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M100-S24

Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fourth Informational Supplement

This document provides updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02-A11, M07-A9, and M11-A8.

An informational supplement for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Fourth Informational Supplement

Abstract

The supplemental information presented in this document is intended for use with the antimicrobial susceptibility testing procedures published in the following Clinical and Laboratory Standards Institute (CLSI)–approved standards: M02-A11—*Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard—Eleventh Edition;* M07-A9—*Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Ninth Edition;* and M11-A8—*Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Eighth Edition.* The standards contain information about both disk (M02) and dilution (M07 and M11) test procedures for aerobic and anaerobic bacteria.

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

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

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The data in the interpretive tables in this supplement are valid only if the methodologies in M02-A11—*Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard—Eleventh Edition;* M07-A9—*Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Ninth Edition;* and M11-A8—*Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Eighth Edition* are followed.

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Contents

Table of Contents

Contents (Continued)

Contents (Continued)

Contents (Continued)

The Clinical and Laboratory Standards Institute consensus process, which is the mechanism for moving a document through two or more levels of review by the health care community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of CLSI documents. Current editions are listed in the CLSI catalog and posted on our website at www.clsi.org. If you or your organization is not a member and would like to become one, and to request a copy of the catalog, contact us at: Telephone: +610.688.0100; Fax: +610.688.0700; E-mail: customerservice@clsi.org; Website: www.clsi.org.

Summary of Major Changes in This Document

This list includes the "major" changes in this document. Other minor or editorial changes were made to the general formatting and to some of the table footnotes and comments. Changes to the tables since the previous edition appear in boldface type.

Additions, Changes, and Deletions

The following are additions or changes unless otherwise noted as a ***"deletion."***

New educational information explaining the cefepime breakpoint change for *Enterobacteriaceae* and introduction of susceptible-dose dependent (SDD) interpretive category (p. 18). Also, refer to p. 52 for new (revised) cefepime disk diffusion and MIC interpretive criteria and p. 206 for a new Appendix E showing dosing regimens used to establish susceptible or SDD interpretive criteria.

Instructions for Use of Tables

Added definition for susceptible-dose dependent (SDD) (p. 29).

Added an example and explanation for antimicrobial agents having only susceptible interpretive criteria (p. 31).

Revised the "Further Testing or Confirmation Required?" recommendations for the penicillin disk diffusion zone-edge test for *S. aureus* (p. 34).

Added "Further Testing or Confirmation Required?" recommendations for a chromogenic cephalosporin screen test for *S. aureus* (p. 34).

Tables 1A, 1B, 1C – Drugs Recommended for Testing and Reporting

Enterobacteriaceae:
Cefazolin added to Test Report Group U as a surrogate test for uncomplicated UTI (p. 38).

Staphylococcus spp.:
Noted use of cefoxitin as a surrogate test for oxacillin (p. 38).

Acinetobacter spp.:
Doripenem added to Test Report Group A (p. 39).

Minocycline placed in own box in Test Report Group B (p. 39).

Additional information added for reporting first- and second-generation cephalosporins and cephamycins for *Salmonella* spp. and *Shigella* spp. (p. 40).

Tables 2A Through 2J – Interpretive Criteria (Breakpoints)

Enterobacteriaceae **(Table 2A):**
Added *P. aeruginosa* ATCC® 27853 to Routine QC Recommendations box for testing carbapenems (p. 50).

Updated recommendations for the placement of disks on a 100-mm plate (p. 50).

Summary of Major Changes in This Document (Continued)

Added recommendation that testing cefazolin is preferred to testing cephalothin for predicting results for oral cephalosporins when used for therapy of uncomplicated UTIs (p. 52).

New (revised) cefepime disk diffusion and MIC interpretive criteria along with dosage regimens for using susceptible-dose dependent (SDD) interpretive criteria (p. 52).

New cefazolin interpretive criteria and recommendations for use as a surrogate test for uncomplicated UTIs to predict results for oral cephalosporins (p. 53).

Table 2A Supplemental Tables 1, 2, and 3 are now Tables 3A, 3B, and 3C, respectively (pp. 110 through 122).

***Pseudomonas aeruginosa* (Table 2B-1):**
Deleted *E. coli* ATCC® 25922 from the Routine QC Recommendations box.

Updated recommendations for the placement of disks on a 100-mm plate (p. 58).

***Acinetobacter* spp. (Table 2B-2):**
Added recommendations in Routine QC Recommendations box that *E. coli* ATCC® 25922 is for QC testing of tetracyclines and trimethoprim-sulfamethoxazole (p. 62).

Updated recommendations for the placement of disks on a 100-mm plate (p. 62).

New doripenem disk diffusion and MIC interpretive criteria with dosage regimens on which the breakpoints are based (p. 63).

New (revised) imipenem and meropenem disk diffusion and MIC interpretive criteria with dosage regimens on which the breakpoints are based (p. 63).

***Burkholderia cepacia* (Table 2B-3):**
Added recommendations in Routine QC Recommendations box that *E. coli* ATCC® 25922 is for QC testing of chloramphenicol, minocycline, and trimethoprim-sulfamethoxazole (p. 64).

***Stenotrophomonas maltophilia* (Table 2B-4):**
Added recommendations in Routine QC Recommendations box that *E. coli* ATCC® 25922 is for QC testing of chloramphenicol, minocycline, and trimethoprim-sulfamethoxazole (p. 65).

Other Non-*Enterobacteriaceae* (Table 2B-5):
Added recommendations in Routine QC Recommendations box that *E. coli* ATCC® 25922 is for QC testing of chloramphenicol, tetracyclines, sulfonamides, and trimethoprim-sulfamethoxazole (p. 66).

***Staphylococcus* spp. (Table 2C):**
Updated recommendations for the placement of disks on a 100-mm plate (p. 68).

Clarified that the 30-µg cefoxitin disk is used as a surrogate test for oxacillin (p. 71).

Added information regarding vancomycin-susceptible *S. aureus* isolates and prolonged therapy (p. 72).

Deleted interpretive criteria for vancomycin disk diffusion test.

Summary of Major Changes in This Document (Continued)

Recommendations from Table 2C Supplemental Tables 1, 2, and 3 can now be found in Tables 3D, 3E, 3F, 3G, and 3H (pp. 124 through 139).

***Enterococcus* spp. (Table 2D):**
Updated recommendations for the placement of disks on a 100-mm plate (p. 76).

Recommendations from Table 2D Supplemental Table 1 can now be found in Tables 3F and 3I (pp. 132 and 140, respectively).

***Streptococcus pneumoniae* (Table 2G):**
Recommendations from Table 2G Supplemental Table 1 can now be found in Table 3G (p. 134).

Table 3 (New)

New Table 3A was previously Table 2A Supplemental Table 1 (p. 110)

New Table 3B was previously Table 2A Supplemental Table 2 (p. 114).

New Table 3C was previously Table 2A Supplemental Table 3 (p. 118).

Screening tests in the new Table 3D were previously in Table 2C Supplemental Tables 1 and 3 (p. 124).

Screening tests in the new Table 3E were previously in Table 2C Supplemental Tables 1 and 3 (p. 128).

Screening tests in the new Table 3F were previously in Table 2C Supplemental Table 2 and Table 2D Supplemental Table 1 (p. 132).

Screening tests in the new Table 3G were previously in Table 2C Supplemental Table 2, Table 2G Supplemental Table 1, and Table 2H-1 Supplemental Table 1 (p. 134).

Screening tests in the new Table 3H were previously in Table 2C Supplemental Table 2 (p. 138).

Screening tests in the new Table 3I were previously in Table 2D Supplemental Table 1 (p. 140).

Tables 4 and 5 – Quality Control

Table 4A (previously Table 3A) (p. 142):
QC ranges added and/or revised for:

Ceftolozane-tazobactam – *E. coli* ATCC® 25922, *S. aureus* ATCC® 25923, *P. aeruginosa* ATCC® 27853, and *E. coli* ATCC® 35218

Eravacycline – *E. coli* ATCC® 25922 and *S. aureus* ATCC® 25923

Table 4B (previously Table 3B) (p. 146):
QC ranges added and/or revised for:

Ceftazidime-avibactam – *S. pneumoniae* ATCC® 49619

Ceftolozane-tazobactam – *H. influenzae* ATCC® 49247

Eravacycline – *S. pneumoniae* ATCC® 49619

Summary of Major Changes in This Document (Continued)

Table 5A (previously Table 4A) (p. 154):
QC ranges added and/or revised for:

Aztreonam – *E. coli* ATCC® 35218

Biapenem – *S. aureus* ATCC® 29213, *E. coli* ATCC® 25922, *P. aeruginosa* ATCC® 27853, and *E. coli* ATCC® 35218

Aztreonam-avibactam – *E. coli* ATCC® 25922, *P. aeruginosa* ATCC® 27853, and *E. coli* ATCC® 35218

Ceftolozane-tazobactam – *S. aureus* ATCC® 29213, *E. coli* ATCC® 25922, *P. aeruginosa* ATCC® 27853, and *E. coli* ATCC® 35218

Colistin (tested with 0.002% polysorbate 80) – *E. coli* ATCC® 25922 and *P. aeruginosa* ATCC® 27853

Polymyxin B – *P. aeruginosa* ATCC® 27853

Polymyxin B (tested with 0.002% polysorbate 80) – *E. coli* ATCC® 25922 and *P. aeruginosa* ATCC® 27853

Telavancin – *S. aureus* ATCC® 29213 and *E. faecalis* ATCC® 29212

Table 5B (previously Table 4B) (p. 158):
QC ranges added and/or revised for:

Ceftolozane-tazobactam – *H. influenzae* ATCC® 49247

Telavancin – *S. pneumoniae* ATCC® 49619

Table 5D (previously Table 4D) (p. 164):
QC ranges added and/or revised for:

Ceftolozane-tazobactam – *B. fragilis* ATCC® 25285 and *B. thetaiotaomicron* ATCC® 29741

Surotomycin – *C. difficile* ATCC® 700057 and *E. lentum* ATCC® 43055

Table 5E (previously Table 4E) (p. 166):
QC ranges added and/or revised for:

Ceftolozane-tazobactam – *B. fragilis* ATCC® 25285 and *B. thetaiotaomicron* ATCC® 29741

Surotomycin – *C. difficile* ATCC® 700057 and *E. lentum* ATCC® 43055

Table 6A – Solvents and Diluents (previously Table 5A) (p. 176):

Added antimicrobial agents:

Biapenem
Eravacycline
Surotomycin

Summary of Major Changes in This Document (Continued)

Revised diluent for telavancin.

Table 6C – Preparation of Solutions and Media Containing Combinations of Antimicrobial Agents (previously Table 5C) (p. 182):

Added aztreonam-avibactam.

Appendixes and Glossaries

Appendix A. Confirmation of AST Results and Organism Identification:
Added ceftaroline to *H. influenzae; S. aureus; S. pneumoniae;* and *Streptococcus*, β-hemolytic group listings in Appendix A (pp. 189 and 190).

Appendix B2. Non-*Enterobacteriaceae:*
Added information for ampicillin and amoxicillin (p. 194).

New Appendix E. Dosing Regimens Used to Establish Susceptible or Susceptible-Dose Dependent Interpretive Criteria (p. 206):

Glossary I – Added aztreonam-avibactam, biapenem, eravacycline, and surotomycin (pp. 208 to 211).

Glossary II – Added aztreonam-avibactam, biapenem, eravacycline, and surotomycin (pp. 212 to 214).

Cefepime Breakpoint Change for *Enterobacteriaceae* and Introduction of the Susceptible-Dose Dependent (SDD) Interpretive Category

What Changed?

The CLSI Subcommittee on Antimicrobial Susceptibility Testing revised the cefepime interpretive criteria (breakpoints) and is introducing the susceptible-dose dependent (SDD) category with this breakpoint revision. Below is a summary of the changes.

Previous – 2013

Method	Susceptible	Intermediate	Resistant
MIC	≤8 µg/mL	16 µg/mL	≥32 µg/mL
Zone Diameter (Disk Diffusion)	≥18 mm	15–17 mm	≤14 mm

Revised – 2014

Method	Susceptible	Susceptible-Dose Dependent	Resistant
MIC	≤2 µg/mL	4–8 µg/mL	≥16 µg/mL
Zone Diameter (Disk Diffusion)	≥25 mm	19–24 mm	≤18 mm

Abbreviation: MIC, minimal inhibitory concentration.

Why were the cefepime breakpoints reconsidered?

The issue of new breakpoints for cefepime became apparent for several reasons:

- Previous breakpoints were based on a higher dose of cefepime than is often used.
- Clinical failures were noted for isolates with cefepime MICs of 4 and 8 µg/mL, especially when lower doses of cefepime were used.
- There are limited new drugs in the pipeline that show activity against multidrug-resistant gram-negative bacteria; thus, there is a need to optimize use of drugs currently available. Designing susceptibility reports to correlate better with dosages of the drug used is one way to help accomplish this goal.

What does "susceptible-dose dependent" (SDD) mean?

SDD interpretation is a new interpretive category for antibacterial susceptibility testing, although it has been applied for interpretation of antifungal susceptibility test results for several years.

Definition:

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 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. 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). 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.

SDD is recommended instead of "intermediate" when reporting cefepime results for *Enterobacteriaceae* isolates because there are multiple approved dosing options for cefepime, and SDD highlights the option of using higher doses to treat infections caused by isolates when the cefepime MIC is 4 or 8 µg/mL or the zone is 19 to 24 mm.

Why is SDD being used now?

- It has become apparent that there is a growing need to refine susceptibility reporting to maximize clinicians' use of available drugs.
- Intermediate too often means "resistant" to clinicians because they do not appreciate the full definition of "intermediate."
- SDD is more specific and it conveys what we know—a higher dose can be considered for isolates with MICs (or zones) that fall in this interpretive category.
- SDD is already well established for use in antifungal susceptibility testing.
- It is anticipated that reporting a cefepime SDD result will encourage clinicians to consider the possibility that cefepime may be an option for treatment.
- Antibiotic stewardship programs, which emphasize dosing regimen and duration of therapy options, are increasing awareness of appropriate use of antibiotics. Personnel from these programs should be able to describe the significance to clinicians of an SDD result for cefepime.

How should this change be implemented?

- Meet with the appropriate practitioners at your institution (members of the antimicrobial stewardship team, infectious disease staff, pathology group, pharmacy, etc.) to inform them of these changes and agree on a plan to inform your clinicians of this change.
- Talk to the manufacturer of your antimicrobial susceptibility testing device to determine how to implement the revised breakpoints on your device.
  - **NOTE:** Because the US Food and Drug Administration (FDA) has not revised the cefepime breakpoints and commercial manufacturers must use FDA breakpoints, the manufacturer cannot adopt the new CLSI cefepime breakpoints. However, for most systems, you can manually change the breakpoints and implement following a verification study.

- Work with your laboratory information system staff to report "SDD" or "D" for *Enterobacteriaceae* when the cefepime MIC is 4 or 8 µg/mL. Make certain that SDD will be transmitted to the hospital information system and appropriately displayed on reports viewed by clinicians.

- Distribute user-specific educational materials to laboratory staff and clinicians receiving antimicrobial susceptibility testing results from your laboratory. Examples of these materials can be found on the CLSI Subcommittee on Antimicrobial Susceptibility Testing webpage at www.clsi.org.

Additional Questions and Answers:

Q: Does CLSI recommend a comment to be reported with the new cefepime breakpoints?
A: If a laboratory chooses to report a comment explaining the SDD range, CLSI recommends the following: "The interpretive criterion for susceptible is based on a dosage regimen of 1 g every 12 h. The interpretive criterion for susceptible-dose dependent is based on dosing regimens that result in higher cefepime exposure, either higher doses or more frequent doses or both, up to approved maximum dosing regimens."

Q: Will all intermediate ranges become SDD?
A: No, the SDD category will be implemented for drug/organism combinations only when there is sufficient evidence to suggest alternative approved dosing regimens may be appropriate for organisms that have MICs or zone diameters between the susceptible and resistant categories.

Q: Will SDD be applied to other antimicrobial agents?
A: CLSI will examine the SDD category possibility for additional drug/organism combinations where multiple dosing options exist (eg, other extended-spectrum cephalosporins).

Q: How do we perform a verification study before implementing the new cefepime breakpoints on our antimicrobial susceptibility testing device?
A: Guidelines for performance of such a verification study are provided in the following publication:
Clark RB, Lewinski MA, Loeffelholz MJ, Tibbetts RJ. Cumitech 31A: verification and validation of procedures in the clinical microbiology laboratory. Washington, DC: ASM Press; 2009.

Q: Does SDD apply to all patients and specimen types (eg, pediatric, geriatric, immunosuppressed)?
A: Yes, in terms of laboratory reporting. Clinicians must decide how to use an SDD result for a specific patient in consideration of all other clinical and physiological parameters for that patient.

Q: Do the new cefepime breakpoints apply to *Pseudomonas aeruginosa* and other gram-negative bacteria also?
A: No, currently they are only applicable to members of the *Enterobacteriaceae.*

Q: Is any special QC required once the SDD breakpoints are implemented?
A: No, currently recommended routine QC is sufficient.

Q: Will we be required to report SDD on proficiency testingsurvey samples?
A: Sponsors of proficiency testing surveys are aware of the difficulties encountered by clinical laboratories in implementing newer CLSI breakpoints. It is highly unlikely that there will be a mandate to report SDD in the near future, but it would be best to check with your proficiency testing survey provider.

Q: If we can implement the revised cefepime breakpoints but cannot facilitate reporting of SDD, can we report "intermediate" instead of SDD?
A: A decision related to this question should be made following consultation with your laboratory director, antibiotic stewardship team (if available), infectious disease practitioners, pharmacists, and infection control practitioners.

Q: If we can implement the revised cefepime breakpoints but cannot facilitate reporting of SDD, can we report an MIC or zone diameter without an MIC?
A: A zone diameter should never be reported without an interpretation because there is a high risk of misinterpretation of this value and this poses patient safety issues. There is a lesser danger of reporting an MIC without an interpretation, but this should not be done without an accompanying qualifying comment. See answer to question above.

Q: If we are still doing extended-spectrum β-lactamase (ESBL) testing and implement the new cefepime breakpoints, do we change a susceptible or SDD result to resistant for ESBL-positive isolates?
A: No. When CLSI changed the other cephem breakpoints in 2010, the recommendation to perform routine ESBL testing was eliminated. When using the new cefepime breakpoints, there is no need to perform routine ESBL testing for patient reporting purposes. However, ESBL testing might be done for infection control or epidemiological purposes.

Q: What does the dosing information that is given with breakpoints mean?
A: The evolving science of pharmacokinetics-pharmacodynamics has become increasingly important in recent years in determining MIC interpretive criteria. Recently approved susceptible or SDD interpretive criteria for a number of agents have been based on a specific dosing regimen(s); these dosing regimens are listed in Appendix E of M100-S24. Proper application of the interpretive criteria requires drug exposure at the site of infection that corresponds to or exceeds the expected systemic drug exposure, at the dose listed, in adult patients with normal renal function. This information should be shared with pharmacists, infectious disease staff, and others making dosing recommendations for the institution.

Summary of CLSI Processes for Establishing Interpretive Criteria and Quality Control Ranges

The Clinical and Laboratory Standards Institute (CLSI) is an international, voluntary, not-for-profit, interdisciplinary, standards-developing, and educational organization accredited by the American National Standards Institute (ANSI) that develops and promotes use of consensus-developed standards and guidelines within the health care community. These consensus standards and guidelines are developed to address critical areas of diagnostic testing and patient health care, and are developed in an open and consensus-seeking forum. CLSI is open to anyone or any organization that has an interest in diagnostic testing and patient care. Information about CLSI can be found at www.clsi.org.

The CLSI Subcommittee on Antimicrobial Susceptibility Testing reviews data from a variety of sources and studies (eg, *in vitro,* pharmacokinetics-pharmacodynamics, and clinical studies) to establish antimicrobial susceptibility test methods, interpretive criteria, and QC parameters. The details of the data required to establish interpretive criteria, QC parameters, and how the data are presented for evaluation are described in CLSI document M23—*Development of* In Vitro *Susceptibility Testing Criteria and Quality Control Parameters.*

Over time, a microorganism's susceptibility to an antimicrobial agent may decrease, resulting in a lack of clinical efficacy and/or safety. In addition, microbiological methods and QC parameters may be refined to ensure more accurate and better performance of susceptibility test methods. Because of this, CLSI continually monitors and updates information in its documents. Although CLSI standards and guidelines are developed using the most current information and thinking available at the time, the field of science and medicine is ever changing; therefore, standards and guidelines should be used in conjunction with clinical judgment, current knowledge, and clinically relevant laboratory test results to guide patient treatment.

Additional information, updates, and changes in this document are found in the meeting summary minutes of the Subcommittee on Antimicrobial Susceptibility Testing at www.clsi.org.

CLSI Reference Methods vs Commercial Methods and CLSI vs FDA Interpretive Criteria (Breakpoints)

It is important for users of M02-A11, M07-A9, and the M100 Informational Supplement to recognize that the standard methods described in CLSI documents are reference methods. These methods may be used for routine antimicrobial susceptibility testing of clinical isolates, for evaluation of commercial devices that will be used in clinical laboratories, or by drug or device manufacturers for testing of new agents or systems. Results generated by reference methods, such as those contained in CLSI documents, may be used by regulatory authorities to evaluate the performance of commercial susceptibility testing devices as part of the approval process. Clearance by a regulatory authority indicates that the commercial susceptibility testing device provides susceptibility results that are substantially equivalent to results generated using reference methods for the organisms and antimicrobial agents described in the device manufacturer's approved package insert.

CLSI breakpoints may differ from those approved by various regulatory authorities for many reasons, including the following: different databases, differences in interpretation of data, differences in doses used in different parts of the world, and public health policies. Differences also exist because CLSI proactively evaluates the need for changing breakpoints. The reasons why breakpoints may change and the manner in which CLSI evaluates data and determines breakpoints are outlined in CLSI document M23—*Development of* In Vitro *Susceptibility Testing Criteria and Quality Control Parameters.*

Following a decision by CLSI to change an existing breakpoint, regulatory authorities may also review data in order to determine how changing breakpoints may affect the safety and effectiveness of the antimicrobial agent for the approved indications. If the regulatory authority changes breakpoints, commercial device manufacturers may have to conduct a clinical laboratory trial, submit the data to the regulatory authority, and await review and approval. For these reasons, a delay of one or more years may be required if an interpretive breakpoint change is to be implemented by a device manufacturer. In the United States, it is acceptable for laboratories that use US Food and Drug Administration (FDA)–cleared susceptibility testing devices to use existing FDA interpretive breakpoints. Either FDA or CLSI susceptibility interpretive breakpoints are acceptable to clinical laboratory accrediting bodies. Policies in other countries may vary. Each laboratory should check with the manufacturer of its antimicrobial susceptibility test system for additional information on the interpretive criteria used in its system's software.

Following discussions with appropriate stakeholders, such as infectious disease practitioners and the pharmacy department, as well as the Pharmacy and Therapeutics and Infection Control committees of the medical staff, newly approved or revised breakpoints may be implemented by clinical laboratories. Following verification, CLSI disk diffusion test breakpoints may be implemented as soon as they are published in M100. If a device includes antimicrobial test concentrations sufficient to allow interpretation of susceptibility and resistance to an agent using the CLSI breakpoints, a laboratory could choose to, after appropriate verification, interpret and report results using CLSI breakpoints.

CLSI Breakpoint Additions/Revisions Since 2010

Antimicrobial Agent	Date of Revision* (M100 version)	Comments
Enterobacteriaceae		
Aztreonam	January 2010 (M100-S20)	
Cefazolin	January 2010 (M100-S20) January 2011 (M100-S21)	Breakpoints were revised twice since 2010.
Cefazolin	**January 2014 (M100-S24)**	**Breakpoints predict results for oral cephalosporins when used for therapy of uncomplicated UTIs.**
Cefepime	**January 2014 (M100-S24)**	
Cefotaxime	January 2010 (M100-S20)	
Ceftazidime	January 2010 (M100-S20)	
Ceftizoxime	January 2010 (M100-S20)	
Ceftriaxone	January 2010 (M100-S20)	
Doripenem	June 2010 (M100-S20-U)	No previous CLSI breakpoints existed for doripenem.
Ertapenem	June 2010 (M100-S20-U) January 2012 (M100-S22)	Breakpoints were revised twice since 2010.
Imipenem	June 2010 (M100-S20-U)	
Meropenem	June 2010 (M100-S20-U)	
Ciprofloxacin – *Salmonella* spp. (including *S.* Typhi)	January 2012 (M100-S22)	Revised body site–specific breakpoint recommendations in 2013.
Ceftaroline	January 2013 (M100-S23)	No previous CLSI breakpoints existed for ceftaroline.
Levofloxacin – *Salmonella* spp. (including *S.* Typhi)	January 2013 (M100-S23)	
Ofloxacin *Salmonella* spp. (including *S.* Typhi)	June 2013 (M100-S23)	
Pseudomonas aeruginosa		
Piperacillin-tazobactam	January 2012 (M100-S22)	
Ticarcillin-clavulanate	January 2012 (M100-S22)	
Doripenem	January 2012 (M100-S22)	
Imipenem	January 2012 (M100-S22)	
Meropenem	January 2012 (M100-S22)	
Ticarcillin	January 2012 (M100-S22)	
Piperacillin	January 2012 (M100-S22)	
***Acinetobacter* spp.**		
Doripenem	**January 2014 (M100-S24)**	
Ertapenem	**January 2014 (M100-S24)**	
Imipenem	**January 2014 (M100-S24)**	
***Staphylococcus* spp.**		
Ceftaroline	January 2013 (M100-S23)	No previous CLSI breakpoints existed for ceftaroline.
Haemophilus influenzae* and *Haemophilus parainfluenzae		
Ceftaroline	January 2013 (M100-S23)	No previous CLSI breakpoints existed for ceftaroline.

Antimicrobial Agent	Date of Revision* (M100 version)	Comments
Streptococcus pneumoniae		
Ceftaroline	January 2013 (M100-S23)	No previous CLSI breakpoints existed for ceftaroline.
Tetracycline	January 2013 (M100-S23)	
Doxycycline	January 2013 (M100-S23)	No previous CLSI breakpoints existed for doxycycline.
***Streptococcus* spp. β-Hemolytic Group**		
Ceftaroline	January 2013 (M100-S23)	No previous CLSI breakpoints existed for ceftaroline.

* Previous breakpoints can be found in the version of M100 that precedes the document listed here, eg, previous breakpoints for aztreonam are listed in M100-S19 (January 2009).

Abbreviation: UTI, urinary tract infection.

Subcommittee on Antimicrobial Susceptibility Testing Mission Statement

The Subcommittee on Antimicrobial Susceptibility Testing is composed of representatives from the professions, government, and industry, including microbiology laboratories, government agencies, health care providers and educators, and pharmaceutical and diagnostic microbiology industries. Using the CLSI voluntary consensus process, the subcommittee develops standards that promote accurate antimicrobial susceptibility testing and appropriate reporting.

The mission of the Subcommittee on Antimicrobial Susceptibility Testing is to:

- Develop standard reference methods for antimicrobial susceptibility tests.
- Provide QC parameters for standard test methods.
- Establish interpretive criteria for the results of standard antimicrobial susceptibility tests.
- Provide suggestions for testing and reporting strategies that are clinically relevant and cost-effective.
- Continually refine standards and optimize detection of emerging resistance mechanisms through development of new or revised methods, interpretive criteria, and QC parameters.
- Educate users through multimedia communication of standards and guidelines.
- Foster a dialog with users of these methods and those who apply them.

The ultimate purpose of the subcommittee's mission is to provide useful information to enable laboratories to assist the clinician in the selection of appropriate antimicrobial therapy for patient care. The standards and guidelines are meant to be comprehensive and to include all antimicrobial agents for which the data meet established CLSI guidelines. The values that guide this mission are quality, accuracy, fairness, timeliness, teamwork, consensus, and trust.

Instructions for Use of Tables

On the following pages, you will find:

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

2. For each organism group, an additional table (Tables 2A through 2I) contains:
   a. Recommended testing conditions.
   b. Routine QC recommendations. (See also the text documents M02-A11, Section 15 and M07-A9, Section 16.)
   c. General comments for testing the organism group and specific comments for testing particular drug/organism combinations.
   d. Suggested agents that should be considered for routine testing and reporting by clinical microbiology laboratories, as specified in Tables 1A and 1B (test/report groups A, B, C, U).
   e. Additional drugs that have an approved indication for the respective organism group, but would generally not warrant routine testing by a clinical microbiology laboratory in the United States (test/report group O for "other"; test/report group Inv. for "investigational" [not yet FDA approved]).
   f. Zone diameter and minimal inhibitory concentration (MIC) interpretive criteria.

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

4. **Tables 3A to 3I describe screening tests or other tests to detect particular types of resistance in specific organisms or organism groups.**

I. Selecting Antimicrobial Agents for Testing and Reporting

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

B. Drugs listed together in a single box are agents for which interpretive results (susceptible, intermediate, or resistant) and clinical efficacy are similar. Within each box, an "or" between agents indicates those agents for which cross resistance and cross susceptibility are nearly complete. Results from one agent connected by an "or" can be used to predict results for the other agent. For example, *Enterobacteriaceae* susceptible to cefotaxime can be considered susceptible to ceftriaxone. The results obtained from testing cefotaxime could be reported along with a comment that the isolate is also susceptible to ceftriaxone. For drugs connected with an "or," combined major and very major errors are fewer than 3%, and minor errors are fewer than 10%,

based on a large population of bacteria tested **(see CLSI document M23 for description of error types)**. In addition, to qualify for an "or," at least 100 strains with resistance to the agents in question must be tested, and a result of "resistant" must be obtained with all agents for at least 95% of the strains. "Or" is also used for comparable agents when tested against organisms for which "susceptible-only" interpretive criteria are provided (eg, cefotaxime or ceftriaxone with *Haemophilus influenzae*). When no "or" connects agents within a box, testing of one agent cannot be used to predict results for another, owing either to discrepancies or insufficient data.

C. Test/Report Groups

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

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

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

4. **Group U ("urine")** includes antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating urinary tract infections. These agents should not be routinely reported against pathogens recovered from other sites of infection. Other agents with broader indications may be included in Group U for specific urinary pathogens (eg, *P. aeruginosa* and ofloxacin).

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

6. **Group Inv. ("investigational")** includes antimicrobial agents that are investigational for the organism group and have not yet been approved by the FDA for use in the United States.

D. Selective Reporting

Each laboratory should decide which agents in the tables to report routinely (Group A) and which might be reported only selectively (from Group B), in consultation with the infectious disease practitioners, the pharmacy, as well as the Pharmacy and Therapeutics and Infection Control committees of the health care institution. Selective reporting should improve the clinical relevance of test reports and help minimize the selection of multiresistant strains by overuse of broad-spectrum agents. Results for Group B agents tested but not reported routinely should be available on request. Unexpected resistance, when confirmed, should be reported (eg, resistance

to a secondary agent but susceptibility to a primary agent, such as a *P. aeruginosa* isolate resistant to amikacin but susceptible to tobramycin; as such, both drugs should be reported). In addition, each laboratory should develop a protocol to address isolates that are confirmed as resistant to all agents on their routine test panels. This protocol should include options for testing additional agents in-house or sending the isolate to a reference laboratory.

II. Reporting Results

The MIC values determined as described in M07-A9 may be reported directly to clinicians for patient care purposes. However, it is essential that an interpretive category result (S, I, or R) also be provided routinely to facilitate understanding of the MIC report by clinicians. Zone diameter measurements without an interpretive category should not be reported. Recommended interpretive categories for various MIC and zone diameter values are included in tables for each organism group and are based on evaluation of data as described in CLSI document M23.

Recommended MIC and disk diffusion interpretive criteria are based on usual dosage regimens and routes of administration in the United States.

A. Susceptible, **susceptible-dose dependent,** intermediate, or resistant interpretations are reported and defined as follows:

1. Susceptible (S)

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 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. 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). 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 (I)**

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 (R)**

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 (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 **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 (see Appendix A).

6. **Interpretive Criteria**

Interpretive criteria are the MIC or zone diameter values used to indicate susceptible, intermediate, and resistant breakpoints.

Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)		
		S	I	R	S	I	R
X	30 µg	≥20	15–19	≤14	≤4	8–16	≥32
Y	—	—	—	—	≤1	2	≥4
Z	**10 µg**	**≥16**	**—**	**—**	**≤1**	**—**	**—**

For example, for antimicrobial agent X with interpretive criteria in the table **above**, the susceptible breakpoint is 4 µg/mL or 20 mm and the resistant breakpoint is 32 µg/mL or 14 mm.

For some antimicrobial agents **(eg, antimicrobial agent Y)**, only MIC **interpretive** criteria may be available. For these agents, the disk diffusion zone diameters do not correlate with MIC values. Technical issues may also preclude the use of the disk diffusion method for some agents.

For some antimicrobial agents (eg, antimicrobial agent Z) only susceptible criteria exist. For these agents, the absence or rare occurrence of resistant strains precludes defining any results categories other than "susceptible." For strains yielding results suggestive of a "nonsusceptible" category, organism identification and antimicrobial susceptibility test results should be confirmed (see Appendix A).

In both cases, a dash mark (—) indicates that interpretive criteria are not applicable.

Laboratories should only report results for agents listed in the Table 2 specific to the **organism** being tested; it is not appropriate to apply disk diffusion or MIC interpretive criteria taken from an alternative Table 2. There may be rare cases where an agent may be appropriate for an isolate but for which there are no CLSI interpretive criteria (eg, tigecycline). In these cases the FDA prescribing information document for the agent should be consulted.

B. For some organism groups excluded from Tables 2A through 2J, CLSI document M45—*Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria* provides suggestions for standardized methods for susceptibility testing, including information about drug selection, interpretation, and QC. The organism groups covered in that document are *Abiotrophia* and *Granulicatella* spp. (formerly known as nutritionally deficient or nutritionally variant streptococci); *Aeromonas* spp.; *Bacillus* spp. (not *B. anthracis*); *Campylobacter jejuni/coli; Corynebacterium* spp. (including *C. diphtheriae*); *Erysipelothrix rhusiopathiae;* the HACEK group: *Aggregatibacter* spp. (formerly *Haemophilus aphrophilus, H. paraphrophilus, H. segnis,* and *Actinobacillus actinomycetemcomitans*), *Cardiobacterium* spp., *Eikenella corrodens,* and *Kingella* spp.; *Helicobacter pylori; Lactobacillus* spp.; *Leuconostoc* spp.; *Listeria monocytogenes; Moraxella catarrhalis; Pasteurella* spp.; *Pediococcus* spp.; potential agents of bioterrorism; and *Vibrio* spp., including *V. cholerae.*

For organisms other than those in the groups mentioned above, studies are not yet adequate to develop reproducible, definitive standards to interpret results. These organisms may require different media or different atmospheres of incubation, or they may show marked strain-to-strain variation in growth rate. For these microorganisms, consultation with an infectious disease specialist is recommended for guidance in determining the need for susceptibility testing and in the interpretation of results. Published reports in the medical literature and current consensus recommendations for therapy of uncommon microorganisms may obviate the need for testing. If necessary, a dilution method usually is the most appropriate testing method, and this may require submitting the organism to a reference laboratory. Physicians should be informed of the limitations of results and advised to interpret results with caution.

C. Policies regarding the generation of cumulative antibiograms should be developed in concert with the infectious disease service, infection control personnel, and the pharmacy and therapeutics committee. In most circumstances, the percentage of susceptible and intermediate results should not be combined into the same statistics. See CLSI document M39—*Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data.*

III. Therapy-Related Comments

Some of the comments in the tables relate to therapy concerns. These are denoted with an ***Rx*** symbol. It may be appropriate to include some of these comments (or modifications thereof) on the patient report. An example would be inclusion of a comment on *Enterococcus* susceptibility reports from blood cultures that "combination therapy with ampicillin, penicillin, or vancomycin (for susceptible strains) plus an aminoglycoside is usually indicated for serious enterococcal infections, such as endocarditis, unless high-level resistance to both gentamicin and streptomycin

is documented; such combinations are predicted to result in synergistic killing of the *Enterococcus*."

Antimicrobial dosage regimens often vary widely among practitioners and institutions. In some cases, the MIC interpretive criteria rely on pharmacokinetic-pharmacodynamic data, using specific human dosage regimens. In cases where specific dosage regimens are important for proper application of breakpoints, the dosage regimen is listed. These dosage regimen comments are not intended for use on individual patient reports.

IV. Confirmation of Patient Results

Multiple test parameters are monitored by following the QC recommendations described in this standard. However, acceptable results derived from testing QC strains do not guarantee accurate results when testing patient isolates. It is important to review all of the results obtained from all drugs tested on a patient's isolate before reporting the results. This should include, but not be limited to, ensuring that 1) the antimicrobial susceptibility results are consistent with the identification of the isolate; 2) the results from individual agents within a specific drug class follow the established hierarchy of activity rules (eg, in general, third-generation cephems are more active than first- or second-generation cephems against *Enterobacteriaceae*); and 3) the isolate is susceptible to those agents for which resistance has not been documented (eg, vancomycin and *Streptococcus* spp.) and for which only "susceptible" interpretive criteria exist in M100.

Unusual or inconsistent results should be confirmed by rechecking various parameters of testing detailed in Appendix A. Each laboratory must develop its own policies for confirmation of unusual or inconsistent antimicrobial susceptibility test results. The list provided in Appendix A emphasizes those results that are most likely to affect patient care.

V. Development of Resistance and Testing of Repeat Isolates

Isolates that are initially susceptible may become intermediate or resistant after initiation of therapy. Therefore, subsequent isolates of the same species from a similar body site should be tested in order to detect resistance that may have developed. This can occur within as little as three to four days and has been noted most frequently in *Enterobacter, Citrobacter,* and *Serratia* spp. with third-generation cephalosporins; in *P. aeruginosa* with all antimicrobial agents; and in staphylococci with quinolones. For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy.

In certain circumstances, testing of subsequent isolates to detect resistance that may have developed might be warranted earlier than within three to four days. The decision to do so requires knowledge of the specific situation and the severity of the patient's condition (eg, an isolate of *Enterobacter cloacae* from a blood culture on a premature infant). Laboratory guidelines on when to perform susceptibility testing on repeat isolates should be determined after consultation with the medical staff.

VI. Warning

Some of the comments in the tables relate to dangerously misleading results that can occur when certain antimicrobial agents are tested and reported as susceptible against specific organisms. These are denoted with the word **"Warning."**

"Warning": The following antimicrobial agent/organism combinations may appear active *in vitro*, but are not effective clinically and should not be reported as susceptible.		
Location	Organism	Antimicrobial Agents That Must Not Be Reported as Susceptible
Table 2A	*Salmonella* spp., *Shigella* spp.	1st- and 2nd-generation cephalosporins, cephamycins, and aminoglycosides
Table 2C	Oxacillin-resistant *Staphylococcus* spp.	Penicillins, β-lactam/β-lactamase inhibitor combinations, antistaphylococcal cephems (except cephalosporins with anti-MRSA activity), and carbapenems
Table 2D	*Enterococcus* spp.	Aminoglycosides (except high concentrations), cephalosporins, clindamycin, and trimethoprim-sulfamethoxazole

VII. Screening Tests

Screening tests, as described in this document, characterize an isolate based on a specific resistance mechanism or phenotype. Some screening tests have sufficient sensitivity and specificity such that results of the screen can be reported without additional testing. Others provide presumptive results and require further testing for confirmation. A summary of the screening tests is provided here; the details for each screening test, including test specifications, limitations, and additional tests needed for confirmation, are provided in the Supplemental Tables listed below.

Organism Group	**Table Location**	**Resistance Phenotype or Mechanism**	**Screening Tests**	**Further Testing or Confirmation Required?**
Enterobacteriaceae	**3A**	ESBL production	Broth microdilution and disk diffusion with various cephalosporins and aztreonam	Yes, if screen test positive[a]
	3B and 3C	Carbapenemase production	Broth microdilution and disk diffusion with various carbapenems	Yes, if screen test positive

Organism Group	Table Location	Resistance Phenotype or Mechanism	Screening Tests	Further Testing or Confirmation Required?
Staphylococcus aureus	**3D**	β-lactamase production	Penicillin disk diffusion zone-edge test	**No**
			Chromogenic cephalosporin	**No, if the test is positive; report the results as positive for β-lactamase (or penicillin resistant).** **Yes, if test is negative the penicillin zone-edge test should be performed before reporting the isolate as penicillin susceptible.**
	3E	Oxacillin resistance	Agar dilution; MHA with 4% NaCl and 6 µg/mL oxacillin	No
		mecA-mediated oxacillin resistance	Broth microdilution and disk diffusion with cefoxitin	No
	3F	Vancomycin MIC ≥8 µg/mL	Agar dilution; BHI with 6 µg/mL vancomycin	Yes, if screen test positive
	3G	Inducible clindamycin resistance	Broth microdilution and disk diffusion with clindamycin and erythromycin	No
	3H	High-level mupirocin resistance	Broth microdilution and disk diffusion with mupirocin	No
Coagulase-negative staphylococci	**3D**	β-lactamase production	Chromogenic cephalosporin or other method	**No, if the test is positive; report the results as positive for β-lactamase (or penicillin resistant).** Yes, if screen test negative: **the penicillin zone-edge test should be performed before reporting the isolate as penicillin susceptible.**
	3E	*mecA*-Mediated oxacillin resistance	Disk diffusion with cefoxitin	No
	3G	Inducible clindamycin resistance	Broth microdilution and disk diffusion with clindamycin and erythromycin	No
Enterococci	**3F**	Vancomycin MIC ≥8 µg/mL	Agar dilution; BHI with 6 µg/mL vancomycin with vancomycin	Yes, if screen test positive
	3I	HLAR	Broth microdilution, agar dilution, and disk diffusion with gentamicin and streptomycin	No for MIC; yes for disk, if inconclusive
Streptococcus pneumoniae	2G	Penicillin resistance	Disk diffusion with oxacillin	Yes, if nonsusceptible **(oxacillin zone ≤19 mm)**

Organism Group	Table Location	Resistance Phenotype or Mechanism	Screening Tests	Further Testing or Confirmation Required?
Streptococcus pneumoniae	**3G**	Inducible clindamycin resistance	Broth microdilution and disk diffusion with clindamycin and erythromycin	No
Streptococcus spp. β-hemolytic Group	**3G**	Inducible clindamycin resistance	Broth microdilution and disk diffusion with clindamycin and erythromycin	No

[a] If the current cephalosporin, aztreonam, and carbapenem breakpoints are used, ESBL and/or modified Hodge testing is not required, but may be used to determine the presence of a resistance mechanism that may be of epidemiological significance. However, if the ESBL and/or carbapenemase screen is performed and positive, the confirmatory test must be performed to establish the presence of an ESBL or a carbapenemase.

Abbreviations: BHI, Brain Heart Infusion; ESBL, extended-spectrum β-lactamase; FDA, US Food and Drug Administration; HLAR, high-level aminoglycoside resistance; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration.

VIII. Quality Control and Verification

Recommendations for QC are addressed in various tables and appendixes. Acceptable ranges for QC strains are provided in Tables 4A and 4B for disk diffusion and Tables 5A through 5E for MIC testing. Guidance for frequency of QC and modifications of antimicrobial susceptibility testing (AST) systems is found in Table 4C for disk diffusion and Table 5F for MIC testing. Guidance for troubleshooting out-of-range results is addressed in Table 4D for disks and Table 5G for MIC testing. Additional information is available in Appendix C: Quality Control Strains for Antimicrobial Susceptibility Tests (eg, QC organism characteristics, QC testing recommendations).

