CLINICAL AND LABORATORY STANDARDS INSTITUTE®

33rd Edition

M100

Performance Standards for Antimicrobial Susceptibility Testing

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

A CLSI supplement for global application.

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M100-Ed33
March 2023
Replaces M100-Ed32

Performance Standards for Antimicrobial Susceptibility Testing

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Abstract

The data in the tables are valid only if the methodologies in CLSI documents M02,[1] M07,[2] and M11[3] are followed. These standards contain information about disk diffusion (M02[1]) and dilution (M07[2] and 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 M100 represent the most current information for drug selection, interpretation, and quality control using the procedures standardized in 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.* 33rd ed. CLSI supplement M100 (ISBN 978-1-68440-170-3 [Print]; ISBN 978-1-68440-171-0 [Electronic]). Clinical and Laboratory Standards Institute, USA, 2023.

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

Suggested Citation

CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 33rd ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2023.

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

M100-Ed33
ISBN 978-1-68440-170-3 (Print)
ISBN 978-1-68440-171-0 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2914 (Electronic) Volume 43, Number 3

Contents

Contents (Continued)

Contents (Continued)

Contents (Continued)

Contents (Continued)

Overview of Changes

M100-Ed33 replaces the previous edition of the supplement, M100-Ed32, published in 2022. The major changes in M100-Ed33 are listed below. Other minor or editorial changes were made to the general formatting and to some of the table footnotes and comments. Changes to the tables since the previous edition appear in boldface type. The following are additions or changes unless otherwise noted as "*Deleted.*"

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 Use of outdated documents is strongly discouraged.

Section/Table	Changes
General	
Throughout	Revised text for testing and reporting to clarify relevant institutional stakeholders
CLSI Breakpoint Additions/Revisions Since 2010	**Revised to create 2 separate tables:** • CLSI Breakpoint Additions Since 2010 • CLSI Breakpoint Revisions Since 2010
CLSI Breakpoint Additions Since 2010	**Added:** • Plazomicin disk diffusion and MIC breakpoints for Enterobacterales (p. xxx)
CLSI Breakpoint Revisions Since 2010	**Revised:** • Amikacin – Disk diffusion and MIC breakpoints for Enterobacterales (p. xxxiii) – Disk diffusion and MIC breakpoints for *Pseudomonas aeruginosa* (p. xxxiv) • Gentamicin disk diffusion and MIC breakpoints for Enterobacterales (p. xxxiii) • Piperacillin disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv) • Piperacillin-tazobactam disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv) • Tobramycin – Disk diffusion and MIC breakpoints for Enterobacterales (p. xxxiv) – Disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv) ***Deleted:*** • Gentamicin disk diffusion and MIC breakpoints for *P. aeruginosa* (p. xxxiv)

Overview of Changes (Continued)

Section/Table	Changes
General (Continued)	
CLSI Archived Resources	**Added:** • Former Tables 1A–1C regarding suggested groupings of antimicrobial agents approved by the US Food and Drug Administration for clinical use that should be considered for testing and reporting by microbiology laboratories, which have been replaced by new Tables 1A through 1P (p. xxxvii)
Instructions for Use of Tables	**Added:** • Test/Report Tiers and Additional Designations (pp. 3–5) • Selective and Cascade Reporting (pp. 6–7) **Revised:** • Introductory section to include new Tables 1A through 1P and to update test/report tiers and designations (p. 1) • Appropriate Agents for Routine Testing (p. 2) • Equivalent Agents (pp. 2–3) • Susceptible-dose dependent definition to include extended infusion in the dosage regimen information (p. 9) • Organisms Excluded from Table 2 to clarify *Aeromonas* spp. (p. 11)
Tables 2	**Added (where applicable):** • Urine-only (U) designation and associated footnote • Inv. designation for investigational agents • * designation for "Other" agents not included in Tables 1 ***Deleted:*** • Test/Report column
Tables 1. Antimicrobial Agents That Should Be Considered for Testing and Reporting by Microbiology Laboratories	
Introduction to Tables 1A–1P. Antimicrobial Agents That Should Be Considered for Testing and Reporting by Microbiology Laboratories (new)	**Added:** • Introductory text and warning box for Tables 1A-1P (p. 24)
Table 1A. Enterobacterales (not including inducible AmpC producers and *Salmonella*/*Shigella*) (new table)	**Added:** • Antimicrobial agents for Enterobacterales (not including inducible AmpC producers and *Salmonella*/*Shigella*) (pp. 26–27)
Table 1B. *Salmonella* and *Shigella* spp. (new table)	**Added:** • Antimicrobial agents for *Salmonella* and *Shigella* spp. (p. 28)

