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Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline—Third Edition



This guideline provides definitions of analytical intervals, planning of quality control procedures, and guidance for quality control applications.

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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Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline—Third Edition

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James O. Westgard, PhD
W. Gregory Miller, PhD
Kathleen Allen, MD
Donald Joe Boone, PhD
Patrick Caines, PhD, MBA
Greg Cooper, CLS, MHA

Carl Garber, PhD, FACB
Neil Greenberg, PhD
Chandra P. Jain
Kristian Linnet, MD, PhD
Estelle Russek-Cohen, PhD
Jeffrey E. Vaks, PhD

Abstract

Clinical and Laboratory Standards Institute document C24-A3—*Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline—Third Edition* addresses the principles of statistical quality control (QC), with particular attention to the planning of a QC strategy, the definition of an analytical run, and the application of statistical QC in a healthcare laboratory. While these principles are of interest to manufacturers, this guideline is intended for use by a healthcare laboratory to provide a QC procedure that employs control materials that are independent and external to a reagent kit, an instrument, or analytical system. This guideline is a revision of an earlier guideline and includes the original definition for user-defined run length. Changes in the second edition included a strong emphasis on defining quality up front to guide the selection of control rules and the number of control measurements. The third edition adds example applications that make use of a simple sigma-metrics QC planning tool.

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Committee Membership

Area Committee on Clinical Chemistry and Toxicology

David A. Armbruster, PhD,
DABCC, FACB
Chairholder
Abbott Laboratories
Abbott Park, Illinois

W. Gregory Miller, PhD
Vice-Chairholder
Virginia Commonwealth
University
Richmond, Virginia

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

David M. Bunk, PhD
National Institute of Standards and
Technology
Gaithersburg, Maryland

Neil Greenberg, PhD
Ortho-Clinical Diagnostics, Inc.
Rochester, New York

Christopher M. Lehman, MD
Univ. of Utah Health Sciences
Center
Salt Lake City, Utah

Richard R. Miller, Jr.
Dade Behring Inc.
Newark, Delaware

Linda Thienpont, PhD
University of Ghent
Ghent, Belgium

Hubert Vesper, PhD
Centers for Disease Control and
Prevention
Atlanta, Georgia

Advisors

Mary F. Burritt, PhD
Mayo Clinic
Rochester, Minnesota

Paul D'Orazio, PhD
Instrumentation Laboratory
Lexington, Massachusetts

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

Uttam Garg, PhD, DABCC
The Children's Mercy Hospital
Kansas City, Missouri

Harvey W. Kaufman, MD
Quest Diagnostics, Incorporated
Lyndhurst, New Jersey

Gary L. Myers, PhD
Centers for Disease Control and
Prevention
Atlanta, Georgia

David Sacks, MD
Brigham and Women's Hospital
and Harvard Medical School
Boston, Massachusetts

Bette Seamonds, PhD
Mercy Health Laboratory
Swarthmore, Pennsylvania

Dietmar Stöckl, PhD
University of Ghent
Ghent, Belgium

Thomas L. Williams, MD
Nebraska Methodist Hospital
Omaha, Nebraska

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

Working Group on Statistical Quality Control

James O. Westgard, PhD
Chairholder
University of Wisconsin
Madison, Wisconsin

Kathleen Allen, MD
Quest Diagnostics Incorporated
Pittsburgh, Pennsylvania

Donald Joe Boone, PhD
Centers for Disease Control and
Prevention
Atlanta, Georgia

Patrick Caines, PhD, MBA
Ortho Clinical Diagnostics
Rochester, New York

Greg Cooper, CLS, MHA
Bio-Rad Laboratories, Inc.
Irvine, California

Chandra P. Jain
Beckman Coulter, Inc.
Brea, California

Kristian Linnet, MD, PhD
Psychiatric University Hospital
Risskov, Denmark

Estelle Russek-Cohen, PhD
U.S. Food and Drug Administration
Rockville, Maryland

Advisors

F. Philip Anderson, PhD
Virginia Commonwealth University
Richmond, Virginia

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

Jeffrey E. Vaks, PhD
Irvine, California

Staff

Clinical and Laboratory Standards
Institute
Wayne, Pennsylvania

John J. Zlockie, MBA
Vice President, Standards

Tracy A. Dooley, BS, MLT (ASCP)
Staff Liaison

Patrice E. Polgar
Projects Coordinator

Donna M. Wilhelm
Editor

Melissa A. Lewis
Assistant Editor

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Foreword

This document is the third edition of a guideline that has been in use by the clinical laboratory community for about fifteen years. Statistical QC is still critically important in laboratories today to ensure the quality of the test results produced by any measurement procedure. The almost universal applicability of statistical QC to quantitative measurement procedures provides laboratories with a quality management tool that can be deployed whenever and wherever needed. It also allows laboratories to verify and validate independently the ongoing performance of *in vitro* diagnostic device manufacturers' built-in quality control measures and monitors.