Implementation of any new diagnostic test requires verification.[1] Each laboratory that introduces a new AST system or adds a new antimicrobial agent to an existing AST system must verify or establish that, before reporting patient test results, the system meets performance specifications for that system. Verification generally involves testing clinical isolates with the new AST system and comparing results to those obtained with an established reference method or a system that has been previously verified. Testing clinical isolates may be done concurrently with the two systems. Alternatively, organisms with known MICs or zone sizes may be used for the verification. Guidance on verification studies is not addressed in this document. Other publications describe verification of AST systems (eg, ASM Cumitech 31A[2]).

References

1 Centers for Medicare & Medicaid Services, US Department of Health and Human Services. *Part 493—Laboratory Requirements; Standard: Establishment and verification of performance specifications* (Codified at 42 CFR §493.1253). US Government Printing Office; published annually.

2 Clark RB, Lewinski MA, Loeffelholz MJ, Tibbetts RJ. Cumitech 31A: verification and validation of procedures in the clinical microbiology laboratory. Washington, DC: ASM Press; 2009.

IX. Abbreviations and Acronyms

AST	antimicrobial susceptibility testing
ATCC	American Type Culture Collection
BHI	Brain Heart Infusion
BLNAR	β-lactamase negative, ampicillin-resistant
BSC	biological safety cabinet
BSL-2	Biosafety Level 2

BSL-3	Biosafety Level 3
CAMHB	cation-adjusted Mueller-Hinton broth
CDC	Centers for Disease Control and Prevention
CFU	colony-forming unit
CMRNG	chromosomally mediated penicillin-resistant *Neisseria gonorrhoeae*
CoNS	coagulase-negative staphylococci
CSF	cerebrospinal fluid
DMF	dimethylformamide
DMSO	dimethyl sulfoxide
ESBL	extended-spectrum β-lactamase
FDA	US Food and Drug Administration
HLAR	high-level aminoglycoside resistance
HTM	*Haemophilus* Test Medium
I	intermediate
ID	identification
KPC	*Klebsiella pneumoniae* carbapenemase
LHB	lysed horse blood
MHA	Mueller-Hinton agar
MHB	Mueller-Hinton broth
MHT	modified Hodge test
MIC	minimal inhibitory concentration
MRS	methicillin-resistant staphylococci
MRSA	methicillin-resistant *S. aureus*
NAD	nicotinamide adenine dinucleotide
NDM	New Delhi metallo-β-lactamase
PBP 2a	penicillin-binding protein 2a
PCR	polymerase chain reaction
PK-PD	pharmacokinetic-pharmacodynamic
QC	quality control
QCP	quality control plan
R	resistant
S	susceptible
SDD	**susceptible-dose dependent**
TSA	tryptic soy agar
UTI	**urinary tract infection**

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Table 1A. Suggested Groupings of Antimicrobial Agents With FDA Clinical Indications That Should Be Considered for Routine Testing and Reporting on Nonfastidious Organisms by Clinical Microbiology Laboratories in the United States

	Enterobacteriaceae	*Pseudomonas aeruginosa*	*Staphylococcus* spp.	*Enterococcus* spp.[m]
GROUP A PRIMARY TEST AND REPORT	Ampicillin[d]	Ceftazidime	Azithromycin[b] or clarithromycin[b] or erythromycin[b]	Ampicillin[n] Penicillin[o]
			Clindamycin[b]	
			*,†Oxacillin[i,k] †Cefoxitin[i,k] **(surrogate test for oxacillin)**	
	Cefazolin[e]	Gentamicin Tobramycin	Penicillin[i]	
	Gentamicin Tobramycin	Piperacillin	Trimethoprim-sulfamethoxazole	
GROUP B PRIMARY TEST REPORT SELECTIVELY	Amikacin	Amikacin	Ceftaroline[h]	*Daptomycin[j]
			*Daptomycin[j]	
		Aztreonam	Linezolid	Linezolid
	Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam Ticarcillin-clavulanate	Cefepime	Doxycycline Minocycline[b] Tetracycline[a]	
	Cefuroxime			Vancomycin
		Ciprofloxacin Levofloxacin	*,†Vancomycin	
	Cefepime	Doripenem Imipenem Meropenem	Rifampin[g]	
	Cefotetan Cefoxitin	Piperacillin-tazobactam Ticarcillin		
	Cefotaxime[d,e] or ceftriaxone[d,e]			
	Ciprofloxacin[d] Levofloxacin[d]			
	Doripenem Ertapenem Imipenem Meropenem			
	Piperacillin			
	Trimethoprim-sulfamethoxazole[d]			
GROUP C SUPPLEMENTAL REPORT SELECTIVELY	*Enterobacteriaceae*	*Pseudomonas aeruginosa*	*Staphylococcus* spp.	*Enterococcus* spp.[m]
	Aztreonam Ceftazidime		Chloramphenicol[b]	Gentamicin (high-level resistance screen only)
	Ceftaroline		Ciprofloxacin or levofloxacin or ofloxacin Moxifloxacin	Streptomycin (high-level resistance screen only)
	Chloramphenicol[b,d]		Gentamicin[l]	
	Tetracycline[a]			
GROUP U SUPPLEMENTAL FOR URINE ONLY	**Cefazolin[c] (surrogate test for uncomplicated UTI)**	Lomefloxacin or ofloxacin Norfloxacin	Lomefloxacin Norfloxacin	Ciprofloxacin Levofloxacin Norfloxacin
	Lomefloxacin or ofloxacin Norfloxacin			
	Nitrofurantoin		Nitrofurantoin	Nitrofurantoin
	Sulfisoxazole		Sulfisoxazole	
	Trimethoprim		Trimethoprim	Tetracycline[a]

* MIC testing only; disk diffusion test unreliable.
† See oxacillin, cefoxitin, and vancomycin comments in Table 2C for using cefoxitin as a surrogate for oxacillin.

Table 1A. (Continued)

	Acinetobacter spp.	*Burkholderia cepacia*	*Stenotrophomonas maltophilia*	*Other Non-*Enterobacteriaceae*[f]
GROUP A PRIMARY TEST AND REPORT	Ampicillin-sulbactam	Trimethoprim-sulfamethoxazole	Trimethoprim-sulfamethoxazole	Ceftazidime
	Ceftazidime			
	Ciprofloxacin Levofloxacin			Gentamicin Tobramycin
	Doripenem Imipenem Meropenem			
	Gentamicin Tobramycin			Piperacillin
GROUP B PRIMARY TEST REPORT SELECTIVELY	Amikacin	Ceftazidime	*Ceftazidime	Amikacin
		*Chloramphenicol[b]	*Chloramphenicol[b]	Aztreonam
		*Levofloxacin	Levofloxacin	Cefepime
	Piperacillin-tazobactam Ticarcillin-clavulanate	Meropenem	Minocycline	Ciprofloxacin Levofloxacin
		Minocycline	*Ticarcillin-clavulanate	Imipenem Meropenem
		*Ticarcillin-clavulanate		
	Cefepime			Piperacillin-tazobactam Ticarcillin-clavulanate
	Cefotaxime Ceftriaxone			
	Doxycycline Tetracycline			Trimethoprim-sulfamethoxazole
	Minocycline			
	Piperacillin			
	Trimethoprim-sulfamethoxazole			
GROUP C SUPPLEMENTAL REPORT SELECTIVELY				Cefotaxime Ceftriaxone
				Chloramphenicol[b]
GROUP U SUPPLEMENTAL FOR URINE ONLY				Lomefloxacin or ofloxacin Norfloxacin
				Sulfisoxazole
				Tetracycline[a]

Abbreviations: FDA, US Food and Drug Administration; MIC, minimal inhibitory concentration, UTI, urinary tract infection.
* MIC testing only; disk diffusion test unreliable.

Table 1A. (Continued)

"Warning": The following antimicrobial agents should not be routinely reported for bacteria isolated from CSF that are included in this document. These antimicrobial agents are not the drugs of choice and may not be effective for treating CSF infections caused by these organisms (ie, the bacteria included in Tables 2A through 2J):

agents administered by oral route only
1st- and 2nd-generation cephalosporins (except cefuroxime parenteral)
and cephamycins
clindamycin
macrolides
tetracyclines
fluoroquinolones

NOTE 1: For information about the selection of appropriate antimicrobial agents; explanation of Test and Report Groups A, B, C, and U; and explanation of the listing of agents within boxes, including the meaning of "or" between agents, refer to the Instructions for Use of Tables that precede Table 1A.

NOTE 2: Information in boldface type is new or modified since the previous edition.

Footnotes

General Comments

a. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.

b. Not routinely reported on organisms isolated from the urinary tract.

Enterobacteriaceae

c. ***Rx*: Cefazolin results predict results for the oral agents cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime axetil, cephalexin, and loracarbef when used for therapy of uncomplicated UTIs due to *E. coli, K. pneumoniae,* and *P. mirabilis.* Cefpodoxime, cefdinir, and cefuroxime axetil may be tested individually because some isolates may be susceptible to these agents while testing resistant to cefazolin.**

d. **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.**

When fecal isolates of *Salmonella* and *Shigella* spp. are tested, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely. In addition, for extraintestinal isolates of *Salmonella* spp., a third-generation cephalosporin should be tested and reported, and chloramphenicol may be tested and reported, if requested. Susceptibility testing is indicated for typhoidal Salmonella (*S.* Typhi and *Salmonella* Paratyphi A–C) isolated from extraintestinal and intestinal sources. Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources.

e. Cefotaxime **or** ceftriaxone should be tested and reported on isolates from CSF in place of cefazolin.

Table 1A. (Continued)

Other Non-*Enterobacteriaceae*

f. Other non-*Enterobacteriaceae* include *Pseudomonas* spp. and other nonfastidious, glucose-nonfermenting, gram-negative bacilli, but exclude *Pseudomonas aeruginosa, Acinetobacter* spp., *Burkholderia cepacia,* and *Stenotrophomonas maltophilia,* because there are separate lists of suggested drugs to test and report for them.

Recommendations for testing and reporting of ***Aeromonas hydrophila*** **complex,** *B. mallei, B. pseudomallei,* ***Plesiomonas shigelloides,*** **and** ***Vibrio*** **species (including** ***V. cholerae)*** are found in CLSI document M45.

Staphylococcus spp.

g. ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.

h. For *S. aureus* only including methicillin-resistant *Staphylococcus aureus* (MRSA).

i. Penicillin-susceptible staphylococci are also susceptible to other β-lactam agents with established clinical efficacy for staphylococcal infections. Penicillin-resistant staphylococci are resistant to penicillinase-labile penicillins. Oxacillin-resistant staphylococci are resistant to all currently available β-lactam antimicrobial agents, with the exception of the newer cephalosporins with anti-MRSA activity. Thus, susceptibility or resistance to a wide array of β-lactam antimicrobial agents may be deduced from testing only penicillin and either cefoxitin or oxacillin. Routine testing of other β-lactam agents, except those with anti-MRSA activity, is not advised.

j. Daptomycin should not be reported for isolates from the respiratory tract.

k. The results of either cefoxitin disk diffusion or cefoxitin MIC tests can be used to predict the presence of *mecA*-mediated oxacillin resistance in *S. aureus* and *S. lugdunensis.* For coagulase-negative staphylococci (except *S. lugdunensis*), the cefoxitin disk diffusion test is the preferred method for detection of *mecA*-mediated oxacillin resistance. Cefoxitin is used as a surrogate for detection of oxacillin resistance; report oxacillin as susceptible or resistant based on cefoxitin results. If a penicillinase-stable penicillin is tested, oxacillin is the preferred agent, and results can be applied to the other penicillinase-stable penicillins, cloxacillin, dicloxacillin, flucloxacillin**, methicillin, and nafcillin**.

l. For staphylococci that test susceptible, aminoglycosides are used only in combination with other active agents that test susceptible.

Enterococcus spp.

m. **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.

n. The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. Ampicillin results may be used to predict susceptibility to amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin, and piperacillin-tazobactam among non–β-lactamase-producing enterococci. Ampicillin susceptibility can be used to predict imipenem susceptibility, providing the species is confirmed to be *E. faecalis.*

Table 1A. (Continued)

o. Enterococci susceptible to penicillin are predictably susceptible to ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, piperacillin, and piperacillin-tazobactam for non–β-lactamase–producing enterococci. However, enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin. If penicillin results are needed, testing of penicillin is required. ***Rx:*** Combination therapy with ampicillin, penicillin, or vancomycin (for susceptible strains) plus an aminoglycoside is usually indicated for serious enterococcal infections, such as endocarditis, unless high-level resistance to both gentamicin and streptomycin is documented; such combinations are predicted to result in synergistic killing of the *Enterococcus.*

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Table 1B. Suggested Groupings of Antimicrobial Agents With FDA Clinical Indications That Should Be Considered for Routine Testing and Reporting on Fastidious Organisms by Clinical Microbiology Laboratories in the United States

	***Haemophilus influenzae* and *Haemophilus parainfluenzae*[d]**	***Neisseria gonorrhoeae*[i]**	***Streptococcus pneumoniae*[j]**	***Streptococcus* spp. β-Hemolytic Group[q]**	***Streptococcus* spp. Viridans Group[q]**
GROUP A PRIMARY TEST AND REPORT	Ampicillin[d,f]	†Ceftriaxone †Cefixime	Erythromycin[a,c]	Clindamycin[c,p]	*Ampicillin[m] *Penicillin[m]
				Erythromycin[a,c,p]	
		†Ciprofloxacin	Penicillin[k] (oxacillin disk)	†Penicillin[n] or †ampicillin[n]	
	Trimethoprim-sulfamethoxazole	†Tetracycline[b]	Trimethoprim-sulfamethoxazole		
GROUP B PRIMARY TEST REPORT SELECTIVELY	Ampicillin-sulbactam		*Cefepime *Cefotaxime[k] *Ceftriaxone[k]	Cefepime or cefotaxime or ceftriaxone	Cefepime Cefotaxime Ceftriaxone
	Cefuroxime (parenteral)				
			Clindamycin[c]		
			Doxycycline		
	Cefotaxime[d] or ceftazidime[d] or ceftriaxone[d]		Gemifloxacin[j] Levofloxacin[j] Moxifloxacin[j] Ofloxacin	Vancomycin	Vancomycin
	Chloramphenicol[c,d]		*Meropenem[k]		
			Telithromycin		
	Meropenem[d]		Tetracycline[b]		
			Vancomycin[k]		
GROUP C SUPPLEMENTAL REPORT SELECTIVELY	Azithromycin[e] Clarithromycin[e]		*Amoxicillin *Amoxicillin-clavulanate	Ceftaroline	Chloramphenicol[c]
	Aztreonam			Chloramphenicol[c]	Clindamycin[c]
	Amoxicillin-clavulanate[e]			*Daptomycin[r]	Erythromycin[a,c]
	Cefaclor[e] Cefprozil[e]		*Cefuroxime		
	Cefdinir[e] or cefixime[e] or cefpodoxime[e]		Ceftaroline	Levofloxacin Ofloxacin	
	Ceftaroline[g]				
	Cefuroxime (oral)[e]		Chloramphenicol[c]	Linezolid	Linezolid
				Quinupristin-dalfopristin[o]	
	Ciprofloxacin or levofloxacin or lomefloxacin or moxifloxacin or ofloxacin	Spectinomycin	*Ertapenem *Imipenem		
	Gemifloxacin		Linezolid		
	Ertapenem or imipenem		Rifampin[l]		
	Rifampin[h]				
	Telithromycin[e]				
	Tetracycline[b]				

Abbreviations: FDA, US Food and Drug Administration, MIC, minimal inhibitory concentration.

* MIC testing only; disk diffusion test unreliable.
† Routine testing is not necessary (see footnotes i and n).

Table 1B. (Continued)

"Warning": The following antimicrobial agents should not be routinely reported for bacteria isolated from CSF that are included in this document. These antimicrobial agents are not the drugs of choice and may not be effective for treating CSF infections caused by these organisms (ie, the bacteria included in Tables 2A through 2J):
agents administered by oral route only 1st- and 2nd-generation cephalosporins (except cefuroxime parenteral) and cephamycins clindamycin macrolides tetracyclines fluoroquinolones

NOTE 1: For information about the selection of appropriate antimicrobial agents; explanation of Test and Report Groups A, B, C, and U; and explanation of the listing of agents within boxes, including the meaning of "or" between agents, refer to the Instructions for Use of Tables that precede Table 1A.

NOTE 2: Information in boldface type is new or modified since the previous edition.

Footnotes

General Comments

a. Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin.

b. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.

c. Not routinely reported for organisms isolated from the urinary tract.

Haemophilus spp.

d. For isolates of *H. influenzae* from CSF, only results of testing with ampicillin, one of the third-generation cephalosporins, chloramphenicol, and meropenem are appropriate to report routinely.

e. Amoxicillin-clavulanate, azithromycin, cefaclor, cefdinir, cefixime, cefpodoxime, cefprozil, cefuroxime, clarithromycin, loracarbef, and telithromycin are oral agents that may be used as empiric therapy for respiratory tract infections due to *Haemophilus* spp. The results of susceptibility tests with these antimicrobial agents are often not useful for management of individual patients. However, susceptibility testing of *Haemophilus* spp. with these compounds may be appropriate for surveillance or epidemiological studies.

f. The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. The majority of isolates of *H. influenzae* that are resistant to ampicillin and amoxicillin produce a TEM-type β-lactamase. In most cases, a direct β-lactamase test can provide a rapid means of detecting ampicillin and amoxicillin resistance.

g. For *H. influenzae* only.

h. May be appropriate only for prophylaxis of case contacts. Refer to Table 2E.

Table 1B. (Continued)

Neisseria gonorrhoeae

i. Culture and susceptibility testing of *N. gonorrhoeae* should be considered in cases of treatment failure. Antimicrobial agents recommended for testing include, at a minimum, those agents listed in Group A. The most recent CDC guidelines for treatment and testing are available at http://www.cdc.gov/std/Gonorrhea/.

Streptococcus pneumoniae

j. *S. pneumoniae* isolates susceptible to levofloxacin are predictably susceptible to gemifloxacin and moxifloxacin. However, *S. pneumoniae* susceptible to gemifloxacin or moxifloxacin cannot be assumed to be susceptible to levofloxacin.

k. Penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method (such as that described in M07-A9), and reported routinely with CSF isolates of *S. pneumoniae*. Such isolates can also be tested against vancomycin using the MIC or disk method. With isolates from other sites, the oxacillin disk screening test may be used. If the oxacillin zone size is ≤ 19 mm, penicillin, cefotaxime, ceftriaxone, or meropenem MICs should be determined.

l. ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.

Streptococcus spp.

m. ***Rx:*** Penicillin- or ampicillin-intermediate isolates may require combined therapy with an aminoglycoside for bactericidal action.

n. Penicillin and ampicillin are drugs of choice for treatment of β-hemolytic streptococcal infections. Susceptibility testing of penicillins and other β-lactams approved by the FDA for treatment of β-hemolytic streptococcal infections need not be performed routinely, because nonsusceptible isolates (ie, penicillin MICs > 0.12 and ampicillin MICs > 0.25 μg/mL) are extremely rare in any β-hemolytic streptococcus and have not been reported for *Streptococcus pyogenes.* If testing is performed, any β-hemolytic streptococcal isolate found to be nonsusceptible should be re-identified, retested, and, if confirmed, submitted to a public health laboratory. (See Appendix A for further instructions.)

o. Report against *S. pyogenes.*

p. ***Rx:*** Recommendations for intrapartum prophylaxis for Group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin. Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin, but may be resistant to erythromycin and clindamycin. When Group B *Streptococcus* is isolated from a pregnant woman with severe penicillin allergy (high risk for anaphylaxis), erythromycin and clindamycin (including inducible clindamycin resistance) should be tested, and only clindamycin should be reported. See Table **3G**.

q. For this table, the β-hemolytic group includes the large colony–forming pyogenic strains of streptococci with Group A (*S. pyogenes*), C, or G antigens and strains with Group B (*S. agalactiae*) antigen. Small colony–forming β-hemolytic strains with Group A, C, F, or G antigens (*S. anginosus* group, previously termed *"S. milleri"*) are considered part of the viridans group, and interpretive criteria for the viridans group should be used.

r. Daptomycin should not be reported for isolates from the respiratory tract.

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Table 1C. Suggested Groupings of Antimicrobial Agents That Should Be Considered for Routine Testing and Reporting on Anaerobic Organisms

	***Bacteroides fragilis* Group and Other Gram-Negative Anaerobes**	**Gram-Positive Anaerobes[b]**
Group A Primary Test and Report	Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam Ticarcillin-clavulanate	Ampicillin[a] Penicillin[a]
		Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam Ticarcillin-clavulanate
	Clindamycin	
	Doripenem Ertapenem Imipenem Meropenem	Clindamycin
		Doripenem Ertapenem Imipenem Meropenem
	Metronidazole	
		Metronidazole
Group C Supplemental Report Selectively	Penicillin[a] Ampicillin[a]	Ceftizoxime Ceftriaxone
	Ceftizoxime Ceftriaxone	Cefotetan Cefoxitin
	Chloramphenicol	
	Cefotetan Cefoxitin	Piperacillin Ticarcillin
		Tetracycline
		Moxifloxacin
	Piperacillin Ticarcillin	
	Moxifloxacin	

Table 1C. (Continued)

NOTE 1: For information about the selection of appropriate antimicrobial agents; explanation of Test and Report Groups A and C; and explanation of the listing of agents within boxes, refer to the Instructions for Use of Tables that precede Table 1A.

NOTE 2: Most anaerobic infections are polymicrobial, including both β-lactamase–positive and β-lactamase–negative strains. Susceptibility of the most resistant strain must be considered first and reported. In the case of an infection caused by a single β-lactamase–negative strain, penicillin or ampicillin may be appropriate for testing and reporting.

NOTE 3: Many gram-positive anaerobes are isolated from polymicrobial infections with potentially resistant organisms; however, some *Clostridium* species (eg, *C. perfringens, C. septicum, C. sordellii)* may be the singular cause of an infection, are typically susceptible to penicillin and ampicillin, and should be tested and reported.

NOTE 4: Information in boldface type is new or modified since the previous edition.

Footnotes

General Comment

a. If β-lactamase positive, report as resistant to penicillin and ampicillin. Be aware that β-lactamase–negative isolates may be resistant to **penicillin and ampicillin** by other mechanisms.

Gram-positive Anaerobes

b. Many non–spore-forming, gram-positive anaerobic rods are resistant to metronidazole.

Table 2A. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Enterobacteriaceae*

Testing Conditions	
Medium:	Disk diffusion: Mueller-Hinton agar (MHA) Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB) Agar dilution: MHA
Inoculum:	Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation:	35±2°C; ambient air; Disk diffusion: 16 to 18 hours Dilution methods: 16 to 20 hours

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Escherichia coli ATCC®* 25922
***Pseudomonas aeruginosa* ATCC® 27853 (for carbapenems)**
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

* ATCC is a registered trademark of the American Type Culture Collection.

Refer to Table**s 3A, 3B, and 3C** for additional **testing** recommendations, reporting suggestions, and QC.

General Comments

(1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and **up to 6** disks on a 100-mm plate**; disks should be placed no less than 24 mm apart, center to center** (M02, Section 9.2 **will be updated during its next scheduled revision to include this recommendation**). **Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement.** Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. Strains of *Proteus* spp. may swarm into areas of inhibited growth around certain antimicrobial agents. With *Proteus* spp., ignore the thin veil of swarming growth in an otherwise obvious zone of growth inhibition. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

(2) When fecal isolates of *Salmonella* and *Shigella* spp. are tested, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely. In addition, for extraintestinal isolates of *Salmonella* spp., a third-generation cephalosporin should be tested and reported, and chloramphenicol may be tested and reported if requested. Susceptibility testing is indicated for typhoidal Salmonella (*S.* Typhi and *Salmonella* Paratyphi A–C) isolated from extraintestinal and intestinal sources. Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources.

(3) The dosage regimens shown in the comment column below are those required to achieve plasma drug exposures (in adults with normal renal and hepatic functions) on which breakpoints were based. When implementing new breakpoints, it is strongly recommended that laboratories share this information with infectious disease practitioners, pharmacists, pharmacy and therapeutics committees, and infection control committees.

NOTE: Information in boldface type is new or modified since the previous edition.

Table 2A. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm) S	SDD	I	R	MIC Interpretive Criteria (µg/mL) S	SDD	I	R	Comments
PENICILLINS											
A	Ampicillin	10 µg	≥17		14–16	≤13	≤8		16	≥32	(4) Results of ampicillin testing can be used to predict results for amoxicillin. See comment (2).
B	Piperacillin	100 µg	≥21		18–20	≤17	≤16		32–64	≥128	
O	Mecillinam	10 µg	≥15		12–14	≤11	≤8		16	≥32	(5) For testing and reporting of *E. coli* urinary tract isolates only.
O	Ticarcillin	75 µg	≥ 20		15–19	≤ 14	≤ 16		32–64	≥ 128	
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS											
B	Amoxicillin-clavulanate	20/10 µg	≥18		14–17	≤13	≤8/4		16/8	≥32/16	
B	Ampicillin-sulbactam	10/10 µg	≥15		12–14	≤11	≤8/4		16/8	≥32/16	
B	Piperacillin-tazobactam	100/10 µg	≥21		18–20	≤17	≤16/4		32/4–64/4	≥128/4	
B	Ticarcillin-clavulanate	75/10 µg	≥20		15–19	≤14	≤16/2		32/2–64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (6) **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. (7) Following evaluation of PK-PD properties, limited clinical data, and MIC distributions, revised interpretive criteria for cephalosporins (cefazolin, cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone) and aztreonam were first published in January 2010 (M100-S20) and are listed in this table. Cefuroxime (parenteral) was also evaluated; however, no change in interpretive criteria was required for the dosage indicated below. When using the current interpretive criteria, routine ESBL testing is no longer necessary before reporting results (ie, it is no longer necessary to edit results for cephalosporins, aztreonam, or penicillins from susceptible to resistant). However, ESBL testing may still be useful for epidemiological or infection control purposes. For laboratories that have not implemented the current interpretive criteria, ESBL testing should be performed as described in Table **3A**. Note that interpretive criteria for drugs with limited availability in many countries (eg, moxalactam, cefonicid, cefamandole, and cefoperazone) were not evaluated. If considering use of these drugs for *E. coli, Klebsiella,* or *Proteus* spp., ESBL testing should be performed (see Table **3A**). If isolates test ESBL positive, the results for moxalactam, cefonicid, cefamandole, and cefoperazone should be reported as resistant. (8) *Enterobacter, Citrobacter,* and *Serratia* may develop resistance during prolonged therapy with third-generation cephalosporins as a result of derepression of AmpC β-lactamase. Therefore, isolates that are initially susceptible may become resistant within three to four days after initiation of therapy. Testing of repeat isolates may be warranted.										
A	Cefazolin	30 µg	≥23		20–22	≤19	≤2		4	≥8	(9) Interpretive criteria are based on a dosage regimen of 2 g every 8 h. See comment (7). **For UTI interpretive criteria, see below under CEPHEMS (ORAL).**
C	Ceftaroline	30 µg	≥23		20–22	≤19	≤0.5		1	≥2	(10) Interpretive criteria are based on a dosage regimen of 600 mg every 12 h.

Table 2A. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)				MIC Interpretive Criteria (µg/mL)				Comments
			S	SDD	I	R	S	SDD	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)											
U	Cephalothin **(surrogate test for uncomplicated UTI)**	30 µg	≥18		15–17	≤14	≤8		16	≥32	(11) Cephalothin interpretive criteria can be used only to predict **susceptibility** to the oral agents, cefadroxil, cefpodoxime, cephalexin, and loracarbef. Older data that suggest that cephalothin results could predict susceptibility to some other cephalosporins may still be correct, but there are no recent data to confirm this. **(12) To predict results for oral cephalosporins when used for therapy of uncomplicated UTIs, testing cefazolin is preferred to testing cephalothin.**
B	Cefepime	30 µg	**≥25**	**19–24**	**–**	**≤18**	**≤2**	**4–8**	**–**	**≥16**	(13) **The interpretive criterion for susceptible is based on a dosage regimen of 1 g every 12 h. The interpretive criterion for SDD is based on dosing regimens that result in higher cefepime exposure, either higher doses or more frequent doses or both, up to approved maximum dosing regimens. See Appendix E for more information about interpretive criteria and dosing regimens. Also see the definition of SDD in the Instructions for Use of Tables section.**
B B	Cefotaxime or ceftriaxone	30 µg 30 µg	≥26 ≥23		23–25 20–22	≤22 ≤19	≤1 ≤1		2 2	≥4 ≥4	(14) Interpretive criteria are based on a dosage regimen of 1 g every 24 h for ceftriaxone and 1 g every 8 h for cefotaxime. See comment (7).
B	Cefotetan	30 µg	≥16		13–15	≤12	≤16		32	≥64	

Table 2A. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)				MIC Interpretive Criteria (µg/mL)				Comments
			S	SDD	I	R	S	SDD	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)											
B	Cefoxitin	30 µg	≥18		15–17	≤14	≤8		16	≥32	(15) The interpretive criteria are based on a dosage regimen of at least 8 g per day (eg, 2 g every 6 h).
B	Cefuroxime (parenteral)	30 µg	≥18		15–17	≤14	≤8		16	≥32	(16) Interpretive criteria are based on a dosage regimen of 1.5 g every 8 h. See comment (7).
C	Ceftazidime	30 µg	≥21		18–20	≤17	≤4		8	≥16	(17) Interpretive criteria are based on a dosage regimen of 1 g every 8 h. See comment (7).
O	Cefamandole	30 µg	≥18		15–17	≤14	≤8		16	≥32	See comment (7).
O	Cefmetazole	30 µg	≥16		13–15	≤12	≤16		32	≥64	(18) Insufficient new data exist to reevaluate interpretive criteria listed here.
O	Cefonicid	30 µg	≥18		15–17	≤14	≤8		16	≥32	See comment (7).
O	Cefoperazone	75 µg	≥21		16–20	≤15	≤16		32	≥64	See comment (7).
O	Ceftizoxime	30 µg	≥25		22–24	≤21	≤1		2	≥4	(19) Interpretive criteria are based on a dosage regimen of 1 g every 12 h. See comment (7).
O	Moxalactam	30 µg	≥23		15–22	≤14	≤8		16–32	≥64	See comment (7).
CEPHEMS (ORAL)											
B	Cefuroxime (oral)	30 µg	≥23		15–22	≤14	≤4		8–16	≥32	**See comments (12 and 20).**
U	**Cefazolin (surrogate test for uncomplicated UTI)**	**30 µg**	**≥15**		**–**	**≤14**	**≤16**	**–**	**–**	**≥32**	**(20) *Rx:* Cefazolin results predict results for the oral agents cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime axetil, cephalexin, and loracarbef when used for therapy of uncomplicated UTIs due to *E. coli, K. pneumoniae,* and *P. mirabilis.* Cefpodoxime, cefdinir, and cefuroxime axetil may be tested individually because some isolates may be susceptible to these agents while testing resistant to cefazolin. See comment (12).**

Table 2A. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)				MIC Interpretive Criteria (µg/mL)				Comments
			S	SDD	I	R	S	SDD	I	R	
CEPHEMS (ORAL) (Continued)											
O	Loracarbef	30 µg	≥18		15–17	≤14	≤8		16	≥32	(21) Do not test *Citrobacter, Providencia,* or *Enterobacter* spp. with cefdinir or loracarbef by disk diffusion because false-susceptible results have been reported. **See comments (12 and 20).**
O	Cefaclor	30 µg	≥18		15–17	≤14	≤8		16	≥32	**See comments (12 and 20).**
O	Cefdinir	5 µg	≥20		17–19	≤16	≤1		2	≥4	See comment**s** (12, **20, and 21**).
O	Cefixime	5 µg	≥19		16–18	≤15	≤1		2	≥4	(22) Do not test *Morganella* spp. with cefixime**, cefpodoxime, or cefetamet** by disk diffusion.
O	Cefpodoxime	10 µg	≥21		18–20	≤17	≤2		4	≥8	See comment**s** (**12, 20**, **and 22**).
O	Cefprozil	30 µg	≥18		15–17	≤14	≤8		16	≥32	(23) Do not test *Providencia* spp. with cefprozil by disk diffusion because false-susceptible results have been reported. **See comments (12 and 20).**
Inv.	Cefetamet	10 µg	≥18		15–17	≤14	≤4		8	≥16	See comment (22).
Inv.	Ceftibuten	30 µg	≥21		18–20	≤17	≤8		16	≥32	(24) For testing and reporting of urine isolates only.
MONOBACTAMS											
C	Aztreonam	30 µg	≥21		18–20	≤17	≤4		8	≥16	(25) Interpretive criteria are based on a dosage regimen of 1 g every 8 h. See comment (7).

Table 2A. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm) S	SDD	I	R	MIC Interpretive Criteria (µg/mL) S	SDD	I	R	Comments
CARBAPENEMS (26) Following evaluation of PK-PD properties, limited clinical data, and MIC distributions that include recently described carbapenemase-producing strains, revised interpretive criteria for carbapenems were first published in June 2010 (M100-S20-U) and are listed below. Because of limited treatment options for infections caused by organisms with carbapenem MICs or zone diameters in the intermediate range, clinicians may wish to design carbapenem dosage regimens that use maximum recommended doses and possibly prolonged intravenous infusion regimens, as has been reported in the literature.[1-4] Consultation with an infectious diseases practitioner is recommended for isolates for which the carbapenem MICs or zone diameter results from disk diffusion testing are in the intermediate or resistant ranges. Until laboratories can implement the current interpretive criteria, the modified Hodge test (MHT) should be performed as described in Table **3C**. After implementation of the current interpretive criteria, the MHT does not need to be performed other than for epidemiological or infection control purposes (refer to Table **3B**). The following information is provided as background on carbapenemases in *Enterobacteriaceae* that are largely responsible for MICs and zone diameters in the intermediate and resistant ranges, and thus the rationale for setting revised carbapenem breakpoints: • The clinical effectiveness of carbapenem treatment of infections produced by isolates for which the carbapenem MIC or disk diffusion test results are within the intermediate (I) range is uncertain due to lack of controlled clinical studies. • Imipenem MICs for *Proteus* spp., *Providencia* spp., and *Morganella morganii* tend to be higher (eg, MICs in the intermediate or resistant range) than meropenem or doripenem MICs. These isolates may have elevated imipenem MICs by mechanisms other than production of carbapenemases.											
B	Doripenem	10 µg	≥23		20–22	≤19	≤1		2	≥4	(27) Interpretive criteria are based on a dosage regimen of 500 mg every 8 h.
B	Ertapenem	10 µg	≥22		19–21	≤18	≤0.5		1	≥2	(28) Interpretive criteria are based on a dosage regimen of 1 g every 24 h.
B	Imipenem	10 µg	≥23		20–22	≤19	≤1		2	≥4	(29) Interpretive criteria are based on a dosage regimen of 500 mg every 6 h or 1 g every 8 h.
B	Meropenem	10 µg	≥23		20–22	≤19	≤1		2	≥4	(30) Interpretive criteria are based on a dosage regimen of 1 g every 8 h.
AMINOGLYCOSIDES (31) **WARNING:** For *Salmonella* spp. and *Shigella* spp., aminoglycosides may appear active *in vitro* but are not effective clinically and should not be reported as susceptible.											
A A	Gentamicin Tobramycin	10 µg 10 µg	≥15 ≥15		13–14 13–14	≤12 ≤12	≤4 ≤4		8 8	≥16 ≥16	
B	Amikacin	30 µg	≥17		15–16	≤14	≤16		32	≥64	
O	Kanamycin	30 µg	≥18		14–17	≤13	≤16		32	≥64	
O	Netilmicin	30 µg	≥15		13–14	≤12	≤8		16	≥32	
O	Streptomycin	10 µg	≥15		12–14	≤11	–		–	–	(32) There are no MIC interpretive standards.

Table 2A. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)				MIC Interpretive Criteria (µg/mL)				Comments
			S	SDD	I	R	S	SDD	I	R	
TETRACYCLINES (33) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.											
C	Tetracycline	30 µg	≥15		12–14	≤11	≤4		8	≥16	
O	Doxycycline	30 µg	≥14		11–13	≤10	≤4		8	≥16	
O	Minocycline	30 µg	≥16		13–15	≤12	≤4		8	≥16	
FLUOROQUINOLONES **NOTE:** Reevaluation of fluoroquinolones is ongoing. See comment (2).											
B	Ciprofloxacin	5 µg	≥21		16–20	≤15	≤1		2	≥4	(34) For testing and reporting of *Enterobacteriaceae* except for *Salmonella* spp.
B	Levofloxacin	5 µg	≥17		14–16	≤13	≤2		4	≥8	
B	Ciprofloxacin	5 µg	≥31		21-30	≤20	≤0.06		0.12–0.5	≥1	(35) For testing and reporting of *Salmonella* spp. (including *S.* Typhi and *S.* Paratyphi A–C). See comment (2).
B	Levofloxacin	–	–		–	–	≤0.12		0.25–1	≥2	(36) If MIC testing is not performed or if interpretive criteria cannot be implemented, see comment (39).
B	Ofloxacin	–	–		–	–	≤0.12		0.25–1	≥2	
U	Lomefloxacin or	10 µg	≥22		19–21	≤18	≤2		4	≥8	
U	ofloxacin	5 µg	≥16		13–15	≤12	≤2		4	≥8	
U	Norfloxacin	10 µg	≥17		13–16	≤12	≤4		8	≥16	
O	Enoxacin	10 µg	≥18		15–17	≤14	≤2		4	≥8	
O	Gatifloxacin	5 µg	≥18		15–17	≤14	≤2		4	≥8	
O	Gemifloxacin	5 µg	≥20		16–19	≤15	≤0.25		0.5	≥1	(37) FDA-approved for *Klebsiella pneumoniae.*
O	Grepafloxacin	5 µg	≥18		15–17	≤14	≤1		2	≥4	
Inv.	Fleroxacin	5 µg	≥19		16–18	≤15	≤2		4	≥8	

Table 2A. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)				MIC Interpretive Criteria (µg/mL)				Comments
			S	SDD	I	R	S	SDD	I	R	
QUINOLONES											
O	Cinoxacin	100 µg	≥19		15–18	≤14	≤16		32	≥64	See comment (24).
O	Nalidixic acid	30 µg	≥19		14–18	≤13	≤16		–	≥32	(38) These interpretive criteria are for urinary tract isolates of *Enterobacteriaceae* and for all isolates of *Salmonella.* (39) Until laboratories can implement the current interpretive criteria for ciprofloxacin, levofloxacin, and/or ofloxacin, nalidixic acid may be used to test for reduced fluoroquinolone susceptibility in *Salmonella*. Strains of *Salmonella* that test resistant to nalidixic acid may be associated with clinical failure or delayed response in fluoroquinolone-treated patients with salmonellosis. Note that nalidixic acid may not detect all mechanisms of fluoroquinolone resistance.
FOLATE PATHWAY INHIBITORS											
B	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16		11–15	≤10	≤2/38		–	≥4/76	See comment (2).
U	Sulfonamides	250 or 300 µg	≥17		13–16	≤12	≤256		–	≥512	(40) Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations.
U	Trimethoprim	5 µg	≥16		11–15	≤10	≤8		–	≥16	
PHENICOLS											
C	Chloramphenicol	30 µg	≥18		13–17	≤12	≤8		16	≥32	(41) Not routinely reported on isolates from the urinary tract.
FOSFOMYCINS											
O	Fosfomycin	200 µg	≥16		13–15	≤12	≤64		128	≥256	(42) For testing and reporting of *E. coli* urinary tract isolates only. (43) The 200-µg fosfomycin disk contains 50 µg of glucose-6-phosphate. (44) The only approved MIC method for testing is agar dilution using agar media supplemented with 25 µg/mL of glucose-6-phosphate. Broth dilution MIC testing should not be performed.
NITROFURANS											
U	Nitrofurantoin	300 µg	≥17		15–16	≤14	≤32		64	≥128	

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; ESBL, extended-spectrum β-lactamase; FDA, US Food and Drug Administration; MIC, minimal inhibitory concentration; MHA, Mueller-Hinton agar; MHT, modified Hodge test; MIC, minimal inhibitory concentration; PK-PD, pharmacokinetic-pharmacodynamic; QC, quality control; SDD, susceptible-dose dependent; UTI, urinary tract infection.

Table 2B-1. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Pseudomonas aeruginosa*

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA)
Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB)
Agar dilution: MHA

Inoculum: Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard

Incubation: 35 ± 2°C; ambient air;
Disk diffusion: 16 to 18 hours
Dilution methods: 16 to 20 hours

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Pseudomonas aeruginosa ATCC® 27853
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

General Comments

(1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and **up to 6** disks on a 100-mm plate**; disks should be placed no less than 24 mm apart, center to center** (M02, Section 9.2 **will be updated during its next scheduled revision to include this recommendation**). **Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement.** Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth.

(2) The susceptibility of *P. aeruginosa* isolated from patients with cystic fibrosis can be reliably determined by disk diffusion or dilution methods, but may require extended incubation for up to 24 hours before reporting as susceptible.

(3) *P. aeruginosa* may develop resistance during prolonged therapy with all antimicrobial agents. Therefore, isolates that are initially susceptible may become resistant within three to four days after initiation of therapy. Testing of repeat isolates may be warranted.

(4) The dosage regimens shown in the comment column below are those required to achieve plasma drug exposures (in adults with normal renal and hepatic functions) on which breakpoints were derived. When implementing new breakpoints, it is strongly recommended that laboratories share this information with infectious disease practitioners, pharmacists, pharmacy and therapeutics committees, and infection control committees.

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
A	Piperacillin	100 µg	≥21	15–20	≤14	≤16	32–64	≥128	(5) Interpretive criteria for piperacillin (alone or with tazobactam) are based on a piperacillin dosage regimen of at least 3 g every 6 h.