Overview of Changes (Continued)

Section/Table	Changes
Tables 1. (Continued)	
Table 1C. *Pseudomonas aeruginosa* (new table)	**Added:** • Antimicrobial agents for *P. aeruginosa* (p. 30)
Table 1D. *Acinetobacter* spp. (new table)	**Added:** • Antimicrobial agents for *Acinetobacter* spp. (p. 32)
Table 1E. *Burkholderia cepacia* complex (new table)	**Added:** • Antimicrobial agents for *B. cepacia* complex (p. 34)
Table 1F. *Stenotrophomonas maltophilia* (new table)	**Added:** • Antimicrobial agents for *S. maltophilia* (p. 36)
Table 1G. Other Non-Enterobacterales (new table)	**Added:** • Antimicrobial agents for other non-Enterobacterales (p. 38)
Table 1H. *Staphylococcus* spp. (new table)	**Added:** • Antimicrobial agents for *Staphylococcus* spp. (pp. 40–41)
Table 1I. *Enterococcus* spp. (new table)	**Added:** • Antimicrobial agents for *Enterococcus* spp. (pp. 42–43)
Table 1J. *Haemophilus influenzae* and *Haemophilus parainfluenzae* (new table)	**Added:** • Antimicrobial agents for *H. influenzae* and *H. parainfluenzae* (pp. 44–45)
Table 1K. *Neisseria gonorrhoeae* (new table)	**Added:** • Antimicrobial agents for *N. gonorrhoeae* (p. 46)
Table 1L. *Streptococcus pneumoniae* (new table)	**Added:** • Antimicrobial agents for *S. pneumoniae* (pp. 48–49)
Table 1M. *Streptococcus* spp. ß-Hemolytic Group (new table)	**Added:** • Antimicrobial agents for *Streptococcus* spp. ß-hemolytic group (pp. 50–51)
Table 1N. *Streptococcus* spp. Viridans Group (new table)	**Added:** • Antimicrobial agents for *Streptococcus* spp. viridans group (p. 52)
Table 1O. Gram-Negative Anaerobes (new table)	**Added:** • Antimicrobial agents for gram-negative anaerobes (p. 54)
Table 1P. Gram-Positive Anaerobes (new table)	**Added:** • Antimicrobial agents for gram-positive anaerobes (p. 56)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. Zone Diameter and/or MIC Breakpoints	
Table 2A. Zone Diameter and MIC Breakpoints for Enterobacterales	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 58) • Reference for comments regarding cephems and routine ESBL testing and cephems and third-generation cephalosporin resistance (p. 62) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 64) • Gentamicin, tobramycin, and amikacin combination therapy comment (p. 68) • Gentamicin, tobramycin, and amikacin dosage regimen comments (p. 68) • Plazomicin disk diffusion and MIC breakpoints and associated comments (p. 68) **Revised:** • General comment regarding testing fecal isolates of *Salmonella* and *Shigella* spp. (p. 58) • Comment regarding therapy for oral ampicillin (p. 60) • Comment regarding cephems and routine ESBL testing (p. 62) • Comment regarding cephems and third-generation cephalosporin resistance (p. 62) • Comment regarding carbapenems and elevated MICs (p. 66) • Gentamicin, tobramycin, and amikacin disk diffusion and MIC breakpoints (p. 68) • Gemifloxacin reporting comment (p. 69)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2B-1. Zone Diameter and MIC Breakpoints for *Pseudomonas aeruginosa*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 74) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 76) • Comment regarding combination therapy for tobramycin and amikacin (p. 78) • Tobramycin and amikacin dosage regimen comments (p. 78) **Revised:** • Piperacillin disk diffusion and MIC breakpoints and associated dosage regimen comment (p. 76) • Piperacillin-tazobactam disk diffusion and MIC breakpoints and associated dosage regimen comment (p. 76) • Tobramycin disk diffusion and MIC breakpoints (p. 78) • U designation for amikacin (p. 78) ***Deleted:*** • Gentamicin disk diffusion and MIC breakpoints
Table 2B-2. Zone Diameter and MIC Breakpoints for *Acinetobacter* spp.	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 80) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 81)

