Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Third 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.
Clinical and Laboratory Standards Institute

Advancing Quality in Health Care Testing

Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) is an international, interdisciplinary, nonprofit, standards-developing, and educational organization that promotes the development and use of voluntary consensus standards and guidelines within the health care community. It is recognized worldwide for the application of its unique consensus process in the development of standards and guidelines for patient testing and related health care issues. Our process is based on the principle that consensus is an effective and cost-effective way to improve patient testing and health care services.

In addition to developing and promoting the use of voluntary consensus standards and guidelines, we provide an open and unbiased forum to address critical issues affecting the quality of patient testing and health care.

PUBLICATIONS

A document is published as a standard, guideline, or committee report.

Standard A document developed through the consensus process that clearly identifies specific, essential requirements for materials, methods, or practices for use in an unmodified form. A standard may, in addition, contain discretionary elements, which are clearly identified.

Guideline A document developed through the consensus process describing criteria for a general operating practice, procedure, or material for voluntary use. A guideline may be used as written or modified by the user to fit specific needs.

Report A document that has not been subjected to consensus review and is released by the Board of Directors.

CONSENSUS PROCESS

The CLSI voluntary consensus process is a protocol establishing formal criteria for:

- the authorization of a project
- the development and open review of documents
- the revision of documents in response to comments by users
- the acceptance of a document as a consensus standard or guideline.

Most documents are subject to two levels of consensus—“proposed” and “approved.” Depending on the need for field evaluation or data collection, documents may also be made available for review at an intermediate consensus level.

Proposed A consensus document undergoes the first stage of review by the health care community as a proposed standard or guideline. The document should receive a wide and thorough technical review, including an overall review of its scope, approach, and utility, and a line-by-line review of its technical and editorial content.

Approved An approved standard or guideline has achieved consensus within the health care community. It should be reviewed to assess the utility of the final document, to ensure attainment of consensus (i.e., that comments on earlier versions have been satisfactorily addressed), and to identify the need for additional consensus documents.

Our standards and guidelines represent a consensus opinion on good practices and reflect the substantial agreement by materially affected, competent, and interested parties obtained by following CLSI’s established consensus procedures. Provisions in CLSI standards and guidelines may be more or less stringent than applicable regulations. Consequently, conformance to this voluntary consensus document does not relieve the user of responsibility for compliance with applicable regulations.

COMMENTS

The comments of users are essential to the consensus process. Anyone may submit a comment, and all comments are addressed, according to the consensus process, by the committee that wrote the document. All comments, including those that result in a change to the document when published at the next consensus level and those that do not result in a change, are responded to by the committee in an appendix to the document. Readers are strongly encouraged to comment in any form and at any time on any document. Address comments to Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

VOLUNTEER PARTICIPATION

Health care professionals in all specialties are urged to volunteer for participation in CLSI projects. Please contact us at customerservice@clsi.org or +610.688.0100 for additional information on committee participation.
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-A3—Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Third Edition is an attempt: 1) to develop guidelines for clinical laboratories and their 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 for effective use of their cumulative susceptibility statistics.

Copyright ©2009 Clinical and Laboratory Standards Institute. Except as stated below, neither this publication nor any portion thereof may be adapted, copied, or otherwise reproduced, by any means (electronic, mechanical, photocopying, recording, or otherwise) without prior written permission from Clinical and Laboratory Standards Institute (“CLSI”).

CLSI hereby grants permission to each individual member or purchaser to make a single reproduction of this publication for use in its laboratory procedure manual at a single site. To request permission to use this publication in any other manner, contact the Executive Vice President, Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA.

