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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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Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: +1.610.688.0100
F: +1.610.688.0700
www.clsi.org
standard@clsi.org

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

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Janet A. Hindler, MCLS, MT(ASCP)
Michael Barton, PharmD
Sharon M. Erdman, PharmD
Alan T. Evangelista, PhD, D(ABMM)
Stephen G. Jenkins, PhD, D(ABMM), F(AAM)
Judith Johnston, MS
James S. Lewis II, PharmD
Dyan Luper, BS, MT(ASCP)SM, MB
Ronald N. Master, MS, SM(AAM)
Graeme Nimmo, MBBS, MSc, MPH, MD
John Stelling, MD, MPH

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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Committee Membership

Consensus Committee on Microbiology

Subcommittee on Antimicrobial Susceptibility Testing

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

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

Michael Barton, PharmD
Health Catalyst
Salt Lake City, Utah, USA

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

Alan T. Evangelista, PhD, D(ABMM)
Tenet Healthcare
Philadelphia, Pennsylvania, USA

Stephen G. Jenkins, PhD, D(ABMM), F(AAM)
New York Presbyterian Hospital
New York, New York, USA

Judith Johnston, MS
Carmichael, California, USA

James S. Lewis II, PharmD
Oregon Health & Science University
Portland, Oregon, USA

Dyan Luper, BS, MT(ASCP)SM, MB
BD Diagnostic Systems
Sparks, Maryland, USA

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

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

John Stelling, MD, MPH
Brigham and Women's Hospital-Microbiology
Boston, Massachusetts, USA

Staff

Clinical and Laboratory Standards Institute
Wayne, Pennsylvania, USA

Luann Ochs, MS
Senior Vice President – Operations

Tracy A. Dooley, MLT(ASCP)
Staff Liaison

Megan L. Tertel, MA
Editor

Joanne P. Christopher, MA
Assistant Editor

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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

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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.

1) **susceptible** – the "susceptible" category implies that isolates are inhibited by the usually achievable concentrations of antimicrobial agent when the dosage recommended to treat the site of infection is used.

2) **susceptible-dose dependent (SDD)** – the "susceptible-dose dependent" category implies that susceptibility of an isolate is dependent on the dosing regimen that is used in the patient. In order to achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either minimal inhibitory concentrations [MICs] or disk diffusion) are in the SDD category, it is necessary to use a dosing regimen (ie, higher doses, more frequent doses, or both) that results in higher drug exposure than the dose that was used to establish the susceptible breakpoint. Consideration should be given to the maximum approved dosage regimen, because higher exposure gives the highest probability of adequate coverage of an SDD isolate. The dosing regimens used to set the SDD interpretive criterion are provided in Appendix E of CLSI document M100.[1] The drug label should be consulted for recommended doses and adjustment for organ function.

   NOTE: The SDD interpretation is a new category for antibacterial susceptibility testing, although it has been previously applied for interpretation of antifungal susceptibility test results (see CLSI document M27-S4).[4] The concept of SDD has been included within the intermediate category definition for antibacterials. However, this is often overlooked or not understood by clinicians and microbiologists when an intermediate result is reported. The SDD category may be assigned when doses well above those used to calculate the susceptible breakpoint are approved and used clinically, and where sufficient data to justify the designation exist and have been reviewed. When the intermediate category is used, its definition remains unchanged.

3) **intermediate** – the "intermediate" category includes isolates with antimicrobial agent MICs that approach usually attainable blood and tissue levels, and for which response rates may be lower than for susceptible isolates. The intermediate category implies clinical efficacy in body sites where the drugs are physiologically concentrated (eg, quinolones and β-lactams in urine) or when a higher than normal dosage of a drug can be used (eg, β-lactams). This category also includes a buffer zone, which should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins.

4) **resistant** – the "resistant" category implies that isolates are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules, and/or that demonstrate MICs or zone diameters that fall in the range where specific microbial resistance mechanisms (eg, β-lactamases) are likely, and clinical efficacy of the agent against the isolate has not been reliably shown in treatment studies.

5) **nonsusceptible** – a category used for isolates for which only a susceptible interpretive criterion has been designated because of the absence or rare occurrence of resistant strains. Isolates for which the antimicrobial agent MICs are above or zone diameters below the value indicated for the susceptible breakpoint should be reported as nonsusceptible; **NOTE 1:** An isolate that is interpreted as nonsusceptible does not necessarily mean that the isolate has a resistance mechanism. It is possible that isolates with MICs above the susceptible breakpoint that lack resistance mechanisms may be encountered within the wild-type distribution subsequent to the time the susceptible-only breakpoint is set; **NOTE 2:** For strains yielding results in the "nonsusceptible" category, organism identification and antimicrobial susceptibility test results should be confirmed.

cascade reporting – strategy of reporting antimicrobial susceptibility test results in which secondary (eg, broader spectrum, more costly) agents may only be reported if an organism is resistant to primary agents within a particular drug class; **NOTE:** Cascade reporting is one type of selective reporting.

cumulative antibiogram – see **cumulative antimicrobial susceptibility test data summary.**

cumulative antimicrobial susceptibility test data summary – the report generated by analysis of results on isolates from a particular institution(s) in a defined period of time that reflects the percentage of first isolates (per patient) of a given species that is susceptible to each of the antimicrobial agents routinely tested.

empirical therapy – treatment initiated before determining the diagnosis of infection in a patient and/or before a specific etiological agent is identified and/or characterized as related to an infectious disease.

first isolate – refers to the initial microbial isolate of a particular species recovered from a patient during the time period analyzed regardless of body source, specimen type, or antimicrobial susceptibility profile; **NOTE:** If analysis of a subset of isolates is being performed (eg, isolates from blood cultures or methicillin-resistant *Staphylococcus aureus* [MRSA] isolates), "first isolate" would refer to the first isolate in that particular subset (ie, the patient's first blood or MRSA isolate).

hospital/health care information system – the computer system used to manage data collected and generated by various services, laboratories, and facilities served by a hospital/health care system.

interpretive criteria (breakpoint) – minimal inhibitory concentration (MIC) or zone diameter values used to indicate susceptible, intermediate, and resistant as defined by the interpretive criteria.

For example, for antimicrobial X with interpretive criteria of:

	MIC (μg/mL)	Zone Diameter (mm)
Susceptible	≤4	≥20
Intermediate	8–16	15–19
Resistant	≥32	≤14

"Susceptible breakpoint" is 4 μg/mL or 20 mm.
"Resistant breakpoint" is 32 μg/mL or 14 mm.

laboratory information system (LIS) – the computer system used to manage data collected and generated by a clinical laboratory, frequently integrated into a hospital/health care information system.

line listing of antimicrobial susceptibility test data – a summary of antimicrobial susceptibility test results for individual isolates with each line containing susceptibility results for all agents tested against the isolate together with other pertinent information (eg, patient hospital number, organism, isolate source, specimen collection date) for that isolate.

multidrug-resistant organism (MDRO) – an organism resistant to multiple classes of antimicrobial agents. The definition can be based on recently published global recommendations[5] or defined by a particular facility.

multiple isolates – isolates of the same species recovered from separate cultures, regardless of body site, specimen type, or antimicrobial susceptibility profile, obtained from a given patient during a defined time period.

patient location – location of the patient at the time a specimen for culture is obtained; **NOTE:** The location may be a specific hospital designation or a less specific designation, such as inpatient, outpatient, intensive care unit, or nursing home facility.

resistant breakpoint – the lowest minimal inhibitory concentration or the largest zone diameter value for which the interpretive category is considered resistant.

selective reporting – reporting of certain antimicrobial susceptibility test results on an individual patient's isolate based on defined criteria, such as organism identification, body site, and overall susceptibility profile; **NOTE:** Cascade reporting is one type of selective reporting.

spreadsheet – a table of values arranged in rows and columns.

suppression reporting – see **cascade reporting.**

surveillance isolates – organisms obtained from cultures of specimens that are collected for the purpose of determining if a patient is harboring a particular organism and are not from cultures that are obtained as part of the clinical evaluation of a patient's illness; **NOTE:** For example, rectal cultures are sometimes performed to determine if a patient is colonized with vancomycin-resistant enterococci, and nares cultures may be performed to determine if a patient is colonized with methicillin-resistant *Staphylococcus aureus*.

susceptible breakpoint – the highest minimal inhibitory concentration or the smallest zone diameter value considered susceptible.

4.2 Abbreviations and Acronyms

%I	percent intermediate
%R	percent resistant
%S	percent susceptible
%SDD	percent susceptible-dose dependent
ASP	antibiotic stewardship program
CA-MRSA	community-associated methicillin-resistant *Staphylococcus aureus*
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CoNS	coagulase-negative staphylococci
CSF	cerebrospinal fluid
ESBL	extended-spectrum β-lactamase
I	intermediate
ICU	intensive care unit
KPC	*Klebsiella pneumoniae* carbapenemase
LIS	laboratory information system
MDR	multidrug-resistant
MDRO	multidrug-resistant organism
MIC	minimal inhibitory concentration
MICU	medical intensive care unit
MRS	methicillin-resistant staphylococci
MRSA	methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-susceptible *Staphylococcus aureus*
NS	nonsusceptible
R	resistant
QA	quality assurance
S	susceptible
VISA	vancomycin-intermediate *Staphylococcus aureus*
VRE	vancomycin-resistant enterococci
VRSA	vancomycin-resistant *Staphylococcus aureus*

5 Information System Design

Most clinical laboratories are likely to use a locally developed or commercial data management computer application to analyze their cumulative antimicrobial susceptibility data. This software may be an integrated component of their LIS system, an analysis utility provided with their antimicrobial susceptibility test instrument, or a desktop software application. The guidelines below recommend a number of desirable characteristics of the data analysis software and data elements that should be considered for inclusion in the analysis database. As for all data analysis systems, it is important to remember that the quality of data extracted from a system depends on the quality of data entered. Some analytical software may be limited by the entry of incomplete data. It is hoped that commercial vendors of software for the analysis of microbiology data will consider the guidelines proposed herein.

5.1 Data Export or Transmission

If the data analysis software is not fully integrated into a laboratory's primary data management system (eg, LIS or antimicrobial susceptibility test instrument), the data system must have the capability to either send data through a real-time interface or, alternatively, to periodically export results to an analysis program. For example:

- Extracted data files should have a consistent format that facilitates the analysis and interpretation of data. This can be accomplished, for example, by organizing results into simple rows and defined columns. Examples of structured files include spreadsheets, delimited "flat" text files, and database tables.

- For data fields to be used in analyses, such as organism, specimen type, patient location, and susceptibility test method, the use of consistent, unambiguous codes or values is important. Because of the potential for spelling errors and inconsistencies in data entry among laboratory personnel, the use of manually entered "free-text" is discouraged.

- When extracted data are saved in a structured file or communicated through an interface, the logical relationship of the results to each other should be preserved. For example, if a blood culture yields two bacterial isolates, Isolate 1 and Isolate 2, the susceptibility test results of the first isolate should unambiguously be associated with Isolate 1, while the results from the second isolate should be clearly associated with Isolate 2, as depicted in the table below. Furthermore, it should be clear that Isolate 1 and Isolate 2 were obtained from the same blood culture, in this case, specimen 105579.

Date Collected	Specimen Number	Isolate Number	Source	Isolate	Test	Result (µg/mL)	Interpretation	Continued
1/14/10	105579	1	Blood	*S. aureus*	OXA	0.5	S	…
1/14/10	105579	2	Blood	*Staphylococcus epidermidis*	OXA	≤0.25	S	…

Abbreviations: OXA, oxacillin; S, susceptible.

- If multiple test panels are used for a single isolate, the system must associate drug results from all panels with the one isolate and not store results as separate isolates. In the example below, there should be only one record containing *S. aureus* susceptibility test results for specimen 16482 Isolate 1. The Panel 2 results should not be resulted or stored as a second isolate.

			Panel 1				Panel 2		
Specimen Number	**Isolate Number**	**Isolate**	**ERY**	**CLI**	**OXA**	**VAN**	**DAP**	**LNZ**	**QDA**
16482	1	*S. aureus*	R	R	R	S	S	S	S

Abbreviations: CLI, clindamycin; DAP, daptomycin; ERY, erythromycin; LNZ, linezolid; OXA, oxacillin; QDA, quinupristin-dalfopristin; R, resistant; S, susceptible; VAN, vancomycin.

5.2 Desirable Attributes of the Data Analysis System

The data analysis program should be able to import all verified, finalized antimicrobial susceptibility test results generated by the laboratory with the required data elements described below. Optionally, the system may also capture the results of specimens for which none of the recovered organisms (if any) had an antimicrobial susceptibility test performed (eg, fungi, "normal or usual flora," negative cultures).

The software must be versatile and flexible and have the ability to:

- Analyze data for a defined time period to generate cumulative antibiogram data and line listings as described below.
- Remove or edit incorrect data in the database.

5.3 Patient Demographic Information

5.3.1 Required

- A unique patient identification number
- Health care facility (for laboratories serving multiple facilities)

5.3.2 Desirable

- Date of birth (preferred) or age
- Sex
- Patient location at the time the specimen was obtained: inpatient ward, nursing unit, clinic (eg, surgical clinic, medical ICU [MICU], emergency room, diabetes clinic), nursing home, or long-term care facility
- Clinical service, if applicable (eg, medicine, surgery, obstetrics)
- Admission date

5.4 Specimen Information

5.4.1 Required

- Specimen number (or other unique identifier for original specimen)

- Specimen type (eg, blood, CSF, urine)
  - The system should have a mechanism for identifying specimens submitted for purposes other than diagnosing infection in patients (eg, infection control, quality control, proficiency testing, screening, surveillance).

- Date of specimen collection

5.4.2 Desirable

- Body site from which original specimen was obtained (eg, right leg wound)

5.5 Organism Information

5.5.1 Required

- Identification (preferably genus and species; genus or organism group [eg, *Enterococcus* spp., viridans group streptococci] when species is not available)

5.5.2 Desirable

- An isolate number, particularly if more than one isolate of a given species is encountered in a culture.

- A mechanism to permit the comparison of organism results over time, regardless of code or taxonomic name changes that occur during the interval under study (eg, *Pseudomonas maltophilia*, *Xanthomonas maltophilia*, and *Stenotrophomonas maltophilia* are different names that have been used at different times to designate the same organism).

- Supplemental information from infection control or clinical services:
  - Colonization or infection
  - Community acquired or health care associated (nosocomial)

5.6 Antimicrobial Susceptibility Test Information

5.6.1 Required

The following are required:

- Quantitative test measurements (minimal inhibitory concentration [MIC] or disk diffusion zone diameters) and/or final test interpretations as would be reported to clinicians (susceptible, intermediate, resistant, or nonsusceptible). If the laboratory uses microbiology "expert rules," then the "expert" interpretation should be stored. For example, many systems will change the interpretation of clindamycin to resistant for isolates of staphylococci, pneumococci, or β-hemolytic streptococci that test erythromycin resistant and clindamycin susceptible but are shown to have inducible clindamycin resistance.

- Database that includes the results of all antimicrobial agents tested, including those agents that may not be routinely reported to clinicians (eg, when selective, suppression, or cascade reporting algorithms are applied). If selective reporting rules are implemented by a commercial antimicrobial susceptibility testing instrument, suppressed antimicrobial susceptibility test results may be absent from the LIS's main data repository, potentially introducing a significant bias in cumulative antimicrobial susceptibility statistics. Efforts should be made to transfer the results of all antimicrobial agents tested (before selective reporting rules suppress any results) to the LIS or

directly to the epidemiology software package. If this is not possible, the cumulative antimicrobial susceptibility statistics, which are likely to be highly biased for antimicrobial agents selectively reported, should not be reported to clinicians.

- Susceptibility test method employed in obtaining a given result (disk diffusion or MIC).

- Specialized test results if they represent a primary testing method used to determine susceptibility or resistance (eg, β-lactamase test, agar screening test, *mecA* detection by polymerase chain reaction, latex agglutination test for penicillin-binding protein 2a).

5.6.2 Desirable

The following antimicrobial susceptibility test result information is desirable:

- Individual data fields for the MIC or zone measurement values and the final interpretation reported in the patient medical record (susceptible, intermediate, or resistant). Besides other uses, the quantitative measurements (MIC or zone diameter) are needed for the analysis of historical data in the event that breakpoints change over time.

- Specific susceptibility test system used (eg, broth microdilution, agar dilution, commercial system, specific MIC panel)

Part I. The Routine Cumulative Antibiogram

6 Data Analysis

Certain criteria, as listed below, must be considered to produce the most meaningful and useful routine cumulative antimicrobial susceptibility report.

6.1 Data Verification

Only final, verified results should be included. It is important to confirm all antimicrobial susceptibility test results on every patient's isolate before reporting the results as final and, by extension, before including these data in the dataset to be analyzed for the cumulative antibiogram report. Many LIS and commercial susceptibility testing instrument data management systems include software (eg, expert systems) that automatically checks all results to ensure they appear reasonable, and also cautions the user to confirm unusual results (see Appendix A).

Examples include:

- Meropenem resistance in *Escherichia coli*, which is uncommon in many facilities

- Vancomycin resistance in *S. pneumoniae*, which (to date of publication) has not been confirmed in a clinical isolate

- Amikacin resistance coexisting with gentamicin and tobramycin susceptibility in *E. coli*
  - Because amikacin is typically more active than gentamicin or tobramycin *in vitro* against *E. coli*, such results are unusual.

6.2 Facility

Cumulative antimicrobial susceptibility test reports should be based on local facility-specific susceptibility data. Separate reports should be generated for each health care facility served by a laboratory, provided sufficient numbers of isolates have been tested from each facility to allow reasonable statistical validity of the estimate of percent susceptibility. Where isolate numbers are too low for meaningful susceptibility estimates, it may be possible to aggregate data from multiple smaller facilities, provided they have a similar clinical case mix and serve a similar population in the same geographical area.

6.3 Frequency

For the purpose of providing reasonably current data to guide empirical antimicrobial therapy choices, it is recommended that data be analyzed at least annually. More frequent analysis may be performed when large numbers of isolates are tested, when new antimicrobial agents are tested, or when other clinically important changes occur or are perceived. Presentation of data on a more frequent basis may be complicated by seasonal variations in resistance rates and imprecise measures due to small numbers of isolates.

6.4 Isolates

Multiple isolates of the same species are frequently recovered from successive cultures from the same patient. These isolates may or may not represent identical strains. For purposes of infection control, QA, detection of rare phenotypes, assessing resistance profiles among isolates encountered in a facility, and monitoring the development of resistant isolates in a patient over time, inclusion of the results of all isolates in the analysis database is of great value and is recommended. Omitting these isolates from the database may result in a significant loss of information regarding bacterial populations. However, inclusion of multiple isolates from an individual patient in analyses of cumulative susceptibility rates for a specific time period can significantly bias estimates in favor of the isolates recovered from patients who are cultured most frequently. The risk of acquiring a resistant strain for a typical patient may thus be significantly overstated.

Therefore, when preparing a cumulative antibiogram to guide clinical decisions about empirical antimicrobial therapy of initial infections, **only the first isolate of a given species per patient, per analysis period (eg, one year) should be included, irrespective of body site, antimicrobial susceptibility profile, or other phenotypical characteristics (eg, biotype).** The first isolate is easily identified, and cumulative antimicrobial susceptibility test data prepared using the first isolate are generally comparable to cumulative antimicrobial susceptibility test data calculated by other methods, providing duplicate isolates are excluded. Further rationale supporting this view is presented in Appendix B. It is recommended that the database stores results from all isolates tested by the laboratory, but that the analytical software should select only "first isolates" when calculating cumulative %S rates. To obtain a reasonable statistical estimate of cumulative %S rates, it is desirable to include only organisms with 30 or more isolates tested during the analysis period (see Section 7.2.2).

Include isolates from human patient specimens collected for diagnostic purposes only. Do not include data on isolates recovered from surveillance cultures (eg, vancomycin-resistant enterococci [VRE], MRSA), environmental cultures, or other nonpatient sources.

In some cases (eg, when small numbers of a species are tested per year and the %S rates have not changed significantly), a facility may wish to analyze data for several years combined (eg, 2005 to 2010). Here, it is suggested that the first isolate per patient per calendar year be included in the analysis, and that a footnote be added to the antibiogram alerting clinicians of the combined data.

6.5 Antimicrobial Agents

6.5.1 Selection of Antimicrobial Agents

Include only antimicrobial agents routinely tested against the population of isolates to be analyzed, making certain each antimicrobial agent reported is appropriate for the species (see Section 6.7.2).

When testing surrogate antimicrobial agents, store the data generated from testing the surrogate agent and report the agent represented by the surrogate. For example, when using the cefoxitin test as a surrogate for detection of oxacillin-resistant staphylococci, present %S for oxacillin and do not report %S for cefoxitin in the cumulative antimicrobial susceptibility report. Likewise, when using the oxacillin disk diffusion screen as a surrogate for detection of penicillin-susceptible *S. pneumoniae*, present %S for penicillin and do not report %S for oxacillin.

6.5.2 Selective Reporting

Selective or cascade reporting criteria are often developed by a multidisciplinary health care team of an institution (eg, physicians, pharmacists, microbiologists) to guide the appropriate use of antimicrobial agents based on the organism identification or infection type. Cascade or selective reporting occurs when the antimicrobial susceptibility test results of secondary antimicrobial agents (eg, broader spectrum, more costly) are only reported if an organism is resistant to primary agents within a particular drug class. An exception would be for those uncommon situations where the primary agent is susceptible and the secondary agent is resistant, in which case the unexpected resistant result should always be reported to the clinician. For purposes of the cumulative antibiogram, results for all antimicrobial agents tested, and not just those results that are selectively reported to the clinician, should be analyzed (see Section 5.6.1). If results for the secondary agents are only available for isolates resistant to primary agents, %S statistics for secondary agents presented in the cumulative antibiogram would generally be biased toward higher levels of resistance. Consequently, such misleading statistics could encourage clinicians to unnecessarily avoid the use of appropriate, effective secondary agents.

It is thus recommended to prepare routine antibiograms using the results of all antimicrobials routinely tested that represent therapeutic alternatives for the species, even if they are not routinely reported to clinicians. If the results of suppressed agents are available to the data analyst in the analysis software, this is simple to accomplish. Unfortunately, the results for suppressed antimicrobial agents often are not available to the analyst. For example, if selective reporting rules are implemented by a laboratory instrument, then the full set of test results may not be available in the dataset used for data analysis and antibiogram preparation. In the absence of complete test results for secondary agents, it is not possible to precisely calculate the %S.

The following example illustrates an approach that could be considered for estimating %S for secondary agents, even when some test results are missing. A satisfactory outcome of this approach will depend on the details of the suppression rules, as well as how consistently they are applied in laboratory reporting.

In this example, the assumption is that a laboratory has implemented two selective reporting rules: 1) if an *E. coli* is susceptible to gentamicin, amikacin is not reported; and 2) if an *E. coli* is susceptible to ceftriaxone, then meropenem is not reported. It is also assumed that the suppressed amikacin and meropenem results are not available in the dataset that will be used for the analysis. By analyzing only the test results available to the data analyst, the following results may be observed:

Organism	No. Strains	%S						
		AMK	AMP	CFZ	CRO	GEN	MEM	SXT
E. coli	1356	48* (n = 353)	35	30	65	74	90† (n = 475)	55

* Amikacin reported only on *E. coli* intermediate or resistant to gentamicin (26% of the 1356 isolates or 353 isolates).

† Meropenem reported only on *E. coli* intermediate or resistant to ceftriaxone (35% of the 1356 isolates or 475 isolates).

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CFZ, cefazolin; CRO, ceftriaxone; GEN, gentamicin; MEM, meropenem; No., number; SXT, trimethoprim-sulfamethoxazole.

Here, the statistics presented for amikacin and meropenem are misleading. With amikacin, only 48% of the isolates appear to be susceptible. However, this represents only a small subset (n = 353) of 1356 *E. coli* tested, and these 353 isolates are likely to be fairly resistant (at least to aminoglycosides) when compared to the rest of the isolates (n = 1003) for which the amikacin result is not available.

Thus, it is appealing to try to estimate the %S for amikacin against all 1356 isolates tested, even though only 353 amikacin results are available. Among the available amikacin results, one knows from the table that 169 of them are amikacin susceptible (48% of 353), and one can make the assumption that the remaining 1003 isolates (1356 − 353) are susceptible to gentamicin (and amikacin was suppressed on these isolates). Because gentamicin-susceptible *E. coli* are usually (though not always) susceptible to amikacin, one can estimate that the total number of amikacin-susceptible strains is 1172 (1003 + 169), which represents 85% susceptible and suggests to clinicians that amikacin actually has much greater efficacy than would be suggested when only the amikacin test results that are available are analyzed (48% susceptible).

Similarly, there were 427 *E. coli* isolates observed to be susceptible to meropenem (90% of 475 isolates) and an additional 881 isolates (1356 − 475) that are probably susceptible to meropenem. This is a total of 1308 likely susceptible isolates, or 96% of all *E. coli* isolates. So, for purposes of the cumulative antibiogram, it would be reasonable to report the amikacin and meropenem results with the indicated footnote in the following manner:

Organism	No. Strains	%S						
		AMK	AMP	CFZ	CRO	GEN	MEM	SXT
E. coli	1356	86*	35	30	65	74	96*	55

* Because of selective reporting rules, actual results obtained for this antimicrobial were not available for all isolates tested. The %S statistic presented in the table is an adjusted estimate of %S based on the data available and an assumption that suppressed susceptibility test results were susceptible.

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CFZ, cefazolin; CRO, ceftriaxone; GEN, gentamicin; MEM, meropenem; No., number; SXT, trimethoprim-sulfamethoxazole.

Thus, in this approach, suppressed antimicrobial agent results were hypothesized to be susceptible. The calculations presented are easy to apply, and can provide valuable information to clinicians about these important second-line agents.

However, the hypothesis that suppressed results are susceptible may not always hold, so the statistics derived should only be considered estimates of the true values. For example, it is possible that some *E. coli* susceptible to gentamicin may, in fact, be resistant to amikacin. Such isolates have been reported, and, in some countries, are relatively common. A clinically important strategy in this scenario would be to

add an additional criterion to the set of reporting rules: if the result of the secondary agent is resistant, then report this result to the clinician. For example, if a strain is resistant to amikacin, then always report the unexpected result, irrespective of whether the gentamicin finding was susceptible or resistant. Most laboratories have these types of reporting rules because they are recommended by CLSI. In addition, fluoroquinolone results may be suppressed in antimicrobial susceptibility reports for children, irrespective of resistance characteristics, because they are not recommended for clinical therapy, or cefazolin may be suppressed in reports on isolates from CSF because cefazolin is not recommended for the treatment of meningitis. In these latter cases, it cannot be assumed that the suppressed results are susceptible.

Consequently, if the data analyst chooses to use the above mentioned approach for estimating %S for antimicrobials with incomplete data, it is important to thoroughly understand the suppression rules and whether this estimation approach is appropriate. To repeat an earlier point, the recommendation is to prepare antibiograms using observed results from all antimicrobials routinely tested when feasible, not only the subset of results that are reported to clinicians.

6.5.3 Supplemental Drug Testing

Some laboratories maintain additional antimicrobial agents or panels of antimicrobial agents that are tested only on isolates demonstrating significant resistance or in response to a physician's request to test additional agents. For example, *Pseudomonas aeruginosa* isolates that are resistant to all antimicrobial agents on the primary panel may be tested against additional or restricted agents (eg, colistin). Additionally, agents may be selectively tested when certain results are obtained with screening tests. For example, some laboratories selectively test extended-spectrum cephalosporins and fluoroquinolones only against isolates of *S. pneumoniae* that are not susceptible to oxacillin using the disk diffusion screen (zones ≤ 19 mm) to determine penicillin susceptibility. The results of testing supplemental agents, or agents tested selectively, should not be included in the routine cumulative antimicrobial susceptibility test report. The supplemental agents would be biased toward lower levels of susceptibility because they were tested only against a less susceptible subgroup of the isolates. For special reports, see Section 6.8.

6.6 Calculations

Include only the percentage of isolates that test susceptible to the listed antimicrobial agent. The percentage of isolates that have an intermediate interpretation should not be included in the %S statistic. For viridans group *Streptococcus* spp. and penicillin, calculate both the %S and the %I separately and list both statistics on the cumulative antibiogram report (see Section 6.8.2).

Susceptible, intermediate, resistant, and nonsusceptible interpretations for a specific organism/antimicrobial agent combination are based primarily on CLSI MIC or disk diffusion zone diameter interpretive criteria (see CLSI document M100).[1] However, for certain organism/antimicrobial agent combinations, the correct interpretation may be determined by findings other than the MIC or zone diameter (eg, clindamycin is correctly reported as resistant for isolates of staphylococci, pneumococci, or β-hemolytic streptococci that test erythromycin resistant and clindamycin susceptible but are shown to have inducible clindamycin resistance). Use the corrected interpretation when calculating the %S.

The "N" value, or total number of isolates tested, will include isolates that have a susceptible, intermediate, resistant, or nonsusceptible interpretation.