Section/Table	Changes
Tables 2. (Continued)	
Table 2B-3. Zone Diameter and MIC Breakpoints for *Burkholderia cepacia* complex	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 84) **Revised:** • Chloramphenicol reporting comment (p. 85)
Table 2B-4. Zone Diameter and MIC Breakpoints for *Stenotrophomonas maltophilia*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 86) • Comment regarding the accuracy and reproducibility of cefiderocol testing results (p. 87) • Levofloxacin ***Rx*** monotherapy comment (p. 87) **Revised:** • Chloramphenicol reporting comment (p. 87)
Table 2B-5. MIC Breakpoints for Other Non-Enterobacterales	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 90) **Revised:** • Comment regarding recommendations for testing and reporting *Aeromonas* spp. (p. 90) • Chloramphenicol reporting comment (p. 92)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2C. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 94) **Revised:** • Daptomycin reporting comment (p. 101) • Quinupristin-dalfopristin reporting comment (p. 102)
Table 2D. Zone Diameter and MIC Breakpoints for *Enterococcus* spp.	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 106) **Revised:** • Dalbavancin and daptomycin (*E. faecium* only) reporting comment (p. 109) • Erythromycin and fosfomycin reporting comments (p. 110) • Quinupristin-dalfopristin and tedizolid reporting comments (p. 111)
Table 2E. Zone Diameter and MIC Breakpoints for *Haemophilus influenzae* and *Haemophilus parainfluenzae*	**Added:** • MH-F agar as a medium for disk diffusion to the testing conditions box for *H. influenzae* (p. 112) • MH-F broth as a medium for broth dilution to the testing conditions box for *H. influenzae* (p. 112) • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 112) • General comment regarding the use of MH-F broth vs HTM broth in MIC testing (p. 113) • General comment regarding the use of MH-F agar broth vs HTM broth in disk diffusion testing (p. 113) **Revised:** • Routine QC recommendations box to clarify media for each QC strain (p. 112) • Ceftolozane-tazobactam reporting comment (p. 115)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2F. Zone Diameter and MIC Breakpoints for *Neisseria gonorrhoeae*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 118)
Table 2G. Zone Diameter and MIC Breakpoints for *Streptococcus pneumoniae*	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 122) **Revised:** • Medium information for disk diffusion in testing conditions box (p. 122) • General comment regarding MIC testing of cefotaxime, ceftriaxone, meropenem, or penicillin reported with *S. pneumoniae* isolated from CSF (p. 123) • Comment regarding susceptibility to gemifloxacin, levofloxacin, and moxifloxacin (p. 127)
Table 2H-1. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. ß-Hemolytic Group	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 130) **Revised:** • Dalbavancin and daptomycin reporting comments (p. 132) • Erythromycin, azithromycin, clarithromycin, and dirithromycin dosage regimen comment (p. 133) • Tedizolid reporting comment (p. 134)
Table 2H-2. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. Viridans Group	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 136) **Revised:** • Dalbavancin and daptomycin reporting comments (p. 138)
Table 2I. Zone Diameter and MIC Breakpoints for *Neisseria meningitidis*	**Revised:** • Chloramphenicol reporting comment (p. 142)

Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2J. MIC Breakpoints for Anaerobes	**Added:** • General comment regarding antimicrobial agents that should be considered for testing and reporting (p. 144) **Revised:** • Ampicillin and penicillin testing and reporting comment to include test/report tiers (p. 145) • Metronidazole resistance comment to refer users to Appendix D (p. 146)
Tables 3. Specialized Resistance Testing	
Table 3A. Tests for Extended-Spectrum β-Lactamases in *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Escherichia coli*, and *Proteus mirabilis*	**Added:** • Introductory text regarding reporting of ESBL test results (p. 148) **Revised:** • **NOTE** regarding ESBL testing (p. 148)
Introduction to Tables 3B and 3C. Tests for Carbapenemases in Enterobacterales and *Pseudomonas aeruginosa*	**Revised:** • Introductory text and associated reference (p. 152)
Table 3B. CarbaNP Test for Suspected Carbapenemase Production in Enterobacterales and *Pseudomonas aeruginosa*	**Revised:** • Indications for when to perform test (p. 154) ***Deleted:*** • **NOTE** regarding the use of former MIC breakpoints for carbapenems
Table 3B-1. Modifications of Table 3B When Using MIC Breakpoints for Carbapenems Described in M100-S20 (January 2010)	***Deleted:*** • Table 3B-1
Table 3C. Modified Carbapenem Inactivation Methods for Suspected Carbapenemase Production in Enterobacterales and *Pseudomonas aeruginosa*	**Revised:** • Indications for when to perform test (p. 162) ***Deleted:*** • **NOTE** regarding the use of former MIC breakpoints for carbapenems
Table 3C-1. Modifications of Table 3C When Using MIC Breakpoints for Carbapenems Described in M100-S20 (January 2010)	***Deleted:*** • Table 3C-1

Overview of Changes (Continued)

Section/Table	Changes
Tables 3. (Continued)	
Table 3D. Tests for Colistin Resistance for Enterobacterales and *Pseudomonas aeruginosa*	**Revised:** • "QC recommendations – routine" row (p. 176) • QC strain in Figures 1 and 2 legends (pp. 178-179)
Table 3E-1. Test for Performing Disk Diffusion Directly From Positive Blood Culture Broth	**Revised:** • Incubation length recommendations to refer users to Tables 3E-2 and 3E-3 (p. 180)
Table 3E-2. Zone Diameter Disk Diffusion Breakpoints for Enterobacterales Direct From Blood Culture	**Added:** • General comment regarding organism identification (p. 182) • Breakpoints for ampicillin 8-10 h, meropenem 8-10 h and 16-18 h, and ciprofloxacin excluding *Salmonella* 8-10 h and 16-18 h (p. 183) ***Deleted:*** • Test/Report Group column
Table 3E-3. Zone Diameter Disk Diffusion Breakpoints for *Pseudomonas aeruginosa* Direct From Blood Culture	**Added:** • General comment regarding organism identification (p. 184) • Breakpoints for meropenem 8-10 h (p. 184) ***Deleted:*** • Test/Report Group column
Table 3I. Tests for Detecting Inducible Clindamycin Resistance in *Staphylococcus* spp., *Streptococcus pneumoniae*, and *Streptococcus* spp. ß-Hemolytic Group	**Added:** • Comment regarding QC disk diffusion recommendations (p. 197)

Overview of Changes (Continued)

Section/Table	Changes
Tables 4. Disk Diffusion QC Ranges and Associated Tables	
Table 4A-2. Disk Diffusion QC Ranges for Nonfastidious Organisms and β-Lactam Combination Agents	**Added:** • Organism characteristic OXA-1 for *E. coli* NCTC 13353 (p. 210) • Footnote e regarding colony morphologies for *K. pneumoniae* ATCC® 700603 (p. 212) • Ceftibuten QC range for *E. coli* NCTC 13353 • Ceftibuten-ledaborbactam QC range for *E. coli* NCTC 13353
Table 4B. Disk Diffusion QC Ranges for Fastidious Organisms	**Added:** • Footnote f regarding chloramphenicol QC range for *H. influenzae* ATCC® 49247 in MH-F agar (p. 216) • Gentamicin QC range for *N. gonorrhoeae* ATCC® 49226 (p. 215) • MH-F agar medium for *H. influenzae* (p. 216) **Revised:** • Footnote e regarding *H. influenzae* ATCC® 49247 or 49766 to indicate its use with HTM and to indicate that *H. influenzae* ATCC® 49247 should be used with MH-F (p. 216) • Footnote g regarding QC ranges for delafloxacin, levonadifloxacin, and nafithromycin to include clarithromycin with MH-F agar (p. 216) • Incubation temperatures for *H. influenzae*, *N. gonorrhoeae*, and streptococci and *N. meningitidis* (p. 216)
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:** • Footnote f regarding ceftibuten and tebipenem lack of established equivalency (p. 228) • Footnote j regarding colistin preparation and handling (p. 228) • **NOTE** stating that MIC ranges in table apply to both broth microdilution and agar dilution unless otherwise specified (p. 230) **Revised:** • Ceftibuten QC range for *E. coli* ATCC® 25922 • Footnote i regarding additional colistin QC ranges for *E. coli* NCTC 13846 (p. 228) • Footnote m regarding exebacase QC ranges, including figures showing determination of exebacase *S. aureus* ATCC® 29213 end points (pp. 228-229)

