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# Establishing Molecular Testing in Clinical Laboratory Environments; Proposed Guideline

*PLEASE*

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This proposed document is published for wide and thorough review in the Clinical and Laboratory Standards Institute (CLSI) consensus-review process. The document will undergo concurrent consensus review, Board review, and delegate voting (ie, candidate for advancement) for 60 days.

Please send your comments on scope, approach, and technical and editorial content to CLSI.

Comment period ends

1 August 2011

The subcommittee responsible for this document will assess all comments received by the end of the comment period. Based on this assessment, a new version of the document will be issued. Readers are encouraged to send their comments to Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898 USA; Fax: +610.688.0700, or to the following e-mail address: standard@clsi.org.

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*COMMENT*

This guideline provides comprehensive guidance for planning and implementation of molecular diagnostic testing, including strategic planning, regulatory requirements, implementation, quality management, and special considerations for the subspecialties of molecular genetics, infectious diseases, oncology, and pharmacogenetics.

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

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*Advancing Quality in Health Care Testing*

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# Establishing Molecular Testing in Clinical Laboratory Environments; Proposed Guideline

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## Abstract

Clinical and Laboratory Standards Institute document MM19-P—*Establishing Molecular Testing in Clinical Laboratory Environments; Proposed Guideline* provides a framework for decision making and implementation of clinical molecular diagnostics, and is intended for those in established clinical laboratories that are implementing a molecular program for the first time. When implementing any diagnostic test for patient care, many elements should be addressed before the test is brought "online." This document focuses on the path of workflow, including laboratory safety and the quality management system, with emphasis on considerations for molecular diagnostics. An organized approach to strategic planning with SWOT (strengths, weaknesses, opportunities, and threats) is presented. Relevant regulatory requirements and the implementation plan are discussed in detail.

Importantly, separate sections are devoted to each of the following subspecialty areas: heritable diseases, oncology and malignant hematology, pharmacogenomics, and infectious diseases. Each of these sections addresses special considerations for molecular testing for each subspecialty.

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## Contents

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## Foreword

This guideline was written in response to the growing migration of common molecular diagnostic tests from solely esoteric laboratories to the more routine clinical environment. Molecular assays are becoming more attractive to routine clinical laboratories based on the availability of *in vitro* diagnostic devices and the relative ease of their implementation. Incorporating molecular testing into the routine menu decreases the need for sendouts, thus improving turnaround time and the financial health of the laboratory.

## Key Words

Molecular diagnostics, molecular genetics, molecular hematopathology, molecular infectious disease, molecular regulatory requirements, strategic planning, unidirectional workflow

# Establishing Molecular Testing in Clinical Laboratory Environments; Proposed Guideline

## 1 Scope

This document was written by experienced molecular laboratory professionals to provide an introduction to molecular diagnostics for nonmolecular, routine clinical laboratories, as well as a framework for decision making and implementation of molecular testing. The target audience of this guideline is the stakeholders who play a role in the strategic decision to implement a molecular diagnostic program, including the:

- Medical and technical directors who may not have previous experience with molecular testing
- Supervisory technical staff who implement molecular assays for the first time
- Quality systems group who will adapt the quality plan to incorporate the unique aspects of the new program
- Production staff that will perform and maintain all aspects of the assays

Because molecular diagnostics encompasses a very broad area, this document focuses on clinical applications and technologies most likely to be used in a laboratory that is venturing into molecular testing for the first time. The laboratory may have a concentration in a specific subspecialty (eg, microbiology) or not. However, given that this document is written for nonmolecular experts, several more complex areas of molecular testing were excluded from the scope, including:

- Complex technologies, including, but not limited to, laboratory-developed tests (LDTs) that require primer and/or probe design, proteomics, pulsed-field gel electrophoresis, multiple locus sequence testing, and repetitive extragenic palindromic sequence-based polymerase chain reaction (PCR)
- Complex reflex testing algorithms
- Laboratory tests that require a high degree of clinical expertise to interpret, such as donor-recipient compatibility typing, and molecular typing of strains possibly related in an outbreak
- Tests for sexual abuse and forensics
- Tests of the blood and tissue supply (eg, blood banks)

It is also out of the scope of this guideline to consider assays that should remain in specialized or esoteric testing facilities, such as:

- Methods for detecting pathogens such as bioterrorism agents that require biosafety levels (BSL) 3 or greater, which are otherwise handled in specialized facilities
- Prenatal diagnosis and preimplantation genetic diagnosis (PGD) of heritable disease

## 2 Introduction

Nucleic acid testing for infectious diseases, human genetics, and molecular oncology is the fastest growing field in laboratory medicine. In the past few years, the complete sequencing of the human genome and ever-increasing numbers of viral and bacterial genomes have been reported, leading to a rapid expansion of assays available to clinical laboratories. The ability to detect small deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) sequence variations has provided tools that improve the ability not only to diagnose, but also identify those at risk for disease.

Until recently, the vast majority of molecular testing has been offered by esoteric laboratories that have great depth of resources in both the technical and clinical aspects of molecular biology. However,