Perform calculations using the interpretive breakpoints and rules current at the time of the analysis.

6.6.1 Changes in Interpretive Breakpoints

Analysis of historical data, including descriptions of susceptibility trends over time, require the storage of the quantitative test measurements (MIC or zone diameter value) with reinterpretation of results using

interpretive criteria or breakpoints current at the time of analysis. If it is not feasible for the computer system to determine the "updated" MIC or zone diameter interpretation, then reports and graphs should indicate that susceptibility estimates may not be directly comparable over time for those antimicrobials for which a breakpoint change has occurred. In addition, a footnote should be included in the susceptibility trend report indicating the year(s) in which the breakpoint changes occurred.

The following table illustrates an example of a routine cumulative antibiogram report that emphasizes how interpretive criteria have changed since the previous cumulative antibiogram report was distributed (see Appendix I, Glossary II for abbreviations of antimicrobial agents).

Organism	No. Strains	%S									
		AMK	**AMP**	**CFZ**	**CRO***	**CIP**	**GEN**	**MEM***	**PTZ**	**SXT**	**TOB**
E. coli	1165	100	62	88	94	88	100	100	88	74	100
Enterobacter cloacae	223	100	–	–	82	91	91	99	82	72	100
Klebsiella pneumoniae	521	100	–	–	78	94	93	93	86	75	100

* Revised (2010) CLSI *Enterobacteriaceae* interpretive criteria (µg/mL) for susceptible are being used for the first time to calculate %S; these are ≤ 1 µg/mL for ceftriaxone and ≤ 1 µg/mL for meropenem. Previous CLSI interpretive criteria for susceptible were ≤8 µg/mL and ≤4 µg/mL values for ceftriaxone and meropenem, respectively.

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CIP, ciprofloxacin; CFZ, cefazolin; CRO, ceftriaxone; GEN, gentamicin; MEM, meropenem; No., number; PTZ, piperacillin-tazobactam; SXT, trimethoprim-sulfamethoxazole; TOB, tobramycin.

The effect of MIC breakpoint changes on susceptibility trend reports can vary depending on the magnitude of the breakpoint change, its relation to the wild-type MIC distribution for the organism/antimicrobial agent combination, and the magnitude of changes in MICs produced by acquisition of resistance mechanisms. For example, the change in penicillin MIC breakpoints for nonmeningitis isolates of *S. pneumoniae* illustrates the effect of a major change in susceptibility breakpoints as shown in the following graph (see Figure 1).

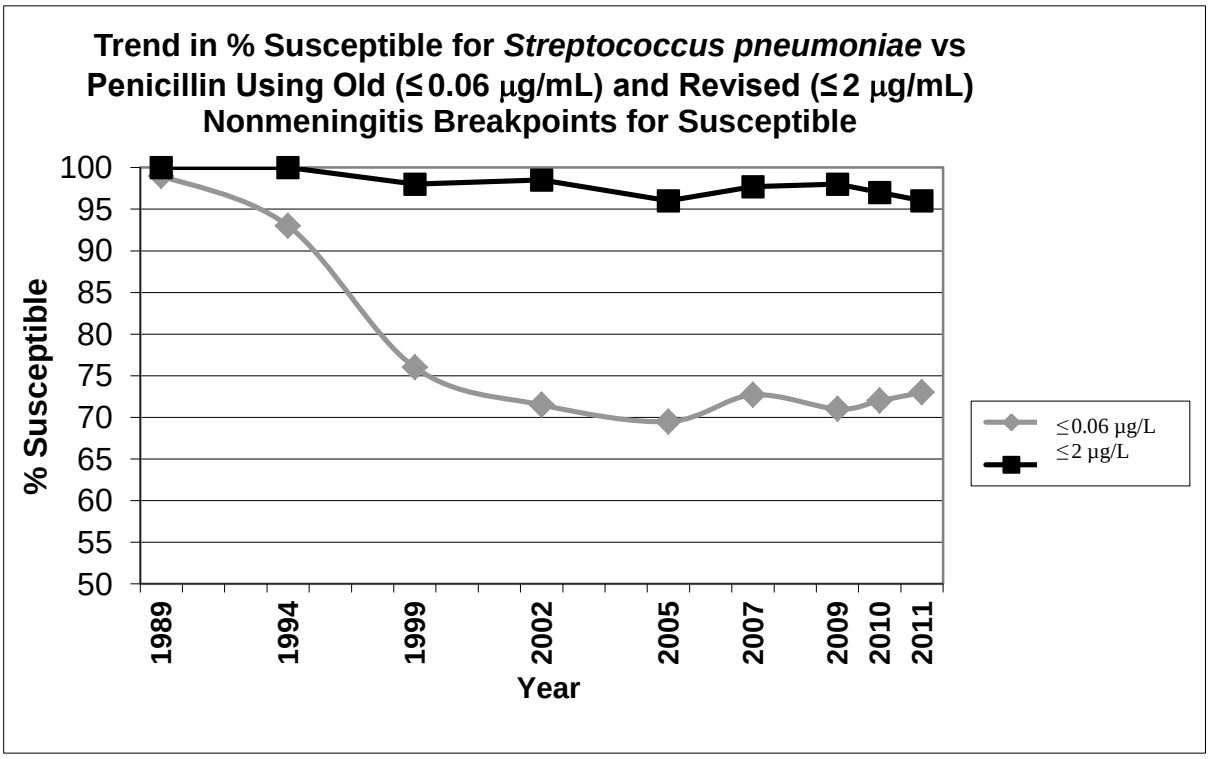

Figure 1. Trend Report for *S. pneumoniae* vs Penicillin

An unfortunate consequence of changing interpretative criteria is that off-scale values that could be interpreted as susceptible, intermediate, or resistant using former breakpoints may no longer be interpretable with newer criteria. For example, in the case of meropenem, the breakpoints initially were S ≤ 4 µg/mL and R ≥ 16 µg/mL. Consequently, an MIC recorded as MIC ≤ 2 µg/mL in 2009 would have been interpreted at that time as susceptible. The current breakpoints are S ≤ 1 µg/mL and R ≥ 4 µg/mL. So, for an isolate with an MIC ≤ 2 µg/mL, it is not possible to ascertain whether the isolate is susceptible or intermediate to meropenem with the new interpretive criteria, so the result could thus be recorded as "no interpretation possible" or "nonresistant." Unfortunately, because routine MIC testing by susceptibility test instruments often involves only a few antimicrobial dilutions per agent, changes in interpretative criteria can greatly decrease the ability to examine susceptibility trends over time (see Section 6.6.2.3).

6.6.2 Issues Related to Determining the Interpretation of Minimal Inhibitory Concentration Values

6.6.2.1 Decimal Minimal Inhibitory Concentration Values

There is a potential for error when interpreting MIC values in cases in which susceptibility and/or resistance breakpoints are < 1 µg/mL. Consider the hypothetical example for a specific drug: MIC values ≤ 0.12 µg/mL are considered susceptible and MICs of 0.25 to 2 µg/mL are intermediate. Thus, an MIC value of 0.12 µg/mL should be interpreted as susceptible. However, because of differences in recording practices, laboratories that record MIC values as 0.125 µg/mL may incorrectly interpret these values to be intermediate. MIC values are recorded to two decimal places only, thereby dropping any numbers beyond the second decimal place. See the examples below:

If MICs Are Recorded as:	Then Report MICs as:
0.015 µg/mL	0.01 µg/mL
0.125 µg/mL	0.12 µg/mL

Abbreviation: MIC, minimal inhibitory concentration.

It is recommended that laboratories verify and ensure that decimal points entered into the data analysis system are formatted in such a way that interpretations are made correctly.

6.6.2.2 Dilutions Other Than Twofold

Some laboratories and commercial systems determine MIC values using dilutions of antimicrobial agents that are not addressed in the CLSI standards. For example, in addition to dilutions of 1, 2, 4, and 8 µg/mL, a laboratory may determine MIC values at levels of 1.5, 3, and 6 µg/mL. The actual MIC obtained should be recorded in the information system; however, it should be given the interpretation at the next higher twofold dilution listed in the CLSI standards. For example, for information systems that have this capability, if the CLSI resistant breakpoint is ≥8 µg/mL, an MIC of 6 µg/mL should be recorded in the database as 6 µg/mL with an interpretation of resistant for purposes of the cumulative antibiogram. For the actual patient report, a laboratory may elect to edit 6 µg/mL to 8 µg/mL.

6.6.2.3 Off-scale Minimal Inhibitory Concentration Values

Individual MIC values frequently lie outside the range of tested dilutions, particularly when only a limited range of concentrations is evaluated. Such values may be recorded, for example, as MIC ≤ 1 µg/mL or MIC > 256 µg/mL. Although values at the low end of the range are typically susceptible and values at the high end are resistant, the ability to interpret such off-scale results may be compromised if interpretive criteria change over time or if the concentrations tested do not overlap with interpretive breakpoints. For example, an MIC value of > 4 µg/mL would be considered resistant if the resistant breakpoint is 4 µg/mL. However, if the resistant breakpoint is revised at some point to 16 µg/mL, then a result recorded as > 4 µg/mL would not be interpretable according to more recent interpretive criteria. In this circumstance, the laboratory may wish to report the values as "uninterpretable by current standards" or report the interpretations using the breakpoints that were in use during the year in which the isolate was reported. A note may be included that these interpretations may not be comparable over time.

6.7 Validation of Calculations

Line listings (see Appendix C) of data should be used as a QA check to ensure that the analytical software is calculating data accurately and that the selection criteria have been met. Data from the computer-generated cumulative reports should be validated by comparison with data generated from manual calculations of data obtained from complete line listings of several organisms. This should be done the first time the program is used, and subsequently if any changes are made to the MIC or disk diffusion interpretive criteria or analytical software.

6.7.1 Validation Suggestions

Using the computer-generated cumulative report, select a time frame that will include 20 to 100 consecutive isolates and a species for which some patients have multiple isolates (eg, MRSA, *P. aeruginosa*, *Acinetobacter baumannii*, *S. pneumoniae*). Print a line listing that contains all isolates of the species, including multiple isolates from each patient. Compare the %S results manually calculated from the line listing to the actual %S results generated from the LIS, susceptibility test instrument, or other computer system to document the accuracy and completeness of the LIS-generated (or susceptibility test instrument or other computer system–generated) data. Verify that manual calculations using patient first isolates from the line listing agree with the software-determined values for:

- The total number of patients
- The %S for each antimicrobial agent

An alternative approach to validating analyses is to compare the results generated from one computer system (eg, LIS) to those generated from another (eg, the antimicrobial susceptibility test instrument), provided both systems use the same calculation algorithms for the cumulative antimicrobial susceptibility test report.

If %S results for the various analyses do not coincide, the reason for the discrepancy should be determined before results are reported in the cumulative antibiogram report.

6.7.2 Validation of Completed Cumulative Antibiogram

Once the cumulative antibiogram report is complete, examine the data to ensure completion of the following items:

1. Include only species for which there are 30 or more isolates. If data are listed for organisms with fewer than 30 isolates available, determine if it is essential to include the species; if yes, append a note to indicate less statistical validity of the estimates of %S. Alternatively, consider analyzing data from a longer time frame (eg, two years) and footnote this exception on the cumulative antibiogram report (see Section 7.2.2).

2. Define all abbreviations.

3. Only include %S data for antimicrobial agents that are appropriate for the species.
   - There may be antimicrobial agents on the test panel that are inappropriate for certain species tested on that panel (eg, trimethoprim-sulfamethoxazole for *P. aeruginosa* tested on a gram-negative panel). Check Table 2 in CLSI document M100[1] to determine which organism/antimicrobial agent combinations are appropriate to report. If interpretive criteria are listed for the specific drug and organism, it is acceptable, but not essential, to include the antimicrobial agent in the cumulative antibiogram report.

   - Some organism/antimicrobial agent combinations may display susceptible results *in vitro*, but the antimicrobial agents are clinically inappropriate for the specific organism. On occasion, such antimicrobial agents may be appropriate in combination therapy, but they should not be included in the cumulative susceptibility report. For example, "appropriate" antimicrobial agents for most *Enterobacteriaceae* include first- and second-generation cephalosporins, cephamycins, and aminoglycosides. However, these agents are inappropriate for *Salmonella* spp. and *Shigella* spp., even if the isolate tests susceptible. Therefore, %S data should not be listed for *Salmonella* spp. and *Shigella* spp. with these agents.

4. For antimicrobial agents listed in CLSI document M100[1] for which only "susceptible" interpretive criteria are provided, any %S calculation that is not 100% should be investigated. For some organism/antimicrobial agent combinations for which there are only "susceptible" interpretive criteria, a "nonsusceptible" result may occur on rare occasions and warrant further investigation. This should be done at the time the observation is made and before reporting results on the individual patient report. See Appendix A, which lists nonsusceptible results that should be verified before reporting patient results.

6.8 Supplemental Analyses and Selection Criteria Options for the Routine Cumulative Antibiogram

For the organism/antimicrobial agent combinations below, perform supplemental analyses as outlined in addition to calculating %S.

6.8.1 *S. pneumoniae*

- **Penicillin:** For all isolates tested, regardless of body site, calculate and list the %S using meningitis, nonmeningitis, and penicillin V (oral penicillin) breakpoints; **NOTE:** It may not be necessary to include data for penicillin V if that information is not used in the facility.

- **Cefotaxime and ceftriaxone:** For all isolates tested, regardless of body site, calculate and list the %S using both meningitis and nonmeningitis breakpoints.

- **Cefepime:** In countries where cefepime is approved for treating both meningitis and nonmeningitis, calculate and list the %S using both meningitis and nonmeningitis breakpoints.

Example:

Organism	No. Strains	%S									
		AMX	CTX	CRO	CLI	ERY	LVX	PEN (IV)	PEN (oral)	SXT	VAN
S. pneumoniae	110	94	–*	–*	81	64	99	–*	64	69	100
Meningitis	110	–	85	84	–	–	–	64	–	–	–
Nonmeningitis	110	–	95	96	–	–	–	84	–	–	–

* Breakpoints differ for cefotaxime, ceftriaxone, and penicillin based on diagnosis. Cefotaxime, ceftriaxone, and penicillin meningitis applies to susceptibility of pneumococci for patients who have meningitis; cefotaxime, ceftriaxone, and penicillin nonmeningitis applies to susceptibility of pneumococci for patients who do not have meningitis.

Abbreviations: %S, percent susceptible; AMX, amoxicillin; CLI, clindamycin; CRO, ceftriaxone; CTX, cefotaxime; ERY, erythromycin; IV, intravenous; LVX, levofloxacin; No., number; PEN, penicillin; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

In this example, isolates from all sources were used to calculate %S using both meningitis and nonmeningitis breakpoints. Ideally, calculation of %S using meningitis breakpoints should be performed on isolates from CSF, and calculation of %S using nonmeningitis breakpoints should be performed on isolates from sources other than CSF. However, most facilities have very few CSF isolates, which makes the ideal strategy unrealistic.

6.8.2 Viridans Group *Streptococcus* spp.

For penicillin: in addition to the %S to penicillin, calculate and list separately the %S and %I to penicillin. The %I can be indicated in a footnote. For example, if 80% are susceptible to penicillin, list that in the table. The footnote might then read: "For the 20% nonsusceptible, 15% were intermediate (MIC 0.25 to 2 µg/mL) and 5% were resistant (MIC ≥4 µg/mL) to penicillin." Only include data from organisms isolated from sterile body sites.

6.8.3 Susceptible-Dose Dependent

For antimicrobial agents that have susceptible dose-dependent (SDD) interpretive criteria (eg, cefepime and *Enterobacteriaceae*), in addition to the %S to cefepime, calculate and list separately the %S and percent SDD (%SDD) to cefepime for each organism. The %SDD can be indicated in a footnote. For

example, with *E. cloacae*, if 89% of isolates are susceptible to cefepime, list that in the table. The footnote might then read: "In addition to the 89% susceptible results, 8% of the isolates were susceptible-dose dependent (MIC 4 to 8 µg/mL) and 3% were resistant (MIC ≥ 16 µg/mL) to cefepime." A laboratory may elect to include the definition of SDD on the cumulative antibiogram report (see Section 4.1).

6.8.4 *S. aureus*

It may be useful to perform a separate analysis for oxacillin-resistant *S. aureus* (MRSA) and oxacillin-susceptible *S. aureus* (eg, use the selection criterion of oxacillin susceptibility or resistance) to demonstrate that many MRSA have lower %S to other antistaphylococcal agents.

Example:

Organism	No. Strains	%S								
		CLI	**DOX**	**ERY**	**GEN**	**OXA**	**PEN**	**RIF**	**SXT**	**VAN**
All *S. aureus*	1317	80	98	50	93	68	13	98	96	100
Oxacillin-resistant *S. aureus* (MRSA)	449	44	96	4	79	0	0	95	94	100
Oxacillin-susceptible *S. aureus* (MSSA)	904	97	99	72	99	100	18	99	97	100

Abbreviations: %S, percent susceptible; CLI, clindamycin; DOX, doxycycline; ERY, erythromycin; GEN, gentamicin; MRSA, methicillin-resistant *S. aureus;* MSSA, methicillin-susceptible *S. aureus;* No., number; OXA, oxacillin; PEN, penicillin; RIF, rifampin; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

NOTE: In this example, the sum of observations for MRSA (n = 449) and MSSA (n = 904) is greater than the number of observations for "all *S. aureus* (n = 1317)." This is because three analyses are being performed: one on a dataset containing all *S. aureus;* one on a dataset containing MRSA only; and one on a dataset containing MSSA only. The first isolate/patient is included in each of the three separate analyses. Thirty-six patients had both MRSA and MSSA isolates during the analysis period (eg, one year).

6.8.5 *Enterococcus* spp.

- Because of differences in susceptibility profiles for *Enterococcus faecalis* and *Enterococcus faecium*, a separate analysis for *E. faecalis*, *E. faecium*, and then for all enterococci as a group might be performed. This can be especially useful when laboratories only identify select enterococcal isolates (eg, sterile body site isolates and isolates identified as VRE) to the species level.

- For high-level aminoglycoside resistance testing, add a footnote indicating the percent resistant (%R) to both gentamicin and streptomycin.

Example:

Organism	No. Strains	%S						
		AMP	DOX	PEN	QDA	VAN	GEN Syn	STR Syn
E. faecalis[*]	77	100	84	100	1	95	60	71
E. faecium[†]	261	2	89	2	99	13	40	14
All *Enterococcus* spp.[‡] (including *E. faecalis*, *E. faecium*, and other)	1525	74	69	74	32	83	71	60

[*] 16% high-level resistance to both gentamicin and streptomycin.
[†] 55% high-level resistance to both gentamicin and streptomycin.
[‡] The laboratory performed susceptibility testing on isolates from sterile and nonsterile sources, but only identified the isolates from sterile sources to species level. The 1525 isolates (many from urine) likely contain mostly the common *Enterococcus* species (eg, *E. faecalis* and *E. faecium*).

Abbreviations: %S, percent susceptible; AMP, ampicillin; DOX, doxycycline; GEN Syn, gentamicin synergy; No., number; PEN, penicillin; QDA, quinupristin-dalfopristin; STR Syn, streptomycin synergy; VAN, vancomycin.

7 Data Presentation

For the cumulative antimicrobial susceptibility test data report, present data in tabular form. Examples of two formats are shown in Appendixes E1 and E2.

7.1 Items to Consider in Constructing the Table

7.1.1 Inclusive Dates of the Report

List the inclusive dates used to create the cumulative antimicrobial susceptibility test data report.

7.1.2 Name of Laboratory or Facility

Include contact information for those responsible for preparing or interpreting the report, if desired.

7.1.3 Comments on Methodology

When the recommendations included in this guideline are used to prepare the cumulative antimicrobial susceptibility test data report for the first time, make a notation indicating that a new analytical method has been applied to generate the data, and comparisons with previous reports must be made with caution.

It may be helpful to provide an explanation of how data were generated, such as:

"The %S for each organism/antimicrobial combination was generated by including only the first isolate of that organism recovered from a given patient during the time period analyzed."

7.2 Items to Consider Within Specific Tables

7.2.1 Organisms

Prepare separate tables for clinically important gram-negative, gram-positive, and, if applicable, anaerobic bacteria and yeasts. For gram-negative organisms, it may be helpful to separate results for glucose-fermenting bacilli (eg, *E. coli*, *Klebsiella* spp., *Enterobacter*) from nonglucose-fermenting bacilli (eg, *A. baumannii*, *P. aeruginosa*).

- List organisms alphabetically, by organism group, or by prevalence. Analyze by organism group or genus if species information is not routinely available.

Species recommended for inclusion when sufficient numbers of isolates are tested:

Gram-negative:

- *A. baumannii*
- *Citrobacter freundii*
- *Enterobacter aerogenes*
- *Enterobacter cloacae*
- *E. coli*
- *Haemophilus influenzae* (β-lactamase results for this organism [eg, percent β-lactamase positive] may be reported as a footnote to the table)
- *K. oxytoca*
- *K. pneumoniae*
- *Morganella morganii*
- *Proteus mirabilis*
- *Providencia* spp.
- *P. aeruginosa*
- *Salmonella* spp.
- *Serratia marcescens*
- *Shigella* spp.
- *S. maltophilia*

Gram-positive:

- *Enterococcus* spp. (it is preferable to separate into *E. faecalis* and *E. faecium* when identified to species level)
- *S. aureus*
- Coagulase-negative staphylococci (CoNS) (consider excluding *Staphylococcus lugdunensis* and *Staphylococcus saprophyticus*, which could be listed separately if sufficient numbers of isolates are tested)
- *S. pneumoniae*

- Viridans group streptococci (from usually sterile body sites only)

Anaerobes:

- *Bacteroides fragilis*
- *Bacteroides fragilis* group (other than *B. fragilis*)
- *Clostridium perfringens*

7.2.2 Number of Organisms

It is best to report only bacteria for which 30 or more isolates of a given species are available. If data are included for organisms with fewer than 30 isolates, a note should be appended to indicate less statistical validity of the estimates of %S. This note might state: "Calculated from fewer than the standard recommendation of 30 isolates." When there are fewer than 30 isolates, it may be appropriate to group several species within a genus together (eg, *Shigella* spp.). This suggestion for reporting %S data only when results for at least 30 isolates are available is based on a desire to include a reasonable number of isolates upon which to calculate the %S, while allowing the reporting of clinically relevant organisms that are isolated in small numbers (see Sections 6.4 and 9.2, and Appendix H).

Include the number of observations (N) for each organism listed on the cumulative report, which allows the users to interpret the relative frequency of each organism as a cause of infection at their institution(s), as well as to estimate the relative precision of the %S value.

7.2.3 Antimicrobial Agents

Use complete antimicrobial agent names, abbreviations listed in Glossary II (see Appendix I), or abbreviations used on patient reports in the institution.

7.2.4 Data

Enter the %S for each organism/antimicrobial agent in the respective box.

Place an "R" in the data box when it is known that the species or organism group is intrinsically resistant to the antimicrobial agent (see example in Appendixes E1 and E2 and intrinsic resistance profiles in Appendix J).

Place a dash (–) in the data box if an antimicrobial agent is not tested, or is known to be clinically ineffective (eg, the *Salmonella* spp. and narrow-spectrum cephalosporins).

7.3 Other Presentation Options

7.3.1 Variations in Drug Panels Tested Routinely

Laboratories may use different panels of antimicrobial agents for the testing of isolates from various organism groups or body sites. For example, one set of antimicrobial agents may be used for testing urine gram-negative isolates and another for nonurine gram-negative isolates.

Include the number of observations (N) based on the highest number of organism/antimicrobial agent combinations tested. If a subset of isolates (eg, urine isolates) is not tested against all antimicrobial agents, the clinical relevance of the cumulative antimicrobial susceptibility test report data may or may not be affected. Sometimes, it might be necessary to report subsets separately. For the following

examples, assume both ciprofloxacin and levofloxacin were tested on the gram-negative nonurine panel, but only ciprofloxacin was tested on the urine panel. Ciprofloxacin appears to have a higher %S than levofloxacin due to the more restricted testing of levofloxacin against only nonurine *E. coli* isolates, which, in this example, were considerably fewer in number and relatively more resistant than the urine isolates. If one considers only the nonurine isolates, the two compounds display identical activity. Therefore, a footnote could be added to the results for all isolates (see Example 1) or the results could be listed for all isolates, as well as for both isolate subsets (see Example 2).

Example 1:

Organism	No. Strains	%S								
		AMP	CFZ	CRO	CIP	GEN	IPM	LVX*	PTZ	SXT
E. coli (All)	3636	61	92	99	92	93	100	80	96	76

* Tested on nonurine isolates only (n = 292). Therefore, results should not be compared to those of other antimicrobial agents listed, all of which were tested against both urine and nonurine isolates.

Abbreviations: %S, percent susceptible; AMP, ampicillin; CIP, ciprofloxacin; CFZ, cefazolin; CRO, ceftriaxone; GEN, gentamicin; IPM, imipenem; LVX, levofloxacin; No., number; PTZ, piperacillin-tazobactam; SXT, trimethoprim-sulfamethoxazole.

Example 2:

Organism	No. Strains	%S								
		AMP	CFZ	CRO	CIP	GEN	IPM	LVX*	PTZ	SXT
E. coli (All)	3636	61	92	99	92	93	100	80	96	76
E. coli (Nonurine)	292	44	82	96	80	87	100	80	93	62
E. coli (Urine)	3417	63	93	99	93	94	100	NT	97	77

* Tested on nonurine isolates only (n = 292). Therefore, results should not be compared to those of other antimicrobial agents listed, all of which were tested against both urine and nonurine isolates.

Abbreviations: %S, percent susceptible; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CRO, ceftriaxone; GEN, gentamicin; IPM, imipenem; LVX, levofloxacin; No., number; PTZ, piperacillin-tazobactam; SXT, trimethoprim-sulfamethoxazole.

NOTE: See Section 6.8.4 for an explanation of why the number of isolates from two subsets of data (eg, urine and nonurine isolates) does not add up to the total number of strains for all *E. coli.*

7.3.2 Change in Drug Panel During Analysis Period (eg, Antimicrobial Agent Is Removed or Added to Routine Testing Panel)

The antimicrobial agents on a laboratory's routine testing panel may change during the analysis period because of: 1) changes in the antimicrobial formulary at the facility; 2) manufacturer changes in available panels; 3) use of an alternate panel to better serve clinician's needs. When such changes occur, the data available can be analyzed and %S results highlighted with a footnote indicating testing has been performed for a limited number of isolates (see example below).

Organism	No. Strains	%S									
		AMP	CFZ	CPM*	CRO	CTZ	CIP	GEN	IPM	PTZ	SXT
E. cloacae	44	R	R	86	75	76	93	95	98	84	90
E. coli	378	49	90	96	95	95	77	91	100	86	74
K. pneumoniae	97	R	94	96	94	93	95	100	98	95	86
P. aeruginosa	73	R	R	86	R	85	79	91	93	92	R

* Added to test panel August 2012. Results for CPM should not be compared directly to those of other agents because CPM was not tested on all isolates.

Abbreviations: %S, percent susceptible; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CPM, cefepime; CRO, ceftriaxone; CTZ, ceftizoxime; GEN, gentamicin; IPM, imipenem; No., number; PTZ, piperacillin-tazobactam; R, resistant; SXT, trimethoprim-sulfamethoxazole.

8 Use of Cumulative Antimicrobial Susceptibility Reports

The following sections provide suggestions for educational efforts to facilitate understanding and use of the cumulative antimicrobial susceptibility test data report.

8.1 Use of the Report

The cumulative antimicrobial susceptibility test data report should only be used as a general guide for empirical antimicrobial therapy until such time that specific antimicrobial susceptibility test results for a patient's infecting organism become available. Clinical application of the cumulative antimicrobial susceptibility test data in an initial choice of antimicrobial agents depends on a variety of factors, including the organism, the antimicrobial agent, patient characteristics, site of infection, and the other clinical parameters. Thus, the patient's physician uses the susceptibility data as one, but not the only, criterion for drug choice.

The cumulative antibiogram is increasing in importance as ASPs evolve in health care facilities. Individuals responsible for ASPs and those preparing cumulative antibiograms must work together to ensure these reports are prepared, distributed, and used optimally.

8.2 Distribution of the Report

8.2.1 "Pocket" Guides

The report should be available in a format that is easily accessible to clinicians. A foldout card with a readable font size (no smaller than 8-point) that fits in the pocket of a laboratory coat is useful. A laminated sheet containing the cumulative antibiogram report might also be placed at the front of each new patient's chart. The amount of material presented on the pocket or chart cumulative antibiogram report should be limited, compared to that on a website or other repository of comprehensive information.

8.2.2 Website Application or Portable Document Format

Presentation of the report on an institution's website (either in graphical form or as a downloadable file) may also meet the needs of some clinicians. It is important to provide reports in each of the formats most frequently used by prescribing physicians. For example, many institutions provide portable devices for use by nurses, medical students, residents, and house staff who may not wish to carry an additional printed pocket version. However, a printed version should also be available in most settings.