Table 2B-1. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS (Continued)									
B	Ticarcillin	75 µg	≥24	16–23	≤15	≤16	32–64	≥128	(6) Interpretive criteria for ticarcillin (alone or with clavulanate) are based on a ticarcillin dosage regimen of at least 3 g every 6 h.
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS See comment (4).									
B	Piperacillin-tazobactam	100/10 µg	≥21	15–20	≤14	≤16/4	32/4–64/4	≥128/4	(7) Interpretive criteria for piperacillin (alone or with tazobactam) are based on a piperacillin dosage regimen of at least 3 g every 6 h.
O	Ticarcillin-clavulanate	75/10 µg	≥24	16–23	≤15	≤16/2	32/2–64/2	≥128/2	(8) Interpretive criteria for ticarcillin (alone or with clavulanate) are based on a ticarcillin dosage regimen of at least 3 g every 6 h.
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftazidime	30 µg	≥18	15–17	≤14	≤8	16	≥32	(9) Interpretive criteria are based on a dosage regimen of 1 g every 6 h or 2 g every 8 h.
B	Cefepime	30 µg	≥18	15–17	≤14	≤8	16	≥32	(10) Interpretive criteria are based on a dosage regimen of 1 g every 8 h or 2 g every 12 h.
MONOBACTAMS									
B	Aztreonam	30 µg	≥22	16–21	≤15	≤8	16	≥32	(11) Interpretive criteria are based on a dosage regimen of 1 g every 6 h or 2 g every 8 h.
CARBAPENEMS									
B	Doripenem	10 µg	≥19	16–18	≤15	≤2	4	≥8	(12) Interpretive criteria for doripenem are based on a dosage regimen of 500 mg every 8 h.
B	Imipenem	10 µg	≥19	16–18	≤15	≤2	4	≥8	(13) Interpretive criteria for imipenem are based on a dosage regimen of 1 g every 8 h or 500 mg every 6 h.
B	Meropenem	10 µg	≥19	16–18	≤15	≤2	4	≥8	(14) Interpretive criteria for meropenem are based on a dosage regimen of 1 g every 8 h.
LIPOPEPTIDES									
O	Colistin	10 µg	≥11	–	≤10	≤2	4	≥8	
O	Polymyxin B	300 units	≥12	–	≤11	≤2	4	≥8	
AMINOGLYCOSIDES									
A	Gentamicin	10 µg	≥15	13–14	≤12	≤4	8	≥16	
A	Tobramycin	10 µg	≥15	13–14	≤12	≤4	8	≥16	
B	Amikacin	30 µg	≥17	15–16	≤14	≤16	32	≥64	
O	Netilmicin	30 µg	≥15	13–14	≤12	≤8	16	≥32	

Table 2B-1. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
FLUOROQUINOLONES									
B	Ciprofloxacin	5 µg	≥21	16–20	≤15	≤ 1	2	≥4	
B	Levofloxacin	5 µg	≥17	14–16	≤13	≤ 2	4	≥8	
U	Lomefloxacin or ofloxacin	10 µg	≥22	19–21	≤18	≤ 2	4	≥8	
U		5 µg	≥16	13–15	≤12	≤ 2	4	≥8	
U	Norfloxacin	10 µg	≥17	13–16	≤12	≤ 4	8	≥16	
O	Gatifloxacin	5 µg	≥18	15–17	≤14	≤ 2	4	≥8	(15) For testing and reporting of urinary tract isolates only.

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

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Table 2B-2. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Acinetobacter* spp.

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA)
Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB)
Agar dilution: MHA
Inoculum: Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation: 35±2°C; ambient air; 20 to 24 hours, all methods

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Pseudomonas aeruginosa ATCC® 27853
Escherichia coli ATCC® 25922 **(for tetracyclines and trimethoprim-sulfamethoxazole)**
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

General Comments

(1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and **up to 6** disks on a 100-mm plate**; disks should be placed no less than 24 mm apart, center to center** (M02, Section 9.2 **will be updated during its next scheduled revision to include this recommendation**). **Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement.** Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
B	Piperacillin	100 µg	≥21	18–20	≤17	≤16	32–64	≥128	
O	Mezlocillin	75 µg	≥21	18–20	≤17	≤16	32–64	≥128	
O	Ticarcillin	75 µg	≥20	15–19	≤14	≤16	32–64	≥128	
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
A	Ampicillin-sulbactam	10/10 µg	≥15	12–14	≤11	≤8/4	16/8	≥32/16	
B	Piperacillin-tazobactam	100/10 µg	≥21	18–20	≤17	≤16/4	32/4–64/4	≥128/4	
B	Ticarcillin-clavulanate	75/10 µg	≥20	15–19	≤14	≤16/2	32/2–64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftazidime	30 µg	≥18	15–17	≤14	≤8	16	≥32	
B	Cefepime	30 µg	≥18	15–17	≤14	≤8	16	≥32	
B	Cefotaxime	30 µg	≥23	15–22	≤14	≤8	16–32	≥64	
B	Ceftriaxone	30 µg	≥21	14–20	≤13	≤8	16–32	≥64	

Table 2B-2. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
CARBAPENEMS									
A	**Doripenem**	**10 µg**	**≥18**	**15–17**	**≤14**	**≤2**	**4**	**≥8**	**(2) Interpretive criteria for doripenem are based on a dosage regimen of 500 mg every 8 h.**
A	Imipenem	10 µg	**≥22**	**19–21**	**≤18**	**≤2**	**4**	**≥8**	**(3) Interpretive criteria for imipenem are based on a dosage regimen of 500 mg every 6 h.**
A	Meropenem	10 µg	**≥18**	**15–17**	**≤14**	**≤2**	**4**	**≥8**	**(4) Interpretive criteria for meropenem are based on a dosage regimen of 1 g every 8 h or 500 mg every 6 h.**
LIPOPEPTIDES									
O	Polymyxin B	–	–	–	–	≤2	–	≥4	
O	Colistin		–	–	–	≤2	–	≥4	
AMINOGLYCOSIDES									
A	Gentamicin	10 µg	≥15	13–14	≤12	≤4	8	≥16	
A	Tobramycin	10 µg	≥15	13–14	≤12	≤4	8	≥16	
B	Amikacin	30 µg	≥17	15–16	≤14	≤16	32	≥64	
O	Netilmicin	–	–	–	–	≤8	16	≥32	
TETRACYCLINES (5) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.									
B	Tetracycline	30 µg	≥15	12–14	≤11	≤4	8	≥16	
B	Doxycycline	30 µg	≥13	10–12	≤9	≤4	8	≥16	
B	Minocycline	30 µg	≥16	13–15	≤12	≤4	8	≥16	
FLUOROQUINOLONES									
A	Ciprofloxacin	5 µg	≥21	16–20	≤15	≤1	2	≥4	
A	Levofloxacin	5 µg	≥17	14–16	≤13	≤2	4	≥8	
O	Gatifloxacin	5 µg	≥18	15–17	≤14	≤2	4	≥8	
FOLATE PATHWAY INHIBITORS									
B	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥ 16	11–15	≤10	≤2/38	–	≥4/76	

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 2B-3. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Burkholderia cepacia*

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA)
Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB)
Agar dilution: MHA
Inoculum: Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation: 35±2°C; ambient air; 20 to 24 hours, all methods

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Pseudomonas aeruginosa ATCC® 27853
Escherichia coli ATCC® 25922 **(for chloramphenicol, minocycline, and trimethoprim-sulfamethoxazole)**
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

General Comments

(1) For disk diffusion, measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
B	Ticarcillin-clavulanate	–	–	–	–	≤16/2	32/2–64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
B	Ceftazidime	30 µg	≥21	18–20	≤17	≤8	16	≥32	
CARBAPENEMS									
B	Meropenem	10 µg	≥20	16–19	≤15	≤4	8	≥16	
TETRACYCLINES									
B	Minocycline	30 µg	≥19	15–18	≤14	≤4	8	≥16	
FLUOROQUINOLONES									
B	Levofloxacin	–	–	–	–	≤2	4	≥8	
FOLATE PATHWAY INHIBITORS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16	11–15	≤10	≤2/38	–	≥4/76	
PHENICOLS									
B	Chloramphenicol	–	–	–	–	≤8	16	≥32	(2) Not routinely reported on isolates from the urinary tract.

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 2B-4. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Stenotrophomonas maltophilia*

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA)
Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB)
Agar dilution: MHA
Inoculum: Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation: 35±2°C; ambient air; 20 to 24 hours, all methods

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Pseudomonas aeruginosa ATCC® 27853
Escherichia coli ATCC® 25922 **(for chloramphenicol, minocycline, and trimethoprim-sulfamethoxazole)**
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

General Comments

(1) For disk diffusion, measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
B	Ticarcillin-clavulanate	–	–	–	–	≤16/2	32/2–64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
B	Ceftazidime	–	–	–	–	≤8	16	≥32	
TETRACYCLINES									
B	Minocycline	30 µg	≥19	15–18	≤14	≤4	8	≥16	
FLUOROQUINOLONES									
B	Levofloxacin	5 µg	≥17	14–16	≤13	≤2	4	≥8	
FOLATE PATHWAY INHIBITORS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥ 16	11–15	≤ 10	≤2/38	–	≥4/76	
PHENICOLS									
B	Chloramphenicol	–	–	–	–	≤8	16	≥32	(2) Not routinely reported on isolates from the urinary tract.

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 2B-5. Minimal Inhibitory Concentration (MIC) Interpretive Standards (μg/mL) for Other Non-*Enterobacteriaceae* (Refer to Comment 1)

Testing Conditions

Medium: Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB)
Agar dilution: Mueller-Hinton agar (MHA)
Inoculum: Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation: 35 ± 2°C; ambient air; 16 to 20 hours

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Pseudomonas aeruginosa ATCC® 27853
Escherichia coli ATCC® 25922 **(for chloramphenicol, tetracyclines, sulfonamides, and trimethoprim-sulfamethoxazole)**
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

General Comments

(1) Other non-*Enterobacteriaceae* include *Pseudomonas* spp. (not *P. aeruginosa*) and other nonfastidious, glucose-nonfermenting, gram-negative bacilli, but exclude *P. aeruginosa, Acinetobacter* spp., *Burkholderia cepacia, B. mallei, B. pseudomallei,* and *Stenotrophomonas maltophilia.* Refer to Tables 2B-2, 2B-3, and 2B-4 for testing of *Acinetobacter* spp., *B. cepacia,* and *S. maltophilia,* respectively, and CLSI document M45 for testing of *Burkholderia mallei* and *B. pseudomallei.*

(2) For other non-*Enterobacteriaceae,* the disk diffusion method has not been systematically studied by the subcommittee nor have clinical data been collected for review. Therefore, for this organism group, disk diffusion testing is not currently recommended.

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (μg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
A	Piperacillin	–	–	–	–	≤16	32–64	≥128	
O	Mezlocillin	–	–	–	–	≤16	32–64	≥128	
O	Ticarcillin	–	–	–	–	≤16	32–64	≥128	
O	Carbenicillin	–	–	–	–	≤16	32	≥64	
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
B	Ticarcillin-clavulanate	–	–	–	–	≤16/2	32/2–64/2	≥128/2	
B	Piperacillin-tazobactam	–	–	–	–	≤16/4	32/4–64/4	≥128/4	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftazidime	–	–	–	–	≤8	16	≥32	
B	Cefepime	–	–	–	–	≤8	16	≥32	
C	Cefotaxime	–	–	–	–	≤8	16–32	≥64	
C	Ceftriaxone	–	–	–	–	≤8	16–32	≥64	
O	Cefoperazone	–	–	–	–	≤16	32	≥64	
O	Ceftizoxime	–	–	–	–	≤8	16–32	≥64	
O	Moxalactam	–	–	–	–	≤8	16–32	≥64	

Table 2B-5. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
MONOBACTAMS									
B	Aztreonam	–	–	–	–	≤8	16	≥32	
CARBAPENEMS									
B	Imipenem	–	–	–	–	≤4	8	≥16	
B	Meropenem	–	–	–	–	≤4	8	≥16	
LIPOPEPTIDES									
O	Colistin	–	–	–	–	≤2	4	≥8	
O	Polymyxin B	–	–	–	–	≤2	4	≥8	
AMINOGLYCOSIDES									
A	Gentamicin	–	–	–	–	≤4	8	≥16	
A	Tobramycin	–	–	–	–	≤4	8	≥16	
B	Amikacin	–	–	–	–	≤16	32	≥64	
O	Netilmicin	–	–	–	–	≤8	16	≥32	
TETRACYCLINES (3) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.									
U	Tetracycline	–	–	–	–	≤4	8	≥16	
O	Doxycycline	–	–	–	–	≤4	8	≥16	
O	Minocycline	–	–	–	–	≤4	8	≥16	
FLUOROQUINOLONES									
B	Ciprofloxacin	–	–	–	–	≤1	2	≥4	
B	Levofloxacin	–	–			≤2	4	≥8	
U	Lomefloxacin or	–	–	–	–	≤2	4	≥8	
U	ofloxacin	–	–	–	–	≤2	4	≥8	
U	Norfloxacin	–	–	–	–	≤4	8	≥16	
O	Gatifloxacin	–	–	–	–	≤2	4	≥8	(4) For testing and reporting of urinary tract isolates only.
FOLATE PATHWAY INHIBITORS									
B	Trimethoprim-sulfamethoxazole	–	–	–	–	≤2/38	–	≥4/76	
U	Sulfonamides	–	–	–	–	≤256	–	≥512	(5) Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations.
PHENICOLS									
C	Chloramphenicol	–	–	–	–	≤8	16	≥32	(6) Not routinely reported on isolates from the urinary tract.

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 2C. Zone Diameter and Minimum Inhibitory Concentration (MIC) Interpretive Standards for *Staphylococcus* spp.

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA)
Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB); CAMHB + 2% NaCl for oxacillin; CAMHB supplemented to 50 µg/mL calcium for daptomycin
Agar dilution: MHA; MHA + 2% NaCl for oxacillin. Agar dilution has not been validated for daptomycin.

Inoculum: Direct colony suspension, equivalent to a 0.5 McFarland standard

Incubation: 35 ± 2°C; ambient air;
Disk diffusion: 16 to 18 hours; 24 hours (coagulase-negative staphylococci and cefoxitin);
Dilution methods: 16 to 20 hours;
24 hours for oxacillin and vancomycin;
Testing at temperatures above 35°C may not detect methicillin-resistant staphylococci (MRS).

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Staphylococcus aureus ATCC® 25923 (disk diffusion)
Staphylococcus aureus ATCC® 29213 (MIC)

General Comments

(1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and **up to 6** disks on a 100-mm plate**; disks should be placed no less than 24 mm apart, center to center** (M02, Section 9.2 **will be updated during its next scheduled revision to include this recommendation**). **Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement.** Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light, except for linezolid, which should be read with transmitted light (plate held up to light source). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter. For linezolid, any discernible growth within the zone of inhibition is indicative of resistance to the respective agent.

(2) Historically, resistance to the penicillinase-stable penicillins (see Glossary I) has been referred to as “methicillin resistance” or “oxacillin resistance.” MRSAs are those strains of *S. aureus* that express *mecA* or another mechanism of methicillin resistance, such as changes in affinity of penicillin-binding proteins for oxacillin (modified *S. aureus* strains).

Table 2C. (Continued)

(3) In most staphylococcal isolates, oxacillin resistance is mediated by *mecA,* encoding the penicillin-binding protein 2a (PBP 2a, also called PBP2'). Isolates that test positive for *mecA* or PBP 2a should be reported as oxacillin resistant.

Isolates that test resistant by oxacillin MIC, cefoxitin MIC, or cefoxitin disk test should be reported as oxacillin resistant.

Mechanisms of oxacillin resistance other than *mecA* are rare and include a novel *mecA* homologue, *mecC.*[1] MICs for strains with *mecC* are typically in the resistant range for cefoxitin and/or oxacillin; *mecC* resistance cannot be detected by tests directed at *mecA* or PBP 2a.

(4) Oxacillin-resistant *S. aureus* and coagulase-negative staphylococci (CoNS) (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.

(5) Routine testing of urine isolates of *S. saprophyticus* is not advised, because infections respond to concentrations achieved in urine of antimicrobial agents commonly used to treat acute, uncomplicated urinary tract infections (eg, nitrofurantoin, trimethoprim ± sulfamethoxazole, or a fluoroquinolone).

(6) For screening tests for β-lactamase production, oxacillin resistance, *mecA*-mediated oxacillin resistance using cefoxitin, reduced susceptibility to vancomycin, inducible clindamycin resistance, and high-level mupirocin resistance (*S. aureus* only), refer to Tables **3D, 3E, 3F, 3G, and 3H**.

NOTE: Information in boldface type is new or modified since the previous edition.

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[1] García-Álvarez L, Holden MT, Lindsay H, et al. Methicillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infect Dis.* 2011;11(8):595-603.

Table 2C. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm) S	I	R	MIC Interpretive Criteria (µg/mL) S	I	R	Comments
PENICILLINASE-LABILE PENICILLINS (7) Penicillin-susceptible staphylococci are also susceptible to other β-lactam agents with established clinical efficacy for staphylococcal infections. Penicillin-resistant staphylococci are resistant to penicillinase-labile penicillins, including ampicillin, amoxicillin, azlocillin, carbenicillin, mezlocillin, piperacillin, and ticarcillin.									
A	Penicillin	10 units	≥29	–	≤28	≤0.12	–	≥0.25	(8) Penicillin should be used to test the susceptibility of all staphylococci to all penicillinase-labile penicillins. Penicillin-resistant strains of staphylococci produce β-lactamase. Perform test(s) to detect β-lactamase production on staphylococci for which the penicillin MICs are ≤ 0.12 µg/mL or zone diameters ≥ 29 mm before reporting the isolate as penicillin susceptible. Rare isolates of staphylococci that contain genes for β-lactamase production may appear negative by β-lactamase tests. Consequently, for serious infections requiring penicillin therapy, laboratories should perform MIC tests and β-lactamase testing on all subsequent isolates from the same patient. PCR testing of the isolate for the *bla*Z β-lactamase gene may be considered. See Tables **3D and 3E**. (9) For oxacillin-resistant staphylococci report penicillin as resistant or do not report.
PENICILLINASE-STABLE PENICILLINS (10) Oxacillin (or cefoxitin) results can be applied to the other penicillinase-stable penicillins (cloxacillin, dicloxacillin, flucloxacillin, methicillin, and nafcillin). For agents with established clinical efficacy and considering site of infection and appropriate dosing, oxacillin (cefoxitin)-susceptible staphylococci can be considered susceptible to: • β-lactam/β-lactamase inhibitor combinations (amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin-tazobactam, ticarcillin-clavulanate) • Oral cephems (cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, loracarbef) • Parenteral cephems including cephalosporins I, II, III, and IV (cefamandole, cefazolin, cefepime, cefmetazole, cefonicid, cefoperazone, cefotaxime, cefotetan, ceftizoxime, ceftriaxone, cefuroxime, cephalothin, ceftaroline, moxalactam) • Carbapenems (doripenem, ertapenem, imipenem, meropenem) Oxacillin-resistant staphylococci are resistant to all currently available β-lactam antimicrobial agents, with the exception of the newer cephalosporins with anti-MRSA activity. Thus, susceptibility or resistance to a wide array of β-lactam antimicrobial agents may be deduced from testing only penicillin and either cefoxitin or oxacillin. Routine testing of other β-lactam agents, except those with anti-MRSA activity, is not advised. See comment**s** (**3) and (**4). **In addition, further explanation on the use of cefoxitin for prediction of *mecA*-mediated oxacillin resistance can be found in Section 12 of M07-A9 and Section 11 of M02-A11.**									

Table 2C. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm) S	I	R	MIC Interpretive Criteria (µg/mL) S	I	R	Comments
PENICILLINASE-STABLE PENICILLINS (Continued)									
A	Oxacillin For *S. aureus* and *S. lugdunensis.*		–	–	–	≤ 2 (oxacillin)	–	≥ 4 (oxacillin)	For use with *S. aureus* and S. *lugdunensis*. (11) Oxacillin disk testing is not reliable. See cefoxitin and comment (**4**) for reporting oxacillin when **testing** cefoxitin as a surrogate **agent**.
		30 µg cefoxitin **(surrogate test for oxacillin)**	≥ 22	–	≤21	≤ 4 (cefoxitin)	–	≥ 8 (cefoxitin)	(12) Cefoxitin is **tested** as a surrogate for oxacillin; report oxacillin susceptible or resistant based on the cefoxitin result. See comments (4), (7), and (10).
A	Oxacillin For CoNS except *S. lugdunensis.*	–	–	–	–	≤0.25 (oxacillin)	–	≥0.5 (oxacillin)	For use with CoNS except *S. lugdunensis.* (13) Oxacillin MIC interpretive criteria may overcall resistance for some CoNS, because some non–*S. epidermidis* strains for which the oxacillin MICs are 0.5 to 2 µg/mL lack *mecA*. For serious infections with CoNS other than *S. epidermidis,* testing for *mecA* or for PBP 2a or with cefoxitin disk diffusion may be appropriate for strains for which the oxacillin MICs are 0.5 to 2 µg/mL.
		30 µg cefoxitin **(surrogate test for oxacillin)**	≥25	–	≤24	–	–	–	See comments (4), (7), (10), and (12).
CEPHEMS (PARENTERAL)									
B	Ceftaroline	30 µg	≥24	21–23	≤20	≤1	2	≥4	(14) For use with *S. aureus* only, including MRSA. (15) Interpretive criteria are based on a dosage regimen of 600 mg every 12 h.

Table 2C. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
GLYCOPEPTIDES **(16) For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy.**									
B	Vancomycin	–	–	–	–	≤2	4–8	≥16	For use with *S. aureus.* (17) MIC tests should be performed to determine the susceptibility of all isolates of staphylococci to vancomycin. The disk test does not differentiate vancomycin-susceptible isolates of *S. aureus* from vancomycin-intermediate isolates, nor does the test differentiate among vancomycin-susceptible, intermediate, and resistant isolates of CoNS, all of which will give similar size zones of inhibition. (18) Send any *S. aureus* for which the vancomycin is ≥ 8 µg/mL to a reference laboratory. See Appendix A. Also refer to Table **3F** for *S. aureus*, Section 12.1.3 in M07-A9, and Section 11.1.3 in M02-A11.

Table 2C. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
GLYCOPEPTIDES (Continued)									
B	Vancomycin	–	–	–	–	≤4	8–16	≥32	For use with CoNS. See comment (17). (19) Send any CoNS for which the vancomycin MIC is ≥32 µg/mL to a reference laboratory. See Appendix A. See also Section 12.1.3 in M07-A9 and Section 11.1.3 in M02-A11.
Inv.	Teicoplanin	30 µg	≥14	11–13	≤10	≤8	16	≥32	(20) Teicoplanin disk diffusion interpretive criteria were not reevaluated concurrent with the reevaluation of vancomycin disk diffusion interpretive criteria. Therefore, the ability of these teicoplanin interpretive criteria to differentiate teicoplanin-intermediate and teicoplanin-resistant staphylococci from teicoplanin-susceptible strains is not known.
LIPOPEPTIDES									
B	Daptomycin	–	–	–	–	≤1	–	–	(21) Daptomycin should not be reported for isolates from the respiratory tract.
AMINOGLYCOSIDES (22) For staphylococci that test susceptible, aminoglycosides are used only in combination with other active agents that test susceptible.									
C	Gentamicin	10 µg	≥15	13–14	≤12	≤4	8	≥16	
O	Amikacin	30 µg	≥17	15–16	≤14	≤16	32	≥64	
O	Kanamycin	30 µg	≥18	14–17	≤13	≤16	32	≥64	
O	Netilmicin	30 µg	≥15	13–14	≤12	≤8	16	≥32	
O	Tobramycin	10 µg	≥15	13–14	≤12	≤4	8	≥16	

Table 2C. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
MACROLIDES (23) Not routinely reported on organisms isolated from the urinary tract.									
A	Azithromycin or	15 µg	≥18	14–17	≤13	≤2	4	≥8	
A	clarithromycin or	15 µg	≥18	14–17	≤13	≤2	4	≥8	
A	erythromycin	15 µg	≥23	14–22	≤13	≤0.5	1–4	≥8	
O	Telithromycin	15 µg	≥22	19–21	≤18	≤1	2	≥4	
O	Dirithromycin	15 µg	≥19	16–18	≤15	≤2	4	≥8	
TETRACYCLINES (24) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.									
B	Tetracycline	30 µg	≥19	15–18	≤14	≤4	8	≥16	
B	Doxycycline	30 µg	≥16	13–15	≤12	≤4	8	≥16	
B	Minocycline	30 µg	≥19	15–18	≤14	≤4	8	≥16	See comment (23).
FLUOROQUINOLONES (25) *Staphylococcus* spp. may develop resistance during prolonged therapy with quinolones. Therefore, isolates that are initially susceptible may become resistant within three to four days after initiation of therapy. Testing of repeat isolates may be warranted.									
C	Ciprofloxacin or	5 µg	≥21	16–20	≤15	≤1	2	≥4	
C	levofloxacin or	5 µg	≥19	16–18	≤15	≤1	2	≥4	
C	ofloxacin	5 µg	≥18	15–17	≤14	≤1	2	≥4	
C	Moxifloxacin	5 µg	≥24	21–23	≤20	≤0.5	1	≥2	
U	Lomefloxacin	10 µg	≥22	19–21	≤18	≤2	4	≥8	
U	Norfloxacin	10 µg	≥17	13–16	≤12	≤4	8	≥16	
O	Enoxacin	10 µg	≥18	15–17	≤14	≤2	4	≥8	(26) FDA approved for *S. saprophyticus* and *S. epidermidis* (but not for *S. aureus*).
O	Gatifloxacin	5 µg	≥23	20–22	≤19	≤0.5	1	≥2	
O	Grepafloxacin	5 µg	≥18	15–17	≤14	≤1	2	≥4	
O	Sparfloxacin	5 µg	≥19	16–18	≤15	≤0.5	1	≥2	
Inv.	Fleroxacin	5 µg	≥19	16–18	≤15	≤2	4	≥8	

Table 2C. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
NITROFURANTOINS									
U	Nitrofurantoin	300 µg	≥17	15–16	≤14	≤32	64	≥128	
LINCOSAMIDES									
A	Clindamycin	2 µg	≥21	15–20	≤14	≤0.5	1–2	≥4	(27) Inducible clindamycin resistance can be detected by disk diffusion using the D-zone test or by broth microdilution (see Table **3G** and Section 12 in M02-A11, and Section 13 in M07-A9). See comment (23).
FOLATE PATHWAY INHIBITORS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16	11–15	≤10	≤2/38	–	≥4/76	
U	Sulfonamides	250 or 300 µg	≥17	13–16	≤12	≤256	–	≥512	(28) Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations.
U	Trimethoprim	5 µg	≥16	11–15	≤10	≤8	–	≥16	
PHENICOLS									
C	Chloramphenicol	30 µg	≥18	13–17	≤12	≤8	16	≥32	See comment (23).
ANSAMYCINS									
B	Rifampin	5 µg	≥20	17–19	≤16	≤1	2	≥4	(29) ***Rx*:** Rifampin should not be used alone for antimicrobial therapy.
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16–18	≤15	≤1	2	≥4	(30) For reporting against methicillin-susceptible *S. aureus.*
OXAZOLIDINONES									
B	Linezolid	30 µg	≥21	–	≤20	≤ 4	–	≥8	(31) When testing linezolid, disk diffusion zones should be examined using transmitted light. Organisms with resistant results by disk diffusion should be confirmed using an MIC method.

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CoNS, coagulase-negative staphylococci; FDA, US Food and Drug Administration; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRS, methicillin-resistant staphylococci; MRSA, methicillin-resistant *S. aureus;* PBP 2a, penicillin-binding protein 2a; PCR, polymerase chain reaction; QC, quality control.

Table 2D. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Enterococcus* spp.

Testing Conditions	
Medium:	Disk diffusion: Mueller-Hinton agar (MHA) Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB); CAMHB supplemented to 50 µg/mL calcium for daptomycin Agar dilution: MHA; agar dilution has not been validated for daptomycin
Inoculum:	Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation:	35 ± 2°C; ambient air; Disk diffusion: 16 to 18 hours; Dilution methods: 16 to 20 hours; All methods: 24 hours for vancomycin

Routine QC Recommendations (See Tables 4A and 5A for acceptable QC ranges.)

Disk diffusion:
Staphylococcus aureus ATCC® 25923

Dilution methods:
Enterococcus faecalis ATCC® 29212

Refer to Table**s 3F and 3I** for additional **testing** recommendations, reporting suggestions, and QC.

General Comments

(1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and **up to 6** disks on a 100-mm plate**; disks should be placed no less than 24 mm apart, center to center** (M02, Section 9.2 **will be updated during its next scheduled revision to include this recommendation**). **Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement.** Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light, except for vancomycin, which should be read with transmitted light (plate held up to light source). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. Any discernible growth within the zone of inhibition indicates vancomycin resistance.

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

(3) Synergy between ampicillin, penicillin, or vancomycin and an aminoglycoside can be predicted for enterococci by using a high-level aminoglycoside (gentamicin and streptomycin) screening test **(see Table 3I)**.

NOTE: Information in boldface type is new or modified since the previous edition.

Table 2D. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
A A	Penicillin Ampicillin	10 units 10 µg	≥15 ≥17	– –	≤14 ≤16	≤8 ≤8	– –	≥16 ≥16	(4) **The results of** ampicillin **susceptibility tests should be used to predict the activity of** amoxicillin. Ampicillin results may be used to predict susceptibility to amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin, and piperacillin-tazobactam among non–β-lactamase-producing enterococci. Ampicillin susceptibility can be used to predict imipenem susceptibility, providing the species is confirmed to be *E. faecalis.* (5) Enterococci susceptible to penicillin are predictably susceptible to ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, piperacillin, and piperacillin-tazobactam for non–β-lactamase-producing enterococci. However, enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin. If penicillin results are needed, testing of penicillin is required. (6) ***Rx:*** Combination therapy with ampicillin, penicillin, or vancomycin (for susceptible strains), plus an aminoglycoside, is usually indicated for serious enterococcal infections, such as endocarditis, unless high-level resistance to both gentamicin and streptomycin is documented; such combinations are predicted to result in synergistic killing of the *Enterococcus.* (7) Penicillin or ampicillin resistance among enterococci due to β-lactamase production has been reported very rarely. Penicillin or ampicillin resistance due to β-lactamase production is not reliably detected with routine disk or dilution methods, but is detected using a direct, nitrocefin-based β-lactamase test. Because of the rarity of β-lactamase–positive enterococci, this test need not be performed routinely, but can be used in selected cases. A positive β-lactamase test predicts resistance to penicillin, as well as amino- and ureidopenicillins (see Glossary I).

Table 2D. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	15–16	≤14	≤4	8–16	≥32	(8) When testing vancomycin against enterococci, plates should be held a full 24 hours for accurate detection of resistance. Zones should be examined using transmitted light; the presence of a haze or any growth within the zone of inhibition indicates resistance. Organisms with intermediate zones should be tested by an MIC method as described in M07-A9. For isolates for which the vancomycin MICs are 8 to 16 µg/mL, perform biochemical tests for identification as listed under the "Vancomycin MIC ≥8 µg/mL" test found in Table **3F**. See comments (3) and (6).
Inv.	Teicoplanin	30 µg	≥14	11–13	≤10	≤8	16	≥32	
LIPOPEPTIDES									
B	Daptomycin	–	–	–	–	≤4	–	–	(9) Daptomycin should not be reported for isolates from the respiratory tract.
MACROLIDES									
O	Erythromycin	15 µg	≥23	14–22	≤13	≤0.5	1–4	≥8	(10) Not routinely reported on isolates from the urinary tract.
TETRACYCLINES (11) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.									
U	Tetracycline	30 µg	≥19	15–18	≤14	≤4	8	≥16	
O	Doxycycline	30 µg	≥16	13–15	≤12	≤4	8	≥16	
O	Minocycline	30 µg	≥19	15–18	≤14	≤4	8	≥16	
FLUOROQUINOLONES									
U	Ciprofloxacin	5 µg	≥21	16–20	≤15	≤1	2	≥4	
U	Levofloxacin	5 µg	≥17	14–16	≤13	≤2	4	≥8	
U	Norfloxacin	10 µg	≥17	13–16	≤12	≤4	8	≥16	
O	Gatifloxacin	5 µg	≥18	15–17	≤14	≤2	4	≥8	(12) These interpretive criteria apply to urinary tract isolates only.
NITROFURANTOINS									
U	Nitrofurantoin	300 µg	≥17	15–16	≤14	≤32	64	≥128	

Table 2D. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
ANSAMYCINS									
O	Rifampin	5 µg	≥20	17–19	≤16	≤1	2	≥4	(13) ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.
FOSFOMYCINS									
O	Fosfomycin	200 µg	≥16	13–15	≤12	≤64	128	≥256	(14) Indicated for use against *E. faecalis* urinary tract isolates only. (15) The approved MIC testing method is agar dilution. Agar media should be supplemented with 25 µg/mL of glucose-6-phosphate. Broth dilution testing should not be performed. (16) The 200-µg fosfomycin disk contains 50 µg of glucose-6-phosphate.
PHENICOLS									
O	Chloramphenicol	30 µg	≥18	13–17	≤12	≤8	16	≥32	See comment (10).
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16–18	≤15	≤1	2	≥4	(17) For reporting against vancomycin-resistant *E. faecium.*
OXAZOLIDINONES									
B	Linezolid	30 µg	≥23	21–22	≤20	≤2	4	≥8	

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 2E. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Haemophilus influenzae* and *Haemophilus parainfluenzae*

Testing Conditions

Medium: Disk diffusion: *Haemophilus* Test Medium (HTM)
Broth dilution: HTM broth

Inoculum: Direct colony suspension, equivalent to a 0.5 McFarland standard prepared using colonies from an overnight (preferably 20- to 24-hour) chocolate agar plate [see comment (2)]

Incubation: 35 ± 2°C;
Disk diffusion: 5% CO_2; 16 to 18 hours
Broth dilution: ambient air; 20 to 24 hours

Routine QC Recommendations (See Tables 4A, 4B, 5A, and 5B for acceptable QC ranges.)

Haemophilus influenzae ATCC® 49247
Haemophilus influenzae ATCC® 49766
Escherichia coli ATCC® 35218 (when testing amoxicillin-clavulanate)

General Comments

(1) *Haemophilus* spp., as used in this table, includes only *H. influenzae* and *H. parainfluenzae.* See CLSI document M45 for testing and reporting recommendations for other species of *Haemophilus*.

(2) The 0.5 McFarland suspension will contain approximately 1 to 4×10^8 colony-forming units/mL. Exercise care in preparing this suspension, because higher inoculum concentrations may lead to false-resistant results with some β-lactam antimicrobial agents, particularly when β-lactamase–producing strains of *H. influenzae* are tested.

(3) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

(4) For isolates of *H. influenzae* from CSF, only results of testing with ampicillin, one of the third-generation cephalosporins, chloramphenicol, and meropenem are appropriate to report routinely.

(5) Amoxicillin-clavulanate, azithromycin, clarithromycin, cefaclor, cefprozil, loracarbef, cefdinir, cefixime, cefpodoxime, cefuroxime, and telithromycin are oral agents that may be used as empiric therapy for respiratory tract infections due to *Haemophilus* spp. The results of susceptibility tests with these antimicrobial agents are often not useful for management of individual patients. However, susceptibility testing of *Haemophilus* spp. with these compounds may be appropriate for surveillance or epidemiological studies.

(6) To make HTM: Prepare a fresh hematin stock solution by dissolving 50 mg of hematin powder in 100 mL of 0.01 mol/L NaOH with heat and stirring until the powder is thoroughly dissolved. Add 30 mL of the hematin stock solution and 5 g of yeast extract to 1 L of Mueller-Hinton agar and autoclave. After autoclaving and cooling, add 3 mL of a nicotinamide adenine dinucleotide (NAD) stock solution (50 mg of NAD dissolved in 10 mL of distilled water, filter sterilized) aseptically.

Table 2E. (Continued)

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
A	Ampicillin	10 µg	≥22	19–21	≤18	≤1	2	≥4	See comment (4). (7) The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. The majority of isolates of *H. influenzae* that are resistant to ampicillin and amoxicillin produce a TEM-type β-lactamase. In most cases, a direct β-lactamase test can provide a rapid means of detecting resistance to ampicillin and amoxicillin. (8) Rare BLNAR strains of *H. influenzae* should be considered resistant to amoxicillin-clavulanate, ampicillin-sulbactam, cefaclor, cefamandole**,** cefetamet, cefonicid, cefprozil, cefuroxime, loracarbef, and piperacillin-tazobactam, despite apparent *in vitro* susceptibility of some BLNAR strains to these agents.
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
B	Ampicillin-sulbactam	10/10 µg	≥20	–	≤19	≤2/1	–	≥4/2	See comment (8).
C	Amoxicillin-clavulanate	20/10 µg	≥20	–	≤19	≤4/2	–	≥8/4	See comments (5) and (8).
O	Piperacillin-tazobactam	100/10 µg	≥21	–	–	≤1/4	–	≥2/4	See comment (8).

Table 2E. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
B	Cefotaxime or	30 µg	≥26	–	–	≤2	–	–	See comment (4).
B	ceftazidime or	30 µg	≥26	–	–	≤2	–	–	
B	ceftriaxone	30 µg	≥26	–	–	≤2	–	–	
B	Cefuroxime	30 µg	≥20	17–19	≤16	≤4	8	≥16	See comments (5) and (8).
C	Ceftaroline	30 µg	≥30	–	–	≤0.5	–	–	(9) For *H. influenzae* only. (10) Interpretive criteria are based on a dosage regimen of 600 mg every 12 h.
O	Cefonicid	30 µg	≥20	17–19	≤16	≤4	8	≥16	See comment (8).
O	Cefamandole	–	–	–	–	≤4	8	≥16	See comment (8).
O	Cefepime	30 µg	≥26	–	–	≤2	–	–	
O	Ceftizoxime	30 µg	≥26	–	–	≤2	–	–	See comment (4).
CEPHEMS (ORAL)									
C	Cefaclor	30 µg	≥20	17–19	≤16	≤8	16	≥32	See comments (5) and (8).
C	Cefprozil	30 µg	≥18	15–17	≤14	≤8	16	≥32	
C	Cefdinir or	5 µg	≥20	–	–	≤1	–	–	See comment (5).
C	cefixime or	5 µg	≥21	–	–	≤1	–	–	
C	cefpodoxime	10 µg	≥21	–	–	≤2	–	–	
C	Cefuroxime	30 µg	≥20	17–19	≤16	≤4	8	≥16	See comments (5) and (8).
O	Loracarbef	30 µg	≥19	16–18	≤15	≤8	16	≥32	See comments (5) and (8).
O	Ceftibuten	30 µg	≥28	–	–	≤2	–	–	
Inv.	Cefetamet	10 µg	≥18	15–17	≤14	≤4	8	≥16	See comment (8).
MONOBACTAMS									
C	Aztreonam	30 µg	≥26	–	–	≤2	–	–	
CARBAPENEMS									
B	Meropenem	10 µg	≥20	–	–	≤0.5	–	–	See comment (4).
C	Ertapenem or	10 µg	≥19	–	–	≤0.5	–	–	
C	imipenem	10 µg	≥16	–	–	≤4	–	–	
O	Doripenem	10 µg	≥16	–	–	≤1	–	–	
MACROLIDES									
C	Azithromycin	15 µg	≥12	–	–	≤4	–	–	See comment (5).
C	Clarithromycin	15 µg	≥13	11–12	≤10	≤8	16	≥32	See comment (5).
KETOLIDES									
C	Telithromycin	15 µg	≥15	12–14	≤11	≤4	8	≥16	See comment (5).
TETRACYCLINES (11) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.									
C	Tetracycline	30 µg	≥29	26–28	≤25	≤2	4	≥8	

Table 2E. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
FLUOROQUINOLONES									
C	Ciprofloxacin or	5 µg	≥21	–	–	≤1	–	–	
C	levofloxacin or	5 µg	≥17	–	–	≤2	–	–	
C	lomefloxacin or	10 µg	≥22	–	–	≤2	–	–	
C	moxifloxacin or	5 µg	≥18	–	–	≤1	–	–	
C	ofloxacin	5 µg	≥16	–	–	≤2	–	–	
C	Gemifloxacin	5 µg	≥18	–	–	≤0.12	–	–	
O	Gatifloxacin	5 µg	≥18	–	–	≤1	–	–	
O	Grepafloxacin	5 µg	≥24	–	–	≤0.5	–	–	
O	Sparfloxacin	–	–	–	–	≤0.25	–	–	
O	Trovafloxacin	10 µg	≥22	–	–	≤1	–	–	
Inv.	Fleroxacin	5 µg	≥19	–	–	≤2	–	–	
FOLATE PATHWAY INHIBITORS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16	11–15	≤10	≤0.5/9.5	1/19–2/38	≥4/76	
PHENICOLS									
B	Chloramphenicol	30 µg	≥29	26–28	≤25	≤2	4	≥8	See comment (4). (12) Not routinely reported on isolates from the urinary tract.
ANSAMYCINS									
C	Rifampin	5 µg	≥20	17–19	≤16	≤1	2	≥4	(13) May be appropriate only for prophylaxis of case contacts. These interpretive criteria do not apply to therapy of patients with invasive *H. influenzae* disease.

Abbreviations: ATCC, American Type Culture Collection; BLNAR, β-lactamase negative, ampicillin-resistant; CSF, cerebrospinal fluid; HTM, *Haemophilus* Test Medium; MIC, minimal inhibitory concentration; NAD, nicotinamide adenine dinucleotide; QC, quality control.

Table 2F. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Neisseria gonorrhoeae*

Testing Conditions

Medium:	Disk diffusion: GC agar base and 1% defined growth supplement. (The use of a cysteine-free growth supplement is not required for disk diffusion testing.) Agar dilution: GC agar base and 1% defined growth supplement. (The use of a cysteine-free growth supplement is required for agar dilution tests with carbapenems and clavulanate. Cysteine-containing defined growth supplement does not significantly alter dilution test results with other drugs.)
Inoculum:	Direct colony suspension, equivalent to a 0.5 McFarland standard prepared in Mueller-Hinton broth (MHB) or 0.9% phosphate-buffered saline, pH 7.0, using colonies from an overnight (20- to 24-hour) chocolate agar plate incubated in 5% CO_2.
Incubation:	36 ± 1°C (do not exceed 37°C); 5% CO_2; all methods, 20 to 24 hours

Routine QC Recommendations (See Tables 4B and 5C for acceptable QC ranges.)

Neisseria gonorrhoeae ATCC® 49226

General Comments

(1) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. For some agents, eg, fluoroquinolones or cephalosporins, only 2 to 3 disks may be tested per plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth.

(2) The clinical effectiveness of cefmetazole, cefotetan, cefoxitin, and spectinomycin for treating **infections due to** organisms that produce intermediate results with these agents is unknown.

(3) For disk diffusion testing of *N. gonorrhoeae,* an intermediate result for an antimicrobial agent indicates either a technical problem that should be resolved by repeat testing or a lack of clinical experience in treating **infections due to** organisms with these zones. Strains with intermediate zones to agents other than cefmetazole, cefotetan, cefoxitin, and spectinomycin have a documented lower clinical cure rate (85% to 95%) compared with > 95% for susceptible strains.

(4) The recommended medium for testing *N. gonorrhoeae* consists of GC agar to which a 1% defined growth supplement (1.1 g L-cysteine, 0.03 g guanine HCl, 3 mg thiamine HCl, 13 mg para-aminobenzoic acid, 0.01 g B12, 0.1 g cocarboxylase, 0.25 g nicotinamide adenine dinucleotide, 1 g adenine, 10 g L-glutamine, 100 g glucose, 0.02 g ferric nitrate [in 1 L H_2O]) is added after autoclaving.

NOTE: Information in boldface type is new or modified since the previous edition.

