CLINICAL AND LABORATORY STANDARDS INSTITUTE®

35th Edition

CLSI M100™

Performance Standards for Antimicrobial Susceptibility Testing

CLSI M100 includes updated tables for the Clinical and Laboratory Standards Institute antimicrobial susceptibility testing standards CLSI M02, M07, and M11.

A CLSI supplement for global application.

CLSI M100-Ed35
January 2025
Replaces CLSI M100-Ed34

Performance Standards for Antimicrobial Susceptibility Testing

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Abstract

The data in the tables are valid only if the methodologies in CLSI M02,[1] M07,[2] and M11[3] are followed. These standards contain information about disk diffusion (CLSI M02[1]) and dilution (CLSI M07[2] and CLSI M11[3]) test procedures for aerobic and anaerobic bacteria. Clinicians depend heavily on information from the microbiology laboratory for treating their seriously ill patients. The clinical importance of antimicrobial susceptibility test results demands that these tests be performed under optimal conditions and that laboratories have the capability to provide results for the newest antimicrobial agents. The tables presented in CLSI M100 represent the most current information for drug selection, interpretation, and quality control using the procedures standardized in CLSI M02,[1] M07,[2] and M11.[3] Users should replace previously published tables with these new tables. Changes in the tables since the previous edition appear in boldface type.

Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*. 35th ed. CLSI supplement M100 (ISBN 978-1-68440-262-5 [Print]; ISBN 978-1-68440-263-2 [Electronic]). Clinical and Laboratory Standards Institute, USA, 2025.

The Clinical and Laboratory Standards Institute consensus process, which is the mechanism for moving a document through two or more levels of review by the health care community, is an ongoing process. Users should expect revised editions of any given document. Because rapid changes in technology may affect the procedures, methods, and protocols in a standard or guideline, users should replace outdated editions with the current editions of CLSI documents. Current editions are listed in the CLSI catalog and posted on our website at www.clsi.org.

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Suggested Citation

CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 35th ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2025.

Previous Editions:

December 1986, December 1987, December 1991, December 1992, December 1994, December 1995, January 1997, January 1998, January 1999, January 2000, January 2001, January 2002, January 2003, January 2004, January 2005, January 2006, January 2007, January 2008, January 2009, January 2010, June 2010, January 2011, January 2012, January 2013, January 2014, January 2015, January 2016, January 2017, January 2018, January 2019, January 2020, March 2021, February 2022, March 2023, February 2024

CLSI M100-Ed35
ISBN 978-1-68440-262-5 (Print)
ISBN 978-1-68440-263-2 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2914 (Electronic)

Volume 45, Number 1

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Overview of Changes

CLSI M100-Ed35 replaces CLSI M100-Ed34, published in 2024. Major additions, reformatting, and/or table relocation changes are summarized below, followed by additional noteworthy changes detailed by section/table. Changes to content since the previous edition appear in boldface type; however, minor editorial or formatting changes are not listed here, nor highlighted in boldface type. To learn more about the organization of CLSI M100-Ed35, check the "Instructions for Use."

CLSI M100 is updated and reviewed annually as new data and new agents become available. Use of outdated documents is strongly discouraged.