Section/Table	Changes
Tables 5. (Continued)	
Table 5A-2. MIC QC Ranges for Nonfastidious Organisms and β-Lactam Combination Agents	**Added:** • Organism characteristic OXA-1 for *E. coli* NCTC 13353 (p. 232) • Ceftazidime-avibactam QC ranges – *E. coli* NCTC 13353 – *Klebsiella pneumoniae* ATCC® BAA-1705™ – *K. pneumoniae* ATCC® BAA-2814™ • Ceftibuten QC range – *K. pneumoniae* ATCC® 700603 • Ceftibuten-avibactam QC ranges – *E. coli* ATCC® 25922 – *K. pneumoniae* ATCC® 700603 – *E. coli* NCTC 13353 – *K. pneumoniae* ATCC® BAA-1705™ – *K. pneumoniae* ATCC® BAA-2814™ • Ceftibuten-ledaborbactam QC ranges – *Escherichia coli* NCTC 13353 – *K. pneumoniae* ATCC® BAA-1705™ – *K. pneumoniae* ATCC® BAA-2814™ • Meropenem-xeruborbactam QC ranges – *P. aeruginosa* ATCC® 27853 – *K. pneumoniae* ATCC® BAA-2814™

Overview of Changes (Continued)

Section/Table	Changes
Tables 5. (Continued)	
Table 5A-2. MIC QC Ranges for Nonfastidious Organisms and β-Lactam Combination Agents (continued)	**Added (continued):** • Footnote e regarding colony morphologies for *K. pneumoniae* ATCC® 700603 (p. 234) • Footnote h regarding ceftazidime-avibactam, ceftibuten, and ceftibuten-avibactam lack of equivalency (p. 234) • Footnote i regarding meropenem QC range for *P. aeruginosa* ATCC® BAA-3197™ (formerly *P. aeruginosa* PA5257) (p. 234) • Footnote j regarding meropenem-xeruborbactam QC range for *P. aeruginosa* ATCC® BAA-3197™ (formerly *P. aeruginosa* PA5257) (p. 234) • **NOTE** stating that MIC ranges in the table apply to both broth microdilution and agar dilution unless otherwise specified (p. 234) **Revised:** • Ceftibuten QC range for *E. coli* ATCC® 25922 • Piperacillin-tazobactam QC range for *E. coli* ATCC® 25922
Table 5B. MIC QC Ranges for Fastidious Organisms (Broth Dilution Methods)	**Added:** • Tebipenem QC ranges – *H. influenzae* ATCC® 49766 – *S. pneumoniae* ATCC® 49619 • Footnote d regarding ceftazidime-avibactam, ceftibuten, and tebipenem lack of equivalency (p. 239) • Footnote k indicating tebipenem QC range for *H. influenzae* ATCC® 49766 was established with a limited number of media manufacturers (p. 239) • **NOTE** stating that MIC ranges in table apply to both broth microdilution and agar dilution unless otherwise specified (p. 239) **Revised:** • Medium for testing *H. influenzae* to include MH-F broth (p. 238) • Incubation temperature for testing *H. influenzae*, *S. pneumoniae* and streptococci, and *N. meningitidis* (p. 238)