8.2.3 Users of the Report

The report should be readily available to all clinicians using or monitoring antimicrobial agents, as well as to infection control personnel, epidemiologists, pharmacists, and clinical microbiology laboratory personnel.

8.2.4 Steps in Presenting Cumulative Antibiogram Data to Health Care Professionals

See Appendix G for stepwise suggestions for presenting cumulative antimicrobial susceptibility test data. The emphasis of these suggestions is to highlight the most important results in order to help educate others about specific resistance concerns within the institution and elsewhere.

9 Limitations of Data, Data Analysis, and Data Presentation

9.1 Culturing Practices

Antimicrobial susceptibility rates are calculated from the results of patient samples processed by the clinical laboratory and reflect local specimen collection practices. The value of these estimates for guiding policy decisions may be compromised if the clinical samples are poorly representative of the typical patients in the treatment population of interest.

- Susceptibility rates may be biased by more frequent sampling of patients with: a) treatment failure following prior antimicrobial therapy; and/or b) prolonged medical histories or recent hospitalizations. These factors are particularly important in the outpatient setting, in which therapy decisions for uncomplicated infections are frequently made without the benefit of a clinical sample.

- Changes in culturing practices within an institution over time and differences in practices between institutions and patient care areas must be considered when comparing differences in susceptibility rates.

9.2 Influence of Small Numbers of Isolates

The number of isolates per species, which is used to generate the cumulative antimicrobial susceptibility test data report, should be noted. Results of small numbers (< 30) of isolates may be misleading and usually should not be included in the report (see Section 7.2.2). However, such data should be kept on file in the laboratory for easy access.

Possible ways to provide guidance for antimicrobial therapy when the number of tested isolates is small include:

- Combining data on the organism from data collected over more than 12 consecutive months

- Combining data, when applicable, for more than one species within a genus

- Combining data from several comparable institutions in a geographical area (eg, acute care hospitals)
  - Be aware of combining data from different types of care institutions (eg, acute care hospitals plus long-term care facilities). Combining data is only appropriate if the %S data among the institutions are similar.

- Providing data from published summaries and guides

9.2.1 Formula for Combining Data From Two or More Datasets

Dataset	No. of Isolates Tested	% of Isolates S to Drug X	No. of Isolates S to Drug X
#1	18	83%	15
#2	22	68%	15
Total	40	–	30

Abbreviations: No., number; S, susceptible.

Use the following formula to calculate the percentage of isolates susceptible to Drug X in datasets #1 and #2 combined:

- Total number of isolates susceptible to Drug X / Total number of isolates tested

Using data from the example above, the percentage is: 30 / 40 = 75%.

9.3 Comparing Results of Individual Antimicrobial Agent Results

Results may be misleading when agents are tested on different groups of isolates in the dataset (eg, an antimicrobial agent tested only against urine isolates compared with an antimicrobial agent tested against organisms from all sites) (see Section 7.3.1).

9.4 Identification of New Patterns of Resistance

When summaries are based on the first isolate per patient per reporting period, changes related to the emergence of new patterns of resistance may be missed. For example, a second or later isolate of *S. aureus* intermediate to vancomycin would not be represented in the susceptibility summary if the initial isolate of *S. aureus* was susceptible to vancomycin. Detecting and dealing with new or unusual patterns of resistance is more appropriately addressed as part of the day-to-day function of data verification (see Section 6.1) and thorough analysis of the complete database, rather than evaluating only the patients' first isolates.

If it is known that at least one isolate in a dataset is not susceptible to a particular agent (eg, one vancomycin-intermediate *S. aureus* [VISA]), but that isolate is not the first isolate/patient, an option is to report the vancomycin %S as 99% or add a comment with the number of VISA encountered. This conveys the message that not all *S. aureus* in that facility were susceptible to vancomycin.

10 Statistical Considerations

The focus of this document is to summarize the culture and susceptibility findings on isolates processed in a clinical microbiology laboratory. Although detailed descriptions of these isolates are certainly of great interest, their value for decision making and policy development is enhanced when the findings from this observed subset can be considered representative of broader underlying bacterial populations causing clinical disease. It is in this area of extrapolating observed results to broader generalizations that the tools and methods of statistics are of greatest value.
As applied to cumulative antibiograms, the two most common uses of statistical methods are:

- Establishing confidence intervals (CIs) that quantify the precision of a %S estimate
- Ascertaining the statistical significance of differences between two observed %S estimates

10.1 Confidence Intervals

If a laboratory finds that 40 out of 100 isolates of *S. aureus* tested are susceptible to erythromycin, one can say with full certainty that 40 / 100 = 40% of the isolates tested erythromycin-susceptible. This does not imply, however, that precisely 40% of all *S. aureus* potentially causing diseases are susceptible. Forty percent is an **estimate** of the true, but unknown, proportion in the broader population of all *S. aureus* likely to cause disease. The true proportion is unlikely to be precisely 40%, but should be somewhere in that vicinity.

The purpose of a CI is to provide an estimate of how precise the observed %S is when used to guide therapy and policy decisions. Guidance for the determination of CIs is provided in Appendix H. In this example, with a calculated %S of 40% and 100 representative isolates, the suggestions provided in Appendix H indicate that the data analyst can be 95% confident that the value lies between 30% and 50%.

The most important determinant of the precision of the estimate is the sample size (ie, the number of isolates tested). For example, if a laboratory finds that four out of 10 isolates of *S. aureus* are erythromycin-susceptible, the observed %S is still 40% as above, but with a very wide CI (95% CI = 12% to 74%). If 400 out of 1000 isolates are susceptible, the CI is narrow (95% CI = 37% to 43%).

10.2 Statistical Significance of Changes in Susceptibility Rates

Multiple sets of cumulative antimicrobial susceptibility test data are frequently compared to look for differences in susceptibility or resistance rates. Examples include comparisons of %S estimates from the current year to the previous one, from inpatients to outpatients, and from one institution to regional or national averages. A common approach to determine if the difference in susceptibility or resistance rates for a selected organism/antimicrobial agent combination is statistically significant is to use the Chi-square test. A P value of ≤ 0.05 is generally accepted to indicate that the differences seen are not likely due to chance alone.

Appendix H includes Tables H2 and H3, which were expanded from a table presented in the World Health Organization document titled *Surveillance Standards for Antimicrobial Resistance*.[6] These tables are based on the Chi-square test and may be used as a guide to determine whether differences between two cumulative antimicrobial susceptibility test data results are statistically significant. To compare trends from multiple years, "Chi-square analysis for trends" (not presented here) may be a useful approach. Information about Chi-square calculations can be found in biostatistics textbooks (see Appendix H for examples).

"Statistically significant" differences must not be confused with "clinically/epidemiologically important" differences. If the number of isolates is very large, then small changes in %S, such as a drop from 57.2% to 55.8%, may be statistically significant, but unimportant from the perspective of clinical decision making. Conversely, if the number of isolates is small, then a change in %S from 70% to 50% may not be statistically significant at a 95% confidence level, but may still serve as a valuable alert to an emerging trend in resistance. Similarly, a change from 100% susceptible to less than 100% susceptible (ie, the first appearance of new resistance) is always important and merits confirmation and further investigation, regardless of statistical significance.

If statistically significant differences in the %S are identified, the data analyst must consider whether results are due to true changes in the underlying bacterial populations or to artifactual differences attributable to changes in the patient population served by the laboratory, sample collection practices, or laboratory testing and reporting protocols.

10.3 Use and Limitations of Statistical Methods

The statistical methods presented make an important assumption that the available isolates are reasonably representative of a broader bacterial population or subpopulation of clinical or public health interest. The isolates processed by a laboratory reflect the characteristics of the patient population served, criteria for the collection of patient samples, and laboratory isolation and susceptibility testing protocols. Thus, one must consider both: 1) which set of patients is best represented by the observed %S estimates; and 2) how these estimates can be generalized to broader patient populations.

Important conclusions about the resistant bacterial population can be made, even when major biases are present. One can explore the presence or absence of resistance, relative resistance rates, and the presence of cross-resistance between agents. If biases remain similar over time, meaningful comparisons of %S rates are possible. The data analyst must, however, always keep in mind the potential impact that biases may have on the conclusions, particularly when estimates are used to guide policy recommendations. This is especially a concern when drawing conclusions in outpatient care areas or in low-resource settings in which the majority of treatment decisions are empirical.

Part II. The Enhanced Antibiogram

11 Stratifying Cumulative Antibiogram Data by Various Parameters

Each facility or health system may stratify or segregate cumulative antimicrobial susceptibility test data by various parameters (eg, patient location, body site). Before stratifying data, one must determine:

- If additional data stratification is necessary based on the current clinical needs of the facility
- If sufficient numbers of isolates have been tested to allow reasonable statistical validity of the %S for the subgroups (minimum of 30 isolates [see Section 6.7.2])
- The most effective method for communicating the results.

Stratified data may be reported within the annual cumulative antibiogram for the institution or to individual users in separate reports.

When analyzing a specific subset of isolates (eg, blood isolates), only the first isolate of a given species recovered from that particular site (eg, blood) per patient should be included in the analysis, even if the patient had a previous isolate from another body site during the analysis period.

11.1 Examples of Selection Criteria for Supplemental Analyses

Cumulative antibiogram data can be stratified in several ways including the following (see Appendix D for specific examples):

- **By nursing unit or site of care.** Data are segregated by patient location (eg, ICU, burn unit, ward, outpatient clinic, nursing home) at the time the infection is suspected or diagnosed. These reports can be used to guide initial empirical antimicrobial therapy for patients at that site of care, and require predetermined selection of patient types that will be included in each report (eg, ICU reports to include data from ICU patients; inpatient reports to include data from all inpatients except ICU patients; outpatient reports to include data from outpatient clinic and emergency room patients). Unit- or site of care–specific cumulative antibiogram data may be useful in the development of empirical antimicrobial treatment algorithms for patients with infections in that particular unit or site of care (eg, ventilator-associated pneumonia treatment algorithms for patients in the MICU).

- **By an organism's resistance characteristics.** Data are segregated by resistance characteristics of a given organism. This reporting scheme is especially useful for multidrug-resistant (MDR) organisms (MDROs) (eg, MRSA, VRE, MDR *A. baumannii*, *K. pneumoniae* resistant to extended-spectrum cephalosporins, and/or carbapenems).

- **By specimen type or infection site.** Data are segregated by specimen type or infection site (eg, urine isolates, blood isolates). These reports should only include antimicrobial agents useful for empirical therapy of the specific infections (eg, report of urine isolates should include those antimicrobial agents useful in treating urinary tract infections).

- **By clinical service or patient population.** Data are segregated by clinical service, medical or surgical specialty, or specific patient population. These reports can be used to guide empirical antimicrobial therapy for specific patient types (eg, surgical, pediatric, cystic fibrosis, transplant).

12 Supplemental Analyses of Multidrug-Resistant Organisms

12.1 Simple Listing of the Percentage of Resistant Organisms

An estimate of the numbers of MDROs encountered might be included with the routine cumulative antibiogram. The facility would define MDROs based on their needs and the antimicrobial agents routinely tested in their facility and/or use definitions recently proposed.[5] One way to report the percentage of a species that is MDR is to list the percentage next to the organism name in the routine cumulative antibiogram report. Examples include:

Gram-Negative Bacilli

E. coli (3% MDR)
Klebsiella oxytoca (1% MDR)
K. pneumoniae (6% MDR)

NOTE: This facility defined MDR in *Enterobacteriaceae* as resistance to at least three of the following four groupings: ciprofloxacin; ceftriaxone and/or ceftazidime and/or piperacillin-tazobactam and/or ertapenem; gentamicin and/or tobramycin; and meropenem. The definition of MDR could be included on the cumulative antibiogram report.

Gram-Positive Cocci

E. faecalis (< 1% VRE)
E. faecium (48% VRE)
S. aureus (47% MRSA)

12.2 Supplemental Analyses of Multidrug-Resistant Organisms

A facility may wish to further analyze data for species in which multidrug resistance is known to occur. For example:

- *K. pneumoniae*

Routine supplemental testing of *Enterobacteriaceae* for extended-spectrum β-lactamase (ESBL) and/or carbapenemase production (eg, *Klebsiella pneumoniae* carbapenemases [KPCs]) is no longer recommended for the purpose of guiding patient therapy decisions. However, in facilities in which these organisms are frequently isolated, segregation of data by resistance pattern or resistance mechanism, and/or hospital unit

(eg, ICU), may be of value. Because most strains of *K. pneumoniae* that produce ESBLs and/or KPCs exhibit resistance to multiple antimicrobial agents, a report that combines all *K. pneumoniae* strains will not reliably represent the susceptibility results for *K. pneumoniae* and may wrongly indicate resistance to antimicrobial agents potentially useful for empirical therapy. Stratification of isolates may provide a more accurate estimation of the presence or absence of MDR isolates.

The following illustrates segregation of data based on specific MDRO phenotypes.

Example:

Organism	No. Strains	%S									
		AMK	AMP	CFZ	CRO	CIP	GEN	IPM	PTZ	TET	SXT
K. pneumoniae (All)	1163	63	R	44	48	46	74	64	53	84	46
K. pneumoniae (Extended-spectrum cephalosporin resistant)	233	30	R	0	0	6	48	100	0	84	3
K. pneumoniae (Carbapenem-resistant)	361	5	R	0	0	0	28	0	0	82	0
K. pneumoniae (**Not** resistant to extended-spectrum cephalosporins or carbapenems)	569	100	R	84	99	94	96	100	88	87	95

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CRO, ceftriaxone; GEN, gentamicin; IPM, imipenem; No., number; PTZ, piperacillin-tazobactam; TET, tetracycline; R, resistant; SXT, trimethoprim-sulfamethoxazole.

13 Examining Percent Susceptible for Combinations of Antimicrobial Agents

A combination of antimicrobial agents is often used in empirical therapy. It may be useful to examine the percentage of isolates susceptible to one or both drugs in relevant combinations. These data could assist in developing specific empirical combination therapy protocols, and could be particularly useful in settings in which there are significant differences in susceptibility of isolates to each individual drug. The %S data for the combination indicates increased coverage over the individual drugs alone. Such data can also be used to demonstrate the extent of coverage offered by the addition of a second antimicrobial agent. The susceptibility estimates obtained from analyzing %S data from two drugs do not take into account potential synergistic or antagonistic interactions between the compounds, and in no way imply that two drugs are necessarily better than one for treatment of infection caused by the organism under consideration.

As an example, for *P. aeruginosa,* it might be helpful to examine activity for ceftazidime plus ciprofloxacin, imipenem plus ciprofloxacin, ceftazidime plus tobramycin, and imipenem plus tobramycin. The combinations selected for reporting for a particular species should reflect clinically useful combinations used for those species at a particular facility. For the analysis in this example, the search parameters would be set to calculate: 1) the percentage of isolates susceptible to ciprofloxacin, ceftazidime, imipenem, and tobramycin individually; and 2) the percentage of isolates that are susceptible to either of the two agents or both of them (eg, ceftazidime and/or ciprofloxacin includes isolates that are susceptible to ceftazidime and resistant to ciprofloxacin, susceptible to ciprofloxacin and resistant to

ceftazidime, or susceptible to both ceftazidime and ciprofloxacin). The data could be presented as follows:

Example:

Organism	No. Strains	%S							
		CIP	CAZ	IPM	TOB	CAZ and/or CIP*	IPM and/or CIP	CAZ and/or TOB	IMP and/or TOB
P. aeruginosa	814	69	80	79	86	86	84	91	91

* 86% of *P. aeruginosa* are susceptible to CAZ or CIP or to both CAZ and CIP.
Abbreviations: %S, percent susceptible; CAZ, ceftazidime; CIP, ciprofloxacin; IPM, imipenem; No., number; TOB, tobramycin.

The example shows that 80% of *P. aeruginosa* are susceptible to ceftazidime. The addition of ciprofloxacin increases the %S to 86%, while the addition of tobramycin raises it to 91%. If combination empirical therapy is desired, either ceftazidime and tobramycin, or imipenem and tobramycin, appear to offer greater than 90% coverage.

Another way of presenting data to guide the potential use of antimicrobial agent combinations would be to list the actual increase in %S gained when a second agent is added. This can be done for individual species or for groups of organisms. For example, when all gram-negative bacilli combined from respiratory sources are analyzed, the addition of ciprofloxacin, tobramycin, or amikacin to piperacillin-tazobactam can be estimated and presented as follows:

Example. All gram-negative bacilli from blood and respiratory sources (N = 977), 2012

PTZ %S			
79.6	Add	%S Gained	Total % Covered With Two Drugs
	CIP	14.3	93.9
	TOB	18.4	98.0
	AMK	20.4	100

Abbreviations: %S, percent susceptible; AMK, amikacin; CIP, ciprofloxacin; PTZ, piperacillin-tazobactam; TOB, tobramycin.

This example shows that 79.6% of all gram-negative bacilli isolated from blood and respiratory sources are susceptible to piperacillin-tazobactam. Of the 977 isolates, 14.3% of isolates resistant to piperacillin-tazobactam are susceptible to ciprofloxacin, resulting in 93.9% of isolates demonstrating susceptibility to piperacillin-tazobactam or to ciprofloxacin, or to both of these agents.

14 Analysis of Susceptibility Profiles of Select Organisms

The routine cumulative antibiogram lists the percentage of isolates susceptible to individual antimicrobial agents. In special circumstances, and in order to obtain further insight into the resistance patterns of select species, it may be useful to calculate the percentage of patients from whom isolates with various resistance patterns have been encountered. For example, when developing empirical therapy algorithms for patients with presumed *P. aeruginosa* infections, the numbers of patients with isolates resistant to multiple combinations of antipseudomonal agents might be presented. For these analyses, it is suggested that the analysis is performed on all isolates rather than the first isolate per patient. All isolates are analyzed, but for each patient a specific profile is only counted once.

Example:

Resistance Profile	No. Patients*	% Patients
No resistance	519	67.9
CIP	77	10.1
CAZ PTZ	55	7.2
CAZ CIP MEM PTZ	44	5.8
CIP MEM	27	3.5
CAZ CIP MEM PTZ TOB	27	3.5
CAZ CIP PTZ	24	3.1
CAZ MEM PTZ	23	3.0
CIP PTZ	18	2.4
CIP MEM PTZ TOB	18	2.4
CIP MEM PTZ	16	2.1
CAZ CIP PTZ TOB	13	1.7
MEM	12	1.6
Other†		

NOTE: Agents evaluated in this analysis include ceftazidime, ciprofloxacin, meropenem, piperacillin-tazobactam, and tobramycin.

* n = 764 patients, some had *P. aeruginosa* isolates with more than one resistance profile.

† Thirty other resistance profiles were encountered with fewer than 10 patients harboring isolates with each of these profiles.

Abbreviations: CAZ, ceftazidime; CIP, ciprofloxacin; MEM, meropenem; No, number; PTZ, piperacillin-tazobactam; TOB, tobramycin.

15 Calculating Percent Susceptible on Select Groups of Organisms

For positive blood cultures, Gram stain information is usually available several hours or days before the organism identification is known. In these settings, it may be helpful to know the percentages of all gram-negative bacilli isolated from blood that are susceptible to specific antimicrobial agents. This information can be obtained by calculating the %S for all gram-negative bacilli grouped together.

In the following example, 334 patients had blood cultures positive with gram-negative bacilli. These included: *E. coli* (n = 118), *Klebsiella* spp. (n = 75), *P. aeruginosa* (n = 32), *E. cloacae* (n = 30), other *Enterobacteriaceae* (n = 32), *Acinetobacter* spp. (n = 13), *S. maltophilia* (n = 7), *Pseudomonas* spp. (not *P. aeruginosa*), and other gram-negative bacilli (n = 13). The percentages of the 334 gram-negative bacilli isolates combined that are susceptible to individual antimicrobial agents are shown below.

Example:

Organism	No. Strains	%S										
		AMK	AMP	CFZ	CAZ	CRO	CIP	GEN	MEM	PTZ	TOB	SXT
All gram-negative bacilli from blood cultures	334	96	22	52	78	75	84	86	98	89	88	71

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CAZ, ceftazidime; CFZ, cefazolin; CIP, ciprofloxacin; CRO, ceftriaxone; GEN, gentamicin; MEM, meropenem; No., number; PTZ, piperacillin-tazobactam; SXT, trimethoprim-sulfamethoxazole; TOB, tobramycin.

With newer technology, organism identification may be known shortly after blood culture signals positive. In these cases, cumulative antibiograms for specific organisms isolated from blood cultures should be used to guide empirical therapy.

16 Graphic Presentation of Percent Susceptible Data to Illustrate Trends in Susceptibility

16.1 Emerging Resistance Trends

A table or graph with data accumulated over several years can be used to demonstrate emerging resistance in a facility (eg, MRSA, VRE, carbapenem-resistant *Enterobacteriaceae*). In cases of emerging resistance in which the prevalence of the resistant organism is low, it may be useful to chart the %R using a limited scale, or to chart the number of patients from whom a particular resistant organism was isolated during the analysis period. Duplicate isolates from a patient may be misleading when the prevalence of a new resistance mechanism is low, and should not be included. A graph demonstrating susceptibility or resistance to multiple antimicrobial agents over time may also be useful in some situations (see the graph examples in Appendix F). Results that may be of interest to report graphically include:

- *S. aureus* – %R to oxacillin (from all or segregated by inpatients, ICU patients, and outpatients)
- *Enterococcus* spp.– %R to vancomycin (isolates from sterile body sites)
- *E. coli* – %R to trimethoprim-sulfamethoxazole (urine isolates) and %R to fluoroquinolone
- *K. pneumoniae* and *E. coli* – %R to extended-spectrum cephalosporins
- *K. pneumoniae* – %R to carbapenem
- *P. aeruginosa* – %R to fluoroquinolone and %R to carbapenem

17 Local Cumulative Antibiograms vs External Antibiograms (eg, Data From External Surveillance Programs)

17.1 Local Cumulative Antibiograms vs Data From External Surveillance Programs

Cumulative antimicrobial susceptibility test data may be aggregated on several levels including a single facility, health care system, community, region, nation, or multiple nations. Surveillance antimicrobial susceptibility data may be obtained from various sources including public health programs, commercial systems, pharmaceutical company sponsored programs, research activities, health systems, or community collaborations.

17.2 The Use of Local Cumulative Antibiograms

When practical, the use of local cumulative antibiograms is preferred to guide empirical therapy decisions. The CDC Campaign to Prevent Antimicrobial Resistance in Healthcare Settings[7] recommends the use of local cumulative antibiograms, and the CDC Antimicrobial Stewardship Program keys for success include the need to tailor interventions to local problems. According to the CDC, "local issues should be assessed to develop targets for antibiotic stewardship interventions. Addressing local problems will further increase buy-in for the interventions."[8] The CDC also suggests aligning the antimicrobial formulary with local susceptibility data: "It is important to ensure that you have the right antibiotics on your formulary and these decisions should be driven by local susceptibility data."[8]

17.3 The Use of Data From External Surveillance Programs

There are circumstances in which local susceptibility test data are not available, are limited in size or scope, or are subject to significant biases that limit their value for developing cumulative antibiograms at the local level and guiding therapy decisions. Even when local data are reliable, benchmark comparisons with regional or national findings (eg, from surveillance data) can provide insights into local resistance findings and prompt evaluations of antimicrobial use and infection control practices if resistance rates are much higher or lower than external norms.

17.4 Some Situations in Which Data From External Surveillance Programs May Be Useful

These circumstances include:

- Organisms that are not routinely tested because they have "predictable" susceptible profiles to commonly used antimicrobial agents (eg, *Streptococcus pyogenes* and penicillin)

- Organisms that are infrequently isolated, such as *S. pneumoniae, H. influenzae, Salmonella* species, and *Shigella* species

- New antimicrobial agents that are not available for testing on commercial diagnostic test systems
  – This may be particularly important for agents that are very active, to determine if any nonsusceptible isolates have been encountered.

- Antimicrobial agents not routinely tested, such as polymyxin B and colistin

- Clinical settings, especially for community-acquired infections, in which treatment decisions are frequently made empirically without the benefit of a diagnostic specimen
  – In such circumstances, local data available may be so biased as to be misleading in guiding empirical therapy decisions.

- Specific patient types such as outpatients, patients residing in extended care facilities, or patients in smaller health care facilities
  – The antimicrobial susceptibility data represented from these patient subsets may not be adequate for preparation of local cumulative antibiograms.

- Analyses of specific patient subsets (eg, by age), specimen source (eg, blood), or bacteria (eg, specific resistance phenotypes) in which data from a single facility may be insufficient in quantity for preparation of reliable local cumulative antibiograms

17.5 Considerations When Using Data From External Surveillance Programs to Guide Local Empirical Therapy Recommendations

External surveillance data can be of value in guiding local empirical therapy recommendations, as described in the previous section. However, in applying such data it is critical to consider: 1) limitations of the external data due to sampling biases or poor test performance; and 2) relevance of the external data for a particular hospital's patient population and clinical setting.

Questions that should be considered when evaluating appropriateness of specific external surveillance data reports include:

- Were the specimens studied in the external data source collected as part of routine clinical care, in which cases there may be sampling biases similar to those noted in locally generated data? Or, were the specimens collected to be representative of a particular patient population and/or clinical syndrome?

- Do the data include the organisms and antimicrobial agents of interest? Some surveillance programs target limited genera or species and a limited number of antimicrobial agents.

- Do the data come from a relevant geographical area for a recent time period?

- How do patient characteristics, such as patient age, acuity of illness, and patient types (eg, inpatient, outpatient, ICU, extended care facility), culturing practices, and clinical syndromes in the external data source compare with the local patient population of interest?

- What susceptibility test methods and interpretive criteria were used by the testing laboratory/laboratories? The use of different interpretive breakpoints (eg, CLSI, the US Food and Drug Administration, European Committee on Antimicrobial Susceptibility Testing) may be an issue, especially in multinational surveillance collaborations.

- Was testing done by a single centralized laboratory, or by collaborating clinical and/or public health laboratories? Testing performed in multiple laboratories may not be as tightly controlled as testing performed in a centralized laboratory.

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Appendix A. Suggestions for Confirmation of Resistant (R), Intermediate (I), or Nonsusceptible (NS) Antimicrobial Susceptibility Test Results and Organism Identification

Organism or Organism Group	Resistance Phenotype Detected[a]	Occurrence and Significance of Resistance and Actions to Take Following Confirmation of Results[a]		
		Category I	**Category II**	**Category III**
		Not reported or only rarely reported to date	**Uncommon in most institutions**	**May be common, but is generally considered of epidemiological concern**
		Action Steps:		
		• Confirm ID and susceptibility.[a] • Report to infection control. • Send to public health laboratory. • Save isolate. *Note: May be appropriate to notify infection control of preliminary findings before confirmation of results.*	• Confirm ID and susceptibility if uncommon in your institution.[a] • Check with infection control in your facility to determine if special reporting procedures or further action are needed. • Check with your local public health department to determine which isolates should be reported to them and when isolates should be sent to the public health laboratory.	• Confirm ID and susceptibility if uncommon in your institution.[a] • Check with infection control in your facility to determine if special reporting procedures or further action are needed.
Any *Enterobacteriaceae*	Carbapenem – I or R[b]		x	
	Amikacin, gentamicin, and tobramycin – R			x
Escherichia coli *Klebsiella* spp. *Proteus mirabilis*	Extended-spectrum cephalosporin[c] – I or R			x
Salmonella and *Shigella* spp.[d]	Cephalosporin III – I or R		x	
	Fluoroquinolone – I or R		x	
Acinetobacter baumannii	Colistin/polymyxin – R		x	
	Carbapenem – I or R			x
Pseudomonas aeruginosa	Colistin/polymyxin – I or R		x	
	Amikacin, gentamicin, and tobramycin – R Carbapenem – I or R			x

Appendix A. (Continued)

Organism or Organism Group	Resistance Phenotype Detected[a]	Occurrence and Significance of Resistance and Actions to Take Following Confirmation of Results[a]		
		Category I	Category II	Category III
		Not reported or only rarely reported to date	Uncommon in most institutions	May be common, but is generally considered of epidemiological concern
Stenotrophomonas maltophilia	Trimethoprim-sulfamethoxazole – I or R		x	
Haemophilus influenzae	Carbapenem – NS Ceftaroline – NS Extended-spectrum cephalosporin[c] – NS Fluoroquinolone – NS	x		
	Amoxicillin-clavulanate – R Ampicillin – R and β-lactamase negative		x	
Neisseria gonorrhoeae	Extended-spectrum cephalosporin[c] – NS		x	
	Fluoroquinolone – I or R			x
Neisseria meningitidis	Ampicillin or penicillin – R Extended-spectrum cephalosporin[c] – NS Meropenem – NS	x		
	Ampicillin or penicillin – I Azithromycin – NS Chloramphenicol – I or R Fluoroquinolone – I or R Minocycline – NS Rifampin – I or R		x	
Enterococcus spp.	Daptomycin – NS Linezolid – R		x	
	Vancomycin – R High-level aminoglycoside – R			x
Staphylococcus aureus	Vancomycin MIC ≥ 8 µg/mL[e]		x[e]	
	Ceftaroline – R Daptomycin – NS Linezolid – R Quinupristin-dalfopristin – I or R Vancomycin MIC = 4 µg/mL		x	
	Oxacillin – R			x
Staphylococcus, coagulase-negative	Daptomycin – NS Linezolid – R Quinupristin-dalfopristin – I or R Vancomycin – I or R[f]		x	

Appendix A. (Continued)

Organism or Organism Group	Resistance Phenotype Detected[a]	Occurrence and Significance of Resistance and Actions to Take Following Confirmation of Results[a]		
		Category I	Category II	Category III
		Not reported or only rarely reported to date	Uncommon in most institutions	May be common, but is generally considered of epidemiological concern
Streptococcus pneumoniae	Ceftaroline – R Linezolid – NS Vancomycin – NS	x		
	Fluoroquinolone – I or R Imipenem or meropenem – I or R Quinupristin-dalfopristin – I or R Rifampin – I or R		x	
	Using nonmeningitis breakpoints: Amoxicillin or penicillin – R Extended-spectrum cephalosporin[c] – R			x
Streptococcus, β-hemolytic group[g]	Ampicillin or penicillin – NS Ceftaroline – NS Daptomycin – NS Ertapenem or meropenem – NS Extended-spectrum cephalosporin[c] – NS Linezolid – NS Vancomycin – NS	x		
	Quinupristin-dalfopristin – I or R		x	
Streptococcus, viridans group	Daptomycin – NS Ertapenem or meropenem – NS Linezolid – NS Quinupristin-dalfopristin – I or R Vancomycin – NS	x		

Abbreviations: CoNS, coagulase-negative staphylococci; FDA, US Food and Drug Administration; I, intermediate; ID, identification; MIC, minimal inhibitory concentration; NS, nonsusceptible; R, resistant.