Major Additions and/or Revisions
• Throughout: Changed categorization of disk diffusion from a "reference" method to a "standard" method; the disk diffusion method described in CLSI M02[1] is no longer considered a reference method but remains a standard method.
• Throughout: Modified QC testing frequency recommendations from "daily or weekly" to "daily or per IQCP."
• Tables 1: Removed all footnotes related to testing tetracycline and extrapolating results for doxycycline and/or minocycline (Tables 1A-1, 1A-2, 1B-2, 1B-5, 1C, 1D, 1E, 1G, and 1H-1); these comments are retained in the respective Tables 2 where relevant.
• Tables 2: Changed title of "Routine QC Recommendations" box to "QC Recommendations" and removed listings of specific QC strains from the boxes; recommendations for QC strain testing and frequency are now in Appendix I.
• Tables 1 and 2: Removed fluoroquinolones from the "Warning" box that lists agents that should not be reported on CSF isolates.
• Tables 2: Modified comments related to testing tetracycline and extrapolating results for doxycycline and/or minocycline, as appropriate for organisms or organism groups where tetracycline, doxycycline, and/or minocycline breakpoints are listed.
• Table 2A-1, Table 3B, and Table 3C: Enhanced recommendations for the performance of carbapenemase testing, including the identification of the carbapenemase type, for carbapenem-resistant Enterobacterales to support treatment decisions and infection control practices.
• Table 2B-3 and Appendix F: Removed MIC breakpoints which are no longer considered reliable for *Burkholderia cepacia* complex. Added instructions for handling *B. cepacia* complex should AST be requested. Developed ECVs for *B. cepacia* complex and added these to Appendix F.
• Appendix H: Expanded to include testing instructions when an MIC method for any agent is modified beyond the standard CLSI MIC reference method. Added method for testing exebacase (Appendix H2) that includes the instructions for testing exebacase previously located in Tables 5A-1 and 6A.
• Appendix I: Added new appendix with suggestions for development of a QC plan that includes selection of QC strains and QC testing frequency.

Section/Table	Changes
General	
CLSI Breakpoint Revisions Since 2010	**Revised:** • Ampicillin-sulbactam disk diffusion breakpoints for *Acinetobacter* spp. • Minocycline disk diffusion and MIC breakpoints for *Acinetobacter* spp. ***Deleted:*** • Doxycycline disk diffusion and MIC breakpoints for *Acinetobacter* spp. • Tetracycline disk diffusion and MIC breakpoints for *Acinetobacter* spp. • Ceftazidime MIC breakpoints for *B. cepacia* complex • Chloramphenicol MIC breakpoints for *B. cepacia* complex • Levofloxacin MIC breakpoints for *B. cepacia* complex • Meropenem MIC breakpoints for *B. cepacia* complex • Minocycline MIC breakpoints for *B. cepacia* complex • Ticarcillin-clavulanate MIC breakpoints for *B. cepacia* complex • Trimethoprim-sulfamethoxazole MIC breakpoints for *B. cepacia* complex
CLSI Archived Resources	***Deleted:*** • Table with links to archived resources (the archived resources remain on the CLSI website)
Instructions for Use of Tables	***Deleted:*** • Fluoroquinolones from the CSF warning box
Tables 1. Antimicrobial Agents That Should Be Considered for Testing and Reporting by Microbiology Laboratories	
Table 1A-1. Enterobacterales (excluding *Salmonella* and *Shigella* spp.)	**Added:** • Footnote d regarding cascade reporting rules for aztreonam
Table 1B-3. *Burkholderia cepacia* Complex	**Added:** • Comment regarding location of information for testing *B. cepacia* complex ***Deleted***: • All antimicrobial agents for testing and reporting: – Ceftazidime – Levofloxacin – Meropenem – Minocycline – Trimethoprim-sulfamethoxazole

Overview of Changes (Continued)

Section/Table	Changes
Tables 1. (Continued)	
Table 1J. Anaerobes	**Revised:** • Footnote c regarding penicillin testing and the presence of β-lactamases
Tables 2. Zone Diameter and/or MIC Breakpoints	
Table 2A-1. Zone Diameter and MIC Breakpoints for Enterobacterales (excluding *Salmonella* and *Shigella* spp.)	**Revised:** • Comment regarding carbapenem testing for Enterobacterales • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline susceptibility ***Deleted:*** • Comment regarding sulfisoxazole to represent other sulfonamides
Table 2A-2. Zone Diameter and MIC Breakpoints for *Salmonella* and *Shigella* spp.	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline susceptibility
Table 2B-2. Zone Diameter and MIC Breakpoints for *Acinetobacter* spp.	**Added:** • Comment regarding minocycline for isolates that test intermediate by disk diffusion **Revised:** • Ampicillin-sulbactam disk diffusion breakpoints • Minocycline disk diffusion and MIC breakpoints ***Deleted:*** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline • Doxycycline disk diffusion and MIC breakpoints • Tetracycline disk diffusion and MIC breakpoints

