CLINICAL AND LABORATORY STANDARDS INSTITUTE®

3rd Edition

M45

Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria

This guideline informs clinical, public health, and research laboratories on susceptibility testing of infrequently isolated or fastidious bacteria that are not included in CLSI documents M02, M07, or M100. Antimicrobial agent selection, test interpretation, and quality control are addressed.

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

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Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria

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Abstract

If a bacterial pathogen's susceptibility to antimicrobial agents cannot be predicted based on the identity of the organism alone, *in vitro* antimicrobial susceptibility testing of the isolated organism may be indicated. Susceptibility testing is particularly necessary in those situations in which the etiological agent belongs to a bacterial species for which resistance to commonly used antimicrobial agents has been documented, or could arise.

A variety of laboratory techniques can be used to measure the *in vitro* susceptibility of bacteria to antimicrobial agents. Clinical and Laboratory Standards Institute document M45—*Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria* describes the standard microdilution and agar disk diffusion methods. It also includes a series of procedures designed to standardize test performance. The performance, applications, and limitations of the current CLSI-recommended methods are described.

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Foreword

This document provides guidance to clinical or public health microbiology laboratories regarding the performance of standardized susceptibility testing, when needed, for infrequently isolated or fastidious bacteria that are not currently included in CLSI documents M02,[1] M07,[2] or M100.[3] Some of the organisms included are aerobic gram-negative bacilli that are not members of the family *Enterobacteriaceae* but may be tested by the standard CLSI broth microdilution or disk diffusion methods in the same manner as the much more common *Enterobacteriaceae* isolates. Some aerobic gram-positive cocci and bacilli that are encountered periodically by clinical laboratories can also be tested reliably by the standard CLSI minimal inhibitory concentration (MIC) or disk diffusion test methods in a manner analogous to *Staphylococcus* or *Enterococcus* spp. In addition, several genera of fastidious gram-positive and gram-negative bacteria can be tested in the same manner as the streptococci, using blood-supplemented Mueller-Hinton media. For the purpose of this document, the term "fastidious" is used to describe bacteria that require media supplemented with blood or blood components and that possibly need an atmosphere other than ambient air (eg, 5% CO_2) for acceptable growth. Because the standard CLSI media, reagents, and procedures can be used to test the organisms included in this guideline, the QC procedures, strains, and acceptable zone diameter and MIC limits that have been established through previous rigorous studies can also be applied. The working group used a thorough search of the published literature in conjunction with the clinical expertise of its members to apply or adapt interpretive criteria from CLSI document M100[3] to the interpretation of tests for organisms in this document. Users of the guideline should be aware that the very extensive microbiological, clinical, and pharmacodynamic databases normally used for setting breakpoints by CLSI do not exist for the collection of "orphan" organisms described in this document.

It is important for users of M45 to recognize that commercial susceptibility testing devices are not addressed in this guideline. The methods described herein are generic reference procedures that can be used for routine susceptibility testing by clinical laboratories, or that can be used by clinical laboratories to evaluate commercial devices for possible routine use. Results generated by reference methods, such as those contained in CLSI documents, may be used by regulatory authorities to evaluate the performance of commercial systems 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 the reference methods for the organisms and antimicrobial agents described in the manufacturer's approved package insert. Some laboratories could find that a commercial dilution, antibiotic gradient, colorimetric, turbidimetric, fluorometric, or other method is suitable for selective or routine use.

Overview of Changes

The changes in this document supersede the information presented in the previous edition of M45. This list includes "major" changes that appear for the first time in this edition of M45, or that were modified since publication of M45-A2. Other minor or editorial changes that were made to the general formatting are not listed here. Revisions to the document include:

Subchapter 1.2, Background (Section 2 in M45-A2)
Deleted *Plesiomonas* spp. due to reclassification as a member of *Enterobacteriaceae* (addressed in CLSI document M100[3]).

Modified discussion of potential bacterial agents of bioterrorism.

Resistance Mechanisms in Gram-Positive Rods (Section 2.1 in M45-A2)
Deleted section and relocated pertinent information to respective table.

Resistance in Infrequently Isolated or Fastidious Gram-Positive Cocci (Section 2.2 in M45-A2)
Deleted section and relocated pertinent information to respective table.

Infrequently Isolated Nonfastidious Gram-Negative Rods (Section 2.3 in M45-A2)
Deleted section and relocated pertinent information to respective table.

Fastidious Gram-Negative Rods (Section 2.4 in M45-A2)
Deleted section and relocated pertinent information to respective table.

***Moraxella catarrhalis* (Section 2.5 in M45-A2)**
Deleted section and relocated pertinent information to respective table.

Potential Bacterial Agents of Bioterrorism (Section 2.6 in M45-A2)
Deleted section and relocated pertinent information to respective table.

Table 1. *Abiotrophia* spp. and *Granulicatella* spp. (Formerly Known as Nutritionally Deficient or Nutritionally Variant Streptococci)
Added comment regarding combination therapy.

Table 2. *Aerococcus* spp.
Added new table.

Table 3. *Aeromonas* spp. (Includes Members of *Aeromonas caviae* Complex, *Aeromonas hydrophila* Complex, and *Aeromonas veronii* Complex)
Deleted *Plesiomonas* spp. due to reclassification as member of *Enterobacteriaceae* (addressed in CLSI document M100[3]).

Added *Pseudomonas aeruginosa* ATCC® 27583 as recommended QC strain for carbapenems.

Deleted zone diameter and MIC interpretive criteria for amoxicillin-clavulanate, ampicillin-sulbactam, and cefazolin.

Deleted amoxicillin-clavulanate as an agent to consider for primary testing.

Revised zone diameter and MIC interpretive criteria for cefepime.

Added dosing regimen for cefepime.

Added zone diameter and MIC interpretive criteria for doripenem.

Revised zone diameter and MIC interpretive criteria for ertapenem, imipenem, and meropenem.

Added dosing regimen for ertapenem, imipenem, meropenem, and doripenem.

Added a note about ciprofloxacin treatment failures.

Table 4. *Bacillus* spp. (not *Bacillus anthracis*) and Related Genera
Expanded list of related genera for which this table and interpretive criteria apply to include *Brevibacillus, Cohnella, Lysinibacillus, Paenibacillus, Solibacillus,* and *Sporolactobacillus.*

Added MIC interpretive criteria for meropenem.

Table 5. *Campylobacter jejuni/coli*
Modified disk diffusion incubation conditions to 42°C for 24 hours; eliminated 36 to 37°C for 48 hours option.

Added tetracycline to the list of agents to consider for primary testing.

Added susceptible and intermediate and revised resistant disk diffusion interpretive criteria for erythromycin and ciprofloxacin.

Added susceptible, intermediate, and resistant disk diffusion interpretive criteria for tetracycline.

Added a comment regarding susceptibility of doxycycline based on tetracycline results.

Revised description of Derivation of Interpretive Criteria.

Table 6. *Corynebacterium* spp. (Including *Corynebacterium diphtheriae*) and Related Coryneform Genera
Expanded list of coryneform genera for which this table and interpretive criteria apply to include *Arthrobacter, Cellulosimicrobium,* and *Trueperella.*

Added comments that describe antimicrobial susceptibility data available for less common species of coryneforms and related organisms.

Revised susceptible and intermediate interpretive MIC criteria for penicillin.

Removed meningitis comment.

Revised MIC interpretive criteria for meropenem.

Deleted MIC interpretive criteria for imipenem.

Table 8. *Gemella* spp.
Added new table.

Table 9. HACEK Group: *Aggregatibacter* spp., *Cardiobacterium* spp., *Eikenella corrodens,* and *Kingella* spp.
Revised broth recommended for testing to include *Haemophilus* Test Medium and Brucella broth as alternatives for some species.

Table 10. *Helicobacter pylori*
Added note indicating that determination of metronidazole resistance under these testing conditions is not recommended because it does not reliably predict treatment failure.

Added note further emphasizing need for the use of aged blood in agar dilution testing.

Table 11. *Lactobacillus* spp.
Expanded comment indicating species that require anaerobic incubation.

Expanded comment describing species that are intrinsically vancomycin resistant and those that are vancomycin susceptible.

Deleted gentamicin interpretive criteria.

Modified comment regarding combination therapy.

Added meropenem interpretive criteria.

Added note indicating the relationship of meropenem and imipenem MICs.

Table 12. *Lactococcus* spp.
Added new table.

Table 13. *Leuconostoc* spp.
Deleted gentamicin interpretive criteria.

Modified comment regarding combination therapy.

Table 14. *Listeria monocytogenes*
Added meropenem interpretive criteria.

Revised trimethoprim-sulfamethoxazole interpretive criteria to include susceptible only.

Table 15. *Micrococcus* spp.
Added new table.

Table 16. *Moraxella catarrhalis*
Deleted interpretive criteria for cefaclor.

Table 18. *Pediococcus* spp.
Deleted gentamicin interpretive criteria.

Modified comment regarding combination therapy.

Table 19. *Rothia mucilaginosa*
Added new table.

Table 20. *Vibrio* spp. (Including *Vibrio cholerae*)
Added *P. aeruginosa* ATCC® 27853 as recommended QC organism for carbapenems.

Added doxycycline as an agent to consider for primary testing.

Revised zone diameter and MIC interpretive criteria for cefepime.

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Added dosing regimen for cefepime.

Revised zone diameter and MIC interpretive criteria for imipenem and meropenem.

Added dosing regimen for imipenem and meropenem.

Expanded comments for testing/reporting tetracyclines (including doxycycline) on *Vibrio* spp. other than *V. cholerae.*

Table 22. Summary of Testing Conditions and Quality Control Recommendations for Infrequently Isolated or Fastidious Bacteria
Deleted *Plesiomonas shigelloides* (*Plesiomonas* spp. now included with *Enterobacteriaceae* in CLSI document M100[3]).

Added *Aerococcus* spp., *Gemella* spp., *Lactococcus* spp., *Micrococcus* spp., and *Rothia mucilaginosa.*

Added *P. aeruginosa* ATCC® 27583 as a recommended QC strain for carbapenems when testing *Aeromonas hydrophila* complex and *Vibrio* spp. (including *V. cholerae*).

Revised temperature and incubation time for disk diffusion testing of *Campylobacter jejuni/coli.*

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

Updated to include newer antimicrobial agents considered by the CLSI Subcommittee on Antimicrobial Susceptibility Testing, not all of which are currently referenced in M45.

These newer agents are:

- Aztreonam-avibactam
- Ceftaroline-avibactam
- Ceftazidime-avibactam
- Ceftolozane-tazobactam
- Biapenem

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

Updated to include newer antimicrobial agents considered by the CLSI Subcommittee on Antimicrobial Susceptibility Testing, not all of which are currently referenced in M45.

These newer agents are:

- Besifloxacin
- Eravacycline
- Fidaxomicin
- Finafloxacin
- Fusidic acid
- Nitazoxanide
- Pefloxacin
- Plazomicin
- Ramoplanin

- Solithromycin
- Surtomycin
- Tedizolid
- Telithromycin
- Tinidazole
- Tizoxanide
- Ulifloxacin (prulifloxacin)

Glossary II. Abbreviations/Routes of Administration/Drug Class for Antimicrobial Agents Listed in CLSI document M100-S25[3]
Deleted trospectinomycin.

Updated to include newer antimicrobial agents considered by the CLSI Subcommittee on Antimicrobial Susceptibility Testing, not all of which are currently referenced in M45.

These newer agents are:

- Aztreonam-avibactam
- Besifloxacin
- Biapenem
- Ceftaroline-avibactam
- Ceftazidime-avibactam
- Ceftolozane-tazobactam
- Eravacycline
- Fidaxomicin
- Finafloxacin
- Fusidic acid
- Metronidazole
- Nitazoxanide
- Omadacycline
- Pefloxacin
- Plazomicin
- Ramoplanin
- Solithromycin
- Surtomycin
- Tedizolid
- Tinoxanide
- Tinidazole
- Ulifloxacin (prulifloxacin)

Glossary III. List of Identical Abbreviations Used for More Than One Antimicrobial Agent in US Diagnostic Products
Added table for consistency with the current edition of CLSI document M100.[3]

NOTE 1: Mandates are occasionally allowed in CLSI guidelines, in cases in which the working group feels strongly that a particular action is either required or prohibited, or when a guideline addresses provisions based on regulations. In Subchapter 1.2.1, the use of the term “must” was evaluated by the working group and deemed appropriate because the use is based on a requirement.

NOTE 2: The findings and conclusions in this document are those of the authors and do not necessarily reflect the views of the organizations they represent.

Key Words

Agar dilution, antimicrobial agent, antimicrobial susceptibility, antimicrobial susceptibility testing, broth dilution, broth microdilution, disk diffusion, minimal inhibitory concentration, susceptibility testing

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 quality control 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 quality control parameters.
- Educate users through multimedia communication of standards and guidelines.
- Foster a dialogue 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.

Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria

Chapter 1: Introduction

This chapter includes:

- Document scope and applicable exclusions
- Background information pertinent to the document content
- Standard precautions information
- "Note on Terminology" that highlights particular use and/or variation in use of terms and or/definitions
- Terms and definitions used in the document
- Abbreviations and acronyms used in the document

1.1 Scope

CLSI documents M02,[1] M07,[2] and M100[3] describe standardized methods and interpretive criteria for antimicrobial susceptibility testing of common aerobic bacteria, including some fastidious organisms. However, a number of less frequently encountered or fastidious bacteria are not addressed in those CLSI documents despite their potential to cause serious infections. M45 addresses these latter organisms with the goal of providing recommendations for clinical microbiology laboratories on how and when to determine the susceptibility of these diverse organisms. This document also provides guidance for public health laboratory testing of bacteria potentially associated with bioterrorism.

This edition of M45 includes taxonomic updates and several new tables to address organisms more likely to be identified in laboratories using sequencing or matrix-assisted laser desorption/ionization time-of-flight mass spectrometry for the identification of bacteria. The intent of this revision is to assist laboratories in determining an approach for testing that is relevant to their individual practice settings.

The methods provided may be used in clinical, public health, and research laboratories.

This guideline does not address commercial susceptibility testing devices.

1.2 Background

Organisms that previously lacked defined methods for susceptibility testing and interpretive criteria included various coryneform bacteria, *Bacillus* spp. (other than *Bacillus anthracis*), *Abiotrophia* spp., *Granulicatella* spp., several genera of gram-positive bacteria with intrinsic glycopeptide resistance (eg, *Erysipelothrix* spp., *Leuconostoc* spp., and *Pediococcus* spp.), as well as several species of fastidious gram-negative bacteria (eg, HACEK group organisms and *Pasteurella* spp.). In addition, more detailed guidance for test performance and interpretation was needed, especially breakpoints for *Listeria* spp., *Aeromonas* spp., *Vibrio* spp., *Moraxella catarrhalis,* and *Campylobacter* spp. The lack of test methods or interpretive criteria made it difficult to assess the frequency of acquired resistance in these less frequently isolated or fastidious organisms and discouraged the testing of individual patient isolates by clinical laboratories.

However, concerns had been raised that resistance exists in some of these organisms, and that laboratories should be prepared to test them when appropriate.[4,5] Subsequently, methods previously described in CLSI document M100[3] for testing *Helicobacter pylori*, *Vibrio cholerae*, and potential bacterial agents of bioterrorism were relocated to M45. Recently, it was determined that methods for testing *Aerococcus* spp., *Gemella* spp., *Lactococcus* spp., *Micrococcus* spp. and *Rothia mucilaginosa* were needed and these were added to M45.

Because infections due to organisms addressed in M45 occur less frequently than many of the organisms presently covered in CLSI documents M02,[1] M07,[2] and M100,[3] and because many of the antimicrobial agents of interest have been marketed for a number of years, it is not reasonable to expect the intensive CLSI document M23[6]–specified studies to be conducted on this special group of organisms. Instead, the goal of this document is to recommend test conditions and interpretive criteria based on a careful review of published microbiological data (distributions of minimal inhibitory concentrations [MICs]), limited animal model studies, the extant medical literature regarding therapy for these organisms, and, in a few instances, a review of existing pharmacokinetic data on the drugs of interest. In some cases, limited *in vitro* studies were performed.

