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35th Edition

CLSI M100™

Performance Standards for Antimicrobial Susceptibility Testing

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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.

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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 Use of outdated documents is strongly discouraged.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.

Overview of Changes (Continued)

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*

Overview of Changes (Continued)

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

Overview of Changes (Continued)

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.

CLSI Breakpoint Additions Since 2010

This table includes the CLSI M100 edition in which specific antimicrobial agent breakpoints were added for the first time for a specific organism group.

Antimicrobial Agent	Date of Addition (CLSI M100 edition)	Disk Diffusion Breakpoints	MIC Breakpoints	Comments
Enterobacterales				
Azithromycin	January 2015 (M100-S25)	X	X	*Salmonella enterica* ser. Typhi only
	March 2021 (M100-Ed31)	X	X	*Shigella* spp. Previously assigned an ECV
Cefiderocol	January 2019 (M100, 29th ed.)		X	
	January 2020 (M100, 30th ed.)	X		
Ceftaroline	January 2013 (M100-S23)	X	X	
Ceftazidime-avibactam	January 2018 (M100, 28th ed.)	X	X	
Ceftolozane-tazobactam	January 2016 (M100-S26)		X	
	January 2018 (M100, 28th ed.)	X		
Colistin	January 2020 (M100, 30th ed.)		X	Previously assigned an ECV
Doripenem	June 2010 (M100-S20-U)	X	X	
Imipenem-relebactam	March 2021 (M100-Ed31)	X	X	
Meropenem-vaborbactam	January 2019 (M100, 29th ed.)	X	X	
Pefloxacin	January 2015 (M100-S25)	X		*Salmonella* spp. (including *S. enterica* ser. Typhi) Surrogate test for ciprofloxacin
Plazomicin	March 2023 (M100-Ed33)	X	X	
Polymyxin B	January 2020 (M100, 30th ed.)		X	
Pseudomonas aeruginosa				
Cefiderocol	January 2019 (M100, 29th ed.)		X	
	January 2020 (M100, 30th ed.)	X		
Ceftazidime-avibactam	January 2018 (M100, 28th ed.)	X	X	
Doripenem	January 2012 (M100-S22)	X	X	
Imipenem-relebactam	March 2021 (M100-Ed31)	X	X	

CLSI Breakpoint Additions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition (CLSI M100 edition)	Disk Diffusion Breakpoints	MIC Breakpoints	Comments
***Acinetobacter* spp.**				
Cefiderocol	January 2019 (M100, 29th ed.)		X	
	January 2020 (M100, 30th ed.)	X		
Doripenem	January 2014 (M100-S24)	X	X	
Sulbactam-durlobactam	February 2024 (M100-Ed34)	X	X	
Stenotrophomonas maltophilia				
Cefiderocol	January 2019 (M100, 29th ed.)		X	
	January 2020 (M100, 30th ed.)	X		
***Staphylococcus* spp.**				
Ceftaroline	January 2013 (M100-S23)	X	X	
Dalbavancin	January 2018 (M100, 28th ed.)		X	
Lefamulin	March 2021 (M100-Ed31)	X	X	
Oritavancin	January 2016 (M100-S26)		X	
Tedizolid	January 2016 (M100-S26)		X	*S. aureus* only
	February 2024 (M100-Ed34)	X		*S. aureus* only
Telavancin	January 2016 (M100-S26)	X	X	
***Enterococcus* spp.**				
Dalbavancin	January 2018 (M100, 28th ed.)		X	
Oritavancin	January 2016 (M100-S26)		X	
Tedizolid	January 2016 (M100-S26)		X	
Telavancin	January 2016 (M100-S26)	X	X	
Haemophilus influenzae* and *Haemophilus parainfluenzae				
Ceftaroline	January 2013 (M100-S23)	X	X	
Ceftolozane-tazobactam	March 2021 (M100-Ed31)		X	
Doripenem	January 2012 (M100-S22)	X	X	
Lefamulin	March 2021 (M100-Ed31)	X	X	
Neisseria gonorrhoeae				
Azithromycin	January 2019 (M100, 29th ed.)		X	Previously assigned an ECV
	March 2021 (M100-Ed31)	X		

