 × 2 design are also discussed. Appendix C is devoted to advanced models—multifactor designs—for use when a 2-factor design lacks the ability to do justice to the major sources of variation affecting an assay's within-laboratory precision. Depending on the assay, some of these models should also prove useful to manufacturers for the insights they can yield both during assay development and optimization and after the assay enters routine production.

To help foster understanding of basic concepts, the new edition includes an extensive tutorial for the nonstatistician (see Subchapter 1.5). Numerical examples illustrating a single-site 20 × 2 × 2 study and a complete multisite 3 × 5 × 5 study are presented in the appendixes.

Because of the complex nature of the calculations in CLSI EP05, it is recommended that the user have access to a computer and statistical software.

CLSI EP05 is largely consistent with recommendations in the International Organization for Standardization (ISO) 5725 series of standards, particularly ISO 5725-3.[2] CLSI EP05's single-site study incorporates the basic concepts in ISO 5725-2.[3] Whereas the ISO 5725 perspective places primary emphasis on interlaboratory sources of variation, CLSI EP05 has focused on within-laboratory sources of variation accumulating over time. However, CLSI EP05's

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