1.2.1 Potential Bacterial Agents of Bioterrorism

Potential bacterial agents of bioterrorism are included in M45 and should be forwarded to appropriate reference or public health laboratories for identification, confirmation, and possible susceptibility testing. The procedures included in this document are intended for use by those reference or public health laboratories. All of the bacterial species identified by the Select Agent Regulations[7] could pose a severe threat to public health and safety. Entities that possess, use, or transfer these select agents must be registered with the US Departments of Health and Human Services and Agriculture. Clinical laboratories that are not registered should transfer these agents to a registered reference or public health laboratory in accordance with the Select Agent Regulations. Laboratories outside the United States should check local public health requirements for handling and reporting of potential bacterial agents of bioterrorism. In Canada, such agents fall under the Human Pathogens and Toxins Act (http://www.phac-aspc.gc.ca/lab-bio/regul/hpta-lapht-eng.php). Suspect isolates should be forwarded to the National Microbiology Laboratory in Winnipeg (BADD.NML@phac-aspc.gc.ca) or a member of the Canadian Laboratory Response Network for antimicrobial susceptibility testing.

1.2.2 The Development of Interpretive Criteria or Breakpoints

In order to establish MIC interpretive criteria or breakpoints for new antimicrobial agents, modify existing breakpoints, or establish breakpoints for organisms that have not previously existed in CLSI documents M02[1] and M07,[2] the Subcommittee on Antimicrobial Susceptibility Testing used an intensive analysis of MIC ranges of a particular drug with isolates that lack known resistance mechanisms, as well as with isolates that contain known resistance mechanisms that affect the activity of the particular drug class. In addition, clinical and bacteriological response data collected during large clinical trials of new agents, as well as pharmacokinetic and pharmacodynamic simulations, are considered. The process of integrating these types of data is described in detail in CLSI document M23.[6] Notably, however, when establishing or reestablishing breakpoints for older drugs or for organisms that have previously lacked breakpoints, large prospectively collected clinical data are often not available. This guideline was developed to assist clinical microbiology laboratories in developing a strategy for susceptibility testing of infrequently encountered or fastidious organisms when circumstances indicate that testing of individual isolates would be helpful for clinical management, or for surveys of resistance for public health or research purposes. The testing methods and interpretive breakpoints included in this guideline were proposed based on an exhaustive search of the medical literature and the experiences of the working group members. In many cases, breakpoints were adapted from those for other, related organisms with approved CLSI breakpoints (see CLSI document M100[3]) because of the similarities between MIC distributions and types of infections that the organisms caused. The derivation of the breakpoint is noted in the table for each organism. As stated,

the large databases requested in CLSI document M23[6] have not been available for assessment with the "orphan" organisms included in this guideline.

1.3 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens are treated as infectious and handled according to "standard precautions." Standard precautions are guidelines that combine the major features of "universal precautions and body substance isolation" practices. Standard precautions cover the transmission of all known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of bloodborne pathogens. The Centers for Disease Control and Prevention addresses this topic in published guidelines that address the daily operations of diagnostic medicine in humans and animals while encouraging a culture of safety in the laboratory.[8] For specific precautions for preventing the laboratory transmission of all known infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all known infectious diseases, refer to CLSI document M29.[9]

1.4 Terminology

1.4.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization wherever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in the United States, Europe, and elsewhere; that these differences are reflected in CLSI, International Organization for Standardization, and European Committee for Standardization (CEN) documents; and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. In light of this, CLSI's consensus process focuses on harmonization of terms to facilitate the global application of standards and guidelines.

1.4.2 Definitions

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

1) **susceptible (S)** – a category that 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) **intermediate (I)** – a category that includes isolates with antimicrobial agent minimal inhibitory concentrations (MICs) that approach usually attainable blood and tissue levels and for which response rates may be lower than for susceptible isolates; **NOTE:** 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.

3) **resistant (R)** – a category that implies that isolates are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules and/or that demonstrate zone diameters that fall in the range in which 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.

4) **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.

minimal inhibitory concentration (MIC) – the lowest concentration of an antimicrobial agent that prevents visible growth of a microorganism in an agar or broth dilution susceptibility test.

quality control (QC) – the operational techniques and activities that are used to fulfill requirements for quality; **NOTE 1:** In health care testing, the set of procedures designed to monitor the test method and the results to ensure test system performance; **NOTE 2:** QC includes testing control materials, charting the results and analyzing them to identify sources of error, and evaluating and documenting any remedial action taken as a result of this analysis.

1.4.3 Abbreviations and Acronyms

ATCC®[a]	American Type Culture Collection
BAP	blood agar plate
BMHA	Mueller-Hinton agar with 5% sheep blood
BSL-2	Biosafety Level 2
BSL-3	Biosafety Level 3
CAMHB	cation-adjusted Mueller-Hinton broth
CAMHB-LHB	cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood
CDC	Centers for Disease Control and Prevention
CFU	colony-forming unit(s)
CSF	cerebrospinal fluid
HTM	*Haemophilus* Test Medium
I	intermediate
LHB	lysed horse blood
MHA	Mueller-Hinton agar
MIC	minimal inhibitory concentration
QC	quality control
R	resistant
RNA	ribonucleic acid
rRNA	ribosomal ribonucleic acid
S	susceptible

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

Chapter 2: Indications for Performing Susceptibility Tests

This chapter includes:

- An overview of indications for performing susceptibility testing

Susceptibility testing is indicated when therapy is warranted for an infection caused by an organism for which the susceptibility profile cannot be reliably predicted. Susceptibility tests are most often indicated when the causative organism is thought to belong to a species capable of exhibiting resistance to commonly used antimicrobial agents. Certain organisms included in this guideline comprise part of the normal microbiota of human skin and mucous membranes (eg, *Aerococcus* spp., *Corynebacterium* spp., *Abiotrophia* spp., *Granulicatella* spp., *Lactobacillus* spp., *Micrococcus* spp., *Pediococcus* spp., *Leuconostoc* spp.) or represent environmental organisms (*Bacillus* spp.). Susceptibility testing of these organisms should not be performed on isolates from nonsterile or superficial sources. The need for susceptibility testing of *Aeromonas* spp. and *Vibrio* spp. isolates recovered from feces is controversial.

Generally, testing of the organisms included in this document should be limited to isolates recovered from normally sterile sites (eg, blood, CSF, joint or bone specimens, prosthetic devices, or long-term indwelling catheters), serious wound infections (*Aeromonas* spp. and *Vibrio* spp.), and refractory or persistent diarrhea due to *Campylobacter jejuni/coli* or gastritis due to *H. pylori*. When the nature of the infection is not clear and the specimen contains mixed growth of normal flora in which the organisms probably bear little relationship to the infectious process, susceptibility tests are often unnecessary, and the results may be misleading. Many times, therapy of individual patients infected with the organisms included in this guideline will be empiric, based on the fact that a genus or species is very likely susceptible to a highly effective drug such that susceptibility testing would not be required. Consultation with an infectious disease–trained physician is recommended for assistance in determining the need for testing and the interpretation of results.

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Chapter 3: Methods for Antimicrobial Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria

This chapter includes:

- Recommendations for selection of antimicrobial agents
- Methods for dilution antimicrobial susceptibility testing
- Methods for disk diffusion antimicrobial susceptibility testing
- Information on detection of resistance to some β-lactams by a direct β-lactamase test
- Therapy-related comments

This document uses the standard broth microdilution and agar dilution techniques (*H. pylori* only). Both techniques are taken from CLSI document M07[2] and based largely on information gathered from the International Collaborative Study on Antibiotic Sensitivity Testing.[10] Although the broth microdilution method is primarily a standard reference method, it may be sufficiently practical to warrant its use in both clinical and research laboratories. The details of performing the broth microdilution procedure are not repeated in this document. Readers should refer to CLSI document M07[2] for procedural details. However, key elements of the recommended methods are highlighted in each organism table for easy reference.

3.1 Selection of Antimicrobial Agents

To make routine susceptibility testing relevant and practical, the number of antimicrobial agents tested should be limited. In each organism table in this document, the consensus primary antimicrobial agents for testing are highlighted in a box labeled "Agents to Consider for Primary Testing." Interpretive criteria are provided for the primary agents and several potentially useful alternatives for each organism (see Tables 1 to 21). This presentation does not imply that testing of every agent in each table should be undertaken. In consultation with the clinicians caring for the patient, a priority list of critical drugs for a specific patient's isolate can be developed. It is inappropriate to report some agents on isolates from specific body sites because of poor delivery of those agents to the sites.

Agents that should not be reported on isolates from CSF include:

- Agents administered by oral route only
- First- and second-generation cephalosporins (except cefuroxime parenteral) and cephamycins
- Clindamycin
- Macrolides
- Tetracyclines
- Fluoroquinolones

Agents that should not be reported on isolates from urine specimens include:

- Chloramphenicol
- Clindamycin
- Erythromycin

Agents that should not be reported on isolates from respiratory specimens include:

- Daptomycin

For a comprehensive review of antimicrobial agent classes, including those in this document, refer to CLSI document M07.[2]

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3.2 Dilution Antimicrobial Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria

3.2.1 Broth Microdilution Procedure

The broth microdilution procedure using cation-adjusted Mueller-Hinton broth (CAMHB), CAMHB supplemented with lysed horse blood (CAMHB-LHB) (2.5% to 5% v/v) or defined growth supplement, *Haemophilus* Test Medium (HTM) or Brucella broth are used for the various fastidious organisms, as indicated in the individual tables and described in detail in CLSI document M07.[2] Users should consult CLSI document M07[2] for the details of medium preparation, drug dilutions, inoculum preparation, incubation, and reading of MIC end points.

3.2.2 Agar Dilution Procedure

The agar dilution procedure is recommended only for testing *H. pylori.*

3.2.3 Interpretive Categories

In addition to the MICs generated with one or more antimicrobial agents on a particular isolate, an interpretive category of susceptible, intermediate, resistant, or nonsusceptible can be assigned based on the tables in M45. Definitions of those categories are found in CLSI document M07[2] and in Subchapter 1.4.2.

3.3 Antimicrobial Disk Diffusion Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria

In many clinical microbiology laboratories, the agar disk diffusion method is used for testing common, rapidly growing bacterial pathogens and sometimes for fastidious species. In laboratories that routinely perform dilution testing or use an automated susceptibility testing device, the disk diffusion test may represent a convenient method for testing the infrequently isolated organisms described in this guideline. The standardized disk diffusion testing method recommended by the CLSI Subcommittee on Antimicrobial Susceptibility Testing is described in CLSI document M02.[1]

Disk diffusion testing interpretive criteria are provided, where possible. It is best suited to testing the rapidly growing pathogens (including *Aeromonas* spp. and *Vibrio* spp.) and modified for testing some fastidious organisms, such as *C. jejuni/coli, M. catarrhalis,* and *Pasteurella* spp. Adequate studies have not been conducted to recommend reproducible disk diffusion breakpoints for many of the organisms in this guideline. For those organisms, only the broth microdilution test or agar dilution (*H. pylori*) should be performed.

The preparation of Mueller-Hinton agar (MHA) including supplementation with 5% defibrinated sheep blood for fastidious organisms is described in CLSI document M02.[1]

3.4 Detection of Resistance to Some β-Lactams by a Direct β-Lactamase Test

Testing for β-lactamase activity using a chromogenic, cephalosporin-based method such as nitrocefin may yield clinically relevant information earlier than the results of an MIC test. A positive β-lactamase test result predicts resistance to penicillin, ampicillin, and amoxicillin among *Aggregatibacter* spp., *Cardiobacterium hominis, Eikenella corrodens, Haemophilus* spp., *Kingella* spp., *M. catarrhalis,* and *Pasteurella* spp.

A negative β-lactamase test result does not rule out resistance due to other mechanisms. β-lactamase testing should only be performed on the organisms listed above.

3.5 Therapy-Related Comments

Some of the table comments 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 indicating that "Rifampin should not be used alone for antimicrobial therapy."

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Chapter 4: Quality System Essentials for Antimicrobial Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria

This chapter includes:

- Overview of QC for antimicrobial susceptibility testing for infrequently isolated or fastidious bacteria
- Minimum laboratory requirements for testing infrequently isolated or fastidious bacteria

4.1 Quality Control

An effective QC program is designed to monitor the accuracy of a susceptibility test procedure, the performance of reagents and equipment, and the performance of persons who conduct the tests. These goals are best realized with the use of standard reference strains selected for their genetic stability and for their usefulness in the particular method. A detailed approach to performance of routine QC testing and maintenance of QC strains is outlined in CLSI documents M02[1] and M07.[2] The most current editions of those documents should be consulted for the recommended QC procedures. Rather than attempting to identify numerous new QC reference strains that correspond to the many genera and species included in this guideline, the standard control strains listed in CLSI documents M02,[1] M07,[2] and M100[3] are applicable to QC of the media, antimicrobial agents, and procedures recommended in M45. For that reason, an abbreviated list of acceptable limits of MICs and zone diameters was extracted from CLSI document M100[3] for inclusion in Tables 23A, 23B, 23E, 23F, 24A, and 24B of M45. Other control values may be extracted from CLSI document M100,[3] if needed, to provide on-scale MICs for individual test panels. For *Campylobacter* spp. and *H. pylori,* QC strains representing these species were identified and added to Tables 23C and 23D, respectively.

4.2 Minimum Laboratory Requirements for Testing Infrequently Isolated or Fastidious Bacteria

Most MIC and disk diffusion tests described in M45 should be performed only in select situations by qualified laboratorians experienced with the recommended procedures. Criteria that can be used to determine qualifications include:

- Performs antimicrobial susceptibility testing at least once per week using a CLSI broth microdilution reference method, or a US Food and Drug Administration–cleared commercial method or other approved methods that may be used by laboratories outside the United States with visual interpretations of MICs, and that may be adapted and validated for the testing conditions described in this guideline
- Performs antimicrobial susceptibility testing at least once per week using a CLSI disk diffusion reference method
  - If *Aeromonas* spp., *Vibrio* spp., *C. jejuni/coli, M. catarrhalis,* or *Pasteurella* spp. will be tested by disk diffusion
- Possesses the most current editions of CLSI documents (ie, M02,[1] M07,[2] and M100[3])
- Is part of a clinical microbiology laboratory directed by a doctoral-level clinical microbiologist, infectious diseases physician, or pathologist with expertise in antimicrobial susceptibility testing
- Possesses appropriate biosafety facilities and legal authority to work with potential agents of bioterrorism, if these organisms are being tested

Information and Interpretive Criteria for Susceptibility Testing

Table 1. *Abiotrophia* spp. and *Granulicatella* spp. (Formerly Known as Nutritionally Deficient or Nutritionally Variant Streptococci)

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) and 0.001% (ie, 10 µg/mL) pyridoxal hydrochloride **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 20 to 24 hours	*S. pneumoniae* ATCC®* 49619 **See QC Table 23B.**	Cefotaxime or ceftriaxone Penicillin Vancomycin

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

General Comments

(1) Growth characteristics on routine media: very fastidious; requires cysteine or pyridoxal for growth. Some strains may grow marginally on enriched chocolate agar or anaerobe agar formulations supplemented with added cysteine; 5% CO_2; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria S	I	R	Comments
PENICILLINS					**(3) Combined therapy with a penicillin (or vancomycin) and gentamicin is recommended for endocarditis.**
	Penicillin	≤0.12	0.25–2	≥4	
	Ampicillin	≤0.25	0.5–4	≥8	
CEPHEMS					
	Cefepime	≤1	2	≥4	
	Cefotaxime	≤1	2	≥4	
	Ceftriaxone	≤1	2	≥4	
CARBAPENEMS					
	Imipenem	≤0.5	1	≥2	
	Meropenem	≤0.5	1	≥2	
GLYCOPEPTIDES					
	Vancomycin	≤1	–	–	See comments (2) **and (3).**
MACROLIDES					
	Erythromycin	≤0.25	0.5	≥1	

Table 1. (Continued)

