CLINICAL AND LABORATORY STANDARDS INSTITUTE®

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M39-A4

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition

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.

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

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Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition

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Abstract

Susceptibility statistical data, consisting of the cumulative and ongoing summary of the patterns of antimicrobial susceptibility of clinically important microorganisms, are important to the practice of medicine on several levels.

If the methods used to create, record, and analyze the data are not reliable and consistent, many of the most important applications and benefits of the data will not be realized. Clinical and Laboratory Standards Institute document M39-A4—*Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition* is an attempt 1) to develop guidelines for clinical laboratories and data analysis software providers for the routine generation and storage of susceptibility data, and for the compilation of susceptibility statistics; and 2) to provide suggestions to clinical laboratories and clinicians for effective use of their cumulative susceptibility statistics.

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Foreword

The antimicrobial susceptibility data generated from testing individual patients' microbial isolates are helpful if cumulative data from such tests are assembled and appropriately reported at regular intervals. For the cumulative reports to be useful and comparable with those of previous years or other institutions, data must be obtained and presented in a clear and consistent manner.

The primary aim of this document is to guide the preparation of cumulative antimicrobial susceptibility test data reports that will prove useful to clinicians in the selection of the most appropriate agents for initial empirical antimicrobial therapy. Other analyses of antimicrobial susceptibility test data may also be of significant value to clinicians, infection control personnel, epidemiologists, pharmacists, and others. These reports are often used to support antibiotic stewardship efforts. Several examples are included in M39.

Overview of Changes From M39-A3

Below is a summary of the changes in this document, which supersede the information presented in previous editions of M39. The list includes "major" changes. Other minor or editorial changes that have been made to the general formatting are not listed here.

General

M39 has been reorganized into two parts: Part I describes the routine cumulative antibiogram, and Part II describes what is referred to as the "enhanced antibiogram." Part II includes suggestions for analyzing and presenting cumulative antibiogram data to answer specific questions about susceptibility patterns in a particular facility. These reports may not be needed on a routine basis.

During this revision, the following sections were updated and relocated to Part II:

Section 6.8.2, Supplemental Analyses of Multidrug-Resistant Organisms (now Section 12)

Section 6.8.3, Additional Data Stratification (now Section 11, Stratifying Cumulative Antibiogram Data by Various Parameters)

Section 6.8.4, Examples of Selection Criteria for Supplemental Analyses (now Section 11.1)

Section 6.8.5, Examining Percent Susceptible for Combinations of Antimicrobial Agents (now Section 13)

Section 7.3.2, Specific Locations (now Section 11, Stratifying Cumulative Antibiogram Data by Various Parameters)

Section 7.3.3, Emerging Resistance Trends (now Section 16.1)

Part I

Section 1, Scope
Added notation that those involved with antibiotic stewardship programs often use cumulative antibiogram data.

Definitions
Added definitions for antimicrobial susceptibility test interpretive categories (susceptible, susceptible-dose dependent, intermediate, resistant, nonsusceptible); line listing of antimicrobial susceptibility test data; multidrug-resistant organism.

Section 6.5.2, Selective Reporting
Expanded section and described a method that could be used to estimate the percent susceptible (%S) for drugs routinely tested but reported selectively.

Section 6.6.1, Changes in Interpretive Breakpoints (previously Section 6.6)
Expanded recommendations for handling changes in interpretive breakpoints and included a table and graphic examples that highlight the changes.

Section 6.6.2, Issues Related to Determining the Interpretation of Minimal Inhibitory Concentration Values (previously Section 6.6.1)
Added an example.

Section 6.8.1, *S. pneumoniae*
Modified footnotes to *Streptococcus pneumoniae* example of reporting %S for drugs that have both meningitis and nonmeningitis breakpoints.

Section 6.8.3, Susceptible-Dose Dependent
Added information for reporting antimicrobial agents that have susceptible-dose dependent interpretive criteria.

Section 7.2.1, Organisms
For gram negatives:
Added *Klebsiella oxytoca*.

Suggested that it may be useful to separate gram-negative organisms into glucose-fermenting and nonglucose-fermenting bacilli in antibiogram tables.

For anaerobes:
Added *Bacteroides fragilis* group (other than *B. fragilis*).

Section 7.3.2, Change in Drug Panel During Analysis Period (eg, Antimicrobial Agent Is Removed or Added to Routine Testing Panel)
Added suggestions for analyzing data when drugs included on a specific panel change during analysis period.

Part II

Added, updated, expanded, and relocated information contained in the following sections of the previous edition of M39:

Section 6.8.3, Additional Data Stratification
Section 6.8.4, Examples of Selection Criteria for Supplemental Analyses
Section 6.8.5, Examining Percent Susceptible for Combinations of Antimicrobial Agents

Section 7.3.2, Specific Locations
Section 7.3.3, Emerging Resistance Trends

The following represent substantive additions to the original recommendations:

Section 12, Supplemental Analyses of Multidrug-Resistant Organisms
Added suggestions for highlighting multidrug-resistant organisms (MDROs) on a routine cumulative antibiogram report and added example (*Klebsiella pneumoniae*) of a supplemental report that might be generated for MDROs.

