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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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- the revision of documents in response to comments by users
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Most documents are subject to two levels of consensus—"proposed" and "approved." Depending on the need for field evaluation or data collection, documents may also be made available for review at an intermediate consensus level.

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Healthcare professionals in all specialties are urged to volunteer for participation in CLSI projects. Please contact us at customerservice@clsi.org or +610.688.0100 for additional information on committee participation.

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

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Abstract

Clinical and Laboratory Standards Institute document EP10-A3—*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.

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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.

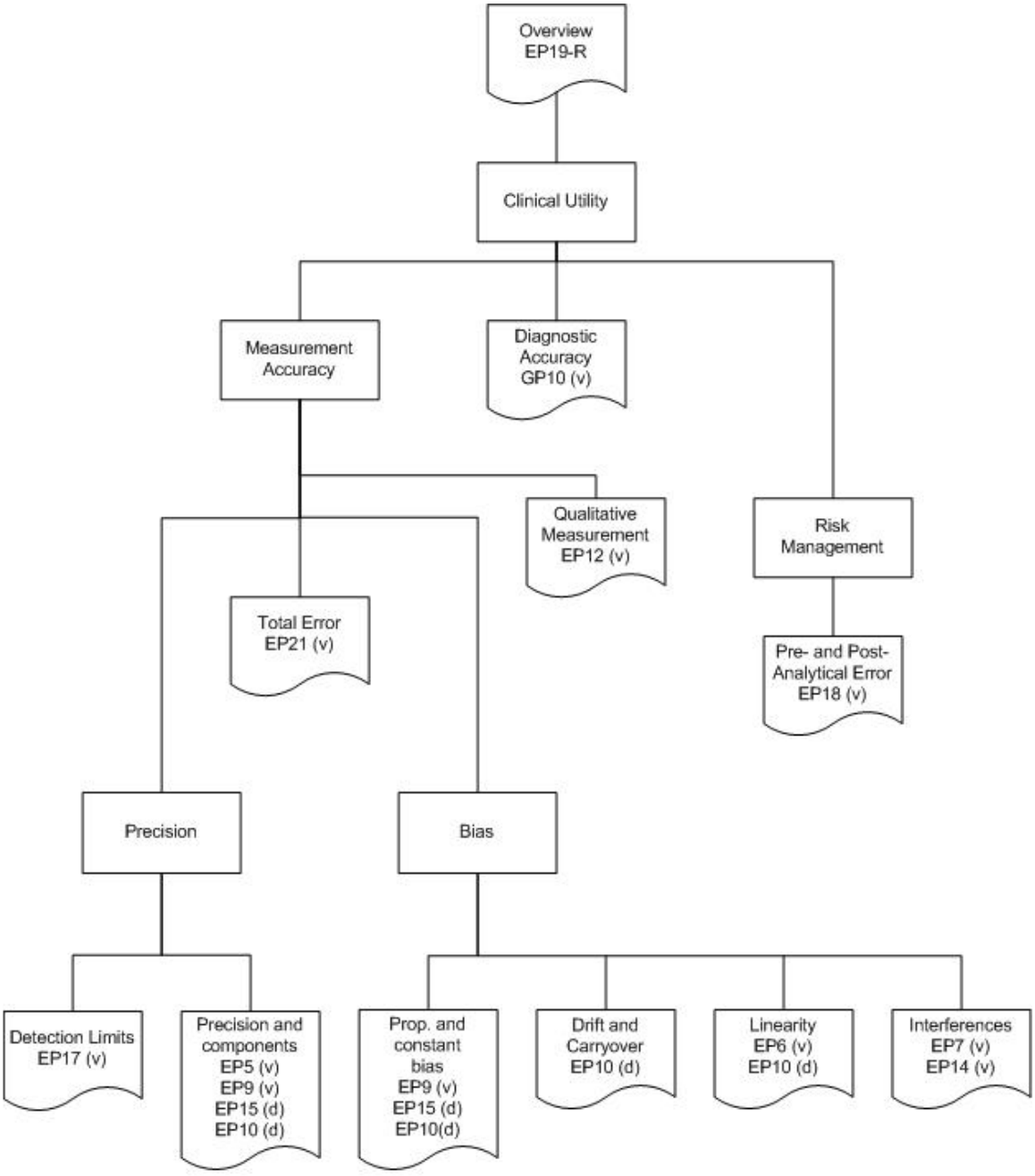
Additional revisions since the last edition of EP10 (2002) include:

- 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 in Excel;
- revised references; and
- revised definitions.

Key Words

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

Laboratory Error Sources and CLSI Evaluation Protocols Documents



Laboratory Error Sources and CLSI Evaluation Protocols Documents.[a] This figure illustrates the relationship among parameters estimated by EP documents. Items higher up in the figure are more comprehensive whereas lower level items are more specific. Overall, the figure is much like a cause-and-effect diagram. Documents marked (d) provide guidance for demonstrating that a source of measurement inaccuracy is within acceptable limits. Documents marked (v) provide guidance for more rigorous evaluation of inaccuracy components.

[a] For a description of each of the documents listed, please see page 53.

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 the most current edition of CLSI document EP15—*User Verification of Performance for Precision and Trueness*).

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.[1] 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.