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## Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline—Second Edition

This guideline describes risk management techniques that will aid in identifying, understanding, and managing sources of failure (potential failure modes) and help to ensure correct results. Although intended primarily for *in vitro* diagnostics, this document will also serve as a reference for clinical laboratory managers and supervisors who wish to learn about risk management techniques and processes.

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

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Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: 610.688.0100
F: 610.688.0700
www.clsi.org
standard@clsi.org

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# Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline—Second Edition

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Jan S. Krouwer, PhD
Abdel-Baset Halim, DPharm, PhD, DABCC
Aristides T. Hatjimihail, MD, PhD
Ellis Jacobs, PhD, DABCC, FACB
Adam Manasterski, PhD
James H. Nichols, PhD, DABCC, FACB

## Abstract

Clinical and Laboratory Standards Institute document EP18-A2—*Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline—Second Edition* recommends a quality management system for *in vitro* diagnostic test systems that is based on expert opinion, is practical to implement, and is applicable to various devices and settings, so sources of failure (potential failure modes) are identified, understood, and managed. This system will assist device manufacturers, regulators, accrediting agencies, and laboratory directors in ensuring correct results. It addresses regulatory considerations (eg, principles and accountability), recommends the development of a partnership between users and manufacturers, provides a source-of-failures matrix, and suggests approaches to quality monitoring/identification of the problems.

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# Committee Membership

## Area Committee on Evaluation Protocols

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**Plano, Texas, USA**

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John Rex Astles, PhD, FACB
Centers for Disease Control and Prevention
Atlanta, Georgia, USA

Jeffrey R. Budd, PhD
Beckman Coulter, Inc.
Chaska, Minnesota, USA

George S. Cembrowski, MD, PhD
University of Alberta Hospital
Edmonton, Alberta, Canada

David L. Duewer, PhD
National Institute of Standards and Technology
Gaithersburg, Maryland, USA

Anders Kallner, MD, PhD
Karolinska Hospital
Stockholm, Sweden

James F. Pierson-Perry
Siemens Healthcare Diagnostics
Newark, Delaware, USA

Mitchell G. Scott, PhD
Washington University School of Medicine
St. Louis, Missouri, USA

Lakshmi Vishnuvajjala, PhD
FDA Center for Devices and Radiological Health
Rockville, Maryland, USA

**Advisors**

David A. Armbruster, PhD, DABCC, FACB
Abbott Diagnostics
Abbott Park, Illinois, USA

Carl C. Garber, PhD, FACB
Quest Diagnostics, Incorporated
Lyndhurst, New Jersey, USA

Patricia E. Garrett, PhD
SeraCare Life Sciences, Inc.
Portland, Maine, USA

Claude Giroud, PhD
Bio-Rad Laboratories, Inc.
Marnes-La-Coquette, France

Martin H. Kroll, MD
Boston Medical Center
Boston, Massachusetts, USA

Jan S. Krouwer, PhD
Krouwer Consulting
Sherborn, Massachusetts, USA

Jacob (Jack) B. Levine, MBA
Siemens Healthcare Diagnostics
Tarrytown, New York, USA

Kristian Linnet, MD, PhD
University of Copenhagen
Copenhagen, Denmark

Robert J. McEnroe, PhD
Roche Diagnostics Operations, Inc.
Indianapolis, Indiana, USA

James H. Nichols, PhD, DABCC, FACB
Baystate Medical Center
Springfield, Massachusetts, USA

Luann Ochs, MS
BD Diagnostics-TriPath
Durham, North Carolina, USA

Donald R. Parker, PhD
Bayer HealthCare, LLC
Elkhart, Indiana, USA

Nils B. Person, PhD, FACB
Siemens Healthcare Diagnostics
Flanders, New Jersey, USA

Donald M. Powers, PhD
Powers Consulting Services
Pittsford, New York, USA

Max Robinowitz, MD
FDA Center for Devices and Radiological Health
Rockville, Maryland, USA

Michele M. Schoonmaker, PhD
Cepheid
Sunnyvale, California, USA

Daniel W. Tholen, MS
American Association for Laboratory Accreditation
Traverse City, Michigan, USA

Jack Zakowski, PhD, FACB
Beckman Coulter, Inc.
Brea, California, USA

## Subcommittee on Risk Management Techniques to Identify and Control Laboratory Error Sources

**Jan S. Krouwer, PhD**
**Chairholder**
**Krouwer Consulting**
**Sherborn, Massachusetts, USA**

Sousan S. Altaie, PhD
FDA Center for Devices and Radiological Health
Rockville, Maryland, USA

Aristides T. Hatjimihail, MD, PhD
Hellenic Complex Systems Laboratory
Drama, Greece

Ellis Jacobs, PhD, DABCC, FACB
NY City Health & Hospital Corporation
New York, New York, USA

Christine Krenc
Abbott Diagnostics
Abbott Park, Illinois, USA

James H. Nichols, PhD, DABCC, FACB
Baystate Medical Center
Springfield, Massachusetts, USA

Anthony O. Okorodudu, PhD, DABCC, FACB
University of Texas Medical Branch
Galveston, Texas, USA