Nonsusceptible (NS): A category used for isolates for which only a susceptible interpretive criterion has been designated because of the absence or rare occurrence of resistant strains. Isolates that have MICs above or zone diameters below the value indicated for the susceptible breakpoint should be reported as nonsusceptible.

NOTE 1: An isolate that is interpreted as nonsusceptible does not necessarily mean that the isolate has a resistance mechanism. It is possible that isolates with MICs above the susceptible breakpoint that lack resistance mechanisms may be encountered within the wild-type distribution subsequent to the time the susceptible-only breakpoint is set.

Appendix A. (Continued)

NOTE 2: For strains yielding results in the "nonsusceptible" category, organism identification and antimicrobial susceptibility test results should be confirmed (see footnote "a").

a. Ensure antimicrobial susceptibility test results and organism identification are accurate and reproducible. Consider the following steps:
   1. Check for transcription errors, contamination, or defective panel, plate, or card.
   2. Check previous reports on the patient to determine if the isolate was encountered and confirmed earlier.
   3. Repeat organism identification and antimicrobial susceptibility tests with initial method to ensure they reproduce. (For category I and II, may elect to skip step 3 and go to steps 4 and 5. For category III, repeat and/or confirmatory testing may not be needed if resistance is common in your institution.)
   4. Confirm organism identification with second method performed in-house or at a referral laboratory.
   5. Confirm antimicrobial susceptibility results with second method (eg, in-house or referral laboratory). The second method might be a CLSI reference method (eg, broth microdilution, agar dilution, or disk diffusion) or an FDA-cleared commercial test.

b. Imipenem MICs for *Proteus* spp., *Providencia* spp., and *Morganella morganii* tend to be higher (eg, MICs in the new intermediate or resistant category first published in June 2010 [M100-S20-U[1]]) than those with meropenem or doripenem MICs. These isolates may have elevated MICs by mechanisms other than production of carbapenemases.

c. Extended-spectrum cephalosporin = cephalosporin III or IV (see Appendix I, Glossary I).

d. When submitting the report to a public health department, include antimicrobial susceptibility results for *Salmonella* spp. that are intermediate or resistant to third-generation cephalosporins (cephalosporin III) and/or intermediate or resistant to fluoroquinolone or resistant to nalidixic acid.

e. Rarely encountered. Because of significant infection control and public health implications, follow Category I recommendations for notifying infection control and public health authorities.

f. There are some species of CoNS for which vancomycin MICs may test within the intermediate range. In contrast, vancomycin-resistant CoNS are rare.

g. Confirm that Groups C and G are large colony and not small colony variants. Group C and G small colony variants are included with the viridans group.

Reference for Appendix A

[1] CLSI. *Performance Standards for Antimicrobial Susceptibility Testing; Twentieth Informational Supplement (June 2010 Update).* CLSI document M100-S20-U. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.

Appendix B. Rationale Behind the "First Isolate per Patient" Analysis Recommendation

There is no single "correct" way to estimate susceptibility and resistance rates. A variety of calculation approaches and variations exist, and each may be more or less appropriate for certain data applications. For example, each of the following percent susceptible (%S) values is equally correct for the database represented in the table below, and provides somewhat different, but complementary, views of the data.

Calculation Method	N	%S
Isolate-based estimate		
All isolates	1892 isolates	54
Patient-based estimates		
Most susceptible	1019 patients	69
First isolate	1019 patients	67
Weighted average	1019 patients	66
Most resistant	1019 patients	64
Episode-based estimates		
First isolate, 30-day interval	1060 episodes	66
First isolate, 7-day interval	1262 episodes	61
Phenotype-based estimates		
First isolate, major or minor differences in oxacillin only	1070 "strains"	66
First isolate, major differences in any antimicrobial agent	1311 "strains"	61

Abbreviation: %S, percent susceptible.

The following definitions have been used:

- **"All isolates"** – calculations include all isolates of a given species equally, even those of patients with multiple isolates.

- **"First isolate" per patient** – calculations include the results of only the first isolate of a given species recovered from each patient during the investigated time interval, regardless of susceptibility profile, body source, or specimen type.

- **"Most resistant" interpretation per patient** – calculations include only the most resistant interpretation observed for each separate antimicrobial agent tested among all isolates of a given species from an individual patient. This estimate gives the "worst-case" scenario for patient-based %S. A useful application of this algorithm is ascertaining the percent of patients who are observed to have, in at least one isolate, a particular resistance finding, for example, in answering the question: "What percent of patients was found to have at least one MRSA [methicillin-resistant *Staphylococcus aureus*] isolate?"

Appendix B. (Continued)

- **"Most susceptible" interpretation per patient** – calculations include only the most susceptible interpretation observed for each separate antimicrobial agent tested among all isolates of a given species from an individual patient. This estimate gives the "best-case" scenario for patient-based %S.

- **"Weighted average"** – calculations include all isolates from each patient. The average %S for each antimicrobial agent is calculated separately for each patient. Then, the cumulative %S statistic is calculated as the overall average of the individual patient average %S values.

- **"First isolate per episode (seven-day interval)"/"First isolate per episode (30-day interval)"** – calculations include the first isolate of a given species recovered from each episode of infection. An episode is defined as the set of all isolates from a patient in which the interval between consecutive isolates is less than or equal to seven days/30 days.

- **"First isolate, major or minor differences in oxacillin only"** – calculations include the first isolate of a given species recovered from each resistance phenotype. A resistance phenotype is defined as the set of all isolates from a patient with the same oxacillin interpretation. An intermediate result is considered as distinct from susceptible and resistant results.

- **"First isolate, major differences in any antimicrobial agent"** – calculations include the first isolate of a given species recovered from each resistance phenotype. A resistance phenotype is defined as the set of all isolates from a patient with the same interpretation for all antimicrobials. An intermediate result is considered consistent with either a susceptible or a resistant result.

If multiple isolates are common in a database, the "all isolates" approach can exhibit much lower estimates of susceptibility (thus, overestimating the risk of resistance in the patient population) than with other methods, and should be avoided. In many instances, patient-, episode-, and phenotype-based approaches yield similar estimates of susceptibility, so any of these approaches could be acceptable; but, episode- and phenotype-based approaches have significant unappreciated limitations that compromise their use in characterizing and comparing trends in resistance and when applied to clinical decision making. Multiple sampling of resistant isolates will inflate resistance rates for an institution that will influence empirical antimicrobial agent use.

- **Epidemiological bias:** The main problem with the isolate-based method is resistance estimates are heavily weighted toward findings in those patients with multiple cultures—frequently, patients with long hospital stays, treatment failures, or complicated clinical histories. Episode- and phenotype-based approaches suffer from this same deficiency, and are thus highly influenced by local sample collection practices and patient hospitalization demographics. The usefulness of phenotype-based approaches is further compromised by local susceptibility test practices; one would expect that a laboratory that tests a large number of antimicrobials would find more distinct "strains," defined with the full set of antimicrobials tested, than a laboratory that tests fewer antimicrobials. Because patients with multiple strains tend to have higher rates of resistance than patients with single strains, one is left with an unexpected skew toward higher estimates of resistance in laboratories that test isolates against broader antimicrobial panels.

Appendix B. (Continued)

- **Technical difficulties:** Another factor that limits the use of phenotype- and episode-based approaches as a general recommendation to clinical laboratories is challenges in implementing the desired calculations: Should the same episode time interval be used for all species? Should all antimicrobial agents tested be used to define a resistance phenotype or certain subsets for distinct species? Should strains with intermediate results be considered distinct from strains with resistant or susceptible results? How should isolates with different sets of antimicrobials be compared (eg, comparing a urine isolate with a blood isolate, or with an isolate in which two individual results are missing because of technical problems identified on a susceptibility test)? Because data managers and software programmers may address these issues differently, resistance estimates between institutions may not be directly comparable.

With these considerations in mind, this document makes the following recommendations:

- For the routine cumulative antibiogram, the "first isolate per patient" approach is an epidemiologically relevant approach for guiding clinical decisions about initial, empirical therapy (ie, for those patients for whom microbiological data do not yet exist to target treatment). It has the additional benefit of computational simplicity compared to other nonisolate-based approaches.

- In many instances, the microbiologist may be interested in estimating resistance rates in a stratified subset of the dataset (eg, in blood isolates or ICU isolates). In this situation, the above algorithms should apply to the subset of interest (eg, the "first blood isolate" or "first ICU isolate").

- If the microbiologist is concerned about missing the initial appearance of a rare phenotype that could perhaps be excluded in the "first isolate" approach, a supplemental analysis using the "all isolates" or "weighted average" approach could be considered for the organisms of concern. The "weighted average" approach may be particularly useful for following underlying trends in resistance, especially for rare resistance phenotypes that may be missed by a "first isolate" approach. Fortunately, resistance estimates from these two approaches are usually very close (< 2% difference in the majority of datasets examined).

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

Table C1. Statistics Generated for *Streptococcus pneumoniae* by the Analysis Software

Organism	n	CRO Meningitis	CRO Nonmeningitis	CLI	ERY	LVX	MEM	PEN Meningitis	PEN Nonmeningitis	PEN oral	SXT	VAN
spn	35	77% S	94% S	77% S	60% S	100% S	74% S	54% S	100% S	54% S	71% S	100% S
		17% I	6% I					NA		29% I		
		6% R	0% R					46% R		17% R		

Abbreviations: %I, percent intermediate; %R, percent resistant; %S, percent susceptible; CLI, clindamycin; CRO, ceftriaxone; ERY, erythromycin; LVX, levofloxacin; MEM, meropenem; NA, not applicable; PEN, penicillin; spn, *S. pneumoniae*, SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

Table C2. Line Listing of All Isolates of This Organism Stored in the Database. Most patients had a single isolate; although two patients, highlighted in gray, had two isolates each.

Identification number	Location	Specimen number	Specimen date	Specimen type	Organism	CRO	CRO Meningitis	CRO non-Mening.	CLI	CLI	ERY	ERY	LVX	LVX	MEM	MEM	PEN	PEN Meningitis	PEN non-Meningitis	PEN Oral	SXT	SXT	VAN	VAN
4816018	odopp	03231	1/14/2004	Eye	spn	0.016	S	S	≤0.125	S	≤0.062	S	1	S	0.016	S	0.016	S	S	S	≤0.25	S	0.5	S
9506097	emc	04890	1/18/2004	Blood	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
2281181	emc	07102	1/22/2004	Sputum	spn	1	I	S	≤0.125	S	1	R	2	S	0.5	I	2	R	S	R	2	I	0.25	S
3300705	emc	09638	1/30/2004	Blood	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
4281299	10w	12169	2/5/2004	Blood	spn	1	I	S	≤0.125	S	>8	R	1	S	0.5	I	2	R	S	R	4	R	0.25	S
4281299	bcmed	12174	2/5/2004	Sputum	spn	1	I	S	0.5	I	>8	R	1	S	0.5	I	2	R	S	R	4	R	0.25	S
7160647	5w	13901	2/7/2004	CSF	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
9391100	n3s	14082	2/21/2004	Blood	spn	0.031	S	S	≤0.125	S	≤0.062	S	1	S	0.016	S	0.031	S	S	S	≤0.25	S	0.25	S
2451279	rsmp1	14292	2/18/2004	Sinus	spn	1	I	S	>1	R	4	R	1	S	0.5	I	2	R	S	R	4	R	0.25	S
3221041	mppul	16873	2/23/2004	Sinus	spn	2	R	I	≤0.125	S	≤0.062	S	1	S	0.062	S	0.125	R	S	I	≤0.25	S	0.25	S
1001274	5e	17461	3/12/2004	Sputum	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.031	S	S	S	≤0.25	S	0.5	S
7540889	emc	22032	3/14/2004	BAL	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
5720879	clmpl	24628	4/5/2004	Sputum	spn	1	I	S	>1	R	> 8	R	≤0.5	S	0.5	I	2	R	S	R	2	I	0.25	S
7921171	5w	27014	4/14/2004	Blood	spn	0.5	S	S	0.5	I	1	R	1	S	0.25	S	1	R	S	I	2	I	0.25	S
6694400	emc	29984	4/19/2004	Sputum	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
8146200	msint	30775	5/1/2004	Blood	spn	0.062	S	S	≤0.125	S	≤0.062	S	1	S	0.016	S	0.031	S	S	S	0.5	S	0.5	S
4282299	bcmed	32510	5/27/2004	Sputum	spn	0.5	S	S	>1	R	>8	R	≤0.5	S	0.125	S	1	R	S	I	2	I	0.25	S
6061178	jsei	37304	5/29/2004	Eye	spn	0.25	S	S	>1	R	>8	R	≤0.5	S	0.016	S	0.062	S	S	S	0.5	S	0.25	S
2888880	mppul	41973	6/8/2004	BAL	spn	0.5	S	S	0.25	S	>8	R	1	S	0.125	S	1	R	S	I	0.5	S	0.25	S
3841271	6ei	43966	6/28/2004	Blood	spn	0.125	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.031	S	0.125	R	S	I	≤0.25	S	0.25	S
4401180	6w	48701	7/17/2004	Blood	spn	0.5	S	S	≤0.125	S	0.125	S	≤0.5	S	0.5	I	1	R	S	I	≤0.25	S	0.25	S
642204	9e	50462	7/15/2004	CSF	spn	0.062	S	S	≤0.125	S	2	R	≤0.5	S	0.125	S	0.5	R	S	I	≤0.25	S	0.5	S
8928269	rsctb	54411	7/31/2004	Sputum	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	≤0.125	S
2577890	acidc	66457	8/17/2004	Sputum	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
5415768	4w	63405	8/30/2004	CSF	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
3211875	emc	71423	10/26/2004	Blood	spn	0.031	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.031	S	S	S	≤0.25	S	0.25	S
4391182	emc	73572	10/31/2004	Sputum	spn	0.031	S	S	≤0.125	S	≤0.062	S	1	S	0.016	S	0.031	S	S	S	≤0.25	S	0.25	S
8281011	emc	75558	11/1/2004	CSF	spn	1	I	S	≤0.125	S	2	R	≤0.5	S	0.5	I	1	R	S	I	1	I	0.25	S
8281011	emc	79032	11/1/2004	Sputum	spn	1	I	S	≤0.125	S	2	R	≤0.5	S	0.5	I	1	R	S	I	1	I	0.25	S
7891125	9fi	81700	11/5/2004	Blood	spn	0.031	S	S	≤0.125	S	≤0.062	S	1	S	0.016	S	0.031	S	S	S	≤0.25	S	0.25	S
6644488	emc	84723	11/17/2004	Blood	spn	0.5	S	S	≤0.125	S	≤0.062	S	1	S	0.5	I	2	R	S	R	≤0.25	S	0.25	S
8347063	emc	86997	11/23/2004	Blood	spn	0.5	S	S	>1	R	>8	R	1	S	0.5	I	1	R	S	I	2	I	0.5	S
8667207	clmpl	89420	12/1/2004	BAL	spn	1	I	S	≤0.125	S	2	R	≤0.5	S	0.5	I	1	R	S	I	1	I	0.25	S
7920715	5w	91473	12/12/2004	CSF	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S
5162516	hnsrg	93245	12/15/2004	Ear	spn	2	R	I	>1	R	>8	R	1	S	0.5	S	2	R	S	R	>4	R	0.25	S
5276155	7wi	94570	12/17/2004	BAL	spn	0.062	S	S	>1	R	>8	R	≤0.5	S	0.016	S	0.031	S	S	S	≤0.25	S	0.25	S
9981207	9e	97804	12/31/2004	Sputum	spn	0.016	S	S	≤0.125	S	≤0.062	S	≤0.5	S	0.016	S	0.016	S	S	S	≤0.25	S	0.25	S

Abbreviations: BAL, bronchoalveolar lavage; CLI, clindamycin; CRO, ceftriaxone; CSF, cerebrospinal fluid; ERY, erythromycin; I, intermediate; LVX, levofloxacin; MEM, meropenem; PEN, penicillin; R, resistant; S, susceptible; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

Appendix C. (Continued)

Table C3 shows the results of calculations performed manually. In compiling these results, only the first isolate from each patient encountered in the line listing above was included in the totals. This can be accomplished by deleting the noninitial isolates (per patient) from the above listing. The total number of susceptible, and optionally resistant and intermediate, strains can be determined by simple counting or by the use of a counting function, as offered by many spreadsheet programs. Finally, the %S, %R, and %I are calculated.

Table C3. Results of Manual Calculations

Organism	CRO Men.	CRO Non-men.	CLI	ERY	LVX	MEM	PEN-Men.	PEN-Non-men.	PEN oral	SXT	VAN
Number S	27	33	27	21	35	26	19	35	19	25	35
%S	77%	94%	77%	60%	100%	74%	54%	100%	54%	71%	100%
Number I	6	2	1	0	0	9	0	0	10	7	0
%I	17%	6%	3%	0%	0%	26%	0%	0%	29%	20%	0%
Number R	2	0	7	14	0	0	16	0	6	3	0
%R	6%	0%	20%	40%	0%	0%	46%	0%	17%	9%	0%
Total	35	35	35	35	35	35	35	35	35	35	35
Total %	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Abbreviations: %I, percent intermediate; %R, percent resistant; %S, percent susceptible; CLI, clindamycin; CRO, ceftriaxone; ERY, erythromycin; I, intermediate; LVX, levofloxacin; MEM, meropenem; Men., Meningitis; Non-men., Nonmeningitis; PEN, penicillin; R, resistant; S, susceptible; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

The manual estimates in Table C3 agree perfectly with the system-calculated estimates in Table C1, supporting the reliability of estimates performed by the analysis software. The above-described process of validation may miss some errors in calculation algorithms, so the analyst should always be alert to the need for subsequent verification of the analysis software.

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

Example D1. *Staphylococcus aureus* by patient location

Organism	Location	No. Strains	%S							
			CLI	DAP	ERY	OXA	PEN	LNZ	SXT	VAN
S. aureus	OP	781	86	99	54	75	4	99	96	100
	IP	461	66	99	42	53	5	99	95	100
	ICU	231	70	99	44	54	5	99	96	100

Abbreviations: %S, percent susceptible; CLI, clindamycin; DAP, daptomycin; ERY, erythromycin; ICU, intensive care unit; IP, inpatient (non-ICU); LNZ, linezolid; No., number; OP, outpatient; OXA, oxacillin; PEN, penicillin; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

Example D2. Urine isolates from inpatients and from outpatients for selected uropathogens

Organism	Location	No. Strains	%S						
			AMP	CFZ	CTX	CIP	NIT	GEN	SXT
Escherichia coli	OP	1205	56	91	98	84	98	90	72
	IP	436	39	83	93	62	97	78	60
Klebsiella pneumoniae	OP	517	R	95	97	95	50	97	86
	IP	138	R	77	85	91	52	88	70
Proteus mirabilis	OP	271	83	95	100	88	R	96	82
	IP	32	74	94	94	81	R	88	75
Pseudomonas aeruginosa	OP	131	R	R	R	67	R	84	R
	IP	169	R	R	R	56	R	75	R

Abbreviations: %S, percent susceptible; AMP, ampicillin; CFZ, cefazolin; CIP, ciprofloxacin; CTX, cefotaxime; GEN, gentamicin; IP, inpatient (non-ICU); NIT, nitrofurantoin; No., number; OP, outpatient; R, resistant; SXT, trimethoprim-sulfamethoxazole.

Appendix D. (Continued)

Example D3. Bloodstream isolates for selected pathogens from all patients

Organism	No. Strains	%S											
		AMP	CLI	DAP	ERY	LNZ	OXA	PEN	QDA	SXT	VAN	GEN Syn	STR Syn
S. aureus	107	5	71	99	60	99	57	5	99	97	100	–	–
Enterococcus faecalis[*]	54	100	–	99	16	100	–	100	0	–	96	54	62
Enterococcus faecium[†]	128	8	–	98	4	97	–	8	96	–	23	61	60

[*] 19% high-level resistance to both GEN Syn and STR Syn.
[†] 25% high-level resistance to both GEN Syn and STR Syn.

Abbreviations: %S, percent susceptible; AMP, ampicillin; CLI, clindamycin; DAP, daptomycin; ERY, erythromycin; GEN Syn, gentamicin synergy; LNZ, linezolid; No., number; OXA, oxacillin; PEN, penicillin; QDA, quinupristin-dalfopristin; STR, streptomycin synergy; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

Example D3. Bloodstream isolates for selected pathogens from all patients (continued)

Organism	No. Strains	%S										
		AMK	AMP	CFZ	CAZ	CTX	CIP	GEN	IPM	PTZ	SXT	TOB
E. coli	120	100	54	77	95	95	71	84	100	90	70	90
K. pneumoniae	73	100	R	81	92	86	84	87	99	82	75	94
P. aeruginosa	41	94	R	–	79	R	71	84	79	87	R	88

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CAZ, ceftazidime; CFZ, cefazolin; CIP, ciprofloxacin; CTX, cefotaxime; GEN, gentamicin; IPM, imipenem; No., number; PTZ, piperacillin-tazobactam; R, resistant; SXT, trimethoprim-sulfamethoxazole; TOB, tobramycin.

Example D4. Isolates from all sites for selected pathogens from burn patients

Organism	No. strains	%S										
		AMK	AMP	CFZ	CAZ	CTX	CIP	GEN	IPM	PTZ	SXT	TOB
E. coli	46	100	62	88	94	94	88	100	100	88	74	100
Enterobacter cloacae	31	100	R	R	82	82	91	91	100	82	72	100
P. aeruginosa	70	70	R	R	70	R	70	70	65	60	R	70

Abbreviations: %S, percent susceptible; AMK, amikacin; AMP, ampicillin; CAZ, ceftazidime; CFZ, cefazolin; CIP, ciprofloxacin; CTX, cefotaxime; GEN, gentamicin; IPM, imipenem; No., number; PTZ, piperacillin-tazobactam; R, resistant; SXT, trimethoprim-sulfamethoxazole; TOB, tobramycin.

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

Memorial Medical Center
1 January – 31 December 2012 Cumulative Antimicrobial Susceptibility Report*
Percent Susceptible

Gram-Negative Organisms	No. Strains	Amikacin	Ampicillin	Cefazolin	Cefotaxime	Ceftazidime	Ciprofloxacin	Nitrofurantoin†	Gentamicin	Meropenem	Piperacillin-tazobactam	Trimethoprim-sulfamethoxazole	Tobramycin
Acinetobacter baumannii	32	80	R	R	34	52	51	–‡	60	80	46	58	59
Citrobacter freundii	49	100	R	R	72	67	90	78	100	99	67	67	100
Enterobacter aerogenes	31	100	R	R	68	69	92	85	91	99	74	95	91
Enterobacter cloacae	76	99	R	R	61	62	92	81	90	99	77	84	90
Escherichia coli	1433	99	36	68	96	94	72	98	91	99	51	65	92
Klebsiella pneumoniae	543	99	R	72	91	92	84	74	94	95	86	81	94
Morganella morganii	44	100	R	R	85	81	99	R	100	99	64	75	100
Proteus mirabilis	88	100	87	80	99	99	89	R	90	100	70	73	93
Pseudomonas aeruginosa	397	97	R	R	R	76	75	R	80	80	85	R	83
Salmonella spp.	32	–	88	–	97	97	90	–	–	100	91	86	–
Serratia marcescens	50	100	R	R	82	94	95	R	94	99	94	91	89
Shigella spp.	33	–	64	–	100	100	95	–	–	100	84	69	–
Stenotrophomonas maltophilia	72	R	R	R	R	63	6	R	R	R	–	98	R

* The percent susceptible for each organism/antimicrobial combination was generated by including the first isolate of that organism encountered on a given patient.
† Nitrofurantoin data from testing urine isolates only.
‡ (–) drug not tested or drug not indicated.
Abbreviations: No., number; R, intrinsic resistance.

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

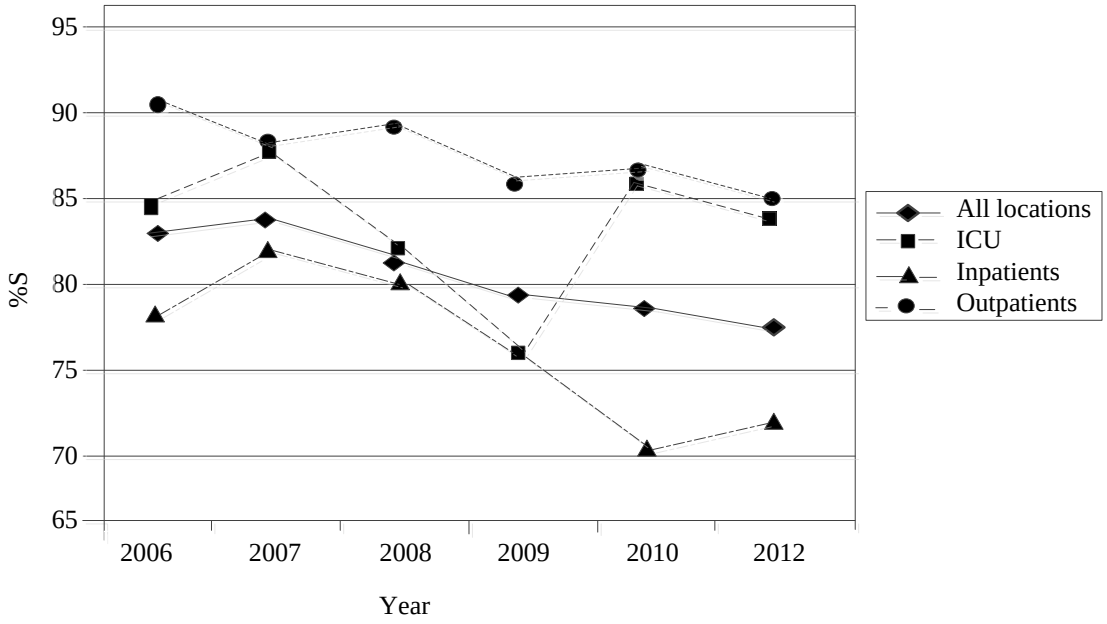
Memorial Medical Center
1 January – 31 December 2012 Cumulative Antimicrobial Susceptibility Report*
Percent Susceptible

Gram-Negative Organisms	No. Strains	β-lactams						Aminoglycosides			FQs	Other	
		Ampicillin	Cefazolin	Cefotaxime	Ceftazidime	Meropenem	Piperacillin-tazobactam	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Nitrofurantoin†	Trimethoprim-sulfamethoxazole
Acinetobacter baumannii	32	R	R	34	52	80	46	80	60	59	51	–‡	58
Citrobacter freundii	49	R	R	72	67	99	67	100	100	100	90	78	67
Enterobacter aerogenes	31	R	R	68	69	99	74	100	91	91	92	85	95
Enterobacter cloacae	76	R	R	61	62	99	77	99	90	90	92	81	84
Escherichia coli	1433	36	68	96	94	99	51	99	91	92	72	98	65
Klebsiella pneumoniae	543	R	72	91	92	99	86	99	94	94	84	74	81
Morganella morganii	44	R	R	85	81	99	64	100	100	100	99	R	75
Proteus mirabilis	88	87	80	99	99	100	70	100	90	93	89	R	73
Pseudomonas aeruginosa	397	R	R	R	76	80	85	97	80	83	75	R	R
Salmonella spp.	32	88	–	97	97	100	91	–	–	–	90	–	86
Serratia marcescens	50	R	R	82	94	99	94	100	94	89	95	R	91
Shigella spp.	33	64	–	100	100	100	84	–	–	–	95	–	69
Stenotrophomonas maltophilia	72	R	R	R	63	R	R	R	R	R	6	R	98

* The percent susceptible for each organism/antimicrobial combination was generated by including the first isolate of that organism encountered on a given patient.
† Nitrofurantoin data from testing urine isolates only.
‡ (–) drug not tested or drug not indicated.
Abbreviations: FQ, fluoroquinolone; R, intrinsic resistance.