When the first edition of this document was developed, laboratories were experiencing changes in measurement technology and instrument systems that made many of the conventional quality control practices difficult to apply. In response to those needs, the first edition of this document clarified the fundamental principles and definitions of statistical quality control that should be considered when managing any laboratory measurement process.

- An example of an important concept in statistical quality control was the definition of an “analytical run,” which in the past often corresponded to the batch of specimens being analyzed for a particular quantity. With many modern analytical systems, the definition of a run is not nearly as clear. An analytical run is better understood in terms of the time or number of measurements for which the measurement procedure is stable.

The second edition continued that tradition to appraise, clarify, and define concepts, approaches, and practices that should be generally useful in developing a specific quality control strategy for testing with quantitative measurements. It maintained a focus on statistical quality control because of the capability of this technique in monitoring the effects of many instrument, reagent, environment, and operator variables on the outcome of a measurement process.

- An example of an important approach was the planning of a quality control procedure. The second edition described the principles for developing a specific quality control strategy that takes into account the quality requirements of the test, the performance available from a method, the error detection capability of different QC strategies, and the goals set by the laboratory for QC performance.
- An example of an important practice was steps that the laboratory should take to respond to an out-of-control condition. Following guidelines on statistical quality control proposed by a European working group of the External Quality Assessment (proficiency testing) Organizers (EQA-Organizers),¹ it was recommended that there should be a strong emphasis on troubleshooting the measurement process to detect a root cause of an out-of-control condition. This response is appropriate when the quality control procedure is carefully planned and control rules are appropriately selected to minimize false alarms or false rejections.

This third edition aims to provide more practical guidance in planning of statistical QC procedures. While there are many possible approaches for implementing a QC planning process, some practical tools have emerged that make it easy to select appropriate QC procedures on the basis of their probabilities of rejecting analytical runs with various magnitudes of error. There are other approaches that make use of probabilities of reporting a patient test result with unacceptable measurement error or average run lengths and related characteristics. A practical and achievable approach is critically important today if individual laboratories are to achieve the performance required for the patient populations they serve. This revision provides detailed examples of a recommended QC planning approach in an appendix, applying practical quality-planning tools.

Responsibility for the laboratory quality management program generally resides with the director(s) of the laboratory. Particularly important is the definition of quality requirements for the tests being performed by the laboratory, which generally resides with the medical director of the laboratory. The responsibility

for utilizing those quality requirements to select and validate appropriate measurement and control procedures can reside with managers, supervisors, laboratory scientists, and quality specialists. Given access to the proper planning tools and training and practice in the use of those tools, clinical laboratory scientists can optimize the statistical QC practices of their laboratories. The approach described here is directed to clinical laboratory scientists who have the knowledge of routine QC practices and the responsibility and opportunity to implement improvements. This approach provides laboratory scientists with practical guidance on how to satisfy the ISO 15189:2003 recommendation (Clause 5.6.1) that “the laboratory shall design internal quality control systems that verify the attainment of the intended quality of the results.”

This document does *not* attempt to define specific quality-control strategies that are appropriate for an individual device or technology, nor does it attempt to describe alternatives to statistical process control. It should also be noted that there are other types of random errors that may affect measurements performed on individual samples, rather than a whole group of samples, and those errors will not be detected by a statistical QC procedure. Such errors may be due to the specific design of an analytical system (e.g., effect of sample viscosity, carryover from a previous sample, or specimen-specific interferences) or possible operator errors that affect individual samples, as well as preanalytical errors of sample preparation, storage, and transportation. Special QC procedures may be needed to monitor known special vulnerabilities that relate to a particular device or system design.

