CLINICAL AND LABORATORY STANDARDS INSTITUTE®

May 2014

EP10-A3-AMD

Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures; Approved Guideline—Third Edition

This guideline provides experimental design and data analysis for preliminary evaluation of the performance of a measurement procedure or device.

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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EP10-A3-AMD
Vol. 26 No. 34
ISBN 1-56238-622-0 Replaces EP10-A2
ISSN 0273-3099 Vol. 22 No. 29

Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures; Approved Guideline—Third Edition

Volume 26 Number 34

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Abstract

Clinical and Laboratory Standards Institute document EP10-A3-AMD—*Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures; Approved Guideline—Third Edition* is intended to facilitate a limited, preliminary evaluation of the performance of a measurement procedure or device. Using the experimental design and data analysis procedure described, determination of whether a device has problems that require further evaluation or referral to the manufacturer can be done with a minimum expenditure of time and material. Included in Appendixes A and B are sample data sheets that should facilitate the analysis of the data. Appendix C contains a more sophisticated, powerful, statistical method for determining the possible causes of imprecision.

Clinical and Laboratory Standards Institute (CLSI). *Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures; Approved Guideline—Third Edition.* CLSI document EP10-A3-AMD (ISBN 1-56238-622-0). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2014.

Suggested Citation

CLSI. *Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures; Approved Guideline—Third Edition.* CLSI document EP10-A3-AMD. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

Previous Editions:
December 1985, June 1989, September 1993, May 1998, December 2002, November 2006

Reaffirmed:
September 2019

ISBN 1-56238-622-0
ISSN 0273-3099

Committee Membership

The changes in this amendment were approved by the Consensus Committee on Evaluation Protocol as follows.

Consensus Committee on Evaluation Protocols

Acknowledgment

CLSI and the Consensus Committee on Evaluation Protocols gratefully acknowledge the following individuals for reviewing all data and providing all appropriate amendments to this document:

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Working Group on Evaluation of Quantitative Clinical Laboratory Methods

Acknowledgment

CLSI, the Area Committee on Evaluation Protocols, and the Working Group on Evaluation of Quantitative Clinical Laboratory Methods gratefully acknowledge Stanley Bauer, MD, a longtime contributor to CLSI, who had the foresight to commission Cuthbert Daniel, an award-winning statistical consultant, to prepare efficient protocols to evaluate commercial analyzers, and John Kennedy, also a dedicated contributor to CLSI, who chaired the original subcommittee that developed the EP10 consensus guideline.

Contents

Contents (Continued)

Summary of Changes in EP10 Amendment

Foreword

- Deleted existing reference to "Excel," but added trade name statement regarding its use in Section 16, per CLSI policy.

Laboratory Error Sources and CLSI Evaluation Protocols Documents

- For consistency with current CLSI publications, the flow chart on Laboratory Error Sources and CLSI Evaluation Protocols Documents was removed.

Section 4.2

- For clarification, added definitions for "commutable" and "continuous flow analyzer."

- For clarification, modified definition of linear drift to state "a change in measurement value that is directly proportional to duration."

Section 5

- For clarification, changed "useful interval" to "desired interval" in the first sentence of the third paragraph.

Section 6

- For clarification, added the phrase, "in the exact sequence specified" in the fifth sentence of the first paragraph.

- For clarification, added the statement "It is important to understand the protocol used by the analyzer to determine which sample will be pipetted next, and, if necessary, configure or program the analyzer to process the samples in the strict order outlined above."

Section 8

- For clarification, added the statement "It is especially important to know what steps are necessary to ensure that the samples are tested in the strict order specified."

Section 11

- For clarification, the first paragraph was shortened to state the following:

  The imprecision of this experiment can be done by estimating the components of variance due to within-run, between-run (if more than one run is done per day), and between-day factors, as given by the formulas and procedures described in Appendixes A and C. These components of variance should then be added and the square root calculated to yield the "corrected" imprecision of this experiment. The relative sizes of the components may then be examined to investigate the sources of imprecision. This provides a more robust estimate of imprecision compared to simple calculation of the standard deviation of the data collected.

Section 11.1

- For clarification, reference to Data Summary Sheet #3 was changed to Appendix A and the following statement was added: "Note that the imprecision goals should take into account the confidence limits from the estimate of imprecision due to the small sample sizes used in this procedure. CLSI document EP15[1] covers this topic."

Section 12.1.1

- For clarification, the first sentence was revised to "Analysis of an aliquot should be done by a measurement procedure of known accuracy (a reference method is ideal)."

Section 12.2.1

- For clarification, reference to page 30 was changed to Appendix A.

Section 16

- Deleted reference to "Excel" in the section title.

- For clarification, the first paragraph was revised to state the following:

  This section describes how to perform the multiple regression calculations using the software program Microsoft® Excel (or the equivalent). Users of other software should be able to follow the description and implement the steps as appropriate. **NOTE:** This section uses the example ethanol data from Appendix B.

- For clarification, deleted "and does not need to be purchased separately" from the NOTE in the second paragraph.