Diane I. Szamosi, MA, MT(ASCP)SH
Becton Dickinson
Franklin Lakes, New Jersey, USA

**Advisors**

Patricia E. Garrett, PhD
SeraCare Life Sciences, Inc.
Portland, Maine, USA

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CLSI and the Subcommittee on Risk Management Techniques to Identify and Control Laboratory Failure Sources gratefully acknowledge the following volunteer for his important contributions to the development and/or completion of this document:

Adam Manasterski, PhD (CDC/retired)
Atlanta, Georgia, USA

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## Foreword

*In vitro* diagnostic (IVD) devices play a crucial role in patient care, and the quality and reliability of IVD results are paramount. However, all devices and methods may be subject to preanalytical, analytical, and postanalytical (preexamination, examination, and postexamination) failure. The relative importance and probability (ie, the risk) of a specific failure condition may vary with the device design, the user, the medical application, and the operating environment. A single quality assurance and quality control (QA/QC) regimen that optimally mitigates risk for all devices does not exist. As a greater variety of devices and tests become available to meet clinical demands in various environments, including outside the traditional laboratory at the point of patient care, a pressing need to ensure and control quality in the most effective and efficient manner has been noted. Such QA/QC regimens should be based on the characteristics of the device in use, taking into consideration local variables, such as the intended use of the test and the testing environment and users. Furthermore, QA/QC procedures should be developed systematically using established quality management tools, such as Failure Modes and Effects Analysis (FMEA) and Failure Reporting, Analysis, and Corrective Action Systems (FRACAS).

The original version of this document, EP18-A—*Quality Management for Unit-Use Testing*, was limited to unit-use devices (see Appendix E). The impetus for the original document was that

*"Conventional quality assurance and quality control methods in and of themselves do not assure quality. A one-size-fits-all or prescribed quality control testing protocol such as 'two levels per day of use' may not be appropriate for all testing systems. The diversity among regulatory requirements, accreditation practices, and user needs, coupled with the financial aspects of this QC method, led to the formation of the CLSI Subcommittee on Unit-Use Testing.*

*It is the subcommittee's intent to provide a comprehensive and flexible guideline that will enable users, manufacturers, and regulators to identify potential sources of failures in unit-use test systems and implement processes to manage these failures using new quality management models."*

The original subcommittee anticipated that a broader based guideline could be created that would address both unit-use and multiuse systems. Accordingly, this revision of EP18 is applicable to all IVDs.

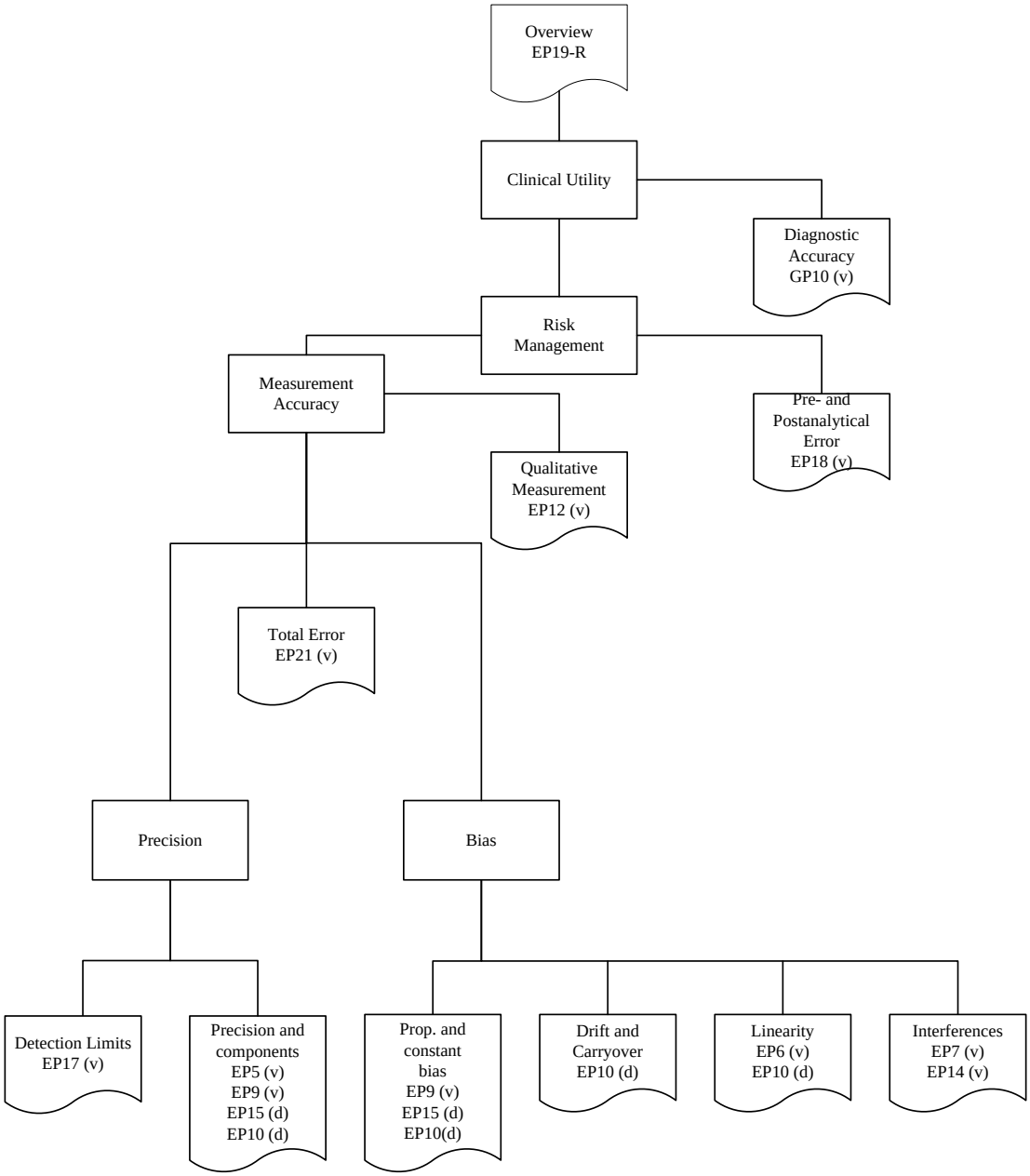
As represented in the table below, this document is intended to provide guidance to manufacturers of IVD devices and laboratory directors to assist in identifying potential risks and developing a strategy to control quality and mitigate potential failures.

