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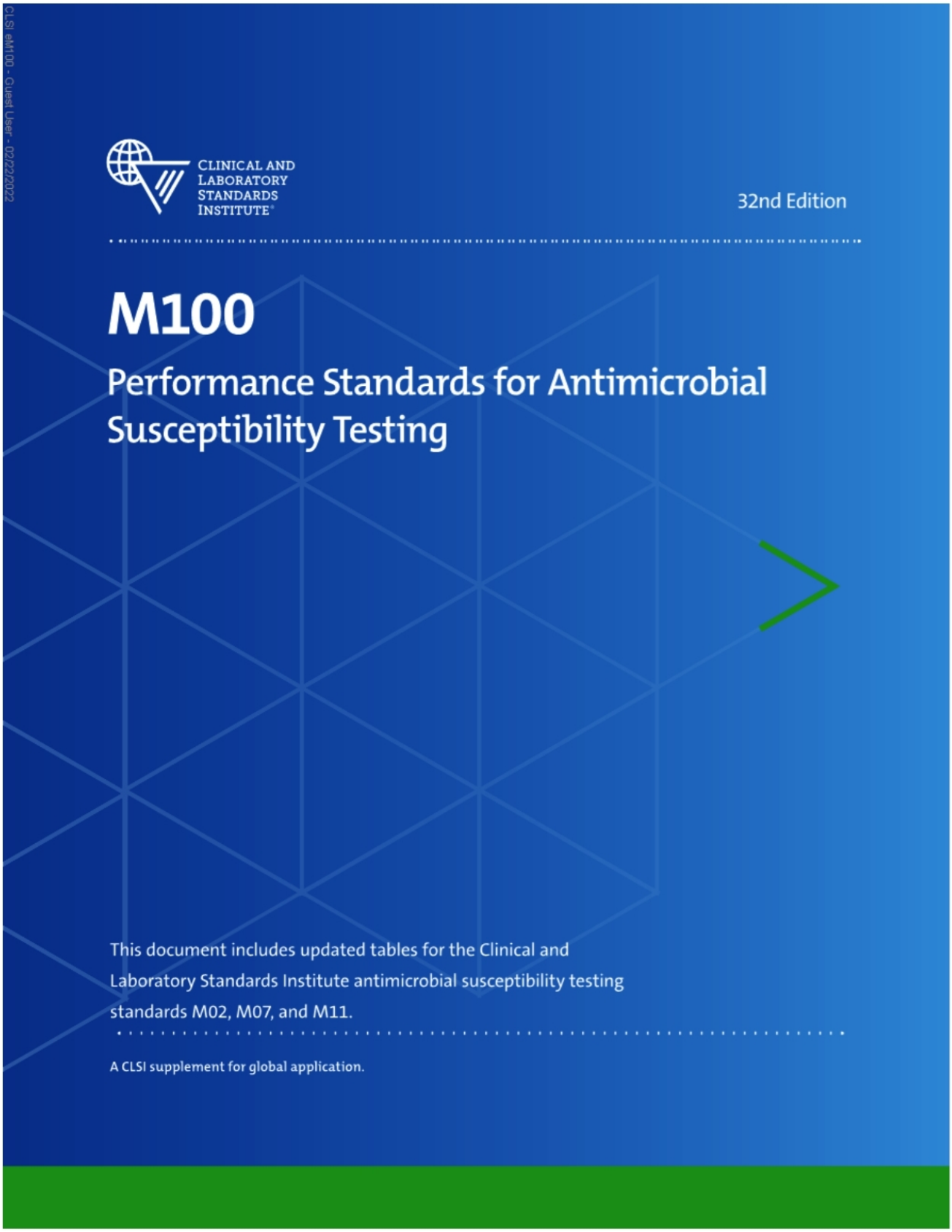

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Overview of Changes

M100-Ed32 replaces the previous edition of the supplement, M100-Ed31, published in 2021. The major changes in M100-Ed32 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 a "***deletion***."

