CLINICAL AND LABORATORY STANDARDS INSTITUTE®

27th Edition

M100

Performance Standards for Antimicrobial Susceptibility Testing

This document includes updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02-A12, M07-A10, and M11-A8.

An informational supplement 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.

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

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Performance Standards for Antimicrobial Susceptibility Testing

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Abstract

The data in the interpretive tables in this supplement are valid only if the methodologies in the following Clinical and Laboratory Standards Institute (CLSI)–approved standards are followed: M02-A12—*Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard—Twelfth Edition;* M07-A10—*Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Tenth Edition;* and M11-A8—*Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Eighth Edition.* The standards contain information about both disk (M02) and dilution (M07 and M11) test procedures for aerobic and anaerobic bacteria.

Clinicians depend heavily on information from the microbiology laboratory for treatment of their seriously ill patients. The clinical importance of antimicrobial susceptibility test results demands that these tests be performed under optimal conditions and that laboratories have the capability to provide results for the newest antimicrobial agents.

The tabular information presented here represents the most current information for drug selection, interpretation, and QC using the procedures standardized in the most current editions of M02, M07, and M11. Users should replace the tables published earlier with these new tables. (Changes in the tables since the previous edition appear in boldface type.)

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Instructions for Use of Tables

The following pages include:

1. Tables 1A and 1B—Suggested groupings of antimicrobial agents that should be considered for testing and reporting by microbiology laboratories. These guidelines are based on drugs **approved by the US Food and Drug Administration (FDA) for clinical use in the United States.** In other countries, placement of antimicrobial agents in Tables 1A and 1B should be based on available drugs approved for clinical use by relevant regulatory agencies.

2. For each organism group, an additional table (Tables 2A through 2I) contains:
   - Recommended testing conditions
   - Routine QC recommendations (See also Chapter 4 in M02-A12 and M07-A10.)
   - General comments for testing the organism group and specific comments for testing particular drug/organism combinations
   - Suggested agents that should be considered for routine testing and reporting by clinical microbiology laboratories, as specified in Tables 1A and 1B (test/report groups A, B, C, U)
   - Additional drugs that have an approved indication for the respective organism group, but would generally not warrant routine testing by a clinical microbiology laboratory in the United States (test/report group O for "other"; test/report group Inv. for "investigational" [not yet FDA approved])
   - Zone diameter and MIC **breakpoints**

3. Tables 1C and 2J-1 address specific recommendations for testing and reporting results on anaerobes and contain some of the information listed in 1 and 2 above.

4. Tables 3A to 3J describe tests to detect particular types of resistance in specific organisms or organism groups.

I. Selecting Antimicrobial Agents for Testing and Reporting

A. Selection of the most appropriate antimicrobial agents to test and to report is a decision best made by each laboratory in consultation with the infectious diseases practitioners and the pharmacy, as well as the pharmacy and therapeutics and infection control committees of the medical staff. The recommendations for each organism group include agents of proven efficacy that show acceptable *in vitro* test performance. Considerations in the assignment of agents to specific test/report groups include clinical efficacy, prevalence of resistance, minimizing emergence of resistance, cost, FDA clinical indications for use, and current consensus recommendations for first-choice and alternative drugs. Tests of selected agents may be useful for infection control purposes.

B. Drugs listed together in a single box are agents for which interpretive results (susceptible, intermediate, or resistant) and clinical efficacy are similar. Within each box, an "or" between agents indicates those agents for which cross-resistance and cross-susceptibility are nearly complete. Results from one agent connected by an "or" can be used to predict results for the other agent. For example, *Enterobacteriaceae* susceptible to cefotaxime can be considered susceptible to ceftriaxone. The results obtained from testing cefotaxime could be reported along with a comment that the isolate is also susceptible to ceftriaxone. For drugs connected with an "or," combined major and very major errors are fewer than 3%, and minor errors are fewer than 10%, based on a large population of bacteria tested (see CLSI document M23 for description of error types). In addition, to qualify for an "or," at least 100 strains with resistance to the agents in question must be tested, and a result of "resistant" must be obtained with all agents for at least 95% of the strains. "Or" is also used for comparable agents when tested against organisms for which "susceptible-only" **breakpoints** are provided (eg, cefotaxime or ceftriaxone with *H. influenzae*). When no "or" connects agents within a box, testing of one agent cannot be used to predict results for another, owing either to discrepancies or insufficient data.

C. Test/Report Groups

1. As listed in Tables 1A, 1B, and 1C, agents in **Group A** are considered appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism groups.

2. **Group B** includes antimicrobial agents that may warrant primary testing, but they may be reported only selectively, such as when the organism is resistant to agents of the same antimicrobial class, as in Group A. Other indications for reporting the result might include a selected specimen source (eg, a third-generation cephalosporin for enteric bacilli from CSF or trimethoprim-sulfamethoxazole for urinary tract isolates); a polymicrobial infection; infections involving multiple sites; cases of patient allergy, intolerance, or failure to respond to an antimicrobial agent in Group A; or for purposes of infection control.

3. **Group C** includes alternative or supplemental antimicrobial agents that may necessitate testing in those institutions that harbor endemic or epidemic strains resistant to several of the primary drugs (especially in the same class, eg, β-lactams); for treatment of patients allergic to primary drugs; for treatment of unusual organisms (eg, chloramphenicol for extraintestinal isolates of *Salmonella* spp.); or for reporting to infection control as an epidemiological aid.

4. **Group U ("urine")** includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating urinary tract infections (UTIs). These agents should not be routinely reported against pathogens recovered from other sites of infection. An exception to this rule is for *Enterobacteriaceae* in Table 1A, where cefazolin is listed as a surrogate agent for oral cephalosporins. Other antimicrobial agents with broader indications may be included in Group U for specific urinary pathogens (eg, *Enterococcus* and ciprofloxacin).