**Suggested Citation**


**Proposed Guideline**

December 2000

**Approved Guideline**

May 2002

**Approved Guideline—Second Edition**

November 2005

**Approved Guideline—Third Edition**

February 2009

ISBN 1-56238-692-1

ISSN 0273-3099
Committee Membership

Area Committee on Microbiology

Mary Jane Ferraro, PhD, MPH
Chairholder
Massachusetts General Hospital
Boston, Massachusetts

John H. Rex, MD, FACP
Vice-Chairholder
AstraZeneca
Cheshire, United Kingdom

Barbara Ann Body, PhD, D(ABMM)
Laboratory Corporation of America
Burlington, North Carolina

Betty (Betz) A. Forbes, PhD, D(ABMM)
Medical College of Virginia Campus
Richmond, Virginia

Freddie Mae Poole
FDA Center for Devices and Radiological Health
Rockville, Maryland

Daniel F. Sahm, PhD
Eurofins Medinet
Herndon, Virginia

Fred C. Tenover, PhD, ABMM
Cepheid
Sunnyvale, California

John D. Turnidge, MD
Women’s and Children’s Hospital
North Adelaide, Australia

Advisors

Mary L. Wilson, MD
Denver Health Medical Center
Denver, Colorado

Nancy L. Anderson, MMSc, MT(ASCP)
Centers for Disease Control and Prevention
Atlanta, Georgia

Ellen Jo Baron, PhD
Stanford Hospital and Clinics
Palo Alto, California

Donald R. Callihan, PhD
BD Diagnostic Systems
Sparks, Maryland

Lynne S. Garcia, MS
LSG & Associates
Santa Monica, California

Richard L. Hodinka, PhD
Children’s Hospital of Philadelphia
Philadelphia, Pennsylvania

James H. Jorgensen, PhD
University of Texas Health Science Center
San Antonio, Texas

Subcommittee on Antimicrobial Susceptibility Testing

Matthew A. Wikler, MD, MBA, FIDSA
Chairholder
Pacific Beach BioSciences, Inc.
San Diego, California

Franklin R. Cockerill, III, MD
Vice-Chairholder
Mayo Clinic/Mayo Foundation
Rochester, Minnesota

Karen Bush, PhD
Johnson & Johnson Pharmaceutical Research and Development
Raritan, New Jersey

Michael N. Dudley, PharmD
Mpex Pharmaceuticals
San Diego, California

George M. Eliopoulos, MD
Beth Israel Deaconess Medical Center
Boston, Massachusetts

Dwight J. Hardy, PhD
University of Rochester Medical Center
Rochester, New York

David W. Hecht, MD
Loyola University Medical Center
Maywood, Illinois

Janet F. Hindler, MCLS, MT(ASCP)
UCLA Medical Center
Los Angeles, California

Jean B. Patel, PhD, D(ABMM)
Centers for Disease Control and Prevention
Atlanta, Georgia

Mair Powell, MD, FRCP, FRCPath
MHRA
London, United Kingdom

John D. Turnidge, MD
Women’s and Children’s Hospital
North Adelaide, Australia

Melvin P. Weinstein, MD
Robert Wood Johnson University Hospital
New Brunswick, New Jersey

Matthew A. Wikler, MD, MBA, FIDSA
Pacific Beach BioSciences, Inc.
San Diego, California

Gail L. Woods, MD
Central Arkansas Veterans Healthcare System
Little Rock, Arkansas
Members (Continued)
Barbara L. Zimmer, PhD
Siemens Healthcare Diagnostics
West Sacramento, California

Advisors
Paul G. Ambrose, PharmD, FIDSA
ICPD/Orway Research Institute
Albany, New York
Patricia A. Bradford, PhD
Wyeth Research
Pearl River, New York
Steven D. Brown, PhD
The Clinical Microbiology Institute
Wilsonville, Oregon
Karen Carroll, MD
Johns Hopkins Medical Institutions
Baltimore, Maryland
Edward M. Cox, Jr., MD, MPH
FDA Center for Drug Evaluation and Research
Rockville, Maryland
William A. Craig, MD
University of Wisconsin
Madison, Wisconsin
Cynthia L. Fowler, MD
bioMérieux, Inc.
Durham, North Carolina
Lawrence V. Friedrich, PharmD
Cubist Pharmaceuticals
Mt. Pleasant, South Carolina

Working Group on Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data

Janet F. Hindler, MCLS, MT(ASCP)
Chairholder
UCLA Medical Center
Los Angeles, California

Michael Barton, PharmD
TheraDoc
Salt Lake City, Utah

Donald R. Callihan, PhD
BD Diagnostic Systems
Sparks, Maryland

Sharon M. Erdman, PharmD
Purdue University
School of Pharmacy
Indianapolis, Indiana