Table 2F. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
O	Penicillin	10 units	≥47	27–46	≤26	≤0.06	0.12–1	≥2	See comment (3). (5) A positive β-lactamase test predicts resistance to penicillin, ampicillin, and amoxicillin. (6) A β-lactamase test detects one form of penicillin resistance in *N. gonorrhoeae* and also may be used to provide epidemiological information. Strains with chromosomally mediated resistance can be detected only by the disk diffusion method or the agar dilution MIC method. (7) Gonococci that produce zones of inhibition of ≤19 mm around a 10-unit penicillin disk are likely to be β-lactamase–producing strains. However, the β-lactamase test remains preferable to other susceptibility methods for rapid, accurate recognition of this plasmid-mediated penicillin resistance.
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftriaxone	30 µg	≥35	–	–	≤0.25	–	–	
O	Cefoxitin	30 µg	≥28	24–27	≤23	≤2	4	≥8	See comment (2).
O	Cefuroxime	30 µg	≥31	26–30	≤25	≤1	2	≥4	See comment (3).
O	Cefepime	30 µg	≥31	–	–	≤0.5	–	–	
O	Cefmetazole	30 µg	≥33	28–32	≤27	≤2	4	≥8	See comment (2).
O	Cefotaxime	30 µg	≥31	–	–	≤0.5	–	–	
O	Cefotetan	30 µg	≥26	20–25	≤19	≤2	4	≥8	See comment (2).
O	Ceftazidime	30 µg	≥31	–	–	≤0.5	–	–	
O	Ceftizoxime	30 µg	≥38	–	–	≤0.5	–	–	
CEPHEMS (ORAL)									
A	Cefixime	5 µg	≥31	–	–	≤0.25	–	–	
O	Cefpodoxime	10 µg	≥29	–	–	≤0.5	–	–	
Inv.	Cefetamet	10 µg	≥29	–	–	≤0.5	–	–	

Table 2F. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
TETRACYCLINES (8) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.									
A	Tetracycline	30 µg	≥38	31–37	≤30	≤0.25	0.5–1	≥2	(9) Gonococci with 30-µg tetracycline disk zone diameters of ≤ 19 mm usually indicate a plasmid-mediated tetracycline-resistant *Neisseria gonorrhoeae* isolate. Resistance in these strains should be confirmed by a dilution test (MIC ≥ 16 µg/mL).
FLUOROQUINOLONES									See comment (3).
A	Ciprofloxacin	5 µg	≥41	28–40	≤27	≤ 0.06	0.12–0.5	≥1	
O	Enoxacin	10 µg	≥36	32–35	≤31	≤ 0.5	1	≥2	
O	Gatifloxacin	5 µg	≥38	34–37	≤33	≤ 0.125	0.25	≥0.5	
O	Grepafloxacin	5 µg	≥37	28–36	≤27	≤ 0.06	0.12–0.5	≥1	
O	Lomefloxacin	10 µg	≥38	27–37	≤26	≤ 0.12	0.25–1	≥2	
O	Ofloxacin	5 µg	≥31	25–30	≤24	≤ 0.25	0.5–1	≥2	
O	Trovafloxacin	10 µg	≥34	–	–	≤ 0.25	–	–	
Inv.	Fleroxacin	5 µg	≥35	29–34	≤28	≤ 0.25	0.5	≥1	
AMINOCYCLITOLS									
C	Spectinomycin	100 µg	≥18	15–17	≤14	≤ 32	64	≥128	See comment (2).

Abbreviations: ATCC, American Type Culture Collection; MHB, Mueller-Hinton broth; MIC, minimal inhibitory concentration; QC, quality control.

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Table 2G. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Streptococcus pneumoniae*

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA) with 5% sheep blood
Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB) with lysed horse blood (LHB) (2.5% to 5% v/v)
(see M07-A9 for instructions for preparation of LHB)
Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.

Inoculum: Direct colony suspension, equivalent to a 0.5 McFarland standard, prepared using colonies from an overnight (18- to 20-hour) sheep blood agar plate

Incubation: 35 ± 2°C
Disk diffusion: 5% CO_2; 20 to 24 hours
Dilution methods: ambient air; 20 to 24 hours (CO_2 if necessary for growth with agar dilution).

Routine QC Recommendations (See Tables 4B and 5B for acceptable QC ranges.)

Streptococcus pneumoniae ATCC® 49619

General Comments

(1) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Do not measure the zone of inhibition of hemolysis. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

(2) Amoxicillin, ampicillin, cefepime, cefotaxime, ceftriaxone, cefuroxime, ertapenem, imipenem, and meropenem may be used to treat pneumococcal infections; however, reliable disk diffusion susceptibility tests with these agents do not yet exist. Their *in vitro* activity is best determined using an MIC method.

(3) For *S. pneumoniae* isolated from CSF, penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method (such as that described in M07-A9), and reported routinely. Such isolates can also be tested against vancomycin using the MIC or disk method.

NOTE: Information in boldface type is new or modified since the previous edition.

Table 2G. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS (4) For nonmeningitis isolates, a penicillin MIC of ≤0.06 µg/mL (or oxacillin zone ≥20 mm) can predict susceptibility to the following β-lactams: ampicillin (oral or parenteral), ampicillin-sulbactam, amoxicillin, amoxicillin-clavulanate, cefaclor, cefdinir, cefditoren, cefepime, cefotaxime, cefpodoxime, cefprozil, ceftaroline, ceftizoxime, ceftriaxone, cefuroxime, doripenem, ertapenem, imipenem, loracarbef, meropenem, and penicillin (oral or parenteral). See comment (3).									
A	Penicillin	1 µg oxacillin	≥20	–	–	–	–	–	(5) Isolates of pneumococci with oxacillin zone sizes of ≥ 20 mm are susceptible (MIC ≤ 0.06 µg/mL) to penicillin. Penicillin and cefotaxime, ceftriaxone, or meropenem MICs should be determined for those isolates with oxacillin zone diameters of ≤ 19 mm, because zones of ≤ 19 mm occur with penicillin-resistant, intermediate, or certain susceptible strains. For isolates with oxacillin zones ≤ 19 mm, do not report penicillin as resistant without performing a penicillin MIC test.
A	Penicillin parenteral (nonmeningitis)	–	–	–	–	≤2	4	≥8	(6) ***Rx*:** Doses of intravenous penicillin of at least 2 million units every four hours in adults with normal renal function (12 million units per day) can be used to treat nonmeningeal pneumococcal infections due to strains with penicillin MICs ≤ 2 µg/mL. Strains with an intermediate MIC of 4 µg/mL may require penicillin doses of 18 to 24 million units per day. (7) For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.
A	Penicillin parenteral (meningitis)	–	–	–	–	≤0.06	–	≥0.12	(8) ***Rx*:** Use of penicillin in meningitis requires therapy with maximum doses of intravenous penicillin (eg, at least 3 million units every four hours in adults with normal renal function). (9) For CSF isolates, report only meningitis interpretations.
A	Penicillin (oral penicillin V)	–	–	–	–	≤0.06	0.12–1	≥2	(10) Interpretations for oral penicillin may be reported for isolates other than those from CSF.

Table 2G. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS (Continued)									
C	Amoxicillin (nonmeningitis)	–	–	–	–	≤2	4	≥8	
C	Amoxicillin-clavulanate (nonmeningitis)					≤2/1	4/2	≥8/4	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
O	Cefepime (meningitis)	–	–	–	–	≤0.5	1	≥2	(11) In the United States, for CSF isolates, report only nonmeningitis interpretations. There is not an FDA–approved indication for the use of cefepime for meningitis in the United States.
B	Cefepime (nonmeningitis)	–	–	–	–	≤1	2	≥4	(12) In the United States, only report interpretations for nonmeningitis and include the nonmeningitis notation on the report.
B	Cefotaxime (meningitis)	–	–	–	–	≤0.5	1	≥2	(13) For CSF isolates, report only meningitis interpretations.
B	Ceftriaxone (meningitis)	–	–	–	–	≤0.5	1	≥2	(14) ***Rx*:** Use of cefotaxime or ceftriaxone in meningitis requires therapy with maximum doses. See comment (3).
B	Cefotaxime (nonmeningitis)	–	–	–	–	≤1	2	≥4	(15) For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.
B	Ceftriaxone (nonmeningitis)	–	–	–	–	≤1	2	≥4	
C	Ceftaroline (nonmeningitis)	30 µg	≥26	–	–	≤0.5	–	–	(16) Interpretive criteria are based on a dosage regimen of 600 mg every 12 h.
C	Cefuroxime (parenteral)	–	–	–	–	≤0.5	1	≥2	
CEPHEMS (ORAL) **See comment (4)**									
C	Cefuroxime (oral)	–	–	–	–	≤1	2	≥4	
O	Cefaclor	–	–	–	–	≤1	2	≥4	
O	Cefdinir	–	–	–	–	≤0.5	1	≥2	
O	Cefpodoxime	–	–	–	–	≤0.5	1	≥2	
O	Cefprozil	–	–	–	–	≤2	4	≥8	
O	Loracarbef	–	–	–	–	≤2	4	≥8	
CARBAPENEMS **See comment (4)**									
B	Meropenem	–	–	–	–	≤0.25	0.5	≥1	See comments (3) and (5).
C	Ertapenem	–	–	–	–	≤1	2	≥4	
C	Imipenem	–	–	–	–	≤0.12	0.25–0.5	≥1	
O	Doripenem	–	–	–	–	≤1	–	–	

Table 2G. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	–	–	≤1	–	–	See comment (3).
MACROLIDES (17) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. (18) Not routinely reported for organisms isolated from the urinary tract.									
A	Erythromycin	15 µg	≥21	16–20	≤15	≤0.25	0.5	≥1	
B	Telithromycin	15 µg	≥19	16–18	≤15	≤1	2	≥4	
O	Azithromycin	15 µg	≥18	14–17	≤13	≤0.5	1	≥2	
O	Clarithromycin	15 µg	≥21	17–20	≤16	≤0.25	0.5	≥1	
O	Dirithromycin	15 µg	≥18	14–17	≤13	≤0.5	1	≥2	
TETRACYCLINES (19) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.									
B	Tetracycline	30 µg	≥28	25–27	≤24	≤1	2	≥4	
B	Doxycycline	30 µg	≥28	25–27	≤24	≤0.25	0.5	≥1	
FLUOROQUINOLONES									
B	Gemifloxacin	5 µg	≥23	20–22	≤19	≤0.12	0.25	≥0.5	(20) *S. pneumoniae* isolates susceptible to levofloxacin are predictably susceptible to gemifloxacin and moxifloxacin. However, *S. pneumoniae* susceptible to gemifloxacin or moxifloxacin cannot be assumed to be susceptible to levofloxacin.
B	Levofloxacin	5 µg	≥17	14–16	≤13	≤2	4	≥8	
B	Moxifloxacin	5 µg	≥18	15–17	≤14	≤1	2	≥4	
B	Ofloxacin	5 µg	≥16	13–15	≤12	≤2	4	≥8	
O	Gatifloxacin	5 µg	≥21	18–20	≤17	≤1	2	≥4	
O	Grepafloxacin	5 µg	≥19	16–18	≤15	≤0.5	1	≥2	
O	Sparfloxacin	5 µg	≥19	16–18	≤15	≤0.5	1	≥2	
O	Trovafloxacin	10 µg	≥19	16–18	≤15	≤1	2	≥4	
FOLATE PATHWAY INHIBITORS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥19	16–18	≤15	≤0.5/9.5	1/19–2/38	≥4/76	
PHENICOLS									
C	Chloramphenicol	30 µg	≥21	–	≤20	≤4	–	≥8	See comment (18).
ANSAMYCINS									
C	Rifampin	5 µg	≥19	17–18	≤16	≤1	2	≥4	(21) ***Rx*:** Rifampin should not be used alone for antimicrobial therapy.

Table 2G. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
LINCOSAMIDES									
B	Clindamycin	2 µg	≥19	16–18	≤15	≤0.25	0.5	≥1	(22) Inducible clindamycin resistance can be detected by disk diffusion using the D-zone test or **by** broth microdilution **using the single-well test (containing both erythromycin and clindamycin)** (see Table **3G**, Section 12 in M02-A11, and Section 13 in M07-A9). See comment (18).
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16–18	≤15	≤1	2	≥4	
OXAZOLIDINONES									
C	Linezolid	30 µg	≥21	–	–	≤2	–	–	

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CSF, cerebrospinal fluid; FDA, US Food and Drug Administration; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

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Table 2H-1. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Streptococcus* spp. β-Hemolytic Group

Testing Conditions

Medium:	Disk diffusion: Mueller-Hinton agar (MHA) with 5% sheep blood Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB) with lysed horse blood (LHB) (2.5% to 5% v/v); the CAMHB should be supplemented to 50 µg/mL calcium for daptomycin (see M07-A9 for instructions for preparation of LHB) Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.
Inoculum:	Direct colony suspension, equivalent to a 0.5 McFarland standard, using colonies from an overnight (18- to 20-hour) sheep blood agar plate
Incubation:	35 ± 2°C; Disk diffusion: 5% CO_2; 20 to 24 hours Dilution methods: ambient air; 20 to 24 hours (CO_2 if necessary for growth with agar dilution)

Routine QC Recommendations (See Tables 4B and 5B for acceptable QC ranges.)

Streptococcus pneumoniae ATCC® 49619

Refer to Table **3G** for additional **testing** recommendations, reporting suggestions, and QC.

General Comments

(1) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Do not measure the zone of inhibition of hemolysis. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth.

(2) For this table, the β-hemolytic group includes the large colony–forming pyogenic strains of streptococci with Group A (*S. pyogenes*), C, or G antigens and strains with Group B (*S. agalactiae*) antigen. Small colony–forming β-hemolytic strains with Group A, C, F, or G antigens (*S. anginosus* group, previously termed *"S. milleri"*) are considered part of the viridans group, and interpretive criteria for the viridans group should be used (see Table 2H-2).

(3) Penicillin and ampicillin are drugs of choice for treatment of β-hemolytic streptococcal infections. Susceptibility testing of penicillins and other β-lactams approved by the US Food and Drug Administration for treatment of β-hemolytic streptococcal infections need not be performed routinely, because nonsusceptible isolates (ie, penicillin MICs > 0.12 and ampicillin MICs > 0.25 µg/mL) are extremely rare in any β-hemolytic streptococcus and have not been reported for *Streptococcus pyogenes*. If testing is performed, any β-hemolytic streptococcal isolate found to be nonsusceptible should be re-identified, retested, and, if confirmed, submitted to a public health laboratory. (See Appendix A for further instructions.)

(4) Interpretive criteria for *Streptococcus* spp. β-hemolytic group are proposed based on population distributions of various species, pharmacokinetics of the antimicrobial agents, previously published literature, and the clinical experience of members of the subcommittee. Systematically collected clinical data were not available for review with many of the **antimicrobial agents** in **this table**.

Table 2H-1. (Continued)

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS (5) For the following organism groups, an organism that is susceptible to penicillin can be considered susceptible to the listed antimicrobial agents when used for approved indications. For β-hemolytic streptococci (Groups A, B, C, G): ampicillin, amoxicillin, amoxicillin-clavulanate, ampicillin-sulbactam, cefazolin, cefepime, ceftaroline, cephradine, cephalothin, cefotaxime, ceftriaxone, ceftizoxime, imipenem, ertapenem, and meropenem. In addition, for **β-hemolytic** streptococci Group A: cefaclor, cefdinir, cefprozil, ceftibuten, cefuroxime, cefpodoxime, and cephapirin.										
A A	Penicillin or ampicillin	10 units 10 µg	≥24 ≥24	– –	– –	≤0.12 ≤0.25	– –	– –	See comment (3).
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) See comment (5).									
B B B	Cefepime or cefotaxime or ceftriaxone	30 µg 30 µg 30 µg	≥24 ≥24 ≥24	– – –	– – –	≤0.5 ≤0.5 ≤0.5	– – –	– – –	
C	Ceftaroline	30 µg	≥26	–	–	≤0.5	–	–	(6) Interpretive criteria are based on a dosage regimen of 600 mg every 12 h.
CARBAPENEMS See comment (5).									
O	Doripenem	–	–	–	–	≤0.12	–	–	
O	Ertapenem	–	–	–	–	≤1	–	–	
O	Meropenem	–	–	–	–	≤0.5	–	–	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	–	–	≤1	–	–	
LIPOPEPTIDES									
C	Daptomycin	–	–	–	–	≤1	–	–	(7) Daptomycin should not be reported for isolates from the respiratory tract.

Table 2H-1. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
MACROLIDES (8) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. (9) Not routinely reported on isolates from the urinary tract.									
A	Erythromycin	15 µg	≥21	16–20	≤15	≤0.25	0.5	≥1	(10) ***Rx:*** Recommendations for intrapartum prophylaxis for Group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin. Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin, but may be resistant to erythromycin and clindamycin. When a Group B *Streptococcus* is isolated from a pregnant woman with severe penicillin allergy (high risk for anaphylaxis), erythromycin and clindamycin (including inducible clindamycin resistance) should be tested, and only clindamycin should be reported. See Table **3G**.
O	Azithromycin	15 µg	≥18	14–17	≤13	≤0.5	1	≥2	
O	Clarithromycin	15 µg	≥21	17–20	≤16	≤0.25	0.5	≥1	
O	Dirithromycin	15 µg	≥18	14–17	≤13	≤0.5	1	≥2	
TETRACYCLINES (11) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.									
O	Tetracycline	30 µg	≥23	19–22	≤18	≤2	4	≥8	
FLUOROQUINOLONES									
C	Levofloxacin	5 µg	≥17	14–16	≤13	≤2	4	≥8	
C	Ofloxacin	5 µg	≥16	13–15	≤12	≤2	4	≥8	
O	Gatifloxacin	5 µg	≥21	18–20	≤17	≤1	2	≥4	
O	Grepafloxacin	5 µg	≥19	16–18	≤15	≤0.5	1	≥2	
O	Trovafloxacin	10 µg	≥19	16–18	≤15	≤1	2	≥4	
PHENICOLS									
C	Chloramphenicol	30 µg	≥21	18–20	≤17	≤4	8	≥16	See comment (9).
LINCOSAMIDES									
A	Clindamycin	2 µg	≥19	16–18	≤15	≤0.25	0.5	≥1	See comments (9) and (10). (12) Inducible clindamycin resistance can be detected by disk diffusion using the D-zone test and broth microdilution. See Table **3G** and Section 12 in M02-A11 and Section 13 in M07-A9.

Table 2H-1. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
STREPTOGRAMINS									
C	Quinupristin-dalfopristin	15 µg	≥19	16–18	≤15	≤1	2	≥4	(13) Report against *S. pyogenes.*
OXAZOLIDINONES									
C	Linezolid	30 µg	≥21	–	–	≤2	–	–	

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 2H-2. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Streptococcus* spp. Viridans Group

Testing Conditions

Medium:	Disk diffusion: Mueller-Hinton agar (MHA) with 5% sheep blood Broth dilution: cation-adjusted Mueller-Hinton broth (CAMHB) with lysed horse blood (LHB) (2.5% to 5% v/v); the CAMHB should be supplemented to 50 µg/mL calcium for daptomycin (see M07-A9 for instructions for preparation of LHB) Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.
Inoculum:	Direct colony suspension, equivalent to a 0.5 McFarland standard using colonies from an overnight (18- to 20-hour) sheep blood agar plate
Incubation:	35±2°C; Disk diffusion: 5% CO_2; 20 to 24 hours Dilution methods: ambient air; 20 to 24 hours (CO_2 if necessary for growth with agar dilution)

Routine QC Recommendations (See Tables 4B and 5B for acceptable QC ranges.)

Streptococcus pneumoniae ATCC® 49619

General Comments

(1) For disk diffusion, measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Do not measure the zone of inhibition of hemolysis. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth.

(2) The viridans group of streptococci includes the following five groups, with several species within each group: *mutans* group, *salivarius* group, *bovis* group, *anginosus* group (previously "*S. milleri*" group), and *mitis* group. The *anginosus* group includes small colony–forming β-hemolytic strains with Groups A, C, F, and G antigens. For detailed information on the species within the groups, please refer to recent clinical microbiology literature.

(3) Interpretive criteria for *Streptococcus* spp. viridans group are proposed based on population distributions of various species, pharmacokinetics of the antimicrobial agents, previously published literature, and the clinical experience of members of the subcommittee. Systematically collected clinical data were not available for review with many of the **antimicrobial agents** in **this table**.

NOTE: Information in boldface type is new or modified since the previous edition.

Table 2H-2. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
A A	Penicillin Ampicillin	–	–	–	–	≤0.12 ≤0.25	0.25–2 0.5–4	≥4 ≥8	(4) Viridans streptococci isolated from normally sterile body sites (eg, CSF, blood, bone) should be tested for penicillin susceptibility using an MIC method. (5) ***Rx:*** Penicillin- or ampicillin-intermediate isolates may require combined therapy with an aminoglycoside for bactericidal action.
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
B B B	Cefepime Cefotaxime Ceftriaxone	30 µg 30 µg 30 µg	≥24 ≥28 ≥27	22–23 26–27 25–26	≤21 ≤25 ≤24	≤1 ≤1 ≤1	2 2 2	≥4 ≥4 ≥4	
CARBAPENEMS									
O	Doripenem	–	–	–	–	≤1	–	–	
O	Ertapenem	–	–	–	–	≤1	–	–	
O	Meropenem	–	–	–	–	≤0.5	–	–	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	–	–	≤1	–	–	
LIPOPEPTIDES									
O	Daptomycin	–	–	–	–	≤1	–	–	(6) Daptomycin should not be reported for isolates from the respiratory tract.
MACROLIDES (7) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. (8) Not routinely reported on isolates from the urinary tract.									
C	Erythromycin	15 µg	≥21	16–20	≤15	≤0.25	0.5	≥1	
O	Azithromycin	15 µg	≥18	14–17	≤13	≤0.5	1	≥2	
O	Clarithromycin	15 µg	≥21	17–20	≤16	≤0.25	0.5	≥1	
O	Dirithromycin	15 µg	≥18	14–17	≤13	≤0.5	1	≥2	
TETRACYCLINES (9) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.									
O	Tetracycline	30 µg	≥23	19–22	≤18	≤2	4	≥8	

Table 2H-2. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
FLUOROQUINOLONES									
O	Levofloxacin	5 µg	≥17	14–16	≤13	≤2	4	≥8	
O	Ofloxacin	5 µg	≥16	13–15	≤12	≤2	4	≥8	
O	Gatifloxacin	5 µg	≥21	18–20	≤17	≤1	2	≥4	
O	Grepafloxacin	5 µg	≥19	16–18	≤15	≤0.5	1	≥2	
O	Trovafloxacin	10 µg	≥19	16–18	≤15	≤1	2	≥4	
PHENICOLS									
C	Chloramphenicol	30 µg	≥21	18–20	≤17	≤4	8	≥16	See comment (8).
LINCOSAMIDES									
C	Clindamycin	2 µg	≥19	16–18	≤15	≤0.25	0.5	≥1	See comment (8).
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16–18	≤15	≤1	2	≥4	
OXAZOLIDINONES									
C	Linezolid	30 µg	≥21	–	–	≤2	–	–	

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CSF, cerebrospinal fluid; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

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Table 2I. Zone Diameter and Minimal Inhibitory Concentration (MIC) Interpretive Standards for *Neisseria meningitidis*

Testing Conditions

Medium: Disk diffusion: Mueller-Hinton agar (MHA) with 5% sheep blood
Broth microdilution: cation-adjusted Mueller-Hinton broth (CAMHB) supplemented with lysed horse blood (LHB) (2.5% to 5% v/v) (see M07-A9 for preparation of LHB)
Agar dilution: MHA supplemented with sheep blood (5% v/v)

Inoculum: Direct colony suspension from 20 to 24 hours growth from chocolate agar incubated at 35°C; 5% CO_2; equivalent to a 0.5 McFarland standard. Colonies grown on sheep blood agar may be used for inoculum preparation. However, the 0.5 McFarland suspension obtained from sheep blood agar will contain approximately 50% fewer CFU/mL. This must be taken into account when preparing the final dilution before panel inoculation, as guided by colony counts.

Incubation: 35±2°C; 5% CO_2; 20 to 24 hours

Routine QC Recommendations (See Tables 4A, 4B, 5A, and 5B for acceptable QC ranges.)

Streptococcus pneumoniae ATCC® 49619:

Disk diffusion: incubate in 5% CO_2.

Broth microdilution: incubate in ambient air or CO_2 (except azithromycin QC tests that must be incubated in ambient air).

E. coli ATCC® 25922

Disk diffusion, broth microdilution or agar dilution for ciprofloxacin, nalidixic acid, minocycline, and sulfisoxazole: incubate in ambient air or CO_2.

General Comments

Important: For complete information on safety precautions, see *Biosafety in Microbiological and Biomedical Laboratories.* 5th ed. Washington, DC: US Department of Health and Human Services; 2010. http://www.cdc.gov/biosafety/publications/bmbl5/.

(1) **Recommended precautions:** Perform all antimicrobial susceptibility testing (AST) of *N. meningitidis* in a biological safety cabinet (BSC). Manipulating *N. meningitidis* outside a BSC is associated with increased risk for contracting meningococcal disease. Laboratory-acquired meningococcal disease is associated with a case fatality rate of 50%. Exposure to droplets or aerosols of *N. meningitidis* is the most likely risk for laboratory-acquired infection. Rigorous protection from droplets or aerosols is mandated when microbiological procedures (including AST) are performed on all *N. meningitidis* isolates.

(2) If a BSC is unavailable, manipulation of these isolates should be minimized, limited to Gram staining or serogroup identification using phenolized saline solution while wearing a laboratory coat and gloves, and working behind a full face splash shield. Use Biosafety Level 3 (BSL-3) practices, procedures, and containment equipment for activities with a high potential for droplet or aerosol production and for activities involving production quantities or high concentrations of infectious materials. If Biosafety Level 2 (BSL-2) or BSL-3 facilities are not available, forward isolates to a reference or public health laboratory with a minimum of BSL-2 facilities.

(3) Laboratorians who are exposed routinely to potential aerosols of *N. meningitidis* should consider vaccination according to the current recommendations of the CDC Advisory Committee on Immunization Practices (http://www.cdc.gov/vaccines/acip/index.html). Vaccination will decrease, but not eliminate, the risk of infection, because it is less than 100% effective and does not provide protection against serogroup B, a frequent cause of laboratory-acquired cases.

Table 2I. (Continued)

(4) For disk diffusion, test a maximum of 5 disks on a 150-mm plate and 2 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

(5) Interpretive criteria are based on population distributions of MICs of various agents, pharmacokinetics of the agents, previously published literature, and the clinical experience of members of the subcommittee. Systematically collected clinical data were not available to review with many of the antimicrobial agents in this table.

(6) With azithromycin, interpretive criteria were developed initially using MICs determined by incubation in ambient air for the pharmacodynamic calculations.

NOTE: Information in boldface type is new or modified since the previous edition.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
C C	Penicillin Ampicillin		– –	– –	– –	≤0.06 ≤0.12	0.12–0.25 0.25–1	≥0.5 ≥2	
CEPHEMS									
C C	Cefotaxime or ceftriaxone	30 µg 30 µg	≥34 ≥34	– –	– –	≤0.12 ≤0.12	– –	– –	
CARBAPENEMS									
C	Meropenem	10 µg	≥30	–	–	≤0.25	–	–	
MACROLIDES									
C	Azithromycin	15 µg	≥20	–	–	≤2	–	–	See comment (6). (7) May be appropriate only for prophylaxis of meningococcal case contacts. These interpretive criteria do not apply to therapy of patients with invasive meningococcal disease.

Table 2I. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria (nearest whole mm)			MIC Interpretive Criteria (µg/mL)			Comments
			S	I	R	S	I	R	
TETRACYCLINES									
C	Minocycline	30 µg	≥26	–	–	≤2	–	–	See comment (7).
FLUOROQUINOLONES									
(8) For surveillance purposes, a nalidixic acid MIC ≥ 8 µg/mL or a zone ≤ 25 mm may correlate with diminished fluoroquinolone susceptibility.									
C	Ciprofloxacin	5 µg	≥35	33–34	≤32	≤0.03	0.06	≥0.12	See comment (7).
C	Levofloxacin	–	–	–	–	≤0.03	0.06	≥0.12	
FOLATE PATHWAY INHIBITORS									
C	Sulfisoxazole	–	–	–	–	≤2	4	≥8	See comment (7).
C	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥30	26–29	≤25	≤0.12/2.4	0.25/4.75	≥0.5/9.5	(9) **Trimethoprim-sulfamethoxazole** is the preferred disk for detection of sulfonamide resistance. Trimethoprim-sulfamethoxazole testing predicts susceptibility and resistance to trimethoprim-sulfamethoxazole and sulfonamides. Sulfonamides may be appropriate only for prophylaxis of meningococcal case contacts.
PHENICOLS									
C	Chloramphenicol	30 µg	≥26	20–25	≤19	≤2	4	≥8	(10) Not routinely reported on isolates from the urinary tract.
ANSAMYCINS									
C	Rifampin	5 µg	≥25	20–24	≤19	≤0.5	1	≥2	See comment (7).

Abbreviations: AST, antimicrobial susceptibility testing; ATCC, American Type Culture Collection; BSC, biological safety cabinet; BSL-2, Biosafety Level 2; BSL-3, Biosafety Level 3; CAMHB, cation-adjusted Mueller-Hinton broth; CDC, Centers for Disease Control and Prevention; CFU, colony-forming unit; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

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Table 2J. Minimal Inhibitory Concentration (MIC) Interpretive Standards for Anaerobes

Testing Conditions

Medium: Agar dilution: (for all anaerobes) Brucella agar supplemented with hemin (5 μg/mL), Vitamin K_1 (1 μg/mL), and laked sheep blood (5% v/v)
Broth microdilution (for *Bacteroides fragilis* group only): Brucella broth supplemented with hemin (5 μg/mL), Vitamin K_1 (1 μg/mL), and lysed horse blood (5% v/v)

Inoculum: Growth method or direct colony suspension, equivalent to 0.5 McFarland suspension;
Agar: 10^5 CFU per spot
Broth: 10^6 CFU/mL

Incubation: 36 ± 1°C, anaerobically
Broth microdilution: 46 to 48 hours
Agar dilution: 42 to 48 hours

Routine QC Recommendations (See Tables 5D and 5E for acceptable QC ranges.)

Bacteroides fragilis ATCC® 25285
Bacteroides thetaiotaomicron ATCC® 29741
Test either strain for broth microdilution method.

For testing antimicrobial agents active against gram-positive organisms:
Clostridium difficile ATCC® 700057
Eubacterium lentum ATCC® 43055

Test any two of the four strains for each 30 isolates for the agar dilution method.

General Comments

(1) The intermediate range was established because of the difficulty in reading end points and the clustering of MICs at or near breakpoint concentrations. Where data are available, the interpretive guidelines are based on pharmacokinetic data, population distributions of MICs, and studies of clinical efficacy. To achieve the best possible levels of a drug in abscesses and/or poorly perfused tissues, which are encountered commonly in these infections, maximum approved dosages of antimicrobial agents are recommended for therapy of anaerobic infections. When maximum dosages are used along with appropriate ancillary therapy, it is believed that organisms with MICs in the susceptible range are generally amenable to therapy, and those with MICs in the intermediate range may respond, but patient response should be carefully monitored. Ancillary therapy, such as drainage procedures and debridement, are of great importance for the proper management of anaerobic infections.

(2) MIC values using either Brucella blood agar or Wilkins Chalgren agar (former reference medium) are considered equivalent.

(3) Broth microdilution is only recommended for testing the *B. fragilis* group. MIC values for agar or broth microdilution are considered equivalent for that group.

(4) Until further studies are performed to validate broth microdilution for testing other organisms, it should be used only for testing members of the *B. fragilis* group.

NOTE: Information in boldface type is new or modified since the previous edition.

Table 2J. (Continued)

Test/Report Group	Antimicrobial Agent	MIC Interpretive Criteria (µg/mL) S	I	R	Comments
PENICILLINS					
A/C	Ampicillin[a]	≤0.5	1	≥2	(5) Ampicillin and penicillin are recommended for primary testing for gram-positive organisms (Group A) because most of them are β-lactamase negative, but not for gram-negative organisms (Group C) because many are β-lactamase positive. (6) Members of the *Bacteroides fragilis* group are presumed to be resistant. Other gram-negative and gram-positive anaerobes may be screened for β-lactamase activity with a chromogenic cephalosporin; if β-lactamase positive, report as resistant to penicillin, ampicillin, and amoxicillin. Be aware that β-lactamase–negative isolates may be resistant to β-lactams by other mechanisms. Because higher blood levels are achievable, infection with non–β-lactamase producing organisms with higher MICs (2–4 µg/mL) with adequate dosage regimen might be treatable. Amoxicillin breakpoints are considered equivalent to ampicillin breakpoints. Limited *in vitro* data indicate that these two agents appear identical in MIC testing against anaerobic bacteria; however, breakpoints for amoxicillin have not been established.
A/C	Penicillin[a]	≤0.5	1	≥2	
C	Piperacillin	≤32	64	≥128	
C	Ticarcillin	≤32	64	≥128	
C	Mezlocillin	≤32	64	≥128	
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS					
A	Amoxicillin-clavulanate	≤4/2	8/4	≥16/8	
A	Ampicillin-sulbactam	≤8/4	16/8	≥32/16	
A	Piperacillin-tazobactam	≤32/4	64/4	≥128/4	
A	Ticarcillin-clavulanate	≤32/2	64/2	≥128/2	
CEPHEMS (PARENTERAL) Please refer to Glossary I.					
C	Cefotetan	≤16	32	≥64	
C	Cefoxitin	≤16	32	≥64	
C	Ceftizoxime	≤32	64	≥128	
C	Ceftriaxone	≤16	32	≥64	
O	Cefmetazole	≤16	32	≥64	
O	Cefoperazone	≤16	32	≥64	
O	Cefotaxime	≤16	32	≥64	

Table 2J. (Continued)

Test/Report Group	Antimicrobial Agent	MIC Interpretive Criteria (µg/mL)			Comments
		S	I	R	
CARBAPENEMS					
A	Doripenem	≤2	4	≥8	
A	Ertapenem	≤4	8	≥16	
A	Imipenem	≤4	8	≥16	
A	Meropenem	≤4	8	≥16	
TETRACYCLINES					
C	Tetracycline	≤4	8	≥16	
FLUOROQUINOLONES					
C	Moxifloxacin	≤2	4	≥8	
LINCOSAMIDES					
A	Clindamycin	≤2	4	≥8	
PHENICOLS					
C	Chloramphenicol	≤8	16	≥32	
NITROIMIDAZOLES					
A	Metronidazole	≤8	16	≥32	(7) Many non–spore-forming, gram-positive anaerobic rods are resistant to metronidazole.

Abbreviations: ATCC, American Type Culture Collection; CFU, colony-forming unit; MIC, minimal inhibitory concentration; QC, quality control.

Footnote

a. A/C: Group A for gram-positive organisms and Group C for *B. fragilis* and other gram-negative organisms. Refer to Table 1C.

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Table 3A. Screening and Confirmatory Tests for Extended-Spectrum β-Lactamases (ESBLs) in *Klebsiella pneumoniae, Klebsiella oxytoca, Escherichia coli,* and *Proteus mirabilis*

NOTE: Following evaluation of pharmacokinetic-pharmacodynamic (PK-PD) properties, limited clinical data, and minimal inhibitory concentration (MIC) distributions, revised interpretive criteria for cefazolin, cefotaxime, ceftazidime, ceftizoxime, ceftriaxone, and aztreonam were published in January 2010 (M100-S20) and are listed in Table 2A. Cefuroxime (parenteral) was also evaluated; however, no change in interpretive criteria was required with the dosage. When using the current interpretive criteria, routine ESBL testing is no longer necessary before reporting results (ie, it is no longer necessary to edit results for cephalosporins, aztreonam, or penicillins to resistant). However, ESBL testing may still be useful for epidemiological or infection control purposes. For laboratories that have not implemented the current interpretive criteria, ESBL testing should be performed as described in this table.

Test	Initial Screen Test		Phenotypic Confirmatory Test	
Test method	Disk diffusion	Broth microdilution	Disk diffusion	Broth microdilution
Medium	MHA	CAMHB	MHA	CAMHB
Antimicrobial concentration	For *K. pneumoniae, K. oxytoca,* and *E. coli*: Cefpodoxime 10 μg or Ceftazidime 30 μg or Aztreonam 30 μg or Cefotaxime 30 μg or Ceftriaxone 30 μg For *P. mirabilis*: Cefpodoxime 10 μg or Ceftazidime 30 μg or Cefotaxime 30 μg (The use of more than one antimicrobial agent for screening improves the sensitivity of ESBL detection.)	For *K. pneumoniae, K. oxytoca,* and *E. coli*: Cefpodoxime 4 μg/mL or Ceftazidime 1 μg/mL or Aztreonam 1 μg/mL or Cefotaxime 1 μg/mL or Ceftriaxone 1 μg/mL For *P. mirabilis*: Cefpodoxime 1 μg/mL or Ceftazidime 1 μg/mL or Cefotaxime 1 μg/mL (The use of more than one antimicrobial agent for screening improves the sensitivity of ESBL detection.)	Ceftazidime 30 μg Ceftazidime-clavulanate[a] 30/10 μg and Cefotaxime 30 μg Cefotaxime-clavulanate 30/10 μg (Confirmatory testing requires use of both cefotaxime and ceftazidime, alone and in combination with clavulanate.)	Ceftazidime 0.25–128 μg/mL Ceftazidime-clavulanate 0.25/4–128/4 μg/mL and Cefotaxime 0.25–64 μg/mL Cefotaxime-clavulanate 0.25/4–64/4 μg/mL (Confirmatory testing requires use of both cefotaxime and ceftazidime, alone and in combination with clavulanate.)
Inoculum	Standard disk diffusion procedure	Standard broth dilution procedure	Standard disk diffusion procedure	Standard broth dilution procedure
Incubation conditions	35±2°C; ambient air	35±2°C; ambient air	35±2°C; ambient air	35±2°C; ambient air
Incubation length	16–18 hours	16–20 hours	16–18 hours	16–20 hours

Table 3A. (Continued)

Test	Initial Screen Test		Phenotypic Confirmatory Test	
Test Method	Disk diffusion	Broth microdilution	Disk diffusion	Broth microdilution
Results	For *K. pneumoniae, K. oxytoca,* and *E. coli*: Cefpodoxime zone ≤17 mm Ceftazidime zone ≤22 mm Aztreonam zone ≤27 mm Cefotaxime zone ≤27 mm Ceftriaxone zone ≤25 mm For *P. mirabilis*: Cefpodoxime zone ≤22 mm Ceftazidime zone ≤22 mm Cefotaxime zone ≤27 mm Zones above may indicate ESBL production.	Growth at or above the screening concentrations may indicate ESBL production (ie, for *E. coli, K. pneumoniae,* and *K. oxytoca,* MIC ≥ 8 μg/mL for cefpodoxime or MIC ≥ 2 μg/mL for ceftazidime, aztreonam, cefotaxime, or ceftriaxone; and for *P. mirabilis,* MIC ≥ 2 μg/mL for cefpodoxime, ceftazidime, or cefotaxime).	A ≥ 5-mm increase in a zone diameter for either antimicrobial agent tested in combination with clavulanate vs the zone diameter of the agent when tested alone = ESBL (eg, ceftazidime zone = 16; ceftazidime-clavulanate zone = 21).	A ≥ 3 twofold concentration decrease in an MIC for either antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone = ESBL (eg, ceftazidime MIC = 8 μg/mL; ceftazidime-clavulanate MIC = 1 μg/mL).
Reporting			For all confirmed ESBL-producing strains: If laboratories do not use current cephalosporin and aztreonam interpretive criteria, the test interpretation should be reported as resistant for all penicillins, cephalosporins, and aztreonam. If laboratories use current cephalosporin and aztreonam interpretive criteria, then test interpretations for these agents do not need to be changed from susceptible to resistant.	

Table 3A. (Continued)

Test	Initial Screen Test		Phenotypic Confirmatory Test	
Test Method	Disk diffusion	Broth microdilution	Disk diffusion	Broth microdilution
QC Recommendations	When testing ESBL-screening antimicrobial agents, *K. pneumoniae* ATCC® 700603 is provided as a supplemental QC strain (eg, for training, competency, or test evaluation). Either strain, *K. pneumoniae* ATCC® 700603 or *E. coli* ATCC® 25922, may then be used for routine QC (eg, weekly or daily). *E. coli* ATCC® 25922 (see acceptable QC ranges in Table 4A) *K. pneumoniae* ATCC® 700603: Cefpodoxime zone 9–16 mm Ceftazidime zone 10–18 mm Aztreonam zone 9–17 mm Cefotaxime zone 17–25 mm Ceftriaxone zone 16–24 mm	When testing ESBL-screening antimicrobial agents, *K. pneumoniae* ATCC® 700603 is provided as a supplemental QC strain (eg, for training, competency, or test evaluation). Either strain, *K. pneumoniae* ATCC® 700603 or *E. coli* ATCC® 25922, may then be used for routine QC (eg, weekly or daily). *E. coli* ATCC® 25922 = No growth (also see acceptable QC ranges listed in Table 5A). *K. pneumoniae* ATCC® 700603 = Growth: Cefpodoxime MIC ≥ 8 μg/mL Ceftazidime MIC ≥ 2 μg/mL Aztreonam MIC ≥ 2 μg/mL Cefotaxime MIC ≥ 2 μg/mL Ceftriaxone MIC ≥ 2 μg/mL	When performing the ESBL confirmatory tests, *K. pneumoniae* ATCC® 700603 and *E. coli* ATCC® 25922 should be used for routine QC (eg, weekly or daily). **Acceptable QC:** *E. coli* ATCC® 25922: ≤ 2-mm increase in zone diameter for antimicrobial agent tested in combination with clavulanate vs the zone diameter when tested alone. *K. pneumoniae* ATCC® 700603: ≥ 5-mm increase in zone diameter of ceftazidime-clavulanate vs ceftazidime alone; ≥ 3-mm increase in zone diameter of cefotaxime-clavulanate vs cefotaxime alone.	When performing the ESBL confirmatory tests, *K. pneumoniae* ATCC® 700603 and *E. coli* ATCC® 25922 should be tested routinely (eg, weekly or daily). **Acceptable QC:** *E. coli* ATCC® 25922: < 3 twofold concentration decrease in MIC for antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone. *K. pneumoniae* ATCC® 700603: ≥ 3 twofold concentration decrease in MIC for an antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone.

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; ESBL, extended-spectrum β-lactamase; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; PK-PD, pharmacokinetic-pharmacodynamic; QC, quality control.

Footnote

a. Preparation of ceftazidime-clavulanate (30 μg/10 μg) and cefotaxime-clavulanate (30 μg/10 μg) disks: Using a stock solution of clavulanate at 1000 μg/mL (either freshly prepared or taken from small aliquots that have been frozen at −70°C), add 10 μL of clavulanate to ceftazidime (30 μg) and cefotaxime (30 μg) disks. Use a micropipette to apply the 10 μL of stock solution to the ceftazidime and cefotaxime disks within one hour before they are applied to the plates, allowing about 30 minutes for the clavulanate to absorb and the disks to be dry enough for application. Use disks immediately after preparation or discard; do not store.

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Table 3B. Confirmatory Test for Suspected Carbapenemase Production in *Enterobacteriaceae*

Until laboratories can implement the revised carbapenem interpretive criteria (now considered current), the modified Hodge test (MHT) should be performed as described in Table **3C**. If using current interpretive criteria, the MHT does not need to be performed other than for epidemiological or infection control purposes and no change in the interpretation of carbapenem susceptibility test results is required for MHT-positive isolates.