Section/Table	Changes
Tables 5. (Continued)	
Table 5G. MIC Troubleshooting Guide	**Added:** • Ceftriaxone troubleshooting comments for *P. aeruginosa* ATCC® 27853 (p. 249) • Colistin troubleshooting comments (p. 249) and associated footnote b (p. 252) for *E. coli* ATCC® 25922, *P. aeruginosa* ATCC® 27853, *E. coli* NCTC 13846, and *E. coli* ATCC® BAA-3170™ • Various agents troubleshooting comments for *Enterococcus faecalis* ATCC® 51299 (p. 250) **Revised:** • Carbenicillin troubleshooting comment for *P. aeruginosa* ATCC® 27853 (p. 248) • Various agents troubleshooting comments for *S. pneumoniae* ATCC® 49619 (p. 250)
Tables 6. Preparing Antimicrobial Agent Stock Solutions	
Table 6A. Solvents and Diluents for Preparing Stock Solutions of Antimicrobial Agents	**Added:** • Ledaborbactam (p. 256) • Footnote i regarding exebacase handling instructions (p. 259) • Footnote j regarding exebacase preparation instructions (p. 259) • Xeruborbactam (p. 258) **Revised:** • Ceftibuten solvent and diluent for preparing stock solutions (p. 254) • Exebacase diluent for preparing stock solutions (p. 255) ***Deleted:*** • DMSO as a solvent for ceftibuten
Table 6C. Preparing Solutions and Media Containing Combinations of Antimicrobial Agents	**Added:** • Ceftibuten-avibactam (p. 264) • Ceftibuten-ledaborbactam (p. 264) • Meropenem-xeruborbactam (p. 265)

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:** • Enterobacterales (p. 274) – Imipenem-relebactam – Cefiderocol • *Acinetobacter baumannii* complex (p. 275) – Cefiderocol • *P. aeruginosa* (p. 275) – Ceftazidime-avibactam – Imipenem-relebactam – Cefiderocol • *S. maltophilia* (p. 275) – Cefiderocol • *Bacteroides* spp. and *Parabacteroides* spp. (p. 279) – Imipenem-relebactam
Appendix B. Intrinsic Resistance; B1. Enterobacterales	**Added:** • Footnote g regarding *Serratia marcescens* and tobramycin (p. 284) **Revised:** • **NOTE** regarding agents not listed because there is no intrinsic resistance (p. 285)
Appendix C. QC Strains for Antimicrobial Susceptibility Tests	**Added:** • Organism characteristic OXA-1 for *E. coli* NCTC 13353 (p. 291) • Comment regarding colony morphologies for *K. pneumoniae* ATCC® 700603 (p. 291)

Overview of Changes (Continued)

Section/Table	Changes
Appendixes (Continued)	
Appendix E. Dosage Regimens Used to Establish Susceptible or Susceptible-Dose Dependent Breakpoints	**Added:** • Enterobacterales – Amikacin (p. 302) – Gentamicin (p. 303) – Plazomicin (excluding family Morganellaceae) (p. 304) – Tobramycin (p. 304) • *P. aeruginosa* – Amikacin (p. 304) – Tobramycin (p. 304) **Revised:** • Dosage for piperacillin and piperacillin-tazobactam for *P. aeruginosa* (p. 304)
Appendix I. Cefiderocol Broth Preparation and Reading Broth Microdilution Minimal Inhibitory Concentration End Points	**Revised:** • Step for preparing iron-depleted cation-adjusted Mueller-Hinton broth (p. 335)
Glossaries	
Glossary I (Part 1). B-Lactams: Class and Subclass Designations and Generic Names	**Added:** • Ceftibuten-avibactam • Ceftibuten-ledaborbactam • Meropenem-xeruborbactam
Glossary II. Antimicrobial Agent Abbreviations, Routes of Administration, and Drug Class	**Added:** • Ceftibuten-avibactam • Ceftibuten-ledaborbactam • Meropenem-xeruborbactam

Abbreviations: ATCC®, American Type Culture Collection; CSF, cerebrospinal fluid; MH-F agar, Mueller-Hinton fastidious agar; MH-F broth, Mueller-Hinton fastidious broth; MIC, minimal inhibitory concentration; UTI, urinary tract infection.

Footnote

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

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 breakpoints and interpretive categories for the results of standard antimicrobial susceptibility tests and provide epidemiological cutoff values when breakpoints are not available.
- 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, breakpoints, 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.

Instructions for Use of Tables

These instructions apply to:

- **Tables 1A through 1P:** 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 1P** should be based on available drugs approved for clinical use by relevant regulatory organizations.