Alan T. Evangelista, PhD
Ortho-McNeil Pharmaceutical
Raritan, New Jersey

Stephen G. Jenkins, PhD, D(ABMM), F(AAM)
Mount Sinai Medical Center
New York, New York

Judith Johnston, MS
Siemens Healthcare Diagnostics Inc.
West Sacramento, California

Ronald N. Master, MS, SM(AAM)
Quest Diagnostics Nichols Institute
Chantilly, Virginia

John E. McGowan, Jr., MD
Emory University, Rollins School of Public Health
Atlanta, Georgia

Graeme Nimmo, MBBS, MSc, MPH
Queensland Health Pathology and Scientific Services
Herston, Australia

Yoichi Hirakata, MD, PhD
Tohoku University Graduate School of Medicine
Sendai, Japan

Ronald N. Jones, MD
JMI Laboratories
North Liberty, Iowa

Gunnar Kahlmeter, MD, PhD
ESCIMD
Växjö, Sweden

Frederic J. Marsik, PhD, ABMM
FDA Center for Drug Evaluation and Research
Rockville, Maryland

Janice Pohlman, MD, MPH
FDA Center for Drug Evaluation & Research
Silver Spring, Maryland

Freddie Mae Poole
FDA Center for Devices and Radiological Health
Rockville, Maryland

Sandra S. Richter, MD, D(ABMM)
University of Iowa Carver College of Medicine
Iowa City, Iowa

Flavia Rossi, MD
University of Sao Paulo
Sao Paulo, Brazil

Dale A. Schwab, PhD, D(ABMM)
Quest Diagnostics, Nichols Institute
San Juan Capistrano, California

Daniel J. Sheehan, PhD
Greenwich, Connecticut

Jana M. Swenson, MMSc
Centers for Disease Control and Prevention
Atlanta, Georgia

George H. Talbot, MD
Talbot Advisors LLC
Wayne, Pennsylvania

Fred C. Tenover, PhD, ABMM
Cepheid
Sunnyvale, California

Richard B. Thomson, Jr., PhD
Northwestern University, Feinberg School of Medicine
Evanston, Illinois

John Stelling, MD, MPH
Brigham and Women’s Hospital
Boston, Massachusetts

Lois M. Schmidt, DA
Vice President, Standards Development and Marketing
Wayne, Pennsylvania

Melissa A. Lewis
Editor
## Contents

Abstract .................................................................................................................................................... i

Committee Membership........................................................................................................................ iii

Foreword .............................................................................................................................................. vii

1 Scope .......................................................................................................................................... 1

2 Introduction ................................................................................................................................ 1

3 Standard Precautions.................................................................................................................. 2

4 Terminology ............................................................................................................................... 2
  4.1 Definitions ................................................................................................................... . 2
  4.2 Abbreviations/Acronyms .............................................................................................. 4

5 Information System Design ....................................................................................................... 4
  5.1 Data Export or Transmission ........................................................................................ 4
  5.2 Desirable Attributes of the Data Analysis System ......................................................... 5
  5.3 Patient Demographic Information.................................................................................... 5
  5.4 Specimen Information ....................................................................................................... 6
  5.5 Organism Information ....................................................................................................... 6
  5.6 Antimicrobial Susceptibility Test Information ............................................................. 6

6 Data Analysis ............................................................................................................................. 7
  6.1 Data Verification ........................................................................................................... 7
  6.2 Facility .......................................................................................................................... 8
  6.3 Frequency ...................................................................................................................... 8
  6.4 Isolates .......................................................................................................................... 8
  6.5 Antimicrobial Agents ...................................................................................................... 9
  6.6 Calculations ..................................................................................................................... 9
  6.7 Validation of Calculations .......................................................................................... 11
  6.8 Supplemental Analyses and Selection Criteria ........................................................... 12

7 Data Presentation ..................................................................................................................... 16
  7.1 Items to Be Considered in Constructing the Table ..................................................... 16
  7.2 Items to Be Considered Within Specific Tables ......................................................... 17
  7.3 Other Presentation Options ......................................................................................... 19

