



MM14-A2

Design of Molecular Proficiency Testing/ External Quality Assessment; Approved Guideline—Second Edition

This document provides guidelines for a quality proficiency testing/external quality assessment program, including reliable databases; design control in the choice of materials and measurements; good manufacturing processes; documentation procedures; complaint handling; corrective and preventive action plans; and responsive timing of reports.

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

Clinical and Laboratory Standards Institute

Setting the standard for quality in medical laboratory testing around the world.

The Clinical and Laboratory Standards Institute (CLSI) is a not-for-profit membership organization that brings together the varied perspectives and expertise of the worldwide laboratory community for the advancement of a common cause: to foster excellence in laboratory medicine by developing and implementing medical laboratory standards and guidelines that help laboratories fulfill their responsibilities with efficiency, effectiveness, and global applicability.

Consensus Process

Consensus—the substantial agreement by materially affected, competent, and interested parties—is core to the development of all CLSI documents. It does not always connote unanimous agreement, but does mean that the participants in the development of a consensus document have considered and resolved all relevant objections and accept the resulting agreement.

Commenting on Documents

CLSI documents undergo periodic evaluation and modification to keep pace with advancements in technologies, procedures, methods, and protocols affecting the laboratory or health care.

CLSI's consensus process depends on experts who volunteer to serve as contributing authors and/or as participants in the reviewing and commenting process. At the end of each comment period, the committee that developed the document is obligated to review all comments, respond in writing to all substantive comments, and revise the draft document as appropriate.

Comments on published CLSI documents are equally essential, and may be submitted by anyone, at any time, on any document. All comments are managed according to the consensus process by a committee of experts.

Appeals Process

When it is believed that an objection has not been adequately considered and responded to, the process for appeals, documented in the CLSI Standards Development Policies and Processes, is followed.

All comments and responses submitted on draft and published documents are retained on file at CLSI and are available upon request.

Get Involved—Volunteer!

Do you use CLSI documents in your workplace? Do you see room for improvement? Would you like to get involved in the revision process? Or maybe you see a need to develop a new document for an emerging technology? CLSI wants to hear from you. We are always looking for volunteers. By donating your time and talents to improve the standards that affect your own work, you will play an active role in improving public health across the globe.

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

Clinical and Laboratory Standards Institute

500 West Valley Road, Suite 2500

Wayne, PA 19087 USA

T: +1.610.688.0100

F: +1.610.688.0700

www.clsi.org

standard@clsi.org

ISBN 1-56238-873-8 (Print)
ISBN 1-56238-874-6 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2914 (Electronic)

MM14-A2
Vol. 33 No. 5
Replaces MM14-A
Vol. 25 No. 24

Design of Molecular Proficiency Testing/External Quality Assessment; Approved Guideline—Second Edition

Volume 33 Number 5

Lisa Kalman, PhD
Roberta M. Madej, CLS, MS, MBA
Elisabeth Dequeker, Prof Dr, PhD
Marie C. Earley, PhD
Vivianne Gomo, MPH, BSc
Cynthia L. Jackson, PhD

Lawrence J. Jennings, MD, PhD
Mario Pazzagli, PhD
Ted E. Schutzbank, PhD, D(ABM-M)
Heather Stang, MS
Paul Wallace, PhD
Amanda E. Weiss, MT, S, (SCP)

Abstract

As medical laboratory tests involving detection of nucleic acids become more common, well-designed and executed proficiency schemes are needed to assure quality and to further the development of this complex and rapidly growing area of laboratory medicine. MM14-A2—*Design of Molecular Proficiency Testing/External Quality Assessment; Approved Guideline—Second Edition* has been developed to guide the individuals and organizations responsible for providing proficiency testing (PT). It will also serve medical laboratories with a benchmark for evaluation of new programs or to facilitate development of laboratory-based PT or alternative assessment schemes when appropriate schemes are not available from formal programs. Specific sections discuss the design of PT programs; sources of materials; production, manufacture, and QA of samples; sample distribution; receipt and evaluation of data; and reporting responsibilities. Also discussed are examples of method-based PT programs and alternative assessment strategies and how they can be used to evaluate laboratory test performance. This document also lists and describes relevant regulatory and guidance documents related to PT.

Clinical and Laboratory Standards Institute (CLSI). *Design of Molecular Proficiency Testing/External Quality Assessment; Approved Guideline—Second Edition*. CLSI document MM14-A2 (ISBN 1-56238-873-8 [Print]; ISBN 1-56238-874-6 [Electronic]). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2013.