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria			Comments
		S	I	R	
FLUOROQUINOLONES					
	Ciprofloxacin	≤1	2	≥4	
	Levofloxacin	≤2	4	≥8	
PHENICOLS					
	Chloramphenicol	≤4	–	≥8	
LINCOSAMIDES					
	Clindamycin	≤0.25	0.5	≥1	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Abiotrophia spp. and *Granulicatella* spp. may demonstrate diminished susceptibility to penicillin, resulting in greater difficulty in treatment of patients with endocarditis. Fluoroquinolone resistance has been reported in an isolate from an immunosuppressed patient.[11,12]

Reasons for Testing/Not Testing:
For isolates from respiratory sources or wounds, testing is usually not necessary. Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue, implanted prosthetic devices) may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for viridans group *Streptococcus* spp., as published in CLSI document M100.[3] Key citations used in derivation of interpretive breakpoints are referenced.[13,14]

Testing Notes:
Many laboratories cannot readily distinguish *Abiotrophia* spp. from *Granulicatella* spp. or determine species-level identification. The requirement for cysteine or pyridoxal in the medium or satellite growth is characteristic for both *Abiotrophia* and *Granulicatella.*

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

Table 2. *Aerococcus* spp.[a]

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; 5% CO_2; 20 to 24 hours	***S. pneumoniae*** **ATCC®* 49619** **See QC Table 23B.**	**Penicillin** **Ceftriaxone** **Vancomycin**

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

General Comments

(1) Growth characteristics on routine media: often fastidious, requires blood-supplemented media for adequate growth; CO_2; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Penicillin	**≤0.12**	**0.25–2**	**≥4**	
CEPHEMS					
	Cefotaxime	**≤1**	**2**	**≥4**	
	Ceftriaxone	**≤1**	**2**	**≥4**	
CARBAPENEMS					
	Meropenem	**≤0.5**	**–**	**–**	**See comment (2).**
GLYCOPEPTIDES					
	Vancomycin	**≤1**	**–**	**–**	**See comment (2).**
FLUOROQUINOLONES					
	Ciprofloxacin	**≤1**	**2**	**≥4**	
	Levofloxacin	**≤2**	**4**	**≥8**	
TETRACYCLINES					
	Tetracycline	**≤2**	**4**	**≥ 8**	
FOLATE PATHWAY INHIBITORS					
	Trimethoprim-sulfamethoxazole	**≤2/38**	**–**	**≥4/76**	
OXAZOLIDINONES					
	Linezolid	**≤2**	**–**	**–**	**See comment (2).**

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Footnote

a. Data evaluated for this guideline include only *Aerococcus urinae, Aerococcus viridans,* and *Aerococcus sanguinocola.*

Table 2. (Continued)

Supplemental Information

Resistance:
***Aerococcus* spp. are usually susceptible to β-lactams and vancomycin. Resistance has been described to the fluoroquinolones, associated with mutations to the quinolone resistance determining region of *gyrA* or *parC*. *A. sanguinocola* and *A. viridans* isolates commonly display resistance to levofloxacin.[15,16]**

Reasons for Testing/Not Testing:
Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue, implanted prosthetic devices) may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for viridans group *Streptococcus* spp., as published in CLSI document M100,[3] with the exception of trimethoprim-sulfamethoxazole, which are adapted from those for *Staphylococcus* spp., as published in CLSI document M100.[3] In addition to the references listed at the end of this document, data from organism collections tested by two of the working group members and MIC data provided by several clinical laboratories were used to derive the interpretive breakpoints.[17]

Testing Notes:
***A. urinae* may appear susceptible to trimethoprim-sulfamethoxazole *in vitro* when tested on media supplemented with LHB, which contains thymidine phosphorylase. However, *in vivo* susceptibility may depend on urinary folate concentrations, which differ based on the patient's diet. For this reason, trimethoprim-sulfamethoxazole testing should not be performed on *A. urinae*.**

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

Table 3. *Aeromonas* spp. (Includes Members of *Aeromonas caviae* Complex, *Aeromonas hydrophila* Complex, and *Aeromonas veronii* Complex)[a]

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB for microdilution; Disk diffusion: MHA **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; Disk diffusion: 16 to 18 hours Broth microdilution method: 16 to 20 hours	*E. coli* ATCC®* 25922 ***P. aeruginosa* ATCC® 27853 (for carbapenems)** *E. coli* ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations) **See QC Tables 23A and 24A.**	3rd- or 4th-generation cephalosporins Fluoroquinolones Trimethoprim-sulfamethoxazole

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

General Comment

(1) Growth characteristics on routine media: nonfastidious; grows well on a blood agar plate; ambient air; 16 to 20 hours.

Antimicrobial Class	Antimicrobial Agent	Disk Content	Zone Diameter (mm) Interpretive Criteria			MIC (µg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
PENICILLINS AND β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
	Piperacillin-tazobactam	100/10 µg	≥21	18–20	≤17	≤ 16/4	32/4–64/4	≥128/4	
CEPHEMS									
	Cefepime	30 µg	**≥25**	**19–24**	**≤18**	**≤2**	**4–8**	**≥16**	**Interpretive criteria are based on a dosage regimen of 1 g every 12 h.**
	Cefotaxime	30 µg	≥26	23–25	≤22	≤1	2	≥4	Interpretive criteria are based on a dosage regimen of 1 g every 8 h.
	Cefoxitin	30 µg	≥18	15–17	≤14	≤8	16	≥32	
	Ceftazidime	30 µg	≥21	18–20	≤ 17	≤ 4	8	≥16	Interpretive criteria are based on a dosage regimen of 1 g every 8 h.
	Ceftriaxone	30 µg	≥23	20–22	≤19	≤1	2	≥4	Interpretive criteria are based on a dosage regimen of 1 g every 24 h.
	Cefuroxime sodium (parenteral)	30 µg	≥18	15–17	≤14	≤8	16	≥32	Interpretive criteria are based on a dosage regimen of 1.5 g every 8 h.
CARBAPENEMS									
	Doripenem	**10 µg**	**≥23**	**20–22**	**≤19**	**≤1**	**2**	**≥4**	**Interpretive criteria are based on a dosage regimen of 500 mg every 8 h.**
	Ertapenem	10 µg	**≥22**	**19–21**	**≤18**	**≤0.5**	**1**	**≥2**	**Interpretive criteria are based on a dosage regimen of 1 g every 24 h.**
	Imipenem	10 µg	**≥ 23**	**20–22**	**≤ 19**	**≤ 1**	**2**	**≥ 4**	**Interpretive criteria are based on a dosage regimen of 500 mg every 6 h or 1 g every 8 h.**

Table 3. (Continued)

Antimicrobial Class	Antimicrobial Agent	Disk Content	Zone Diameter (mm) Interpretive Criteria			MIC (μg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
CARBAPENEMS (Continued)									
	Meropenem	10 μg	**≥ 23**	**20–22**	**≤ 19**	**≤ 1**	**2**	**≥ 4**	**Interpretive criteria are based on a dosage regimen of 1 g every 8 h.**
MONOBACTAMS									
	Aztreonam	30 μg	≥ 21	18–20	≤ 17	≤ 4	8	≥ 16	Interpretive criteria are based on a dosage regimen of 1 g every 8 h.
AMINOGLYCOSIDES									
	Amikacin	30 μg	≥ 17	15–16	≤ 14	≤ 16	32	≥ 64	
	Gentamicin	10 μg	≥ 15	13–14	≤ 12	≤ 4	8	≥ 16	
TETRACYCLINES									
	Tetracycline	30 μg	≥ 15	12–14	≤ 11	≤ 4	8	≥ 16	
FLUOROQUINOLONES									
	Ciprofloxacin	5 μg	≥ 21	16–20	≤ 15	≤ 1	2	≥ 4	
	Levofloxacin	5 μg	≥ 17	14–16	≤ 13	≤ 2	4	≥ 8	
FOLATE PATHWAY INHIBITORS									
	Trimethoprim-sulfamethoxazole	1.25/23.75 μg	≥ 16	11–15	≤ 10	≤ 2/38	–	≥ 4/76	
PHENICOLS									
	Chloramphenicol	30 μg	≥ 18	13–17	≤ 12	≤ 8	16	≥ 32	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Footnote

a. Most of the published data on susceptibility testing are limited to these three *Aeromonas* spp.

Supplemental Information

Resistance:

Aeromonas spp. are uniformly resistant to ampicillin**, amoxicillin-clavulanate, and cefazolin.** *Aeromonas* strains may possess multiple, distinct, inducible β-lactamases, and like other genera with inducible β-lactamases, resistance to extended-spectrum cephalosporins may emerge during therapy with a β-lactam. **The significance of the carbapenemase produced by some strains is not fully understood.[18] Treatment failures have been noted for *Aeromonas* spp. with elevated but susceptible ciprofloxacin MICs.[19]**

Reasons for Testing/Not Testing:

Testing is **usually** limited to isolates from extraintestinal sites.

Table 3. (Continued)

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for *Enterobacteriaceae,* as published in CLSI document M100.[3] Key citations used in derivation of interpretive breakpoints are referenced.[20-28]

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

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Table 4. *Bacillus* spp. (Not *Bacillus anthracis*) and Related Genera[a]

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 16 to 20 hours	*S. aureus* ATCC®* 29213 **See QC Table 23A.**	Clindamycin Fluoroquinolones Vancomycin

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

General Comments

(1) Growth characteristics on routine media: nonfastidious; grows well on blood plates; ambient air; 16 to 20 hours.

(2) For some organism/antimicrobial combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Penicillin	≤0.12	–	≥0.25	
	Ampicillin	≤0.25	–	≥0.5	
CARBAPENEMS					
	Imipenem	≤4	8	≥16	
	Meropenem	**≤4**	**8**	**≥16**	
GLYCOPEPTIDES					
	Vancomycin	≤4	–	–	See comment (2).
AMINOGLYCOSIDES					
	Amikacin	≤16	32	≥64	
	Gentamicin	≤4	8	≥16	
MACROLIDES					
	Erythromycin	≤0.5	1–4	≥8	
TETRACYCLINES					
	Tetracycline	≤4	8	≥16	
FLUOROQUINOLONES					
	Ciprofloxacin	≤1	2	≥4	
	Levofloxacin	≤2	4	≥8	
LINCOSAMIDES					
	Clindamycin	≤0.5	1–2	≥4	

Table 4. (Continued)

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria			Comments
		S	I	R	
FOLATE PATHWAY INHIBITORS					
	Trimethoprim-sulfamethoxazole	≤2/38	–	≥4/76	
PHENICOLS					
	Chloramphenicol	≤8	16	≥32	
ANSAMYCINS					
	Rifampin	≤1	2	≥4	(3) *Rx:* **Rifampin should not be used alone for antimicrobial therapy.**

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MIC, minimal inhibitory concentration, QC, quality control, R, resistant; S, susceptible.

Footnote

a. Related genera include *Brevibacillus, Cohnella, Lysinibacillus, Paenibacillus,* and *Sporolactobacillus.*

Supplemental Information

Resistance:
Bacillus cereus **and *Bacillus thuringiensis* are generally resistant to penicillins and cephalosporins due to production of a potent broad-spectrum β-lactamase.[29] *Bacillus* spp. are usually susceptible to several other drug classes including vancomycin, aminoglycosides, macrolides, and quinolones.**

Reasons for Testing/Not Testing:
Bacillus spp. are frequently encountered as contaminating bacteria in cultures. Testing of isolates from normally sterile sources (eg, deep tissue, CSF, multiple positive blood cultures) may be warranted, especially in patients with an implanted prosthetic device, immunosuppression, or history of intravenous drug abuse.

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for *Staphylococcus* spp., as published in CLSI document M100.[3] Interpretive criteria for carbapenems were initially adapted in 2012 (CLSI document M100-S22), before removing breakpoints for these β-lactams from the *Staphylococcus* spp. table. Key citations used in derivation of interpretive breakpoints are referenced.[29-32]

Testing Notes:
Although many *Bacillus* spp. produce β-lactamase, β-lactamase testing of this genus is unreliable.

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

Table 5. *Campylobacter jejuni/coli*

Testing Conditions

Medium: Broth microdilution: CAMHB-LHB (2.5% to 5% v/v)
Disk diffusion: BMHA
Inoculum: Direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation: Broth microdilution method: 36 to 37°C for 48 hours; 42°C for 24 hours (Incubation at less than 36°C or greater than 42°C may not yield satisfactory growth.)
Disk diffusion: 42°C for 24 hours
Microaerobic atmosphere equivalent to 10% CO_2, 5% O_2, and 85% N_2. Use of a compressed gas incubator is preferable; however, acceptable performance may be achieved using microaerobic gas-generating sachets. Sealed plastic bags or pouches do not result in reproducible data and are not recommended.

NOTE: Agar dilution testing is described in CLSI documents **VET01[33] and VET01S.**[34]

Routine QC Recommendations

Microdilution:
C. jejuni ATCC®* 33560, 36 to 37°C for 48 hours or 42°C for 24 hours

Disk Diffusion:
S. aureus ATCC® 25923, MHA, 35 to 37°C for 16 to 18 hours in ambient air

See QC Tables 23C and 24A.

Agents to Consider for Primary Testing

Ciprofloxacin
Erythromycin
Tetracycline

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

General Comment

(1) Growth characteristics on routine media: fastidious; grows on media such as BMHA; requires a microaerobic atmosphere (10% CO_2, 5% O_2, and 85% N_2); 36 to 37°C for 48 hours or 42°C for 24 hours.

Antimicrobial Class	Antimicrobial Agent	Disk Content	Zone Diameter (mm) Interpretive Criteria			MIC (µg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
MACROLIDE									
	Erythromycin	15 µg	**≥16**	**13–15**	**≤12**	≤8	16	≥32	**(2) Susceptibility and resistance to azithromycin can be predicted by testing erythromycin.**
FLUOROQUINOLONE									
	Ciprofloxacin	5 µg	**≥24**	**21–23**	**≤20**	≤1	2	≥4	
TETRACYCLINES									
	Tetracycline	30 µg	**≥26**	**23–25**	**≤22**	≤4	8	≥16	
	Doxycycline	–	–	–	–	≤2	4	≥8	**Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline.**

Abbreviations: ATCC®, American Type Culture Collection; BMHA, Mueller-Hinton agar with 5% sheep blood; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MHA, Mueller-Hinton Agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Table 5. (Continued)

Supplemental Information

Resistance:
Resistance among *C. jejuni/C. coli* is known to occur with erythromycin (0% to 11%) but is more problematic with fluoroquinolones and is highly variable from country to country, with rates of 10% to as high as 40% being reported. Emergence of resistance to ciprofloxacin may occur while the patient is on therapy. Strains resistant to both macrolides and fluoroquinolones have been reported.

Reasons for Testing/Not Testing:
Testing may be useful for epidemiological purposes or for management of patients with prolonged or severe symptoms.

Derivation of Interpretive Criteria:
MIC interpretive criteria are adapted from those for *Enterobacteriaceae* (ciprofloxacin and tetracycline), as published in CLSI document M100.[3] **MIC** interpretive criteria for erythromycin and doxycycline are based on population distributions following testing of 150 strains of wild-type *C. jejuni/coli* at 36 to 37°C, using a microaerobic atmosphere for 48 hours. **Disk diffusion interpretive criteria for erythromycin, ciprofloxacin, and tetracycline were developed by testing 206 *C. jejuni* and 101 *C. coli* isolates with MIC-zone diameter regression analysis and error-rate bounding showing only minor errors (< 2%).** Key citations used in derivation of interpretive breakpoints are referenced (see CLSI documents VET01[33] and VET01S[34]).[35-37]

Testing Notes:
To improve reading of zones, BMHA plates should be dried before inoculation (at 20 to 25ºC overnight or at 35ºC with the lid removed for 15 minutes). Disk diffusion zone diameters are determined after tilting the plate and measuring the smallest zone with no growth of inner colonies.