- **Tables 2A through 2I:** tables for each organism group that contain:
  - Recommended testing conditions
  - Routine QC recommendations (also see Chapter 4 in M02[1] and 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 1P** (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 1O, 1P, 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 3K:** 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-1P 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 document 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 *H. 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).**

C. Test/Report Tiers and Additional Designations

Antimicrobial Agent Test and Report Tiers and Additional Considerations for Agents Listed in Tables 1

Tier	Definition	Test	Report[a]	Additional Testing and Reporting Considerations
1	Antimicrobial agents that are appropriate for routine, primary testing and reporting	Routine	Routine	
2	Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Routine	Cascade[b]	• Report following cascade reporting rules due to resistance to agent(s) in Tier 1. • May be reported routinely based on institution-specific guidelines.
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[c]	Routine or by request	Cascade[b]	Test routinely based on institution-specific guidelines or by clinician request and report following cascade reporting rules due to resistance to agent(s) in Tiers 1 and 2.

Table 1A. Enterobacterales (not including inducible AmpC producers and *Salmonella/Shigella*)[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			
Cefazolin	Cefuroxime		
Cefotaxime or ceftriaxone[b]	Cefepime[c]		
	Ertapenem Imipenem Meropenem	Cefiderocol	
		Ceftazidime-avibactam	
		Imipenem-relebactam	
		Meropenem-vaborbactam	
Amoxicillin-clavulanate Ampicillin-sulbactam			
Piperacillin-tazobactam			
Gentamicin	Tobramycin	Plazomicin	
	Amikacin		
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
	Cefotetan Cefoxitin		
	Tetracycline[d]		
			Aztreonam
			Ceftaroline[b]
			Ceftazidime[b]
			Ceftolozane-tazobactam
Urine Only			
Cefazolin (surrogate for uncomplicated UTI)[e]			
Nitrofurantoin			
		Fosfomycin[f] (*Escherichia coli*)	

Abbreviations: MDRO, multidrug-resistant organism; UTI, urinary tract infection.

Table 1A. Enterobacterales (Continued)

Footnotes

a. See Appendix B for species-specific intrinsic resistance profiles. If an antimicrobial agent-organism combination that is defined as intrinsically resistant is tested, the result hould be reported as resistant. Consideration may be given to adding comments regarding intrinsic resistance of agents not tested.

b. *Citrobacter freundii* complex, *Enterobacter cloacae* complex, *Hafnia alvei*, *Klebsiella* (formerly *Enterobacter) aerogenes*, *Morganella morganii*, *Providencia* spp., *Serratia marcescens*, and *Yersinia enterocolitica* may test susceptible to ceftriaxone, cefotaxime, ceftazidime, and ceftaroline, but these agents may be ineffective against these genera within a few days after initiation of therapy due to derepression of inducible AmpC ß-lactamase. The risk of AmpC derepression during therapy is moderate to high with *C. freundii* complex, *E. cloacae complex*, and *K. aerogenes* and appears to be less frequent with *M. morganii*, *Providencia* spp., and *S. marcescens*.[1] Therefore, isolates that are initially susceptible may become resistant. Testing subsequent isolates may be warranted if clinically indicated.

c. Cefepime should be considered a Tier 1 agent for testing and/or reporting of *C. freundii* complex, *E. cloacae* complex, *H. alvei*, *K. aerogenes*, *M. morganii*, *Providencia* spp., *S. marcescens*, and *Y. enterocolitica* (see footnote b).[1]

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

e. See cefazolin comments in Table 2A for using cefazolin as a surrogate test for oral cephalosporins and for reporting cefazolin when used for therapy in uncomplicated UTIs.

f. Report only on *E. coli* isolated from the urinary tract.

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

Reference for Table 1A

[1] Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. IDSA Guidance on the treatment of antimicrobial-restant gram-negative infections: version 2.0. Infectious Diseases Society of America; 2022. Accessed 10 January 2023. https://www.idsociety.org/practice-guideline/amr-guidance-2.0/

Table 1B. *Salmonella* and *Shigella* spp.[a,b]

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			
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
Cefotaxime or ceftriaxone			Ertapenem[c] Imipenem[c] Meropenem[c]
	Azithromycin[d]		
			Tetracycline[e]

Abbreviation: MDRO, multidrug-resistant organism.