When to Do This Test:	Institutional infection control procedures or epidemiological investigations may require identification of carbapenemase-producing *Enterobacteriaceae.* Carbapenemase-producing isolates usually test intermediate or resistant to one or more carbapenems using the current interpretive criteria as listed in Table 2A (Note: Ertapenem nonsusceptibility is the most sensitive indicator of carbapenemase production), and usually test resistant to one or more agents in cephalosporin subclass III (eg, cefoperazone, cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone). Therefore, for infection control or epidemiological investigations, testing could be limited to isolates with these characteristics.
Test Method	MHT
Medium	MHA
Antimicrobial Concentration	Ertapenem disk 10 μg or Meropenem disk 10 μg
Inoculum	(1) Prepare a 0.5 McFarland standard suspension (using either direct colony suspension or growth method) of *E. coli* ATCC® 25922 (the indicator organism) in broth or saline, and dilute 1:10 in saline or broth. Inoculate an MHA plate as for the routine disk diffusion procedure. Allow the plate to dry 3 to 10 minutes. Place the appropriate number of ertapenem or meropenem disks on the plate as noted below and shown in Figures 1 and 2. (2) Using a 10-μL loop or swab, pick 3 to 5 colonies of test or QC organism grown overnight on a blood agar plate and inoculate in a straight line out from the edge of the disk. The streak should be at least 20 to 25 mm in length. Test the number of isolates per plate as noted below and shown in Figures 1 and 2. Capacity of small and large MHA plates (100-mm or 150-mm diameter, respectively): Small Large Disks 1 1–4 Test isolates 1 1–6 QC isolates 2 2
Incubation Conditions	35 ± 2°C; ambient air
Incubation Length	16 to 20 hours

Table 3B. (Continued)

Results	Following incubation, examine the MHA plate for enhanced growth around the test or QC organism streak at the intersection of the streak and the zone of inhibition (see Figures 1 and 2). Enhanced growth = positive for carbapenemase production. No enhanced growth = negative for carbapenemase production. Some test isolates may produce substances that will inhibit growth of *E. coli* ATCC® 25922. When this occurs, a clear area will be seen around the streak (see Figure 3), and the MHT is uninterpretable for these isolates. **NOTE:** Not all carbapenemase-producing isolates of *Enterobacteriaceae* are MHT positive, and MHT-positive results may be encountered in isolates with carbapenem resistance mechanisms other than carbapenemase production.
Reporting	Report results of the MHT to infection control or those requesting epidemiological information. No change in the interpretation of carbapenem susceptibility test results is required for MHT-positive isolates**.**
QC Recommendations	Test positive and negative QC organisms each day of testing. *K. pneumoniae* ATCC® BAA-1705—MHT positive *K. pneumoniae* ATCC® BAA-1706—MHT negative

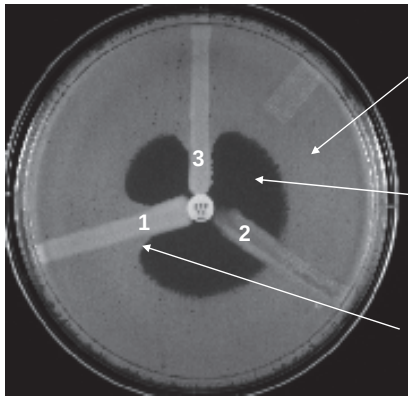
Abbreviations: ATCC, American Type Culture Collection; KPC, *Klebsiella pneumoniae* carbapenemase; MHA, Mueller-Hinton agar; MHT, modified Hodge test; NDM, New Delhi metallo-β-lactamase; QC, quality control.

NOTES:

1. Test recommendations were largely derived following testing of US isolates of *Enterobacteriaceae,* and provide for a high level of sensitivity (> 90%) and specificity (> 90%) in detecting KPC-type carbapenemases in these isolates. The sensitivity and specificity of the test for detecting other carbapenemase production can vary. For example, the sensitivity of the test for detecting NDM-type carbapenemases is low (ie, 11%).

2. No data exist on the usefulness of these tests for the detection of carbapenemase production in nonfermenting gram-negative bacilli.

Table 3B. (Continued)



E. coli ATCC® 25922

Inhibition of *E. coli* ATCC® 25922 by ertapenem

Enhanced growth of *E. coli* ATCC® 25922. Carbapenemase produced by *K. pneumoniae* ATCC ® BAA-1705 inactivated ertapenem that diffused into the media. Thus, there is no longer sufficient ertapenem here to inhibit *E. coli* ATCC® 25922 and an indentation of the zone is noted.

Figure 1. The MHT Performed on a Small MHA Plate.
(1) *K. pneumoniae* ATCC® BAA-1705, positive result;
(2) *K. pneumoniae* ATCC® BAA-1706, negative result;
and (3) a clinical isolate, positive result.

Table 3B. (Continued)

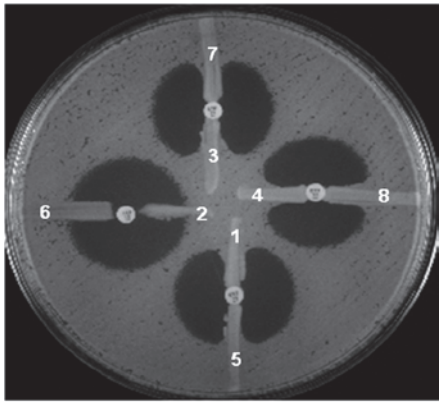


Figure 2. The MHT Performed on a Large MHA Plate With Ertapenem. (1) *K. pneumoniae* ATCC® BAA-1705, positive result; (2) *K. pneumoniae* ATCC® BAA-1706, negative result; (3–8) clinical isolates; (6) negative result; (3, 4, 5, 7, 8) positive result.

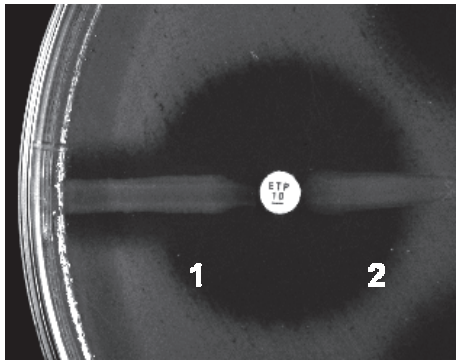


Figure 3. An Example of an Indeterminate Result. (1) A clinical isolate with an indeterminate result; and (2) a clinical isolate with a negative result.

Table 3C. Screening and Confirmatory Tests for Suspected Carbapenemase Production in *Enterobacteriaceae* When Using Interpretive Criteria for Carbapenems Listed in M100-S20 (2010)

Until the current interpretive criteria for carbapenems are implemented, the screen and confirmatory tests should be performed and reported using the instructions for a positive modified Hodge test (MHT) described below. It is not necessary to test an isolate for a carbapenemase by the MHT when all of the carbapenems that are reported by a laboratory test as either intermediate or resistant (ie, intermediate or resistant results should be reported as tested). However, if the isolate tests intermediate or resistant, the MHT may be performed for epidemiological purposes to determine if a carbapenemase is present.

Test	Initial Screen Test		Phenotypic Confirmatory Test
When to Do This Test:	The following applies ONLY when using interpretive criteria for carbapenems described in M100-S20 (January 2010).		Positive screening test and resistance to one or more agents in cephalosporin subclass III (eg, cefoperazone, cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone).
Test Method	Disk diffusion	Broth microdilution	MHT
Medium	MHA	CAMHB	MHA
Antimicrobial Concentration	Ertapenem 10 μg or Meropenem 10 μg (NOTE: The imipenem disk test performs poorly as a screen for carbapenemases.)	Ertapenem 1 μg/mL or Imipenem 1 μg/mL or Meropenem 1 μg/mL	Ertapenem disk 10 μg or Meropenem disk 10 μg
Inoculum	Standard disk diffusion procedure	Standard broth dilution procedure	(1) Prepare a 0.5 McFarland standard suspension (using either direct colony suspension or growth method) of *E. coli* ATCC® 25922 (the indicator organism) in broth or saline, and dilute 1:10 in saline or broth. Inoculate an MHA plate as for the routine disk diffusion procedure. Allow the plate to dry 3 to 10 minutes. Place the appropriate number of ertapenem or meropenem disks on the plate as noted below and shown in Figures 1 and 2. (2) Using a 10-μL loop or swab, pick 3 to 5 colonies of test or QC organism grown overnight on a blood agar plate, and inoculate in a straight line out from the edge of the disk. The streak should be at least 20 to 25 mm in length. Test the number of isolates per plate as noted below and shown in Figures 1 and 2. Capacity of small and large MHA plates (100-mm or 150-mm diameter, respectively): Small / Large Disks: 1 / 1–4 Test isolates: 1 / 1–6 QC isolates: 2 / 2
Incubation Conditions	35±2°C; ambient air	35±2°C; ambient air	35±2°C; ambient air

Table 3C. (Continued)

Test	Initial Screen Test		Phenotypic Confirmatory Test
Incubation Length	16–18 hours	16–20 hours	16–20 hours
Results	Ertapenem 19–21 mm Meropenem 16–21 mm The zone diameters of inhibition listed above may indicate carbapenemase production, despite the fact that they are in the old susceptible interpretive categories. For confirmation, perform the MHT. (NOTE: The imipenem disk test performs poorly as a screen for carbapenemases.)	Ertapenem 2 µg/mL Imipenem 2–4 µg/mL Meropenem 2–4 µg/mL MICs listed above may indicate carbapenemase production, despite the fact that they are in the old susceptible interpretive categories in M100-S20 (January 2010). For confirmation, perform the MHT.	Following incubation, examine the MHA plate for enhanced growth around the test or QC organism streak at the intersection of the streak and the zone of inhibition (see Figures 1 and 2). Enhanced growth = positive for carbapenemase production. No enhanced growth = negative for carbapenemase production. Some test isolates may produce substances that will inhibit growth of *E. coli* ATCC® 25922. When this occurs, a clear area will be seen around the streak (see Figure 3) and the MHT is uninterpretable for these isolates. For isolates positive with the ertapenem or meropenem disk screen AND positive with the MHT, perform the MIC test before reporting any carbapenem results.
Reporting			The following applies ONLY when using interpretive criteria for carbapenems described in M100-S20 (January 2010). For isolates that are MHT positive and have an ertapenem MIC of 2–4 µg/mL, imipenem MIC of 2–8 µg/mL, or meropenem MIC of 2–8 µg/mL, report all carbapenems as resistant. If the MHT is negative, interpret the carbapenem MICs using CLSI interpretive criteria as listed in Table 2A in M100-S20 (January 2010). NOTE: Not all carbapenemase-producing isolates of *Enterobacteriaceae* are MHT positive and MHT-positive results may be encountered in isolates with carbapenem resistance mechanisms other than carbapenemase production.
QC Recommendations	*E. coli* ATCC® 25922 (see acceptable QC ranges in Table 4A).	*E. coli* ATCC® 25922 (see acceptable QC ranges in Table 5A).	Test positive and negative QC organisms each day of testing. *K. pneumoniae* ATCC® BAA-1705—MHT positive *K. pneumoniae* ATCC® BAA-1706—MHT negative

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; KPC, *Klebsiella pneumoniae* carbapenemase; MHA, Mueller-Hinton agar; MHT, modified Hodge test; MIC, minimal inhibitory concentration; NDM, New Delhi metallo-β-lactamase; QC, quality control.

Table 3C. (Continued)

NOTES:

1. *Proteus* spp., *Providencia* spp., and *Morganella* spp. may have elevated MICs to imipenem by mechanisms other than production of carbapenemases; thus, the usefulness of the imipenem MIC screen test for the detection of carbapenemases in these three genera is not established. Also, the imipenem disk test performs poorly as a screen for carbapenemases for all *Enterobacteriaceae*.

2. The screening and confirmatory test recommendations were largely derived following testing of US isolates of *Enterobacteriaceae,* and provide for a high level of sensitivity (> 90%) and specificity (> 90%) in detecting KPC-type carbapenemases in these isolates. The sensitivity and specificity of the test for detecting other carbapenemase production can vary. For example, the sensitivity of the test for detecting NDM-type carbapenemases is low (ie, 11%).

3. No data exist on the usefulness of these tests for the detection of carbapenemase production in nonfermenting gram-negative bacilli.

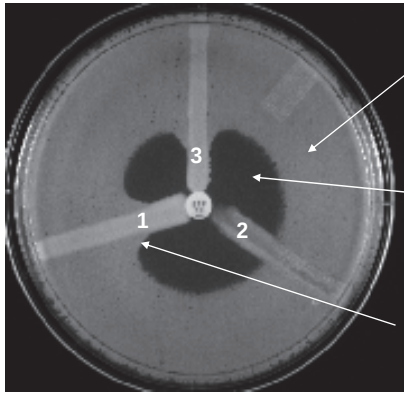


Figure 1. The MHT Performed on a Small MHA Plate.
(1) *K. pneumoniae* ATCC® BAA-1705, positive result;
(2) *K. pneumoniae* ATCC® BAA-1706, negative result;
and (3) a clinical isolate, positive result.

Table 3C. (Continued)

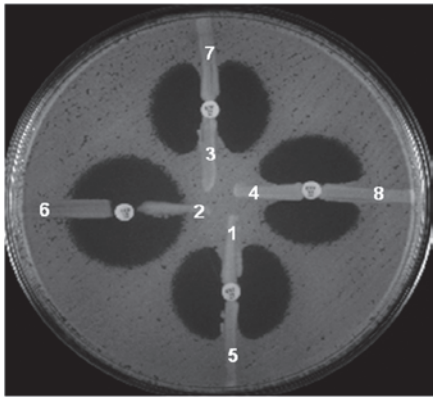


Figure 2. The MHT Performed on a Large MHA Plate With Ertapenem. (1) *K. pneumoniae* ATCC® BAA-1705, positive result; (2) *K. pneumoniae* ATCC® BAA-1706, negative result; (3–8) clinical isolates; (6) negative result; (3, 4, 5, 7, 8) positive result.

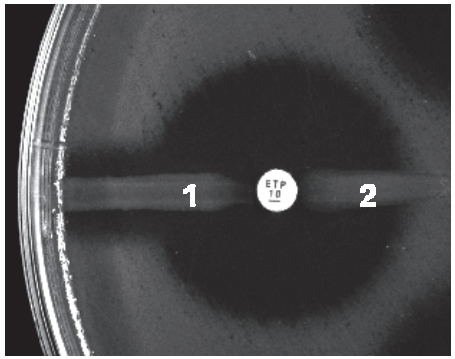


Figure 3. An Example of an Indeterminate Result. (1) A clinical isolate with an indeterminate result; and (2) a clinical isolate with a negative result.

Table 3C. (Continued)

References

[1] Perrott J, Mabasa VH, Ensom MH. Comparing outcomes of meropenem administration strategies based on pharmacokinetic and pharmacodynamic principles: A qualitative systematic review. *Ann Pharmacother.* 2010;44:557-564.

[2] Cirillo I, Vaccaro N, Turner K, Solanki B, Natarajan J, Redman R. Pharmacokinetics, safety, and tolerability of doripenem after 0.5-, 1-, and 4-hour infusions in healthy volunteers. *J Clin Pharmacol.* 2009;49:798-806.

[3] Sakka SG, Glauner AK, Bulitta JB, et al. Population pharmacokinetics and pharmacodynamics of continuous versus short-term infusion of imipenem-cilastatin in critically ill patients in a randomized, controlled trial. *Antimicrob Agents Chemother*. 2007;51:3304-3310.

[4] Peleg AY, Hooper DC. Hospital-acquired infections due to Gram-negative bacteria. *N Engl J Med.* 2010;362:1804-1813.

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Table 3D. Screening Test for Detection of β-Lactamase Production in *Staphylococcus* species

Screen Test	β-Lactamase Production	
Organism Group	*S. aureus* with penicillin MICs ≤ 0.12 µg/mL or zones ≥ 29 mm[a]	*S. aureus*[a] and CoNS (including *S. lugdunensis*[b]) with penicillin MICs ≤ 0.12 µg/mL or zones ≥ 29 mm
Test Method	Disk diffusion (Penicillin zone-edge test)	Nitrocefin-based test
Medium	MHA	NA
Antimicrobial Concentration	10 units penicillin disk	NA
Inoculum	Standard disk diffusion procedure	Induced growth (ie, growth taken from the zone margin surrounding a penicillin or cefoxitin disk test on either MHA or a blood agar plate after 16–18 hours of incubation)
Incubation Conditions	35 ± 2°C; ambient air	Room temperature
Incubation Length	16–18 hours	Up to 1 hour for nitrocefin-based test or follow manufacturer's directions
Results	Sharp zone edge ("cliff") = β-lactamase positive. Fuzzy zone edge ("beach") = β-lactamase negative.	Nitrocefin-based test: conversion from yellow to red/pink = β-lactamase positive.

Table 3D. (Continued)

Screen Test	β-Lactamase Production	
Organism Group	*S. aureus* with penicillin MICs ≤ 0.12 µg/mL or zones ≥ 29 mm[a]	*S. aureus*[a] and CoNS (including *S. lugdunensis*[b]) with penicillin MICs ≤ 0.12 µg/mL or zones ≥ 29 mm
Test Method	Disk diffusion (Penicillin zone-edge test)	Nitrocefin-based test
Further Testing and Reporting	β-lactamase–positive staphylococci are resistant to penicillin, amino-, carboxy-, and ureidopenicillins.	Nitrocefin-based tests can be used for *S. aureus*, but negative results should be confirmed with the penicillin zone-edge test before reporting penicillin as susceptible. β-lactamase–positive staphylococci are resistant to penicillin, amino-, carboxy-, and ureidopenicillins.
QC Recommendations – Routine[c]	*S. aureus* ATCC® 25923 for routine QC of penicillin disk to include examination of zone edge test (fuzzy edge = "beach")	
QC Recommendations – Lot/shipment[d]		*S. aureus* ATCC® 29213 – positive *S. aureus* ATCC® 25923 – negative (or see local regulations and manufacturers' recommendations)
QC Recommendations –Supplemental[e]	***S. aureus* ATCC® 29213 – positive pencillin zone-edge test (sharp edge = "cliff")**	

Abbreviations: AST, antimicrobial susceptibility testing; ATCC, American Type Culture Collection; CoNS, coagulase-negative staphylococci; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 3D. (Continued)

Footnotes

a. The penicillin disk diffusion zone-edge test was shown to be more sensitive than nitrocefin-based tests for detection of β-lactamase production in *S. aureus.* The penicillin zone-edge test is recommended if only one test is used for β-lactamase detection. However, some laboratories may choose to perform a nitrocefin-based test first and, if this test is positive, report the results as positive for β-lactamase (or penicillin resistant). If the nitrocefin test is negative, the penicillin zone-edge test should be performed before reporting the isolate as penicillin susceptible in cases where penicillin may be used for therapy (eg, endocarditis).

References:

Kaase M, Lenga S, Friedrich S, et al. Comparison of phenotypic methods for penicillinase detection in *Staphylococcus aureus*. *Clin Microbiol Infect.* 2008;14(6):614-616.

Gill VJ, Manning CB, and Ingalls CM. Correlation of penicillin minimum inhibitory concentrations and penicillin zone edge appearance with staphylococcal beta-lactamase production. *J Clin Microbiol.* 1981;14(4):437-440.

b. For *S. lugdunensis*, tests for β-lactamase detection are not necessary because isolates producing a β-lactamase will test penicillin resistant (MIC > 0.12 µg/mL and zone diameters < 29 mm). If a laboratory is using a method other than the CLSI disk diffusion or MIC reference method and is unsure if the method can reliably detect penicillin resistance with contemporary isolates of *S. lugdunensis,* the laboratory should perform an induced nitrocefin assay or other CLSI reference method on isolates that test penicillin susceptible before reporting the isolate as penicillin susceptible.

c. QC recommendations – Routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Section 15.7.2.1 in M02 or Section 16.7.2.1 in M07)
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

d. QC recommendations – Lot/shipment

Test positive (resistant) QC strain at minimum with each new lot/shipment of testing materials.

e. QC recommendations – Supplemental

- **Supplemental QC strains can be used to assess a new test, for training personnel, and for competency assessment. It is not necessary to include supplemental QC strains in routine daily or weekly AST QC programs. See Appendix C, footnote g, which describes use of supplemental QC strains.**

Table 3D. (Continued)

Figure 1. A Positive Penicillin Disk Zone-Edge Test for β-Lactamase Detection. The zone edge is sharp or like a “cliff” indicating β-lactamase production.

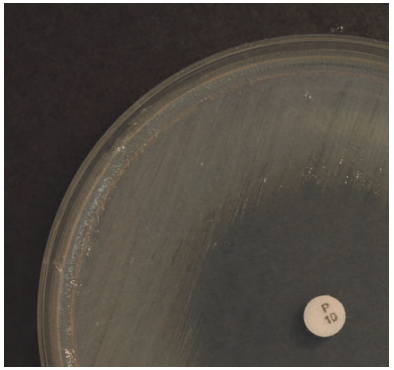

Figure 2. A Negative Penicillin Disk Zone-Edge Test for β-Lactamase Detection. The zone edge is fuzzy or like a “beach” indicating no β-lactamase production.

Table 3E. Screening Tests for Detection of Methicillin Resistance (Oxacillin Resistance) in *Staphylococcus* species

Screen Test	Oxacillin Resistance	*mecA*-Mediated Oxacillin Resistance Using Cefoxitin		
Organism group	*S. aureus*	*S. aureus* and *S. lugdunensis*	CoNS[a]	*S. aureus* and *S. lugdunensis*
Test Method	Agar dilution	Disk diffusion		Broth microdilution
Medium	MHA with 4% NaCl	MHA		CAMHB
Antimicrobial Concentration	6 μg/mL oxacillin	30 μg cefoxitin disk		4 μg/mL cefoxitin
Inoculum	Direct colony suspension to obtain 0.5 McFarland turbidity. Using a 1-μL loop that was dipped in the suspension, spot an area 10–15 mm in diameter. Alternatively, using a swab dipped in the suspension and expressed, spot a similar area or streak an entire quadrant.	Standard disk diffusion procedure		Standard broth microdilution procedure
Incubation Conditions	33 to 35°C; ambient air. (Testing at temperatures above 35°C may not detect MRSA.)	33 to 35°C; ambient air. (Testing at temperatures above 35°C may not detect MRSA)		33 to 35°C; ambient air. (Testing at temperatures above 35°C may not detect MRSA.)
Incubation Length	24 hours; read with transmitted light	16–18 hours	24 hours (may be reported after 18 hours, if resistant)	16–20 hours

Table 3E. (Continued)

Screen Test	Oxacillin Resistance	*mecA*-Mediated Oxacillin Resistance Using Cefoxitin		
Organism group	*S. aureus*	*S. aureus* and *S. lugdunensis*	CoNS[a]	*S. aureus* and *S. lugdunensis*
Test Method	Agar dilution	Disk diffusion		Broth microdilution
Results	Examine carefully with transmitted light for > 1 colony or light film of growth. > 1 colony = oxacillin resistant	≤ 21 mm = *mecA* positive ≥ 22 mm = *mecA* negative	≤ 24 mm = *mecA* positive; ≥ 25 mm = *mecA* negative.	> 4 µg/mL = *mecA* positive ≤ 4 µg/mL = *mecA* negative
Further Testing and Reporting	Oxacillin-resistant staphylococci are resistant to all β-lactam agents; other β-lactam agents should be reported as resistant or should not be reported.	Cefoxitin is used as a surrogate for *mecA*-mediated oxacillin resistance. Isolates that test as *mecA* positive should be reported as oxacillin (not cefoxitin) resistant; other β-lactam agents**, except those with anti-MRSA activity**, should be reported as resistant or should not be reported.		Cefoxitin is used as a surrogate for *mecA*-mediated oxacillin resistance. Isolates that test as *mecA* positive should be reported as oxacillin (not cefoxitin) resistant; other β-lactam agents should be reported as resistant or should not be reported. Because of the rare occurrence of oxacillin resistance mechanisms other than *mecA*, isolates that test as *mecA* negative, but for which the oxacillin MICs are resistant (MIC ≥ 4 µg/mL), should be reported as oxacillin resistant.
QC Recommend-ations – Routine[b]	*S. aureus* ATCC® 29213 – Susceptible (with each test day)	*S. aureus* ATCC® 25923 – *mecA* negative (**cefoxitin** zone 23–29 mm)		*S. aureus* ATCC® 29213 – *mecA* negative (**cefoxitin** MIC 1–4 µg/mL)
QC Recommend-ations – Lot/shipment[c]	*S. aureus* ATCC® 43300 – Resistant	*S. aureus* ATCC® 43300 – *mecA* positive (zone ≤ 21 mm)		*S. aureus* ATCC® 43300 – *mecA* positive (MIC > 4 µg/mL)

Abbreviations: CoNS, coagulase-negative staphylocci; CAMHB, cation-adjusted Mueller-Hinton broth; CoNS, coagulase-negative staphylococci; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRSA, methicillin-resistant *S. aureus;* QC quality control.

Table 3E. (Continued)

Footnotes

a. Except *S. lugdunensis* which is included in the *S. aureus* group.

b. QC recommendations – Routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Section 15.7.2.1 in M02 or Section 16.7.2.1 in M07)
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

c. QC recommendations – Lot/shipment

Test positive (resistant) QC strain at minimum with each new lot/shipment of testing materials.

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Table 3F. Screening Test for Detection of Vancomycin Minimal Inhibitory Concentration (MIC) ≥ 8 µg/mL in *Staphylococcus aureus* and *Enterococcus* species

Screen Test	Vancomycin MIC≥8 µg/mL	
Organism Group	*S. aureus*	*Enterococcus* spp.
Test Method	Agar dilution	Agar dilution
Medium	BHI agar	BHI[a] agar
Antimicrobial Concentration	6 µg/mL vancomycin	6 µg/mL vancomycin
Inoculum	Direct colony suspension to obtain 0.5 McFarland turbidity. Preferably, using a micropipette, spot a 10-µL drop onto agar surface. Alternatively, using a swab dipped in the suspension and the excess liquid expressed, spot an area 10 to 15 mm in diameter or streak a portion of the plate.	Direct colony suspension to obtain 0.5 McFarland turbidity. Preferably, using a micropipette, spot a 10-µL drop onto agar surface. Alternatively, using a swab dipped in the suspension and the excess liquid expressed, spot an area 10 to 15 mm in diameter or streak a portion of the plate.
Incubation Conditions	35± 2°C; ambient air	35 ± 2°C; ambient air
Incubation Length	24 hours	24 hours
Results	Examine carefully with transmitted light for>1 colony or light film of growth. >1 colony=presumptive reduced susceptibility to vancomycin	> 1 colony = Presumptive vancomycin resistance
Further Testing and Reporting	Perform a vancomycin MIC using a validated MIC method to determine vancomycin MICs on *S. aureus* that grow on BHI–vancomycin screening agar. Testing on BHI–vancomycin screening agar does not reliably detect all vancomycin-intermediate *S. aureus* strains. Some strains for which the vancomycin MICs are 4 µg/mL will fail to grow.	Perform vancomycin MIC **on *Enterococcus* spp. that grow on BHI–vancomycin screening agar** and test for motility and pigment production to distinguish species with acquired resistance (eg, *vanA* and *vanB*) from those with intrinsic, intermediate-level resistance to vancomycin (eg, *vanC*), such as *Enterococcus gallinarum* and *Enterococcus casseliflavus*, which often grow on the vancomycin screen plate. In contrast to other enterococci, *E. casseliflavus* and *E. gallinarum* with vancomycin MICs of 8–16 µg/mL (intermediate) differ from vancomycin-resistant enterococcus for infection control purposes.
QC Recommendations – Routine[b]	*Enterococcus faecalis* ATCC® 29212 – Susceptible	*E. faecalis* ATCC® 29212 – Susceptible
QC Recommendations – Lot/shipment[c]	*E. faecalis* ATCC® 51299 – Resistant	*E. faecalis* ATCC® 51299 – Resistant

Abbreviations: BHI, Brain Heart Infusion; MIC, minimal inhibitory concentration; QC, quality control.

Table 3F. (Continued)

Footnotes

a. BHI: even though not as widely available, dextrose phosphate agar and broth have been shown in limited testing to perform comparably.

b. QC recommendations – Routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the screening test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Section 15.7.2.1 in M02 or Section 16.7.2.1 in M07)
- Daily if the screening test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

c. QC recommendations – Lot/shipment

Test positive (resistant) QC strain at minimum with each new lot/shipment of testing materials.

Table 3G. Screening Test for Detection of Inducible Clindamycin Resistance in *Staphylococcus* species, *Streptococcus pneumoniae,* and *Streptococcus* spp. β-Hemolytic Group[a]

Screen Test	Inducible Clindamycin Resistance			
Test Method	**Disk Diffusion (D-zone test)**		**Broth Microdilution**	
Organism Group (applies only to organisms resistant to erythromycin and susceptible or intermediate to clindamycin)	***S. aureus, S. lugdunensis,* and CoNS**	***S. pneumoniae* and β-hemolytic *Streptococcus* spp.**	***S. aureus, S. lugdunensis*, and CoNS[b]**	***S. pneumoniae* and β-hemolytic *Streptococcus* spp.**
Medium	MHA or blood agar purity plate used with MIC tests	MHA supplemented with sheep blood (5% v/v) or TSA supplemented with sheep blood (5% v/v)	CAMHB	CAMHB with LHB (2.5% to 5% v/v)
Antimicrobial Concentration	15-µg erythromycin and 2-µg clindamycin disks spaced 15–26 mm apart	15-µg erythromycin disk and 2-µg clindamycin disk spaced 12 mm apart	4 µg/mL erythromycin and 0.5 µg/mL clindamycin in same well	1 µg/mL erythromycin and 0.5 µg/mL clindamycin in same well
Inoculum	Standard disk diffusion procedure or heavily inoculated area of purity plate	Standard disk diffusion procedure	Standard broth microdilution procedure	
Incubation Conditions	35 ± 2°C; ambient air	35 ± 2°C; 5% CO_2	35 ± 2°C; ambient air	
Incubation Length	16–18 hours	20–24 hours	18–24 hours	20–24 hours
Results	Flattening of the zone of inhibition adjacent to the erythromycin disk (referred to as a D-zone) = inducible clindamycin resistance. Hazy growth within the zone of inhibition around clindamycin = clindamycin resistance, even if no D-zone is apparent.		Any growth = inducible clindamycin resistance. No growth = no inducible clindamycin resistance.	

Table 3G. (Continued)

Screen Test	Inducible Clindamycin Resistance			
Test Method	Disk diffusion (D-zone test)		Broth microdilution	
Organism Group (applies only to organisms resistant to erythromycin and susceptible or intermediate to clindamycin).	***S. aureus, S. lugdunensis*, and CoNS**	***S. pneumoniae* and β-hemolytic *Streptococcus* spp.**	***S. aureus, S. lugdunensis*, and CoNS[b]**	***S. pneumoniae* and β-hemolytic *Streptococcus* spp.**
Further Testing and Reporting	Report isolates with inducible clindamycin resistance as "clindamycin resistant." **The following** comment may be included with the report**:** "This isolate is presumed to be resistant based on detection of inducible clindamycin resistance."			
QC Recommendations – Routine[b]	*S. aureus* ATCC® 25923 for routine QC of erythromycin and clindamycin disks	*S. pneumoniae* ATCC® 49619 for routine QC of **erythromycin and clindamycin** disks; See Appendix C for use of supplemental QC strains.	*S. aureus* ATCC® BAA-976 or *S. aureus* ATCC® 29213 – no growth	*S. pneumoniae* ATCC® 49619 or *S. aureus* ATCC® BAA-976 – no growth
QC Recommendations – Lot/shipment[c]			*S. aureus* ATCC® BAA-977 – growth	
QC Recommendations – Supplemental[d]	***S. aureus* ATCC® BAA-976 (D-zone test negative)** ***S. aureus* ATCC® BAA-977 (D-zone test positive)** **Use of unsupplemented MHA is acceptable for these strains.**		***S. aureus* ATCC® BAA-976 (no growth)** ***S. aureus* ATCC® BAA-977 (growth)**	

Abbreviations: AST, antimicrobial susceptibility testing; ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CDC, Centers for Disease Control and Prevention; CoNS, coagulase-negative staphylococci; MHA, Mueller-Hinton agar; QC, quality control; TSA, tryptic soy agar.

Footnotes

a. **NOTE:** AST of β-hemolytic streptococci need not be performed routinely (see comment [3] in Table 2H-1). When susceptibility testing is clinically indicated, it should include testing for inducible clindamycin resistance. In accordance with 2010 CDC guidance, colonizing isolates of group B streptococci from penicillin-allergic pregnant women should be tested for inducible clindamycin resistance. (See comment [10] in Table 2H-1.)

Table 3G. (Continued)

Reference

Verani JR, McGee L, Schrag SJ; Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease – revised guidelines from CDC, 2010. *MMWR Recomm Rep.* 2010;59(RR-10):1-36.

b. QC recommendations – Routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the screening test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Section 15.7.2.1 in M02 or Section 16.7.2.1 in M07)
- Daily if the screening test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

c. QC recommendations – Lot/shipment

Test positive (resistant) QC strain at minimum with each new lot/shipment of testing materials.

d. QC recommendations – Supplemental

- **Supplemental QC strains can be used to assess a new test, for training personnel, and for competency assessment. It is not necessary to include supplemental QC strains in routine daily or weekly AST QC programs. See Appendix C, footnote g, which describes use of supplemental QC strains.**

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Table 3H. Screening Test for Detection of High-Level Mupirocin Resistance in *Staphylococcus aureus*

Screen Test	High-Level Mupirocin Resistance[a,b]	
Organism Group	*S. aureus*	
Test Method	Disk diffusion	Broth microdilution
Medium	MHA	CAMHB
Antimicrobial Concentration	200-µg mupirocin disk	Single mupirocin 256-µg/mL well
Inoculum	Standard disk diffusion procedure	Standard broth microdilution procedure
Incubation Conditions	35 ± 2°C; ambient air	35 ± 2°C; ambient air
Incubation Length	24 hours; read with transmitted light	24 hours
Results	Examine carefully with transmitted light for light growth within the zone of inhibition. No zone = high-level mupirocin resistance. Any zone = the absence of high-level mupirocin resistance.	For single 256-µg/mL well: Growth = high-level mupirocin resistance. No growth = the absence of high-level mupirocin resistance.
Further Testing and Reporting	Report isolates with no zone as high-level mupirocin resistant. Report any zone of inhibition as the absence of high-level resistance.	Report growth in the 256-µg/mL well as high-level mupirocin resistant. Report no growth in the 256-µg/mL well as the absence of high-level resistance.
QC Recommend-ations – Routine[c]	*S. aureus* ATCC® 25923 (200-µg disk) – *mupA* negative (zone 29–38 mm)	*S. aureus* ATCC® 29213 – *mupA* negative (MIC 0.06–0.5 µg/mL) or *E. faecalis* ATCC® 29212 – *mupA* negative (MIC 16–128 µg/mL)
QC Recommend-ations – Lot/shipment[d]	*S. aureus* ATCC® BAA-1708 – *mupA* positive (no zone)	*S. aureus* ATCC® BAA-1708 – *mupA* positive (growth in 256-µg/mL well)

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Footnotes

a. Although not formally validated by CLSI document M23–based analyses, some studies have linked a lack of response to mupirocin-based decolonization regimens with isolates for which the mupirocin MICs are ≥ 512 µg/mL. Although this document does not provide guidance on interpretive criteria for mupirocin, disk-based testing and the MIC screening test described here identify isolates for which the mupirocin MICs are ≥ 512 µg/mL.

b. References:

Simor AE. Randomized controlled trial of chlorhexidine gluconate for washing intranasal mupirocin, and rifampin and doxycycline versus no treatment for the eradication of methicillin-resistant *Staphylococcus aureus* colonization. *Clin Infect Dis.* 2007;44:178-185.

Harbarth S, Dharan S, Liassine N, Herrault P, Auckenthaler R, Pittet D. Randomized, placebo-controlled, double-blind trial to evaluate the efficacy of mupirocin for eradicating carriage of methicillin-resistant *Staphylococcus aureus. Antimicrob Agents Chemother.* 1999;43:1412-1416.

Walker ES, Vasquez JE, Dula R, Bullock H, Sarubbi FA. Mupirocin-resistant, methicillin-resistant *Staphylococcus aureus;* does mupirocin remain effective? *Infect Control Hosp Epidemiol.* 2003;24:342-346.

Table 3H. (Continued)

c. QC recommendations – Routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the screening test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Section 15.7.2.1 in M02 or Section 16.7.2.1 in M07)
- Daily if the screening test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

d. QC recommendations – Lot/shipment

Test positive (resistant) QC strain at minimum with each new lot/shipment of testing materials.

Table 3I. Screening Test for Detection of High-Level Aminoglycoside Resistance (HLAR) in *Enterococcus* species[a]

Screen Test	Gentamicin HLAR			Streptomycin HLAR		
Test Method	Disk diffusion	Broth microdilution	Agar dilution	Disk diffusion	Broth microdilution	Agar dilution
Medium	MHA	BHI[b] broth	BHI[b] agar	MHA	BHI[b] broth	BHI[b] agar
Antimicrobial Concentration	120-µg gentamicin disk	Gentamicin, 500 µg/mL	Gentamicin, 500 µg/mL	300-µg streptomycin disk	Streptomycin, 1000 µg/mL	Streptomycin, 2000 µg/mL
Inoculum	Standard disk diffusion procedure	Standard broth dilution procedure	10 µL of a 0.5 McFarland suspension spotted onto agar surface	Standard disk diffusion procedure	Standard broth dilution procedure	10 µL of a 0.5 McFarland suspension spotted onto agar surface
Incubation Conditions	35±2°C; ambient air	35±2°C; ambient air	35±2°C; ambient air	35±2°C; ambient air	35±2°C; ambient air	35±2°C; ambient air
Incubation Length	16–18 hours	24 hours	24 hours	16–18 hours	24–48 hours (if susceptible at 24 hours, reincubate)	24–48 hours (if susceptible at 24 hours, reincubate)
Results	6 mm = Resistant; 7–9 mm = Inconclusive; ≥10 mm = Susceptible. MIC correlates: R = >500 µg/mL S = ≤500 µg/mL	Any growth = Resistant	>1 colony = Resistant	6 mm = Resistant; 7–9 mm = Inconclusive; ≥10 mm = Susceptible MIC correlates: R = >1000 µg/mL (broth) and >2000 µg/mL (agar); S = ≤500 µg/mL (broth) and ≤1000 µg/mL (agar)	Any growth = Resistant	>1 colony = Resistant
Further Testing and Reporting	Resistant: is not synergistic with cell wall–active agent (eg, ampicillin, penicillin, and vancomycin). Susceptible: is synergistic with cell wall–active agent (eg, ampicillin, penicillin, and vancomycin) that is also susceptible. If disk diffusion result is inconclusive: perform an agar dilution or broth microdilution test to confirm.					
QC Recommendations – Routine[c]	*E. faecalis* ATCC® 29212: 16–23 mm	*E. faecalis* ATCC® 29212 – Susceptible	*E. faecalis* ATCC® 29212 – Susceptible	*E. faecalis* ATCC® 29212: 14–20 mm	*E. faecalis* ATCC® 29212 – Susceptible	*E. faecalis* ATCC® 29212 – Susceptible
QC Recommendations – Lot/shipment[d]		*E. faecalis* ATCC® 51299 – Resistant	*E. faecalis* ATCC® 51299 – Resistant		*E. faecalis* ATCC® 51299 – Resistant	*E. faecalis* ATCC® 51299 – Resistant

Abbreviations: ATCC, American Type Culture Collection; BHI, Brain Heart Infusion; HLAR, high-level aminoglycoside resistance; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 3I. (Continued)

Footnotes

a. **Other aminoglycosides need not be tested, because their activities against enterococci are not superior to gentamicin and streptomycin.**

b. BHI: even though not as widely available, dextrose phosphate agar and broth have been shown in limited testing to perform comparably.

c. QC recommendations – Routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the screening test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Section 15.7.2.1 in M02 or Section 16.7.2.1 in M07)
- Daily if the screening test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

d. QC recommendations – Lot/shipment

Test positive (resistant) QC strain at minimum with each new lot/shipment of testing materials.

Table 4A. Disk Diffusion: Quality Control Ranges for Nonfastidious Organisms (Unsupplemented Mueller-Hinton Medium)

Antimicrobial Agent	Disk Content	*Escherichia coli* ATCC®[a] 25922	*Staphylococcus aureus* ATCC® 25923	*Pseudomonas aeruginosa* ATCC® 27853	*Escherichia coli* ATCC® 35218[b,c]
Amikacin	30 µg	19–26	20–26	18–26	–
Amoxicillin-clavulanate	20/10 µg	18–24	28–36	–	17–22
Ampicillin	10 µg	16–22	27–35	–	6
Ampicillin-sulbactam	10/10 µg	19–24	29–37	–	13–19
Azithromycin	15 µg	–	21–26	–	–
Azlocillin	75 µg	–	–	24–30	–
Aztreonam	30 µg	28–36	–	23–29	–
Carbenicillin	100 µg	23–29	–	18–24	–
Cefaclor	30 µg	23–27	27–31	–	–
Cefamandole	30 µg	26–32	26–34	–	–
Cefazolin	30 µg	21–27	29–35	–	–
Cefdinir	5 µg	24–28	25–32	–	–
Cefditoren	5 µg	22–28	20–28	–	–
Cefepime	30 µg	31–37	23–29	24–30	–
Cefetamet	10 µg	24–29	–	–	–
Cefixime	5 µg	23–27	–	–	–
Cefmetazole	30 µg	26–32	25–34	–	–
Cefonicid	30 µg	25–29	22–28	–	–
Cefoperazone	75 µg	28–34	24–33	23–29	–
Cefotaxime	30 µg	29–35	25–31	18–22	–
Cefotetan	30 µg	28–34	17–23	–	–
Cefoxitin	30 µg	23–29	23–29	–	–
Cefpodoxime	10 µg	23–28	19–25	–	–
Cefprozil	30 µg	21–27	27–33	–	–
Ceftaroline	30 µg	26–34	26–35	–	–
Ceftaroline-avibactam[d]	30/15 µg	27–34	25–34	17–26	27–35
Ceftazidime	30 µg	25–32	16–20	22–29	–
Ceftazidime-avibactam[d]	30/20 µg	27–35	16–22	25–31	28–35
Ceftibuten	30 µg	27–35	–	–	–
Ceftizoxime	30 µg	30–36	27–35	12–17	–
Ceftobiprole	30 µg	30–36	26–34	24–30	–
Ceftolozane-tazobactam[e]	**30/10 µg**	**24–32**	**10–18**	**25–31**	**25–31**
Ceftriaxone	30 µg	29–35	22–28	17–23	–
Cefuroxime	30 µg	20–26	27–35	–	–
Cephalothin	30 µg	15–21	29–37	–	–
Chloramphenicol	30 µg	21–27	19–26	–	–
Cinoxacin	100 µg	26–32	–	–	–
Ciprofloxacin	5 µg	30–40	22–30	25–33	–
Clarithromycin	15 µg	–	26–32	–	–
Clinafloxacin	5 µg	31–40	28–37	27–35	–
Clindamycin[f]	2 µg	–	24–30	–	–
Colistin	10 µg	11–17	–	11–17	–
Dirithromycin	15 µg	–	18–26	–	–
Doripenem	10 µg	27–35	33–42	28–35	–
Doxycycline	30 µg	18–24	23–29	–	–
Enoxacin	10 µg	28–36	22–28	22–28	–
Eravacycline	**20 µg**	**16–23**	**19–26**	**–**	**–**
Ertapenem	10 µg	29–36	24–31	13–21	–
Erythromycin[f]	15 µg	–	22–30	–	–
Faropenem	5 µg	20–26	27–34	–	–
Fleroxacin	5 µg	28–34	21–27	12–20	–
Fosfomycin[g]	200 µg	22–30	25–33	–	–
Fusidic acid	10 µg	–	24–32	–	–
Garenoxacin	5 µg	28–35	30–36	19–25	–
Gatifloxacin	5 µg	30–37	27–33	20–28	–
Gemifloxacin	5 µg	29–36	27–33	19–25	–
Gentamicin[h]	10 µg	19–26	19–27	17–23	–
Grepafloxacin	5 µg	28–36	26–31	20–27	–
Iclaprim	5 µg	14–22	25–33	–	–
Imipenem	10 µg	26–32	–	20–28	–
Kanamycin	30 µg	17–25	19–26	–	–
Levofloxacin	5 µg	29–37	25–30	19–26	–
Linezolid	30 µg	–	25–32	–	–
Linopristin-flopristin	10 µg	–	25–31	–	–
Lomefloxacin	10 µg	27–33	23–29	22–28	–

Table 4A. (Continued)

Antimicrobial Agent	Disk Content	*Escherichia coli* ATCC® 25922	*Staphylococcus aureus* ATCC® 25923	*Pseudomonas aeruginosa* ATCC® 27853	*Escherichia coli* ATCC® 35218[b,c]
Loracarbef	30 μg	23–29	23–31	–	–
Mecillinam	10 μg	24–30	–	–	–
Meropenem	10 μg	28–34	29–37	27–33	–
Methicillin	5 μg	–	17–22	–	–
Mezlocillin	75 μg	23–29	–	19–25	–
Minocycline	30 μg	19–25	25–30	–	–
Moxalactam	30 μg	28–35	18–24	17–25	–
Moxifloxacin	5 μg	28–35	28–35	17–25	–
Nafcillin	1 μg	–	16–22	–	–
Nalidixic acid	30 μg	22–28	–	–	–
Netilmicin	30 μg	22–30	22–31	17–23	–
Nitrofurantoin	300 μg	20–25	18–22	–	–
Norfloxacin	10 μg	28–35	17–28	22–29	–
Ofloxacin	5 μg	29–33	24–28	17–21	–
Omadacycline	30 μg	22–28	22–30	–	–
Oxacillin	1 μg	–	18–24	–	–
Penicillin	10 units	–	26–37	–	–
Piperacillin	100 μg	24–30	–	25–33	12–18
Piperacillin-tazobactam	100/10 μg	24–30	27–36	25–33	24–30
Plazomicin	30 μg	21–27	19–25	15–21	–
Polymyxin B	300 units	13–19	–	14–18	–
Quinupristin-dalfopristin	15 μg	–	21–28	–	–
Razupenem	10 μg	21–26	–[k]	–	–
Rifampin	5 μg	8–10	26–34	–	–
Solithromycin	15 μg	–	22–30	–	–
Sparfloxacin	5 μg	30–38	27–33	21–29	–
Streptomycin[h]	10 μg	12–20	14–22	–	–
Sulfisoxazole[j]	250 μg or 300 μg	15–23	24–34	–	–
Tedizolid	20 μg	–	22–29	–	–
Teicoplanin	30 μg	–	15–21	–	–
Telavancin	30 μg	–	16–20	–	–
Telithromycin	15 μg	–	24–30	–	–
Tetracycline	30 μg	18–25	24–30	–	–
Ticarcillin	75 μg	24–30	–	21–27	6
Ticarcillin-clavulanate	75/10 μg	24–30	29–37	20–28	21–25
Tigecycline	15 μg	20–27	20–25	9–13	–
Tobramycin	10 μg	18–26	19–29	20–26	–
Trimethoprim[j]	5 μg	21–28	19–26	–	–
Trimethoprim-sulfamethoxazole[j]	1.25/23.75 μg	23–29	24–32	–	–
Trospectomycin	30 μg	10–16	15–20	–	–
Trovafloxacin	10 μg	29–36	29–35	21–27	–
Ulifloxacin (prulifloxacin)[i]	5 μg	32–38	20–26	27–33	–
Vancomycin	30 μg	–	17–21	–	–

Abbreviations: AST, antimicrobial susceptibility testing; ATCC, American Type Culture Collection; MHA, Mueller-Hinton agar; QC, quality control.