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

Table 6. *Corynebacterium* spp. (Including *Corynebacterium diphtheriae*) and Related Coryneform Genera[a]

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v). If testing daptomycin, the medium should contain 50 µg/mL calcium. **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 24 to 48 hours (see Testing Notes)	*S. pneumoniae* ATCC®* 49619 *E. coli* ATCC® 25922 for gentamicin **See QC Table 23B.**	Erythromycin Gentamicin Penicillin Vancomycin

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

General Comments

(1) Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; ambient air; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Penicillin	**≤0.12**	**0.25–2**	**≥4**	
CEPHEMS					
	Cefepime	≤1	2	≥4	
	Cefotaxime	≤1	2	≥4	
	Ceftriaxone	≤1	2	≥4	
CARBAPENEMS					
	Meropenem	**≤ 0.25**	**0.5**	**≥1**	
GLYCOPEPTIDES					
	Vancomycin	≤2	–	–	See comment (2).
LIPOPEPTIDES					
	Daptomycin	≤1	–	–	See comment (2).
AMINOGLYCOSIDES					
	Gentamicin	≤4	8	≥16	
MACROLIDES					
	Erythromycin	≤0.5	1	≥2	
FLUOROQUINOLONES					
	Ciprofloxacin	≤1	2	≥4	

Table 6. (Continued)

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria S	I	R	Comments
TETRACYCLINES					
	Doxycycline	≤4	8	≥16	
	Tetracycline	≤4	8	≥16	
LINCOSAMIDES					
	Clindamycin	≤0.5	1–2	≥4	
FOLATE PATHWAY INHIBITORS					
	Trimethoprim-sulfamethoxazole	≤2/38	–	≥4/76	
ANSAMYCINS					
	Rifampin	≤1	2	≥4	(3) *Rx:* **Rifampin should not be used alone for antimicrobial therapy.**
STREPTOGRAMINS					
	Quinupristin-dalfopristin	≤1	2	≥4	
OXAZOLIDINONES					
	Linezolid	≤2	–	–	See comment (2).

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Footnote

a. Coryneform genera include: *Arcanobacterium,* ***Arthrobacter,*** *Brevibacterium, Cellulomonas,* ***Cellulosimicrobium,*** *Dermabacter, Leifsonia, Microbacterium, Oerskovia, Rothia* (**excluding *Rothia mucilaginosa;* see Table 19),** ***Trueperella,*** and *Turicella.*

Supplemental Information

Resistance:

Resistance to β-lactams, macrolides, and aminoglycosides, as well as quinolones or folate pathway inhibitors, has been reported in *Corynebacterium afermentans, Corynebacterium amycolatum, Corynebacterium aurimucosum, Corynebacterium auris, Corynebacterium coyleae, C. diphtheriae, Corynebacterium glucuronolyticum, Corynebacterium jeikeium, Corynebacterium propinquum, Corynebacterium pseudodiphtheriticum, Corynebacterium resistens, Corynebacterium striatum, Corynebacterium tuberculostearicum* (which includes nearly all CDC group G-2 isolates), *Corynebacterium urealyticum*, and *Corynebacterium ureicelerivorans*. Resistance to erythromycin and clindamycin is nearly always attributable to the presence of the *ermX* or, occasionally, *ermB* gene.[38] Resistance to quinolones has been observed due to mutations in *gyrA.* Ophthalmic infections caused by *Corynebacterium macginleyi* are more difficult to treat with fluoroquinolone eye drops if a *gyrA* mutation is present.[39] Based on several recent reviews, all *Corynebacterium* remain susceptible to vancomycin, linezolid,[40,41] and tigecycline.[40] In addition, from among nearly 500 *Corynebacterium* strains, most were susceptible to daptomycin (99.6%) and quinupristin-dalfopristin (95.3%), with > 85% of isolates susceptible to rifampin, tetracycline, gentamicin, and meropenem (based on data collected by one member of the working group). A single daptomycin nonsusceptible *C. jeikeium* isolate has been reported.[42]

There are limited antimicrobial susceptibility and resistance mechanism data for other coryneform genera. In contrast to *Corynebacterium* spp., reduced susceptibility to daptomycin appears to be relatively common in other coryneform genera (based on data collected by one member of the working group). *Arcanobacterium haemolyticum* and *Trueperella* (formerly *Arcanobacterium*) *bernardiae* may be resistant to tetracycline.[43-45] *Arthrobacter* spp. have been reported to be resistant to aminoglycosides and quinolones.[46] *Brevibacterium* spp., particularly *Brevibacterium casei* and *Brevibacterium otitidis,* may demonstrate resistance to β-lactams and clindamycin.[47] *Dermabacter hominis* and *Turicella otitidis* may be macrolide and clindamycin resistant.[47] *Leifsonia aquatica* has been reported to have diminished vancomycin and penicillin susceptibility.[48] *Microbacterium resistens* and other *Microbacterium* spp. may be nonsusceptible to vancomycin.[49]

Table 6. (Continued)

Reasons for Testing/Not Testing:
Coryneforms are frequently encountered as contaminating bacteria in cultures. Testing of isolates from normally sterile sources (eg, deep tissue, CSF, multiple positive blood cultures) may be warranted, especially in patients with an implanted prosthetic device or immunosuppression.

Derivation of Interpretive Criteria:
Interpretive criteria for erythromycin are based primarily on MIC distributions following testing of a large number of isolates. Penicillin, cephalosporin, and meropenem interpretive criteria are adapted from those for *Streptococcus* spp., linezolid interpretive criteria are adapted from those for *Enterococcus* spp., and remaining interpretive criteria are adapted from those for *Staphylococcus* spp., as published in CLSI document M100.[3] **In addition to MIC data provided by clinical laboratories,** citations listed under Additional References were used to derive the interpretive breakpoints.

Testing Notes:
Isolates demonstrating susceptible results for β-lactams at 24 hours should be reincubated and results for that agent reported at 48 hours. Susceptible results for other agents can be reported after 24 hours of incubation if the control well shows adequate growth.

Lipophilic *Corynebacterium* species (*Corynebacterium kroppenstedtii, C. tuberculostearicum), Microbacterium hatanonsis*, and *Microbacterium oleivorans* may not grow sufficiently to be tested using the method described.

Limited data are available to support the use of these methods for *Auritidibacter, Curtobacterium, Exiguobacterium, Helcobacillus, Janibacter, Knoellia,* and *Pseudoclavibacter* spp.

The following asporogenous, gram-positive bacilli have been tested reliably using the methods recommended here but are not considered "coryneforms": aerotolerant strains of *Actinomyces* (*Actinomyces bovis, Actinomyces europaeus, Actinomyces graevenitzii, Actinomyces johnsonii, Actinomyces naeslundii, Actinomyces neuii, Actinomyces odontolyticus, Actinomyces oris* group, *Actinomyces radingae, Actinomyces turicensis, Actinomyces urogenitalis, Actinomyces viscosus*), aerotolerant strains of *Bifidobacterium* (*Bifidobacterium scardovii* and *Bifidobacterium tsurumense*), and some *Varibaculum* spp. Other *Actinomyces* spp. (eg, *Actinomyces dentalis* and *Actinomyces israelii), Actinobaculum* spp., and *Rothia dentocariosa* should be tested following anaerobic protocols.

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

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Table 7. *Erysipelothrix rhusiopathiae*

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 20 to 24 hours	*S. pneumoniae* ATCC®* 49619 **See QC Table 23B.**	Ampicillin or penicillin

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

General Comments

(1) Growth characteristics on routine media: fastidious; may take one to three days for colonies to grow on blood agar or chocolate agar; ambient air. At 24 hours, growth may be pinpoint colonies.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Ampicillin	≤0.25	–	–	See comment (2).
	Penicillin	≤0.12	–	–	See comment (2).
CEPHEMS					
	Cefepime	≤1	–	–	See comment (2).
	Cefotaxime	≤1	–	–	See comment (2).
	Ceftriaxone	≤1	–	–	See comment (2).
CARBAPENEMS					
	Imipenem	≤0.5	–	–	See comment (2).
	Meropenem	≤0.5	–	–	See comment (2).
MACROLIDES					
	Erythromycin	≤0.25	0.5	≥1	
FLUOROQUINOLONES					
	Ciprofloxacin	≤1	–	–	See comment (2).
	Gatifloxacin	≤1	–	–	See comment (2).
	Levofloxacin	≤2	–	–	See comment (2).
LINCOSAMIDES					
	Clindamycin	≤0.25	0.5	≥1	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Table 7. (Continued)

Supplemental Information

Resistance:
E. rhusiopathiae is considered intrinsically resistant to vancomycin **and aminoglycosides;** routine testing of these agents is not necessary.

Reasons for Testing/Not Testing:
Although antimicrobial susceptibility testing is not required, it is important to identify this organism promptly because of its potentially fulminant nature when causing endocarditis and the fact that it is intrinsically resistant to vancomycin, which is the therapy often used empirically for gram-positive organisms. For patients with penicillin allergy, testing of erythromycin and clindamycin may be warranted.

Derivation of Interpretive Criteria:
Interpretive criteria for ciprofloxacin are adapted from those for *Staphylococcus* spp., as published in CLSI document M100.[3] Interpretive criteria for all other antimicrobial agents are adapted from those for *Streptococcus* spp., as published in CLSI document M100.[3] **Key citations used in derivation of interpretive breakpoints are referenced.**[50-53]

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

Table 8. *Gemella* spp.

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** **Direct colony suspension, equivalent to a 0.5 McFarland standard** **Incubation:** **35°C; 5% CO_2; 24 to 48 hours**	***S. pneumoniae* ATCC®* 49619** **See QC Table 23B.**	**Cefotaxime or ceftriaxone** **Penicillin** **Vancomycin**

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

General Comments

(1) Growth characteristics on routine media: fastidious; requires blood-supplemented media for adequate growth; 5% CO_2 24 to 48 hours. *Gemella haemolysans* tends to prefer aerobic growth environments, while *Gemella morbillorum* is a facultative anaerobe.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Penicillin	**≤0.12**	**0.25–2**	**≥4**	**(3) Combined therapy with a penicillin (or vancomycin) and gentamicin is recommended for endocarditis.**
CEPHEMS					
	Cefotaxime	**≤1**	**2**	**≥4**	
	Ceftriaxone	**≤1**	**2**	**≥4**	
CARBAPENEMS					
	Meropenem	**≤0.5**	**1**	**≥2**	
GLYCOPEPTIDES					
	Vancomycin	**≤1**	**–**	**–**	**See comments (2) and (3).**
MACROLIDES					
	Erythromycin	**≤0.25**	**0.5**	**≥1**	
FLUOROQUINOLONES					
	Levofloxacin	**≤2**	**4**	**≥8**	
LINCOSAMIDES					
	Clindamycin	**≤0.25**	**0.5**	**≥1**	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Table 8. (Continued)

Supplemental Information

Resistance:
Limited data in the literature and data provided from working group members have shown *Gemella* spp. to be very susceptible to many antimicrobial agents, including penicillin.

Reasons for Testing/Not Testing:
Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue, implanted prosthetic devices) may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:
Interpretive criteria are from those for viridans group *Streptococcus* spp., as published in CLSI document M100.[3] In addition to MIC data provided by clinical laboratories, key references were used to derive interpretive breakpoints.[54,55]

Testing Notes:
Most isolates require 48-hour incubation to obtain adequate growth.

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

Table 9. HACEK Group: *Aggregatibacter* spp., *Cardiobacterium* spp., *Eikenella corrodens,* and *Kingella* spp.

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: **CAMHB-LHB (2.5% to 5% v/v)** **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; 5% CO_2; 24 to 48 hours **Medium:** **Alternatively HTM or Brucella broth with vitamin K (1 µg/mL), hemin (5 µg/mL) and 5% LHB (see Testing Notes)**	*S. pneumoniae* ATCC®* 49619 *E. coli* ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations) **See QC Table 23B.**	Ampicillin Amoxicillin-**clavulanate** Ceftriaxone or cefotaxime Ciprofloxacin or levofloxacin Imipenem Penicillin Trimethoprim-sulfamethoxazole

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

General Comments

(1) Growth characteristics on routine media: very fastidious; most will grow on blood agar or chocolate agar in CO_2; 24 to 48 hours. **Some strains behave as strict anaerobes and require anaerobic incubation.** See Testing Notes.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS AND β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS					
	Ampicillin	≤1	2	≥4	
	Ampicillin-sulbactam	≤2/1	–	≥4/2	
	Amoxicillin-clavulanate	≤4/2	–	≥8/4	
	Penicillin	≤1	2	≥4	
CEPHEMS					
	Ceftriaxone	≤2	–	–	See comment (2).
	Cefotaxime	≤2	–	–	See comment (2).
CARBAPENEMS					
	Imipenem (*Aggregatibacter* spp.)	≤4	8	≥16	
	Imipenem (all other species)	≤0.5	1	≥2	
	Meropenem (*Aggregatibacter* spp.)	≤4	8	≥16	
	Meropenem (all other species)	≤0.5	1	≥2	
MACROLIDES					
	Azithromycin	≤4	–	–	See comment (2).
	Clarithromycin	≤8	16	≥32	

Table 9. (Continued)

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria			Comments
		S	I	R	
FLUOROQUINOLONES					
	Ciprofloxacin	≤1	2	≥4	
	Levofloxacin	≤2	4	≥8	
TETRACYCLINES					
	Tetracycline	≤2	4	≥8	
PHENICOLS					
	Chloramphenicol	≤4	8	≥16	
ANSAMYCINS					
	Rifampin	≤1	2	≥4	(3) *Rx:* **Rifampin should not be used alone for antimicrobial therapy**.
FOLATE PATHWAY INHIBITORS					
	Trimethoprim-sulfamethoxazole	≤0.5/9.5	1/19–2/38	≥4/76	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; CFU, colony-forming unit(s); HTM, *Haemophilus* Test Medium; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:

Ampicillin and penicillin resistance due to β-lactamases that are inhibited by clavulanate has been reported for HACEK organisms. Some isolates may be β-lactam resistant due to mechanisms other than β-lactamase production. Macrolide and aminoglycoside resistance has been reported in *Aggregatibacter actinomycetemcomitans.*[56]

Reasons for Testing/Not Testing:

Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue), may be warranted, especially in patients with an implanted prosthetic device, immunosuppression, or β-lactam allergy. For isolates of *Eikenella* spp. from bite wound infections, testing may not be necessary when using amoxicillin-clavulanate, considering the high probability of susceptibility to amoxicillin-clavulanate.

Derivation of Interpretive Criteria:

Interpretive criteria for penicillin are based primarily on MIC distributions. Chloramphenicol interpretive criteria are adapted from those for viridans *Streptococcus* spp.; all others are adapted from those for *Haemophilus influenzae.* **In addition to MIC data provided by clinical laboratories,** key references, listed under Additional References, were used to derive interpretive breakpoints.

Testing Notes:

Routine performance of a β-lactamase test **(chromogenic cephalosporin method)** is recommended. A positive β-lactamase test result predicts resistance to penicillin, ampicillin, and amoxicillin. A negative β-lactamase test result does not rule out resistance due to other mechanisms.

It may be difficult to obtain satisfactory antimicrobial susceptibility test results with some HACEK group isolates due to their fastidious nature and poor growth in broth media.

Table 9. (Continued)

When tested by broth microdilution, some HACEK group isolates, such as those belonging to *Aggregatibacter* spp., have been shown to grow better in HTM broth. *Eikenella* spp. isolates may grow better in Brucella broth supplemented with vitamin K_1, hemin, and 5% lysed horse blood (LHB), the broth recommended in CLSI document M11[57] for anaerobic bacteria. Limited studies (unpublished data) demonstrated results obtained with MIC tests performed in HTM (*Aggregatibacter* spp., *Cardiobacterium* spp., and *Kingella* spp.) and Brucella broth (*Eikenella* spp.) are comparable to tests performed in CAMHB-LHB.

If using either HTM or **Brucella broth supplemented with vitamin K_1, hemin, and 5% LHB,** use QC organisms and QC ranges as listed in CLSI document M100.[3]

Although extensive studies have not been performed, methods outlined here may be appropriate for rare HACEK group organisms from the genera *Haemophilus* (eg, *Haemophilus haemolyticus, Haemophilus parahaemolyticus*).[58]

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

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Table 10. *Helicobacter pylori*

Testing Conditions	
Medium:	Agar dilution: MHA and aged (≥2-week-old) sheep blood (5% v/v)
Inoculum:	A saline suspension equivalent to a 2.0 McFarland standard (containing 1×10^7 to 1×10^8 CFU/mL), to be prepared from a 72-hour-old subculture from a BAP. The inoculum (1 to 3 μL per spot) is replicated directly onto the antimicrobial agent–containing agar dilution plates.
Incubation:	35°C ± 2°C; 72 hours; microaerobic atmosphere equivalent to 10% CO_2, 5% O_2, and 85% N_2. Use of a compressed gas incubator is preferable; however, acceptable performance may be achieved using microaerobic gas-generating sachets.

