CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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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 measurands; 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.

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

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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.

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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

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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