Appendix F. Examples of Graphs to Illustrate Trends in Susceptibility

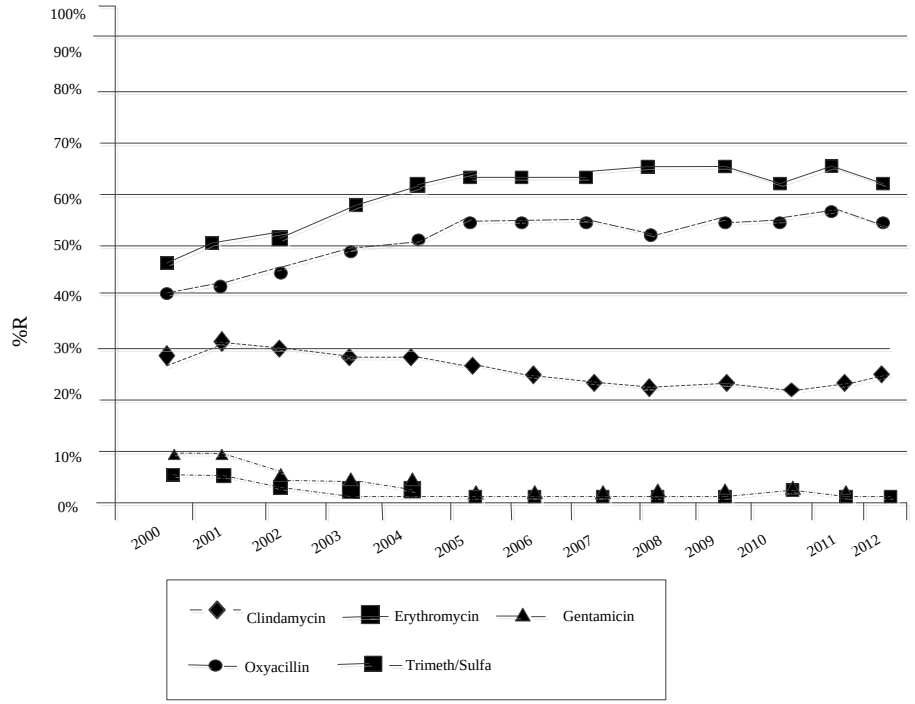
Graphic presentation of data can be useful to demonstrate changes in the percent susceptible (%S) (or the percent resistant [%R]) over time. This can be done in various ways, as presented in the Figures F1 to F4. The %S statistics were determined as described in Section 6.4 in this document. Percent resistant statistics were obtained by subtracting the sum of %S plus the percent intermediate from 100%. In cases in which the incidence of resistance is very low (eg, < 1%), it may be useful to indicate the numbers of patients from which an organism with a specific resistance phenotype was isolated, as illustrated in Figure F4.



Abbreviation: ICU, intensive care unit.

Figure F1. Five-Year Trend – Oxacillin %S for *Staphylococcus aureus* From All Locations and by Patient Care Area 2006 to 2012

Appendix F. (Continued)



Abbreviation: trimeth/sulfa, trimethoprim-sulfamethoxazole.

Figure F2. *S. aureus* %R 2000 to 2012

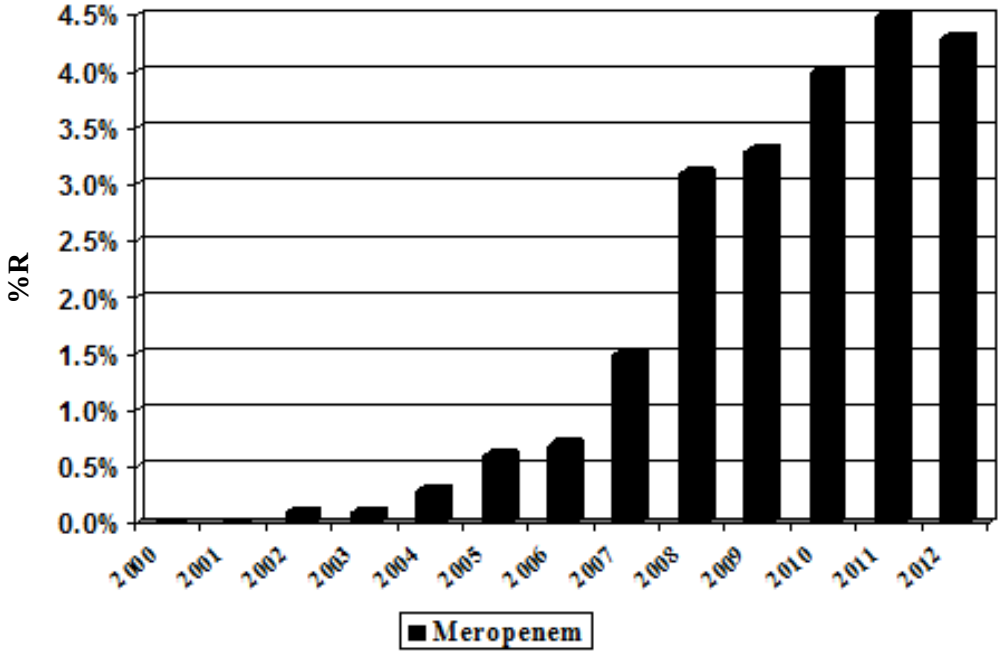


Figure F3. *Klebsiella pneumoniae* – Meropenem %R 2000 to 2012

Appendix F. (Continued)

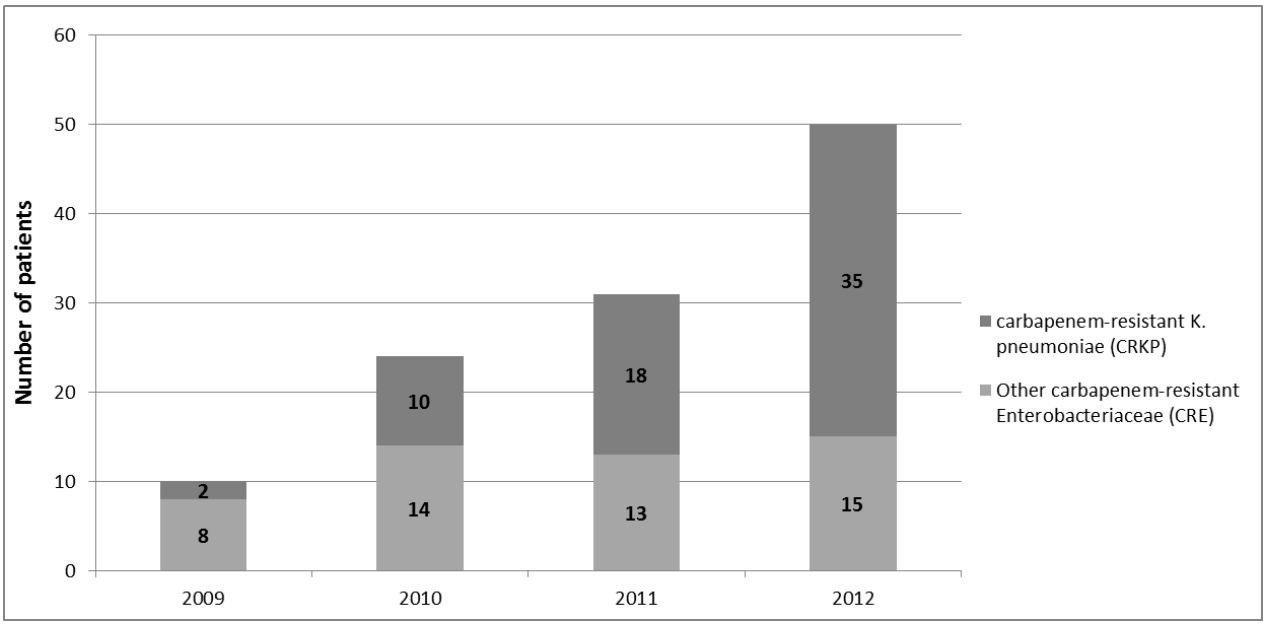


Figure F4. Number of Patients With Carbapenem-Resistant *Enterobacteriaceae* 2009 to 2012

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

Below are stepwise suggestions for presenting cumulative antimicrobial susceptibility test data to health care professionals. The emphasis is to highlight the most important results to help educate those using the report on specific resistance concerns within a specific institution and elsewhere.

1. Explain the purpose of the local cumulative antibiogram and CLSI recommendations for preparing this report.
   - Recommendations in M39 are for preparation of a cumulative antimicrobial susceptibility test data report that can be used to support clinical decisions regarding empirical therapy of initial infections, particularly when used in conjunction with antibiotic stewardship programs.

   - The primary recommendations for analysis and presentation of the data include:
     – Prepare a report annually.

     – Include only species with testing data for ≥30 isolates.

     – Exclude surveillance isolates.

     – Include only results from the first isolate of a given species encountered for a patient, and ignore multiple isolates of the same species irrespective of their source or overall susceptibility profile.

     – Report results for all drugs tested that are appropriate for the species. Do not report supplemental drugs that are selectively tested on resistant isolates only.

     – Report the percent susceptible (%S) and do not include the percent intermediate in the statistic.

2. Explain any limitations of the software to analyze data according to CLSI recommendations. For example, if the software only eliminates isolates with identical susceptibility profiles to those of previous isolates, the %S statistics will likely differ from those that would be generated by including only the first isolate per patient. It is difficult to compare the %S data among facilities in which isolates are removed using different exclusion criteria. Additionally, if the data include surveillance isolates, this is not consistent with M39 recommendations.

3. Describe the plan used to separate data into subgroups for the report (eg, inpatient vs outpatient, urine vs nonurine).

4. Present graphs and charts for trends that are monitored from year to year (see Appendix F).

5. Consider highlighting data or information related to the following if it is an important problem in the institution.
   - *Staphylococcus aureus*
     – Susceptibility to oxacillin (methicillin-susceptible *S. aureus* [MSSA] vs methicillin-resistant *S. aureus* [MRSA])

     – The *mecA* testing option for select isolates

Appendix G. (Continued)

  - Various strain types of MRSA that might be encountered (eg, community-associated MRSA [CA-MRSA], hospital-associated MRSA); presence of multidrug resistance among MRSA vs MSSA

  - Use of penicillin and oxacillin results to predict results for all β-lactams; MRSA are resistant to all currently available β-lactams (except cephems with anti-MRSA activity, such as ceftaroline)

  - Susceptibility to vancomycin, and current global status of vancomycin-intermediate *S. aureus* (VISA) and vancomycin-resistant *S. aureus* (VRSA)

  - Susceptibility to clindamycin and erythromycin, and tests for inducible clindamycin resistance in erythromycin-resistant, clindamycin-susceptible isolates

- Coagulase-negative staphylococci (CoNS)
  - Susceptibility to oxacillin

  - Limitation for overcalling oxacillin resistance in some CoNS other than *Staphylococcus epidermidis*

  - The *mecA* testing option for select isolates

  - Susceptibility testing policies for CoNS and circumstances in which CoNS may be a contaminant

- *Enterococcus* spp.
  - Susceptibility to gentamicin and streptomycin synergy screens (nonurine isolates)

  - Reporting policies and CLSI notes regarding combination therapy for serious enterococcal infections

  - Presence of vancomycin-resistant enterococci, which are usually *Enterococcus faecium* and often ampicillin- and penicillin-resistant and quinupristin-dalfopristin, linezolid-, and daptomycin-susceptible

  - Presence of *Enterococcus faecalis*, which are usually ampicillin- and penicillin-susceptible and nearly always quinupristin-dalfopristin-resistant

  - Limitations of some results (eg, ampicillin, penicillin, and quinupristin-dalfopristin if all enterococcal species are grouped together and reported as "*Enterococcus* spp.")

- *Streptococcus pneumoniae*
  - No vancomycin resistance reported to date
  - Susceptibility to penicillin; meningitis vs nonmeningitis vs oral penicillin V breakpoints
  - Susceptibility to cefotaxime or ceftriaxone; meningitis vs nonmeningitis breakpoints

- Viridans group *Streptococcus* spp.
  - No vancomycin resistance reported to date

Appendix G. (Continued)

  - Presence of penicillin-intermediate and penicillin-susceptible, and significance for blood culture isolates

- *Streptococcus* spp., β-hemolytic group
  - No penicillin or vancomycin resistance reported to date
  - Susceptibility to clindamycin and erythromycin, and tests for inducible clindamycin resistance in erythromycin-resistant, clindamycin-susceptible isolates; clindamycin significance in *Streptococcus agalactiae* and also *Streptococcus pyogenes*

- *Escherichia coli*
  - Susceptibility to ampicillin, cefazolin (IV [intravenous] use), cefazolin (to predict oral cephalosporins), trimethoprim-sulfamethoxazole, and fluoroquinolones
  - Presence of multidrug-resistant (MDR) isolates (eg, ampicillin, ciprofloxacin, gentamicin, and trimethoprim-sulfamethoxazole)
  - Presence of isolates resistant to third-generation cephalosporins
  - Profiles of urine isolates vs those from other sites

- *Klebsiella pneumoniae*
  - Susceptibility to third-generation cephalosporins
  - Susceptibility to carbapenems and an MDR profile for carbapenem-resistant *Enterobacteriaceae*
  - Susceptibility to fluoroquinolones

- *Enterobacter* spp.
  - Susceptibility to third- and fourth-generation cephalosporins
  - Susceptibility to carbapenems
  - Susceptibility to fluoroquinolones

- *Pseudomonas aeruginosa*
  - Susceptibility to aminoglycosides
  - Susceptibility to fluoroquinolones
  - Susceptibility to antipseudomonal penicillins
  - Susceptibility to third- and fourth-generation cephalosporins
  - Susceptibility to carbapenems
  - Presence of MDR isolates (eg, ceftazidime/cefepime, gentamicin, imipenem, fluoroquinolone)
  - Colistin/polymyxin B testing options

- *Haemophilus influenzae*
  - Incidence of β-lactamase-positive isolates

Appendix G. (Continued)

6. An example of cumulative susceptibility data for *S. aureus* and comments that might be made regarding these data:

S. aureus

Organism	No. Strains	%S							
		CLI	ERY	GEN	OXA	PEN	RIF	SXT	VAN
All *S. aureus*	1317	80	50	93	58	13	98	96	100
Oxacillin-resistant *S. aureus* (MRSA)	449	44	4	79	0	0	95	94	100
Oxacillin-susceptible *S. aureus* (MSSA)	904	97	72	99	100	18	99	97	100

Abbreviations: %S, percent susceptible; CLI, clindamycin; ERY, erythromycin; GEN, gentamicin; MRSA, methicillin-resistant *S. aureus;* MSSA, methicillin-susceptible *S. aureus;* No., number; OXA, oxacillin; PEN, penicillin; RIF, rifampin; SXT, trimethoprim-sulfamethoxazole; VAN, vancomycin.

Comments:

1. Oxacillin-resistant staphylococci are resistant to cefazolin and all other currently available β-lactams (except cephems with anti-MRSA activity such as ceftaroline).

2. Hospital-associated MRSA are typically more resistant to other antistaphylococcal agents than MSSA.

3. Significant numbers of MRSA are seen in patients from the community, and the strain type for these is often different from the strain types associated with MRSA that have been noted in hospitalized patients for years. The CA-MRSA are often (but not always) more susceptible to other antistaphylococcal agents (eg, clindamycin and trimethoprim-sulfamethoxazole); CA-MRSA can be encountered in hospitalized patients. There are currently no practical tests for the clinical laboratory to distinguish community-associated from hospital-associated strain types of MRSA, although the resistance profile can often give some indication of this.

4. Many *S. aureus* that appear to be erythromycin-resistant and clindamycin-susceptible with routine susceptibility tests in fact possess a gene conferring inducible clindamycin resistance. Use of clindamycin to treat infections caused by strains with inducible clindamycin resistance may result in clinical failure. Tests are available to detect inducible clindamycin resistance.

5. As of November 2012, in the United States, VRSA has been isolated from 12 patients; VISA has been reported from at least 100 patients.

Appendix H. Statistical Methods for Examining Percent Susceptible

H1 Confidence Intervals

The effect of sample size on the reliability of resistance rates can be illustrated by calculating confidence intervals (CIs). Table H1 lists CIs for selected sample sizes and susceptibility rates. The first column lists the sample size. The second and third columns list the lower and upper confidence limits for a 95% confidence level for a 10% susceptibility rate. For example, if a sample of 30 isolates of *Streptococcus pneumoniae* is tested for susceptibility to erythromycin and 27 (90%) of the isolates are susceptible, the 95% CI for the susceptibility rate is 74% to 97%. A 95% CI of 74% to 97% means that there is a 95% certainty that the true susceptibility rate of the population is between 74% and 97%, assuming the sample collected is reasonably representative.

Table H1. 95% CIs for Selected Sample Sizes*

	Susceptible or Resistant Rate																	
Sample Size	10%		20%		30%		40%		50%		60%		70%		80%		90%	
10	0	43	5	52	10	61	17	69	24	76	31	83	39	90	48	95	57	100
20	2	31	7	42	14	52	22	61	30	70	39	78	48	86	58	93	69	98
30	3	26	9	38	17	48	25	58	33	67	42	75	52	83	62	91	74	97
40	3	24	10	35	18	46	26	55	35	65	45	74	54	82	65	90	76	97
50	4	22	11	33	19	44	28	54	37	63	46	72	56	81	67	89	78	96
60	4	20	12	32	20	43	29	53	38	62	47	71	57	80	68	88	80	96
70	5	20	12	31	20	42	29	52	39	61	48	71	58	80	69	88	80	95
80	5	19	13	30	21	41	30	51	39	61	49	70	59	79	70	87	81	95
90	5	18	13	30	21	40	30	50	40	60	50	70	60	79	70	87	82	95
100	5	18	13	29	22	40	31	50	40	60	50	69	60	78	71	87	82	95
200	7	15	15	26	24	37	33	47	43	57	53	67	63	76	74	85	85	93
400	7	13	16	24	26	35	35	45	45	55	55	65	65	74	76	84	87	93
600	8	13	17	23	26	34	36	44	46	54	56	64	66	74	77	83	87	92
1000	8	12	18	23	27	33	37	43	47	53	57	63	67	73	77	82	88	92

* CIs were calculated using the Agresti-Coull interval.
Abbreviation: CI, confidence interval.

Table H1 is provided as a general guide. Laboratories may also wish to calculate CIs for percent susceptible (%S) or percent resistant (%R) more precisely. This can be done either with "approximate" or "exact" methods.

The simplest approach is with a "Normal approximation to a binomial distribution," also known as the "Wald" method. The Normal approximation is a convenient and simple approach that is frequently used in the literature. However, it is not reliable if the number of isolates is small or if the %S or %R is close to 0%, in which case calculations for %S may include meaningless negative values. Consequently, this approach is not recommended.

A much better approximate method is the Agresti-Coull interval, which is a simple modification of the previous approach.[1-4] It is also known as the "Add 4" interval because the calculations are identical to those used to calculate the binomial proportion after two "successes" (susceptible) and two "failures" (resistant) have been added to the observed dataset. The 95% CI is calculated with the following formula where "*S*" is the number of susceptible isolates and "N" is the total number of isolates tested.

Appendix H. (Continued)

$$\tilde{p} = \frac{S + 2}{\mathrm{N} + 4}$$

The 95% CI for %S is:

$$\tilde{p} \pm 1.96 \sqrt{\frac{\tilde{p}(1 - \tilde{p})}{\mathrm{N} + 4}}$$

Example 1: 517 of 584 *Escherichia coli* isolates are susceptible to a drug. The %S is 517/584 = 0.885 = 88.5%. The 95% CI is calculated as follows:

$$95\%\ \mathrm{CI} = 0.882653 \pm 1.96 \sqrt{\frac{0.882653(1 - 0.882653)}{584 + 4}} = 0.882653 \pm 0.026013 = [85.7\% - 90.9\%] \approx [86\% - 91\%]$$

By this approximation, there is 95% certainty that the true proportion susceptible for the general population lies somewhere between 85.7% and 90.9%.

If the number of isolates is below 30, the Agresti-Coull approximation is not as accurate as other recommended approaches. Alternative estimates which can be applied include the Wilson interval without continuity correction (Agresti-Coull was designed as an approximation to the Wilson interval, so the CIs are very similar), the more conservative Wilson interval with continuity correction, or the even more conservative Clopper-Pearson method. Conservative CIs are a bit wider than nonconservative CIs to improve the likelihood that the 95% CI estimated from the data indeed includes the true 95% CI. So, with a given dataset, a conservative 95% CI may in fact be a 97% or 98% CI. Calculations for all of the methods mentioned can be found in the below references.[1-10]

H2 Statistical Significance of a Difference in Two Proportions

Tables H2 and H3 contain data that may be used to determine whether differences between two proportions are statistically significant. The first column of each table contains an initial susceptibility rate, the top row contains the size of each sample, and the grid contains the new susceptibility rate that would be statistically significant at a *P* value of 0.05 when about the same number of isolates is tested in both years. The same tables can be used to provide estimates in the change of %R in place of %S.

For example, if a cumulative antimicrobial susceptibility test dataset from 2007 contains 100 isolates of *Proteus mirabilis* with an ampicillin susceptibility rate of 80%, a cumulative antibiogram that includes data from 2008 for a similar number of isolates of *P. mirabilis* would need to show a decrease in ampicillin susceptibility to 66% or less to be statistically significant (see Table H2).

Appendix H. (Continued)

Table H2. Percent Susceptible Decreases

	Sample Size							
Initial %S	10	20	50	100	200	400	600	1000
98	–	–	84	90	93	95	95	96
95	–	65	78	85	89	91	92	92
90	30	55	72	78	82	85	86	87
80	20	45	60	66	71	73	75	76
70	10	30	48	55	60	63	64	65
60	0	20	38	45	49	52	54	55
50	0	15	28	35	39	42	44	45
40	NS	5	20	25	30	33	34	35
30	NS	0	12	17	20	23	24	25
20	NS	NS	4	9	12	14	15	16
10	NS	NS	NS	2	4	5	6	7

Abbreviations: %s, percent susceptible; NS, nonsusceptible.

Table H3. Percent Susceptible Increases

	Sample Size							
Initial %S	10	20	50	100	200	400	600	1000
98	–	–	NS	NS	NS	100	100	100
95	–	NS	NS	NS	99	98	98	97
90	NS	NS	NS	98	96	95	94	93
80	NS	NS	96	91	88	86	85	84
70	NS	100	88	83	80	77	76	75
60	NS	95	80	75	70	67	66	65
50	100	85	72	65	61	58	56	55
40	100	80	62	55	51	48	46	45
30	90	70	52	45	40	37	36	35
20	80	55	40	34	29	27	25	24
10	70	45	28	22	18	15	14	13

Abbreviations: %s, percent susceptible; NS, nonsusceptible.

Calculations were performed using the Chi-square test and Fisher's exact test.

These tables are valid for comparisons of two datasets of the same size. For example, when comparing data from different years, the tables are useful if the sample size (number of isolates) does not vary significantly from year to year. However, if there were 100 isolates in 2003 and 1000 isolates in 2004, these tables would not be valid.

Appendix H. (Continued)

In the case of unequal sample sizes, a more formal statistical analysis must be applied. There are a number of possible "approximate" and "exact" tests, but the statistic most commonly used in the literature for this purpose is the Chi-square test or the Chi-square test with continuity correction. This method does not work well if the number of isolates is small, or if the %R or %S is close to 0%. In these circumstances, an "exact" approach, such as Fisher's exact test or the Agresti-Caffo method for comparison of binomial proportions, would be appropriate.

H3 Multiple Comparisons

The previous section explores the statistical significance of a difference in two proportions, for example, the difference in %S for *E. coli* and ciprofloxacin between 2005 and 2006. However, if one is comparing the results for multiple organisms and multiple antibiotics between two years, one must repeat the calculations for each organism and antibiotic of interest. This raises a problem in statistical testing known as "multiple comparisons." By performing multiple statistical tests, there is a high risk that some of the "significant" differences identified represent spurious artifacts attributable to normal random fluctuations in the data samples, not to true changes in the underlying bacterial populations.

There are a number of statistical approaches for controlling the statistical significance when performing multiple comparisons, and a more complete discussion can be found in the references.[1-10] However, in common practice in the literature, the issue of multiple comparisons is often ignored. This practice is widespread and generally accepted in many contexts. However, it is advisable in such cases to add a note indicating that "no adjustments were made for multiple statistical comparisons."

H4 Statistical Significance of Proportion Trends Over Time

A common concern of health care providers and public health authorities is whether resistance trends change over time. If only two years are to be compared, then the approach described in the previous sections can be applied. To examine trends over a longer period, however, this approach is inadequate. For example, important gradual changes in susceptibility over a five-year period may be missed if the year-to-year changes are too small to be statistically significant. A useful statistical test that is commonly applied in this situation is the Chi-square for trend test. Mathematically, it is similar to a simple linear regression test.

H5 Statistically Significant Changes in Percent Susceptible Between Analysis Periods

It is difficult to visually inspect routine cumulative antibiograms from successive time periods to determine if changes in %S have occurred. Statistically significant changes in %S from one year to the next can be highlighted in the routine cumulative antibiogram (see Example A) or listed in a separate table (see Example B). For the latter, the table could include changes in %S for all organism/antimicrobial agent combinations or only for those that showed a statistically significant change.

It is important to note that changes in %S that are statistically significant (decreases or increases) may not always be clinically significant. Similarly, there may be clinically significant increases in resistant organisms, but these may not be apparent by looking at decreases in %S in the routine cumulative antibiogram. Subtle changes in resistance are best noted with other types of analyses, such as monitoring the numbers of patients from which a specific type of resistant organism was isolated (see Section 16 of this document and Appendix F).

Appendix H. (Continued)

Section 10 of this document describes how to determine the statistical significance of changes in %S. When the "N" is small (eg, < 500 isolates), the change in %S must be substantial (eg, > 5%) for the change to be statistically significant.

Appendix H. (Continued)

Example A. Routine cumulative antibiogram

Memorial Medical Center
1 January – 31 December 2012 Cumulative Antimicrobial Susceptibility Report*
Percent Susceptible

Gram-Negative Organisms	No. Strains	β-lactams						Aminoglycosides			FQs	Other	
		Ampicillin	Cefazolin	Ceftriaxone	Ceftazidime	Meropenem	Piperacillin-tazobactam	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Nitrofurantoin†	Trimethoprim-sulfamethoxazole
Acinetobacter baumannii	32	34	42	34	52	80	46	80	60	59	51	–‡	58
Citrobacter freundii	49	R	R	72	67	99	67	100	100	100	90	78	67
Enterobacter aerogenes	31	R	R	68	69	99	74	100	91	91	92	85	95
Enterobacter cloacae	76	R	R	61	62	99	77	99	90	90	92	81	84
E. coli	1433	36	68 ↓	96	94	99	51	99	91	92	62↓	98	65
Klebsiella pneumoniae	543	R	69	91	92	95	86	99	94	94	84	74	81↓
Morganella morganii	44	R	R	85	81	99	64	100	100	100	99	R	75
P. mirabilis	88	87	80	99	99	100	70	100	90	93	89	R	73
Pseudomonas aeruginosa	397	R	R	R	76	80	85	97	80	83	75	R	R
Salmonella spp.	32	88	–	97	–	100	91	–	–	–	90	–	86
Serratia marcescens	50	R	R	82	94	99	94	100	94	89	95	R	91
Shigella spp.	33	64	–	100	100	100	84	–	–	–	95	–	69
Stenotrophomonas maltophilia	72	R	R	R	63	R	R	R	R	R	6	R	98

* The %S for each organism/antimicrobial combination was generated by including the first isolate of that organism encountered on a given patient.
† Nitrofurantoin data from testing urine isolates only.
‡ (–) drug not tested or drug not indicated.

Appendix H. (Continued)

Shading with ↓ indicates a statistically significant decrease in %S from 2011; **NOTE:** Not all decreases in %S are clinically significant, and not all clinically significant emerging resistance is detected by changes in %S in routine antibiograms.

Abbreviations: FQ, fluoroquinolone; No., number; R, intrinsic resistance.

Example B. Organism/antimicrobial agents showing statistically significant changes in %S from 2011 to 2012

Organism	No. Strains	CFZ	CIP	SXT
E. coli	1433	68* (9%↓)†	62 (7%↓)	
K. pneumoniae	543			81 (7%↓)

NOTE: Not all decreases in %S are clinically significant, and not all clinically significant emerging resistance is detected by changes in %S in routine antibiograms.

* %S.

† Percent decrease (↓) in %S from 2011 to 2012 cumulative antibiogram.