Routine QC Recommendations
H. pylori ATCC®* 43504
See QC Table 23D.

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

General Comment

(1) Growth characteristics on routine media: fastidious; optimal growth occurs on media supplemented with blood or serum; requires a microaerobic atmosphere (10% CO_2, 5% O_2, and 85% N_2); 36 to 37°C for at least 72 hours.

Test/Report Group	Antimicrobial Agent	MIC Interpretive Standard (μg/mL)			Comments
		S	I	R	
A	Clarithromycin	≤0.25	0.5	≥1.0	(2) These breakpoints presume that clarithromycin will be used in an approved regimen that includes a proton-pump inhibitor and possibly one or more additional antimicrobial agents.

Abbreviations: ATCC®, American Type Culture Collection; BAP, blood agar plate; CFU, colony-forming unit(s); I, intermediate; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Macrolide resistance in *H. pylori* has been ascribed to 23S ribosomal RNA (rRNA) point mutations (primarily 2143 and 2142 positions) and the resistance-nodulation cell division efflux pump system.[59]

Reasons for Testing/Not Testing:
Laboratories may be asked to culture and perform susceptibility testing on *H. pylori* isolates from apparent treatment failures.

Table 10. (Continued)

***In vitro* resistance to metronidazole under the test conditions described here does not reliably predict *in vivo* treatment failure; therefore, testing for metronidazole is not recommended.**

Derivation of Interpretive Criteria:
Clarithromycin interpretive criteria were initially published in 2010 (CLSI document M100-S20) after review of MIC distribution, clinical outcome, 23S rRNA sequence analysis, and pharmacokinetic data.

Testing Notes:
Aged sheep blood provides superior growth compared to plates prepared with fresh sheep blood.

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

Table 11. *Lactobacillus* spp.

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v); if testing daptomycin, the medium should contain 50 µg/mL calcium. **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; 5% CO_2; 24 to 48 hours	*S. pneumoniae* ATCC®* 49619 **See QC Table 23B.**	Ampicillin or penicillin

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

General Comments

(1) Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; 5% CO_2; 24 to 48 hours. **Vaginal strains such as *Lactobacillus crispatus, Lactobacillus gasseri, Lactobacillus iners* (often misidentified as *Lactobacillus acidophilus* by phenotypic tests), and *Lactobacillus jensenii,* grow poorly under 5% CO_2 and require anaerobic conditions for optimal growth.**

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					**(3) Therapy of serious infections such as endocarditis often involves combined therapy with a penicillin and gentamicin.**
	Penicillin	≤8	–	–	See comment (2).
	Ampicillin	≤8	–	–	
CARBAPENEMS					
	Imipenem	≤0.5	1	≥2	
	Meropenem	**≤1**	**2**	**≥4**	
GLYCOPEPTIDES					
	Vancomycin	≤2	4–8	≥16	
LIPOPEPTIDES					
	Daptomycin	≤4	–	–	See comment (2).
MACROLIDES					
	Erythromycin	≤0.5	1–4	≥8	
LINCOSAMIDES					
	Clindamycin	≤0.5	1	≥2	
OXAZOLIDINONES					
	Linezolid	≤4	–	–	See comment (2).

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Table 11. (Continued)

Supplemental Information

Resistance:
Many species of *Lactobacillus* spp. that grow well in ambient air (***Lactobacillus casei, Lactobacillus fermentum, Lactobacillus plantarum, Lactobacillus reuteri, Lactobacillus rhamnosus, Lactobacillus salivarius, Lactobacillus vaginalis,*** **and** ***Lactobacillus zeae*****) are intrinsically resistant to vancomycin. Vancomycin-susceptible species include** ***L. acidophilus, L. crispatus, L. gasseri, L. iners, L. jensenii, Lactobacillus johnsonii,*** **and** ***Lactobacillus lactis.***

Reasons for Testing/Not Testing:
Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue) may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:
Interpretive criteria for linezolid and vancomycin are adapted from those for *Staphylococcus* spp., as published in CLSI document M100.[3] Interpretive criteria for clindamycin and imipenem are based on MIC distributions following testing of a large number of isolates and data presented in various publications listed in the Additional References. **Interpretive criteria for meropenem are based on MIC distributions examined following testing of a subset of isolates with both meropenem and imipenem.** Interpretive criteria for all other antimicrobial agents are adapted from those for *Enterococcus* spp., as published in CLSI document M100.[3] **In addition to MIC data provided by clinical laboratories,** key references were used to derive interpretive breakpoints.[60-68]

Testing Notes:
Meropenem MICs are typically two to three dilutions higher than those of imipenem.

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

Table 12. *Lactococcus* spp.

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 20 to 24 hours	*S. pneumoniae* ATCC®* 49619 See QC Table 23B.	Ceftriaxone Clindamycin Erythromycin Penicillin or ampicillin Vancomycin

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

General Comments

(1) **Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; ambient air; 20 to 24 hours.**

(2) **For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.**

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					(3) Therapy of serious infections such as endocarditis often involves combined therapy with a penicillin (or vancomycin) and gentamicin.
	Penicillin	≤1	2	≥4	
	Ampicillin	≤1	2	≥4	
CEPHEMS					
	Ceftriaxone	≤1	2	≥4	
CARBAPENEMS					
	Meropenem	≤0.25	0.5	≥1	
GLYCOPEPTIDES					
	Vancomycin	≤2	–	–	See comments (2) and (3).
TETRACYCLINES					
	Tetracycline	≤2	4	≥8	
MACROLIDES					
	Erythromycin	≤0.5	1–4	≥8	
LINCOSAMIDES					
	Clindamycin	≤0.5	1–2	≥4	

Table 12. (Continued)

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
FLUOROQUINOLONES					
	Levofloxacin	**≤2**	**4**	**≥8**	
FOLATE PATHWAY INHIBITORS					
	Trimethoprim-sulfamethoxazole	**≤2/38**	**–**	**≥4/76**	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Lactococcus garvieae* is intrinsically resistant to clindamycin. Resistance to clindamycin and erythromycin mediated by *ermB* has been reported in veterinary isolates of *Lactococcus lactis* subsp*. lactis.* Tetracycline resistance attributed to *tetM* or *tetS* has been detected in *L. lactis* subsp. *lactis* and *L. garvieae.

Reasons for Testing/Not Testing:
Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue) may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:
Interpretive criteria for penicillin and ampicillin are based primarily on MIC distributions. Interpretive criteria for vancomycin, clindamycin, erythromycin, and trimethoprim-sulfamethoxazole are adapted from those for *Staphylococcus* spp.; meropenem interpretive criteria are adapted from those for *S. pneumoniae;* and interpretive criteria for all other antimicrobial agents are adapted from those for viridans group streptococci, as published in CLSI document M100.[3] In addition to MIC data provided by clinical laboratories, key references were used to derive interpretive breakpoints.[69-72]

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

Table 13. *Leuconostoc* spp.

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C: ambient air: 20 to 24 hours	*S. pneumoniae* ATCC®* 49619 **See QC Table 23B.**	Ampicillin or penicillin

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

General Comments

(1) Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; ambient air; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria S	I	R	Comments
PENICILLINS					**(3) Therapy of serious infections such as endocarditis often involves combined therapy with a penicillin and gentamicin.**
	Penicillin	≤8	–	–	See comment (2).
	Ampicillin	≤8	–	–	
TETRACYCLINES					
	Minocycline	≤4	8	≥16	
PHENICOLS					
	Chloramphenicol	≤8	16	≥32	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Leuconostoc spp. are considered intrinsically resistant to vancomycin; routine testing of vancomycin is not necessary. **Resistance to carbapenems and cephalosporins has been reported.[73]**

Reasons for Testing/Not Testing:
Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue) may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for *Enterococcus* spp., as published in CLSI document M100.[3] Key citations used in derivation of interpretive breakpoints are referenced.[63,67]

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

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Table 14. *Listeria monocytogenes*

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 20 to 24 hours	*S. pneumoniae* ATCC®* 49619 **See QC Table 23B.**	Ampicillin or penicillin Trimethoprim-sulfamethoxazole

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

General Comments

(1) Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; ambient air; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Penicillin	≤2	–	–	See comment (2).
	Ampicillin	≤2	–	–	See comment (2).
FOLATE PATHWAY INHIBITORS					
	Trimethoprim-sulfamethoxazole	≤0.5/9.5	**–**	**–**	**See comment (2).**
CARBAPENEMS					
	Meropenem	**≤0.25**	**–**	**–**	**See comment (2).**

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
L. monocytogenes is intrinsically resistant to cephalosporins.

Reasons for Testing/Not Testing:
Resistance to ampicillin or penicillin has not been described. Testing may be limited to suspected treatment failures or for patients with a penicillin allergy.

Derivation of Interpretive Criteria:
Interpretive criteria for penicillin and ampicillin were initially published in 2005 (CLSI document M100-S15). Interpretive criteria for trimethoprim-sulfamethoxazole are adapted from those for *Streptococcus* spp., and **interpretive criteria for meropenem are adapted from those for *S. pneumoniae*** as published in CLSI document M100.[3] **In addition to MIC data provided by clinical laboratories,** key references were used to derive interpretive breakpoints.[74,75]

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

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Table 15. *Micrococcus*[a] spp.

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 20 to 24 hours	***S. aureus* ATCC®* 29213** **See QC Table 23A.**	**Penicillin** **Vancomycin**

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

General Comments

(1) Growth characteristics on routine media: nonfastidious; grows well on BAP; ambient air; 16 to 20 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Penicillin	**≤0.12**	**–**	**≥0.25**	
GLYCOPEPTIDES					
	Vancomycin	**≤2**	**–**	**–**	**See comment (2).**
MACROLIDES					
	Erythromycin	**≤0.5**	**1–4**	**≥8**	
LINCOSAMIDES					
	Clindamycin	**≤0.5**	**1–2**	**≥4**	

Abbreviations: ATCC®, American Type Culture Collection; BAP, blood agar plate; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MIC, minimal inhibitory concentration, QC, quality control; R, resistant; S, susceptible.

Footnote

a. Although there are few supportive antimicrobial susceptibility testing data, application of these criteria to organisms formerly included in the genus *Micrococcus* (ie, *Kocuria* spp., *Nesterenkonia* spp., *Dermacoccus* spp., *Kytococcus* spp.) may be considered.

Supplemental Information

Resistance:
***Micrococcus* spp. with resistance to β-lactams and erythromycin have been reported.**

Reasons for Testing/Not Testing:
***Micrococcus* spp. often represent contaminating bacteria in cultures. Testing of isolates from patients with multiple positive blood cultures or implanted prosthetic devices may be warranted.**

Table 15. (Continued)

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for *Staphylococcus* spp. as published in CLSI document M100.[3] In addition to MIC data provided by clinical laboratories, key references were used to derive interpretive breakpoints.[76,77]

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

Table 16. *Moraxella catarrhalis*

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB; Disk diffusion: MHA **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C Disk diffusion: 5% CO_2, 20 to 24 hours Broth microdilution method: ambient air; 20 to 24 hours	*S. aureus* ATCC®* 29213 (MIC) *E. coli* ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations) *S. aureus* ATCC® 25923 disk diffusion) **See QC Tables 23A and 24A.**	Amoxicillin-clavulanate Cefuroxime Trimethoprim-sulfamethoxazole

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

General Comments

(1) Growth characteristics on routine media: nonfastidious; grows well on blood agar; ambient air; 16 to 20 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	Disk Content	Zone Diameter (mm) Interpretive Criteria			MIC (μg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
PENICILLINS AND β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
	Amoxicillin-clavulanate	20/10 μg	≥24	–	≤23	≤4/2	–	≥8/4	
CEPHEMS									
	Cefuroxime (oral)	–	–	–	–	≤4	8	≥16	
	Cefotaxime	–	–	–	–	≤2	–	–	See comment (2).
	Ceftazidime	–	–	–	–	≤2	–	–	See comment (2).
	Ceftriaxone	–	–	–	–	≤2	–	–	See comment (2).
MACROLIDES									
	Azithromycin	15 μg	≥26	–	–	≤0.25	–	–	See comment (2).
	Clarithromycin	15 μg	≥24	–	–	≤1	–	–	See comment (2).
	Erythromycin	15 μg	≥21	–	–	≤2	–	–	See comment (2).
FLUOROQUINOLONES									
	Ciprofloxacin	–	–	–	–	≤1	–	–	See comment (2).
	Levofloxacin	–	–	–	–	≤2	–	–	See comment (2).
TETRACYCLINES									
	Tetracycline	30 μg	≥29	25–28	≤24	≤2	4	≥8	
LINCOSAMIDE									
	Clindamycin	–	–	–	–	≤0.5	1–2	≥4	

Table 16. (Continued)

Antimicrobial Class	Antimicrobial Agent	Disk Content	Zone Diameter (mm) Interpretive Criteria			MIC (µg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
FOLATE PATHWAY INHIBITORS									
	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥13	11–12	≤10	≤0.5/9.5	1/19–2/38	≥4/76	
PHENICOLS									
	Chloramphenicol	–	–	–	–	≤2	4	≥8	
ANSAMYCINS									
	Rifampin	–	–	–	–	≤1	2	≥4	(3) *Rx:* **Rifampin should not be used alone for antimicrobial therapy**.

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Most strains of *M. catarrhalis* produce one of two β-lactamases (BRO-1, or less commonly, BRO-2), rendering them resistant to penicillin, ampicillin, and amoxicillin.[78] Acquired resistance in *M. catarrhalis* to tetracyclines and trimethoprim-sulfamethoxazole has been reported in some isolates; resistance to macrolides is very rare.

Reasons for Testing/Not Testing:
Testing is not recommended routinely. However, testing may be useful for epidemiological purposes or for management of patients with prolonged or severe infections.

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for *Haemophilus* spp., as published in CLSI document M100[3]; however, for macrolides, interpretive criteria were derived from a large organism collection tested by working group members.

Testing Notes:
If desired, β-lactamase testing can be performed using chromogenic cephalosporin methods such as nitrocefin.

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

Table 17. *Pasteurella* spp.

Testing Conditions

Medium: CAMHB-LHB (2.5% to 5%) for broth microdilution; Disk diffusion: BMHA(see Testing Notes)
Inoculum: Direct colony suspension, equivalent to a 0.5 McFarland standard
Incubation: 35°C; ambient air
Disk diffusion: 16 to 18 hours
Broth microdilution method: 18 to 24 hours

Routine QC Recommendations

S. pneumoniae ATCC®* 49619
E. coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations) *S. aureus* ATCC® 25923 for disk diffusion (amoxicillin-clavulanate)

See QC Tables 23B, 24A, and 24B.

Agents to Consider for Primary Testing
Amoxicillin-clavulanate
Ceftriaxone
Fluoroquinolones
Macrolides
Penicillins
Tetracycline
Trimethoprim-sulfamethoxazole

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

General Comments

(1) Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; ambient air; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	Disk Content	Zone Diameter (mm) Interpretive Criteria			MIC (μg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
PENICILLINS AND β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
	Amoxicillin	–	–	–	–	≤0.5	–	–[a]	See comment (2).
	Amoxicillin-clavulanate	20/10 μg	≥27	–	–	≤0.5/0.25	–	–[a]	See comment (2).
	Ampicillin	10 μg	≥27	–	–	≤0.5	–	–[a]	See comment (2).
	Penicillin	10 units	≥25	–	–	≤0.5	–	–[a]	See comment (2).
CEPHEMS									
	Ceftriaxone	30 μg	≥34	–	–	≤0.12	–	–	See comment (2).
FLUOROQUINOLONES									
	Levofloxacin	5 μg	≥28	–	–	≤0.06	–	–	See comment (2).
	Moxifloxacin	5 μg	≥28	–	–	≤0.06	–	–	See comment (2).
TETRACYCLINES									
	Doxycycline	30 μg	≥23	–	–	≤0.5	–	–	See comment (2).
	Tetracycline	30 μg	≥23	–	–	≤1	–	–	See comment (2).
MACROLIDES									
	Azithromycin	15 μg	≥20	–	–	≤1	–	–	See comment (2).
	Erythromycin	15 μg	≥27	25–26	≤24	≤0.5	1	≥2	

Table 17. (Continued)

Antimicrobial Class	Antimicrobial Agent	Disk Content	Zone Diameter (mm) Interpretive Criteria			MIC (µg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
OTHERS									
	Chloramphenicol	30 µg	≥ 28	–	–	≤ 2	–	–	See comment (2).
	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥ 24	–	–	≤ 0.5/9.5	–	–	See comment (2).