CLSI Breakpoint Additions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition (CLSI M100 edition)	Disk Diffusion Breakpoints	MIC Breakpoints	Comments
Streptococcus pneumoniae				
Ceftaroline	January 2013 (M100-S23)	X	X	
Doripenem	January 2012 (M100-S22)		X	
Doxycycline	January 2013 (M100-S23)	X	X	
Lefamulin	March 2021 (M100-Ed31)	X	X	
***Streptococcus* spp. β-Hemolytic Group**				
Ceftaroline	January 2013 (M100-S23)	X	X	
Dalbavancin	January 2018 (M100, 28th ed.)		X	
Doripenem	January 2012 (M100-S22)		X	
Oritavancin	January 2016 (M100-S26)		X	
Tedizolid	January 2016 (M100-S26)		X	
	February 2024 (M100-Ed34)	X		*S. pyogenes* and *S. agalactiae* only
Telavancin	January 2016 (M100-S26)	X	X	
***Streptococcus* spp. Viridans Group**				
Ceftolozane-tazobactam	January 2016 (M100-S26)		X	
Dalbavancin	January 2018 (M100, 28th ed.)		X	
Doripenem	January 2012 (M100-S22)		X	
Oritavancin	January 2016 (M100-S26)		X	
Tedizolid	January 2016 (M100-S26)		X	
	February 2024 (M100-Ed34)	X		*S. anginosus* group only
Telavancin	January 2016 (M100-S26)	X	X	
Anaerobes				
Doripenem	January 2012 (M100-S22)		X	
Imipenem-relebactam	March 2021 (M100-Ed31)		X	
Piperacillin-tazobactam	January 2017 (M100, 27th ed.)		X	
	January 2018 (M100, 28th ed.)		X	

Abbreviations: ECV, epidemiological cutoff value; MIC, minimal inhibitory concentration.

CLSI Breakpoint Revisions Since 2010

This table includes the CLSI M100 edition in which specific antimicrobial agent breakpoints were revised, updated, or deleted for a specific organism group. In some cases, unique breakpoints were added for a specific genus or species previously included within the organism or organism group breakpoints (eg, "*Salmonella* spp. [including *Salmonella enterica* ser. Typhi]" was previously grouped with the organism group breakpoints for Enterobacterales). Previous breakpoints for those revised here can be found in the edition of CLSI M100 that precedes the document listed in the column labeled "Date of Revision (CLSI M100 edition)." For example, previous breakpoints for aztreonam are listed in CLSI M100-S20 (January 2010). Deleted breakpoints can be found in CLSI Archived Resources.

Antimicrobial Agent	Date of Revision (CLSI M100 edition)	Disk Diffusion Breakpoints	MIC Breakpoints	Comments
Enterobacterales				
Amikacin	March 2023 (M100-Ed33)	X	X	
Aztreonam	January 2010 (M100-S20)	X	X	
Cefazolin (parenteral)	January 2010 (M100-S20)	X	X	Removed disk diffusion breakpoints
	January 2011 (M100-S21)	X	X	
	January 2016 (M100-S26)	X	X	For uncomplicated UTIs
Cefazolin (oral)	January 2014 (M100-S24)	X	X	Surrogate test for oral cephalosporins and uncomplicated UTIs
Cefepime	January 2014 (M100-S24)	X	X	Revised breakpoints include SDD
Cefiderocol	February 2022 (M100-Ed32)	X		
Cefotaxime	January 2010 (M100-S20)	X	X	
Ceftazidime	January 2010 (M100-S20)	X	X	
Ceftizoxime	January 2010 (M100-S20)	X	X	
Ceftolozane-tazobactam	February 2022 (M100-Ed32)	X		
Ceftriaxone	January 2010 (M100-S20)	X	X	
Ciprofloxacin	January 2012 (M100-S22)	X	X	*Salmonella* spp. (including *S. enterica* ser. Typhi)
	January 2019 (M100, 29th ed.)	X	X	Non-*Salmonella* spp.
Ertapenem	June 2010 (M100-S20-U)	X	X	
	January 2012 (M100-S22)	X	X	
Gentamicin	March 2023 (M100-Ed33)	X	X	
Imipenem	June 2010 (M100-S20-U)	X	X	
Levofloxacin	January 2013 (M100-S23)	X	X	*Salmonella* spp. (including *S. enterica* ser. Typhi)
	January 2019 (M100, 29th ed.)	X	X	Non-*Salmonella* spp.

