



CLINICAL AND  
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STANDARDS  
INSTITUTE

2nd Edition

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# CLSI MM22™

## Microarrays for Diagnosis and Monitoring of Infectious Diseases

This guideline provides recommendations for the laboratory development and use of qualitative nucleic acid microarray methods for the diagnosis and monitoring of infectious diseases. It also presents recommendations for validation and verification, quality control, and interpretation of results.

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

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# Microarrays for Diagnosis and Monitoring of Infectious Diseases

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## Abstract

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Clinical and Laboratory Standards Institute guideline MM22—*Microarrays for Diagnosis and Monitoring of Infectious Diseases* discusses the wide variety of nucleic acid microarray technologies that a growing number of medical laboratories have adopted for diagnostic testing. The different types of microarrays and their uses in various types of laboratories have grown tremendously. MM22 specifically discusses infectious diseases detection, identification, and genotyping, as well as drug resistance determinants. This guideline describes types of microarray platforms and general considerations in microarray development. It also provides recommendations for validation and verification of microarray performance and QC and QA considerations and discusses parameters for data analysis and interpretation.

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## Foreword

Today, a growing number of medical laboratories have adopted a wide variety of microarray platforms for clinical testing, and as a result, the types and associated purposes of such arrays have grown tremendously. Because the scope of this subject is too large to be covered in a single CLSI document, MM22 was developed to focus on the use of nucleic acid microarrays in medical microbiology and immunology laboratories (eg, pathogen profiling) and specifically discusses detection, identification, and genotyping of pathogens, as well as antimicrobial drug resistance determinants.

### Overview of Changes

This guideline replaces MM22-A, published in 2014. Several changes were made in this edition, including:

- Updating platform overview to include newer technologies now in use for microarray tests
- Adding a new subchapter to describe an individualized quality control plan, which permits the laboratory to customize its QC plan
- Reorganizing content to correspond to the path of workflow
- Adding a process flow chart

**NOTE:** The content of this guideline is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

#### KEY WORDS

clinical diagnostics

microarray analysis

pathogen detection

infectious diseases

nucleic acid testing



# Chapter ①

## Introduction

# Microarrays for Diagnosis and Monitoring of Infectious Diseases

## 1 Introduction

### 1.1 Scope

This guideline specifies the requirements and/or recommendations for the use of microarrays for diagnosis and monitoring of microbial infections. It covers infectious diseases pathogen detection and identification, genotyping (strain characterization), and virulence and resistance genetic markers. The intended users of this guideline are clinical and molecular microbiology laboratories, including bacteriology, mycobacteriology, mycology, parasitology, and virology. This guideline may also serve as a reference for government agencies and industry.

MM22 is not intended to provide manufacturing guidelines. Protein microarrays and microarray applications for unknown pathogen discovery, host gene expression profiling, or host genomic polymorphism determination related to microbial infections are not included. Sequencing as a detection and identification method is not covered by this guideline (see CLSI documents MM09<sup>1</sup> and MM18<sup>2</sup>).

### 1.2 Background

Molecular detection techniques have been used increasingly by medical microbiology and immunology laboratories. *In vitro* nucleic acid amplification techniques (eg, PCR) have transformed microbial pathogen detection. The continued advancement of molecular infectious diseases diagnostics depends on multiplexing technologies to easily and reliably detect multiple pathogens in a single clinical specimen. Microarray analysis can be used for multiplex detection, characterization, and monitoring of infectious diseases. A microarray is a collection of microscopic features (most commonly DNA) that can be probed with target molecules to produce either quantitative (gene expression) or qualitative (detection and identification) data. Advancements in fabrication, robotics, and bioinformatics have improved the efficiency, reproducibility, sensitivity, and specificity of microarray technology. Microarray platforms have expanded to include three-dimensional or suspension arrays. These improvements have transitioned microarrays from strictly research to clinical diagnostic applications, which has led to the optimization of the diagnostic potential of microarrays and to the development of commercially available qualitative and semiquantitative detection platforms. A series of microarray-based diagnostic devices are commercially available, and some have received regulatory agency clearance.

MM22 discusses the variety of nucleic acid microarray technologies that can be used for diagnostic testing. This guideline specifically discusses the clinical application of microarrays, including infectious diseases detection, identification, and genotyping, as well as detection of drug resistance determinants. It also describes types of microarray platforms and general considerations in microarray development. MM22 provides recommendations for validation and verification of microarray performance and quality considerations and discusses parameters for data analysis and interpretation. This guideline also reviews the specifications for laboratories to establish an individualized quality control plan (IQCP).<sup>3</sup>