Abbreviations: ATCC®, American Type Culture Collection; BHMA, Mueller-Hinton agar with 5% sheep blood; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration, QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:

Resistance to oxacillin, cephalexin, erythromycin, and clindamycin is common.[79] Tetracycline resistance has been reported. Rare β-lactamase–producing isolates have been encountered with ampicillin, amoxicillin, and penicillin MICs > 0.5 µg/mL.

Reasons for Testing/Not Testing:

For isolates from bite wounds, routine testing is usually not necessary. Multiple organisms are often present in these specimens; therefore, empiric therapy directed toward these organisms is generally effective for *Pasteurella multocida,* as well. Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue, implanted prosthetic devices) and also from respiratory specimens may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:

Interpretive criteria are based primarily on MIC distributions obtained by testing large numbers of isolates recovered from human-animal bite infections. Key references were also used to derive interpretive breakpoints.[80,81]

Testing Notes:

Testing for β-lactamase production using a chromogenic cephalosporin test is recommended for isolates recovered from respiratory or normally sterile sources. β-lactamase–positive isolates are resistant to ampicillin, amoxicillin, and penicillin.

Isolates that do not demonstrate satisfactory growth with the disk diffusion test described here should be tested by broth microdilution.

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

Table 18. *Pediococcus* spp.

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 20 to 24 hours	*S. pneumoniae* ATCC®* 49619 **See QC Table 23B.**	Ampicillin or penicillin

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

General Comments

(1) Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; ambient air; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (μg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					**(3) Therapy of serious infections such as endocarditis often involves combined therapy with a penicillin and gentamicin.**
	Ampicillin	≤8	–	–	See comment (2).
	Penicillin	≤8	–	–	
CARBAPENEMS					
	Imipenem	≤0.5	–	–	See comment (2).
PHENICOLS					
	Chloramphenicol	≤8	16	≥32	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Pediococcus spp. are considered intrinsically resistant to vancomycin; routine testing of vancomycin is not necessary.

Reasons for Testing/Not Testing:
Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue, implanted prosthetic devices) may be warranted, especially in immunodeficient patients.

Derivation of Interpretive Criteria:
Interpretive criteria are adapted from those for *Enterococcus* spp., as published in CLSI document M100.[3] Key citations used in derivation of interpretive breakpoints are referenced.[63,64,67,82]

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

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Table 19. *Rothia mucilaginosa*

Testing Conditions	Routine QC Recommendations	Agents to Consider for Primary Testing
Medium: CAMHB-LHB (2.5% to 5% v/v) **Inoculum:** Direct colony suspension, equivalent to a 0.5 McFarland standard **Incubation:** 35°C; ambient air; 20 to 24 hours	***S. pneumoniae* ATCC®* 49619** **See QC Table 23B.**	**Penicillin** **Vancomycin**

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

General Comments

(1) Growth characteristics on routine media: often fastidious; requires blood-supplemented media for adequate growth; ambient air; 20 to 24 hours.

(2) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

Antimicrobial Class	Antimicrobial Agent	MIC (µg/mL) Interpretive Criteria			Comments
		S	I	R	
PENICILLINS					
	Penicillin	**≤0.12**	**0.25–2**	**≥4**	
GLYCOPEPTIDES					
	Vancomycin	**≤2**	**–**	**–**	See comment (2).
MACROLIDES					
	Erythromycin	**≤0.5**	**1–4**	**≥8**	
LINCOSAMIDES					
	Clindamycin	**≤0.5**	**1–2**	**≥4**	
FLUOROQUINOLONES					
	Levofloxacin	**≤1**	**2**	**≥4**	
FOLATE PATHWAY INHIBITORS					
	Trimethoprim-sulfamethoxazole	**≤2/38**	**–**	**≥4/76**	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Resistance to β-lactams, clindamycin, erythromycin, and fluoroquinolones has been reported.

Reasons for Testing/Not Testing:
Testing of isolates from normally sterile sources (eg, blood cultures, deep tissue) may be warranted, especially in immunodeficient patients.

Table 19. (Continued)

Derivation of Interpretive Criteria:
Interpretive criteria for penicillin are based primarily on MIC. All other interpretive criteria are adapted from those for *Staphylococcus* spp. as published in CLSI document M100.[3] In addition to MIC data provided by clinical laboratories, key references were used to derive interpretive criteria.[76,83,84]

Testing Notes:
Some strains of *R. mucilaginosa* grow satisfactorily in cation-adjusted Mueller-Hinton broth and this medium could be considered as an alternative for testing.

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

Table 20. *Vibrio* spp. (Including *Vibrio cholerae*)

Testing Conditions

Medium: CAMHB for microdilution; Disk diffusion: MHA
Inoculum: Growth method or direct colony suspension, equivalent to a 0.5 McFarland standard. Prepare inoculum in 0.85% NaCl (normal saline).
Incubation: 35°C ± 2 °C; ambient air;
Disk diffusion: 16 to 18 hours
Broth microdilution method: 16 to 20 hours

Routine QC Recommendations

E. coli ATCC®* 25922
***P. aeruginosa* ATCC® 27853 (for carbapenems)**
E. coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

See QC Tables 23A and 24A.

Agents to Consider for Primary Testing

For *V. cholerae:*
Ampicillin
Azithromycin
Chloramphenicol
Sulfonamides
Tetracycline or doxycycline
Trimethoprim-sulfamethoxazole

For other *Vibrio* spp.:
Cefotaxime
Ceftazidime
Fluoroquinolones
Tetracycline **or doxycycline**

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

General Comment

(1) Growth characteristics on routine media: halophilic; grows well on blood agar plates; ambient air; 20 to 24 hours.

Antimicrobial Class	Antimicrobial Agent	Disk Diffusion	Zone Diameter (mm) Interpretive Criteria			MIC (µg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
PENICILLINS AND β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
	Ampicillin	10 µg	≥17	14–16	≤13	≤8	16	≥32	(2) Class representative for ampicillin and amoxicillin.
	Amoxicillin-**clavulanate**	20/10 µg	≥18	14–17	≤13	≤8/4	16/8	≥32/16	(3) For *Vibrio* spp. other than *V. cholerae.*
	Ampicillin-sulbactam	10/10 µg	≥15	12–14	≤11	≤8/4	16/8	≥32/16	See comment (3).
	Piperacillin	100 µg	≥21	18–20	≤17	≤16	32–64	≥128	See comment (3).
	Piperacillin-tazobactam	100/10 µg	≥21	18–20	≤17	≤16/4	32/4–64/4	≥128/4	See comment (3).
CEPHEMS									**See comment (3).**
	Cefazolin	30 µg	–	–	–	≤2	4	≥8	Breakpoints are based on a dosage regimen of 2 g every 8 h.
	Cefepime	30 µg	**≥25**	**19–24**	**≤18**	**≤2**	**4–8**	**≥16**	**Breakpoints are based on a dosage regimen of 1 g every 12 h.**
	Cefotaxime	30 µg	≥26	23–25	≤22	≤1	2	≥4	Breakpoints are based on a dosage regimen of 1 g every 8 h.
	Cefoxitin	30 µg	≥18	15–17	≤14	≤8	16	≥32	

Table 20. (Continued)

Antimicrobial Class	Antimicrobial Agent	Disk Diffusion	Zone Diameter (mm) Interpretive Criteria			MIC (μg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
CEPHEMS (Continued)									**See comment (3).**
	Ceftazidime	30 μg	≥21	18–20	≤17	≤4	8	≥16	Breakpoints are based on a dosage regimen of 1 g every 8 h.
	Cefuroxime sodium (parenteral)	30 μg	≥18	15–17	≤14	≤8	16	≥32	Breakpoints are based on a dosage regimen of 1.5 g every 8 h.
CARBAPENEMS									**See comment (3).**
	Imipenem	10 μg	**≥23**	**20–22**	**≤19**	**≤1**	**2**	**≥4**	**Breakpoints are based on a dosage regimen of 500 mg every 6 h or 1 g every 8 h.**
	Meropenem	10 μg	**≥23**	**20–22**	**≤19**	**≤1**	**2**	**≥4**	**Breakpoints are based on a dosage regimen of 1 g every 8 h.**
MACROLIDES									
	Azithromycin	–	–	–	–	≤2	–	–	**(4) Due to limited clinical or *in vitro* MIC data for azithromycin and doxycycline, the utility of these interpretive criteria for *Vibrio* spp. other than *V. cholerae* is uncertain.**
AMINOGLYCOSIDES									See comment (3).
	Amikacin	30 μg	≥17	15–16	≤14	≤16	32	≥64	
	Gentamicin	10 μg	≥15	13–14	≤12	≤4	8	≥16	
TETRACYCLINES									(5) For *V. cholerae,* isolates susceptible to tetracycline are also susceptible to doxycycline.
	Doxycycline	–	–	–	–	≤4	8	≥16	**See comment (4).**
	Tetracycline	30 μg	≥15	12–14	≤11	≤4	8	≥16	
FLUOROQUINOLONES									**See comment (3).**
	Ciprofloxacin	5 μg	≥21	16–20	≤15	≤1	2	≥4	
	Levofloxacin	5 μg	≥17	14–16	≤13	≤2	4	≥8	
	Ofloxacin	5 μg	≥16	13–15	≤12	≤2	4	≥8	
FOLATE PATHWAY INHIBITORS									
	Sulfonamides	250 μg or 300 μg	≥17	13–16	≤12	≤256	–	≥512	(6) Sulfasoxazole can be used to represent any of the current available sulfonamide preparations. (7) For *V. cholerae* only.
	Trimethoprim-sulfamethoxazole	1.25/23.75 μg	≥16	11–15	≤10	≤2/38	–	≥4/76	

Table 20. (Continued)

Antimicrobial Class	Antimicrobial Agent	Disk Diffusion	Zone Diameter (mm) Interpretive Criteria			MIC (μg/mL) Interpretive Criteria			Comments
			S	I	R	S	I	R	
PHENICOLS									
	Chloramphenicol	30 μg	≥18	13–17	≤12	≤8	16	≥32	(8) Use with caution for disk diffusion as the disk diffusion test may misclassify many organisms (higher minor error rate). (9) Not routinely reported on isolates from the urinary tract. (10) For *V. cholerae* only.

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Supplemental Information

Resistance:
Halophilic *Vibrio* spp. are **often** resistant to sulfonamides, penicillins, and older cephalosporins (cephalothin, cefuroxime).

Reasons for Testing/Not Testing:
Testing is **usually** limited to isolates from extraintestinal sites.

Derivation of Interpretive Criteria:
With the exception of azithromycin, interpretive criteria are adapted from those for *Enterobacteriaceae,* as published in CLSI document M100.[3] Azithromycin susceptible criterion is adapted from *Staphylococcus* spp. Key citations used in derivation of interpretive breakpoints are referenced.[85-93]

Testing Notes:
Inoculum suspension should be prepared in 0.85% NaCl (normal saline). This will allow most isolates of *Vibrio* spp. to grow satisfactorily on MHA and CAMHB without adding supplemental NaCl to these test media.

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

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Table 21. Potential Bacterial Agents of Bioterrorism: *Bacillus anthracis, Yersinia pestis, Burkholderia mallei, Burkholderia pseudomallei, Francisella tularensis,* and *Brucella* spp.

Testing Conditions

Medium: Broth microdilution: unsupplemented Brucella broth pH adjusted to 7.1±0.1 for *Brucella* spp.; CAMHB + 2% defined growth supplement for *F. tularensis;* CAMHB for all other organisms

Inoculum: Growth method or direct colony suspension in CAMHB, equivalent to a 0.5 McFarland standard; for *F. tularensis,* prepare inoculum as a direct colony suspension from a chocolate agar plate.

Incubation: 35°C±2 °C; ambient air; 16 to 20 hours; for *Y. pestis,* incubate 24 hours and if unacceptable growth in the control well, reincubate an additional 24 hours; for *F. tularensis* and *Brucella* spp., incubate 48 hours (see comment 8).

Routine QC Recommendations (See Table 23A [CAMHB], Table 23E [CAMHB + 2% defined growth supplement], and Table 23F [Brucella broth] for acceptable QC ranges).

E. coli ATCC®* 25922 (all organisms)
E. coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations and *B. pseudomallei*)
S. aureus ATCC® 29213 (for *B. anthracis* and *F. tularensis*)
P. aeruginosa ATCC® 27853 (for *B. mallei/pseudomallei* and *F. tularensis*)
S. pneumoniae ATCC® 49619 (for *Brucella* spp. only)

See QC Tables 23A, 23E, and 23F.

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

Agents to Consider for Primary Testing

B. anthracis	***Y. pestis***	***B. mallei***	***B. pseudomallei***	***F. tularensis***	***Brucella* spp.**
Penicillin[a]	Gentamicin	Ceftazidime	Amoxicillin-clavulanate	Gentamicin Streptomycin	Gentamicin Streptomycin
Doxycycline Tetracycline	Streptomycin	Imipenem	Ceftazidime	Doxycycline Tetracycline	Doxycycline Tetracycline
Ciprofloxacin	Doxycycline Tetracycline	Doxycycline Tetracycline	Imipenem	Ciprofloxacin or levofloxacin	Trimethoprim- sulfamethoxazole
	Ciprofloxacin		Doxycycline Tetracycline	Chloramphenicol	
	Trimethoprim- sulfamethoxazole		Trimethoprim- sulfamethoxazole		
	Chloramphenicol				

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; QC, quality control.

Footnote

a. Organisms that are susceptible to penicillin are also considered susceptible to amoxicillin.

Table 21. (Continued)

General Comments

Important: For complete information on safety precautions, see *Biosafety in Microbiological and Biomedical Laboratories.* 5th ed. Washington, DC: US Government Printing Office; 2009. http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf. Accessed August 25, 2015.

(1) **Extreme Caution:** Notify public health officials of all isolates presumptively identified as *B. anthracis, Y. pestis, B. mallei, B. pseudomallei, Brucella* spp., or *F. tularensis.* Confirmation of isolates of these bacteria may require specialized testing that is available only in referral or public health laboratories.

(2) Recommended precautions: Use Biosafety Level 2 (BSL-2) practices, containment equipment, and facilities for activities using clinical materials and diagnostic quantities of infectious cultures. Use Biosafety Level 3 (BSL-3) practices, containment equipment, and facilities for work involving production quantities or concentrations of cultures and for activities with a high potential for aerosol production. If BSL-2 or BSL-3 facilities are not available, forward isolates to a referral or public health laboratory with a minimum of BSL-2 facilities for susceptibility testing.

(3) Interpretive criteria are based on microorganism MIC population distributions, pharmacokinetics, and pharmacodynamics of the antimicrobial agents, and/or animal model data.

(4) Test method and interpretive criteria for *B. anthracis* do not apply to other *Bacillus* spp.

(5) **WARNING:** For *Y. pestis,* studies have demonstrated that although β-lactam antimicrobial agents may appear active *in vitro,* they lack efficacy in animal models of infection. *Y. pestis* should be reported as resistant to these antimicrobial agents. ***Rx:*** Retrospective clinical data suggest that β-lactam antimicrobial agents are not effective clinically.