Users of M100-Ed32 should note recent formatting changes to Tables 2, including:

- **An intermediate (I) with a ^ in Tables 2 indicates agents that have the potential to concentrate in the urine. The I^ is for informational use only. The decision to report I^ is best made by each laboratory based on institution-specific guidelines and in consultation with appropriate medical personnel.**

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 Use of outdated documents is strongly discouraged.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	
CLSI Breakpoint Additions/Revisions Since 2010	**Revised:** • Cefiderocol – Disk diffusion breakpoints for Enterobacterales (p. xxiii) and *Acinetobacter* spp. (p. xxv) – Disk diffusion and MIC breakpoints for *Stenotrophomonas maltophilia* (p. xxvi) • Ceftolozane-tazobactam disk diffusion breakpoints for Enterobacterales (p. xxiii) • Piperacillin MIC breakpoints for Enterobacterales (p. xxiv) • Piperacillin-tazobactam disk diffusion and MIC breakpoints for Enterobacterales (p. xxiv) • Amoxicillin-clavulanate MIC breakpoints for *Haemophilus influenzae* and *Haemophilus parainfluenzae* (p. xxvii) • Lefamulin disk diffusion breakpoints for *H. influenzae* only (p. xxvii) and *Streptococcus pneumoniae* (p. xxviii) ***Deleted***: • Piperacillin disk diffusion breakpoints for Enterobacterales • Amoxicillin-clavulanate disk diffusion breakpoints for *H. influenzae*

Overview of Changes (Continued)

Section/Table	Changes
Tables 1. 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 in the United States	
Table 1A. Nonfastidious Organisms	**Added:** Cefiderocol to Group B for Enterobacterales, *Pseudomonas aeruginosa*, *Acinetobacter* spp., and *S. maltophilia* (pp. 20 and 22)
Tables 2. Zone Diameter and/or MIC Breakpoints	
Table 2A. Zone Diameter and MIC Breakpoints for Enterobacterales	**Added:** • Ampicillin dosage regimen comments for parenteral and oral administration (p. 36) • Comment clarifying removal of piperacillin disk diffusion breakpoints (p. 36) • Comment for β-lactam combination agents regarding susceptibility of combination agents when the primary single agent is susceptible (replaced previous imipenem-relebactam surrogate testing comment) (p. 37) • Amoxicillin-clavulanate dosage regimen comments for parenteral and oral administration (p. 37) • Ampicillin-sulbactam dosage regimen comment (p. 37) • Piperacillin-tazobactam dosage regimen comment (p. 38) **Revised:** • General comment regarding reporting of results of amoxicillin testing with ampicillin (p. 34) • General comment regarding I^ (p. 35) • General comment and reference to associated tables regarding direct blood culture susceptibility testing of Enterobacterales with select antimicrobial agents (p. 35) • Piperacillin MIC breakpoints (p. 36) • Ceftolozane-tazobactam disk diffusion breakpoints and associated dosage regimen comment (p. 37) • Piperacillin-tazobactam disk diffusion and MIC breakpoints (p. 38) • Cefiderocol test group and disk diffusion breakpoints (p. 40) ***Deleted:*** • Piperacillin disk diffusion breakpoints • Imipenem-relebactam surrogate testing comment

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Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2B-1. Zone Diameter and MIC Breakpoints for *Pseudomonas aeruginosa*	**Added:** • Positive blood culture broth as an inoculum to the testing conditions box (p. 48) • General comment regarding direct blood culture susceptibility testing of *P. aeruginosa* with select antimicrobial agents (p. 49) • Comment for ß-lactam combination agents regarding susceptibility of combination agents when the primary single agent is susceptible (replaced previous imipenem-relebactam surrogate testing comment) (p. 50) **Revised:** • General comment regarding I^ (p. 48) • Ceftolozane-tazobactam dosage regimen comment (p. 50) • Cefiderocol test group (p. 50) ***Deleted:*** • Imipenem-relebactam surrogate testing comment
Table 2B-2. Zone Diameter and MIC Breakpoints for *Acinetobacter* spp.	**Added:** • Comment for ß-lactam combination agents regarding susceptibility of combination agents when the primary single agent is susceptible (p. 55) • Cefiderocol testing and reporting comment (p. 55) **Revised:** • Cefiderocol test group, disk diffusion breakpoints, and associated dosage regimen comment (p. 55)
Table 2B-4. Zone Diameter and MIC Breakpoints for *Stenotrophomonas maltophilia*	**Revised:** • Cefiderocol test group, disk diffusion and MIC breakpoints, and reporting comment (p. 61)
Table 2B-5. MIC Breakpoints for Other Non-Enterobacterales	**Added:** • Comment for ß-lactam combination agents regarding susceptibility of combination agents when the primary single agent is susceptible (p. 63)
Table 2C. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.	**Added:** • Dalbavancin, oritavancin, and telavancin dosage regimen comments (p. 72) • Tedizolid dosage regimen comment (p. 75) **Revised:** • *Staphylococcus* spp. indications for vancomycin (p. 72) and lefamulin (p. 75) to include methicillin-resistant *S. aureus*