NOTE: Information in boldface type is new or modified since the previous edition.

Footnotes

a. ATCC is a registered trademark of the American Type Culture Collection.

b. QC strain recommended when testing β-lactam/β-lactamase inhibitors.

c. This strain may lose its plasmid and develop susceptibility to β-lactam antimicrobial agents after repeated transfers onto culture media. Minimize by removing new culture from storage at least monthly or whenever the strain begins to show increased zone diameters to ampicillin, piperacillin, or ticarcillin; refer to M02-A11, Section 15.4.

d. QC limits for *K. pneumoniae* ATCC® 700603 with ceftaroline-avibactam and ceftazidime-avibactam is 21–27 mm. This strain is considered supplemental QC only and is not required as routine user QC testing.

Table 4A. (Continued)

e. QC limits for *K. pneumoniae* ATCC® 700603 with ceftolozane-tazobactam are 17–25 mm. This strain is considered supplemental QC only and is not required as routine user QC testing.

f. When disk approximation tests are performed with erythromycin and clindamycin, *S. aureus* ATCC® BAA-977 (containing inducible *ermA*-mediated resistance) and *S. aureus* ATCC® BAA-976 (containing *msrA*-mediated macrolide-only efflux) are recommended as supplemental QC strains (eg, for training, competency assessment, or test evaluation). *S. aureus* ATCC® BAA-977 should demonstrate inducible clindamycin resistance (ie, a positive D-zone test), whereas *S. aureus* ATCC® BAA-976 should not demonstrate inducible clindamycin resistance. *S. aureus* ATCC® 25923 should be used for routine QC (eg, weekly or daily) of erythromycin and clindamycin disks using standard MHA.

g. The 200-μg fosfomycin disk contains 50 μg of glucose-6-phosphate.

h. For control limits of gentamicin 120-μg and streptomycin 300-μg disks, use *E. faecalis* ATCC® 29212 (gentamicin: 16–23 mm; streptomycin: 14–20 mm).

i. Ulifloxacin is the active metabolite of the prodrug prulifloxacin. Only ulifloxacin should be used for AST.

j. These agents can be affected by excess levels of thymidine and thymine. See M02-A11, Section 7.1.3 for guidance, should a problem with QC occur.

k. Razupenem tested with *S. aureus* ATCC® 25923 can often produce the double or target zone phenomenon. For accurate QC results, use *S. aureus* ATCC® 29213 (no double zones) with acceptable limit 33–39 mm.

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Table 4B. Disk Diffusion: Quality Control Ranges for Fastidious Organisms

Antimicrobial Agent	Disk Content	*Haemophilus influenzae* ATCC® 49247	*Haemophilus influenzae* ATCC® 49766	*Neisseria gonorrhoeae* ATCC® 49226	*Streptococcus pneumoniae* ATCC® 49619[a]
Amoxicillin-clavulanate[b]	20/10 μg	15–23	–	–	–
Ampicillin	10 μg	13–21	–	–	30–36
Ampicillin-sulbactam	10/10 μg	14–22	–	–	–
Azithromycin	15 μg	13–21	–	–	19–25
Aztreonam	30 μg	30–38	–	–	–
Cefaclor	30 μg	–	25–31	–	24–32
Cefdinir	5 μg	–	24–31	40–49	26–31
Cefditoren	5 μg	25–34	–	–	27–35
Cefepime	30 μg	25–31	–	37–46	28–35
Cefetamet	10 μg	23–28	–	35–43	–
Cefixime	5 μg	25–33	–	37–45	16–23
Cefmetazole	30 μg	16–21	–	31–36	–
Cefonicid	30 μg	–	30–38	–	–
Cefotaxime	30 μg	31–39	–	38–48	31–39
Cefotetan	30 μg	–	–	30–36	–
Cefoxitin	30 μg	–	–	33–41	–
Cefpodoxime	10 μg	25–31	–	35–43	28–34
Cefprozil	30 μg	–	20–27	–	25–32
Ceftaroline	30 μg	29–39	–	–	31–41
Ceftaroline-avibactam[c]	30/15 μg	30–38	–	–	–
Ceftazidime	30 μg	27–35	–	35–43	–
Ceftazidime-avibactam[c]	30/20 μg	28–34	–	–	**23–31**
Ceftibuten	30 μg	29–36	–	–	–
Ceftizoxime	30 μg	29–39	–	42–51	28–34
Ceftobiprole[d]	30 μg	28–36	30–38	–	33–39
Ceftolozane-tazobactam[c]	30/10 μg	**23–29**	–	–	21–29
Ceftriaxone	30 μg	31–39	–	39–51	30–35
Cefuroxime	30 μg	–	28–36	33–41	–
Cephalothin	30 μg	–	–	–	26–32
Chloramphenicol	30 μg	31–40	–	–	23–27
Ciprofloxacin	5 μg	34–42	–	48–58	–
Clarithromycin	15 μg	11–17	–	–	25–31
Clinafloxacin	5 μg	34–43	–	–	27–34
Clindamycin	2 μg	–	–	–	19–25
Dirithromycin	15 μg	–	–	–	18–25
Doripenem	10 μg	21–31	–	–	30–38
Doxycycline	30 μg	–	–	–	25–34
Enoxacin	10 μg	–	–	43–51	–
Eravacycline	**20 μg**	**–**	**–**	**–**	**23–30**
Ertapenem[d]	10 μg	20–28	27–33	–	28–35
Erythromycin	15 μg	–	–	–	25–30
Faropenem	5 μg	15–22	–	–	27–35
Fleroxacin	5 μg	30–38	–	43–51	–
Fusidic acid	10 μg	–	–	–	9–16
Garenoxacin	5 μg	33–41	–	–	26–33
Gatifloxacin	5 μg	33–41	–	45–56	24–31
Gemifloxacin	5 μg	30–37	–	–	28–34
Grepafloxacin	5 μg	32–39	–	44–52	21–28
Iclaprim	5 μg	24–33	–	–	21–29
Imipenem	10 μg	21–29	–	–	–
Levofloxacin	5 μg	32–40	–	–	20–25
Linezolid	30 μg	–	–	–	25–34
Linopristin-flopristin	10 μg	25–31	–	–	22–28
Lomefloxacin	10 μg	33–41	–	45–54	–
Loracarbef	30 μg	–	26–32	–	22–28
Meropenem	10 μg	20–28	–	–	28–35
Moxifloxacin	5 μg	31–39	–	–	25–31
Nitrofurantoin	300 μg	–	–	–	23–29
Norfloxacin	10 μg	–	–	–	15–21
Ofloxacin	5 μg	31–40	–	43–51	16–21
Omadacycline	30 μg	21–29	–	–	24–32
Oxacillin	1 μg	–	–	–	≤12[e]
Penicillin	10 units	–	–	26–34	24–30
Piperacillin-tazobactam	100/10 μg	33–38	–	–	–
Quinupristin-dalfopristin	15 μg	15–21	–	–	19–24
Razupenem	10 μg	24–30	–	–	29–36
Rifampin	5 μg	22–30	–	–	25–30

Table 4B. (Continued)

Antimicrobial Agent	Disk Content	*Haemophilus influenzae* ATCC® 49247	*Haemophilus influenzae* ATCC® 49766	*Neisseria gonorrhoeae* ATCC® 49226	*Streptococcus pneumoniae* ATCC® 49619[a]
Solithromycin	15 μg	16–23	–	–	25–33
Sparfloxacin	5 μg	32–40	–	43–51	21–27
Spectinomycin	100 μg	–	–	23–29	–
Tedizolid	20 μg	–	–	–	24–30
Telavancin	30 μg	–	–	–	17–24
Telithromycin	15 μg	17–23	–	–	27–33
Tetracycline	30 μg	14–22	–	30–42	27–31
Tigecycline	15 μg	23–31	–	30–40	23–29
Trimethoprim-sulfamethoxazole	1.25/23.75 μg	24–32	–	–	20–28
Trospectomycin	30 μg	22–29	–	28–35	–
Trovafloxacin	10 μg	32–39	–	42–55	25–32
Vancomycin	30 μg	–	–	–	20–27

Disk Diffusion Testing Conditions for Clinical Isolates and Performance of QC

Organism	*Haemophilus influenzae*	*Neisseria gonorrhoeae*	Streptococci and *Neisseria meningitidis*
Medium	HTM	GC agar base and 1% defined growth supplement. The use of a cysteine-free growth supplement is not required for disk diffusion testing.	MHA supplemented with 5% defibrinated sheep blood
Inoculum	Direct colony suspension	Direct colony suspension	Direct colony suspension
Incubation characteristics	5% CO_2; 16–18 hours; 35°C	5% CO_2; 20–24 hours; 35°C	5% CO_2; 20–24 hours; 35°C

Abbreviations: ATCC, American Type Culture Collection; HTM, *Haemophilus* Test Medium; MHA, Mueller-Hinton agar; QC, quality control.

NOTE: Information in boldface type is new or modified since the previous edition.

Footnotes

a. Despite the lack of reliable disk diffusion interpretive criteria for *S. pneumoniae* with certain β-lactams, *Streptococcus pneumoniae* ATCC® 49619 is the strain designated for QC of all disk diffusion tests with all *Streptococcus* spp.

b. When testing *Haemophilus* on HTM incubated in ambient air, the acceptable QC limits for *E. coli* ATCC® 35218 are 17 to 22 mm for amoxicillin-clavulanate.

c. QC limits for *E. coli* ATCC® 35218 in HTM: ceftaroline-avibactam 26 to 34 mm; ceftazidime-avibactam 27 to 34 mm; **ceftolozane-tazobactam 25 to 31 mm.**

d. Either *H. influenzae* ATCC® 49247 or 49766 may be used for routine QC testing.

e. Deterioration in oxacillin disk content is best assessed with QC organism *S. aureus* ATCC® 25923, with an acceptable zone diameter of 18 to 24 mm.

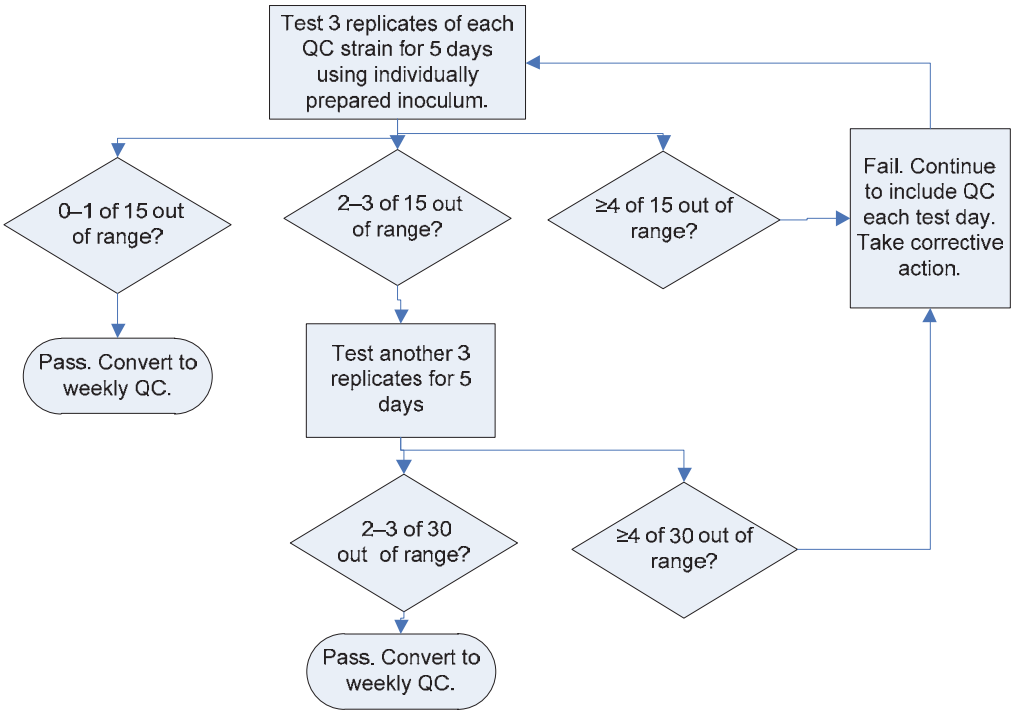
Table 4C. Disk Diffusion: Reference Guide to Quality Control Frequency

Conversion From Daily to Weekly QC

Routine QC is performed each day the test is performed unless an alternative QC plan (QCP) has been established (see CLSI document EP23™).[1] M02-A11, Section 15.7 describes a QCP using a 20- or 30-day plan that, if successfully completed, allows a user to convert from daily to weekly QC. A new alternative QCP using a two-phase, 15-replicate (3 × 5 day) plan is described as follows:

- Test 3 replicates using individual inoculum preparations of the appropriate QC strains for 5 consecutive test days.
- Evaluate each QC strain/antimicrobial agent combination separately using acceptance criteria and following recommended actions as described in the flow diagram below.
- Upon successful completion of the QCP, the laboratory can convert from daily to weekly QC testing. If unsuccessful, investigate, take corrective action as appropriate, and continue daily QC testing until either the 20- or 30-day plan or 15-replicate (3 × 5 day) plan is successfully completed. At that time weekly QC testing can be initiated.

15-Replicate (3 × 5 day) Plan Flow Chart:



For background information that supports the 3 × 5 day plan, refer to the CLSI AST Subcommittee webpage at www.clsi.org for Statisticians' Summary for Alternative QC Frequency Testing Proposal.

Table 4C. (Continued)

15-Replicate (3 × 5 day) Plan: Acceptance Criteria and Recommended Action*

Number Out of Range With Initial Testing (based on 15 replicates)	Conclusion From Initial Testing (based on 15 replicates)	Number Out of Range After Repeat Testing (based on all 30 replicates)	Conclusion After Repeat Testing
0–1	QCP successful. Convert to weekly QC testing.	NA	NA
2–3	Test another 3 replicates for 5 days.	2–3	QCP successful. Can convert to weekly QC testing.
4 or greater	QCP fails. Investigate and take corrective action as appropriate. Continue QC each test day.	4 or greater	QCP fails. Investigate and take corrective action as appropriate. Continue QC each test day.

Abbreviations: NA, not applicable; QC, quality control; QCP, quality control plan.
* Assess each QC strain/antimicrobial agent combination separately.

Test Modifications

This table summarizes the suggested QC frequency when modifications are made to antimicrobial susceptibility test systems. It applies only to antimicrobial agents for which satisfactory results have been obtained with either the 15-replicate (3 × 5 day) plan or 20 or 30 consecutive test day plan.[a] Otherwise QC is required each test day.

	Required QC Frequency[a]			
Test Modification	1 Day	5 Days	15-Replicate Plan or 20- or 30-day Plan	Comments
Disks				
Use new shipment or lot number.	X			
Use new manufacturer.	X			
Addition of new antimicrobial agent to existing system.			X	
Media (prepared agar plates)				
Use new shipment or lot number.	X			
Use new manufacturer.		X		
Inoculum Preparation				
Convert inoculum preparation/ standardization to use of a device that has its own QC protocol.		X		Example: Convert from visual adjustment of turbidity to use of a photometric device for which a QC procedure is provided.
Convert inoculum preparation/ standardization to a method that depends on user technique.			X	Example: Convert from visual adjustment of turbidity to another method that is not based on a photometric device.
Measuring Zones				
Change method of measuring zones.			X	Example: Convert from manual zone measurements to automated zone reader. In addition, perform in-house verification studies.

Table 4C. (Continued)

Test Modification	Required QC Frequency[a] 1 Day	5 Days	15-Replicate Plan or 20- or 30-day Plan	Comments
Instrument/Software (eg, automated zone reader)				
Software update that affects AST results		X		Monitoring all drugs, not just those implicated in software modification
Repair of instrument that affects AST results	X			Depending on extent of repair (eg, critical component such as the photographic device), additional testing may be appropriate (eg, five days).

Abbreviations: AST, antimicrobial susceptibility testing; QC, quality control.

NOTE 1: QC can be performed before or concurrent with testing patient isolates. Patient results can be reported for that day if QC results are within the acceptable limits.

NOTE 2: Manufacturers of commercial or in-house prepared tests should follow their own internal procedures and applicable regulations.

NOTE 3: For troubleshooting out-of-range results, refer to M02-A11, Section 15.8 and M100 Table 4D. Additional information is available in M100 Appendix C, Quality Control Strains for Antimicrobial Susceptibility Tests (eg, QC organism characteristics, QC testing recommendations).

NOTE 4: Broth, saline, and/or water used to prepare an inoculum does not require routine QC.

Footnote

a. M02 will be updated during its next scheduled revision to include both the 15-replicate (3 × 5 day) plan and the 20- or 30-day plan as acceptable QCPs.

Reference

[1] CLSI. *Laboratory Quality Control Based on Risk Management; Approved Guideline.* CLSI document EP23-A™. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.

Definition

quality control plan (QCP) – a document that describes the practices, resources, and sequences of specified activities to control the quality of a particular measuring system or test process to ensure requirements for its intended purpose are met.

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Table 4D. Disk Diffusion: Troubleshooting Guide

This table provides guidance for troubleshooting and corrective action for out-of-range QC, primarily using antimicrobial susceptibility tests with Mueller-Hinton agar (MHA). Refer to M02-A11 (disk diffusion), Section 15, Quality Control and Quality Assurance Procedures for additional information. Out-of-range QC tests should first be repeated. If the issue is unresolved, this troubleshooting guide provides additional suggestions for troubleshooting out-of-range QC results. In addition, if unresolved, manufacturers should be notified of potential product problems.

General Comments

(1) QC organism maintenance: avoid repeated subcultures. Retrieve new QC strain from stock. If using lyophilized strains, follow the maintenance recommendations of the manufacturer. Store *E. coli* ATCC® 35218 and *K. pneumoniae* ATCC® 700603 stock cultures at −60°C or below and prepare working stock cultures weekly.

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Action
Aminoglycosides	Any	Zone too small	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Aminoglycosides	Any	Zone too large	pH of media too high	Acceptable pH range = 7.2–7.4
Aminoglycosides	*P. aeruginosa* ATCC® 27853	Zone too small	Ca++ and/or Mg++ content too high	Use alternative lot of media.
Aminoglycosides	*P. aeruginosa* ATCC® 27853	Zone too large	Ca++ and/or Mg++ content too low	Use alternative lot of media.
Amoxicillin-clavulanate	*E. coli* ATCC® 35218	Zone too small	Clavulanate is labile. Disk has lost potency.	Use alternative lot of disks. Check storage conditions and package integrity.
Ampicillin	*E. coli* ATCC® 35218	Zone too large (should be no zone—resistant)	Spontaneous loss of the plasmid encoding the β-lactamase	See general comment (1) on QC organism maintenance.
β-Lactam group	Any	Zone initially acceptable, but decreases and possibly out of range over time	Disk has lost potency.	Use alternative lot of disks. Check storage conditions and package integrity. Imipenem, clavulanate, and cefaclor are especially labile.
Aztreonam Cefotaxime Cefpodoxime Ceftazidime Ceftriaxone	*K. pneumoniae* ATCC® 700603	Zone too large	Spontaneous loss of the plasmid encoding the β-lactamase	See general comment (1) on QC organism maintenance.
Cefotaxime-clavulanate Ceftazidime-clavulanate	*K. pneumoniae* ATCC® 700603	Negative ESBL confirmatory test	Spontaneous loss of the plasmid encoding the β-lactamase	See general comment (1) on QC organism maintenance.
Penicillins	Any	Zone too large	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Penicillins	Any	Zone too small	pH of media too high	Acceptable pH range = 7.2–7.4
Carbenicillin	*P. aeruginosa* ATCC® 27853	Zone too small	QC strain develops resistance after repeated subculture.	See general comment (1) on QC organism maintenance.
Ticarcillin-clavulanate	*E. coli* ATCC® 35218	Zone too small	Clavulanate is labile. Disk has lost potency.	Use alternative lot of disks. Check storage conditions and package integrity.
Clindamycin	*S. aureus* ATCC® 25923	Zone too small	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Clindamycin	*S. aureus* ATCC® 25923	Zone too large	pH of media too high	Acceptable pH range = 7.2–7.4
Macrolides	*S. aureus* ATCC® 25923	Zone too small	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Macrolides	*S. aureus* ATCC® 25923	Zone too large	pH of media too high	Acceptable pH range = 7.2–7.4

Table 4D. (Continued)

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Action
Quinolones	Any	Zone too small	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Quinolones	Any	Zone too large	pH of media too high	Acceptable pH range = 7.2–7.4
Tetracyclines	Any	Zone too large	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Tetracyclines	Any	Zone too small	pH of media too high	Acceptable pH range = 7.2–7.4
Tetracyclines	Any	Zone too small	Ca++ and/or Mg++ content too high	Use alternative lot of media.
Tetracyclines	Any	Zone too large	Ca++ and/or Mg++ content too low	Use alternative lot of media.
Sulfonamides Trimethoprim Trimethoprim-sulfamethoxazole	*E. faecalis* ATCC® 29212	Zone ≤ 20 mm	Media too high in thymidine content	Use alternative lot of media.
Various	Any	Many zones too large	Inoculum too light Error in inoculum preparation Media depth too thin MHA nutritionally unacceptable	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Use agar with depth approximately 4 mm. Recheck alternate lots of MHA.
Various	Any	Many zones too small	Inoculum too heavy Error in inoculum preparation Media depth too thick MHA nutritionally unacceptable	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Use agar with depth approximately 4 mm. Recheck alternate lots of MHA.
Various	Any	One or more zones too small or too large	Measurement error Transcription error Random defective disk Disk not pressed firmly against agar	Recheck readings for measurement or transcription errors. Retest. If retest results are out of range and no errors are detected, initiate corrective action.
Various	*S. pneumoniae* ATCC® 49619	Zones too large. Lawn of growth scanty.	Inoculum source plate too old and contains too many nonviable cells. Plate used to prepare inoculum should be 18–20 hours.	Subculture QC strain and repeat QC test or retrieve new QC strain from stock.
Various	Any	One QC strain is out of range, but other QC organism(s) are in range with the same antimicrobial agent.	One QC organism may be a better indicator of a QC problem.	Retest this strain to confirm reproducibility of acceptable results. Evaluate with alternative strains with known MICs. Initiate corrective action with problem QC strain/antimicrobial agents.
Various	Any	Two QC strains are out of range with the same antimicrobial agent.	Indicates a problem with the disk	Use alternative lot of disks. Check storage conditions and package integrity.
Various	Any	Zones overlap.	Too many disks per plate	Place no more than 12 disks on a 150-mm plate and 5 disks on a 100-mm plate; for some fastidious bacteria that produce large zones, use fewer.

Abbreviations: ATCC, American Type Culture Collection; ESBL, extended-spectrum β-lactamase; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Table 5A. MIC: Quality Control Ranges for Nonfastidious Organisms (Unsupplemented Mueller-Hinton Medium [Cation-Adjusted if Broth])

Antimicrobial Agent	*Staphylococcus aureus* ATCC®[a] 29213	*Enterococcus faecalis* ATCC® 29212	*Escherichia coli* ATCC® 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Escherichia coli* ATCC® 35218[b,c]
Amikacin	1–4	64–256	0.5–4	1–4	–
Amoxicillin-clavulanate	0.12/0.06–0.5/0.25	0.25/0.12–1.0/0.5	2/1–8/4	–	4/2–16/8
Ampicillin	0.5–2	0.5–2	2–8	–	> 32
Ampicillin-sulbactam	–	–	2/1–8/4	–	8/4–32/16
Azithromycin	0.5–2	–	–	–	–
Azlocillin	2–8	1–4	8–32	2–8	–
Aztreonam	–	–	0.06–0.25	2–8	**0.03–0.12**
Aztreonam-avibactam	**–**	**–**	**0.03/4–0.12/4**	**2/4–8/4**	**0.015/4–0.06/4**
Besifloxacin	0.015–0.06	0.06–0.25	0.06–0.25	1–4	–
Biapenem	**0.03–0.12**	**–**	**0.03–0.12**	**0.5–2**	**0.03–0.12**
Carbenicillin	2–8	16–64	4–16	16–64	–
Cefaclor	1–4	–	1–4	–	–
Cefamandole	0.25–1	–	0.25–1	–	–
Cefazolin	0.25–1	–	1–4	–	–
Cefdinir	0.12–0.5	–	0.12–0.5	–	–
Cefditoren	0.25–2	–	0.12–1	–	–
Cefepime	1–4	–	0.015–0.12	0.5–4	–
Cefetamet	–	–	0.25–1	–	–
Cefixime	8–32	–	0.25–1	–	–
Cefmetazole	0.5–2	–	0.25–1	> 32	–
Cefonicid	1–4	–	0.25–1	–	–
Cefoperazone	1–4	–	0.12–0.5	2–8	–
Cefotaxime	1–4	–	0.03–0.12	8–32	–
Cefotetan	4–16	–	0.06–0.25	–	–
Cefoxitin	1–4	–	2–8	–	–
Cefpodoxime	1–8	–	0.25–1	–	–
Cefprozil	0.25–1	–	1–4	–	–
Ceftaroline	0.12–0.5	0.25–2[d]	0.03–0.12	–	–
Ceftaroline-avibactam	0.12/4–0.5/4	–	0.03/4–0.12/4	–	0.015/4–0.06/4[d]
Ceftazidime	4–16	–	0.06–0.5	1–4	–
Ceftazidime-avibactam	4/4–16/4	–	0.06/4–0.5/4	0.5/4–4/4	0.03/4–0.12/4
Ceftibuten	–	–	0.12–0.5	–	–
Ceftizoxime	2–8	–	0.03–0.12	16–64	–
Ceftobiprole	0.12–1	0.06–0.5	0.03–0.12	1–4	–
Ceftolozane-tazobactam	**16/4–64/4**	**–**	**0.12/4–0.5/4**	**0.25/4–1/4**	**0.06/4–0.25/4**
Ceftriaxone	1–8	–	0.03–0.12	8–64	–
Cefuroxime	0.5–2	–	2–8	–	–
Cephalothin	0.12–0.5	–	4–16	–	–
Chloramphenicol	2–16	4–16	2–8	–	–
Cinoxacin	–	–	2–8	–	–
Ciprofloxacin[e]	0.12–0.5	0.25–2	0.004–0.015	0.25–1	–
Clarithromycin	0.12–0.5	–	–	–	–
Clinafloxacin	0.008–0.06	0.03–0.25	0.002–0.015	0.06–0.5	–
Clindamycin[f]	0.06–0.25	4–16	–	–	–
Colistin	–	–	0.25–2	0.5–4	–
Colistin (tested with 0.002% polysorbate 80)	**–**	**–**	**0.03–0.25**	**0.12–0.5**	**–**
Dalbavancin[h]	0.03–0.12	0.03–0.12	–	–	–
Daptomycin[i]	0.12–1	1–4	–	–	–
Dirithromycin	1–4	–	–	–	–
Doripenem	0.015–0.06	1–4	0.015–0.06	0.12–0.5	–
Doxycycline	0.12–0.5	2–8	0.5–2	–	–
Enoxacin	0.5–2	2–16	0.06–0.25	2–8	–
Ertapenem	0.06–0.25	4–16	0.004–0.015	2–8	–
Erythromycin[f]	0.25–1	1–4	–	–	–

Table 5A. (Continued)

Antimicrobial Agent	*Staphylococcus aureus* ATCC®[a] 29213	*Enterococcus faecalis* ATCC® 29212	*Escherichia coli* ATCC® 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Escherichia coli* ATCC® 35218[b,c]
Faropenem	0.03–0.12	–	0.25–1	–	–
Fidaxomicin	2–16	1–4	–	–	–
Finafloxacin	0.03–0.25	0.25–1	0.004–0.03	1–8	–
Fleroxacin	0.25–1	2–8	0.03–0.12	1–4	–
Fosfomycin[j]	0.5–4	32–128	0.5–2	2–8	–
Fusidic acid	0.06–0.25	–	–	–	–
Garenoxacin	0.004–0.03	0.03–0.25	0.004–0.03	0.5–2	–
Gatifloxacin	0.03–0.12	0.12–1.0	0.008–0.03	0.5–2	–
Gemifloxacin	0.008–0.03	0.015–0.12	0.004–0.015	0.25–1	–
Gentamicin[k]	0.12–1	4–16	0.25–1	0.5–2	–
Grepafloxacin	0.03–0.12	0.12–0.5	0.004–0.03	0.25–2.0	–
Iclaprim	0.06–0.25	0.004–0.03	1–4	–	–
Imipenem	0.015–0.06	0.5–2	0.06–0.25	1–4	–
Kanamycin	1–4	16–64	1–4	–	–
Levofloxacin	0.06–0.5	0.25–2	0.008–0.06	0.5–4	–
Linezolid	1–4	1–4	–	–	–
Linopristin-flopristin	0.06–0.25	0.5–2	–	–	–
Lomefloxacin	0.25–2	2–8	0.03–0.12	1–4	–
Loracarbef	0.5–2	–	0.5–2	>8	–
Mecillinam	–	–	0.03–0.25[l]	–	–
Meropenem	0.03–0.12	2–8	0.008–0.06	0.25–1	–
Methicillin	0.5–2	>16	–	–	–
Mezlocillin	1–4	1–4	2–8	8–32	–
Minocycline[e]	0.06–0.5	1–4	0.25–1	–	–
Moxalactam	4–16	–	0.12–0.5	8–32	–
Moxifloxacin	0.015–0.12	0.06–0.5	0.008–0.06	1–8	–
Nafcillin	0.12–0.5	2–8	–	–	–
Nalidixic acid[e]	–	–	1–4	–	–
Netilmicin	≤0.25	4–16	≤0.5–1	0.5–8	–
Nitrofurantoin	8–32	4–16	4–16	–	–
Norfloxacin	0.5–2	2–8	0.03–0.12	1–4	–
Ofloxacin	0.12–1	1–4	0.015–0.12	1–8	–
Omadacycline[g]	0.12–1	0.06–0.5	0.25–2	–	–
Oritavancin[h]	0.015–0.12	0.008–0.03	–	–	–
Oxacillin	0.12–0.5	8–32	–	–	–
Penicillin	0.25–2	1–4	–	–	–
Piperacillin	1–4	1–4	1–4	1–8	>64
Piperacillin-tazobactam	0.25/4–2/4	1/4–4/4	1/4–4/4	1/4–8/4	0.5/4–2/4
Plazomicin	0.25–2	32–128	0.25–2	1–4	–
Polymyxin B	–	–	0.25–2	**0.5–2**	–
Polymyxin B (tested with 0.002% polysorbate 80)	**–**	**–**	**0.03–0.25**	**0.06–0.5**	**–**
Quinupristin-dalfopristin	0.25–1	2–8	–	–	–
Razupenem	0.008–0.03	0.25–1	0.06–0.5	–	–
Rifampin	0.004–0.015	0.5–4	4–16	16–64	–
Solithromycin	0.03–0.12	0.015–0.06	–	–	–
Sparfloxacin	0.03–0.12	0.12–0.5	0.004–0.015	0.5–2	–
Sulfisoxazole[e,n]	32–128	32–128	8–32	–	–
Sulopenem	0.015–0.12	2–8	0.015–0.06	–	–

Table 5A. (Continued)

Antimicrobial Agent	*Staphylococcus aureus* ATCC® 29213	*Enterococcus faecalis* ATCC® 29212	*Escherichia coli* ATCC® 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Escherichia coli* ATCC® 35218[b,c]
Tedizolid	0.25–1	0.25–1	–	–	–
Teicoplanin	0.25–1	0.25–1	–	–	–
Telavancin[h]	**0.03–0.12**	**0.03–0.12**	–	–	–
Telithromycin	0.06–0.25	0.015–0.12	–	–	–
Tetracycline	0.12–1	8–32	0.5–2	8–32	–
Ticarcillin	2–8	16–64	4–16	8–32	>128
Ticarcillin-clavulanate	0.5/2–2/2	16/2–64/2	4/2–16/2	8/2–32/2	8/2–32/2
Tigecycline[g]	0.03–0.25	0.03–0.12	0.03–0.25	–	–
Tobramycin	0.12–1	8–32	0.25–1	0.25–1	–
Trimethoprim[n]	1–4	0.12–0.5	0.5–2	>64	–
Trimethoprim-sulfamethoxazole	≤0.5/9.5	≤0.5/9.5	≤0.5/9.5	8/152–32/608	–
Trospectomycin	2–16	2–8	8–32	–	–
Trovafloxacin	0.008–0.03	0.06–0.25	0.004–0.015	0.25–2	–
Ulifloxacin (prulifloxacin)[m]	–	–	0.004–0.015	0.12–0.5	–
Vancomycin[o]	0.5–2	1–4	–	–	–

Abbreviations: AST, antimicrobial susceptibility testing; ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; HTM, *Haemophilus* Test Medium; LHB, lysed horse blood; MHB, Mueller-Hinton broth; MIC, minimal inhibitory concentration.

Quality Control Ranges for *Klebsiella pneumoniae* ATCC® 700603 as supplemental QC

Antimicrobial Agent	*Klebsiella pneumoniae* ATCC 700603
Aztreonam	**8–64**
Aztreonam-avibactam	**0.06/4–0.5/4**
Biapenem	**0.03–0.12**
Ceftaroline-avibactam	**0.25/4–1/4**
Ceftazidime-avibactam*	**0.25/4–2/4**
Ceftolozane-tazobactam	**0.5/4–2/4**

* *K. pneumoniae* ATCC® 700603 should be tested against ceftazidime-avibactam and ceftazidime alone to confirm the activity of avibactam in the combination and to ensure that the plasmid encoding the β-lactamase has not been lost in this strain. The acceptable range for ceftazidime alone is >16 µg/mL.

NOTE 1: These MICs were obtained in several reference laboratories by dilution methods. If four or fewer concentrations are tested, QC may be more difficult.

NOTE 2: Information in boldface type is new or modified since the previous edition.

Footnotes

a. ATCC is a registered trademark of the American Type Culture Collection.

b. QC strain recommended when testing β-lactam/β-lactamase inhibitors.

c. This strain may lose its plasmid and develop susceptibility to β-lactam antimicrobial agents after repeated transfers onto culture media. Minimize by removing new culture from storage at least monthly or whenever the strain begins to show decreased MICs to ampicillin, piperacillin, or ticarcillin; refer to M07-A9, Section 16.4.

d. Testing this strain with this antimicrobial agent is considered supplemental QC only and is not required as routine user QC testing.

e. QC limits for *E. coli* ATCC® 25922 with ciprofloxacin, nalidixic acid, minocycline, and sulfisoxazole when tested in CAMHB with 2.5% to 5% LHB incubated either in ambient air or 5% CO_2 (when testing *N. meningitidis*) are the same as those listed in Table 5A.

Table 5A. (Continued)

f. When the erythromycin/clindamycin combination well for detection of inducible clindamycin resistance is used, *S. aureus* ATCC® BAA-977 (containing inducible *ermA*-mediated resistance) and *S. aureus* ATCC® 29213 or *S. aureus* ATCC® BAA-976 (containing *msrA*-mediated macrolide-only efflux) are recommended for QC purposes. *S. aureus* ATCC® BAA-977 should demonstrate inducible clindamycin resistance (ie, growth in the well), whereas *S. aureus* ATCC® 29213 and *S. aureus* ATCC® BAA-976 should not demonstrate inducible clindamycin resistance (ie, no growth in the well).

g. For broth microdilution testing of omadacycline and tigecycline, when MIC panels are prepared, the medium must be prepared fresh on the day of use. The medium must be no more than 12 hours old at the time the panels are made; however, the panels may then be frozen for later use.

h. QC ranges reflect MICs obtained when CAMHB is supplemented with 0.002% polysorbate-80.

i. QC ranges reflect MICs obtained when MHB is supplemented with calcium to a final concentration of 50 μg/mL. Agar dilution has not been validated for daptomycin.

j. The approved MIC susceptibility testing method is agar dilution. Agar media should be supplemented with 25 μg/mL of glucose-6-phosphate. Broth dilution should not be performed.

k. For control organisms for gentamicin and streptomycin high-level aminoglycoside screen tests for enterococci, see Table **3I**.

l. This test should be performed by agar dilution only.

m. Ulifloxacin is the active metabolite of the prodrug prulifloxacin. Only ulifloxacin should be used for AST.

n. Very medium-dependent, especially with enterococci.

o. For QC organisms for vancomycin screen test for enterococci, see Table **3F**.

Table 5B. MIC: Quality Control Ranges for Fastidious Organisms (Broth Dilution Methods)

Antimicrobial Agent	*Haemophilus influenzae* ATCC® 49247	*Haemophilus influenzae* ATCC® 49766	*Streptococcus pneumoniae* ATCC® 49619
Amoxicillin[a]	–	–	0.03–0.12
Amoxicillin-clavulanate[a]	2/1–16/8	–	0.03/0.015–0.12/0.06
Ampicillin	2–8	–	0.06–0.25
Ampicillin-sulbactam	2/1–8/4	–	–
Azithromycin	1–4	–	0.06–0.25
Aztreonam	0.12–0.5	–	–
Besifloxacin	0.015–0.06	–	0.03–0.12
Cefaclor	–	1–4	1–4
Cefamandole	–	0.25–1	–
Cefdinir	–	0.12–0.5	0.03–0.25
Cefditoren	0.06–0.25	–	0.015–0.12
Cefepime	0.5–2	–	0.03–0.25
Cefetamet	0.5–2	–	0.5–2
Cefixime	0.12–1	–	–
Cefmetazole	2–16	–	–
Cefonicid	–	0.06–0.25	–
Cefotaxime	0.12–0.5	–	0.03–0.12
Cefotetan	–	–	–
Cefoxitin	–	–	–
Cefpirome	0.25–1	–	–
Cefpodoxime	0.25–1	–	0.03–0.12
Cefprozil	–	1–4	0.25–1
Ceftaroline	0.03–0.12	–	0.008–0.03
Ceftaroline-avibactam	0.015/4–0.12/4	–	–
Ceftazidime	0.12–1	–	–
Ceftazidime-avibactam[b]	0.06/4–0.5/4	0.015/4–0.06/4	0.25/4–2/4
Ceftibuten	0.25–1	–	–
Ceftizoxime	0.06–0.5	–	0.12–0.5
Ceftobiprole[c]	0.12–1	0.016–0.06	0.004–0.03
Ceftolozane-tazobactam	**0.5/4–2/4**	–	0.25/4–1/4
Ceftriaxone	0.06–0.25	–	0.03–0.12
Cefuroxime	–	0.25–1	0.25–1
Cephalothin	–	–	0.5–2
Chloramphenicol	0.25–1	–	2–8
Ciprofloxacin[d]	0.004–0.03	–	–
Clarithromycin	4–16	–	0.03–0.12
Clinafloxacin	0.001–0.008	–	0.03–0.12
Clindamycin	–	–	0.03–0.12
Dalbavancin[f]	–	–	0.008–0.03
Daptomycin[g]	–	–	0.06–0.5
Dirithromycin	8–32	–	0.06–0.25
Doripenem	–	0.06–0.25	0.03–0.12
Doxycycline	–	–	0.015–0.12
Enoxacin	–	–	–
Ertapenem	–	0.015–0.06	0.03–0.25
Erythromycin	–	–	0.03–0.12
Faropenem	–	0.12–0.5	0.03–0.25
Finafloxacin	–	0.002–0.008	0.25–1
Fleroxacin	0.03–0.12	–	–
Fusidic acid	–	–	4–32
Garenoxacin	0.002–0.008	–	0.015–0.06
Gatifloxacin	0.004–0.03	–	0.12–0.5
Gemifloxacin	0.002–0.008	–	0.008–0.03
Gentamicin	–	–	–
Grepafloxacin	0.002–0.015	–	0.06–0.5

Table 5B. (Continued)

Antimicrobial Agent	*Haemophilus influenzae* ATCC® 49247	*Haemophilus influenzae* ATCC® 49766	*Streptococcus pneumoniae* ATCC® 49619
Iclaprim	0.12–1	–	0.03–0.12
Imipenem	–	0.25–1	0.03–0.12
Levofloxacin	0.008–0.03	–	0.5–2
Linezolid	–	–	0.25–2
Linopristin-flopristin	0.25–2	–	0.12–0.5
Lomefloxacin	0.03–0.12	–	–
Loracarbef	–	0.5–2	2–8
Meropenem	–	0.03–0.12	0.06–0.25
Metronidazole	–	–	–
Minocycline[d]	–	–	–
Moxifloxacin	0.008–0.03	–	0.06–0.25
Nalidixic acid[d]	–	–	–
Nitrofurantoin	–	–	4–16
Norfloxacin	–	–	2–8
Ofloxacin	0.015–0.06	–	1–4
Omadacycline[e]	0.5–2	–	0.015–0.12
Oritavancin[f]	–	–	0.001–0.004
Penicillin	–	–	0.25–1
Piperacillin-tazobactam	0.06/4–0.5/4	–	–
Quinupristin-dalfopristin	2–8	–	0.25–1
Razupenem	–	0.008–0.03	0.008–0.06
Rifampin	0.25–1	–	0.015–0.06
Solithromycin	1–4	–	0.004–0.015
Sparfloxacin	0.004–0.015	–	0.12–0.5
Spectinomycin	–	–	–
Sulfisoxazole[d]	–	–	–
Sulopenem	–	0.06–0.25	0.03–0.12
Tedizolid	–	–	0.12–0.5
Telavancin[f]	–	–	0.004–**0.015**
Telithromycin	1–4	–	0.004–0.03
Tetracycline	4–32	–	0.06–0.5
Tigecycline[e]	0.06–0.5	–	0.015–0.12
Trimethoprim-sulfamethoxazole	0.03/0.59–0.25/4.75	–	0.12/2.4–1/19
Trospectomycin	0.5–2	–	1–4
Trovafloxacin	0.004–0.015	–	0.06–0.25
Vancomycin	–	–	0.12–0.5

Table 5B. (Continued)

Testing Conditions for Clinical Isolates and Performance of QC

Organism	*Haemophilus influenzae*	*Streptococcus pneumoniae* and Streptococci	*Neisseria meningitidis*
Medium	Broth dilution: HTM broth	Broth dilution: CAMHB with LHB (2.5% to 5% v/v)	Broth dilution: CAMHB with LHB (2.5% to 5% v/v)
Inoculum	Direct colony suspension	Direct colony suspension	Direct colony suspension
Incubation Characteristics	Ambient air; 20–24 hours; 35°C	Ambient air; 20–24 hours; 35°C	5% CO_2; 20–24 hours; 35°C (for QC with *S. pneumoniae* ATCC® 49619, 5% CO_2 or ambient air, except for azithromycin, ambient air only)

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; HTM, *Haemophilus* Test Medium; LHB, lysed horse blood; MHB, Mueller-Hinton broth; MIC, minimal inhibitory concentration; QC, quality control.