The Clinical and Laboratory Standards Institute consensus process, which is the mechanism for moving a document through two or more levels of review by the health care community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of CLSI documents. Current editions are listed in the CLSI catalog and posted on our website at www.clsi.org. If your organization is not a member and would like to become one, and to request a copy of the catalog, contact us at: Telephone: 610.688.0100; Fax: 610.688.0700; E-Mail: customer-service@cls.org; Website: www.clsi.org.



CLINICAL AND
LABORATORY
STANDARDS
INSTITUTE®



Copyright ©2013 Clinical and Laboratory Standards Institute. Except as stated below, any reproduction of content from a CLSI copyrighted standard, guideline, companion product, or other material requires express written consent from CLSI. All rights reserved. Interested parties may send permission requests to permissions@clsi.org.

CLSI hereby grants permission to each individual member or purchaser to make a single reproduction of this publication for use in its laboratory procedure manual at a single site. To request permission to use this publication in any other manner, e-mail permissions@clsi.org.

Suggested Citation

CLSI. *Design of Molecular Proficiency Testing/External Quality Assessment. Approved Guideline—Second Edition*. CLSI document MM14-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.

Previous Editions:

September 2004, August 2005

Reaffirmed:

September 2018

ISBN 1-56238-873-8 (Print)
ISBN 1-56238-874-6 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2914 (Electronic)

Committee Membership

Consensus Committee on Molecular Methods

Frederick S. Nolte, PhD,
D(ABMM), F(AAM)
Chairholder
Medical University Hospital
Authority
Charleston, South Carolina, USA

Barbara Zehnbaauer, PhD,
FACMG
Vice-Chairholder
Centers for Disease Control and
Prevention
Atlanta, Georgia, USA

Helen Fernandes, PhD
UMDNJ – University Hospital
Newark, New Jersey, USA

Tina M. Hambuch, PhD
Illumina, Inc.
San Diego, California, USA

Charles E. Hill, MD, PhD
Emory University Hospital
Atlanta, Georgia, USA

Penny Keller, BS, MP(ASCP)
Centers for Medicare & Medicaid
Services
Baltimore, Maryland, USA

Thomas J. Lenk, PhD
Celera Diagnostics
Alameda, California, USA

Yi-Wei Tang, MD, PhD,
D(ABMM)
Memorial Sloan Kettering Cancer
Center
New York, New York, USA

Zivana Tezak-Fragale, PhD
FDA Center for Devices and
Radiological Health
Silver Spring, Maryland, USA

Emily S. Winn-Feen, PhD
Rx Dx Advisors, Inc.
San Diego, California, USA

Document Development Committee on Proficiency Testing for Molecular Methods

Lisa Kalman, PhD
Chairholder
Centers for Disease Control and
Prevention
Atlanta, Georgia, USA

Roberta M. Madej, CLS, MS,
MBA
Vice-Chairholder
Cepheid
Sunnyvale, California, USA

Philip D. Cotter, PhD, FACMG
Pacific Diagnostics Clinical
Laboratory
Irvine, California, USA

Elisabeth Dequeker, Prof Dr, PhD
University of Leuven
Leuven, Belgium

Vivianne Gomo, MCH, BSc
ImmunoGen Labs Pvt Ltd
Ruwenzori, Rwanda

Cynthia L. Jackson, PhD
Providence Hospital/Lifespan
Academic Medical Center
Providence, Rhode Island, USA

Lawrence J. Jennings, M. Phil
College of American Pathologists
Northfield, Illinois, USA

Penny Keller, BS, MP(ASCP)
Centers for Medicare & Medicaid
Services
Baltimore, Maryland, USA

Marco Paolaggi, PhD
University of Florence
Florence, Italy

Ted E. Schutzbank, PhD,
D(ABMM)
Covance Central Laboratory
Services
Indianapolis, Indianapolis, USA

Paul Wallace, PhD
QCMD
Glasgow, Scotland, United
Kingdom

Amanda E. Weiss, MLS(ASCP)
Wisconsin State Laboratory of
Hygiene
Madison, Wisconsin, USA

Staff

Clinical and Laboratory Standards
Institute
Wayne, Pennsylvania, USA

Luann Ochs, MS
Senior Vice President – Operations

Tracy A. Dooley, MLT(ASCP)
Staff Liaison

Marcy Hackenbrack, MCM,
M(ASCP)
Project Manager

Megan L. Tertel, MA
Editor

Ryan J. Torres
Assistant Editor

Acknowledgment

This guideline was prepared by CLSI, as part of a cooperative effort with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) to work toward the advancement and dissemination of laboratory standards on a worldwide basis. CLSI gratefully acknowledges the participation of IFCC in this project. The IFCC expert for this project is Mario Pazzagli, PhD.