This document does not consider specific legal requirements that may impose different philosophies or procedures on quality control practices (e.g., a specific approach for defining quality requirements, specific values for quality requirements, or a specific procedure for determining target values for the means of control materials). For example, in some countries or geographic regions, government regulation may define specific laboratory QC requirements that dictate frequency and number of QC data points, QC specimen requirements, target values, and acceptable ranges for results. In the U.S., recent regulatory proposals for application of “equivalent QC” procedures need to be carefully evaluated in light of the concepts, principles, and planning approach presented here. It is not the purpose of this document to make any recommendation about these proposed procedures.

The concepts, approaches, and practices discussed here are interdependent and all must be carefully studied and considered when developing the specific QC strategy for any test procedure, system, or laboratory. In an age when the quality of laboratory tests is often taken for granted by clinicians, this document serves as a reminder that there are technical issues that still require a careful scientific approach to planning QC procedures, if laboratories are to achieve the quality specifications needed by the physicians and patients they serve.

A Note on Terminology

CLSI, as a global leader in standardization, is committed to achieving global harmonization wherever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in the United States, Europe, and elsewhere; that these differences are reflected in CLSI, ISO, and CEN documents; and that legally required use of terms, regional usage, and different consensus timelines are all obstacles to harmonization. In light of this, CLSI recognizes that harmonization of terms facilitates the global application of standards and is an area of immediate attention. Implementation of this policy is an evolutionary and educational process that begins with new projects and revisions of existing documents.

In keeping with CLSI’s commitment to align terminology with that of ISO, the following terms are used in C24: *Measurement procedure* has replaced the term *analytical method* for a set of operations, used in the performance of particular measurements according to a given method; *measuring range* has replaced *reportable range* when referring to a set of values of measurands for which the error of a measuring instrument is intended to lie within specified limits; and *measurement error* is used instead of *analytical error* to describe the result of a measurement minus a true value of the measurand.

The Working Group on Statistical Quality Control has chosen to retain the term *allowable total error* rather than replace it with a term based on measurement error because it represents a different concept in this guideline. Measurement error is the result of a measurement minus a true value (or accepted reference value) of the measurand. *Allowable total error* is an analytical quality requirement that sets a limit for both the imprecision (random error) and bias (systematic error) that are tolerable in a single measurement or single test result.

Key Words

Analytical run, calibration, quality control, quality control rules

Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline—Third Edition

1 Scope

This guideline addresses the purpose of statistical quality control for quantitative measurement procedures; describes an approach for planning quality control for a particular measurement procedure; provides a definition of an analytical run; addresses the use of quality control material and quality control data, including the use of the data in quality assurance and interpretation; and provides detailed examples that demonstrate a practical QC planning process for clinical laboratories. The recommendations given are applicable to quantitative laboratory tests in all fields of laboratory medicine where external stable control materials can be measured like patient specimens. The document does not contain step-by-step procedures for establishing and maintaining a statistical quality control program, or for other aspects of quality control, such as instrument function checks or the use of patient values for quality control purposes.

This guideline applies to a broad spectrum of clinical laboratories, from the low test volume to the high test volume. The analytical performance and quality control required for a measurement procedure must satisfy the medical applications of the particular test, which relate to inherent clinical aspects of the laboratory's patient population regardless of the laboratory's size, location, or complexity. Particularly in the low-volume environment, the decision to implement a given measurement procedure should carefully take into account (in addition to elements such as cost, service requirements, training requirements, and required turnaround time) the complexity and performance characteristics of the procedure. Measurement procedures are selected to meet medical needs. Once implemented, however, quality control is needed to ensure that the test results will continue to satisfy the medical needs.

2 Introduction

Statistical quality control procedures are intended to monitor the analytical performance of a measurement procedure and alert analysts to problems that might limit the usefulness of a test result for its intended medical purpose.

There is abundant literature addressing the theoretical and practical bases for initiating and maintaining statistical quality control (QC) procedures in clinical chemistry.²⁻⁷ However, there still are many difficulties in the routine practice of statistical quality control, and improvements depend on a better understanding of how to:

- (1) Plan QC on the basis of measurement procedure performance and the quality required for a test, including the selection of appropriate control materials, control rules, and numbers of control samples;
- (2) Define an analytical run appropriate for the measurement procedure as operated in an individual laboratory;
- (3) Implement QC and respond to out-of-control situations properly.

The prevalence of a broad range of automated clinical laboratory instruments using widely different analytical principles has complicated the terminology and the steps necessary for establishing statistical quality control procedures. On the other hand, these highly automated systems can often perform specific electronic checks that help detect potential problems and alert the operator to instrument malfunction. The