| | **Prevention** | **Detection** |
|---|---|---|
| Manufacturer | Risk assessment and risk mitigation for manufacturers<br><br>References:<br>• International Organization for Standardization (ISO) 14971[1]<br>• CLSI document EP18 | Embedded instrument checks and controls<br><br>Information regarding design features intended to mitigate risk of potential device failures that can affect the accuracy of test results |
| Laboratory | Techniques (FMEA and FRACAS) to identify and control laboratory failure sources<br><br>Reference:<br>• CLSI document EP18 | Laboratory implemented quality control procedures<br><br>Reference:<br>• ISO 15189[2] |

**Key Words**

Quality assurance, quality control, quality management, quality system, risk management

## Laboratory Failure Sources and CLSI Evaluation Protocols Documents




Adapted from Krouwer JS. Estimating total analytical failure and its sources: techniques to improve method evaluation. *Arch Pathol Lab Med.* 1992;116:726-731.[3] Copyright © 1992 American Medical Association. All rights reserved. Reprinted with permission.

**Laboratory Failure Sources and CLSI Evaluation Protocols (EP) 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 the Related CLSI Reference Materials section at the end of this document.

# Risk Management Techniques to Identify and Control Laboratory Error Sources; Approved Guideline—Second Edition

## 1 Scope

This document provides guidance for risk management activities that include risk analysis (Failure Modes and Effects Analysis [FMEA]), fault trees, and risk monitoring (Failure Reporting, Analysis, and Corrective Action Systems [FRACAS]). These approaches are based on best practices; practical to implement; applicable to all diagnostics assays; and scientifically based, so sources of failure are identified, understood, and managed.

This guideline applies to *in vitro* diagnostic device (IVD) test systems used by providers of health care services in any setting. The scope of this guideline comprises testing components, locations, and users. Specifically, the testing components include preanalytical, analytical, and postanalytical (preexamination, examination, and postexamination) processes.

This document is intended primarily for IVD manufacturers. However, it is also intended as an important reference for clinical laboratory directors and supervisors who wish to learn about risk management techniques and processes. Although the concept of risk reduction is not new in the laboratory, the risk management tools in this guideline may be new to laboratorians, and will create a need for laboratory directors and supervisors to gain an understanding of these techniques so they can apply these principles and processes in development of their customized quality plan. EP18 is intended to help in that effort.

## 2 Introduction

Diagnostic testing presents unique challenges to manufacturers, users, regulators, and accrediting agencies. Manufacturers and the clinical laboratory are faced with the task of keeping systems operational and producing results (reliability), as well as ensuring that the results meet minimum performance standards. Examples include accuracy and those elements that affect accuracy such as precision, bias, and limit of detection. ***Any*** failure source (see Appendix B for some examples of failures) can affect the accuracy and/or reliability of a result.

Risk management attempts to answer four questions:

1. What can go wrong? (process mapping, brainstorming)

2. How bad is it? (severity of harm, especially with downstream events)

3. How often? (probability of occurrence for potential errors, frequency of occurrence for observed errors)

4. What should be done to mitigate/reduce the risk? (prioritization of risks)

Many evaluation protocols documents have focused on evaluating parameters that affect accuracy, such as linearity (see CLSI document EP06),[4] precision (see CLSI document EP05),[5] and bias (see CLSI document EP09).[6] EP18 takes a more global approach regarding accuracy and reliability by using risk analysis methods to ensure that

- The risk of potentially hazardous situations has been lowered to an acceptable level.

- The rate of hazardous situations that have occurred has been lowered to an acceptable level where an acceptable level can be an as low as reasonably practicable (ALARP) level.