Section/Table	Changes
Tables 2. (Continued)	
Table 2B-3. MIC Breakpoints for *Burkholderia cepacia* complex	**Added:** • Comment regarding removal of MIC breakpoints • Comment regarding ECVs • Comment regarding clinical reporting guidance • Comment regarding reference BMD as the only reproducible method ***Deleted:*** • Ceftazidime MIC breakpoints • Chloramphenicol MIC breakpoints • Levofloxacin MIC breakpoints • Meropenem MIC breakpoints • Minocycline MIC breakpoints • Ticarcillin-clavulanate MIC breakpoints • Trimethoprim-sulfamethoxazole MIC breakpoints
Table 2B-5. MIC Breakpoints for Other Non-Enterobacterales	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline ***Deleted:*** • Comment regarding sulfisoxazole to represent other sulfonamides
Table 2C. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.	**Added:** • References describing species included in *Staphylococcus aureus* complex and the species evaluated by CLSI • List of methicillin (oxacillin) methods or targets appropriate for *Staphylococcus coagulans*; addition of *S. coagulans* to listing of species where breakpoints are applicable • Introduction of staphylococci other than *Staphylococcus aureus* (SOSA) terminology **Revised:** • Comment regarding resistance to the penicillinase-stable penicillins • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline • Comment regarding linezolid susceptibility prediction for tedizolid ***Deleted:*** • Comment regarding sulfisoxazole to represent other sulfonamides

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2D. Zone Diameter and MIC Breakpoints for *Enterococcus* spp.	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline • Comment regarding linezolid susceptibility prediction for tedizolid
Table 2E. Zone Diameter and MIC Breakpoints for *Haemophilus influenzae* and *Haemophilus parainfluenzae*	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline
Table 2F. Zone Diameter and MIC Breakpoints for *Neisseria gonorrhoeae*	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline
Table 2G. Zone Diameter and MIC Breakpoints for *Streptococcus pneumoniae*	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline
Table 2H-1. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. β-Hemolytic Group	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline • Comment regarding linezolid susceptibility prediction for tedizolid
Table 2H-2. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. Viridans Group	**Revised:** • Comment regarding tetracycline susceptibility prediction for doxycycline and minocycline • Comment regarding linezolid susceptibility prediction for tedizolid
Table 2I. Zone Diameter and MIC Breakpoints for *Neisseria meningitidis*	***Deleted:*** • Sulfisoxazole MIC breakpoints
Table 2J. MIC Breakpoints for Anaerobes	**Revised:** • Species appropriate for testing by broth microdilution (Testing Conditions box)
Table 2 Dosages. Antimicrobial Agent Dosage Regimens Used to Establish Susceptible or Susceptible-Dose Dependent Breakpoints	**Added:** • Dosage for ampicillin-sulbactam for *Acinetobacter* spp. • Dosage for minocycline for *Acinetobacter* spp. **Revised:** • Dosage for cefepime for *Pseudomonas aeruginosa*

Section/Table	Changes
Tables 3. Specialized Resistance Testing	
Introduction to Tables 3B and 3C. Tests for Carbapenemases in Enterobacterales and *Pseudomonas aeruginosa*	**Added:** • Comment recommending testing for carbapenemase type for carbapenem-resistant Enterobacterales • Comment regarding false-negative eCIM results with isolates coproducing a serine carbapenemase and a metallo-β-lactamase
Table 3C. Modified Carbapenem Inactivation Methods for Suspected Carbapenemase Production in Enterobacterales and *Pseudomonas aeruginosa*	**Added:** • Comment regarding false-negative eCIM results with isolates coproducing a serine carbapenemase and a metallo-β-lactamase; comment includes reporting recommendations • Comment regarding poor sensitivity of eCIM for detection of metallo-β-lactamases in isolates coproducing a serine β-lactamase **Revised:** • QC recommendations box
Table 3D. Aztreonam Plus Ceftazidime-Avibactam Broth Disk Elution Method	**Added:** • Alternative QC strains
Table 3F-1. Test for Performing Disk Diffusion Directly From Positive Blood Culture Broth	**Added:** • Supplemental reading – options • Ranges for early reading (8–10 h) of select QC strain–antimicrobial agent combinations • Breakpoint additions since 2021 for: – Enterobacterales cefepime 8–10 h and 16–18 h – *P. aeruginosa* ceftazidime 8–10 h – *Acinetobacter* spp. ampicillin-sulbactam 8–10 h – *Acinetobacter* spp. ceftazidime 8–10 h – *Acinetobacter* spp. piperacillin-tazobactam 8–10 h and 16–18 h **Revised:** • Breakpoint revisions since 2021 for: – *Acinetobacter* spp. ampicillin-sulbactam 16–18 h
Table 3F-2. Zone Diameter Disk Diffusion Breakpoints for Enterobacterales Direct From Blood Culture	**Added:** • Breakpoints for cefepime 8–10 h and 16–18 h