NOTE 1: Information in boldface type is new or modified since the previous edition.

NOTE 2: For four-dilution ranges, results at the extremes of the acceptable ranges should be suspect. Verify validity with data from other control strains.

Footnotes

a. QC limits for *E. coli* ATCC® 35218 when tested on HTM are 4/2 to 16/8 μg/mL for amoxicillin-clavulanate and ≥ 256 μg/mL for amoxicillin; testing amoxicillin may help to determine if the isolate has maintained its ability to produce β-lactamase.

b. QC limits for *K. pneumoniae* ATCC® 700603 with ceftazidime-avibactam when testing in HTM are 0.25/4–1/4 μg/mL. *K. pneumoniae* ATCC® 700603 should be tested against ceftazidime-avibactam and ceftazidime alone to confirm the activity of avibactam in the combination and to ensure that the plasmid encoding the β-lactamase has not been lost in this strain. The acceptable range for ceftazidime alone is > 16 μg/mL.

c. Either *H. influenzae* ATCC® 49247 or 49766 may be used for routine QC testing.

d. QC limits for *E. coli* ATCC® 25922 with ciprofloxacin, nalidixic acid, minocycline, and sulfisoxazole when tested in CAMHB with 2.5% to 5% LHB incubated either in ambient air or 5% CO_2 (when testing *N. meningitidis*) are the same as those listed in Table 5A.

e. For broth microdilution testing of omadacycline and tigecycline, when MIC panels are prepared, the medium must be prepared fresh on the day of use. The medium must be no more than 12 hours old at the time the panels are made; however, the panels may then be frozen for later use.

f. QC ranges reflect MICs obtained when CAMHB is supplemented with 0.002% polysorbate-80.

g. QC ranges reflect MICs obtained when MHB is supplemented with calcium to a final concentration of 50 μg/mL. Agar dilution has not been validated for daptomycin.

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Table 5C. MIC: Quality Control Ranges for *Neisseria gonorrhoeae* (Agar Dilution Method)

Antimicrobial Agent	***Neisseria gonorrhoeae* ATCC® 49226**
Cefdinir	0.008–0.03
Cefepime	0.015–0.06
Cefetamet	0.015–0.25
Cefixime	0.004–0.03
Cefmetazole	0.5–2
Cefotaxime	0.015–0.06
Cefotetan	0.5–2
Cefoxitin	0.5–2
Cefpodoxime	0.03–0.12
Ceftazidime	0.03–0.12
Ceftizoxime	0.008–0.03
Ceftriaxone	0.004–0.015
Cefuroxime	0.25–1
Ciprofloxacin	0.001–0.008
Enoxacin	0.015–0.06
Fleroxacin	0.008–0.03
Gatifloxacin	0.002–0.015
Grepafloxacin	0.004–0.03
Lomefloxacin	0.008–0.03
Moxifloxacin	0.008–0.03
Ofloxacin	0.004–0.015
Penicillin	0.25–1
Sparfloxacin	0.004–0.015
Spectinomycin	8–32
Tetracycline	0.25–1
Trospectomycin	1–4
Trovafloxacin	0.004–0.015

Testing Conditions for Clinical Isolates and Performance of QC

Organism	*Neisseria gonorrhoeae*
Medium	Agar dilution: GC agar base and 1% defined growth supplement. The use of a cysteine-free supplement is required for agar dilution tests with carbapenems and clavulanate. Cysteine-containing defined growth supplements *do not* significantly alter dilution test results with other drugs.
Inoculum	Direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation Characteristics	36±1°C (do not exceed 37°C); 5% CO_2; 20–24 hours

Abbreviations: ATCC American Type Culture Collection; MIC, minimal inhibitory concentration; QC; quality control.

NOTE 1: Information in boldface type is new or modified since the previous edition.

NOTE 2: For four-dilution ranges, results at the extremes of the acceptable ranges should be suspect. Verify validity with data from other control strains.

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Table 5D. MIC: Quality Control Ranges for Anaerobes (Agar Dilution Method)

Antimicrobial Agent	*Bacteroides fragilis* ATCC® 25285	*Bacteroides thetaiotaomicron* ATCC® 29741	*Clostridium difficile* ATCC® 700057	*Eubacterium lentum* ATCC® 43055
Amoxicillin-clavulanate	0.25/0.125–1/0.5	0.5/0.25–2/1	0.25/0.125–1/0.5	—
Ampicillin	16–64	16–64	1–4	—
Ampicillin-sulbactam	0.5/0.25–2/1	0.5/0.25–2/1	0.5/0.25–4/2	0.25/0.125–2/1
Cefmetazole	8–32	32–128	—	4–16
Cefoperazone	32–128	32–128	—	32–128
Cefotaxime	8–32	16–64	—	64–256
Cefotetan	4–16	32–128	—	32–128
Cefoxitin	4–16	8–32	—	4–16
Ceftaroline	4–32	16–128	2–16	8–32
Ceftaroline-avibactam	0.12/4–0.5/4	4/4–16/4	0.5/4–4/4	4/4–16/4
Ceftizoxime	—	4–16	—	16–64
Ceftolozane-tazobactam	**0.12/4–1/4**	**16/4–128/4**	**—**	**—**
Ceftriaxone	32–128	64–256	—	—
Chloramphenicol	2–8	4–16	—	—
Clinafloxacin	0.03–0.125	0.06–0.5	—	0.03–0.125
Clindamycin	0.5–2	2–8	2–8	0.06–0.25
Doripenem	—	—	0.5–4	—
Ertapenem	0.06–0.25	0.25–1	—	0.5–2
Faropenem	0.03–0.25	0.12–1	—	1–4
Fidaxomicin	—	—	0.06–0.25	—
Finafloxacin	0.12–0.5	1–4	1–4	0.12–0.5
Garenoxacin	0.06–0.5	0.25–1	0.5–2	1–4
Imipenem	0.03–0.125	0.125–0.5	—	0.125–0.5
Linezolid	2–8	2–8	1–4	0.5–2
Meropenem	0.03–0.25	0.125–0.5	0.5–4	0.125–1
Metronidazole	0.25–1	0.5–2	0.125–0.5	—
Mezlocillin	16–64	8–32	—	8–32
Moxifloxacin	0.125–0.5	1–4	1–4	0.125–0.5
Nitazoxanide	—	—	0.06–0.5	—
Omadacycline	0.25–2	0.5–4	0.25–2	0.25–2
Penicillin	8–32	8–32	1–4	—
Piperacillin	2–8	8–32	4–16	8–32
Piperacillin-tazobactam	0.125/4–0.5/4	4/4–16/4	4/4–16/4	4/4–16/4
Ramoplanin	—	—	0.125–0.5	—
Razupenem	0.015–0.12	0.06–0.25	0.06–0.25	0.06–0.5
Rifaximin	—	—	0.0039–0.0156	—
Sulopenem	—	0.06–0.5	1–4	0.5–2
Surotomycin[a]	**—**	**—**	**0.12–1**	**2–8**
Tetracycline	0.125–0.5	8–32	—	—
Ticarcillin	16–64	16–64	16–64	16–64
Ticarcillin-clavulanate	—	0.5/2–2/2	16/2–64/2	16/2–64/2
Tigecycline	0.12–1	0.5–2	0.125–1	0.06–0.5
Tinidazole	—	—	0.125–0.5	—
Tizoxanide	—	—	0.06–0.5	—
Vancomycin	—	—	0.5–4	—

Abbreviations: ATCC, American Type Culture Collection; MIC, minimal inhibitory concentration; QC, quality control.

NOTE 1: Information in boldface type is new or modified since the previous edition.

NOTE 2: Values are in micrograms per milliliter (μg/mL) except for penicillin.

Footnote

a. QC ranges reflect MICs obtained when media are supplemented with calcium to a final concentration of 50 μg/mL.

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Table 5E. MIC: Quality Control Ranges for Anaerobes (Broth Microdilution Method)

Antimicrobial Agent	*Bacteroides fragilis* ATCC® 25285	*Bacteroides thetaiotaomicron* ATCC® 29741	*Clostridium difficile* ATCC® 700057	*Eubacterium lentum* ATCC® 43055
Amoxicillin-clavulanate (2:1)	0.25/0.125–1/0.5	0.25/0.125–1/0.5	—	—
Ampicillin-sulbactam (2:1)	0.5/0.25–2/1	0.5/0.25–2/1	—	0.5/0.25–2/1
Cefotetan	1–8	16–128	—	16–64
Cefoxitin	2–8	8–64	—	2–16
Ceftaroline	2–16	8–64	0.5–4	–
Ceftaroline-avibactam	0.06/4–0.5/4	2/4–8/4	0.25/4–1/4	4/4–16/4
Ceftizoxime	—	—	—	8–32
Ceftolozane-tazobactam	**0.12/4–1/4**	**16/4–64/4**	**—**	**—**
Chloramphenicol	4–16	8–32	—	4–16
Clindamycin	0.5–2	2–8	—	0.06–0.25
Doripenem	0.12–0.5	0.12–1	—	—
Doxycycline	—	2–8	—	2–16
Ertapenem	0.06–0.5	0.5–2	—	0.5–4
Faropenem	0.015–0.06	0.12–1	—	0.5–2
Garenoxacin	0.06–0.25	0.25–2	—	0.5–2
Imipenem	0.03–0.25	0.25–1	—	0.25–2
Linezolid	2–8	2–8	—	0.5–2
Meropenem	0.03–0.25	0.06–0.5	—	0.125–1
Metronidazole	0.25–2	0.5–4	—	0.125–0.5
Moxifloxacin	0.12–0.5	1.0–8	—	0.12–0.5
Omadacycline[a]	0.12–1	0.25–1	0.06–0.25	0.06–5
Penicillin	8–32	8–32	—	—
Piperacillin	4–16	8–64	—	8–32
Piperacillin-tazobactam	0.03/4–0.25/4	2/4–16/4	—	8/4–32/4
Razupenem	0.03–0.25	0.12–0.5	0.06–0.5	0.12–0.5
Sulopenem	—	0.03–0.25	0.5–2	0.25–1
Surotomycin[b]	**—**	**—**	**0.12–1**	**1–4**
Ticarcillin-clavulanate	0.06/2–0.5/2	0.5/2–2/2	—	8/2–32/2
Tigecycline[a]	0.06–0.5	0.25–1	0.03–0.12	—

Abbreviations: ATCC, American Type Culture Collection; MIC, minimal inhibitory concentration; QC, quality control.

NOTE 1: Information in boldface type is new or modified since the previous edition.

NOTE 2: For four-dilution ranges, results at the extremes of the acceptable range(s) should be suspect. Verify validity of the antimicrobial concentration with data from other quality control strains.

Footnotes

a. For broth microdilution testing of tigecycline and omadacycline, when MIC panels are prepared, the medium must be prepared fresh on the day of use. The medium must be no greater than 12 hours old at the time the panels are made; however, the panels may then be frozen for later use.

b. QC ranges reflect MICs obtained when broth is supplemented with calcium to a final concentration of 50 μg/mL.

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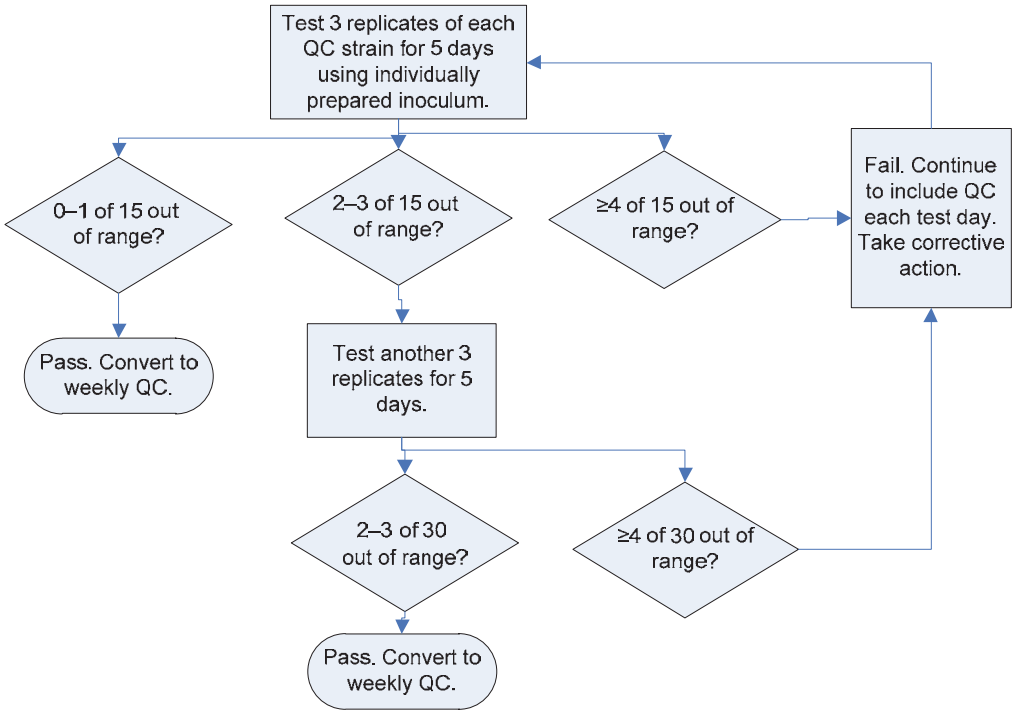
Table 5F. MIC: Reference Guide to Quality Control Frequency

Conversion From Daily to Weekly QC

Routine QC is performed each day the test is performed unless an alternative QC plan (QCP) has been established (see CLSI document EP23[1]). M07-A9, Section 16.7 describes a QCP using a 20- or 30-day plan that, if successfully completed, allows a user to convert from daily to weekly QC. A new alternative QCP using a two-phase, 15-replicate (3 × 5 day) plan is described as follows:

- Test 3 replicates using individual inoculum preparations of the appropriate QC strains for 5 consecutive test days.
- Evaluate each QC strain/antimicrobial agent combination separately using acceptance criteria and following recommended actions as described in the flow diagram below.
- Upon successful completion of the QCP, the laboratory can convert from daily to weekly QC testing. If unsuccessful, investigate, take corrective action as appropriate, and continue daily QC testing until either the 20- or 30-day plan or 15-replicate (3 × 5 day) plan is successfully completed. At that time weekly QC testing can be initiated.

15-Replicate (3 × 5 day) Plan Flow Chart:



For background information that supports the 3 × 5 day plan, refer to the CLSI AST Subcommittee webpage at www.clsi.org for Statisticians' Summary for Alternative QC Frequency Testing Proposal.

Table 5F. (Continued)

15-Replicate (3 × 5 day) Plan: Acceptance Criteria and Recommended Action*

Number Out of Range With Initial Testing (based on 15 replicates)	Conclusion From Initial Testing (based on 15 replicates)	Number Out of Range After Repeat Testing (based on all 30 replicates)	Conclusion After Repeat Testing
0–1	QCP successful. Convert to weekly QC testing.	NA	NA
2–3	Test another 3 replicates for 5 days.	2–3	QCP successful. Can convert to weekly QC testing.
4 or greater	QCP fails. Investigate and take corrective action as appropriate. Continue QC each test day.	4 or greater	QCP fails. Investigate and take corrective action as appropriate. Continue QC each test day.

Abbreviations: NA, not applicable; QC, quality control; QCP, quality control plan.
*Assess each QC strain/antimicrobial agent combination separately.

Test Modifications

This table summarizes the suggested QC frequency when modifications are made to antimicrobial susceptibility test systems. It applies only to antimicrobial agents for which satisfactory results have been obtained with either the 15-replicate (3 × 5 day) plan or 20 or 30 consecutive test day plan.[a] Otherwise QC is required each test day.

	Required QC Frequency[a]			
Test Modification	1 Day	5 Days	15-Replicate Plan or 20- or 30-day Plan	Comments
MIC Tests(s)				
Use new shipment or lot number.	X			
Expand dilution range.	X			Example: Convert from breakpoint to expanded range MIC panels.
Reduce dilution range.	X			Example: Convert from expanded dilution range to breakpoint panels.
Use new method (same company).			X	Examples: Convert from visual to instrument reading of panel. Convert from overnight to rapid MIC test. In addition, perform in-house verification studies.
Use new manufacturer of MIC test.			X	In addition, perform in-house verification studies.
Use new manufacturer of broth or agar.		X		
Addition of new antimicrobial agent to existing system			X	
Inoculum Preparation				
Convert inoculum preparation/ standardization to use of a device that has its own QC protocol.		X		Example: Convert from visual adjustment of turbidity to use of a photometric device for which a QC procedure is provided.
Convert inoculum preparation/ standardization to a method that is dependent on user technique.			X	Example: Convert from visual adjustment of turbidity to another method that is not based on a photometric device.

Table 5F. (Continued)

Test Modification	Required QC Frequency[a] 1 Day	5 Days	15-Replicate Plan or 20- or 30-day Plan	Comments
Instrument/Software				
Software update that affects AST results		X		Monitor all drugs, not just those implicated in software modification.
Repair of instrument that affects AST results	X			Depending on extent of repair (eg, critical component such as the optics), additional testing may be appropriate (eg, five days).

Abbreviations: AST, antimicrobial susceptibility testing; FDA, US Food and Drug Administration; MIC, minimal inhibitory concentration; QC, quality control.

NOTE 1: QC can be performed before or concurrent with testing patient isolates. Patient results can be reported for that day if QC results are within the acceptable limits.

NOTE 2: Manufacturers of commercial or in-house prepared tests should follow their own internal procedures and applicable regulations.

NOTE 3: Acceptable MIC QC limits for FDA-cleared antimicrobial susceptibility tests may differ slightly from acceptable CLSI QC limits. Users of each device should use the manufacturer's procedures and QC limits as indicated in the instructions for use.

NOTE 4: For troubleshooting out-of-range results, refer to M07-A9, Section 16.9 and M100 Table 5G. Additional information is available in M100 Appendix C, Quality Control Strains for Antimicrobial Susceptibility Tests (eg, organism characteristics, QC testing recommendations).

NOTE 5: Broth, saline, and/or water used to prepare an inoculum does not require routine QC.

Footnote

a. M07 will be updated during its next scheduled revision to include both the 15-replicate (3 × 5 day) plan and the 20- or 30-day plan as acceptable QCPs.

Reference

[1] CLSI. *Laboratory Quality Control Based on Risk Management; Approved Guideline.* CLSI document EP23-A™. Wayne, PA: Clinical and Laboratory Standards Institute; 2011.

Definition

quality control plan (QCP) – a document that describes the practices, resources, and sequences of specified activities to control the quality of a particular measuring system or test process to ensure requirements for its intended purpose are met.

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Table 5G. MIC: Troubleshooting Guide

This table provides guidance for troubleshooting and corrective action for out-of-range QC primarily using antimicrobial susceptibility tests with cation-adjusted Mueller-Hinton broth (CAMHB) for broth microdilution. Refer to M07-A9 (MIC), Section 16, Quality Control and Quality Assurance Procedures. Out-of-range QC tests should first be repeated. If the issue is unresolved, this troubleshooting guide provides additional suggestions for troubleshooting out-of-range QC results and unusual clinical isolate results. In addition, if unresolved, manufacturers should be notified of potential product problems.

General Comments

(1) QC organism maintenance: Avoid repeated subcultures. Retrieve new QC strain from stock. If using lyophilized strains, follow the maintenance recommendations of the manufacturer. Store *E. coli* ATCC® 35218 and *K. pneumoniae* ATCC® 700603 stock cultures at −60°C or below and prepare working stock cultures weekly.

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
Aminoglycosides	Any	MIC too high	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Aminoglycosides	Any	MIC too low	pH of media too high	Acceptable pH range = 7.2–7.4
Aminoglycosides	*P. aeruginosa* ATCC® 27853	MIC too high	Ca++ and/or Mg++ content too high	Acceptable range = Ca++ 20–25 mg/L Mg++ 10–12.5 mg/L
Aminoglycosides	*P. aeruginosa* ATCC® 27853	MIC too low	Ca++ and/or Mg++ content too low	Acceptable range = Ca++ 20–25 mg/L Mg++ 10–12.5 mg/L
Amoxicillin-clavulanate	*E. coli* ATCC® 35218	MIC too high	Clavulanate is labile. Antimicrobial agent is degrading.	Use alternative lot. Check storage and package integrity.
β-Lactam group	Any	MIC initially acceptable, but increases possibly out of range over time	Antimicrobial agent is degrading.	Use alternative lot. Check storage and package integrity. Imipenem, cefaclor, and clavulanate are especially labile.
Aztreonam Cefotaxime Cefpodoxime Ceftazidime Ceftriaxone	*K. pneumoniae* ATCC® 700603	MIC too low	Spontaneous loss of the plasmid encoding the β-lactamase.	See general comment (1) on QC organism maintenance.
Cefotaxime-clavulanate Ceftazidime-clavulanate	*K. pneumoniae* ATCC® 700603	Negative ESBL confirmatory test	Spontaneous loss of the plasmid encoding the β-lactamase.	See general comment (1) on QC organism maintenance.
Carbapenems	*P. aeruginosa* ATCC® 27853	MIC too high	Zn++ concentration in media is too high.	Use alternative lot.
Carbapenems	*P. aeruginosa* ATCC® 27853	MIC too high	Antimicrobial agent is degrading.	Use alternative lot. Check storage and package integrity. Repeated imipenem results of 4 μg/mL with *P. aeruginosa* ATCC® 27853 may indicate deterioration of the drug.
Penicillin	*S. aureus* ATCC® 29213	MIC too high	QC strain is a β-lactamase producer; overinoculation may yield increased MICs.	Repeat with a carefully adjusted inoculum.
Penicillins	Any	MIC too low	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Penicillins	Any	MIC too high	pH of media too high	Acceptable pH range = 7.2–7.4
Carbenicillin	*P. aeruginosa* ATCC® 27853	MIC too high	QC strain develops resistance after repeated subculture.	See general comment (1) on QC organism maintenance.
Ticarcillin-clavulanate	*E. coli* ATCC® 35218	MIC too high	Clavulanate is labile. Antimicrobial agent is degrading.	Use alternative lot. Check storage and package integrity.
Clindamycin	*S. aureus* ATCC® 29213 *E. faecalis* ATCC® 29212	MIC too high	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.

Table 5G. (Continued)

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
Clindamycin	*S. aureus* ATCC® 29213 *E. faecalis* ATCC® 29212	MIC too low	pH of media too high	Acceptable pH range = 7.2–7.4
Daptomycin	*S. aureus* ATCC® 29213 *E. faecalis* ATCC® 29212	MICs too high MICs too low	Ca++ content too low Ca++ content too high	Acceptable Ca++ content 50 µg/mL in CAMHB Adjust Ca++ concentration in or try alternative lots.
Macrolides and Ketolides	*S. aureus* ATCC® 29213 *E. faecalis* ATCC® 29212	MIC too high	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Macrolides and Ketolides	*S. aureus* ATCC® 29213 *E. faecalis* ATCC® 29212	MIC too low	pH of media too high	Acceptable pH range = 7.2–7.4
Quinolones	Any	MIC too high	pH of media too low	Acceptable pH range = 7.2–7.4 Avoid CO_2 incubation, which lowers pH.
Quinolones	Any	MIC too low	pH of media too high	Acceptable pH range = 7.2–7.4
Tetracyclines	Any	MIC too low	pH of media too low	Acceptable pH range = 7.2–7.4
Tetracyclines	Any	MIC too high	pH of media too high	Acceptable pH range = 7.2–7.4
Tetracyclines	Any	MIC too high	Ca++ and/or Mg++ content too high	Acceptable range = Ca++ 20–25 mg/L Mg++ 10–12.5 mg/L
Tetracyclines	Any	MIC too low	Ca++ and/or Mg++ content too low	Acceptable range = Ca++ 20–25 mg/L Mg++ 10–12.5 mg/L
Omadacycline Tigecycline	Any	MIC too high	CAMHB has not been freshly prepared.	Reference panels must be used or frozen within 12 hours of CAMHB preparation.
Various	Any	Many MICs too low	Inoculum too light; error in inoculum preparation	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Check steps in inoculum preparation and inoculation procedure. Perform colony count check of growth control well immediately after inoculation and before incubation (*E. coli* ATCC® 25922 closely approximates 5×10^5 CFU/mL).
Various	Any	Many MICs too high or too low	CAMHB not optimal	Use alternative lot.
Various	Any	Many MICs too high	Inoculum too heavy	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Check steps in inoculum preparation and inoculation procedure. Perform colony count check of growth control well immediately after inoculation and before incubation (*E. coli* ATCC® 25922 closely approximates 5×10^5 CFU/mL).
Various	Any	Skipped wells	Contamination. Improper inoculation of panel or inadequate mixing of inoculum. Actual concentration of drug in wells inaccurate. Volume of broth in wells inaccurate.	Repeat QC test. Use alternative lot.
Various	Any	Several MICs too high or too low	Possible reading/transcription error	Recheck readings. Use alternative lot.

Table 5G. (Continued)

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
Various	*S. pneumoniae* ATCC® 49619	MICs too low	Inoculum source plate too old and contains too many nonviable cells. Plate used to prepare inoculum should be 18–20 hours. MHB with LHB not optimal.	Subculture QC strain and repeat QC test; or subculture new QC strain from stock culture. Use alternative lot.
Various	Any	One QC strain is out of range, but other QC strains are in range with the same antimicrobial agent.	One QC organism may be a better indicator of a QC problem (eg, *P. aeruginosa* ATCC® 27853 is a better indicator of imipenem deterioration than *E. coli* ATCC® 25922).	Determine if the in-range QC strain has an on-scale end point for the agent in question. Retest this strain to confirm reproducibility of acceptable results. Evaluate with alternative strains with known MICs. Initiate corrective action with problem QC strain/antimicrobial agent(s).
Various	Any	Two QC strains are out of range with the same antimicrobial agent.	Indicates a problem with the antimicrobial agent. May be a systemic problem.	Initiate corrective action.
Various	Any	One QC result is out of range, but the antimicrobial agent is not an agent reported for patient results (eg, not on hospital formulary).		If antimicrobial agent is not normally reported, no repeat is necessary if adequate controls are in place to prevent reporting of the out-of-range antimicrobial agent. Carefully check antimicrobial agents of the same class for similar trend toward out-of-control results. If the antimicrobial agent in question is consistently out of control, contact the manufacturer.

Abbreviations: ATCC, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CFU, colony-forming unit; ESBL, extended-spectrum β-lactamase; LHB, lysed horse blood; MHB, Mueller-Hinton broth; MIC, minimal inhibitory concentration; QC, quality control.

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Table 6A. Solvents and Diluents for Preparation of Stock Solutions of Antimicrobial Agents[e]

Antimicrobial Agent	Solvent	Diluent
	Unless otherwise stated, use a minimum amount of the listed solvent to solubilize the antimicrobial powder.	**Finish diluting the final stock solution as stated below.**
Amikacin	Water	Water
Amoxicillin	Phosphate buffer, pH 6.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Ampicillin	Phosphate buffer, pH 8.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Avibactam	Water	Water
Azithromycin	95% ethanol or glacial acetic acid[e,f]	Broth media
Azlocillin	Water	Water
Aztreonam	Saturated solution sodium bicarbonate	Water
Besifloxacin	Methanol	Water
Biapenem	**Saline[m]**	**Saline[m]**
Carbenicillin	Water	Water
Cefaclor	Water	Water
Cefadroxil	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Cefamandole	Water	Water
Cefazolin	Phosphate buffer, pH 6.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Cefdinir	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Cefditoren	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Cefepime	Phosphate buffer, pH 6.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Cefetamet	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Cefixime	Phosphate buffer, pH 7.0, 0.1 mol/L	Phosphate buffer, pH 7.0, 0.1 mol/L
Cefmetazole	Water	Water
Cefonicid	Water	Water
Cefoperazone	Water	Water
Cefotaxime	Water	Water
Cefotetan	DMSO[e]	Water
Cefoxitin	Water	Water
Cefpodoxime	0.10% (11.9 mmol/L) aqueous sodium bicarbonate	Water
Cefprozil	Water	Water
Ceftaroline	DMSO[e] to 30% of total volume	Saline[m]
Ceftazidime	Sodium carbonate[d]	Water
Ceftibuten	1/10 vol DMSO[e]	Water
Ceftizoxime	Water	Water
Ceftobiprole	DMSO plus glacial acetic acid[e,h]	Water, vortex vigorously
Ceftolozane	Water or saline[m]	Water or saline[m]
Ceftriaxone	Water	Water
Cefuroxime	Phosphate buffer, pH 6.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Cephalexin	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Cephalothin	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Cephapirin	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Cephradine	Phosphate buffer, pH 6.0, 0.1 mol/L	Water
Chloramphenicol	95% ethanol	Water
Cinoxacin	1/2 volume of water, then add 1 mol/L NaOH dropwise to dissolve	Water
Ciprofloxacin	Water	Water
Clarithromycin	Methanol[e] or glacial acetic acid[e,f]	Phosphate buffer, pH 6.5, 0.1 mol/L
Clavulanate	Phosphate buffer, pH 6.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Clinafloxacin	Water	Water
Clindamycin	Water	Water
Colistin[a]	Water	Water
Dalbavancin	DMSO[e]	DMSO[e,g]
Daptomycin	Water	Water

Table 6A. (Continued)

Antimicrobial Agent	Solvent	Diluent
	Unless otherwise stated, use a minimum amount of the listed solvent to solubilize the antimicrobial powder.	**Finish diluting the final stock solution as stated below.**
Dirithromycin	Glacial acetic acid[f]	Water
Doripenem	Saline[m]	Saline[m]
Doxycycline	Water	Water
Enoxacin	1/2 volume of water, then 0.1 mol/L NaOH dropwise to dissolve	Water
Eravacycline	**Water**	**Water**
Ertapenem	Phosphate buffer, pH 7.2, 0.01 mol/L	Phosphate buffer, pH 7.2, 0.01 mol/L
Erythromycin	95% ethanol or glacial acetic acid[e,f]	Water
Faropenem	Water	Water
Fidaxomicin	DMSO[e]	Water
Finafloxacin	Water	Water
Fleroxacin	1/2 volume of water, then 0.1 mol/L NaOH dropwise to dissolve	Water
Fosfomycin	Water	Water
Fusidic acid	Water	Water
Garenoxacin	Water (with stirring)	Water
Gatifloxacin	Water (with stirring)	Water
Gemifloxacin	Water	Water
Gentamicin	Water	Water
Iclaprim	DMSO[e]	Water
Imipenem	Phosphate buffer, pH 7.2, 0.01 mol/L	Phosphate buffer, pH 7.2, 0.01 mol/L
Kanamycin	Water	Water
Levofloxacin	1/2 volume of water, then 0.1 mol/L NaOH dropwise to dissolve	Water
Linezolid	Water	Water
Linopristin-flopristin	DMF[k]	Water
Lomefloxacin	Water	Water
Loracarbef	Water	Water
Mecillinam	Water	Water
Meropenem	Water	Water
Methicillin	Water	Water
Metronidazole	DMSO[e]	Water
Mezlocillin	Water	Water
Minocycline	Water	Water
Moxalactam (diammonium salt)[b]	0.04 mol/L HCl (let sit for 1.5 to 2 hours)	Phosphate buffer, pH 6.0, 0.1 mol/L
Moxifloxacin	Water	Water
Mupirocin	Water	Water
Nafcillin	Water	Water
Nalidixic acid	1/2 volume of water, then add 1 mol/L NaOH dropwise to dissolve	
Netilmicin	Water	Water
Nitazoxanide	DMSO[e,l]	DMSO[e,l]
Nitrofurantoin[c]	Phosphate buffer, pH 8.0, 0.1 mol/L	Phosphate buffer, pH 8.0, 0.1 mol/L
Norfloxacin	1/2 volume of water, then 0.1 mol/L NaOH dropwise to dissolve	Water

Table 6A. (Continued)

Antimicrobial Agent	Solvent	Diluent
	Unless otherwise stated, use a minimum amount of the listed solvent to solubilize the antimicrobial powder.	**Finish diluting the final stock solution as stated below.**
Ofloxacin	1/2 volume of water, then 0.1 mol/L NaOH dropwise to dissolve	Water
Omadacycline	Water	Water
Oritavancin	0.002% polysorbate-80 in water[i]	0.002% polysorbate-80 in water[i]
Oxacillin	Water	Water
Penicillin	Water	Water
Piperacillin	Water	Water
Plazomicin	Water	Water
Polymyxin B	Water	Water
Quinupristin-dalfopristin	Water	Water
Ramoplanin	Water	Water
Razupenem	Phosphate buffer, pH 7.2, 0.01 mol/L	Phosphate buffer, pH 7.2, 0.01 mol/L
Rifampin	Methanol[e] (maximum concentration = 640 μg/mL)	Water (with stirring)
Rifaximin	Methanol[e]	0.1 M phosphate buffer, pH 7.4 + 0.45% sodium dodecyl sulfonate
Solithromycin	Glacial acetic acid[f]	Water
Sparfloxacin	Water	Water
Spectinomycin	Water	Water
Streptomycin	Water	Water
Sulbactam	Water	Water
Sulfonamides	1/2 volume hot water and minimal amount of 2.5 mol/L NaOH to dissolve	Water
Sulopenem[j]	0.01 M phosphate buffer, pH 7.2, vortex to dissolve	0.01 M phosphate buffer, pH 7.2
Surotomycin	**Water**	**Water**
Tazobactam	Water	Water
Teicoplanin	Water	Water
Telavancin	DMSO[e]	**DSMO[e,g]**
Telithromycin	Glacial acetic acid[e,f]	Water
Tetracycline	Water	Water
Ticarcillin	Phosphate buffer, pH 6.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Ticarcillin-clavulanate	Phosphate buffer, pH 6.0, 0.1 mol/L	Phosphate buffer, pH 6.0, 0.1 mol/L
Tigecycline	Water	Water
Tinidazole	DMSO[e,l]	Water
Tizoxanide	DMSO[e,l]	DMSO[e,l]
Tobramycin	Water	Water
Tedizolid	DMSO[e]	Water
Trimethoprim	0.05 mol/L lactic[e] or hydrochloric[e] acid, 10% of final volume	Water (may require heat)
Trimethoprim (if lactate)	Water	Water
Trospectomycin	Water	Water
Ulifloxacin (prulifloxacin)	DMSO[e]	Water
Vancomycin	Water	Water

Abbreviations: CAMHB, cation-adjusted Mueller-Hinton broth; DMF, dimethylformamide; DMSO, dimethyl sulfoxide.

NOTE: Information in boldface type is new or modified since the previous edition.

Footnotes

a. The formulation of colistin reference standard powder used in antimicrobial susceptibility tests is colistin sulfate and not colistin methane sulfonate (sulfomethate).

b. The diammonium salt of moxalactam is very stable, but it is almost pure R isomer. Moxalactam for clinical use is a 1:1 mixture of R and S isomers. Therefore, the salt is dissolved in 0.04 mol/L HCl and allowed to react for 1.5 to 2 hours to convert it to equal parts of both isomers.

Table 6A. (Continued)

c. Alternatively, nitrofurantoin is dissolved in DMSO.

d. Anhydrous sodium carbonate is used at a weight of exactly 10% of the ceftazidime to be used. The sodium carbonate is dissolved in solution in most of the required water. The antimicrobial agent is dissolved in this sodium carbonate solution, and water is added to the desired volume. The solution is to be used as soon as possible, but it can be stored up to six hours at no more than 25°C.

e. Consult the safety data sheets before working with any antimicrobial reference standard powder, solvent, or diluent. Some of the compounds (eg, solvents such as DMSO, methanol) are more toxic than others and may necessitate handling in a chemical fume hood.

f. For glacial acetic acid, use 1/2 volume of water, then add glacial acetic acid dropwise until dissolved, not to exceed 2.5 µL/mL.

g. Starting stock solutions of dalbavancin **and telavancin** should be prepared at concentrations no higher than 1600 µg/mL. Intermediate 100× concentrations should then be diluted in DMSO. Final 1:100 dilutions should then be made directly into CAMHB supplemented with 0.002% (v/v) polysorbate-80, so the final concentration of DMSO in the wells is no greater than 1%. See also Table 8B.

h. For each 1.5 mg of ceftobiprole, add 110 µL of a 10:1 mixture of DMSO and glacial acetic acid. Vortex vigorously for one minute, then intermittently for 15 minutes. Dilute to 1.0 mL with distilled water.

i. Starting stock solutions of oritavancin should be prepared at concentrations no higher than 1600 µg/mL in 0.002% polysorbate-80 in water. Intermediate 100× oritavancin concentrations should then be prepared in 0.002% polysorbate-80 in water. Final 1:100 dilutions should be made directly into CAMHB supplemented with 0.002% polysorbate-80, so the final concentration of polysorbate-80 in the wells is 0.002%.

j. Must be made *fresh* on the day of use.

k. DMF to 25% of final volume/water.

l. Final concentration of DMSO should not exceed 1%. This may be accomplished as follows: 1) prepare the stock solution at 10 times higher concentration than planned stock solution (ie, prepare at 12 800 µg/mL, rather than 1280 µg/mL); 2) add 1.8 mL sterile water to each agar deep; 3) add 0.2 mL of each antibiotic dilution to each agar deep.

m. Saline – a solution of 0.85% to 0.9% NaCl (w/v).

Table 6B. Preparation of Stock Solutions for Antimicrobial Agents Provided With Activity Expressed as Units

Antimicrobial Agent	Pure Agent (reference)	Calculation for µg/mg	Example
Potassium Penicillin G	0.625 µg/unit[1]	Multiply the activity expressed in units/mg by 0.625 µg/unit.	Activity units/mg × 0.625 µg/unit = Activity µg/mg (eg, 1592 units/mg × 0.625 µg/unit = 995 µg/mg)
Sodium Penicillin G	0.6 µg/unit[1]	Multiply the activity expressed in units/mg by 0.6 µg/unit.	Activity units/mg × 0.6 µg/unit = Activity µg/mg (eg, 1477 units/mg × 0.6 µg/unit = 886.2 µg/mg)
olymyxin B	10 000 units/mg = 10 units/µg = 0.1 µg/unit[2]	Multiply the activity expressed in units/mg by 0.1 µg/unit.	Activity units/mg × 0.1 µg/unit = Activity µg/mg (eg, 8120 units/mg × 0.1 µg/unit = 812 µg/mg)
		Divide the activity expressed in units/mg by 10 units/µg.	Activity units/mg / 10 units/µg = Activity µg/mg (eg, 8120 units/mg / 10 units/mg = 812 µg/mg)
Colistin sulfate[a]	30 000 units/mg = 30 units/µg = 0.03333 µg/unit[2]	Multiply the activity expressed in units/mg by 0.03333 µg/unit.	Activity units/mg × 0.03333 µg/unit = Activity µg/mg (eg, 20 277 units/mg × 0.03333 µg/unit = 676 µg/mg)
		Divide the activity expressed in units/mg by 30 units/mg.	Activity units/mg / 30 units/µg = Activity µg/mg (eg, 20 277 units/mg / 30 units/µg = 676 µg/mg)
Streptomycin	785 units/mg[3]	Divide the number of units given for the powder by 785. This will give the percent purity of the powder. Multiply the percent purity by 850, which is the amount in the purest form of streptomycin. This will equal the activity factor in µg/mg.	([Potency units/mg] / [785 units/mg]) × (850 µg/mg) = Potency µg/mg (eg, [751 units/mg / 785 units/mg] × 850 µg/mg = 813 µg/mg) If powder contains 2.8% water: 813 × (1 – 0.028) = potency 813 × 0.972 = 790 µg/mg

Footnote

a. Do not use colistin methanesulfonate for *in vitro* antimicrobial susceptibility tests.

References for Table 6B

1 Kucers A, Crowe SM, Grayson ML, Hoy JF. Penicillin G (Pen G). *The Use of Antibiotics.* 5th ed. Oxford, UK: Butterworth-Heinemann; 1997:3-70.
2 Kucers A, Crowe SM, Grayson ML, Hoy JF. Polymyxins. *The Use of Antibiotics.* 5th ed. Oxford, UK: Butterworth-Heinemann; 1997:667-675.
3 United States Department of Agriculture, OPHS, Laboratory QA/QC Division. *Bioassay for the detection, identification and quantitation of antimicrobial residues in meat and poultry tissue*. 2004;1-58, vol. MLG 34.01.