CLSI Breakpoint Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Revision (CLSI M100 edition)	Disk Diffusion Breakpoints	MIC Breakpoints	Comments
Enterobacterales (Continued)				
Meropenem	June 2010 (M100-S20-U)	X	X	
Norfloxacin	January 2020 (M100, 30th ed.)	X	X	Reinstated breakpoints deleted from M100, 29th ed.
Ofloxacin	January 2013 (M100-S23)		X	*Salmonella* spp. (including *S. enterica* ser. Typhi)
Piperacillin	February 2022 (M100-Ed32)		X	Removed disk diffusion breakpoints due to reassessment of disk correlates for revised MIC breakpoints
Piperacillin-tazobactam	February 2022 (M100-Ed32)	X	X	
Tobramycin	March 2023 (M100-Ed33)	X	X	
Pseudomonas aeruginosa				
Amikacin	March 2023 (M100-Ed33)	X	X	Report only on organisms isolated from the urinary tract
Ciprofloxacin	January 2019 (M100, 29th ed.)	X	X	
Colistin	January 2017 (M100, 27th ed.)		X	
	January 2020 (M100, 30th ed.)		X	
Gentamicin	March 2023 (M100-Ed33)			Removed disk diffusion and MIC breakpoints
Imipenem	January 2012 (M100-S22)	X	X	
Levofloxacin	January 2019 (M100, 29th ed.)	X	X	
Meropenem	January 2012 (M100-S22)	X	X	
Norfloxacin	January 2020 (M100, 30th ed.)	X	X	Reinstated breakpoints deleted from M100, 29th ed.
Piperacillin	January 2012 (M100-S22)	X	X	
	March 2023 (M100-Ed33)	X	X	
Piperacillin-tazobactam	January 2012 (M100-S22)	X	X	
	March 2023 (M100-Ed33)	X	X	
Polymyxin B	January 2020 (M100, 30th ed.)		X	
Ticarcillin	January 2012 (M100-S22)	X	X	
Ticarcillin-clavulanate	January 2012 (M100-S22)	X	X	
Tobramycin	March 2023 (M100-Ed33)	X	X	

CLSI Breakpoint Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Revision (CLSI M100 edition)	Disk Diffusion Breakpoints	MIC Breakpoints	Comments
***Acinetobacter* spp.**				
Ampicillin-sulbactam	**January 2025 (M100-Ed35)**	**X**		
Cefiderocol	February 2022 (M100-Ed32)	X		
Colistin	January 2020 (M100, 30th ed.)		X	
Doxycycline	**January 2025 (M100-Ed35)**			**Removed disk diffusion and MIC breakpoints**
Imipenem	January 2014 (M100-S24)	X	X	
Meropenem	January 2014 (M100-S24)	X	X	
Minocycline	**January 2025 (M100-Ed35)**	**X**	**X**	
Polymyxin B	January 2020 (M100, 30th ed.)		X	
Tetracycline	**January 2025 (M100-Ed35)**			**Removed disk diffusion and MIC breakpoints**
***Burkholderia cepacia* complex**				
Ceftazidime	February 2024 (M100-Ed34)			Removed disk diffusion breakpoints
	January 2025 (M100-Ed35)			**Removed MIC breakpoints**
Chloramphenicol	**January 2025 (M100-Ed35)**			**Removed MIC breakpoints**
Levofloxacin	**January 2025 (M100-Ed35)**			**Removed MIC breakpoints**
Meropenem	February 2024 (M100-Ed34)			Removed disk diffusion breakpoints
	January 2025 (M100-Ed35)			**Removed MIC breakpoints**
Minocycline	February 2024 (M100-Ed34)			Removed disk diffusion breakpoints
	January 2025 (M100-Ed35)			**Removed MIC breakpoints**
Ticarcillin-clavulanate	**January 2025 (M100-Ed35)**			**Removed MIC breakpoints**
Trimethoprim-sulfamethoxazole	February 2024 (M100-Ed34)			Removed disk diffusion breakpoints
	January 2025 (M100-Ed35)			**Removed MIC breakpoints**
Stenotrophomonas maltophilia				
Cefiderocol	February 2022 (M100-Ed32)	X	X	
Ceftazidime	February 2024 (M100-Ed34)			Removed MIC breakpoints
Minocycline	February 2024 (M100-Ed34)	X	X	
Other Non-Enterobacterales				
Norfloxacin	January 2020 (M100, 30th ed.)	X	X	Reinstated breakpoints deleted from M100, 29th ed.