8 Use of Cumulative Antimicrobial Susceptibility Reports ................................................. 20
  8.1 Use of the Report ........................................................................................................ 20
  8.2 Distribution of the Report ........................................................................................... 20

9 Limitations of Data, Data Analysis, and Data Presentation ..................................................... 21
  9.1 Culturing Practices ....................................................................................................... 21
  9.2 Influence of Small Numbers of Isolates ..................................................................... 21
  9.3 Comparing Results of Individual Antimicrobial Agent Results ................................ 22
  9.4 Identification of New Patterns of Resistance ............................................................ 22

10 Statistical Considerations......................................................................................................... 22
  10.1 Confidence Intervals ................................................................................................... 22
Contents (Continued)

10.2 Statistical Significance of Changes in Susceptibility Rates ........................................ 23
10.3 Use and Limitations of Statistical Methods ................................................................. 23

References ............................................................................................................................................. 25

Additional References ........................................................................................................................... 26

Appendix A. Suggestions for Verification of Antimicrobial Susceptibility Test Results and
Confirmation of Organism Identification ............................................................................................. 28

Appendix B. Rationale Behind the “First Isolate per Patient” Analysis Recommendation .......... 30

Appendix C. Example of Using a Line Listing to Verify Susceptibility Rates Determined by the
Analysis Software ................................................................................................................................. 33

Appendix D. Examples of Supplemental Analyses – Stratifying Cumulative Antibiogram Data by
Various Parameters ............................................................................................................................... 34

Appendix E1. Cumulative Antimicrobial Susceptibility Report Example – Antimicrobial Agents
Listed Alphabetically (Hypothetical Data) ........................................................................................... 36

Appendix E2. Cumulative Antimicrobial Susceptibility Report Example – Antimicrobial Agents
Listed by Class (Hypothetical Data) ..................................................................................................... 37

Appendix F. Example of Graph to Illustrate Trend in Susceptibility Over Five Years ............... 38

Appendix G. Steps for Presenting Local Cumulative Antibiogram Report to Health Care
Professionals ......................................................................................................................................... 39

Appendix H. Statistical Methods for Examining Percent Susceptible ............................................ 43

Appendix I. Glossary I (Part 1). β-lactams: Class and Subclass Designation and Generic Name....... 48
Glossary I (Part 2). Non-β-lactams: Class and Subclass Designation and Generic Name ............. 49

Glossary II. Abbreviations/Routes of Administration/Drug Class for Antimicrobial Agents .......... 50

Summary of Delegate Comments and Subcommittee Responses ......................................................... 53

The Quality Management System Approach ........................................................................................ 54

Related CLSI Reference Materials ........................................................................................................ 55
Foreword

The antimicrobial susceptibility data generated from testing individual patients’ microbial isolates can be 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, but lie outside the scope of this document.

Key Words

Antibiogram, antimicrobial agent, cumulative antibiogram, epidemiology, resistance

Updated Information in This Edition

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.

Introduction

Added concise list of criteria required for a cumulative antibiogram report to comply with M39-A3 recommendations (replaced bullets in the Scope section).

Added list of some factors that can impact cumulative antibiogram data—not bold.

Section 3, Standard Precautions

Added new safety recommendations.

Section 4.2, Abbreviations/Acronyms

Added a list of abbreviations and acronyms used in this document.

Section 5.1, Data Export or Transmission

Added description for handing susceptibility results from multiple panels tested on a single organism.

Section 5.5.2, Desirable (organism information)

Added isolate number.

Section 6.4, Isolates

Added guidance for including the first isolate per calendar year when analyzing data for several years combined (eg, 2000-2005).

Section 6.5.2, Selective Reporting

Expanded description of selective reporting.

Section 6.7, Validation of Calculations

Added suggestion to validate software used to perform calculations when changes are made to the minimal inhibitory concentration (MIC) or disk diffusion interpretive criteria.
Section 6.7.1, Validation Suggestions
Added suggestion to validate software used to perform calculations with a species that is likely to be isolated multiple times from a given patient.

Section 6.7.2, Validation of Completed Cumulative Antibiogram
Added suggestion to consider analyzing data from a longer time frame (eg, two years) if fewer than 30 isolates are tested for a given species per year.