Overview of Changes (Continued)

Section/Table	Changes
Tables 3. (Continued)	
Table 3F-3. Zone Diameter Disk Diffusion Breakpoints for *Pseudomonas aeruginosa* Direct From Blood Culture	**Added:** • Breakpoints for ceftazidime 8–10 h • Comment regarding intermediate results for ceftazidime
Table 3F-4. Zone Diameter Disk Diffusion Breakpoints for *Acinetobacter* spp. Direct From Blood Culture	**Added:** • Breakpoints for ampicillin-sulbactam 8–10 h • Breakpoints for ceftazidime 8–10 h • Breakpoints for piperacillin-tazobactam 8–10 h and 16–18 h **Revised:** • Breakpoints for ampicillin-sulbactam 16–18 h
Tables 4. Disk Diffusion QC Ranges and Associated Tables	
Table 4A-1. Disk Diffusion QC Ranges for Nonfastidious Organisms and Antimicrobial Agents Excluding β-Lactam Combination Agents	**Added:** • Footnote that sulfisoxazole can be used to represent any of the currently available sulfonamide preparations **Revised:** • Minocycline QC range for *Escherichia coli* ATCC®[a] 25922 • Footnote d regarding routine QC for erythromycin and clindamycin
Table 4A-2. Disk Diffusion QC Ranges for Nonfastidious Organisms and β-Lactam Combination Agents	**Added:** • Ceftibuten-avibactam QC ranges for: – *E. coli* ATCC® 25922 – *E. coli* NCTC 13353 – *Klebsiella pneumoniae* ATCC® 700603 – *K. pneumoniae* ATCC® BAA-1705™ – *K. pneumoniae* ATCC® BAA-2814™
Table 4C. Disk Diffusion Reference Guide to QC Frequency to Support Modifications to Antimicrobial Susceptibility Test Systems	**Revised:** • Title of table • Introduction regarding approaches to determine QC testing frequency following test modification ***Deleted:*** • Option for 15-replicate plan or 20- or 30-d plan

Section/Table	Changes
Tables 5. MIC QC Ranges and Associated Tables	
Table 5A-1. MIC QC Ranges for Nonfastidious Organisms and Antimicrobial Agents Excluding β-Lactam Combination Agents	**Added:** • Zosurabalpin QC range for *Acinetobacter baumannii* NCTC 13304 • Footnote that sulfisoxazole can be used to represent any of the currently available sulfonamide preparations **Revised:** • Footnote o regarding exebacase testing instructions ***Deleted:*** • Detailed instructions and figures for testing exebacase (now in Appendix H2) • Sulfisoxazole QC instructions for CAMHB with 2.5–5% LHB in footnote h
Table 5A-2. MIC QC Ranges for Nonfastidious Organisms and β-Lactam Combination Agents	**Added:** • Ceftibuten-xeruborbactam QC ranges – *K. pneumoniae* ATCC® 700603 – *K. pneumoniae* ATCC® BAA-1705™ – *K. pneumoniae* ATCC® BAA-2814™
Table 5B. MIC QC Ranges for Fastidious Organisms (Broth Dilution Methods)	***Deleted:*** • Sulfisoxazole QC instructions for CAMHB with 2.5–5% LHB in footnote g
Table 5F. MIC Reference Guide to QC Frequency to Support Modifications to Antimicrobial Susceptibility Test Systems	**Revised:** • Title of table • Introduction regarding approaches to determine QC testing frequency following test modification ***Deleted:*** • Option for 15-replicate plan or 20- or 30-d plan
Tables 6. Preparing Antimicrobial Agent Stock Solutions	
Table 6A. Solvents and Diluents for Preparing Stock Solutions of Antimicrobial Agents	**Added:** • Zosurabalpin **Revised:** • Footnote i regarding exebacase handling instructions • Footnote j regarding CAMHB-HSD preparation instructions (now in Appendix H2)
Table 6C. Preparing Solutions and Media Containing Combinations of Antimicrobial Agents	**Added:** • Ceftibuten-xeruborbactam