Appendix A

- The first footnote of Data Summary Sheet #1 was revised to "* See Appendix C for basis of calculations. Standard deviations use equation 1 of Appendix C. When using software such as a spreadsheet program or statistical software to facilitate the calculations, be sure to use the formula for sample standard deviation with $n-1$ as the denominator."

Appendixes A and B

- Realigned table formats in the data summary sheets.

Summary of Consensus and Delegate Comments and Committee Responses

- The Summary of Consensus and Delegate Comments and Committee Responses was removed as part of this amendment. This summary is on file at the CLSI office and available upon request by contacting CLSI at 610.688.0100 or standard@clsi.org.

Foreword

Before using a new measurement procedure or instrument for *in vitro* diagnostic use, the laboratory must make a preliminary decision about its acceptability. This initial performance check is neither a rigorous characterization of long-term performance nor an evaluation of the many factors that can affect results produced by the device. Rather, this experiment is a quick check to rule out major problems and a starting point for accumulating data and experience that will enable the user to make a final decision. The primary purpose of this document is to help detect performance problems that would warrant immediate correction, referral to the manufacturer, or expanded investigation before a new device is placed into service.

This document may also now be used by manufacturers to either establish the magnitude of factors that can affect performance or verify that such magnitude is acceptable.

Additional revisions since the last edition of EP10 (2002) include:

- a figure to illustrate which error sources the EP10 protocol can detect with respect to all error sources and other EP documents (see page viii);
- suggested sample sizes, so now the document is useful for manufacturers;
- instructions for the multiple regression calculations;
- revised references; and
- revised definitions.

Key Words

Carry-over, comparison of methods, drift, evaluation protocol, experimental design, linearity, multiple regression, outlier, precision

Note that the trade name Microsoft® Excel is included in Section 16 of this document. It is Clinical and Laboratory Standards Institute's policy to avoid using a trade name unless the product identified is the only one available, or it serves solely as an illustrative example of the procedure, practice, or material described. In this case, the working group and consensus committee believe the trade name is an important descriptive adjunct to the document. In such cases, it is acceptable to use the product's trade name, as long as the words, "or the equivalent" are added to the references. It should be understood that information on this product in this standard also applies to any equivalent products. Please include in your comments any information that relates to this aspect of EP10.

Preliminary Evaluation of Quantitative Clinical Laboratory Measurement Procedures; Approved Guideline—Third Edition

1 Scope

Before starting a complete evaluation of a new measurement procedure, kit, or instrument for *in vitro* diagnostic use, it is often necessary to make a preliminary decision about its acceptability. This initial performance check is neither a rigorous investigation into the procedure's long-term performance, nor an evaluation of the many factors that can affect results produced by the device. The primary purpose of this document is to help detect problems that are severe enough to warrant immediate correction, referral to the manufacturer, or expanded investigation. Accreditation bodies may have requirements for verification or validation that exceed the procedures in this document (see CLSI document EP15[1]).

Manufacturers can also benefit by performing this protocol either as assays are developed or when they are validated. By performing more than five runs, manufacturers can detect trends in the effects estimated by EP10 or document their absence.

2 Introduction

This document describes a procedure for the preliminary evaluation of linearity, proportional and constant bias, linear drift, sample carry-over, and precision of a clinical laboratory measurement procedure. Preliminary evaluations should be performed before new procedures are used to test patients' samples and when any modifications of procedures are made. This guideline is based on a protocol and procedure developed for continuous flow analyzers.[2] The rationale for recommending a protocol based on so old a system is explained in Section 13.1. The experiment is intended primarily for evaluating automated instruments but may be appropriate for kits, manual procedures, or other *in vitro* diagnostic devices. By repeating a sequence of only ten samples, performance characteristics may be evaluated by plotting the data and performing some simple calculations. Using a statistical technique called multiple linear regression analysis, further information about the factors influencing accuracy (such as sample carry-over linear drift, and nonlinearity) can be obtained. Instructions are given for simple data analysis, in case a computer is not available.

The experiment is intended to provide preliminary estimates of those performance characteristics that may be used to determine the ultimate acceptability of the device. The results should be used only to determine whether the device has grossly unacceptable performance.

The following sections outline the materials and procedures to be used. Many variations on this basic experiment are possible (such as extending the number of days or eliminating the priming samples when appropriate). Variations should be dictated by the complexities of the device, the particular characteristics of the measurement procedure, and the resources available to the user.

3 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are treated as infectious and handled according to "standard precautions." Standard precautions are guidelines that combine the major features of "universal precautions and body substance isolation" practices. Standard precautions cover the transmission of all infectious agents and thus are more comprehensive than universal precautions which are intended to apply only to transmission of blood-borne pathogens. Standard and universal precaution guidelines are available from the U.S. Centers for Disease Control and Prevention (Garner JS, Hospital Infection Control Practices Advisory Committee. Guideline for isolation precautions in hospitals. *Infect Control Hosp Epidemiol*. 1996;17(1):53-80). For