Footnotes

a. Table 2A should be used for interpreting antimicrobial susceptibility testing results for *Salmonella* and *Shigella* spp.

b. WARNING: For *Salmonella* spp. and *Shigella* spp., aminoglycosides, first- and second-generation cephalosporins, and cephamycins may appear active *in vitro* but are not effective clinically and should not be reported as susceptible. Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources. However, susceptibility testing is indicated for all *Shigella* isolates. When fecal isolates of *Salmonella* and *Shigella* spp. are tested, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely. In addition, for extraintestinal isolates of *Salmonella* spp., a third-generation cephalosporin should be tested and reported. Azithromycin may be tested and reported per institutional guidelines.

c. Ertapenem, imipenem, and/or meropenem might be considered for testing and/or reporting for isolates resistant to all agents in Tiers 1 and 2, although there are limited clinical data suggesting their effectiveness for treating salmonellosis or shigellosis.[1]

d. Report only on *Salmonella enterica* ser. Typhi and *Shigella* spp.

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

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

Reference for Table 1B

1 CDC Health Alert Network. Extensively drug-resistant *Salmonella* typhi infections among US residents without international travel. Accessed 10 January 2023. http://emergency.cdc.gov/han/2021/han00439.asp

Table 2A. Zone Diameter and MIC Breakpoints for Enterobacterales

Testing Conditions

Medium: Disk diffusion: MHA
Broth dilution: CAMHB; iron-depleted CAMHB for cefiderocol (see Appendix I)[1]
Agar dilution: MHA

Inoculum: Broth culture method or colony suspension, equivalent to a 0.5 McFarland standard; positive blood culture broth for select antimicrobial agents with disk diffusion (see general comment [6]).

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

Routine QC Recommendations (see Tables 4A-1 and 5A-1 for acceptable QC ranges)

Escherichia coli ATCC®[a] 25922
Pseudomonas aeruginosa ATCC® 27853 (for carbapenems)
Staphylococcus aureus ATCC® 25923 (for disk diffusion) or *S. aureus* ATCC® 29213 (for dilution methods) when testing azithromycin against *Salmonella enterica* ser. Typhi *or Shigella* spp.
Refer to Tables 4A-2 and 5A-2 to select strains for routine QC of β-lactam combination agents.

When a commercial test system is used for susceptibility testing, refer to the manufacturer's instructions for QC test recommendations and QC ranges.

Refer to Tables 3A, 3B, and 3C for additional testing, reporting, and QC for Enterobacterales.

General Comments

(1) Refer to Tables 1A-1B for antimicrobial agents that should be considered for testing and reporting by microbiology laboratories.

(2) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and no more than 6 disks on a 100-mm plate; disks should be placed no less than 24 mm apart, center to center (see M02,[2] Subchapter 3.6). Each zone diameter should be clearly measurable; overlapping zones prevent accurate measurement. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk (see the *M02 Disk Diffusion Reading Guide*[3]). Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. Strains of *Proteus* spp. may swarm into areas of inhibited growth around certain antimicrobial agents. With *Proteus* spp., ignore the thin veil of swarming growth in an otherwise obvious zone of growth inhibition. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

(3) When fecal isolates of *Salmonella* and *Shigella* spp. are tested, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely. Data regarding whether amoxicillin should be used to treat shigellosis are conflicting. When reporting ampicillin results, state that treatment of shigellosis with amoxicillin might **have poorer efficacy compared with treatment with ampicillin.** In addition, for extraintestinal isolates of *Salmonella* spp., a third-generation cephalosporin should be tested and reported, and chloramphenicol may be tested and reported if requested. Susceptibility testing is indicated for typhoidal *Salmonella* (*S. enterica* ser. Typhi and *S. enterica* ser. Paratyphi A–C) isolated from extraintestinal and intestinal sources. Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources. In contrast, susceptibility testing is indicated for all *Shigella* isolates.

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PRINT ISBN 978-1-68440-170-3

ELECTRONIC ISBN 978-1-68440-171-0

M100-Ed33