Section 13, Examining Percent Susceptible for Combinations of Antimicrobial Agents
Moved from Part I to Part II, and revised to reflect this change.

Section 14, Analysis of Susceptibility Profiles of Select Organisms
Added new section that describes preparation of a report that lists the numbers/percent of patients who harbored an isolate of a given species with a specific resistance profile.

Section 15, Calculating Percent Susceptible on Select Groups of Organisms
Added new section that describes preparation of a report that lists the %S for all isolates within an organism group.

Section 16, Graphic Presentation of Percent Susceptible Data to Illustrate Trends in Susceptibility
Added examples to include various presentation options.

Section 17, Local Cumulative Antibiograms vs External Antibiograms (eg, Data From External Surveillance Programs)
Added new section that discusses use of local vs surveillance data and when either might be advantageous.

Additional References
Updated references.

Appendix A. Suggestions for Confirmation of Resistant (R), Intermediate (I), or Nonsusceptible (NS) Antimicrobial Susceptibility Test Results and Organism Identification
Imported updated table from CLSI document M100.[1]

Appendix C. Example of Using a Line Listing to Verify Susceptibility Rates Determined by the Analysis Software
Updated example data.

Appendix D. Examples of Supplemental Analyses – Stratifying Cumulative Antibiogram Data by Various Parameters
Updated example data.

Appendix E1. Cumulative Antimicrobial Susceptibility Report Example – Antimicrobial Agents Listed Alphabetically (Hypothetical Data)
Incorporated suggestion to insert "R" in cells denoting intrinsic resistance for the drug/organism combination.

Appendix E2. Cumulative Antimicrobial Susceptibility Report Example – Antimicrobial Agents Listed by Class (Hypothetical Data)
Incorporated suggestion to insert "R" in cells denoting intrinsic resistance for the drug/organism combination.

Appendix F. Examples of Graphs to Illustrate Trends in Susceptibility
Added examples to include various presentation options.

Appendix G. Steps for Presenting Local Cumulative Antibiogram Report to Health Care Professionals
Updated primary recommendations for analysis and data to consider highlighting.

Appendix I. Glossaries of β-Lactams and Non–β-Lactams: Class and Subclass Designation and Generic Name, and Abbreviations/Routes of Administration/Drug Class for Antimicrobial Agents
Imported updated table from CLSI document M100.[1]

Appendix J. Intrinsic Resistance
Imported updated table from CLSI document M100.[1]

Key Words

Antibiogram, antimicrobial agent, cumulative antibiogram, epidemiology, resistance

Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition

1 Scope

The recommendations set forth in this document are intended to be used by individuals involved in the following:

- Analyzing and presenting antimicrobial susceptibility test data (eg, clinical microbiologists, pharmacists, physicians)
- Using cumulative antimicrobial susceptibility test data to make clinical decisions and/or participate in antibiotic stewardship programs (ASPs) (eg, clinical microbiologists, infectious disease specialists and other clinicians, infection control practitioners, pharmacists, epidemiologists, other health care personnel, and public health officials)
- Designing information systems for the storage and analysis of antimicrobial susceptibility test data (eg, LIS vendors, manufacturers of diagnostic products that include epidemiology analysis software, and manufacturers of epidemiology analysis or surveillance software)

The cumulative antimicrobial susceptibility report generated, according to recommendations presented in this guideline, may not reveal some trends in emerging resistance, and thus cannot substitute for the careful analysis of all susceptibility data derived from examining and/or analyzing all antimicrobial susceptibility test results for individual patient management. For reports intended for other purposes (eg, emergence of resistance during therapy, empirical therapy of subsequent infections), other inclusion criteria may be appropriate.

2 Introduction

This guideline presents specific recommendations for the collection, analysis, and presentation of cumulative antimicrobial susceptibility test data. Among the issues addressed are the way in which multiple isolates from the same patient should be handled, the species included or combined in a statistic, the frequency of data analysis, and the format for data presentation. This guideline also identifies additional data analysis and presentation options that may be useful to certain clinicians for specialized applications.

It is important to recognize that many of the specific recommendations presented here (eg, inclusion of only the first isolate of a given species from an individual patient during the analysis period) have been made with the primary aim of guiding clinicians in the selection of initial empirical antimicrobial therapy for infections.

The following recommendations have been made with the primary aim of preparing a report to guide clinicians in the selection of empirical antimicrobial therapy for initial infections:

- Analyze and present a cumulative antibiogram report at least annually.
- Include only final, verified test results.
- Include only species with testing data for ≥30 isolates (see Sections 6.4 and 7.2.2).
- Include only diagnostic (not surveillance) isolates (see Section 6.4).