(6) The recommended medium for testing *F. tularensis* consists of CAMHB to which a 2% defined growth supplement (25.9 g L-cysteine HCl, 1.1 g L-cystine, 1 g adenine, 0.03 g guanine HCl, 0.01 g vitamin B_{12}, 0.1 g cocarboxylase, 0.25 g nicotinamide adenine dinucleotide, 10 g L-glutamine, 0.02 g ferric nitrate, 100 g glucose, 3 mg thiamine HCl, and 13 mg p-aminobenzoic acid [in 1 L H_2O]) is added after autoclaving. The pH of the medium should be adjusted to 7.1 ± 0.1.

(7) For some organism/antimicrobial agent combinations, 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. Subsequently, the isolates should be saved and submitted to a referral laboratory for confirmation.

(8) Incubation in 5% CO_2 may be required for growth of some strains of *Brucella* spp., especially *Brucella abortus.* Incubation of broth MIC tests in CO_2 may increase the MIC of aminoglycosides and decrease the MIC of tetracyclines, usually by one doubling dilution.

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

Table 21. (Continued)

Organism Group	Antimicrobial Agent	MIC Interpretive Criteria (µg/mL)			Comments
		S	I	R	
PENICILLINS					
B. anthracis	Penicillin	≤0.12	–	≥0.25	(9) Class representative for amoxicillin. (10) *B. anthracis* strains may contain inducible β-lactamases. *In vitro* penicillinase induction studies suggest that penicillin MICs may increase during therapy. This finding is supported by reduced response rates to penicillin in animal treatment studies of *B. anthracis* infection. However, β-lactamase testing of clinical isolates of *B. anthracis* is unreliable and should not be performed. If MIC susceptibility testing using CLSI methods indicates that *B. anthracis* isolates are susceptible to penicillin, amoxicillin may still be considered for prophylactic use in children and pregnant women.[94]
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS					
B. pseudomallei	Amoxicillin-clavulanate	≤8/4	16/8	≥32/16	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)					
B. mallei *B. pseudomallei*	Ceftazidime	≤8	16	≥32	
CARBAPENEMS					
B. mallei *B. pseudomallei*	Imipenem	≤4	8	≥16	
AMINOGLYCOSIDES					
Y. pestis	Gentamicin	≤4	8	≥16	
	Streptomycin	≤4	8	≥16	
F. tularensis	Gentamicin	≤4	–	–	See comment (7).
Brucella spp.	Streptomycin	≤8	–	–	See comments (7) and (8). (11) The streptomycin-susceptible breakpoint is ≤16 µg/mL when the test is incubated in CO_2 and ≤8 µg/mL when incubated in air.
TETRACYCLINES					(12) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline.
B. anthracis *Brucella* spp.	Doxycycline	≤1	–	–	See comments (7) and (8).
	Tetracycline	≤1	–	–	See comments (7) and (8).
B. mallei *B. pseudomallei* *Y. pestis*	Doxycycline	≤4	8	≥16	
	Tetracycline	≤4	8	≥16	
F. tularensis	Doxycycline	≤4	–	–	See comment (7).
	Tetracycline	≤4	–	–	See comment (7).

Table 21. (Continued)

Organism Group	Antimicrobial Agent	MIC Interpretive Criteria (µg/mL)			Comments
		S	I	R	
FLUOROQUINOLONES					
B. anthracis	Ciprofloxacin	≤0.25	–	–	See comment (7).
	Levofloxacin	≤0.25	–	–	See comment (7).
Y. pestis	Ciprofloxacin	≤0.25	–	–	See comment (7).
	Levofloxacin	≤0.25	–	–	See comment (7).
F. tularensis	Ciprofloxacin	≤0.5	–	–	See comment (7).
	Levofloxacin	≤0.5	–	–	See comment (7).
FOLATE PATHWAY INHIBITORS					
B. pseudomallei *Y. pestis*	Trimethoprim-sulfamethoxazole	≤2/38	–	≥4/76	
Brucella spp.	Trimethoprim-sulfamethoxazole	≤2/38	–	–	See comments (7) and (8).
PHENICOLS					
Y. pestis	Chloramphenicol	≤8	16	≥32	
F. tularensis	Chloramphenicol	≤8	–	–	See comment (7).

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Table 22. Summary of Testing Conditions and Quality Control Recommendations for Infrequently Isolated or Fastidious Bacteria

Table No.	Organism/Organism Group	Broth Microdilution MIC Test Medium	Broth Microdilution MIC Incubation Conditions	Disk Diffusion Test Medium/Incubation Conditions	QC Strain(s) (see Tables for QC Ranges)
1	*Abiotrophia* spp., *Granulicatella* spp.	CAMHB-LHB (2.5% to 5% v/v) + 0.001% pyridoxal HCl	35°C; ambient air; 20–24 h	N/A	*S. pneumoniae* ATCC®[a] 49619
2	***Aerococcus* spp.**	**CAMHB-LHB (2.5% to 5%)**	**35°C; 5% CO_2; 20–24 h**	**N/A**	***S. pneumoniae* ATCC® 49619**
3	*Aeromonas hydrophila* complex	CAMHB	35°C; ambient air; 16–20 h	MHA (unsupplemented/35°C; ambient air; 16–18 h)	*E. coli* ATCC® 25922 *E. coli* ATCC® 35218[b] ***P. aeruginosa* ATCC® 27853[d]**
4	*Bacillus* spp. (not *B. anthracis*)	CAMHB	35°C; ambient air; 16–20 h	N/A	*S. aureus* ATCC® 29213
5	*C. jejuni/coli*	CAMHB-LHB (2.5% to 5% v/v)	36 to 37°C/48 h or 42°C/24 h; 10% CO_2, 5% O_2, 85% N_2 (microaerobic)	MHA with 5% sheep blood/**42°C/24 h**; 10% CO_2, 5% O_2, 85% N_2 (microaerobic)	*C. jejuni* ATCC® 33560 for broth microdilution *S. aureus* ATCC® 25923, for disk diffusion
6	*Corynebacterium* spp.	CAMHB-LHB (2.5% to 5% v/v)	35°C; ambient air; 24–48 h	N/A	*S. pneumoniae* ATCC® 49619 *E. coli* ATCC® 25922 for gentamicin
7	*E. rhusiopathiae*	CAMHB-LHB (2.5% to 5% v/v)	35°C; ambient air; 20–24 h	N/A	*S. pneumoniae* ATCC® 49619
8	***Gemella* spp.**	**CAMHB-LHB (2.5% to 5% v/v)**	**35°C; 5% CO_2; 24–48 h**	**N/A**	***S. pneumoniae* ATCC® 49619**
9	HACEK group	CAMHB-LHB (2.5% to 5% v/v) See Table #9 for additional media suggestions.	35°C; 5% CO_2; 24–48 h	N/A	*S. pneumoniae* ATCC® 49619 *E. coli* ATCC® 35218[b]
10	*H. pylori*	Agar dilution: MHA and aged (≥ 2-week-old) sheep blood (5% v/v)	35°C ± 2 °C; 72 h; 10% CO_2, 5% O_2, 85% N_2 (microaerobic)	N/A	*H. pylori* ATCC® 43504
11	*Lactobacillus* spp.	CAMHB-LHB (2.5% to 5% v/v)	35°C; 5% CO_2; 24–48 h	N/A	*S. pneumoniae* ATCC® 49619
12	***Lactococcus* spp.**	**CAMHB-LHB (2.5% to 5% v/v)**	**35°C; ambient air; 20–24 h**	**N/A**	***S. pneumoniae* ATCC® 49619**
13	*Leuconostoc* spp.	CAMHB-LHB (2.5% to 5% v/v)	35 °C; ambient air; 20–24 h	N/A	*S. pneumoniae* ATCC® 49619 *E. coli* ATCC® 25922 for gentamicin
14	*L. monocytogenes*	CAMHB-LHB (2.5%–5% v/v)	35 °C; ambient air; 20–24 h	N/A	*S. pneumoniae* ATCC® 49619
15	*Micrococccus* spp.	CAMHB	35°C; ambient air; 20–24 h	N/A	*S. aureus ATCC® 29213*
16	*M. catarrhalis*	CAMHB	35°C; ambient air; 20–24 h	MHA (unsupplemented/35°C; 5% CO2; 20–24 h)	*S. aureus ATCC® 29213* *E. coli ATCC® 35218b*
17	*Pasteurella* spp.	CAMHB-LHB (2.5% to 5% v/v)	35°C; ambient air; 18–24 h	MHA with 5% sheep blood/35°C; ambient air; 16–18 h	*S. pneumoniae ATCC® 49619* *E. coli ATCC® 35218b* *S. aureus ATCC® 25923 for disk diffusion*

Table 22. (Continued)

Table No.	Organism/Organism Group	Broth Microdilution MIC Test Medium	Broth Microdilution MIC Incubation Conditions	Disk Diffusion Test Medium/Incubation Conditions	QC Strain(s) (see Tables for QC Ranges)
18	*Pediococcus* spp.	CAMHB-LHB (2.5% to 5% v/v)	35°C; ambient air; 20–24 h	N/A	*S. pneumoniae* ATCC® 49619
19	***R. mucilaginosa***	**CAMHB-LHB (2.5% to 5% v/v)**	**35°C; ambient air; 20–24 h**	**N/A**	***S. pneumoniae* ATCC® 49619**
20	*Vibrio* spp. (including *V. cholerae*)	CAMHB[d]	35°C; ambient air; 16–20 h	MHA (unsupplemented/35°C; ambient air; 16–18 h)[c]	*E. coli* ATCC® 25922 *E. coli* ATCC® 35218[b] ***P. aeruginosa* ATCC® 27583[d]**
Potential Bacterial Agents of Bioterrorism					
21	*B. anthracis*	CAMHB	35°C; ambient air; 16–20 h	N/A	*E. coli* ATCC® 25922 *S. aureus* ATCC® 29213
21	*Brucella* spp.	Unsupplemented Brucella broth pH adjusted to 7.1 ± 0.1	35 °C; ambient air; 48 h	N/A	*E. coli* ATCC® 25922 *S. pneumoniae* ATCC® 49619
21	*B. mallei*	CAMHB	35°C; ambient air; 16–20 h	N/A	*E. coli* ATCC® 25922 *P. aeruginosa* ATCC® 27853
21	*B. pseudomallei*	CAMHB	35°C; ambient air; 16–20 h	N/A	*E. coli* ATCC® 25922 *E. coli* ATCC® 35218[c] *P. aeruginosa* ATCC® 27853
21	*F. tularensis*	CAMHB + 2% defined growth supplement	35°C; ambient air; 48 h	N/A	*E. coli* ATCC® 25922 *S. aureus* ATCC® 29213 *P. aeruginosa* ATCC® 27853
21	*Y. pestis*	CAMHB	35°C ± 2 °C; ambient air; 24 h, and if unacceptable growth in the control well, reincubate an additional 24 h	NA	*E. coli* ATCC® 25922

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CAMHB-LHB, cation-adjusted Mueller-Hinton broth supplemented with lysed horse blood; QC, quality control; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; N/A, not applicable; No., number.

Footnotes

a. ATCC® is a registered trademark of the American Type Culture Collection.
b. *E. coli* ATCC® 35218 is used for QC when testing β-lactam/β-lactamase inhibitor combination drugs.
c. Prepare inoculum in 0.85% NaCl (normal saline).
d. ***P. aeruginosa* ATCC® 27583 is used for QC when testing carbapenems.**

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

Table 23A. MIC: Quality Control Ranges for Nonfastidious Organisms (Unsupplemented Cation-Adjusted Mueller-Hinton Broth)

Antimicrobial Agent	MIC QC Ranges (µg/mL)			
	S. aureus **ATCC®[a] 29213**	***E. coli*** **ATCC® 25922**	***E. coli*** **ATCC® 35218[b]**	***P. aeruginosa*** **ATCC® 27853**
Amikacin	1–4	0.5–4	–	**–**
Amoxicillin-clavulanate	0.12/0.06–0.5/0.25	2/1–8/4	4/2–16/8	**–**
Ampicillin	0.5–2	2–8	>32	**–**
Ampicillin-sulbactam	–	2/1–8/4	8/4–32/16	**–**
Azithromycin	0.5–2	–	–	**–**
Aztreonam	–	0.06–0.25	**0.03–0.12**	**–**
Cefaclor	1–4	1–4	–	**–**
Cefazolin	0.25–1	1–4	–	**–**
Cefepime	1–4	0.015–0.12	–	**–**
Cefotaxime	1–4	0.03–0.12	–	**–**
Cefoxitin	1–4	2–8	–	**–**
Cefpodoxime	1–8	0.25–1	–	**–**
Cefprozil	0.25–1	1–4	–	**–**
Ceftazidime	4–16	0.06–0.5	–	**1–4**
Ceftriaxone	1–8	0.03–0.12	–	**–**
Cefuroxime	0.5–2	2–8	–	**–**
Cephalothin	0.12–0.5	4–16	–	**–**
Chloramphenicol	2–16	2–8	–	**–**
Ciprofloxacin	0.12–0.5	0.004–0.015	–	**–**
Clarithromycin	0.12–0.5	–	–	**–**
Clindamycin	0.06–0.25	–	–	**–**
Doripenem	–	–	–	**0.12–0.5**
Ertapenem	0.06–0.25	0.004–0.015	–	**2–8**
Erythromycin	0.25–1	–	–	**–**
Gentamicin	0.12–1	0.25–1	–	**–**
Imipenem	0.015–0.06	0.06–0.25	–	**1–4**
Levofloxacin	0.06–0.5	0.008–0.06	–	**–**
Meropenem	0.03–0.12	0.008–0.06	–	**0.25–1**
Ofloxacin	0.12–1	0.015–0.12	–	**–**
Penicillin	0.25–2	–	–	**–**
Piperacillin	1–4	1–4	>64	**–**
Piperacillin-tazobactam	0.25/4–2/4	1/4–4/4	0.5/4–2/4	**–**
Rifampin	0.004–0.015	4–16	–	**–**
Tetracycline	0.12–1	0.5–2	–	**8–32**
Trimethoprim-sulfamethoxazole	≤0.5/9.5	≤0.5/9.5	–	**–**
Vancomycin	0.5–2	–	–	**–**

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

Footnotes

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

b. Because *E. coli* ATCC® 35218 may lose its plasmid, careful organism maintenance is required; refer to CLSI document M07.[2]

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

Table 23B. MIC: Quality Control Ranges for Broth Microdilution Methods (Cation-Adjusted Mueller-Hinton Broth With Lysed Horse Blood [2.5% to 5% v/v])

Antimicrobial Agent	MIC QC Ranges (µg/mL)		
	***S. pneumoniae* ATCC®[a] 49619**	***E. coli* ATCC® 25922**	***E. coli* ATCC® 35218[b]**
Amoxicillin	0.03–0.12	–	≥256
Amoxicillin-clavulanate	0.03/0.015–0.12/0.06	–	4/2–16/8[c]
Ampicillin	0.06–0.25	–	–
Ampicillin-sulbactam	–	–	8/4–32/16[c]
Azithromycin	0.06–0.25	–	–
Cefepime	0.03–0.25	–	–
Cefotaxime	0.03–0.12	–	–
Ceftriaxone	0.03–0.12	–	–
Chloramphenicol	2–8	–	–
Ciprofloxacin	0.25–1[b]	–	–
Clarithromycin	0.03–0.12	–	–
Clindamycin	0.03–0.12	–	–
Daptomycin[d]	0.06–0.5	–	–
Doxycycline	0.015–0.12	–	–
Erythromycin	0.03–0.12	–	–
Gatifloxacin	0.12–0.5	–	–
Gentamicin	–	0.25–1[c]	–
Imipenem	0.03–0.12	–	–
Levofloxacin	0.5–2	–	–
Linezolid	0.25–2	–	–
Meropenem	0.06–0.25	–	–
Minocycline	–	0.25–1[c]	–
Moxifloxacin	0.06–0.25	–	–
Penicillin	0.25–1	–	–
Quinupristin-dalfopristin	0.25–1	–	–
Rifampin	0.015–0.06	–	–
Tetracycline	0.06–0.5	–	–
Trimethoprim-sulfamethoxazole	0.12/2.4–1/19	–	–
Vancomycin	0.12–0.5	–	–

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

Footnotes

a. Because ***E. coli* ATCC® 35218** may lose its plasmid, careful organism maintenance is required; refer to CLSI document M07.[2]

b. These QC ranges were validated for tests performed in cation-adjusted Mueller-Hinton broth with lysed horse blood **(2.5% to 5% v/v)** and were not established by the studies outlined in CLSI document M23.[6] The validation studies were conducted in at least three laboratories using multiple lots of media.