CLSI Breakpoint Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Revision (CLSI M100 edition)	Disk Diffusion Breakpoints	MIC Breakpoints	Comments
***Staphylococcus* spp.**				
Cefoxitin	January 2019 (M100, 29th ed.)	X		*S. epidermidis* surrogate test for oxacillin
Ceftaroline	January 2019 (M100, 29th ed.)	X	X	Revised breakpoints include SDD
Linezolid	February 2024 (M100-Ed34)	X		Staphylococci read with reflected light (previously read with transmitted light)
Norfloxacin	January 2020 (M100, 30th ed.)	X	X	Reinstated breakpoints deleted from M100, 29th ed.
Oxacillin	January 2016 (M100-S26)	X	X	*S. pseudintermedius*
	January 2018 (M100, 28th ed.)	X	X	*S. schleiferi*
	January 2019 (M100, 29th ed.)	X		*S. epidermidis*
	March 2021 (M100-Ed31)		X	*Staphylococcus* spp. except *S. aureus* and *S. lugdunensis*
Telavancin	January 2017 (M100, 27th ed.)			Removed disk diffusion breakpoints
***Enterococcus* spp.**				
Daptomycin	January 2019 (M100, 29th ed.)		X	
	January 2020 (M100, 30th ed.)		X	Separated into two sets of breakpoints: • *Enterococcus* spp. other than *E. faecium* • *E. faecium* (including SDD)
Norfloxacin	January 2020 (M100, 30th ed.)	X	X	Reinstated breakpoints deleted from M100, 29th ed.
Telavancin	January 2017 (M100, 27th ed.)			Removed disk diffusion breakpoints
Haemophilus influenzae* and *Haemophilus parainfluenzae				
Amoxicillin-clavulanate	February 2022 (M100-Ed32)		X	Removed disk diffusion breakpoints
Lefamulin	February 2022 (M100-Ed32)	X		For *H. influenzae* only
Streptococcus pneumoniae				
Lefamulin	February 2022 (M100-Ed32)	X		
Tetracycline	January 2013 (M100-S23)	X	X	
***Streptococcus* spp. β-Hemolytic Group**				
Telavancin	January 2017 (M100, 27th ed.)			Removed disk diffusion breakpoints
***Streptococcus* spp. Viridans Group**				
Telavancin	January 2017 (M100, 27th ed.)			Removed disk diffusion breakpoints
Neisseria meningitidis				
Sulfisoxazole	**January 2025 (M100, 35th ed.)**			**Removed MIC breakpoints**

Abbreviations: MIC, minimal inhibitory concentration; SDD, susceptible-dose dependent; UTI, urinary tract infection.

CLSI Archived Resources

The CLSI Archived Resources have been relocated to the CLSI website at www.clsi.org.

NOTE: The content of this document is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

Summary of CLSI Processes for Establishing Breakpoints and QC Ranges

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

The CLSI Subcommittee on Antimicrobial Susceptibility Testing reviews data from a variety of sources and studies (eg, *in vitro*, pharmacokinetics/pharmacodynamics, and clinical studies) to establish antimicrobial susceptibility test methods, breakpoints, and QC parameters. The details of the data necessary to establish breakpoints, QC parameters, and how the data are presented for evaluation are described in CLSI M23.[4]

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

Additional information, updates, and changes in CLSI M100 are found in the meeting summary minutes of the CLSI Subcommittee on Antimicrobial Susceptibility Testing at https://clsi.org/meetings/ast-file-resources/.

CLSI Methods vs Commercial Methods and CLSI vs US Food and Drug Administration Breakpoints

The standard methods described in CLSI M07[2] and CLSI M100 are reference methods. These methods, **and the standard disk diffusion method described in CLSI M02,[1]** may be used for routine antimicrobial susceptibility testing of patient isolates, for evaluating commercial devices that will be used in medical laboratories, by drug or device manufacturers for testing new agents or systems, or for surveillance of antimicrobial resistance. Results generated by reference methods, such as those included in CLSI documents, may be used by regulatory authorities to evaluate the performance of commercial susceptibility testing devices as part of the approval process. Clearance by a regulatory authority indicates the commercial susceptibility testing device provides susceptibility results that are substantially equivalent to results generated using reference methods for the organisms and antimicrobial agents described in the device manufacturer's approved package insert.

CLSI breakpoints may differ from those approved by various regulatory authorities for many reasons, including use of different databases, differences in data interpretation, differences in doses used in different parts of the world, and public health policies. Differences also exist because CLSI proactively evaluates the need for changing breakpoints. The reasons why breakpoints may change and the manner in which CLSI evaluates data and determines breakpoints are outlined in CLSI M23.[4]

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

CLSI Subcommittee on Antimicrobial Susceptibility Testing Mission Statement

The CLSI 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 CLSI Subcommittee on Antimicrobial Susceptibility Testing is to:

- Develop standard reference methods for antimicrobial susceptibility tests.
- Provide QC 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 QC 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 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