Section 6.8.1, Suggested Supplemental Analyses
Modified recommendations for presenting %S data for penicillin and *Streptococcus pneumoniae* based on the new penicillin breakpoints published in CLSI document M100.

Section 6.8.2, Supplemental Analyses on Multidrug-Resistant Organisms (MDRO)
Added new section to describe optional mechanism of presenting data when the incidence of a specific MDRO is significant in a specific facility.

Section 6.8.3, Additional Data Stratification
Revised wording to better explain the concept of data stratification.

Section 6.8.4, Examples of Selection Criteria for Supplemental Analyses
Expanded descriptions of criteria that might be used to perform supplemental analysis of subsets of data. Relocated examples to Appendix D.

Section 6.8.5, Examining Percent Susceptible for Combinations of Antimicrobial Agents
Added new section that describes analysis option to calculate %S to two antimicrobial agents in select settings.

Section 8.2.2, Website Application or Portable Document Format (PDF)
Added suggestion to make cumulative antibiogram report available for download to a portable device, if appropriate for the facility.

Section 9.1, Culturing Practices
Expanded explanation about limitations of cumulative antibiogram data based on culturing practices.

Section 9.2, Influence of Small Numbers of Isolates
Expanded discussion for combining data on organisms with low numbers to include options for collecting data over more than 12 consecutive months and/or collecting data from several comparable institutions in a geographic area.

Section 9.2.1, Formula for Combining Data From Two or More Datasets
Added steps that describe combining data from multiple datasets.

Section 9.4, Identification of New Patterns of Resistance
Included option for presenting %S data for antimicrobial agent/organism combinations where resistance is very rare, but might occur in an isolate other than the first isolate for a given patient.

Section 10, Statistical Considerations
Expanded explanations of applying statistics to cumulative antibiogram data.

Additional References (formerly Bibliography)
Updated all citations, which are now found in the References and Additional References sections.
Appendix D. Examples of Supplemental Analyses – Stratifying Cumulative Antibiogram Data by Various Parameters
Expanded examples previously located in Section 5.8.3.1 of M39-A2.

Appendix E2. Cumulative Antimicrobial Susceptibility Report Example – Antimicrobial Agents Listed by Class
Added a second example of a cumulative antibiogram report with drugs listed by class.

Appendix G. Steps for Presenting Local Cumulative Antibiogram Report to Health Care Professionals
Updated to include contemporary antimicrobial susceptibility and resistance concerns.

Appendix H. Statistical Methods for Examining Percent Susceptible
Added formula for calculating confidence intervals and expanded explanations of applying statistics to cumulative antibiogram data.
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 (e.g., clinical microbiologists, pharmacists, physicians);
- utilizing cumulative antimicrobial susceptibility test data to make clinical decisions (e.g., clinical microbiologists, infectious disease specialists and other clinicians, infection control practitioners, pharmacists, epidemiologists, other health care personnel, and public health officials); and
- designing information systems for the storage and analysis of antimicrobial susceptibility test data (e.g., laboratory information system [LIS] vendors, manufacturers of diagnostic products that include epidemiology software packages).

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 are 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 that may be useful to certain clinicians for specialized applications.

It is important to recognize that many of the specific recommendations presented here (e.g., inclusion of only the first isolate of a given species from an individual patient) have been made with the primary aim of guiding clinicians in the selection of initial empirical antimicrobial therapy for infections. Thus, 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 (e.g., emergence of resistance during therapy, empirical therapy of later infections), other inclusion criteria may be appropriate (see Section 6.4).

A summary of the recommendations in M39-A3 that have been made with the primary aim of preparing a report to guide clinicians in the selection of empirical antimicrobial therapy for initial infections is as follows:

- analyze/present cumulative antibiogram report at least annually;
- include only final, verified test results;
- include only species with testing data for $\geq 30$ 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 profile (see Section 6.4);
- include only antimicrobial agents routinely tested; do not report supplemental agents selectively tested on resistant isolates only (see Section 6.5);
- report %S and do not include %I in the statistic (see Section 6.6);