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Table 6C. Preparation of Solutions and Media Containing Combinations of Antimicrobial Agents

Antimicrobial Agent	Combination Tested	Preparation	Example
Amoxicillin-clavulanate	2:1 ratio (amoxicillin:clavulanate)	Prepare 10× starting concentration as 2:1 ratio and dilute as needed.	For a starting concentration of 128/64 in the panel, prepare a 10× stock concentration of 2560 µg/mL for amoxicillin and 1280 µg/mL for clavulanate. Then combine equal amounts of each to the first dilution tube, which will then contain 1280/640 µg/mL of the combination. Dilute 1:10 with broth to achieve the final concentration in microdilution wells.
Ampicillin-sulbactam	2:1 ratio (ampicillin:sulbactam)	Same as amoxicillin-clavulanate.	
Aztreonam-avibactam	**Fixed concentration of avibactam at 4 µg/mL**	**Prepare 10× starting concentration of aztreonam at twice the concentration needed and dilute as usual using serial twofold dilutions. Add an equal volume of avibactam 80 µg/mL to each of the diluted tubes.**	**For a starting concentration of 128/4 in the panel, prepare a 10× stock concentration of aztreonam at 2560 µg/mL and dilute by serial twofold increments down to the final concentration needed in the panel. Prepare a stock concentration of avibactam at 80 µg/mL. Then add an equal volume of the avibactam 80 µg/mL solution to each diluted tube of aztreonam. For example, 5 mL of 2560 µg/mL aztreonam + 5 mL of 80 µg/mL avibactam = 10 mL of 1280/40 µg/mL aztreonam-avibactam. Dilute 1:10 with broth to achieve the final concentration in microdilution wells.**
Ceftaroline-avibactam	Fixed concentration of avibactam at 4 µg/mL	**Same as aztreonam-avibactam**.	
Ceftazidime-avibactam	Fixed concentration of avibactam at 4 µg/mL	Same as **aztreonam**-avibactam.	
Ceftolozane-tazobactam	Fixed concentration of tazobactam at 4 µg/mL	Same as **aztreonam**-avibactam.	
Piperacillin-tazobactam	Fixed concentration of tazobactam at 4 µg/mL	Same as **aztreonam**-avibactam.	
Ticarcillin-clavulanate	Fixed concentration of clavulanate at 2 µg/mL	Prepare 10× starting concentration of ticarcillin at twice the concentration needed and dilute as usual using serial twofold dilutions. Add an equal volume of clavulanate 40 µg/mL to each of the diluted tubes.	For a starting concentration of 128/2 in the panel, prepare a 10× stock concentration of ticarcillin at 2560 µg/mL and dilute by serial twofold increments down to the final concentration needed. Prepare a stock concentration of clavulanate at 40 µg/mL. Then add an equal volume of the clavulanate 40 µg/mL solution to each diluted tube of ticarcillin. For example, 5 mL of 2560 µg/mL ticarcillin + 5 mL of 40 µg/mL clavulanate = 10 mL of 1280/20 µg/mL ticarcillin-clavulanate. Dilute 1:10 with broth to achieve the final concentration in microdilution wells.

Table 6C. (Continued)

Antimicrobial Agent	Combination Tested	Preparation	Example
Trimethoprim-sulfamethoxazole	1:19 ratio (trimethoprim:sulfamethoxazole)	Prepare a 10× starting concentration of trimethoprim at 1600 µg/mL (or at 1280 µg/mL that will require dilution to 160 µg/mL). Prepare a 10× starting concentration of sulfamethoxazole at a $\log_2$ multiple of 1520 µg/mL (eg, 1520, 3040, or 6080 µg/mL) depending on the starting concentration needed.	For a starting concentration of 8/152 in the panel, prepare a 10× concentration of trimethoprim at 160 µg/mL. Prepare a 10× starting concentration of sulfamethoxazole at 3040 µg/mL. Add an equal volume of the 160 µg/mL trimethoprim and the 3040 µg/mL sulfamethoxazole to the first dilution tube, and then dilute by serial twofold dilutions as usual. For example, 5 mL of 160 µg/mL trimethoprim and 5 mL of 3040 µg/mL sulfamethoxazole = 10 mL of 80/1520 trimethoprim-sulfamethoxazole. Dilute 1:10 with broth to achieve the final concentration in microdilution wells.
Quinupristin-dalfopristin Linopristin-flopristin	Preparation usually not required, because drug powder is received as combination.		

NOTE: To prepare intermediate dilutions of antimicrobial agents, a convenient formula to use is $C_1 \times V_1 = C_2 \times V_2$, where C_1 is the concentration of stock solution of the antimicrobial agent (usually 1280 µg/mL or greater); V_1 is the unknown volume that will be needed to make the intermediate concentration; C_2 is the intermediate concentration needed; and V_2 is the volume of the intermediate stock solution needed.

For example: To prepare 20 mL of a 40 µg/mL solution from a 1280 µg/mL stock solution:

$$C_1 \times V_1 = C_2 \times V_2$$

$$1280\ \mu g/mL \times V_1 = 40\ \mu g/mL \times 20\ mL$$

$$V_1 = \frac{40\ \mu g/mL \times 20\ mL}{1280\ \mu g/mL}$$

$$V_1 = 0.625\ mL$$

Therefore, add 0.625 mL of the 1280 µg/mL stock solution to 19.375 mL of diluent (usually water) for a final volume of 20 mL of a 40 µg/mL solution.

Table 7A. Scheme for Preparing Dilutions of Antimicrobial Agents to Be Used in Agar Dilution Susceptibility Tests

	Antimicrobial Solution						
Step	Concentration (μg/mL)	Source	Volume (mL)	Diluent (mL)	Intermediate Concentration (μg/mL)	Final Concentration at 1:10 Dilution in Agar (μg/mL)	Log_2
	5120	Stock	–	–	5120	512	9
1	5120	Stock	2	2	2560	256	8
2	5120	Stock	1	3	1280	128	7
3	5120	Stock	1	7	640	64	6
4	640	Step 3	2	2	320	32	5
5	640	Step 3	1	3	160	16	4
6	640	Step 3	1	7	80	8	3
7	80	Step 6	2	2	40	4	2
8	80	Step 6	1	3	20	2	1
9	80	Step 6	1	7	10	1	0
10	10	Step 9	2	2	5	0.5	−1
11	10	Step 9	1	3	2.5	0.25	−2
12	10	Step 9	1	7	1.25	0.125	−3

NOTE: This table is modified from Ericsson HM, Sherris JC. Antibiotic sensitivity testing. Report of an international collaborative study. *Acta Pathol Microbiol Scand*. 1971;217(suppl B):1-98.

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Table 8A. Scheme for Preparing Dilutions of Antimicrobial Agents to Be Used in Broth Dilution Susceptibility Tests

	Antimicrobial Solution							
Step	Concentration (μg/mL)	Source	Volume[a] (mL)	+	CAMHB[b] Volume[a] (mL)	=	Final Concentration (μg/mL)	Log_2
1	5120	Stock	1		9		512	9
2	512	Step 1	1		1		256	8
3	512	Step 1	1		3		128	7
4	512	Step 1	1		7		64	6
5	64	Step 4	1		1		32	5
6	64	Step 4	1		3		16	4
7	64	Step 4	1		7		8	3
8	8	Step 7	1		1		4	2
9	8	Step 7	1		3		2	1
10	8	Step 7	1		7		1	0
11	1	Step 10	1		1		0.5	−1
12	1	Step 10	1		3		0.25	−2
13	1	Step 10	1		7		0.125	−3

Abbreviation: CAMHB, cation-adjusted Mueller-Hinton broth.

NOTE: This table is modified from Ericsson HM, Sherris JC. Antibiotic sensitivity testing. Report of an international collaborative study. *Acta Pathol Microbiol Scand*. 1971;217(suppl B):1-90.

Footnotes

a. The volumes selected can be any multiple of these figures, depending on the number of tests to be performed.

b. Adjustment with cations, if necessary, occurs before this step.

Table 8B. Scheme for Preparing Dilutions of Water-Insoluble Antimicrobial Agents to Be Used in Broth Dilution Susceptibility Tests

	Antimicrobial Solution									
Step	Concentration (µg/mL)	Source	Volume (mL)	+	Solvent (mL) (eg, DMSO)	=	Intermediate Concentration (µg/mL)	=	Final Concentration at 1:100 (µg/mL)	Log_2
1	1600	Stock					1600		16	4
2	1600	Stock	0.5		0.5		800		8.0	3
3	1600	Stock	0.5		1.5		400		4.0	2
4	1600	Stock	0.5		3.5		200		2.0	1
5	200	Step 4	0.5		0.5		100		1.0	0
6	200	Step 4	0.5		1.5		50		0.5	−1
7	200	Step 4	0.5		3.5		25		0.25	−2
8	25	Step 7	0.5		0.5		12.5		0.125	−3
9	25	Step 7	0.5		1.5		6.25		0.0625	−4
10	25	Step 7	0.5		3.5		3.1		0.03	−5
11	3.1	Step 10	0.5		0.5		1.6		0.016	−6
12	3.1	Step 10	0.5		1.5		0.8		0.008	−7
13	3.1	Step 10	0.5		3.5		0.4		0.004	−8
14	0.4	Step 13	0.5		0.5		0.2		0.002	−9

Abbreviation: DMSO, dimethyl sulfoxide.

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.

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

Appendix A. (Continued)

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 intermediate or resistant category first published in June 2010 [M100-S20-U]) 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 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. Groups C and G small colony variants are included with the viridans group.

Appendix B. 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 Appendix A, footnote "a."

B1. *Enterobacteriaceae*

Antimicrobial Agent / Organism	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 Table 2A, comment (6) for reporting.												
Serratia marcescens	R	R	R			R	R	R			R	R	
Yersinia enterocolitica	R	R			R	R							

Appendix B. (Continued)

B1. (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 minimal inhibitory concentrations 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.**

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 (with some exceptions) (erythromycin, clarithromycin, azithromycin), quinupristin-dalfopristin, and rifampin.

Appendix B. (Continued)

B2. Non-*Enterobacteriaceae*

Antimicrobial Agent / Organism	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**.

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 B. (Continued)

B3. 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		

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 has not been presented.

Appendix B. (Continued)

B4. *Enterococcus* spp.

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

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

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Appendix C. Quality Control Strains for Antimicrobial Susceptibility Tests

Routine QC Strain	Organism Characteristics	Disk Diffusion Tests	MIC Tests	Screening Tests	Other
B. fragilis ATCC® 25285	• β-lactamase positive		• All anaerobes		
B. thetaiotaomicron ATCC® 29741	• β-lactamase positive		• All anaerobes		
C. difficile ATCC® 700057	• β-lactamase negative		• Gram-positive anaerobes		
E. faecalis ATCC® 29212			• Nonfastidious gram-positive bacteria	• Vancomycin agar • HLAR • **High-level mupirocin resistance MIC test**	• Assess suitability of medium for sulfonamide or trimethoprim MIC tests.[d] • Assess suitability of cation content in each batch/lot of Mueller-Hinton for daptomycin broth microdilution.
E. faecalis ATCC® 51299	• Resistant to vancomycin (*VanB*) and high-level aminoglycosides			• Vancomycin agar • HLAR	
E. coli ATCC® 25922	• β-lactamase negative	• Nonfastidious gram-negative bacteria •*Neisseria meningitidis*	• Nonfastidious gram-negative bacteria •*Neisseria meningitidis*		
E. coli ATCC® 35218	• Contains plasmid-encoded TEM-1 β-lactamase (non-ESBL)[a,b,e,f]	•β-lactam/β-lactamase inhibitor combinations	•β-lactam/β-lactamase inhibitor combinations		
E. lentum ATCC® 43055			• All anaerobes		• Growth on Brucella media not optimum
H. influenzae ATCC® 49247	• BLNAR	•*Haemophilus* spp.	•*Haemophilus* spp.		
H. influenzae ATCC® 49766	• Ampicillin susceptible	•*Haemophilus* spp. (more reproducible with selected β-lactams)	•*Haemophilus* spp. (more reproducible with selected β-lactams)		
K. pneumoniae ATCC® 700603	• Contains SHV-18 ESBL[b,e,f]	•ESBL screen and confirmatory tests	•ESBL screen and confirmatory tests		
N. gonorrhoeae ATCC® 49226	• CMRNG	•*N. gonorrhoeae*	•*N. gonorrhoeae*		

Appendix C. (Continued)

Routine QC Strain	Organism Characteristics	Disk Diffusion Tests	MIC Tests	Screening Tests	Other
P. aeruginosa ATCC® 27853[c]	• Contains inducible AmpC β-lactamase	• Nonfastidious gram-negative bacteria	• Nonfastidious gram-negative bacteria		• Assess suitability of cation content in each batch/lot of Mueller-Hinton for gentamicin MIC and disk diffusion.
S. aureus ATCC® 25923	• β-Lactamase negative • *mecA* negative • Little value in MIC testing due to its extreme susceptibility to most drugs	• Nonfastidious gram-positive bacteria		• **High-level mupirocin resistance disk diffusion test** • **Inducible clindamycin resistance disk diffusion test (D-zone test)**	
S. aureus ATCC® 29213	• Weak β-lactamase producing strain • *mecA* negative		• Nonfastidious gram-positive bacteria	• Oxacillin agar • **High-level mupirocin resistance MIC test** • **Inducible clindamycin resistance MIC test**	• Assess suitability of cation content in each batch/lot of Mueller-Hinton for daptomycin broth microdilution.
S. aureus ATCC® 43300	• Oxacillin-resistant, *mecA* positive	• Cefoxitin disk diffusion testing	• Cefoxitin MIC testing	• Oxacillin agar	
S. aureus ATCC® BAA-1708	• High-level mupirocin resistance mediated by the *mupA* gene			• **High-level mupirocin resistance test**	
S. pneumoniae ATCC® 49619	• Penicillin intermediate by altered penicillin-binding protein	• *S. pneumoniae* • *Streptococcus* spp. • *N. meningitidis*	• *S. pneumoniae* • *Streptococcus* spp. • *N. meningitidis*	• **Inducible clindamycin resistance MIC test**	
Supplemental QC Strains[g]					
E. faecalis ATCC® 29212			• Ceftaroline MIC testing		
E. faecalis ATCC® 33186					• Alternative to *E. faecalis* ATCC® 29212 to assess suitability of medium for sulfonamide or trimethoprim MIC and disk diffusion tests.[d] End points are the same as for *E. faecalis* ATCC® 29212.

Appendix C. (Continued)

Supplemental QC Strains[g]	Organism Characteristics	Disk Diffusion Tests	MIC Tests	Screening Tests	Other
H. influenzae ATCC® 10211					• Assess each batch/lot for growth capabilities of HTM.
K. pneumoniae ATCC® BAA-1705	• KPC-producing strain[b] • MHT positive	• Phenotypic confirmatory test for carbapenemase production (MHT)			
K. pneumoniae ATCC® BAA-1706	• Resistant to carbapenems by mechanisms other than carbapenemase • MHT negative	• Phenotypic confirmatory test for carbapenemase production (MHT)			
S. aureus ATCC® 29213	• Weak β-lactamase producing strain • *mecA* negative			• **Penicillin zone-edge test**	
S. aureus ATCC® BAA-976	• Contains *msrA*-mediated macrolide-only resistance	• Assess disk approximation tests with erythromycin and clindamycin (D-zone test negative).			
S. aureus ATCC® BAA-977	• Contains inducible *ermA*-mediated resistance	• Assess disk approximation tests with erythromycin and clindamycin (D-zone test positive).			

Abbreviations: ATCC, American Type Culture Collection; BLNAR, β-lactamase negative, ampicillin-resistant; CMRNG, chromosomally mediated penicillin resistant *N. gonorrhoeae;* ESBL, extended-spectrum β-lactamase; HLAR, high-level aminoglycoside resistance; HTM, *Haemophilus* Test Medium; KPC, *Klebsiella pneumoniae* carbapenemase; MHT, modified Hodge test; MIC, minimal inhibitory concentration; QC, quality control.

Footnotes

a. *E. coli* ATCC® 35218 is recommended only as a control organism for β-lactamase inhibitor combinations, such as those containing clavulanate, sulbactam, or tazobactam. This strain contains a plasmid-encoded β-lactamase (non-ESBL); subsequently, the organism is resistant to many penicillinase-labile drugs, but susceptible to β-lactam/β-lactamase inhibitor combinations. The plasmid must be present in the QC strain for the QC test to be valid; however, the plasmid may be lost during storage at refrigerator or freezer temperatures. To ensure the plasmid is present, test the strain with a β-lactam agent alone (ampicillin, amoxicillin, piperacillin, or ticarcillin) in addition to a β-lactam/β-lactamase inhibitor agent (eg, amoxicillin-clavulanate). If the strain loses the plasmid, it will be susceptible to the β-lactam agent when tested alone, indicating that the QC test is invalid and a new culture of *E. coli* ATCC® 35218 must be used.

Appendix C. (Continued)

b. Careful attention to organism maintenance (eg, minimal subcultures) and storage (eg, −60°C or below) is especially important for QC strains *E. coli* ATCC® 35218, *K. pneumoniae* ATCC® 700603, and *K. pneumoniae* ATCC® BAA-1705, because spontaneous loss of the plasmid encoding the β-lactamase or carbapenemase has been documented. Plasmid loss leads to QC results outside the acceptable limit, such as decreased MICs for *E. coli* ATCC® 35218 with enzyme-labile penicillins (eg, ampicillin, piperacillin, and ticarcillin), decreased MICs for *K. pneumoniae* ATCC® 700603 with cephalosporins and aztreonam, and false-negative MHT with *K. pneumoniae* ATCC® BAA-1705.

c. Develops resistance to β-lactam antimicrobial agents after repeated transfers onto laboratory media. Minimize by removing new culture from storage at least monthly or whenever the strain begins to show resistance.

d. End points should be easy to read (as 80% or greater reduction in growth as compared with the control) if media have acceptable levels of thymidine.

e. Rasheed JK, Anderson GJ, Yigit H, et al. Characterization of the extended-spectrum beta-lactamase reference strain, *Klebsiella pneumoniae* K6 (ATCC® 700603), which produces the novel enzyme SHV-18. *Antimicrob Agents Chemother.* 2000;44(9):2382-2388.

f. Queenan AM, Foleno B, Gownley C, Wira E, Bush K. Effects of inoculum and beta-lactamase activity in AmpC- and extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* clinical isolates tested by using NCCLS ESBL methodology. *J Clin Microbiol.* 2004;42(1):269-275.

g. QC strains are tested regularly (eg, daily or weekly) to ensure the test system is working and produces results that fall within specified limits listed in M100. The QC strains recommended in this document should be included if a laboratory performs CLSI reference disk diffusion or MIC testing as described herein. For commercial test systems, manufacturer's recommendations should be followed for all QC procedures. Supplemental QC strains are used to assess particular characteristics of a test or test system in select situations, or may represent alternative QC strains. For example, *Haemophilus influenzae* ATCC® 10211 is more fastidious than *H. influenzae* ATCC® 49247 or *H. influenzae* ATCC® 49766, and is used to ensure HTM can adequately support the growth of clinical isolates of *H. influenzae* and *H. parainfluenzae.* Supplemental QC strains may possess susceptibility or resistance characteristics specific for one or more special tests listed in M02-A11 and M07-A9. They can be used to assess a new test, for training new personnel, and for competency assessment. It is not necessary to include supplemental QC strains in routine daily or weekly antimicrobial susceptibility testing QC programs.

Appendix D. Cumulative Antimicrobial Susceptibility Report for Anaerobic Organisms

Isolates collected from selected US hospitals
1 January 2007 – 31 December 2009[a]

***Bacteroides fragilis* Group**

Anaerobic Organisms	Number of Strains	Ampicillin-sulbactam		Piperacillin-tazobactam		Cefoxitin		Ertapenem		Imipenem		Meropenem		Clindamycin		Moxifloxacin		Metronidazole[b]	
Percent Susceptible (%S) and Percent Resistant (%R)[c]		%S	%R	%S	%R	%S	%R	%S	%R	%S	%R	%S	%R	%S	%R	%S	%R	%S	%R
Breakpoints in µg/mL		≤8/4	≥32/16	≤32/4	≥128/4	≤16	≥64	≤4	≥16	≤4	≥16	≤4	≥16	≤2	≥8	≤2	≥8	≤8	≥32
B. fragilis	872	89	4	98	1	85	6	96	2	98	2	97	2	64	28	53	38	100	0
B. thetaiotaomicron	342	86	3	92	2	32	13	96	2	99	0	99	1	27	56	44	34	100	0
B. ovatus	67	93	2	93	2	37	15	98	0	100	0	100	0	54	39	43	39	100	0
B. vulgatus	70	67	6	100	0	83	4	98	2	98	2	98	2	49	51	43	46	100	0
B. uniformis	60	87	2	93	0	42	13	97	0	100	0	98	0	35	52	35	50	100	0
B. eggerthii	58	95	0	100	0	98	2	100	0	100	0	100	0	29	55	28	55	100	0
Parabacteroides distasonis	111	69	11	91	2	41	16	97	0	100	0	99	0	30	41	54	38	100	0
B. fragilis group without *B. fragilis*	708	83	4	93	1	40	12	97	1	99	0	99	0	33	42	43	40	100	0
B. fragilis group (all 7 species listed)	1580	86	4	95	2	65	9	97	1	98	1	98	1	50	39	49	39	100	0

a. Data were generated from unique isolates from patient specimens submitted to three referral laboratories: Tufts New England Medical Center, Boston, MA; Loyola University Medical Center, Maywood, IL; and R.M. Alden Research Laboratory, Culver City, CA. Testing was performed by the agar dilution method.
b. Resistance to metronidazole occurs infrequently.
c. Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.

Appendix D. (Continued)

Isolates collected from selected US hospitals
1 January 2007 – 31 December 2009[a]

Anaerobic Organisms Other Than *Bacteroides fragilis* Group

Anaerobic Organisms	Number of Strains	Ampicillin-sulbactam		Piperacillin-tazobactam		Cefoxitin		Ertapenem		Imipenem		Meropenem	Penicillin/ ampicillin		Clindamycin		Moxifloxacin		Metronidazole	
Percent Susceptible (%S) and Percent Resistant (%R)[d]		%S	%R	%S	%R	%S	%R	%S	%R	%S	%R	%R	%S	%R	%S	%R	%S	%R	%S	%R
Breakpoints in µg/mL		≤8/4	≥32/16	≤32/4	≥128/4	≤16	≥64	≤4	≥16	≤4	≥16	≥16	≤0.5	≥2	≤2	≥8	≤2	≥8	≤8	≥32
Prevotella spp.	173	98	1	99	1	99	1	100	0	100	0	1	40	49	66	30	59	24	100	0
Fusobacterium nucleatum-necrophorum	44	100	0	100	0	100	0	100	0	100	0	0	100	0	100	0	95	5	100	0
Anaerobic gram-positive cocci[e]	168	98	1	100	0	100	0	100	0	100	0	0	96	3	78	20	82	11	98	1
Veillonella spp.[b]	28	100	0	61	7	100	0	100	0	100	0	0	57	28	89	7	79	14	86	11
P. acnes	34	100	0	100	0	100	0	100	0	100	0	0	100	0	91	3	100	0	3	97
Clostridium perfringens	73	100	0	100	0	100	0	100	0	100	0	0	100	0	96	0	99	1	100	0
C. difficile[c]	56	100	0	100	0	0	100	100	0	20	18	0	0	79	5	79	78	22	100	0
Other *Clostridium* spp.	43	100	0	100	0	47	26	100	0	100	0	0	79	9	56	21	74	12	100	0

Appendix D. (Continued)

a. Data were generated from unique isolates from patient specimens submitted to three referral laboratories: Tufts New England Medical Center, Boston, MA; Loyola University Medical Center, Maywood, IL; and R.M. Alden Research Laboratory, Culver City, CA. Testing was performed by the agar dilution method.

b. Calculated from fewer than the CLSI document M39[1] recommendation of 30 isolates.

c. *C. difficile* isolates are from intestinal source; these results do not imply efficacy for intraluminal infections. Vancomycin minimal inhibitory concentrations for all isolates were < 4 µg/mL.

d. Intermediate category is not shown, but can be derived by subtraction of %S and %R for each antimicrobial agent from %100.

e. Anaerobic gram-positive cocci include *Peptococcus, Peptostreptococcus, Finegoldia, Peptoniphilus,* and *Anaerococcus* species.

Reference

[1] CLSI. *Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Third Edition.* CLSI document M39-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2009.

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Appendix E. Dosing Regimens Used to Establish Susceptible or Susceptible-Dose Dependent Interpretive Criteria

The evolving science of pharmacokinetics-pharmacodynamics has become increasingly important in recent years in determining MIC interpretive criteria. Recently approved susceptible or susceptible-dose dependent (SDD) interpretive criteria for a number of agents have been based on a specific dosing regimen(s); these dosing regimens are listed in the table below. Proper application of the interpretive criteria requires drug exposure at the site of infection that corresponds to or exceeds the expected systemic drug exposure at the dose listed in adult patients with normal renal function. This information should be shared with pharmacists, infectious disease staff, and others making dosing recommendations for the institution.

Antimicrobial Agent	Interpretive Criteria			
	Susceptible		SDD	
	MIC (µg/mL)	Dose	MIC (µg/mL)	Dose
Table 2A. *Enterobacteriaceae*				
Aztreonam	≤4	1 g every 8 h	NA	
Cefazolin	≤2	2 g every 8 h	NA	
Ceftaroline	≤0.5	600 mg every 12 h	NA	
Cefepime	≤2	1 g every 12 h	4	1 g every 8 h or 2 g every 12 h
			8 or zone diameter: 19–24 mm	2 g every 8 h (because it is not possible to correlate specific zone diameters with specific MICs, an isolate with a zone diameter in the SDD range should be treated as if it might be an MIC of 8 µg/mL)
Cefotaxime	≤1	1 g every 8 h	NA	
Ceftriaxone	≤1	1 g every 24 h	NA	
Cefoxitin	≤8	8 g per day (eg, 2 g every 6 h)	NA	
Cefuroxime	≤8	1.5 g every 8 h	NA	
Ceftazidime	≤4	1 g every 8 h	NA	
Ceftizoxime	≤1	1 g every 12 h	NA	
Doripenem	≤1	500 mg every 8 h	NA	
Ertapenem	≤0.5	1 g every 24 h	NA	
Imipenem	≤1	500 mg every 6 h or 1 g every 8 h	NA	
Table 2B-1. *Pseudomonas aeruginosa*				
Aztreonam	≤8	1 g every 6 h or 2 g every 8 h	NA	
Cefepime	≤8	1 g every 8 h or 2g every 12 h	NA	
Ceftazidime	≤8	1 g every 6 h or 2 g every 8 h	NA	
Doripenem	≤2	500 mg every 8 h	NA	
Imipenem	≤2	1 g every 8 h or 500 mg every 6 h	NA	
Meropenem	≤2	1 g every 8 h	NA	
Piperacillin	≤16	3 g every 6 h	NA	
Piperacillin-tazobactam	≤16/4	3 g every 6 h	NA	
Ticarcillin	≤16	3 g every 6 h	NA	
Ticarcillin-clavulanate	≤16/2	3 g every 6 h	NA	
Table 2B-2. *Acinetobacter* spp.				
Doripenem	≤2	500 mg every 8 h	NA	
Imipenem	≤2	500 mg every 6 h	NA	
Meropenem	≤2	1 g every 8 h or 500 mg every 6 h	NA	
Table 2C. *Staphylococcus* spp.				
Ceftaroline	≤1	600 mg every 12 h	NA	
Table 2E. *Haemophilus influenzae* and *Haemophilus parainfluenzae*				
Ceftaroline	≤0.5	600 mg every 12 h	NA	

Appendix E. (Continued)

Antimicrobial Agent	Interpretive Criteria			
	Susceptible		SDD	
	MIC (µg/mL)	Dose	MIC (µg/mL)	Dose
Table 2G. *Streptococcus pneumoniae*				
Ceftaroline (nonmeningitis)	≤0.5	600 mg every 12 h	NA	
Penicillin (nonmeningitis)	≤2	2 million units every 4 h (12 million units per day)	NA	
Penicillin parenteral (meningitis)	≤0.06	3 million units every 4 h	NA	
Table 2H-1. *Streptococcus* spp. β-Hemolytic Group				
Ceftaroline	≤0.5	600 mg every 12 h	NA	

Abbreviations: MIC, minimal inhibitory concentration; NA, not applicable; SDD, susceptible-dose dependent.

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

Glossary I (Part 1). (Continued)

Antimicrobial Class	Antimicrobial Subclass	Agents Included; Generic Names
Monobactams		Aztreonam
Penems	Carbapenem	**Biapenem** Doripenem Ertapenem Imipenem Meropenem Razupenem
	Penem	Faropenem Sulopenem

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

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.

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)

Glossary I (Part 2). (Continued)

Antimicrobial Class	Antimicrobial Subclass	Agents Included; Generic Names
Steroidal	Fusidanes	Fusidic acid
Streptogramins		Linopristin-flopristin Quinupristin-dalfopristin
Tetracyclines		Doxycycline **Eravacycline** Minocycline Tetracycline
	Glycylcyclines	Tigecycline
	Aminomethylcycline	Omadacycline
Thiazolide		Nitazoxanide Tizoxanide

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)	CB, Cb, BAR	X				Penicillin
Carbenicillin			X	X		
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

Glossary II. (Continued)

Antimicrobial Agent	Agent Abbreviation[a]	Routes of Administration[b]				Drug Class or Subclass
		PO	IM	IV	Topical	
Cefuroxime (oral)	CXM, CFX, ROX, Crm,	X				Cephem
Cefuroxime (parenteral)	FUR, XM		X	X		
Cephalexin	CN, LEX, CFL	X				Cephem
Cephalothin	CF, Cf, CR, CL, CEP, CE, KF			X		Cephem
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	GM, Gm, CN, GEN		X	X		Aminoglycoside
Gentamicin synergy	GM500, HLG, Gms					
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

Glossary II. (Continued)

Antimicrobial Agent	Agent Abbreviation[a]	Routes of Administration[b]				Drug Class or Subclass
		PO	IM	IV	Topical	
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
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		**Lipoglycopeptide**
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

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

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.

Glossary III. List of Identical Abbreviations Used for More Than One Antimicrobial Agent in US Diagnostic Products

Agent Abbreviation	Antimicrobial Agents for Which Respective Abbreviation Is Used
AZM	Azithromycin, Aztreonam
AZ	Azithromycin, Azlocillin
CB, Cb	Ceftibuten, Carbenicillin
CFR, Cfr	Cefaclor, Cefadroxil
CF, Cf	Cefaclor, Cephalothin
CM	Clindamycin, Cefamandole
CFM, Cfm	Cefixime, Cefamandole
CZ, Cz	Ceftizoxime, Cefazolin
CD, Cd	Clindamycin, Cefdinir
CPZ	Cefprozil, Cefoperazone
CP, Cp	Cephapirin, Cefoperazone, Ciprofloxacin
CN, Cn	Cephalexin, Cefotetan, Cinoxacin, Gentamicin
CFX, Cfx	Cefoxitin, Cefuroxime
CL	Cephalothin, Chloramphenicol
CH	Clarithromycin, Cephradine
DX	Doxycycline, Dicloxacillin
FO	Fleroxacin, Fosfomycin
NIT	Nitrofurantoin
SC	Spectinomycin, Methicillin
SO	Sparfloxacin, Oxacillin
TC	Tetracycline, Ticarcillin

Informational – User Questions and Subcommittee Responses

1. Previously, antibiotic "A" was not on our routine test panel. When we were asked to test antibiotic "A" on a patient's isolate, we tested the patient's isolate and performed QC testing for antibiotic "A" on the same day. Now we want to begin testing antibiotic "A" routinely. Can we use the last 20 consecutive QC results (obtained over the past year) to justify conversion from daily to weekly QC testing of antibiotic "A"? Only one QC result for antibiotic "A" was out of control during the past 20 days on which we tested antibiotic "A," and this corrected upon repeat testing.

- **Yes, you have demonstrated satisfactory performance of "daily QC" by obtaining acceptable results from at least 20 consecutive test days and you can now implement weekly QC testing. "Consecutive test days," or "testing with each use" refers to the actual number of days when a QC test is performed; it is not meant to indicate consecutive calendar days. Don't forget to maintain the records for conversion from daily to weekly QC testing indefinitely. The subcommittee will clarify wording to address this situation in the next editions of the M02 and M07 standards.**

2. I am seeking assistance regarding the following instance: Our laboratory was recently cited during a College of American Pathologists inspection for not following the CLSI guidelines regarding an unacceptable minimal inhibitory concentration value for one drug per one QC organism per one instance with weekly QC done for the month of March. Repeat testing on said organism was acceptable the following day. Please keep in mind that this was only one instance for one drug on one QC organism; aside from this exception, our weekly controls are typically within expected ranges.

- **QC ranges are established based on multilaboratory, multilot QC studies from CLSI document M23. Ranges are established to include ≥ 95% of the results. Therefore, a small number of (random) out-of-range QC results may be obtained even when the test method is performed correctly and materials are maintained adequately. If the cause of the error can be reasonably determined, corrective action can be taken and satisfactory performance confirmed with a single QC repeat. However, if the cause of the error cannot be reasonably determined, additional testing is needed to determine if the cause of the out-of-range result is due to random error, test conditions, or materials.**

  The subcommittee will work on clarifying the wording in Table 4C (and 5F) "Reference Guide to Quality Control Frequency" and modify the next editions of the M02 and M07 standards to provide additional guidance on troubleshooting and corrective action. In addition, we will describe two alternatives to satisfy the requirement to have five QC results to evaluate by allowing use of retrospective QC (if the previous four QC results from the same lot of materials was acceptable) and the ability to test up to three QC replicates in a single day. These alternatives may detect problems faster and minimize cost while providing the same level of confidence in confirming acceptable performance.

The two examples below will be included in the appropriate QC sections of the forthcoming M02 and M07 revisions:

Scenario 1. Ampicillin *E. coli* ATCC® 25922 Acceptable Range: 2–8 µg/mL

Week	Day	Lot #	Result	Action
1	1	3564	4	
2	1	3564	8	
3	1	3564	8	
4	1	3564	4	
5	1	3564	16	Out of range. Repeat QC same day.
5	2	3564	8	In range. Five acceptable in-range QC tests for *E. coli* ATCC® 25922 and ampicillin with lot 3564. Resume weekly QC testing.

Conclusion: Random QC error.

Scenario. 2 Ampicillin *E. coli* ATCC® 25922 Acceptable Range: 2–8 µg/mL

Week	Day	Lot #	Result	Action
1	1	9661	4	
2	1	9661	8	
3	1	9661	16	Out of range. Repeat QC same day.
3	2	9661	8	In range. Three acceptable in-range QC tests for *E. coli* ATCC® 25922 and ampicillin with lot 9661. Repeat QC 2 more consecutive days.
3	3	9661	8	In range.
3	4	9661	8	In range. Five acceptable in-range QC tests for *E. coli* ATCC® 25922 and ampicillin with lot 9661. Resume weekly QC testing.

Conclusion: Random QC error.

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

M100-S24 does not address any of the QSEs. For a description of the documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Organization	Customer Focus	Facilities and Safety	Personnel	Purchasing and Inventory	Equipment	Process Management	Documents and Records	Information Management	Nonconforming Event Management	Assessments	Continual Improvement
						EP23 M02 M07 M11 M23 M27 M27-S4 M39 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.

M100-S24 addresses the clinical laboratory path of workflow steps indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Preexamination				**Examination**			**Postexamination**	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
				X EP23 M02 M07 M11 M27 M27-S4	X EP23 M02 M07 M11 M27 M27-S4	X EP23 M02 M07 M11 M27 M27-S4	X M02 M07 M11 M27 M27-S4	 M27 M27-S4

Related CLSI Reference Materials*

EP23-A™ **Laboratory Quality Control Based on Risk Management; Approved Guideline (2011).** This document provides guidance based on risk management for laboratories to develop quality control plans tailored to the particular combination of measuring system, laboratory setting, and clinical application of the test.

M02-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.

M39-A3 **Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Third Edition (2009).** This document describes methods for recording and analysis of antimicrobial susceptibility test data, consisting of cumulative and ongoing summaries of susceptibility patterns of clinically significant microorganisms.

M45-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.

* 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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(As of 1 December 2013)

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AstraZeneca Pharmaceuticals (MA)
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BD (NJ)
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Diagnostica Stago (NJ)
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Greiner Bio-One Inc. (NC)
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Hologic, Inc. (MA)
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Insmed Incorporated (NJ)
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Intuity Medical (CA)
ITC Corp (NJ)
Johnson & Johnson Pharmaceutical Research & Develop., L.L.C. (NJ)
Kaiser Permanente (CA)
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Laboratory Specialists, Inc. (OH)
Life Laboratories (MA)
LifeLabs (Canada)
LifeLabs Medical Laboratory Services (Canada)
LipoScience, Inc. (NC)
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Merck & Company, Inc. (NJ)
Merial Limited & Newport Laboratories (MO)
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Micromyx, LLC (MI)
Micropoint Bioscience, Inc. (CA)
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. (IL)
Sonic Healthcare USA (TX)
SRL Limited (India)
Streck Laboratories, Inc. (NE)
Sysmex America, Inc. (IL)
Tetraphase Pharmaceuticals (MA)
The Medicines Company (Canada)
Theranos (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)
673rd Medical Group (AK)
Academisch Ziekenhuis-VUB (Belgium)
Academy of Medical Laboratory Sciences (Ireland)
ACG (Colombia)
ACL Laboratories (IL)
ACL Laboratories (WI)
ADNOC Medical Center (United Arab Emirates)
Adventist Health System (FL)
Adventist Medical Center (OR)
Affiliated Laboratory, Inc. (ME)
AFRIMS (Thailand)
Aga Khan University Hospital (Pakistan)
Aggredyne, Inc. (TX)
AHS Morristown (NJ)
Akron Children's Hospital (OH)
Akron General Medical Center (OH)
Al Hada Armed Forces Hospital/TAIF/KSA (Saudi Arabia)
Alamance Regional Medical Center (NC)
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)
Analytisch Diagnostisch Centrum N.V. (Curaçao)
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 Heart Hospital of South Dakota (SD)
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)
Baton Rouge General (LA)
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 Biomedical Laboratories (Canada)
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)
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)
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California Pacific Medical Center (CA)
Cambridge Health Alliance (MA)
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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)
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Cape Cod Hospital (MA)
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Capital Health Regional Medical Center (NJ)
Capital Region Medical Center (MO)
Cardinal Hill Rehabilitation Hospital (KY)
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Carolinas Healthcare System (NC)
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Carroll Hospital Center (MD)
Carteret General Hospital (NC)
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Cass County Memorial Hospital (IA)
Castle Medical Center (HI)
Catholic Health Initiatives (KY)
Catholic Medical Center (NH)
CD Diagnostics, Inc. (PA)
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Cedars-Sinai Medical Center (CA)
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Cellnetix Pathology & Laboratories (WA)
Center for Disease Detection (TX)
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Centers for Disease Control and Prevention (GA)
Centers for Disease Control and Prevention - Ethiopia (Ethiopia)
Centers for Disease Control and Prevention - Tanzania (Tanzania)
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Centers for Medicare & Medicaid Services/CLIA Program (TX)
Centers For Medicare and Medicaid Services (GA)
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Central Maine Medical Center (ME)
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Ceylon Hospitals Limited (Sri Lanka)
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Chaleur Regional Hospital (Canada)

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Champlain Valley Physicians Hospital (NY)
Chang Gung Memorial Hospital (Taiwan)
Charleston Area Medical Center (WV)
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Chester County Hospital (PA)
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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 Hospital - 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)
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Chinese Committee for Clinical Laboratory Standards (China)
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CHU Sainte-Justine: Department of Microbiology and Immunology (Canada)
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CHW-St. Mary's Medical Center (CA)
Cibola General Hospital (NM)
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Clinique St. Luc (Belgium)
CLMA (IL)
CML HealthCare (Canada)
COLA (MD)
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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 (OR)
Columbia St. Mary's Milwaukee (WI)
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)
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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)
Dermatopathology Northwest (WA)
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)
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Dialysis Clinic, Inc. Laboratory (TN)
Dimensions Healthcare System Prince George's Hospital Center (MD)
DMC University Laboratories (MI)
Docro, Inc. (CT)
Doctors Hospital (FL)
Doctors Hospital (OH)
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 Georgia Regional Medical Center (GA)
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)
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)
Excela Health Latrobe Hospital (PA)
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)
FHG- University of Applied Science-Tyrol (Austria)
Firelands Regional Medical Center (OH)
Fisher-Titus Memorial Hospital (OH)
Flagler Hospital Inc. (FL)
Fletcher Allen Health Care (VT)
Florida Department of Health (FL)
Forrest General Hospital (MS)
Forsyth Medical Center (NC)
Fort Loudoun Medical Center (TN)
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Fundacion Mexicana Para la Salud Capitulo Peninsular A.C (Mexico)
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Gateway Regional Medical Center (IL)
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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 Baltimore Medical Center (MD)
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 Diagnostic Laboratory, Inc. (VA)
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)
Highline Medical Center (WA)
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)
INEI-ANLIS "Dr. C. G. Malbrán" (Argentina)
Ingalls Hospital (IL)
Inova Central Laboratory (VA)
Institut Für Klinische Chemie Und Laboratoriumsmedizin Universitätsklinikum (Germany)
Institut National de Sante Publique du Quebec (Canada)
Institut National de Sante Publique du Quebec - INSPQ (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)
Kane Community Hospital (PA)
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)
Lakeway Regional Medical Center (TX)
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)
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 Bucks Hospital (PA)
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)
McCullough-Hyde Memorial Hospital (OH)
MCG Health (GA)
McKenzie-Willamette Medical Center (OR)
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)
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 Medical Center (IL)
Memorial Medical Center (PA)
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)
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)
Montgomery Regional Hospital (VA)
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 Veterinary Institute (Sweden)
Nationwide Children's Hospital (OH)
Naval Health Clinic Charleston (SC)
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)
Oconee Memorial Hospital (SC)
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)
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)
Round Rock Medical Center (TX)
Royal Children's Hospital (Australia)
Royal Hobart Hospital (Australia)
Royal Victoria Hospital (Canada)
Rush Health Systems (MS)
Rush University Medical Center (IL)
Russellville Hospital (AL)
SA Pathology (Australia)
SAAD Specialist Hospital (Saudi Arabia)
Sacred Heart Hospital (FL)
Sacred Heart Hospital (WI)
Sacred Hearth -St. Mary's Hospital Inc (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)
Seoul St. Mary's 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. Croix Regional Medical Center (WI)
St. David's Medical Center (TX)
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)
Tan Tock Seng Hospital (Singapore)
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)
Tethys Bioscience, Inc. (CA)
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 M.D. Anderson Cancer Center (TX)
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)
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)
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 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 Malaya Medical Centre (Malaysia)
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 Connecticut (CT)
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 (MD)
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 North Texas Health Science Center (TX)
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 Southwestern Medical Center (TX)
University of the Ryukyus (Japan)
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University of Wisconsin Medical Foundation (WI)
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Urology of Virginia, PLLC (VA)
USA MEDDAC-Japan
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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)
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VA (Durham) Medical Center (NC)
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 Nebraska Community College (NE)
Western State Hospital (VA)
Whangarei Hospital (New Zealand)
Wheaton Franciscan Laboratories At St. Francis (WI)
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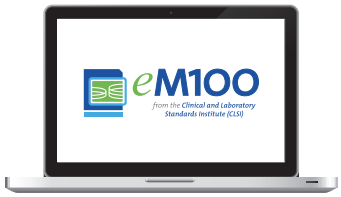

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