- Eliminate duplicates by including only the first isolate of a species/patient/analysis period, irrespective of body site or antimicrobial susceptibility profile (see Section 6.4 and Appendix B).

- Include only antimicrobial agents routinely tested and calculate the percent susceptible (%S) from results reported, as well as those that might be suppressed on patient reports using selective reporting rules; do not report supplemental agents selectively tested on resistant isolates only (see Section 6.5.1).

- Report the %S and do not include the percent intermediate (%I) in the statistic (see Section 6.6).

- *Streptococcus pneumoniae* and cefotaxime/ceftriaxone/penicillin: list the %S using both meningitis and nonmeningitis breakpoints (see Section 6.8.1); for penicillin, also consider indicating the %S using oral breakpoints.

- Viridans group streptococci and penicillin: list both the %I and the %S (see Section 6.8.2).

- *Staphylococcus aureus:* list the %S for all isolates and the methicillin-resistant *S. aureus* (MRSA) subset (see Section 6.8.4).

In addition, some factors that can affect cumulative antibiogram data include:

- Patient population served
- Culturing practices
- Laboratory antimicrobial susceptibility testing and reporting policies
- Temporal outbreaks

See Section 9 for additional information.

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 blood-borne pathogens. The Centers for Disease Control and Prevention (CDC) address this topic in published guidelines that address the daily operations of diagnostic medicine in human and animal medicine while encouraging a culture of safety in the laboratory.[2] 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.[3]

4 Terminology

4.1 Definitions

antibiogram – for the purpose of this document, see **cumulative antimicrobial susceptibility test data summary.**

antimicrobial susceptibility test interpretive category – a classification based on an *in vitro* response of an organism to an antimicrobial agent at levels corresponding to blood or tissue levels attainable with usually prescribed doses of that agent.

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents. The quality management system 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

M39-A4 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 page 80.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
		M29				X M02 M07 M11 M23 M27 M27-S4 M38 M44 M45	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.

M39-A4 addresses the clinical laboratory path of workflow step 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	
				M02 M07 M11 M27 M27-S4 M38	M02 M07 M11 M27 M27-S4 M38 M44 M100	M02 M07 M11 M27 M27-S4 M38 M44 M100	M02 M07 M11 M27 M27-S4 M38 M44 M100	M27 M27-S4 M38

Related CLSI Reference Materials*

M02-A11 **Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard—Eleventh Edition (2012).** This document 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-A9 **Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Ninth Edition (2012).** This document addresses reference methods for the determination of minimal inhibitory concentrations of aerobic bacteria by broth macrodilution, broth microdilution, and agar dilution.

M11-A8 **Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Eighth Edition (2012).** This standard provides reference methods for the determination of minimal inhibitory concentrations of anaerobic bacteria by agar dilution and broth microdilution.

M23-A3 **Development of *In Vitro* Susceptibility Testing Criteria and Quality Control Parameters; Approved Guideline—Third Edition (2008).** This document addresses the required and recommended data needed for the selection of appropriate interpretive criteria and quality control ranges for antimicrobial agents.

M27-A3 **Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard—Third Edition (2008).** This document addresses the selection and preparation of antifungal agents; implementation and interpretation of test procedures; and quality control requirements for susceptibility testing of yeasts that cause invasive fungal infections.

M27-S4 **Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Fourth Informational Supplement (2012).** This document provides updated tables for the CLSI antimicrobial susceptibility testing standard M27-A3.

M29-A3 **Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Third Edition (2005).** 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.

M38-A2 **Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi; Approved Standard—Second Edition (2008).** This document addresses the selection of antifungal agents, preparation of antifungal stock solutions and dilutions for testing implementation and interpretation of test procedures, and quality control requirements for susceptibility testing of filamentous fungi (moulds) that cause invasive and cutaneous fungal infections.

M44-A2 **Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts; Approved Guideline—Second Edition (2009).** This document provides newly established methodology for disk diffusion testing of *Candida* spp., criteria for quality control testing, and interpretive criteria.

M45-A2 **Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria; Approved Guideline—Second Edition (2010).** This document provides guidance to clinical microbiology laboratories for standardized susceptibility testing of infrequently isolated or fastidious bacteria that are not presently included in CLSI documents M02 or M07. The tabular information in this document presents the most current information for drug selection, interpretation, and quality control for the infrequently isolated or fastidious bacterial pathogens included in this guideline.

M100-S24 **Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fourth Informational Supplement (2014).** This document provides updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02-A11, M07-A9, and M11-A8.

* 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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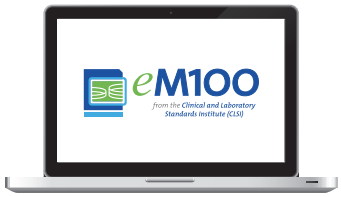

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