Acknowledgment

CLSI and the Consensus Committee on Molecular Methods gratefully acknowledge the following individuals for their help in preparing the second edition of this document:

Marie C. Earley, PhD
Centers for Disease Control and Prevention
Atlanta, Georgia, USA

Heather Stang, MS
Centers for Disease Control and Prevention
Atlanta, Georgia, USA

Contents

Abstract.....	i
Committee Membership.....	iii
Foreword.....	vii
1 Scope.....	1
2 Introduction.....	1
3 Standard Precautions.....	2
4 Terminology.....	2
4.1 A Note on Terminology.....	2
4.2 Definitions.....	3
4.3 Abbreviations and Acronyms.....	6
5 Survey of Regulatory and Guidance Documents Regarding Proficiency Testing.....	7
6 Design.....	7
6.1 Regulatory Considerations.....	9
6.2 Sample Composition.....	9
6.3 Number and Variety of Test Samples.....	10
6.4 Interpretation.....	12
6.5 Process Checklist.....	13
6.6 Handling Complaints and Inquiries.....	13
7 Material Sourcing/Collection.....	14
7.1 Laws and Guidelines Governing Human Specimen Acquisition.....	14
7.2 Confidentiality and Privacy.....	14
7.3 Sample Sourcing.....	15
8 Production/Manufacture.....	16
8.1 Sample Preservation.....	16
8.2 Production.....	18
8.3 Characterization.....	18
8.4 Proficiency Testing Material Stability.....	19
8.5 Sample Retention.....	19
9 Transportation of Samples for Proficiency Testing Programs.....	19
9.1 Specimen Types.....	20
9.2 Packaging and Transport.....	21
9.3 Sample Rejection Criteria.....	22
10 Documentation to Exchange Information.....	23
10.1 Documentation Requirements.....	23
10.2 General Information About the Proficiency Testing/External Quality Assessment Scheme.....	23
10.3 Registration and Confirmation.....	23
10.4 Preparation and Transport of Samples.....	24

Contents (Continued)

10.5	Result Form.....	25
10.6	Reporting of Results to Participants	27
11	Provider Results Review and Evaluation.....	29
11.1	Issues to Be Considered.....	29
11.2	Defining the “Correct” Result.....	30
12	Complementary and Supplementary Approaches to Proficiency Testing/External Quality Assessment Programs	32
12.1	Laboratories Acting as Proficiency Testing Providers	33
12.2	Alternative Proficiency Testing/External Quality Assessment Strategies	32
	References.....	37
	Appendix A. Globally Influential Documents Addressing Proficiency Testing: Relevance to and Impact on Stakeholders.....	42
	Appendix B. Process Checklist Example.....	48
	Appendix C. Useful Websites for Information on Shipping Proficiency Testing/External Quality Assessment Samples	49
	Appendix D. Example Registration Form for Proficiency Testing/External Quality Assessment Challenge/Scheme.....	50
	Appendix E. Example Instructions Manual	52
	Appendix F. Example of Clinical Information Related to the Proficiency Testing/External Quality Assessment Sample.....	54
	Appendix G. Example Sections From a Proficiency Testing/External Quality Assessment Result Reporting Form.....	55
	Appendix H. Example Confidentiality Form.....	58
	Appendix I. Example Data From a Participant Summary Report.....	59
	The Quality Management System Approach	66
	Related CLSI Reference Materials	67

Foreword

This document replaces the first edition of the approved guideline, which was published in 2005. Several changes and additions were made in this edition; chief among them is the revision of the sections describing relevant regulatory and guidance documents and the addition of sections describing examples of method-based proficiency testing (PT) programs and alternative assessment strategies. This edition also recognizes and emphasizes the roles and responsibilities of the medical laboratory in providing PT through informal sample exchange programs.