Overview of Changes (Continued)

Section/Table	Changes
Appendixes	
Appendix A. Suggestions for Confirming Antimicrobial Susceptibility Test Results and Organism Identification for Agents Approved by the US Food and Drug Administration for Clinical Use	**Added:** • Sulbactam-durlobactam for *Acinetobacter baumanii* complex **Revised:** • Organization of organisms to align with organization of Tables 2
Appendix C. Quality Control Strains for Antimicrobial Susceptibility Tests	**Revised:** • NOTE regarding selection of QC strains for routine vs supplemental testing
Appendix F. Epidemiological Cutoff Values	**Added:** • *B. cepacia* complex ECVs for: – Ceftazidime – Levofloxacin – Meropenem – Minocycline – Trimethoprim-sulfamethoxazole **Revised:** • Order of the tables
Appendix H. Modifications of the Minimal Inhibitory Concentration Method for Testing Select Antimicrobial Agents (new)	**Added:** • Introductory text for Appendix H • Exebacase testing instructions in Appendix H, section H2 **Revised:** • Title for Appendix H
Appendix I. Selection of Quality Control Strains and Quality Control Testing Frequency (new)	New Appendix

Section/Table	Changes
Glossaries	
Glossary I (Part 1). β-Lactams: Class and Subclass Designations and Generic Names	**Added:** • Ceftibuten-xeruborbactam
Glossary I (Part 2). Non–β-Lactams: Class and Subclass Designations and Generic Names	**Added:** • Zosurabalpin
Glossary II. Antimicrobial Agent Abbreviations, Routes of Administration, and Drug Class	**Added:** • Ceftibuten-xeruborbactam • Zosurabalpin

Abbreviations: AST, antimicrobial susceptibility testing; ATCC®, American Type Culture Collection; BMD, broth microdilution; CAMHB, cation-adjusted Mueller-Hinton broth; CAMHB-HSD, cation-adjusted Mueller-Hinton broth supplemented with horse serum (25% v/v) and 0.5 mM DL-dithiothreitol (pH 7.2–7.4); CSF, cerebrospinal fluid; d, day(s); eCIM, EDTA-modified carbapenem inactivation method; ECV, epidemiological cutoff value; EDTA, ethylenediaminetetraacetic acid; h, hour(s); **IQCP, individualized quality control plan;** LHB, lysed horse blood; MIC, minimal inhibitory concentration; NCTC, National Collection of Type Cultures; QC, quality control; **SOSA, staphylococci other than *Staphylococcus aureus*.**

Footnote

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

Instructions for Use of Tables

These instructions apply to:

- Tables 1A through 1J: suggested tiers of antimicrobial agents that should be considered for testing and reporting by microbiology laboratories. These suggestions include clinical efficacy, current consensus recommendations for first-choice and alternative drugs, and US Food and Drug Administration (FDA) clinical indications for use. In other countries, placement of antimicrobial agents in Tables 1A through 1J should be based on available drugs approved for clinical use by relevant regulatory organizations.
- Tables 2A through 2J: tables for each organism group that contain:
  - Recommended testing conditions
  - Routine QC recommendations (also see CLSI M02[1] and CLSI M07[2])
  - General comments for testing the organism group and specific comments for testing particular agent/organism combinations
  - Agents that should be considered for routine testing and reporting by medical microbiology laboratories, as specified in Tables 1A through 1J (test/report Tiers 1, 2, 3, and 4), including agents reported only on organisms isolated from the urinary tract (designated by "U")
  - Agents that are appropriate for the respective organism group but are not listed in Tables 1 and would generally not warrant routine testing by a medical microbiology laboratory in the United States (designated with an asterisk as "other"; designated with "Inv." for "investigational" [not yet FDA approved]), including agents reported only on organisms isolated from the urinary tract (designated by "U")
  - Zone diameter and minimal inhibitory concentration (MIC) breakpoints
- Tables 1J and 2J: tables containing specific recommendations for testing and reporting results on anaerobes and some of the information listed in the bullets above
- Tables 3A through 3L: tables describing tests to detect particular resistance types in specific organisms or organism groups

I. Selecting Antimicrobial Agents for Testing and Reporting

A. Appropriate Agents for Routine Testing

Selecting the most appropriate antimicrobial agents to test and report is a decision best made by each laboratory in consultation with the antimicrobial stewardship team and other relevant institutional stakeholders.

The suggestions for each organism group in Tables 1A through 1J include agents of proven efficacy that show acceptable *in vitro* test performance. Considerations in the assignment of agents to specific tiers include:

- Clinical efficacy
- Prevalence of resistance
- Minimizing emergence of resistance
- FDA clinical indications for use
- Current consensus recommendations for first-choice and alternative drugs
- Cost

Tests on selected agents may be useful for infection-prevention purposes (eg, testing ceftazidime for Enterobacterales to indicate potential extended-spectrum β-lactamase production; see Table 3A).

B. Equivalent Agents

Antimicrobial agents listed together in a single box are agents for which interpretive categories (susceptible, intermediate, susceptible-dose dependent, or resistant) and clinical efficacy are similar. A laboratory will often test only one agent from a box routinely, typically the agent that is on its formulary. In some cases, a laboratory may not test any agents from a box, depending on institutional needs.

In some boxes, the agents will be listed with an "or" between them. The "or" identifies agents for which cross-resistance and cross-susceptibility are nearly complete. Results from one agent connected by an "or" can be used to predict results for the other agent (ie, equivalent agents). For example, Enterobacterales susceptible to cefotaxime can be considered susceptible to ceftriaxone. The results obtained from testing cefotaxime could be reported along with a comment that the isolate is also susceptible to ceftriaxone. For drugs connected with an "or," combined major and very major errors are fewer than 3%, and minor errors are fewer than 10%, based on a large population of bacteria tested (see CLSI M23[4] for description of error types). In addition, to qualify for an "or," at least 100 strains with resistance to the agents in question must be tested and a result of "resistant" must be obtained with all agents for at least 95% of the strains. "Or" is also used for comparable agents when tested against organisms for which "susceptible-only" breakpoints are provided (eg, cefotaxime or ceftriaxone with *Haemophilus influenzae*). When no "or" connects agents within a box, testing of one agent cannot be used to predict results for another, owing either to discrepancies or insufficient data (see Section VIII, which describes equivalent agent tests).

Table 1D. *Enterococcus* spp.[a]

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ampicillin[b,c] Penicillin[c,d]			
	Vancomycin		
	Gentamicin[e] (high-level resistance testing only)	Streptomycin[e] (high-level resistance testing only)	
	Daptomycin[f,g]		
	Linezolid	Tedizolid	
			Dalbavancin[f,h]
			Oritavancin[f,h]
			Telavancin[f,h]
Urine Only			
Nitrofurantoin			
	Ciprofloxacin Levofloxacin		
		Fosfomycin[i]	
		Tetracycline	

Abbreviations: HLAR, high-level aminoglycoside resistance; MDRO, multidrug-resistant organism; MIC, minimal inhibitory concentration.

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PRINT ISBN 978-1-68440-262-5

ELECTRONIC ISBN 978-1-68440-263-2

CLSI M100-Ed35