Abbreviations: CFZ, cefazolin; CIP, ciprofloxacin; No., number; SXT, trimethoprim-sulfamethoxazole.

References for Appendix H

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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

Glossary I (Part 1). β-Lactams: Class and Subclass Designation and Generic Name

Antimicrobial Class	Antimicrobial Subclass	Agents Included; Generic Names
Penicillins	Penicillin[a]	Penicillin
	Aminopenicillin[a]	Amoxicillin Ampicillin
	Ureidopenicillin[a]	Azlocillin Mezlocillin Piperacillin
	Carboxypenicillin[a]	Carbenicillin Ticarcillin
	Penicillinase-stable penicillins[b]	Cloxacillin Dicloxacillin Methicillin Nafcillin Oxacillin
	Amidinopenicillin	Mecillinam
β-Lactam/β-lactamase inhibitor combinations		Amoxicillin-clavulanate Ampicillin-sulbactam Aztreonam-avibactam Ceftaroline-avibactam Ceftazidime-avibactam Ceftolozane-tazobactam Piperacillin-tazobactam Ticarcillin-clavulanate
Cephems (parenteral)	Cephalosporin I[c]	Cefazolin Cephalothin Cephapirin Cephradine
	Cephalosporin II[c]	Cefamandole Cefonicid Cefuroxime (parenteral)
	Cephalosporin III[c]	Cefoperazone Cefotaxime Ceftazidime Ceftizoxime Ceftriaxone
	Cephalosporin IV[c]	Cefepime
	Cephalosporins with anti-MRSA activity	Ceftaroline Ceftobiprole
	Cephamycin	Cefmetazole Cefotetan Cefoxitin
	Oxacephem	Moxalactam
Cephems (oral)	Cephalosporin	Cefaclor Cefadroxil Cefdinir Cefditoren Cefetamet Cefixime Cefpodoxime Cefprozil Ceftibuten Cefuroxime (oral) Cephalexin Cephradine
	Carbacephem	Loracarbef
Monobactams		Aztreonam
Penems	Carbapenem	Biapenem Doripenem Ertapenem Imipenem Meropenem Razupenem
	Penem	Faropenem Sulopenem

Appendix I. (Continued)
Glossary I (Part 1) (Continued)

[a] Penicillinase labile; hydrolyzed by staphylococcal penicillinase.
[b] Not hydrolyzed by staphylococcal penicillinase.
[c] Cephalosporin I, II, III, and IV are sometimes referred to as 1st-, 2nd-, 3rd-, and 4th-generation cephalosporins, respectively. Cephalosporin III and IV are also referred to as "extended-spectrum cephalosporins." This does not imply activity against ESBL-producing gram-negative bacteria.

Abbreviations: ESBL, extended-spectrum β-lactamase; MRSA, methicillin-resistant *Staphylococcus aureus.*

Appendix I. (Continued)

Glossary I (Part 2). Non–β-lactams: Class and Subclass Designation and Generic Name

Antimicrobial Class	Antimicrobial Subclass	Agents Included; Generic Names
Aminocyclitols		Spectinomycin
Aminoglycosides		Amikacin Gentamicin Kanamycin Netilmicin Plazomicin Streptomycin Tobramycin
Ansamycins		Rifampin
Folate pathway inhibitors		Iclaprim Sulfonamides Trimethoprim Trimethoprim-sulfamethoxazole
Fosfomycins		Fosfomycin
Glycopeptides	Glycopeptide	Vancomycin
	Lipoglycopeptide	Dalbavancin Oritavancin Teicoplanin Telavancin Ramoplanin
Lincosamides		Clindamycin
Lipopeptides		Daptomycin Surotomycin
	Polymyxins	Colistin Polymyxin B
Macrocyclic		Fidaxomicin
Macrolides		Azithromycin Clarithromycin Dirithromycin Erythromycin
	Ketolide	Telithromycin
	Fluoroketolide	Solithromycin
Nitrofurans		Nitrofurantoin
Nitroimidazoles		Metronidazole Tinidazole
Oxazolidinones		Linezolid Tedizolid
Phenicols		Chloramphenicol
Pseudomonic acid		Mupirocin
Quinolones	Quinolone	Cinoxacin Garenoxacin Nalidixic acid
	Fluoroquinolone	Besifloxacin Ciprofloxacin Clinafloxacin Enoxacin Finafloxacin Fleroxacin Gatifloxacin Gemifloxacin Grepafloxacin Levofloxacin Lomefloxacin Moxifloxacin Norfloxacin Ofloxacin Sparfloxacin Trovafloxacin Ulifloxacin (prulifloxacin)
Steroidal	Fusidanes	Fusidic acid
Streptogramins		Linopristin-flopristin Quinupristin-dalfopristin
Tetracyclines		Doxycycline Eravacycline Minocycline Tetracycline
	Glycylcyclines	Tigecycline
	Aminomethylcycline	Omadacycline
Thiazolide		Nitazoxanide Tizoxanide

Appendix I. (Continued)

Glossary II. Abbreviations/Routes of Administration/Drug Class for Antimicrobial Agents Listed in M100-S24

Antimicrobial Agent	Agent Abbreviation[a]	Routes of Administration[b]				Drug Class or Subclass
		PO	IM	IV	Topical	
Amikacin	AN, AK, Ak, AMI, AMK		X	X		Aminoglycoside
Amoxicillin	AMX, Amx, AMOX, AC	X				Penicillin
Amoxicillin-clavulanate	AMC, Amc, A/C, AUG, Aug, XL, AML	X				β-Lactam/β-lactamase inhibitor
Ampicillin	AM, Am, AMP	X	X	X		Penicillin
Ampicillin-sulbactam	SAM, A/S, AMS, AB			X		β-Lactam/β-lactamase inhibitor
Azithromycin	AZM, Azi, AZI, AZ	X		X		Macrolide
Azlocillin	AZ, Az, AZL		X	X		Penicillin
Aztreonam	ATM, AZT, Azt, AT, AZM			X		Monobactam
Aztreonam-avibactam	AZA			X		β-Lactam/β-lactamase inhibitor
Besifloxacin	BES				X	Fluoroquinolone
Biapenem	BPM			X		Carbapenem
Carbenicillin (indanyl salt) Carbenicillin	CB, Cb, BAR	X	 X	 X		Penicillin
Cefaclor	CEC, CCL, Cfr, FAC, CF	X				Cephem
Cefadroxil	CFR, FAD	X				Cephem
Cefamandole	MA, CM, Cfm, FAM		X	X		Cephem
Cefazolin	CZ, CFZ, Cfz, FAZ, KZ		X	X		Cephem
Cefdinir	CDR, Cdn, DIN, CD, CFD	X				Cephem
Cefditoren	CDN	X				Cephem
Cefepime	FEP, Cpe, PM, CPM		X	X		Cephem
Cefetamet	CAT, FET	X				Cephem
Cefixime	CFM, FIX, Cfe, IX	X				Cephem
Cefmetazole	CMZ, CMZS, CMT		X	X		Cephem
Cefonicid	CID, Cfc, FON, CPO		X	X		Cephem
Cefoperazone	CFP, Cfp, CPZ, PER, FOP, CP		X	X		Cephem
Cefotaxime	CTX, TAX, Cft, FOT, CT		X	X		Cephem
Cefotetan	CTT, CTN, Ctn, CTE, TANS, CN		X	X		Cephem
Cefoxitin	FOX, CX, Cfx, FX		X	X		Cephem
Cefpodoxime	CPD, Cpd, POD, PX	X				Cephem
Cefprozil	CPR, CPZ, FP	X				Cephem
Ceftaroline	CPT			X		Cephem
Ceftaroline-avibactam	CPA			X		β-Lactam/β-lactamase inhibitor
Ceftazidime	CAZ, Caz, TAZ, TZ		X	X		Cephem
Ceftazidime-avibactam	CZA			X		β-Lactam/β-lactamase inhibitor
Ceftibuten	CTB, TIB, CB	X				Cephem
Ceftizoxime	ZOX, CZX, CZ, Cz, CTZ, TIZ		X	X		Cephem
Ceftobiprole	BPR			X		Cephem
Ceftolozane-tazobactam	C/T			X		β-Lactam/β-lactamase inhibitor
Ceftriaxone	CRO, CTR, FRX, Cax, AXO, TX		X	X		Cephem
Cefuroxime (oral) Cefuroxime (parenteral)	CXM, CFX, ROX, Crm, FUR, XM	X	 X	 X		Cephem
Cephalexin	CN, LEX, CFL	X				Cephem
Cephalothin	CF, Cf, CR, CL, CEP, CE, KF			X		Cephem

Appendix I. (Continued)
Glossary II. (Continued)

Antimicrobial Agent	Agent Abbreviation[a]	Routes of Administration[b]				Drug Class or Subclass
		PO	IM	IV	Topical	
Cephapirin	CP, HAP		X	X		Cephem
Cephradine	RAD, CH	X				Cephem
Chloramphenicol	C, CHL, CL	X		X		Phenicol
Cinoxacin	CIN, Cn	X				Quinolone
Ciprofloxacin	CIP, Cp, CI	X		X		Fluoroquinolone
Clarithromycin	CLR, CLM, CLA, Cla, CH	X				Macrolide
Clinafloxacin	CFN, CLX, LF	X		X		Fluoroquinolone
Clindamycin	CC, CM, CD, Cd, CLI, DA	X	X	X		Lincosamide
Colistin	CL, CS, CT			X		Lipopeptide
Dalbavancin	DAL			X		Glycopeptide
Daptomycin	DAP			X		Lipopeptide
Dicloxacillin	DX, DIC	X				Penicillin
Dirithromycin	DTM, DT	X				Macrolide
Doripenem	DOR			X		Carbapenem
Doxycycline	DOX, DC, DOXY	X		X		Tetracycline
Eravacycline	ERV	X		X		Tetracycline
Ertapenem	ETP		X	X		Carbapenem
Erythromycin	E, ERY, EM	X		X		Macrolide
Faropenem	FAR, FARO	X				Penem
Fidaxomicin	FDX	X				Macrocyclic
Finafloxacin	FIN	X		X	X	Fluoroquinolone
Fleroxacin	FLE, Fle, FLX, FO	X		X		Fluoroquinolone
Fosfomycin	FOS, FF, FO, FM	X				Fosfomycin
Fusidic acid	FA, FC	X		X	X	Steroidal
Garenoxacin	GRN	X		X		Quinolone
Gatifloxacin	GAT	X		X		Fluoroquinolone
Gemifloxacin	GEM	X				Fluoroquinolone
Gentamicin Gentamicin synergy	GM, Gm, CN, GEN GM500, HLG, Gms		X	X		Aminoglycoside
Grepafloxacin	GRX, Grx, GRE, GP	X				Fluoroquinolone
Iclaprim	ICL			X		Folate pathway inhibitor
Imipenem	IPM, IMI, Imp, IP			X		Carbapenem
Kanamycin	K, KAN, HLK, KM		X	X		Aminoglycoside
Levofloxacin	LVX, Lvx, LEV, LEVO, LE	X		X		Fluoroquinolone
Linezolid	LNZ, LZ, LZD	X		X		Oxazolidinone
Linopristin-flopristin	LFE	X				Streptogramin
Lomefloxacin	LOM, Lmf	X				Fluoroquinolone
Loracarbef	LOR, Lor, LO	X				Cephem
Mecillinam	MEC	X				Penicillin
Meropenem	MEM, Mer, MERO, MRP, MP			X		Carbapenem
Methicillin	DP, MET, ME, SC		X	X		Penicillin
Metronidazole	MTZ	X		X		Nitroimidazole
Mezlocillin	MZ, Mz, MEZ		X	X		Penicillin
Minocycline	MI, MIN, Min, MN, MNO, MC, MH	X		X		Tetracycline
Moxalactam	MOX		X	X		Cephem
Moxifloxacin	MXF	X		X		Fluoroquinolone
Mupirocin	MUP, MOP, MU				X	Pseudomonic acid
Nafcillin	NF, NAF, Naf		X	X		Penicillin
Nalidixic acid	NA, NAL	X				Quinolone
Netilmicin	NET, Nt, NC		X	X		Aminoglycoside
Nitazoxanide	NIT	X				Thiazolide
Nitrofurantoin	F/M, FD, Fd, FT, NIT, NI, F	X				Nitrofurantoin
Norfloxacin	NOR, Nxn, NX	X				Fluoroquinolone
Ofloxacin	OFX, OFL, Ofl, OF	X	X	X		Fluoroquinolone
Omadacycline	OMC	X		X		Tetracycline

Appendix I. (Continued)
Glossary II. (Continued)

Antimicrobial Agent	Agent Abbreviation[a]	Routes of Administration[b]				Drug Class or Subclass
		PO	IM	IV	Topical	
Oritavancin	ORI			X		Lipoglycopeptide
Oxacillin	OX, Ox, OXS, OXA	X	X	X		Penicillin
Penicillin	P, PEN, PV	X	X	X		Penicillin
Piperacillin	PIP, PI, PP, Pi		X	X		Penicillin
Piperacillin-tazobactam	TZP, PTZ, P/T, PTc			X		β-Lactam/β-lactamase inhibitor combination
Plazomicin	PLZ			X		Aminoglycoside
Polymyxin B	PB			X		Lipopeptide
Quinupristin-dalfopristin	SYN, Syn, QDA, RP			X		Streptogramin
Razupenem	RZM			X		Carbapenem
Ramoplanin	RAM	X				Lipoglycopeptide
Rifampin	RA, RIF, Rif, RI, RD	X		X		Ansamycin
Solithromycin	SOL	X		X	X	Fluoroketolide
Sparfloxacin	SPX, Sfx, SPA, SO	X				Fluoroquinolone
Spectinomycin	SPT, SPE, SC		X	X		Aminocyclitol
Streptomycin Streptomycin synergy	S, STR, StS, SM, ST2000, HLS		X	X		Aminoglycoside
Sulfonamides	SSS, S3	X		X		Folate pathway inhibitor (some PO only)
Sulopenem	SLP, SULO	X		X		Penem
Surotomycin	SUR	X				Lipopeptide
Tedizolid	TZD	X		X		Oxazolidinone
Teicoplanin	TEC, TPN, Tei, TEI, TP, TPL		X	X		Glycopeptide
Telavancin	TLV			X		Lypoglycopeptide
Telithromycin	TEL	X				Ketolide
Tetracycline	TE, Te, TET, TC	X		X		Tetracycline
Ticarcillin	TIC, TC, TI, Ti		X	X		Penicillin
Ticarcillin-clavulanate	TIM, Tim, T/C, TCC, TLc			X		β-Lactam/β-lactamase inhibitor
Tigecycline	TGC			X		Glycylcycline
Tinoxanide	TIN	X				Thiazolide
Tinidazole	TNZ	X				Nitroimidazoles
Tobramycin	NN, TM, TO, To, TOB		X	X		Aminoglycoside
Trimethoprim	TMP, T, TR, W	X				Folate pathway inhibitor
Trimethoprim-sulfamethoxazole	SXT, SxT, T/S, TS, COT	X		X		Folate pathway inhibitor
Trovafloxacin	TVA, Tva, TRV, TV	X		X		Fluoroquinolone
Ulifloxacin (prulifloxacin)	PRU	X				Fluoroquinolone
Vancomycin	VA, Va, VAN	X		X		Glycopeptide

[a] Abbreviations assigned to one or more diagnostic products in the United States. If no diagnostic product is available, abbreviation is that of the manufacturer.
[b] As available in the United States.

Abbreviations: IM, intramuscular; IV, intravenous; PO, per OS (oral).

Appendix J. Intrinsic Resistance

Intrinsic resistance is defined as inherent or innate (not acquired) antimicrobial resistance, which is reflected in wild-type antimicrobial patterns of all or almost all representatives of a species. Intrinsic resistance is so common that susceptibility testing is unnecessary. For example, *Citrobacter* species are intrinsically resistant to ampicillin.

These tables can be helpful in at least three ways: 1) they provide a way to evaluate the accuracy of testing methods; 2) they aid in the recognition of common phenotypes; and 3) they can assist with verification of cumulative antimicrobial susceptibility test data. In the tables, an "R" occurring with an organism-antimicrobial combination means that strains should test resistant. A small percentage (1% to 3%) may appear susceptible due to method variation, mutation, or low levels of resistance expression.

A "susceptible" result should be viewed with caution. Ensure antimicrobial susceptibility test results and identification are accurate and reproducible. See CLSI document M100[1] Appendix A, footnote "a."

J1. *Enterobacteriaceae*

Organism \ Antimicrobial Agent	Ampicillin	Amoxicillin-clavulanate	Ampicillin-sulbactam	Piperacillin	Ticarcillin	Cephalosporin I: Cefazolin, Cephalothin	Cephamycins: Cefoxitin, Cefotetan	Cephalosporin II: Cefuroxime	Imipenem	Tetracyclines/Tigecycline	Nitrofurantoin	Polymyxin B Colistin	Aminoglycosides
Citrobacter freundii	R	R	R			R	R	R					
Citrobacter koseri	R			R	R								
Enterobacter aerogenes	R	R	R			R	R	R					
Enterobacter cloacae	R	R	R			R	R	R					
Escherichia coli	There is no intrinsic resistance to β-lactams in this organism.												
Escherichia hermannii	R				R								
Hafnia alvei	R	R	R			R	R						
Klebsiella pneumoniae	R				R								
Morganella morganii	R	R				R		R	*	R	R	R	
Proteus mirabilis	There is no intrinsic resistance to penicillins and cephalosporins in this organism.								*	R	R	R	
Proteus penneri	R					R		R	*	R	R	R	
Proteus vulgaris	R					R		R	*	R	R	R	
Providencia rettgeri	R	R				R			*	R	R	R	
Providencia stuartii	R	R				R				R	R	R	†
Salmonella and *Shigella* spp.	There is no intrinsic resistance to β-lactams in these organisms; see CLSI document M100[1] Table 2A, comment (6) for reporting.												
Serratia marcescens	R	R	R			R	R	R			R	R	
Yersinia enterocolitica	R	R			R	R							

Appendix J. (Continued)

J1. *Enterobacteriaceae* (Continued)

Warning: For *Salmonella* spp. and *Shigella* spp., first- and second-generation cephalosporins and cephamycins may appear active *in vitro*, but are not effective clinically and should not be reported as susceptible.

[*] *Proteus* species, *Providencia* species, and *Morganella* species may have elevated MICs to imipenem by mechanisms other than by production of carbapenemases. Isolates that test as susceptible should be reported as susceptible.

[†] *Providencia stuartii* should be considered resistant to gentamicin, netilmicin, and tobramycin but not intrinsically resistant to amikacin.

Abbreviations: MIC, minimal inhibitory concentration; R, resistant.

NOTE 1: Cephalosporins III, cefepime, aztreonam, ticarcillin-clavulanate, piperacillin-tazobactam, and the carbapenems are not listed, because there is no intrinsic resistance in *Enterobacteriaceae*.

NOTE 2: *Enterobacteriaceae* are also intrinsically resistant to clindamycin, daptomycin, fusidic acid, glycopeptides (vancomycin, teicoplanin), linezolid, macrolides (erythromycin, clarithromycin, azithromycin), quinupristin-dalfopristin, and rifampin.

Appendix J. (Continued)

J2. Non-*Enterobacteriaceae*

Organism \ Antimicrobial Agent	Ampicillin, Amoxicillin	Piperacillin	Ticarcillin	Ampicillin-sulbactam	Amoxicillin-clavulanate	Piperacillin-tazobactam	Cefotaxime	Ceftriaxone	Ceftazidime	Cefepime	Aztreonam	Imipenem	Meropenem	Ertapenem	Polymyxin B Colistin	Aminoglycosides	Tetracyclines/Tigecycline	Trimethoprim	Trimethoprim-sulfamethoxazole	Chloramphenicol	Fosfomycin
Acinetobacter baumannii/ Acinetobacter calcoaceticus complex	R			*	R						R			R				R		R	R
Burkholderia cepacia complex	R	R	R	R	R	R	R	R		R	R	R		R	R	R		R			R
Pseudomonas aeruginosa	R			R	R		R	R						R			R	R	R	R	R
Stenotrophomonas maltophilia	R	R	R	R	R	R	R	R			R	R	R	R		R	†	R			R

* Acinetobacter baumannii/calcoaceticus may appear to be susceptible to ampicillin-sulbactam due to the activity of sulbactam with this species.

† *Stenotrophomonas maltophilia* is intrinsically resistant to tetracycline, but not to doxycycline, minocycline, or tigecycline.

Abbreviation: R, resistant.

NOTE: These nonfermentative gram-negative bacteria are also intrinsically resistant to aminopenicillins (ampicillin, amoxicillin), cephalosporin I (cephalothin, cefazolin), cephalosporin II (cefuroxime), cephamycins (cefoxitin, cefotetan), clindamycin, daptomycin, fusidic acid, glycopeptides (vancomycin, teicoplanin), linezolid, macrolides (erythromycin, azithromycin, clarithromycin), penicillin (ie, benzylpenicillin), quinupristin-dalfopristin, and rifampin.

Appendix J. (Continued)

J3. Staphylococci

Antimicrobial Agent / Organism	Novobiocin	Fosfomycin	Fusidic Acid
S. aureus/S. lugdunensis	There is no intrinsic resistance in these species.		
S. epidermidis			
S. haemolyticus			
S. saprophyticus	R	R	R
S. capitis		R	
S. cohnii	R		
S. xylosus	R		

Abbreviation: R, resistant.

NOTE 1: Gram-positive bacteria are also intrinsically resistant to aztreonam, polymyxin B/colistin, and nalidixic acid.

NOTE 2: Oxacillin-resistant *S. aureus* and coagulase-negative staphylococci (methicillin-resistant staphylococci [MRS]), are considered resistant to other β-lactam agents, ie, penicillins, β-lactam/β-lactamase inhibitor combinations, cephems (with the exception of the cephalosporins with anti-MRSA activity), and carbapenems. This is because most cases of documented MRS infections have responded poorly to β-lactam therapy, or because convincing clinical data that document clinical efficacy for those agents have not been presented.

Appendix J. (Continued)

J4. *Enterococcus* spp.

Organism \ Antimicrobial Agent	Cephalosporins	Vancomycin	Teicoplanin	Aminoglycosides	Clindamycin	Quinupristin-dalfopristin	Trimethoprim	Trimethoprim-sulfamethoxazole	Fusidic Acid
E. faecalis	R*			R*	R*	R	R	R*	R
E. faecium	R*			R*	R*		R	R*	R
E. gallinarum / *E. casseliflavus*	R*	R		R*	R*	R	R	R*	R

* **Warning:** For *Enterococcus* spp., cephalosporins, aminoglycosides (except for high-level resistance screening), clindamycin, and trimethoprim-sulfamethoxazole may appear active *in vitro*, but are not effective clinically and should not be reported as susceptible.

Abbreviation: R, resistant.

NOTE: Gram-positive bacteria are also intrinsically resistant to aztreonam, polymyxin B/colistin and nalidixic acid.

Reference for Appendix J

[1] CLSI. *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fourth Informational Supplement.* CLSI document M100-S24. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

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
				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	X 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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Nihon Kohden Corporation (Japan)
Nissui Pharmaceutical Co., Ltd. (Japan)
Nova Biomedical Corporation (MA)
NovaBiotics (United Kingdom [GB])
Novartis Institutes for Biomedical Research (CA)
Optimer Pharmaceuticals, Inc. (CA)
Ortho-Clinical Diagnostics, Inc. (NY)
Oxyrase, Inc. (OH)
PathCare Pathology Laboratory (South Africa)
PerkinElmer (Finland)
PerkinElmer Genetics, Inc. (PA)
Pfizer Inc (PA)
Phadia AB (Sweden)
Philips Healthcare Incubator (Netherlands)
QML Pathology (Australia)
Quest Diagnostics Nichols Institute (CA)
Quotient Bioresearch Ltd. (United Kingdom [GB])
Roche Diagnostics, Inc. (Spain)
Sanofi Pasteur (PA)
Sarstedt, Inc. (NC)
Sekisui Diagnostics (MA)
Seventh Sense Biosystems (MA)
Siemens Healthcare Diagnostics Inc. (CA)
Sonic Healthcare USA (TX)
SRL Limited (India)
Streck Laboratories, Inc. (NE)
Sysmex America, Inc. (IL)
Tetraphase Pharmaceuticals (MA)
The Medicines Company (Canada)
Theranos (CA)
Theravance Inc. (CA)
Thermo Fisher Scientific (CA)
Thermo Scientific Microbiology Sdn Bhd (Malaysia)
Ventana Medical Systems Inc. (AZ)
Verinata Health, Inc. (CA)
Viracor-IBT Reference Laboratory (MO)
Wellstat Diagnostics, LLC (MD)
XDx, Inc. (CA)