5. **Group O ("other")** includes antimicrobial agents that have a clinical indication for the organism group but are generally not candidates for routine testing and reporting in the United States.

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

M100 does not cover any of the QSEs. For a description of the 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
						EP23 M02 M07 M11 M23 M27S M39 M45 M52	M07				

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.

M100 covers the medical laboratory path of workflow steps 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.

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
				X EP23 M02 M07 M11 M27S	X EP23 M02 M07 M11 M27S M45	X EP23 M02 M07 M11 M27S M45	X M02 M07 M11 M27S M39 M45	M27S

Related CLSI Reference Materials*

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.

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.

M11 **Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria. 8th ed., 2012.** This standard provides reference methods for the determination of minimal inhibitory concentrations of anaerobic bacteria by agar dilution and broth microdilution.

M23 **Development of *In Vitro* Susceptibility Testing Criteria and Quality Control Parameters. 4th ed., 2016.** This guideline discusses the necessary and recommended data for the selection of appropriate interpretive criteria and quality control ranges for antimicrobial agents.

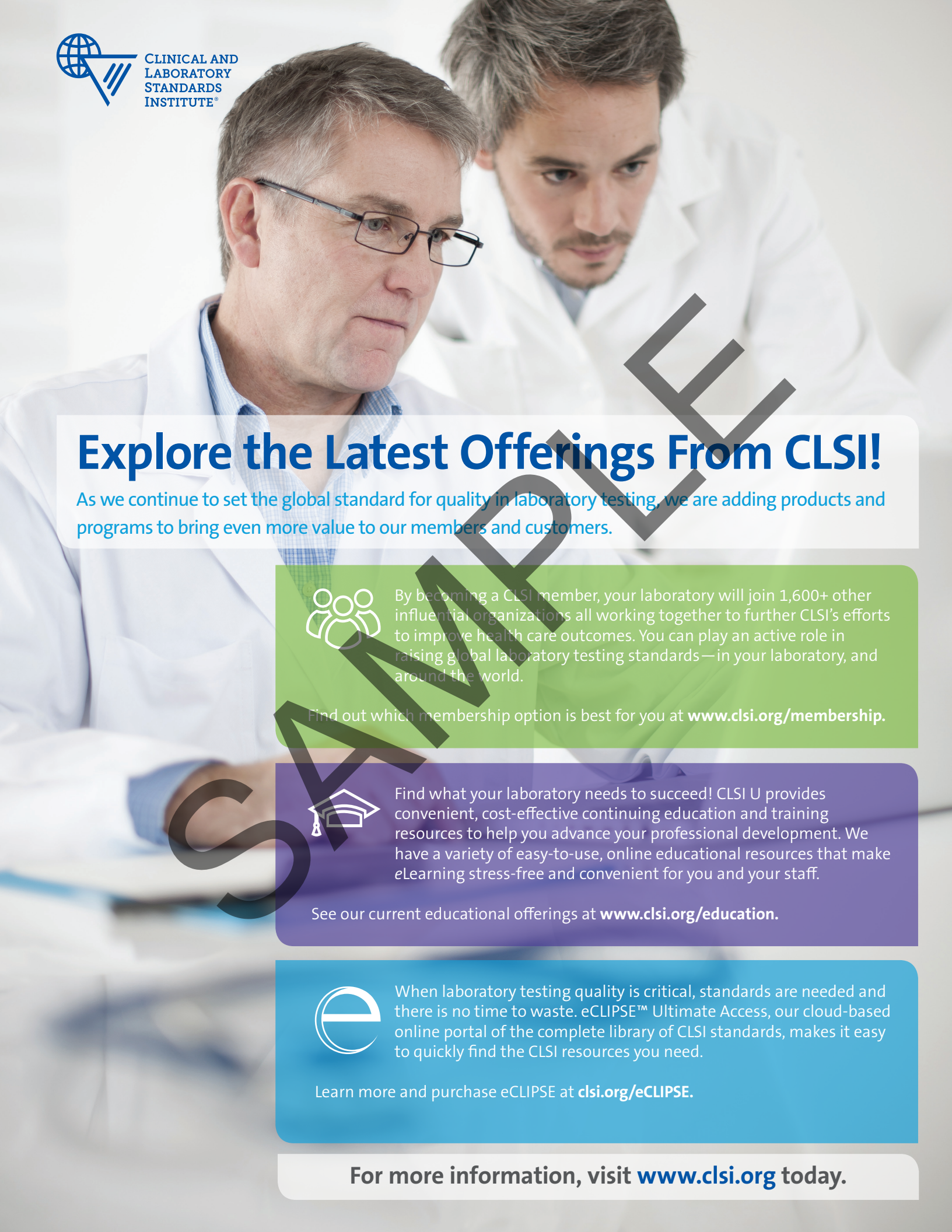
M27S **Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts. 4th ed., 2012.** This document provides updated tables for the CLSI antimicrobial susceptibility testing standard M27-A3.

M39 **Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data. 4th ed., 2014.** This document describes methods for recording and analysis of antimicrobial susceptibility test data, consisting of cumulative and ongoing summaries of susceptibility patterns of clinically significant microorganisms.

M45 **Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria. 3rd ed., 2015.** This guideline informs clinical, public health, and research laboratories on susceptibility testing of infrequently isolated or fastidious bacteria that are not included in CLSI documents M02, M07, or M100. Antimicrobial agent selection, test interpretation, and quality control are addressed.

M52 **Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems. 1st ed., 2015.** 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.

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



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