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

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

Table 23C. MIC: Quality Control Ranges for *Campylobacter jejuni* (Broth Microdilution Method) (Cation-Adjusted Mueller-Hinton Broth With Lysed Horse Blood [2.5% to 5% v/v])

Antimicrobial Agent	*C. jejuni* ATCC®[a] 33560 MIC QC Ranges (µg/mL)	
	36 to 37°C/48 hours	42°C/24 hours
Azithromycin	0.03–0.25	0.03–0.12
Ciprofloxacin	0.06–0.25	0.03–0.12
Doxycycline	0.12–0.5	0.12–0.5
Erythromycin	0.5–2	0.25–2
Gentamicin	0.5–2	0.25–2
Levofloxacin	0.06–0.25	0.03–0.25
Meropenem	0.008–0.03	0.008–0.03
Tetracycline	0.25–2	0.25–1

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

NOTE: These QC ranges were validated for tests performed in cation-adjusted Mueller-Hinton broth with lysed horse blood (2.5% to 5% v/v) and were not established by the studies described in CLSI document M23.[6] The validation studies were conducted in at least three laboratories using multiple lots of media.

Table 23D. MIC: Quality Control Ranges for *Helicobacter pylori* (Agar Dilution Methods) (Mueller-Hinton Agar With Aged [≥2-Week-Old] Sheep Blood)

Antimicrobial Agent	*H. pylori* ATCC®[a] 43504 MIC QC Ranges (µg/mL)
Amoxicillin	0.015–0.12
Clarithromycin	0.015–0.12
Metronidazole	64–256
Telithromycin	0.06–0.5
Tetracycline	0.12–1

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

Table 23E. MIC: Quality Control Ranges for Broth Microdilution Method (Cation-Adjusted Mueller-Hinton Broth + 2% Defined Growth Supplement[a])

Antimicrobial Agent	MIC QC Ranges (µg/mL)					
	S. aureus ATCC®[b] 29213		*E. coli* ATCC® 25922		*P. aeruginosa* ATCC® 27853	
	24 hours	48 hours	24 hours	48 hours	24 hours	48 hours
Chloramphenicol	4–16	4–32	2–8	4–16	–	–
Ciprofloxacin	0.25–1	0.25–1	0.004–0.015	0.004–0.03	0.12–1	0.25–1
Doxycycline	0.12–1	0.25–2	1–4	1–8	4–32	4–32
Gentamicin	0.25–1	0.25–1	0.25–2	0.25–2	0.5–2	0.5–4
Levofloxacin	0.12–0.5	0.12–0.5	0.008–0.03	0.008–0.06	0.5–2	0.5–4
Nalidixic acid	–	–	1–8	2–8	–	–
Streptomycin	8–32	8–64	8–32	8–32	32–128	32–256
Tetracycline	0.25–2	0.5–4	1–4	2–8	8–32	8–64
Trimethoprim-sulfamethoxazole	≤0.25/4.75	≤0.25/4.75	≤0.5/9.5	≤0.5/9.5	–	–

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

Footnote

a. Add 2% defined growth supplement (25.9 g L-cysteine HCl, 1.1 g L-cystine, 1 g adenine, 0.03 g guanine HCl, 0.01 g vitamin B_{12}, 0.1 g cocarboxylase, 0.25 g nicotinamide adenine dinucleotide, 10 g L-glutamine, 0.02 g ferric nitrate, 100 g glucose, 3 mg thiamine HCl, and 13 mg p-aminobenzoic acid [in 1 L H_2O]) to cation-adjusted Mueller-Hinton broth after autoclaving. The pH of medium should be adjusted to 7.1 ± 0.1.

NOTE: When reading *F. tularensis* MIC results at 24 hours, read QC at 24 hours and use 24-hour QC ranges. When reading *F. tularensis* MIC results at 48 hours, read QC at 48 hours and use 48-hour QC ranges.

Table 23F. MIC: Quality Control Ranges for Broth Microdilution Methods (Brucella Broth Without Supplements Adjusted to pH 7.1 ± 0.1)

Antimicrobial Agent	MIC QC Ranges (µg/mL)					
	E. coli ATCC®[a] 25922		*S. aureus* ATCC® 29213		*S. pneumoniae* ATCC® 49619	
	24 hours	48 hours	24 hours	48 hours	24 hours	48 hours
Azithromycin	–	–	2–8	2–16	0.25–1	0.25–1
Chloramphenicol	2–8	4–16	4–16	4–16	1–8	2–8
Ciprofloxacin	–	–	0.25–1	0.25–1	0.25–1	0.25–2
Doxycycline	0.5–2	1–4	0.12–0.5	0.12–0.5	0.03–0.12	0.03–0.25
Gentamicin	1–8	1–8	–	–	–	–
Levofloxacin	–	–	0.06–0.5	0.12–0.5	0.25–1	0.25–2
Rifampin	4–16	4–16	–	–	0.008–0.03	0.008–0.06
Streptomycin	4–32	4–32	8–64	8–64	16–64	16–128
Tetracycline	0.5–2	0.5–4	0.12–1	0.25–1	0.03–0.25	0.06–0.5
Trimethoprim-sulfamethoxazole	–	–	–	–	0.5/9.5–2/38	0.5/9.5–2/38

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

Table 24A. Disk Diffusion: Quality Control Ranges for Nonfastidious Organisms (Unsupplemented Mueller-Hinton Medium)

Antimicrobial Agent	Disk Content	Disk Diffusion QC Ranges (mm)			
		E. coli **ATCC®[a] 25922**	***S. aureus*** **ATCC® 25923**	***E. coli*** **ATCC® 35218[b]**	***P. aeruginosa*** **ATCC® 27853**
Amikacin	30 μg	19–26	20–26	–	**–**
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	–	**–**
Aztreonam	30 μg	28–36	–	–	**–**
Cefazolin	30 μg	21–27	29–35	–	**–**
Cefepime	30 μg	31–37	23–29	–	**–**
Cefotaxime	30 μg	29–35	25–31	–	**–**
Cefoxitin	30 μg	23–29	23–29	–	**–**
Ceftazidime	30 μg	25–32	16–20	–	**–**
Ceftriaxone	30 μg	29–35	22–28	–	**–**
Cefuroxime	30 μg	20–26	27–35	–	**–**
Cephalothin	30 μg	15–21	29–37	–	**–**
Chloramphenicol	30 μg	21–27	19–26	–	**–**
Ciprofloxacin	5 μg	30–40	22–30	–	**–**
Clarithromycin	15 μg	–	26–32	–	**–**
Doripenem	10 μg	–	–	–	**28–35**
Doxycycline	30 μg	18–24	23–29	–	**–**
Ertapenem	10 μg	29–36	24–31	–	**13–21**
Erythromycin	15 μg	–	22–30	–	**–**
Gentamicin	10 μg	19–26	19–27	–	**–**
Imipenem	10 μg	26–32	–	–	**20–28**
Levofloxacin	5 μg	29–37	25–30	–	**–**
Meropenem	10 μg	28–34	29–37	–	**27–33**
Ofloxacin	5 μg	29–33	24–28	–	**–**
Piperacillin	100 μg	24–30	–	12–18	**–**
Piperacillin-tazobactam	100/10 μg	24–30	27–36	24–30	**–**
Tetracycline	30 μg	18–25	24–30	–	**–**
Trimethoprim-sulfamethoxazole	1.25/23.75 μg	23–29	24–32	–	**–**

Abbreviations: ATCC®, American Type Culture Collection; QC, quality control.

Footnotes

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

b. Because ***E. coli*** **ATCC® 35218** may lose its plasmid, careful organism maintenance is required; refer to CLSI document M07.[2]

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

Table 24B. Disk Diffusion: Quality Control Ranges for Fastidious Organisms (Mueller-Hinton Medium With 5% Sheep Blood)

Antimicrobial Agent	Disk Content	*S. pneumoniae* ATCC®[a] 49619
		Disk Diffusion QC Ranges (mm)
Amoxicillin-clavulanate[b]	20/10	–
Ampicillin	10 μg	30–36
Azithromycin	15 μg	19–25
Ceftriaxone	30 μg	30–35
Chloramphenicol	30 μg	23–27
Doxycycline	30 μg	25–34
Erythromycin	15 μg	25–30
Levofloxacin	5 μg	20–25
Moxifloxacin	5 μg	25–31
Penicillin	10 units	24–30
Tetracycline	30 μg	27–31
Trimethoprim-Sulfamethoxazole	1.25/23.75 μg	20–28

Abbreviations: ATCC®, American Type Culture Collection; QC, quality control.

Footnote

a. Testing of *S. aureus* ATCC® 25923 using Mueller-Hinton agar (MHA) supplemented with 5% sheep blood has been shown to produce zones within the acceptable range (28 to 36 mm) noted in CLSI document M100[3] for unsupplemented MHA.

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

Antimicrobial Class	Antimicrobial Subclass		Agents Included; Generic Names
Penicillins	**Penicillinase-labile penicillins**[a]	Penicillin	Penicillin
		Aminopenicillin	Amoxicillin Ampicillin
		Carboxypenicillin	Carbenicillin Ticarcillin
		Ureidopenicillin	Azlocillin Mezlocillin Piperacillin
	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

Abbreviation: MRSA, methicillin-resistant *S. aureus.*

Footnotes

a. **Hydrolyzed by staphylococcal penicillinase.**

b. Not hydrolyzed by staphylococcal penicillinase.

c. Cephalosporin I, II, III, and IV are sometimes referred to as first-, second-, third-, and fourth-generation cephalosporins, respectively. Cephalosporin III and IV are also referred to as "extended-spectrum cephalosporins." This does not imply activity against extended-spectrum β-lactamase–producing gram-negative bacteria.

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

NOTE 2: Users should consult CLSI document M100,[3] which is updated annually, for the most current version of the glossary.

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
	Fluoroketolide	**Solithromycin**
	Ketolide	**Telithromycin**
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 **Pefloxacin** 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 Minocycline Tetracycline
	Fluorocycline	**Eravacycline**
	Glycylcyclines	Tigecycline
	Aminomethylcycline	Omadacycline
Thiazolide		**Nitazoxanide** **Tizoxanide**

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

NOTE 2: Users should consult CLSI document M100,[3] which is updated annually, for the most current version of the glossary.

Glossary II. Abbreviations/Routes of Administration/Drug Class for Antimicrobial Agents Listed in CLSI Document M100-S25[3]

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

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 Gentamicin synergy	GM, Gm, CN, GEN GM500, HLG, Gms		X	X		Aminoglycoside
Grepafloxacin	GRX, Grx, GRE, GP	X				Fluoroquinolone
Iclaprim	ICL			X		Folate pathway inhibitor
Imipenem	IPM, IMI, Imp, IP			X		Carbapenem
Kanamycin	K, KAN, HLK, KM		X	X		Aminoglycoside
Levofloxacin	LVX, Lvx, LEV, LEVO, LE	X		X		Fluoroquinolone
Linezolid	LNZ, LZ, LZD	X		X		Oxazolidinone
Linopristin-flopristin	LFE	X				Streptogramin
Lomefloxacin	LOM, Lmf	X				Fluoroquinolone
Loracarbef	LOR, Lor, LO	X				Cephem
Mecillinam	MEC	X				Penicillin
Meropenem	MEM, Mer, MERO, MRP, MP			X		Carbapenem
Methicillin	DP, MET, ME, SC		X	X		Penicillin
Metronidazole	**MTZ**	**X**		**X**		**Nitroimidazole**
Mezlocillin	MZ, Mz, MEZ		X	X		Penicillin
Minocycline	MI, MIN, Min, MN, MNO, MC, MH	X		X		Tetracycline
Moxalactam	MOX		X	X		Cephem
Moxifloxacin	MXF	X		X		Fluoroquinolone
Mupirocin	MUP, MOP, MU				X	Pseudomonic acid
Nafcillin	NF, NAF, Naf		X	X		Penicillin
Nalidixic acid	NA, NAL	X				Quinolone

Glossary II. (Continued)

Antimicrobial Agent	Agent Abbreviation[a]	Routes of Administration[b]				Drug Class or Subclass
		PO	IM	IV	Topical	
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
Pefloxacin	**PEF, PF**					**Fluoroquinolone**
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.

Footnotes

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.

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

NOTE 2: Users should consult CLSI document M100,[3] which is updated annually, for the most current version of the glossary.

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	**Nitazoxanide, Nitrofurantoin**
SC	**Spectinomycin, Methicillin**
SO	**Sparfloxacin, Oxacillin**
TC	**Tetracycline, Ticarcillin**

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

NOTE 2: Users should consult CLSI document M100,[3] which is updated annually, for the most current version of the glossary.

Chapter 5: Conclusion

This third edition of M45 provides guidance for susceptibility testing of a wide variety of fastidious or infrequently isolated organisms in clinical, research, and public health laboratory settings. The working group is grateful to the individuals who contributed data and expert opinions to draft these recommendations. Users of this document are encouraged to assess these methods and collect clinical outcome data. The goal of this and future revisions is to translate new knowledge regarding organism growth requirements, taxonomy, therapeutic response, and antimicrobial resistance into laboratory guidance that will optimize patient outcomes.

Chapter 6: Supplemental Information

This chapter includes:

- References
- Additional Resources
- The Quality Management System Approach
- Related CLSI Reference Materials

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Additional Resources

General

Baddour LM, Wilson WR, Bayer AS, et al.; Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease; Council on Cardiovascular Disease in the Young; Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia; American Heart Association; Infectious Diseases Society of America. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. *Circulation*. 2005;111(23):e394-e434.

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Table 1. *Abiotrophia* spp. and *Granulicatella* spp. (Formerly Known as Nutritionally Deficient or Nutritionally Variant Streptococci)

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The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system (QMS) approach in the development of standards and guidelines, which facilitates project management; defines a document structure using a template; and provides a process to identify needed documents. The QMS approach applies a core set of "quality system essentials" (QSEs), basic to any organization, to all operations in any health care service's path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager's guide. The QSEs are as follows:

Organization	Personnel	Process Management	Nonconforming Event Management
Customer Focus	Purchasing and Inventory	Documents and Records	Assessments
Facilities and Safety	Equipment	Information Management	Continual Improvement

M45 addresses the QSE indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on 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
		M29				X M02 M07 M11 M23 VET01	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.

M45 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
				M02 M07 M11 VET01	X M02 M07 M11 VET01 VET01S M100	X M02 M07 M11 VET01 VET01S M100	X M02 M07 M11 VET01 VET01S M100	

Related CLSI Reference Materials*

M02 **Performance Standards for Antimicrobial Disk Susceptibility Tests. 12th ed., 2015.** This standard contains the current Clinical and Laboratory Standards Institute–recommended methods for disk susceptibility testing, criteria for quality control testing, and updated tables for interpretive zone diameters.

M07 **Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 10th ed., 2015.** This standard addresses reference methods for the determination of minimal inhibitory concentrations of aerobic bacteria by broth macrodilution, broth microdilution, and agar dilution.

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

M23 **Development of *In Vitro* Susceptibility Testing Criteria and Quality Control Parameters. 3rd ed., 2008.** This document addresses the required and recommended data needed for the selection of appropriate interpretive criteria and quality control ranges for antimicrobial agents.

M29 **Protection of Laboratory Workers From Occupationally Acquired Infections. 4th ed., 2014.** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.

M100S **Performance Standards for Antimicrobial Susceptibility Testing. 25th ed, 2015.** This document provides updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards M02-A12, M07-A10, and M11-A8.

VET01 **Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals. 4th ed., 2013.** This document provides the currently recommended techniques for antimicrobial agent disk and dilution susceptibility testing, criteria for quality control testing, and interpretive criteria for veterinary use.

VET01S **Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals. 3rd ed., 2015.** This document provides updated tables for the CLSI antimicrobial susceptibility testing standard VET01.

* 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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