Heath Care Professions/Government

14 MDSS/SGSL (MS)
436 Medical Group - Dover Air Force Base (DE)
51 MDSS/ Laboratory (AP)
59th MDW/859th MDTS/MTL (TX)
Aberdeen Royal Infirmary (United Kingdom [GB])
Academisch Ziekenhuis-VUB (Belgium)
ACG (Colombia)
ACL Laboratories (WI)
ACL Laboratories (IL)
ADNOC Medical Center (United Arab Emirates)
Advanced Laboratory Services (PA)
Adventist Health System (FL)
Adventist Medical Center (OR)
Affiliated Laboratory, Inc. (ME)
AFRIMS (Thailand)
Aga Khan University Hospital (Pakistan)
AHS Morristown (NJ)
Akron Children's Hospital (OH)
Akron General Medical Center (OH)
Al Hada Armed Forces Hospital/TAIF/KSA (Saudi Arabia)
Al Noor Hospital (United Arab Emirates)
Alamance Regional Medical Center (NC)
Alameda County Medical Center (CA)
Alaska Native Medical Center (AK)
Alaska Regional Hospital (AK)
Alaska State Public Health Laboratories (AK)
Albany College of Pharmacy & Health Sciences (NY)
Albany Medical Center Hospital (NY)
Albemarle Hospital (NC)
Albert Einstein Medical Center (PA)
Alberta Health Services (Canada)
Alexandra Health Pte Ltd (Singapore)
Alfred I. du Pont Hospital for Children (DE)
All Children's Hospital (FL)
Alliance Community Hospital (OH)
Allina Labs - 13201 (MN)
Alpena Regional Medical Center (MI)
Alta Bates Summit Medical Center (CA)
Altru Health Systems (ND)
Alvarado Hospital Medical Center Laboratory (CA)
Alverno Clinical Laboratories, Inc. (IN)
American Association for Clinical Chemistry (DC)
American Association for Laboratory Accreditation (MD)
American Hospital Dubai (United Arab Emirates)
American Medical Laboratories (Israel)
American Medical Technologists (VA)
American Society for Clinical Pathology (IL)
American Society for Microbiology (DC)
American Society of Phlebotomy Technicians (SC)
American Type Culture Collection (VA)
Ampath (South Africa)
Ann & Robert H. Lurie Children's Hospital of Chicago (IL)
Anna Jaques Hospital (MA)
Anne Arundel Medical Center (MD)
Anson General Hospital (Canada)
Appalachian Regional Healthcare System (NC)
Arhus Universitets Hospital (Denmark)
Arizona State Health Laboratory (AZ)
Arkansas Children's Hospital (AR)
Arkansas Dept of Health (AR)
Armed Forces Health Surveillance Center (AFHSC) (MD)
Arnot Ogden Medical Center Laboratory (NY)
Arrowhead Regional Medical Center (CA)
Asan Medical Center (Korea, Republic of)
Asante Health System (OR)
Ashe Memorial Hospital (NC)
Asiri Group of Hospitals Ltd. (Sri Lanka)
Aspen Valley Hospital (CO)
ASPETAR (Qatar Orthopedic and Sports Medicine Hospital) (Qatar)
Aspirus Wausau Hospital (WI)
Associação Das Pioneiras Sociais (Brazil)
Association of Public Health Laboratories (MD)
Atlantic Diagnostics Laboratories (PA)
Atlanticare Regional Medical Center (NJ)
Audie L. Murphy VA Hospital (TX)
Augusta Health (VA)
Aultman Hospital (OH)
Austin Diagnostic Clinic (TX)
Austin Health (Australia)
Austin Regional Clinic, P.A. (TX)
Austin State Hospital (TX)
Avera McKennan Laboratory (SD)
AZ Sint-Jan (Belgium)
AZ Sint-Lucas Hospital (Belgium)
Azienda Ospedale Di Lecco (Italy)
Azienda Ospedaliera Verona (Italy)
B.B.A.G. Ve U. AS., Duzen Laboratories (Turkey)
Baptist Health Medical Center (FL)
Baptist Health Medical Center-Little Rock (AR)
Baptist Health System (TX)
Baptist Hospital East (KY)
Baptist Hospital Laboratory (FL)
Baptist Hospital of Miami (FL)
Baptist Memorial Health Care Corporation - Hospital Laboratories Works (TN)
Barnes-Jewish Hospital (VT)
Bassett Healthcare (NY)
Basurto Hospital (Spain)
Baxter Regional Medical Center (AR)
Bay Area Hospital (OR)
Bay Medical Center (FL)
BayCare Health System (FL)
Bayhealth Medical Center-Kent General Hospital (DE)
Baylor Health Care System (TX)
Bayou Pathology, APMC (LA)
Baystate Medical Center (MA)
BC Centre for Disease Control (Canada)
Beaufort Delta Health and Social Services Authority (Canada)
Beebe Medical Center (DE)
Bellin Hospital (WI)
Beloit Memorial Hospital (WI)
Berkshire Medical Center (MA)
Berlin Memorial Hospital (WI)
Beth Goldstein Consultant (PA)
Beth Israel Deaconess Medical Center (MA)
Beth Israel Medical Center (NY)
Biodesign Institute At ASU (AZ)
Bio-Reference Laboratories (NJ)
Blanchard Valley Hospital (OH)
BloodCenter of Wisconsin (WI)
Blount Memorial Hospital (TN)
Blue Mountain Health System (PA)
Blue Ridge Regional Hospital (NC)
Boca Raton Community Hospital (FL)
Bon Secours Health Partners (VA)
Bon Secours Hospital (Ireland)
Boulder Community Hospital (CO)
Bozeman Deaconess Laboratory (MT)
Braintree Rehabilitation Hospital (MA)
Brandywine Hospital (PA)
Brant Community Healthcare System/Brant General Hospital (Canada)
Brazosport Regional Health System (TX)
Breathitt Veterinary Center, Murray State University (KY)
Brian All Good Community Hospital/121 Combat (CA)
Bridgeport Hospital (CT)
Bristol Hospital (CT)
British Columbia Institute of Technology (Canada)
Brockville General Hospital (Canada)
Bronson Methodist Hospital (MI)
Broward General Medical Center (FL)
Brownwood Regional Medical Center (TX)
Bryan LGH Medical Center (NE)
BSA Health System (TX)
Buena Vista Regional Medical Center (IA)
Bumrungrad Hospital (Thailand)
C. Gregory Bowling, MD APMC (LA)
Cadham Provincial Laboratory-MB Health (Canada)
California Department of Public Health (CA)
California Pacific Medical Center (CA)
Cambridge Health Alliance (MA)
Cambridge Life Science (United Kingdom [GB])
Camden Clark Memorial Hospital (WV)
Campbellford Memorial Hospital (Canada)
Canadian Science Center for Human and Animal Health (Canada)
Canadian Society for Medical Laboratory Science (Canada)
Canberra Hospital (Australia)
Cape Cod Hospital (MA)
Cape Fear Valley Medical Center Laboratory (NC)
Capital Coast Health (New Zealand)
Capital Health Regional Medical Center (NJ)
Capital Region Medical Center (MO)
Cardinal Hill Rehabilitation Hospital (KY)
Caritas Norwood Hospital (MA)
Carl R. Darnall Army Medical Center Department of Pathology (TX)
Carle Foundation Hospital (IL)
Carolinas Healthcare System (NC)
Caromont Regional Medical Center (NC)
Carpermor S.A. de C.V. (Mexico)
Carroll Hospital Center (MD)
Carteret General Hospital (NC)
Cary Medical Center (ME)
Cass County Memorial Hospital (IA)
Castle Medical Center (HI)
Catholic Health Initiatives (KY)
Catholic Medical Center (NH)
CD Diagnostics, Inc. (PA)
CDC - Nigeria (Nigeria)
Cedars-Sinai Medical Center (CA)
Cedimat Medical Center (FL)
Cellnetix Pathology & Laboratories (WA)
Center for Disease Detection (TX)
Center for Phlebotomy Education (IN)
Centers for Disease Control and Prevention (GA)
Centers for Disease Control and Prevention - Ethiopia (Ethiopia)
Centers for Disease Control and Prevention - Tanzania (Tanzania)
Centers for Medicare & Medicaid Services (MD)
Centers for Medicare & Medicaid Services/CLIA Program (TX)
Central Baptist Hospital (KY)
Central Maine Medical Center (ME)
Central Ohio Primary Care Physicians (OH)
Central Pennsylvania Alliance Laboratory (PA)
Central Vermont Medical Center (VT)
Central Washington Hospital (WA)
Centre Hospitalier Anna-Laberge (Canada)
Centre Hospitalier Lyon SUD (France)
Centro Medico Imbanaco (Colombia)
Ceylon Hospitals Limited (Sri Lanka)
CGH Medical Center (IL)
Chaleur Regional Hospital (Canada)
Chambersburg Hospital (PA)
Champlain Valley Physicians Hospital (NY)
Chang Gung Memorial Hospital (Taiwan)
Charleston Area Medical Center (WV)
Chatham - Kent Health Alliance (Canada)
Chesapeake General Hospital (VA)
Chester County Hospital (PA)
Cheyenne Regional Medical Center (WY)
Chi Solutions, Inc. (MI)
Chia-Yi Chang Gung Memorial Hospital (Taiwan)
Chickasaw Nation Division of Health - Chickasaw Nation Medical Center (OK)
Children's Healthcare of Atlanta (GA)
Childrens Hosp.- Kings Daughters (VA)
Children's Hospital (AL)
Children's Hospital & Medical Center (NE)
Children's Hospital Boston (MA)
Childrens Hospital Los Angeles (CA)
Children's Hospital of Central California (CA)
Children's Hospital of Philadelphia (PA)
Childrens Hospital of Wisconsin (WI)
Children's Hospitals and Clinics (MN)
Children's Medical Center (TX)
Chilton Memorial Hospital (NJ)
Chinese Committee for Clinical Laboratory Standards (China)
Chino Valley Medical Center (CA)
Christiana Care Health Services (DE)
Christus Santa Rosa-Westover Hills (TX)
Christus Spohn Hospital Beeville (TX)
Christus St. Patrick Hospital (LA)
CHU Sainte-Justine: Department of Microbiology and Immunology (Canada)
CHUM Hospital Saint-Luc (Canada)
CHW-St. Mary's Medical Center (CA)
Cibola General Hospital (NM)
Cincinnati Children's Hospital Medical Center (OH)
Citizens Memorial Hospital (MO)
City of Hope National Medical Center (CA)

City of Milwaukee Health Department (WI)
Clara Maass Medical Center (NJ)
Cleveland Clinic (OH)
Clifton Fine Hospital (NY)
Clinica Alemana De Santiago (Chile)
Clinica Hospital San Fernando (Panama)
Clinical and Laboratory Standards Institute (PA)
Clinical Hospital Merkur (Croatia/Hrvatska)
Clinique St. Luc (Belgium)
CLMA (IL)
CML HealthCare (Canada)
COLA (MD)
College of American Pathologists (IL)
College of Physicians and Surgeons of Alberta (Canada)
College of Physicians and Surgeons of Saskatchewan (Canada)
College of the North Atlantic (Canada)
College of Veterinary Medicine, Auburn University (AL)
Collingwood General & Marine Hospital (Canada)
Collom & Carney Clinic (TX)
Columbia Memorial Hospital (NY)
Columbia Memorial Hospital (OR)
Columbus Regional Healthcare System (NC)
Commonwealth of Kentucky (KY)
Commonwealth of Virginia (DCLS) (VA)
Community College of Rhode Island-Flanagan Campus (RI)
Community Hospital (IN)
Community Hospital of the Monterey Peninsula (CA)
Community Hospitals of Williams County (OH)
Community Medical Center (MT)
Community Medical Center (NJ)
Complexe Hospitalier de la Sagamie (Canada)
CompuNet Clinical Laboratories (OH)
Coney Island Hospital (NY)
Consultants Laboratory of WI LLC (WI)
Contra Costa Regional Medical Center (CA)
Conway Medical Center (SC)
Cook Children's Medical Center (TX)
Cookeville Regional Medical Center (TN)
Cooper University Hospital (NJ)
Countess of Chester Hospital (United Kingdom [GB])
Counties Manukau District Health Board, Middlemore Hospital (New Zealand)
Covance CLS (IN)
Covenant Medical Center (TX)
Crozer-Chester Medical Center (PA)
CSSS Alphonse-Desjardins (Canada)
CSSS Du Sud De Lanaudiere (Canada)
CSSS Papineau/Hopital de Papineau (Canada)
CSSS St-Jerome (Canada)
Cyruss Tsurgeon (LA)
Dameron Hospital Association (CA)
Danbury Hospital (CT)
Darwin Health Library, NT Dept. of Health (Australia)
Daviess Community Hospital (IN)
Dayton Children's Medical Center (OH)
Deaconess Hospital Laboratory (IN)
Dean Medical Center (WI)
Delaware Public Health Laboratory (DE)
Delnor Community Hospital (IL)
Delta Regional Medical Center (MS)
Denver Health Medical Center (CO)
Department of Veterans Affairs (DC)
DHHS NC State Lab of Public Health (NC)
Diagnostic Accreditation Program (Canada)
Diagnostic Center for Population & Animal Health (MI)
Diagnostic Laboratory Medicine, Inc. (MA)
Diagnostic Laboratory Services, Inc. (HI)
Diagnostic Medicine Services (Iceland)
Diagnostic Services of Manitoba (Canada)
Dialysis Clinic, Inc. Laboratory (TN)
Dimensions Healthcare System Prince George's Hospital Center (MD)
DMC University Laboratories (MI)
Docro, Inc. (CT)
DoctorsManagement (TN)
Donalsonville Hospital (GA)
Door County Medical Center (WI)
Dr Sulaiman Al Habib Medical Group (Saudi Arabia)
Drug Scan Inc. (PA)
DuBois Regional Medical Center (PA)
DUHS Clinical Laboratories (NC)
Duke University Medical Center (NC)
Dynacare Laboratory (WI)
Dynacare NW, Inc - Seattle (WA)
DynaLIFE (Canada)
E. A. Conway Medical Center (LA)
East Houston Regional Medical Center (TX)
East Texas Medical Center - Tyler (TX)
East Texas Medical Center (ETMC) Henderson (TX)
East Texas Medical Center-Pittsburg (TX)
Eastern Gateway Community College (OH)
Eastern Health - Health Sciences Centre (Canada)
Eastern Health Pathology (Australia)
Eastern Ontario Regional Laboratory Association (EORLA) (Canada)
Easton Hospital (PA)
Edgerton Hospital & Health Services (WI)
Edmonds Community College (WA)
Edward Hospital (IL)
Effingham Hospital (GA)
Emerson Hospital Laboratory (MA)
Emory University Hospital (GA)
Emory University School of Medicine (GA)
Empire College (CA)
Ephrata Community Hospital (PA)
Erie County Medical Center Corporation (NY)
Erlanger Health Systems (TN)
ESCMID (Switzerland)
Estes Park Medical Center (CO)
Ethiopian Health and Nutrition Research Institute (Ethiopia)
Evangelical Community Hospital (PA)
Evans Army Community Hospital (CO)
Evanston Hospital, NorthShore University HealthSystem (IL)
Exempla - Saint Joseph Hospital (CO)
Exempla Lutheran Medical Center (CO)
Fairfax County Health Department (VA)
Farrer Park Hospital (Singapore)
Fauquier Hospital (VA)
Fayette County Memorial Hospital (OH)
FDA Ctr. for Devices/Rad. Health (CDRH) (MD)
Federal Medical Center (MN)
Firelands Regional Medical Center (OH)
Fisher-Titus Memorial Hospital (OH)
Flagler Hospital Inc. (FL)
Fletcher Allen Health Care (VT)
Fleury S.A. (Brazil)
Florida Department of Health (FL)
Forrest General Hospital (MS)
Forsyth Medical Center (NC)
Fort Loudoun Medical Center (TN)
Fox Chase Cancer Center (PA)
Franklin Memorial Hospital (ME)
Fresno Community Hospital & Medical Center (CA)
Ft. Belvoir Community Hospital (VA)
Fundacao Faculdade de Medicina (Brazil)
Fundacion Mexicana Para la Salud Capitulo Peninsular A.C (Mexico)
Gamma-Dynacare Laboratories (Canada)
Garden City Hospital (MI)
Gateway Regional Medical Center (IL)
Geary Community Hospital (KS)
Geisinger Medical Center (PA)
Genesis Healthcare System (OH)
Genesis Laboratory Management (NJ)
Genesis Medical Center (IL)
Genome DX (Canada)
George Mason University (VA)
Ghent University Hospital (Belgium)
Glasgow Royal Infirmary (United Kingdom [GB])
Golden Valley Memorial Hospital (MO)
Golwilkar Metropolis (India)
Good Samaritan Hospital (IN)
Good Samaritan Hospital Medical Center (NY)
Good Shepherd Medical Center (TX)
Gottlieb Memorial Hospital (IL)
Grady Memorial Hospital (GA)
Grana S.A. (TX)
Grand River Hospital (Canada)
Grays Harbor Community Hospital (WA)
Great Plains Regional Med. Ctr. (NE)
Great River Medical Center (IA)
Greater Lowell Pediatrics (MA)
Greensboro Pathology (NC)
Greenville Memorial Medical Campus (SC)
Grey Bruce Regional Health Center (Canada)
Gritman Medical Center (ID)
Group Health Cooperative (WA)
Grove City Medical Center (PA)
Guelph General Hospital (Canada)
Gulf Medical College Hospital & Research Centre (United Arab Emirates)
Gundersen Lutheran Medical Center (WI)
Gunnison Valley Hospital (CO)
Guthrie Clinic Laboratories (PA)
Gwinnett Medical Center (GA)
Halton Healthcare Services (Canada)
Hamad Medical Corp-DLMP LAB QM (Qatar)
Hamilton Hospital (TX)
Hamilton Regional Laboratory Medicine Program - St. Joseph's (Canada)
Hanover General Hospital (PA)
Harbor - UCLA Medical Center (CA)
Hardy Diagnostics (CA)
Harford Memorial Hospital (MD)
Harris Methodist HEB Hospital (TX)
Harris Methodist Hospital Southwest (TX)
Hartford Hospital (CT)
Harvard Vanguard Medical Associates (MA)
Hawaii Pathologists Laboratory (HI)
Hawaii State Hospital (HI)
Healdsburg District Hospital (CA)
Health Canada (Canada)
Health Network Lab (PA)
Health Waikato (New Zealand)
Healthscope Pathology (Australia)
Heartland Health (MO)
Helen Hayes Hospital (NY)
Hendrick Regional Laboratory (TX)
Hendricks Regional Health (IN)
Henrico Doctors' Hospital - Parham (VA)
Henry Ford Hospital (MI)
Henry M. Jackson Foundation for the Advancement of Military Medicine-MD (MD)
Henry M. Jackson Foundation-Brook Army Medical Ctr (BAMC) (TX)
Hi-Desert Medical Center (CA)
Highlands Medical Center (AL)
Hillcrest Medical Center (OK)
Hinsdale Pathology Associates (IL)
Hoag Memorial Hospital Presbyterian (CA)
Holstebro Hospital (Denmark)
Holy Name Hospital (NJ)
Holy Redeemer Hospital & Medical Center (PA)
Holy Spirit Hospital (PA)
Holzer Health System (OH)
Hong Kong Accreditation Service Innovation and Technology Commission (Hong Kong)
Hong Kong Sanatorium & Hospital (Hong Kong)
Hopital Charles Lemoyne (Canada)
Hopital Cite de La Sante De Laval (Canada)
Hopital de Granby-CSSS Haute-Yamaska (Canada)
Hopital Maisonneuve-Rosemont (Canada)
Hopital Santa Cabrini Ospedale (Canada)
Hopkins County Memorial Hospital (TX)
Horizon Health Network (Canada)
Hospital Albert Einstein (Brazil)
Hospital de Tjongerschans (Netherlands)
Hospital Italiano Laboratorio Central (Argentina)
Hospital Sacre-Coeur de Montreal (Canada)
Hotel Dieu Grace Hospital Library (Canada)
Houston Medical Center (GA)
Hunt Regional Healthcare (TX)
Hunterdon Medical Center (NJ)
Huntington Memorial Hospital (CA)
Hutchinson Clinic, P.A. (KS)
Hutt Valley Health District Health Board (New Zealand)
IDEXX Reference Laboratories (Canada)
Indiana University - Chlamydia Laboratory (IN)
Indiana University Health Bloomington Hospital (IN)
Indiana University Health Care - Pathology Laboratory (IN)
Industrial Technology Research Institute (ITRI) (Taiwan)
INEI-ANLIS "Dr. C. G. Malbrán" (Argentina)
Ingalls Hospital (IL)
Inova Central Laboratory (VA)
Institut National de Sante Publique du Quebec (Canada)
Institute Health Laboratories (PR)
Institute of Public Health (Slovenia)
Institute of Tropical Medicine Dept. of Clinical Sciences (Belgium)
Institute of Veterinary Bacteriology (Switzerland)
Integrated BioBank (Luxembourg)
Integrated Diagnositcs (WA)
Integrated Regional Laboratories (HCA) (FL)
Interim LSU Hospital/Med. Center of La (LA)
Interior Health (Canada)
International Accreditation New Zealand (New Zealand)
International Federation of Clinical Chemistry (Italy)
International Health Management Associates, Inc. (IL)
Irwin Army Community Hospital (KS)
Istituto Cantonale Di Microbiologia (Switzerland)
Jackson County Memorial Hospital (OK)
Jackson Health System (FL)
Jackson Hospital & Clinic, Inc. (AL)
Jackson Purchase Medical Center (KY)
Jameson Memorial Hospital (PA)
Japan Assn. of Clinical Reagents Industries (Japan)
Jeanetics Laboratory Consulting, LLc (CA)
Jefferson Memorial Hospital (WV)
Jefferson Regional Medical Center (PA)
Jennings American Legion Hospital (LA)
Jersey Shore University Medical Center (NJ)
Jessa Ziekenhuis VZW (Belgium)
Jiao Tong University School of Medicine - Shanghai No. 3 People's Hospital (China)
John C. Lincoln Hospital - N.MT. (AZ)
John D. Archbold Hospital (GA)
John F. Kennedy Medical Center (NJ)
John H. Stroger, Jr. Hospital of Cook County (IL)
John Hopkins APL (MD)
John Muir Health (CA)
Johns Hopkins Medical Institutions (MD)
Johnson City Medical Center Hospital (TN)
Jonathan M. Wainwright Memorial Veterans Affairs Medical Center (WA)
Jones Memorial Hospital (NY)
Jordan Valley Community Health Center (MO)
JPS Health Network (TX)
Jupiter Medical Center (FL)
Kaiser Medical Laboratory (HI)
Kaiser Permanente (GA)
Kaiser Permanente (MD)
Kaiser Permanente Colorado (CO)
Kaiser Permanente Medical Care (CA)
Kaiser Permanente San Francisco (CA)
Kaleida Health Center for Laboratory Medicine (NY)
Kalispell Regional Medical Center (MT)
Kansas State University (KS)
Kaohsiun Chang Gung Memorial Hospital (Taiwan)
Karmanos Cancer Institute (MI)
KCHL St. Elisabeth Hospital (Netherlands)
Keck Hospital of USC (CA)
Keck School of Medicine-USC (CA)
Keelung Chang Gung Memorial Hospital (Taiwan)
Keller Army Community Hospital (NY)
Kennedy Health System (NJ)
Kenora-Rainy River Reg. Lab. Program (Canada)
Kindred Healthcare (KY)
King Abdulaziz Hospital (Saudi Arabia)
King Abdulaziz Medical City-NGHA/DPLM-Riyadh (Saudi Arabia)
King Fahad Specialist Hospital-Dammam, K.S.A. (Saudi Arabia)
King Faisal Specialist Hospital & Research Center (Saudi Arabia)
King Hussein Cancer Center (Jordan)
Kingsbrook Jewish Medical Center (NY)
Kingston General Hospital (Canada)
KK Women's & Children's Hospital (Singapore)
Kuakini Health System (HI)
Kuwait Cancer Control Center (Kuwait)
Kyoto University Hospital (Japan)
La Rabida Childrens Hospital (IL)
Lab Express (AZ)
Lab Médico Santa Luzia LTDA (Brazil)
Labor Stein + Kollegen (Germany)
Laboratorio Bueso Arias (Honduras)
Laboratorio Clinico Amadita P. de Gonzales S.A. (FL)
Laboratorio Médico De Referencia (Colombia)
Laboratory Alliance of Central New York (NY)
Laboratory for Medical Microbiology and Infectious Diseases (Netherlands)
Laboratory Medicin Dalarna (Sweden)
Laboratory of Clinical Biology Ziekenhuis Oost-Limburg (ZOL) (Belgium)
Laboratory of Veterinary Medicine (Luxembourg)
LabPlus Auckland District Health Board (New Zealand)
LAC/USC Medical Center (CA)
Lafayette General Medical Center (LA)
Lahey Clinic (MA)
Lake Charles Memorial Hospital (LA)

Lake Norman Regional Medical Center (NC)
Lakeland Regional Laboratories (MI)
Lakeland Regional Medical Center (FL)
Lakeridge Health Corporation - Oshawa Site (Canada)
Lakeview Medical Center (WI)
Lamb Healthcare Center (TX)
Lancaster General Hospital (PA)
Landstuhl Regional Medical Center (AE)
Lane Regional Medical Center (LA)
Lawrence and Memorial Hospitals (CT)
LeBonheur Children's Hospital (TN)
Lee Memorial Hospital (FL)
Legacy Laboratory Services (OR)
Leiden University Medical Center (Netherlands)
LewisGale Hospital Montgomery (VA)
Lewis-Gale Medical Center (VA)
Lexington Medical Center (SC)
L'Hotel-Dieu de Quebec (Canada)
Licking Memorial Hospital (OH)
LifeBridge Health Sinai Hospital (MD)
LifeCare Medical Center (MN)
Little Company of Mary Hospital (IL)
Littleton Regional Healthcare (NH)
Lodi Memorial Hospital (CA)
Lompoc Valley Medical Center (CA)
London Health Sciences Center (Canada)
Long Beach Memorial Medical Center-LBMMC (CA)
Long Island Jewish Medical Center (NY)
Longmont United Hospital (CO)
Longview Regional Medical Center (TX)
Louisiana Office of Public Health Laboratory (LA)
Louisiana State University Medical Ctr. (LA)
Lower Mainland Laboratories (Canada)
Luke Thiboutot (MA)
Luminex Corporation (TX)
Lummi Tribal Health Center (WA)
Lutheran Hospital of Indiana Inc. (IN)
Lynchburg General (VA)
Lyndon B. Johnson General Hospital (TX)
Lyster Army Health Clinic (AL)
MA Dept. of Public Health Laboratories (MA)
Mackenzie Health (Canada)
Madigan Army Medical Center (WA)
Mafraq Hospital (United Arab Emirates)
Magnolia Regional Health Center (MS)
Main Line Clinical Laboratories, Inc. Lankenau Hospital (PA)
Maine General Medical Center (ME)
Mammoth Hospital Laboratory (CA)
Maria Parham Medical Center (NC)
Marietta Memorial Hospital (OH)
Marin General Hospital (CA)
Marion County Public Health Department (IN)
Marquette General Hospital (MI)
Marshfield Clinic (WI)
Martha Jefferson Hospital (VA)
Martin Luther King, Jr./Drew Medical Center (CA)
Martin Memorial Health Systems (FL)
Mary Greeley Medical Center (IA)
Mary Hitchcock Memorial Hospital (NH)
Mary Washington Hospital (VA)
Massachusetts General Hospital (MA)
Massasoit Community College (MA)
Mater Health Services - Pathology (Australia)
Maury Regional Hospital (TN)
Mayo Clinic (MN)
Mayo Clinic Health Systems in Waycross (GA)
Mayo Clinic Scottsdale (AZ)
McAlester Regional Health Center (OK)
McAllen Medical Center (TX)
McCullough-Hyde Memorial Hospital (OH)
MCG Health (GA)
McLaren Northern Michigan (MI)
MCN Healthcare (CO)
Meadows Regional Medical Center (GA)
Meadville Medical Center (PA)
Med Health Services Laboratory (PA)
Med. Laboratories Duesseldorf (Germany)
Medecin Microbiologiste (Canada)
Media Lab, Inc. (GA)
Medibus (Canada)
Medical Center Enterprise (AL)
Medical Center Hospital (TX)
Medical Center of Central Georgia (GA)
Medical Centre Ljubljana (Slovenia)
Medical College of Virginia Hospital (VA)
Medical Laboratories of Windsor, LTD (Canada)
Medical Laboratory Sciences Council of Nigeria (Nigeria)
Medical University Hospital Authority (SC)
Medical, Laboratory & Technology Consultants, LLC (DC)
Medlab Central (New Zealand)
Medlab Ghana Ltd. (Ghana)
Medstar Health (DC)
Memorial Health System (CO)
Memorial Hermann Healthcare System (TX)
Memorial Hospital at Gulfport (MS)
Memorial Hospital of Carbondale (IL)
Memorial Hospital of Rhode Island (RI)
Memorial Hospital of Texas County (OK)
Memorial Medical Center (PA)
Memorial Medical Center (IL)
Memorial Medical Center (TX)
Memorial Regional Hospital (FL)
Memorial Sloan Kettering Cancer Center (NY)
Menonnite General Hospital (PR)
Mercy Franciscan Mt. Airy (OH)
Mercy Health Center (OK)
Mercy Hospital (IA)
Mercy Hospital (MN)
Mercy Hospital Jefferson (MO)
Mercy Hospital of Tiffin (OH)
Mercy Hospital St. Louis (MO)
Mercy Integrated Laboratories / Mercy St. Vincent (OH)
Mercy Medical Center (CA)
Mercy Medical Center (IA)
Mercy Medical Center (MD)
Mercy Medical Center (OH)
Mercy Regional Medical Center (OH)
Meritus Medical Laboratory (MD)
Methodist Dallas Medical Center (TX)
Methodist Healthcare (TN)
Methodist Hospital (TX)
Methodist Hospital Pathology (NE)
Methodist Medical Center (TN)
Methodist Sugarland Hospital (TX)
MetroHealth Medical Center (OH)
Metropolitan Hospital Center (NY)
Miami Children's Hospital (FL)
Michigan Dept. of Community Health (MI)
Michigan State University (MI)
Microbial Research, Inc. (CO)
Microbiology Specialists, Inc. (TX)
Mid America Clinical Laboratories (IN)
Mid Coast Hospital (ME)
Middelheim General Hospital (Belgium)
Middlesex Hospital (CT)
Midland Memorial Hospital (TX)
Mile Bluff Medical Center/Hess Memorial Hospital (WI)
Milford Regional Hospital (MA)
Ministry of Health - Zambia (Zambia)
Ministry of Health and Social Welfare - Tanzania (Tanzania)
Minneapolis Community and Technical College (MN)
Minneapolis Medical Research Foundation (MN)
Minnesota Department of Health (MN)
MiraVista Diagnostics (IN)
Mission Hospitals Laboratory (NC)
Mississippi Baptist Medical Center (MS)
Mississippi Public Health Lab (MS)
Missouri State Public Health Laboratory (MO)
Mobile Infirmary Association (AL)
Modesto Memorial Hospital (CA)
MolecularMD Corp. (OR)
Monadnock Community Hospital (NH)
Mongolian Agency for Standardization and Metrology (Mongolia)
Monongahela Valley Hospital (PA)
Monongalia General Hospital (WV)
Montana Department of Public Health and Human Services (MT)
Montefiore Medical Center (NY)
Morehead Memorial Hospital (NC)
Morristown Hamblen Hospital (TN)
Mount Nittany Medical Center (PA)
Mt. Auburn Hospital (MA)
Mt. Sinai Hospital (Canada)
Mt. Sinai Hospital - New York (NY)
Mt. Sinai Hospital Medical Center (IL)
MultiCare Health Systems (WA)
Muskoka Algonquin Healthcare (Canada)
Nacogdoches Memorial Hospital (TX)
Nanticoke Memorial Hospital (DE)
Nash General Hospital/Laboratory (NC)
Nassau County Medical Center (NY)
National Cancer Institute, CCR, LP (MD)
National Cancer Institute, CDP, NIH (MD)
National Food Institute Technical University of Denmark (Denmark)
National Health Laboratory Service C/O F&M Import & Export Services (South Africa)
National Institute of Health (Thailand)
National Institute of Health-Maputo, Mozambique (Mozambique)
National Institutes of Health Department of Lab Medicine (MD)
National Jewish Health (CO)
National Pathology Accreditation Advisory Council (Australia)
National Society for Histotechnology, Inc. (MD)
National University Hospital (Singapore) Pte Ltd (Singapore)
National University of Ireland, Galway (NUIG) (Ireland)
National Veterinary Institute (Sweden)
Nationwide Children's Hospital (OH)
Naval Hospital Lemoore (CA)
Naval Hospital Oak Harbor (WA)
Naval Medical Center San Diego (CA)
NB Department of Health (Canada)
Nebraska LabLine (NE)
Nellis Air Force Base (NV)
Netlab SA (Ecuador)
New Brunswick Community College (Canada)
New Brunswick Provincial Veterinary Laboratory (Canada)
New Dar Al Shifa Hospital - Kuwait (Kuwait)
New England Baptist Hospital (MA)
New Hampshire Public Health Labs. (NH)
New Hanover Regional Medical Center (NC)
New Lexington Clinic (KY)
New London Hospital (NH)
New Medical Centre Hospital (United Arab Emirates)
New York City Department of Health and Mental Hygiene (NY)
New York Eye and Ear Infirmary (NY)
New York Presbyterian Hospital (NY)
New York State Dept. of Health (NY)
New York University Medical Center (NY)
New Zealand Blood Service (New Zealand)
Newark Beth Israel Medical Center (NJ)
Newborn Metabolic Screening Program/ Alberta Health Services (Canada)
Newman Regional Health (KS)
Niagara Health System (Canada)
Ninewells Hospital and Medical School (United Kingdom [GB])
Noble's Hospital (United Kingdom [GB])
NorDx - Scarborough Campus (ME)
Norman Regional Hospital (OK)
North Bay Regional Health Center (Canada)
North Carolina Baptist Hospital (NC)
North District Hospital (China)
North Kansas City Hospital (MO)
North Oaks Medical Center (LA)
North Philadelphia Health System-St. Joseph's Hospital (PA)
North Shore Hospital Laboratory (New Zealand)
North Shore Medical Center (MA)
North Shore-Long Island Jewish Health System Laboratories (NY)
North Vista Hospital (NV)
North York General Hospital (Canada)
Northcrest Medical Center (TN)
Northeast Georgia Health System (GA)
Northeastern Vermont Regional Hospital (VT)
Northfield Hospital & Clinics (MN)
Northridge Hospital Medical Center (CA)
Northside Hospital (GA)
Northside Medical Center (OH)
Northumberland Hills Hospital (Canada)
Northwest Arkansas Pathology Associates (AR)
Northwestern Medical Center, Inc. (VT)
Northwestern Memorial Hospital (IL)
Norton Healthcare (KY)
Norwalk Hospital (CT)
Notre Dame Hospital (Canada)
Nova Scotia Association of Clinical Laboratory Managers (Canada)
Nova Scotia Community College (Canada)
Novus Path Labs (India)
NSW Health Pathology (Australia)
NW Physicians Lab (WA)
Oakton Community College (IL)
Ocean County Medical Laboratories (NJ)
Ochsner Clinic Foundation (LA)
Octapharma Plasma (NC)
Odense University Hospital (Denmark)
Office of Medical Services Laboratory (DC)
Ohio Health Laboratory Services (OH)
Ohio State University Hospitals (OH)
Ohio Valley Medical Center (WV)
Oklahoma Heart Hospital, LLC (OK)
Oklahoma State University: Center for Health Sciences (OK)
Olive View-UCLA Medical Center (CA)
Olmsted Medical Center Laboratory (MN)
Ontario Medical Association Quality Management Program-Laboratory Service (Canada)
Onze Lieve Vrouwziekenhuis (Belgium)
Orange County Community College (NY)
Orange Park Medical Center (FL)
Ordre Professionnel Des Technologistes Médicaux Du Québec (Canada)
Orebro University Hospital (Sweden)
Oregon Health and Science University (OR)
Oregon Public Health Laboratory (OR)
Orillia Soldiers Memorial Hospital (Canada)
Orlando Health (FL)
OSF - Saint Anthony Medical Center (IL)
OSU Veterinary Diagnostic Laboratory (OR)
Ottawa Regional Hospital & Healthcare Center (IL)
OU Medical Center (OK)
Our Lady of the Lake Regional Medical Center/FMOL Health System (LA)
Our Lady's Hospital for Sick Children (Ireland)
Overlake Hospital Medical Center (WA)
Ozarks Medical Center (MO)
PA Veterinary Laboratory (PA)
Pacific Diagnostic Laboratories (CA)
Palmer Lutheran Health Center (IA)
Palmetto Baptist Medical Center (SC)
Palmetto Health Baptist Easley (SC)
Palo Alto Medical Foundation (CA)
Pamela Youde Nethersole Eastern Hospital (Hong Kong East Cluster) (Hong Kong)
Paris Community Hospital (IL)
Park Nicollet Methodist Hospital (MN)
Parkview Adventist Medical Center (ME)
Parkview Health Laboratories (IN)
Parkwest Medical Center (TN)
Parrish Medical Center (FL)
Pathgroup (TN)
Pathlab (IA)
Pathology Associates Medical Lab. (WA)
PathWest Laboratory Medicine WA (Australia)
Pavia Hospital Santurce (PR)
PeaceHealth Laboratories (OR)
Peninsula Regional Medical Center (MD)
Penn State Hershey Medical Center (PA)
Pennsylvania Dept. of Health (PA)
Pennsylvania Hospital (PA)
Peoria Tazewell Pathology Group, P.C. (IL)
PEPFAR Tanzania (PA)
PerkinElmer Health Sciences, Inc. (SC)
Peterborough Regional Health Centre (Canada)
Peterson Regional Medical Center (TX)
PHIA Project, NER (CO)
Phoebe Putney Memorial Hospital (GA)
Phoenix Children's Hospital (AZ)
Phoenixville Hospital (PA)
Physicians Choice Laboratory Services (NC)
Physicians Laboratory & SouthEast Community College (NE)
Physicians Preferred Laboratory (TX)
Piedmont Atlanta Hospital (GA)
Piedmont Henry Hospital (GA)
Pioneers Memorial Health Care District (CA)
Placer County Public Health Laboratory (CA)
Plains Memorial Hospital (TX)
Pocono Medical Center School of Medical Technology (PA)
Portneuf Medical Center (ID)
Poudre Valley Hospital (CO)
Prairie Lakes Hospital (SD)
Presbyterian Hospital - Laboratory (NC)
Presbyterian/St. Luke's Medical Center (CO)
Preventive Medicine Foundation (Taiwan)
Prince George Regional Hospital (Canada)
Princess Margaret Hospital (Hong Kong)
Proasecal LTD (Colombia)
ProMedica Laboratory (OH)
Prometheus Laboratories Inc. (CA)
Providence Alaska Medical Center (AK)
Providence Everett Medical Center (WA)
Providence Hospital (AL)
Providence St. Joseph Medical Center (CA)
Providence St. Mary Medical Center (WA)
Provista Diagnostics (AZ)
Public Health Ontario (Canada)
Puget Sound Blood Center (WA)
Pullman Regional Hospital (WA)
Queen Elizabeth Hospital (Canada)
Queen Elizabeth Hospital (China)
Queensland Health Pathology Services (Australia)

