EP15-A3

User Verification of Precision and Estimation of Bias; Approved Guideline—Third Edition

>

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.

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

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For additional information on committee participation or to submit comments, contact CLSI.

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Volume 34 Number 12

User Verification of Precision and Estimation of Bias; Approved Guideline—Third Edition

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Abstract

Clinical and Laboratory Standards Institute document EP15-A3—*User Verification of Precision and Estimation of Bias; Approved Guideline—Third Edition* describes the verification of precision claims and estimation of relative bias for quantitative methods performed within the laboratory. Included are guidelines for duration, experimental designs, materials, data analysis summarization, and interpretation—techniques adaptable for the widest possible range of analytes and device complexity. A balance is created in the document between the complexity of design and formulae, and the simplicity of operation. The protocol is designed to be completed within five working days based on a uniform experimental design yielding estimates of imprecision and bias.

Clinical and Laboratory Standards Institute (CLSI). *User Verification of Precision and Estimation of Bias; Approved Guideline—Third Edition*. CLSI document EP15-A3 (ISBN 1-56238-965-3 [Print]; ISBN 1-56238-966-1 [Electronic]). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2014.

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Suggested Citation

CLSI. *User Verification of Precision and Estimation of Bias; Approved Guideline—Third Edition*. CLSI document EP15-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

Proposed Guideline

December 1998

Approved Guideline

December 2001

Approved Guideline—Second Edition

June 2005

Second Printing

April 2006

Approved Guideline—Third Edition

September 2014

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Foreword

Before a laboratory can introduce a new measurement procedure for reporting results of patient testing, it must evaluate the procedure's analytical performance. Typically, laboratories specify the performance required of the procedure and then verify that the procedure's performance meets the specification. Performance requirements may be defined by regulatory requirements and/or medical usefulness requirements.

In this edition of EP15, the user is **verifying** the manufacturer's claim for precision, and **estimating** bias, because there is unlikely to be a bias claim to verify. The document development committee felt that it was necessary to keep precision and trueness together in one document because the document demonstrates how to measure both in the same experiment.

Most manufacturers follow CLSI document EP05[1] to establish precision claims, and these claims are relatively easily verifiable using the approach prescribed in EP15. The committee chose to keep the number of days in the experiment at five, and to increase the number of replicates per day to five, in order to obtain more reliable estimates of repeatability and within-laboratory imprecision. The most complicated calculations were replaced by tables to make calculations easier and to reduce the opportunities for mathematical errors.

This document is primarily intended for use when an established measurement procedure is initially set up in the laboratory. It may also be used to verify performance after corrective action following a failed proficiency testing event.

⚠ **NOTE:**

Due to the complex nature of the calculations in this guideline, it is recommended that the user have access to a computer and statistical software, such as StatisPro™[2] method evaluation software from CLSI.

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⚠️ **NOTE:**
. . . .

Instead of manual worksheets, calculations may be readily performed with **CLSI's StatisPro[2] software** or generic spreadsheet software.

. . . .

In any case, the user must follow the protocol described   in order to obtain reliable results.

Overview of Changes

In this revision of EP15, the experiment to demonstrate trueness using materials with known concentrations was expanded to five days, with encouragement to work with the same sample materials used in the precision verification experiment. The intention of the document development committee was for the user to perform a single experiment to verify precision and trueness simultaneously. This experiment is designed to produce reliable estimates of bias between the mean measurand concentration observed by use of the candidate measurement procedure and the assigned measurand concentration of the material. The degree to which the observed bias is a measurement of trueness depends on the quality of the measurement procedure used to assign the measurand concentrations of the material. As with the precision experiment, complicated calculations were replaced by tables wherever possible.

Similar to previous editions of the document, the document development committee had two principal goals during the development of EP15. One goal was to develop a testing protocol that is suitable for use in the large clinical laboratory, yet simple enough to be applicable in the point-of-care or physician's office laboratory. The second goal was to develop a protocol that is sufficiently rigorous to provide statistically valid conclusions for verification studies. The bias is assessed by a recovery experiment. Instead of manual worksheets, calculations may be readily performed with CLSI's StatisPro[2] software or generic spreadsheet software (see recommendation below).

The committee feels that it is important to provide the interested user with an explanation of the statistical procedures that are used in the document. If the user has access to software specifically designed to perform the calculations described in the document, such as StatisPro,[2] a detailed understanding of the statistics is not necessary. Flow charts are included to provide the user with the necessary overview of the experiment and data processing. In any case, the user must follow the protocol described as closely as possible in order to obtain reliable results.

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Chapter ❶

Introduction

This chapter includes:

- ▶ Document scope and applicable exclusions

- ▶ Background information pertinent to the document content

- ▶ Standard Precautions information, as applicable

- ▶ Terms and definitions used in the document

- ▶ "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions, where applicable

- ▶ Abbreviations and acronyms used in the document