Medicine is science, experience, and art. While physicians, nurses, and other practitioners provide diagnosis, treatment, counseling, and patient management, their decisions and actions are based on scientific data, as well as their knowledge, experience, and approach. Medical (clinical) laboratories provide a major source of information about the patient to the practitioners; therefore, the accuracy of the data and their interpretation is critical. This fact is intuitive among laboratory professionals. Medical laboratory directors organized blinded-sample testing and sample exchange studies long before the establishment of formal programs or laws and standards prescribing participation. Today, PT/external quality assessment (EQA) is an integral part of laboratory QA and, as such, the organizations that administer these programs carry a great responsibility. Programs should be designed to identify laboratory errors and recognize tests offered by medical laboratories that are not performing as expected. They also have an important role in educating laboratories about how their testing practices compare to those of other laboratories and ways in which they can improve the quality of their tests.

In this guideline, the basic principles and practices for PT/EQA organizations, as well as laboratories that provide PT/EQA through informal sample exchange programs, for molecular tests in the areas of human genetics, infectious disease, molecular oncology, and pharmacogenetics are outlined. In addition, practices such as method-based PT/EQA programs that can increase the scope of laboratory PT and provide valuable educational experiences are described. A section specifically addressing the medical laboratory as a provider of PT and PT materials for internal or external use is also included.

Key Words

Alternative assessment, EQA, external quality assessment, laboratory testing, manufacturers, molecular testing, proficiency testing, proficiency testing material, PT, PT materials, sample exchange

Currently in preview, click buy full version

Design of Molecular Proficiency Testing/External Quality Assessment; Approved Guideline—Second Edition

1 Scope

The purpose of this guideline is to complement currently available regulatory and guidance documents regarding the management and operations of proficiency testing/external quality assessment (PT/EQA) programs. Presently, these documents guide the administration of such programs, but consideration of panel selection, analysis of data for evolving technologies and tests with many possible measurands, method-based PT/EQA, and reporting to participants are not addressed. For molecular methods, these issues are important for all stakeholders, including regulatory agencies, accrediting agencies, PT/EQA providers/organizations, PT/EQA materials manufacturers, medical (clinical) laboratories, and test/reagent manufacturers. This document addresses both large formal PT/EQA programs as well as medical laboratorians who produce, distribute, and administer PT/EQA schemes, and should provide guidance for the development and implementation of new PT/EQA programs for nucleic acid testing or modifying existing schemes.

This guideline does not address the process of testing and reporting PT/EQA in the medical laboratory, medical laboratory inspection, accreditation, or other regulatory processes.

This guideline focuses on nucleic acid (DNA and RNA) PT in the areas of human genetics, infectious disease, molecular oncology, and pharmacogenetics. Though written specifically to address needs in this area, the principles stated may be applicable to programs outside of nucleic acid testing.

Organizations and programs that send blinded samples to laboratories and analyze the submitted results carry several different names. These challenge programs may be called PT/EQA, quality assessment or assurance programs, QC programs, ring trials, sample exchange, and EQA/assurance. Countries or regions may place regulatory distinctions on these names. To facilitate the readability of this document, the terms PT/EQA, PT/EQA provider/organization, and PT/EQA program have been chosen to describe such activities, and regulatory categorization is not implied unless specifically noted.

2 Introduction

PT/EQA is a critical and integral part of the medical laboratory QMS and is required by some accreditation bodies and regulations. All participants of a PT/EQA program receive identical or comparable samples to test for a particular measurand or set of measurands. These results are returned to the PT/EQA provider who analyzes and summarizes the data and provides feedback to the participants. Participation in PT/EQA allows laboratories to compare their analytical performance to that of other laboratories using similar or different methods. Participation in PT/EQA allows laboratories to identify analytical and interpretive errors, and may indicate internal problems with QC, calibration, assay design, or test interpretation. The ability to compare results obtained in different laboratories is especially important for molecular tests because the vast majority of them are developed by the laboratory offering the test (laboratory-developed test). The comparison afforded by participation in PT/EQA provides the laboratories and the accreditation bodies an assurance that the test, as developed by that laboratory, performs comparably to other available tests.

QA for molecular diagnostics is further complicated by the lack of established PT/EQA programs for most molecular genetic tests. This is due in part to the large number of tests available, the small number of laboratories that offer each test, the evolving technologies, and the complexity of the tests. In addition, it is often difficult to obtain suitable PT/EQA samples that represent the full range of measurands detected by the tests. This combination makes it economically and logistically difficult to offer formal PT/EQA