Quest - A Society for Adult Support and Rehabilitation (Canada)
Quinte Healthcare Corp. - Belleville General Site (Canada)
Quintiles Laboratories, Ltd. (GA)
Ramathibodi Hospital (Thailand)
Randers Regional Hospital (Denmark)
Range Regional Health Services (MN)
Rapides Regional Medical Center (LA)
Rappahannock General Hospital (VA)
RCPA Quality Assurance Programs Pty Limited (Australia)
Reading Hospital (PA)
Redlands Community Hospital (CA)
Regina Qu'Appelle Health Region (Canada)
Regional Laboratory of Public Health (Netherlands)
Regional Medical Laboratory, Inc. (OK)
Regions Hospital (MN)
Rehoboth McKinley Christian Health Care Services (NM)
Reid Hospital & Health Care Services (IN)
Renown Regional Medical Center (NV)
Research Institute of Tropical Medicine (Philippines)
Rhode Island Dept. of Health Labs (RI)
Rhode Island Hospital (RI)
Rice Memorial Hospital (MN)
Ridgeview Medical Center (MN)
Riverside Community Hospital (CA)
Riverside Health System (VA)
Riverton Memorial Hospital (WY)
Riverview Healthcare Assoc. (MN)
Riyadh Armed Forces Hospital, Sulaymainia (Saudi Arabia)
RMIT University (Australia)
Robert E. Bush Naval Hospital (CA)
Robert Wood Johnson University Hospital (NJ)
Robert Wood Johnson University Hospital Rahway (NJ)
Rochester General Hospital (NY)
Rockford Memorial Hospital (IL)
Roger Williams Medical Center (RI)
Roosevelt General Hospital (NM)
Roper St. Francis Healthcare (SC)
Ross University School of Veterinary Medicine (Saint Kitts and Nevis)
Roswell Park Cancer Institute (NY)
Rouge Valley Health System (Canada)
Royal Children's Hospital (Australia)
Royal Hobart Hospital (Australia)
Royal Victoria Hospital (Canada)
Rush Copley Medical Center (IL)
Rush Health Systems (MS)
Rush University Medical Center (IL)
Russellville Hospital (AL)
SA Pathology (Australia)
SAAD Specialist Hospital (Saudi Arabia)
Sacred Heart - St. Mary's Hospital Inc (WI)
Sacred Heart Hospital (FL)
Sacred Heart Hospital (WI)
Saddleback Memorial Medical Center (CA)
Sahlgrenska Universitetssjukhuset (Sweden)
Saint Francis Hospital & Medical Center (CT)
Saint Francis Medical Center (IL)
Saint Mary's Regional Medical Center (NV)
Salem Hospital (OR)
Salisbury University (MD)
Salzburger Landeskliniken (SALK) (Austria)
Samaritan Health Services (OR)
Samaritan Regional Health System (OH)
Samkwang Medical Laboratory (Korea, Republic of)
Sampson Regional Medical Center (NC)
Samsung Medical Center (Korea, Republic of)
San Angelo Community Medical Center (TX)
San Francisco General Hospital-University of California San Francisco (CA)
San Jose State University (CA)
San Juan Regional Medical Group (NM)
Sanford Health (ND)
Sanford USD Medical Center (SD)
Santa Clara Valley Health & Hospital Systems (CA)
Santa Rosa Medical Center (FL)
Santiam Memorial Hospital (OR)
Sarasota Memorial Hospital (FL)
Saratoga Hospital (NY)
SARL Laboratoire Caron (France)
Saskatchewan Disease Control Laboratory (Canada)
Saskatoon Health Region (Canada)
Saudi Aramco Medical (TX)
SC Department of Health and Environmental Control (SC)
Schneck Medical Center (IN)
School of Animal and Veterinary Science, University of Adelaide (Australia)
Schuyler Hospital (NY)
Scientific Institute of Public Health (Belgium)
Scott & White Memorial Hospital (TX)
Scripps Health (CA)
Scuola Di Specializzaaione- University Milano Bicocca (Italy)
Seattle Cancer Care Alliance (WA)
Seattle Children's Hospital/Children's Hospital and Regional Medical Center (WA)
Sel Lam Terral (France)
Seminole Hospital District (TX)
Sentara Healthcare (VA)
Sentinel CH SpA (Italy)
Seoul National University Hospital (Korea, Republic of)
Seton Healthcare Network (TX)
Seton Medical Center (CA)
Shands Jacksonville (FL)
Shared Hospital Laboratory (Canada)
Sharon Regional Health System (PA)
Sharp Health Care Laboratory Services (CA)
Shiel Medical Laboratory Inc. (NY)
Shore Memorial Hospital (NJ)
Shriners Hospitals for Children (OH)
Silliman Medical Center (Philippines)
Silverton Health (OR)
SIMeL (Italy)
Singapore General Hospital (Singapore)
Singulex (CA)
Sky Lakes Medical Center (OR)
Slidell Memorial Hospital (LA)
SMDC Clinical Laboratory (MN)
Sociedad Espanola de Bioquimica Clinica y Patologia Molec. (Spain)
Sociedade Brasileira de Analises Clinicas (Brazil)
Sociedade Brasileira de Patologia Clinica (Brazil)
South Bay Hospital (FL)
South Bend Medical Foundation (IN)
South County Hospital (RI)
South Dakota State Health Laboratory (SD)
South Eastern Area Laboratory Services (Australia)
South Miami Hospital (FL)
South Peninsula Hospital (AK)
South Texas Laboratory (TX)
South West Medical Center (KS)
Southeast Alabama Medical Center (AL)
SouthEast Alaska Regional Health Consortium (SEARHC) (AK)
Southern Community Laboratories (New Zealand)
Southern Health Care Network (Australia)
Southern Hills Medical Center (TN)
Southern Maryland Hospital (MD)
Southern Pathology Services, Inc. (PR)
Southwest General Health Center (OH)
Southwestern Regional Medical Center (OK)
Sparrow Hospital (MI)
Spaulding Hospital Cambridge (MA)
Speare Memorial Hospital (NH)
Spectra East (NJ)
St Elizabeth Hospital (WI)
St Rose Dominican Hospital (AZ)
St. Agnes Healthcare (MD)
St. Anthony Hospital (OK)
St. Antonius Ziekenhuis (Netherlands)
St. Barnabas Medical Center (NJ)
St. Charles Medical Center-Bend (OR)
St. Charles Parish Hospital (LA)
St. Clair Hospital (PA)
St. David's South Austin Hospital (TX)
St. Elizabeth Community Hospital (CA)
St. Elizabeth's Medical Center (NY)
St. Francis Health Center (KS)
St. Francis Hospital (MO)
St. Francis Hospital (SC)
St. Francis Hospital & Health Centers (NY)
St. John Hospital and Medical Center (MI)
St. John Medical Center (OH)
St. John's Hospital (IL)
St. John's Regional Health Center (MO)
St. Joseph Health Center (MO)
St. Joseph Hospital (CA)
St. Joseph Hospital (NH)
St. Joseph Medical Center (TX)
St. Joseph Regional Health Center (TX)
St. Joseph's Health Centre (Canada)
St. Joseph's Hospital & Medical Center (AZ)
St. Jude Children's Research Hospital (TN)
St. Jude Medical Center (CA)
St. Luke's Episcopal Hospital (TX)
St. Luke's Hospital (IA)
St. Luke's Hospital (MN)
St. Luke's Hospital (MO)
St. Luke's Hospital (PA)
St. Luke's Hospital at The Vintage (TX)
St. Luke's Medical Center (AZ)
St. Luke's Regional Medical Center (ID)
St. Mark's Hospital (UT)
St. Mary Medical Center (CA)
St. Mary Medical Center (PA)
St. Mary's Good Samaritan (IL)
St. Mary's Health Center (MO)
St. Mary's Hospital (CO)
St. Mary's Hospital (NJ)
St. Mary's Hospital (NY)
St. Mary's Hospital (WI)
St. Mary's Medical Center (IN)
St. Michael's Hospital (WI)
St. Nicholas Hospital (WI)
St. Olavs Hospital (Norway)
St. Peter's Bender Laboratory (NY)
St. Peter's Hospital (MT)
St. Rita's Medical Center (OH)
St. Tammany Parish Hospital (LA)
St. Thomas Hospital (TN)
St. Thomas-Elgin General Hospital (Canada)
St. Vincent Hospital (NM)
St. Vincent's Medical Center (FL)
Stanford Hospital and Clinics (CA)
Stat Veterinary Lab (CA)
State of Alabama (AL)
State of Ohio Corrections Medical Center Laboratory (OH)
State of Washington Public Health Labs (WA)
State of Wyoming Public Health Laboratory (WY)
Statens Serum Institut (Denmark)
Stillwater Medical Center (OK)
Stony Brook University Hospital (NY)
Stormont-Vail Regional Medical Ctr. (KS)
Sturgis Hospital (MI)
Summa Health System (OH)
Sunnybrook Health Sciences Centre (Canada)
Sunrise Hospital and Medical Center (NV)
SUNY Downstate Medical Center (NY)
Susan B. Allen Hospital (KS)
Susquehanna Health System (PA)
Sutter Health Sacramento Sierra Region Laboratories (CA)
Swedish American Health System (IL)
Swedish Medical Center (CO)
Sydney South West Pathology Service Liverpool Hospital (Australia)
Tahoe Forest Hospital (CA)
Taichung Veterans General Hospital (Taiwan)
Taiwan Society of Laboratory Medicine (Taiwan)
Tallaght Hospital (Ireland)
Tampa General Hospital (FL)
Taranaki Medlab (New Zealand)
Tartu University Clinics (Estonia)
Tataa Biocenter (Sweden)
Taylor Regional Hospital (KY)
Temple Community Hospital (CA)
Temple University Hospital - Parkinson Pavilion (PA)
Tenet Healthcare (PA)
Tennessee Department of Health (TN)
Tewksbury Hospital (MA)
Texas A & M University (TX)
Texas Children's Hospital (TX)
Texas Department of State Health Services (TX)
Texas Health Harris Methodist Hospital Cleburne (TX)
Texas Health Harris Methodist Hospital Fort Worth (TX)
Texas Health Presbyterian Hospital Dallas (TX)
Texas Scottish Rite Hospital for Children (TX)
The Broad Institute (MA)
The Charlotte Hungerford Hospital (CT)
The Cheshire Medical Center (NH)
The Children's Mercy Hospital (MO)
The City Hospital Dubai UAE (United Arab Emirates)
The Clinical Microbiology Institute (OR)
The Cooley Dickinson Hospital, Inc. (MA)
The Doctor's Clinic (OR)
The First Hospital of China Medical University (China)
The Good Samaritan Hospital (PA)
The Hospital for Sick Children (Canada)
The Joint Commission (IL)
The Joint Pathology Center (MD)
The Korean Society for Laboratory Medicine (Korea, Republic of)
The Michener Inst. for Applied Health Sciences (Canada)
The Nathan S. Kline Institute (NY)
The Naval Hospital of Jacksonville (FL)
The Nebraska Medical Center (NE)
The Norwegian Institute of Biomedical Science (Norway)
The Ohio State University-Vet Hospital (OH)
The Permanente Medical Group, Inc. (CA)
The University of Texas Medical Branch (TX)
The University of the West Indies, Trinidad Campus (Trinidad and Tobago)
The University of Tokyo (Japan)
Thibodaux Regional Medical Center (LA)
Thomas Jefferson University Hospital, Inc. (PA)
Thunder Bay Regional Health Sciences Centre (Canada)
Torrance Memorial Medical Center (CA)
Touro Infirmary (LA)
Tri-Cities Laboratory (WA)
TriCore Reference Laboratories (NM)
Trident Medical Center (SC)
Trillium Health Partners Credit Valley Hospital (Canada)
Trinity Health Systems (OH)
Trinity Hospital of Augusta (GA)
Trinity Medical Center (AL)
Trinity Muscatine (IA)
Tripler Army Medical Center (HI)
Trumbull Memorial Hospital (OH)
Tucson Medical Center (AZ)
Tuen Mun Hospital, Hospital Authority (Hong Kong)
Tufts Medical Center (MA)
Tulane Medical Center Hospital & Clinic (LA)
Tulane University Health Sciences Center (LA)
Twin Lakes Regional Medical Center (KY)
U.S. Medical Ctr. for Federal Prisoners (MO)
U.S. Naval Hospital, Yokosuka, Japan (AP)
UC Davis Medical Center Department of Pathology & Laboratory Medicine (CA)
UC San Diego Health System Clinical Laboratories (CA)
UCI Medical Center (CA)
UCLA Medical Center (CA)
UCONN Health Center (CT)
UCSF Medical Center China Basin (CA)
UMass Memorial Medical Center (MA)
UMC of El Paso- Laboratory (TX)
UMC of Southern Nevada (NV)
Umea University Hospital (Sweden)
UNC Hospitals (NC)
Union Clinical Laboratory (Taiwan)
United Christian Hospital (Hong Kong)
United Clinical Laboratories (IA)
United Health Services Hospital / Wilson Hospital Lab (NY)
United Memorial Med Center (NY)
United States Air Force School of Aerospace Medicine / PHE (OH)
United States Coast Guard (NJ)
Universidad de Guadalajara (Mexico)
Universidade Federal Do Rio de Janeiro (Brazil)
Universitaet Zuerich (Switzerland)
Universitair Ziekenhuis Antwerpen (Belgium)
University College Hospital (Ireland)
University Health Network Laboratory Medicine Program (Canada)
University Hospital (TX)
University Hospital Center Sherbrooke (CHUS) (Canada)
University Hospitals of Cleveland (OH)
University Medical Center at Princeton (NJ)
University Medical Center of El Paso (TX)
University Medical Center Utrecht (Netherlands)
University of Alabama Hospital Lab (AL)
University of Alberta - Medical Genetics (Canada)
University of Arizona Medical Center (AZ)
University of Arkansas for Medical Sciences (AR)
University of Bonn (Germany)
University of British Columbia (Canada)
University of California Veterinary Medical Teaching Hospital (CA)
University of Chicago Hospitals Laboratories (IL)
University of Cincinnati Medical Center (OH)
University of Cologne Medical Center (Germany)
University of Colorado Health Sciences Center (CO)
University of Colorado Hospital (CO)
University of Delaware (DE)
University of Guelph (Canada)
University of Hong Kong (Hong Kong)
University of Illinois Medical Center (IL)

University of Iowa Hospitals and Clinics (IA)
University of Iowa, Hygienic Lab (IA)
University of Kentucky Medical Center Hospital (KY)
University of Ljubljana Faculty of Medicine (Slovenia)
University of Louisville Hospital (KY)
University of Maryland Medical System (UT)
University of Miami (FL)
University of Miami - Clinical Genetics Labs (FL)
University of Michigan, Department of Pathology (MI)
University of Minnesota Medical Center-Fairview (MN)
University of Missouri Hospital (MO)
University of MS Medical Center (MS)
University of New Mexico (NM)
University of North Carolina - Health Services (NC)
University of Oregon (OR)
University of Pennsylvania (PA)
University of Pennsylvania Health System (PA)
University of Pittsburgh Medical Center (PA)
University of Portsmouth (United Kingdom [GB])
University of Queensland (Australia)
University of Rochester Medical Center (NY)
University of South Alabama Medical Center (AL)
University of Tasmania (Australia)
University of Tennessee, College of Veterinary Medicine (TN)
University of Texas Health Center (Tyler) (TX)
University of Texas Health Science Center (TX)
University of Texas Southwestern Medical Center (TX)
University of the Ryukyus (Japan)
University of Utah Hospital & Clinics (UT)
University of Virginia Medical Center (VA)
University of Washington Medical Center (WA)
University of Wisconsin Health (WI)
University of Wisconsin Medical Foundation (WI)
UPMC Bedford Memorial (PA)
Urology of Virginia, PLLC (VA)
USA MEDDAC-Japan
Uvalde Memorial Hospital (TX)
VA (Asheville) Medical Center (NC)
VA (Bay Pines) Medical Center (FL)
VA (Castle Point) Hudson Valley Health Care System (NY)
VA (Central Texas) Veterans Health Care System (TX)
VA (Dayton) Medical Center (OH)
VA (Indianapolis) Medical Center (IN)
VA (Miami) Medical Center (FL)
VA (Tampa) Hospital (FL)
VA (Tuscaloosa) Medical Center (AL)
Vail Valley Medical Center (CO)
Valley Health / Winchester Medical Center (VA)
Valley Medical Center (WA)
Vancouver Island Health Authority (SI) (Canada)
Vanderbilt University Medical Center (TN)
Vejle Hospital (Denmark)
Vermont Department of Health (VT)
Vernon Memorial Hospital (WI)
Veterans Memorial Hospital (IA)
Via Christi Regional Medical Center (KS)
Virginia Mason Medical Center (WA)
Virginia Physicians, Inc. (VA)
Virginia Regional Medical Center (MN)
Virtua - West Jersey Hospital (NJ)
WakeMed (NC)
Warren Hospital (NJ)
Waterbury Hospital (CT)
Watson Clinic (FL)
Wayne Memorial Hospital (GA)
Weber State University (UT)
Weed Army Community Hospital Laboratory (CA)
Weeneebayko General Hospital (Canada)
Weirton Medical Center (WV)
Wellington Regional Medical Center (FL)
Wellstar Douglas Hospital Laboratory (GA)
Wellstar Health Systems (GA)
WellStar Paulding Hospital (GA)
Wenatchee Valley Medical Center (WA)
Wesley Medical Center (KS)
West Georgia Health Systems (GA)
West Penn Allegheny Health System-Allegheny General Hospital (PA)
West Shore Medical Center (MI)
West Valley Medical Center Laboratory (ID)
West Virginia Bureau for Public Health (WV)
West Virginia Univ. Hospitals (WV)
Westchester Medical Center (NY)
Western Baptist Hospital (KY)
Western Healthcare Corporation (Canada)
Western Missouri Medical Center (MO)
Western State Hospital (VA)
Whangarei Hospital (New Zealand)
Wheaton Franciscan Laboratories At St. Francis (WI)
Wheeling Hospital (WV)
Whitehorse General Hospital (Canada)
Whitman Hospital & Medical Center (WA)
Wickenburg Community Hospital (AZ)
William Beaumont Army Medical Center (TX)
William Beaumont Hospital (MI)
William Osler Health Centre (Canada)
Williamson Medical Center (TN)
Wilson Medical Center (NC)
Winchester Hospital (MA)
Winn Army Community Hospital (GA)
Winter Haven Hospital, Inc. (FL)
Wisconsin State Laboratory of Hygiene (WI)
Wishard Health Sciences (IN)
Womack Army Medical Center (NC)
Women & Infants Hospital (RI)
Womens and Childrens Hospital (LA)
Women's Health Care Group of PA (PA)
Woods Memorial Hospital (TN)
Woodside Health Center (Canada)
WuXi AppTec Co., Ltd. (China)
Wyckoff Heights Medical Center (NY)
Wyoming County Community Hospital (NY)
Yale New Haven Hospital (CT)
York General Health Care Services (NE)
York Hospital (PA)
Yuma Regional Medical Center (AZ)

Individuals

Mohamed O Abdelhalim (Oman)
Shana Ahmad (NY)
Lawal Akeem (Nigeria)
Erika B Ammirati (CA)
Stephen Apfelroth (NY)
Ahmed M Azaybi (Saudi Arabia)
Cary Baird (OH)
Susan Barber (NC)
Nancy Behling (AZ)
Steven Bellistri (PA)
Melissa Bennett (Canada)
Dr. Lynette Y. Berkeley PhD (MD)
Ms. Lucia M. Berte MA, MT(ASCP), SBB (CO)
Bhaskar Bhattacharya (India)
Elma Kamari Bidkorpeh (CA)
Deborah Bishop (WV)
Abbejane Blair (MA)
Ms. Susan Blonshine RRT, RPFT, FAARC (MI)
Elizabeth Brown (PA)
Steven Brown (OR)
Vanessa Buchan (New Zealand)
Karen Bush (IN)
Donald R Callihan (MD)
Ms. Natalie Campbell RT (Canada)
Sheldon Campbell (CT)
Alan T. Cariski (CA)
A. Bjoern Carle (ME)
Dr. Maria Paz Carlos DVM, PhD, MBA (MD)
Eileen Carreiro-Lewandowski (MA)
Dr. Jose B. Casals (Denmark)
Ning Cegielski (WA)
Tony Chan (China)
Mintrude Charles-Young (Canada)
Redintor Dagos (Philippines)
Dr. Jeff Dahlen PhD (CA)
Imelda Daniel (CA)
Saffiatou Darboe (Gambia)
Ms. Arlene Darmanie MS (Trinidad and Tobago)
Dr. Trivikram Dasu PhD (WI)
Ms. Diana R. DeHoyos MS, MT(ASCP) (TX)
Dr. Maria del Pilar Aguinaga PhD, CLDir(NCA) (TN)
Dr. Francois Depasse PharmD, MSc (France)
Narendra Desai (Ca)
Dr. Edward P. Desmond PhD (CA)
Patricia Devine (MA)
Ms. Diana L. Dickson MS, RAC (PA)
Dr. Sherry A. Dunbar PhD (TX)
Mr. A. Paul Durham MA (CA)
Omer Eltoum (Qatar)
Sahar Gamil EL-Wakil (Saudi Arabia)
Mike Ero (CA)
Mr. German Esparza BSc (Colombia)
Galen Eversole (NV)
Dr. William Fales (MO)
Ms. Sue Forrest (Australia)
Dr. Timothy S. Frana DVM, MS, MPH, PhD (IA)
Dr. Jeff Fuller PhD, FCCM, ABMM (Canada)
Mary Lou Gantzer (DE)
Patricia Garrett (ME)
Dr. Valerio M. Genta MD (VA)
Carlos Gonzalez (TX)
Merran Govendir (Australia)
Tanya Graham (SD)
Neil Greenberg (NY)
David Grier (NC)
Jason Gruver (IA)
Dr. W. Harry Hannon PhD (GA)
Dr. Muain Haseeb (Saudi Arabia)
Judy Horton (MD)
B. Y. Hsieh (Taiwan)
Po-Ren Hsueh (Taiwan)
Mr. Darren C. Hudach (OH)
Clark B Inderlied (CA)
T. S Isbell (MO)
Dr. Megan E. Jacob PhD (NC)
Ellis Jacobs (NJ)
Benjamin B John (MA)
Judith Johnston (CA)
Sumy Joseph (NC)
Stephen Kahn (IL)
Jiesheng Kang (MA)
Mr. Bob Kaplanis PBT, MT(ASCP) (AZ)
Dr. Steven C. Kazmierczak PhD, DABCC, FACB (OR)
Harvey Ronald Kennedy, MD (NJ)
Natalie J. Kennel (CA)
Mr. Klaus M. Kjoller MSc (Denmark)
William F. Koch (MD)
Jo Anne Koch-Owens (FL)
Mr. Narayan Krishnaswami MS, MBA (MO)
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