



M52

Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems

This guideline includes recommendations for verification of commercial US Food and Drug Administration–cleared microbial identification and antimicrobial susceptibility testing systems by clinical laboratory professionals to fulfill regulatory or quality assurance requirements for the use of these systems for diagnostic testing.

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

Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems

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Abstract

Clinical and Laboratory Standards Institute document M52—*Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems* provides recommendations for verification of commercial US Food and Drug Administration–cleared antimicrobial susceptibility testing (AST) and microbial identification (ID) systems by clinical laboratory professionals to fulfill regulatory or QA requirements for the use of these systems for diagnostic testing. This guideline focuses on instrument-based systems commonly used in clinical laboratories and may also be applicable to manual methods for ID and AST.

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Foreword

M52 provides recommendations that laboratories may consider while designing their own verification activities. Each laboratory needs to determine what activities are needed to provide accurate results and meet local regulatory requirements. The number of isolates suggested for verification represent the minimum number recommended for testing. Testing additional isolates, especially isolates with unusual identifications and resistance patterns, should be considered. Because antimicrobial resistance continues to evolve, laboratories need to continually review and evaluate patient results as part of their QA activities.

This guideline is based on US regulations and may also serve as a useful resource for a wider audience. The unique tagline on the cover and the imprint of the US flag on the Abstract page and throughout the document footers call attention to M52's national focus and differentiate it from CLSI's global consensus documents. M52 is expected to be used extensively in the United States and globally to guide users on verification of microbial identification and antimicrobial susceptibility testing systems.

In order to clarify and emphasize the difference between a standard and a guideline, the CLSI definitions for standard and guideline documents are provided.

standard – a CLSI document developed through the consensus process, clearly identifying specific, essential requirements for materials, methods, or practices for voluntary use in an unmodified form. A CLSI standard may, in addition, contain discretionary elements. These discretionary elements are clearly identified.

guideline – a CLSI document developed through the consensus process describing criteria for a general operating practice, method, or material for voluntary use. A guideline can be used as written or modified by the user to fit specific needs. Mandates (ie, “must” or “shall”) are occasionally allowed in guidelines, in cases in which the document development committee feels strongly that a particular action is either required or prohibited, or when a guideline addresses provisions based on regulations.

NOTE 1: Mandates are occasionally allowed in CLSI guidelines, in cases in which the document development committee feels strongly that a particular action is either required or prohibited, or when a guideline addresses provisions based on regulations. Throughout M52, the use of the term “must” was evaluated by the document development committee and deemed appropriate because the uses are either 1) based on a requirement or 2) indicative of a necessary step to ensure patient safety or proper fulfillment of a procedure.

NOTE 2: The findings and conclusions in this document are those of the authors and do not necessarily represent the views of the organizations they represent.

Key Words

Antimicrobial susceptibility testing, antimicrobial susceptibility testing system, microbial identification testing, microbial identification testing system, verification

Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems

Chapter 1: Introduction

This chapter includes:

- Document scope and applicable exclusions
- Background information
- Standard precautions information
- “Note on Terminology” that highlights particular use and/or variation in use of terms and/or definitions
- Terms and definitions used in the document
- Abbreviations and acronyms used in the document

1.1 Scope

This guideline provides recommendations for clinical laboratory professionals for verification of commercial microbial identification systems (MIS) and US Food and Drug Administration (FDA)–cleared antimicrobial susceptibility testing systems (ASTS) to fulfill regulatory or QA requirements for use in diagnostic testing. Recommendations for postverification QA are also included. This guideline focuses on instrument-based systems commonly used in clinical laboratories, but the recommendations may also be applicable to manual methods for microbial identification (ID) and antimicrobial susceptibility testing (AST), including disk diffusion and gradient diffusion strips.

This guideline is not intended to provide guidance to manufacturers of *in vitro* diagnostic devices. A manufacturer must perform many studies during the research and development phases and the manufacturing validation phase that are unique to the design of the test system and the manufacturing processes. These studies go beyond the scope of this document. See Appendix A for a description of the FDA requirements for MIS and ASTS clearance.

This document does not address verification of chromogenic media, laboratory-developed methods, or systems using nucleic acid detection methods.

Appendix B addresses studies that may be used to implement alternative interpretive criteria (breakpoints) for ASTS.

1.2 Background

1.2.1 Verification

In this guideline, the term “verification” is used to describe the processes and studies performed when a system is first introduced into a laboratory or when that system is updated by the introduction of new identification substrates, antimicrobial agents, updated databases, software, or hardware.

The purpose of performing a verification study is to:

- Verify the system is performing within manufacturer’s specifications.
- Verify the ability of the laboratory staff to produce accurate and reproducible results.
- Fulfill regulatory requirements.

1.2.2 Postverification Quality Assurance

QA activities are used to describe the on-going processes and procedures performed to ensure that a verified system continues to perform at an acceptable level.

The purpose of QA is to:

- Ensure that the instrument continues to perform within the manufacturer’s specifications
- Ensure that the laboratory staff maintains the ability to produce accurate and reproducible results
- Fulfill regulatory requirements

1.3 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are treated as infectious and handled according to “standard precautions.” Standard precautions are guidelines that combine the major features of “universal precautions and body substance isolation” practices. Standard precautions cover the transmission of all known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of bloodborne pathogens. The Centers for Disease Control and Prevention address this topic in published guidelines that address the daily operations of diagnostic medicine in humans and animals while encouraging a culture of safety in the laboratory.¹ For specific precautions for preventing the laboratory transmission of all known infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all known infectious diseases, refer to CLSI document M29.²

1.4 Terminology

1.4.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly 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, International Organization for Standardization (ISO), and European Committee for Standardization (CEN) documents; and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. In light of this, CLSI’s consensus process focuses on harmonization of terms to facilitate the global application of standards and guidelines.

In order to align M52 with globally harmonized terminology, *validation* is the term used to describe the process that manufacturers follow to set test performance specifications. Validation is also used to describe the process laboratories need to follow to determine test performance specifications for laboratory-developed tests or when FDA-cleared tests are modified by the laboratory. *Verification* is the term used to describe the process users (eg, laboratories) need to follow to prove that an individual laboratory can meet the performance specifications set by the manufacturer under its own conditions when performed by the individual laboratory’s personnel before using the test/instrument for patient testing. Activities (eg, ongoing

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system (QMS) approach in the development of standards and guidelines, which facilitates project management; defines a document structure using a template; and provides a process to identify needed documents. The QMS approach applies a core set of “quality system essentials” (QSEs), basic to any organization, to all operations in any health care service’s path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager’s guide. The QSEs are as follows:

Organization	Personnel	Process Management	Nonconforming Event Management
Customer Focus	Purchasing and Inventory	Documents and Records	Assessments
Facilities and Safety	Equipment	Information Management	Continual Improvement

M52 addresses the QSE indicated by an “X.” For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
QMS01	QMS01	M29 QMS01	QMS01	QMS01 QMS05	QMS01	X AUTO8 EP23 GP27 GP29 LIS02 M02 M07 M50 MM18 QMS01	M07 QMS01	LIS02 QMS01	QMS01	GP27 GP29 QMS01	GP27 QMS01

Path of Workflow

A path of workflow is the description of the necessary processes to deliver the particular product or service that the organization or entity provides. A laboratory path of workflow consists of the sequential processes: preexamination, examination, and postexamination and their respective sequential subprocesses. All laboratories follow these processes to deliver the laboratory’s services, namely quality laboratory information.

M52 does not address any of the clinical laboratory path of workflow steps. For a description of the documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Preexamination				Examination			Postexamination	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
	AUTO8			EP23 M02 M07	EP23 M02 M07 M50 M100	EP23 M02 M07 M50 M100	AUTO8 LIS02 M02 M07 M50 M100	

Related CLSI Reference Materials*

- AUTO8** **Managing and Validating Laboratory Information Systems. 1st ed., 2006.** This document provides guidance for developing a protocol for validation of the laboratory information system (LIS), as well as protocols for assessing the dependability of the LIS when storing, retrieving, and transmitting data.
- EP23™** **Laboratory Quality Control Based on Risk Management. 1st ed., 2011.** This document provides guidance based on risk management for laboratories to develop quality control plans tailored to the particular combination of measuring system, laboratory setting, and clinical application of the test.
- GP27** **Using Proficiency Testing to Improve the Clinical Laboratory. 2nd ed., 2007.** This guideline provides assistance to laboratories in using proficiency testing as a quality improvement tool.
- GP29** **Assessment of Laboratory Tests When Proficiency Testing Is Not Available. 2nd ed., 2008.** This document offers methods to assess test performance when proficiency testing (PT) is not available; these methods include examples with statistical analyses. This document is intended for use by laboratory managers and testing personnel in traditional clinical laboratories as well as in point-of-care and bedside testing environments.
- LIS02** **Specification for Transferring Information Between Clinical Instruments and Information Systems. 2nd ed., 2004.** This document covers the two-way digital transmission of remote requests and results between clinical laboratory instruments and information systems.
- M02** **Performance Standards for Antimicrobial Disk Susceptibility Tests. 12th ed., 2015.** This standard contains the current Clinical and Laboratory Standards Institute–recommended methods for disk susceptibility testing, criteria for quality control testing, and updated tables for interpretive zone diameters.
- M07** **Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 10th ed., 2015.** This standard addresses reference methods for the determination of minimal inhibitory concentrations of aerobic bacteria by broth macrodilution, broth microdilution, and agar dilution.
- M29** **Protection of Laboratory Workers From Occupationally Acquired Infections. 4th ed., 2014.** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.
- M50** **Quality Control for Commercial Microbial Identification Systems. 1st ed., 2008.** This document provides guidance for quality control of commercial systems for microbial identification from culture, including information that pertains to manufacturers, distributors, and laboratory users. The intent is to ensure optimal performance of a microbial identification system in an efficient (streamlined) manner.
- M100S** **Performance Standards for Antimicrobial Susceptibility Testing. 25th ed., 2015.** This document provides updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02-A12, M07-A10, and M11-A8.
- MM18** **Interpretive Criteria for Identification of Bacteria and Fungi by DNA Target Sequencing. 1st ed., 2008.** Sequencing DNA targets of cultured isolates provides a quantitative metric within which to perceive microbial diversity, and can serve as the basis to identify microorganisms. This document is an effort to catalyze the entry of molecular microbiology into clinical usage by establishing interpretive criteria for microorganism identification.
- QMS01** **Quality Management System: A Model for Laboratory Services. 4th ed., 2011.** This document provides a model for medical laboratories that will assist with implementation and maintenance of an effective quality management system.
- QMS05** **Quality Management System: Qualifying, Selecting, and Evaluating a Referral Laboratory. 2nd ed., 2012.** This guideline provides recommended criteria and easily implemented processes for qualifying, selecting, and evaluating a referral laboratory.

* CLSI documents are continually reviewed and revised through the CLSI consensus process; therefore, readers should refer to the most current editions.

SAMPLE



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