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Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2D. Zone Diameter and MIC Breakpoints for *Enterococcus* spp.	**Added:** • Penicillin and ampicillin dosage regimen comments for parenteral and oral administration (p. 79) • Dalbavancin, oritavancin, and telavancin dosage regimen comments (p. 81) • Tedizolid dosage regimen comment (p. 83) **Revised:** • General comment regarding I^ (p. 78) • ***Rx*** combination therapy comment (p. 79)
Table 2E. Zone Diameter and MIC Breakpoints for *Haemophilus influenzae* and *Haemophilus parainfluenzae*	**Added:** • Ampicillin dosage regimen comment (p. 86) • Comment for ß-lactam combination agents regarding susceptibility of combination agents when the primary single agent is susceptible (p. 87) • Ampicillin-sulbactam, amoxicillin-clavulanate, and ceftolozane-tazobactam dosage regimen comments (p. 87) **Revised:** • Amoxicillin-clavulanate MIC breakpoints for susceptible and intermediate (p. 87) • Lefamulin disk diffusion breakpoint (for *H. influenzae* only) (p. 89) ***Deleted:*** • Amoxicillin-clavulanate disk diffusion breakpoints
Table 2F. Zone Diameter and MIC Breakpoints for *Neisseria gonorrhoeae*	**Revised:** • Tetracycline dosage regimen comment (p. 92)
Table 2G. Zone Diameter and MIC Breakpoints for *Streptococcus pneumoniae*	**Added:** • Amoxicillin (nonmeningitis) and amoxicillin-clavulanate (nonmeningitis) dosage regimen comment (p. 96) **Revised:** • Lefamulin disk diffusion breakpoint (p. 98)
Table 2H-1. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. ß-Hemolytic Group	**Added:** • Dalbavancin, oritavancin, and telavancin dosage regimen comments (p. 102) • Tedizolid dosage regimen comment (p. 104)
Table 2H-2. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. Viridans Group	**Added:** • Dalbavancin, oritavancin, and telavancin dosage regimen comments (pp. 107-108) • Tedizolid dosage regimen comment (p. 109)

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Overview of Changes (Continued)

Section/Table	Changes
Tables 2. (Continued)	
Table 2I. Zone Diameter and MIC Breakpoints for *Neisseria meningitidis*	**Added:** • Ampicillin dosage regimen comment (p. 111)
Table 2J. MIC Breakpoints for Anaerobes	**Added:** • Comment for β-lactam combination agents regarding susceptibility of combination agents when the primary single agent is susceptible (replaced previous imipenem-relebactam surrogate testing comment) (p. 115) **Revised:** • Imipenem-relebactam test group (p. 115) ***Deleted:*** • Imipenem-relebactam surrogate testing comment
Tables 3. Specialized Resistance Testing	
Table 3D. Tests for Colistin Resistance for Enterobacterales and *Pseudomonas aeruginosa*	**Revised:** • Nomenclature for *Escherichia coli* ATCC®a BAA-3170™ (formerly *E. coli* AR Bank #0349 *mcr-1*) (p. 148) • QC range for *E. coli* ATCC® BAA-3170™ (p. 148) • QC range for *P. aeruginosa* ATCC® 27853 (p. 148)
Table 3E-1. Test for Performing Disk Diffusion Directly From Positive Blood Culture Broth	**Revised:** • Applicable organism groups (p. 152) • Antimicrobial concentration information (refer to new Tables 3E-2 and 3E-3) (p. 152) • Applicable incubation length (p. 152) • Results reporting procedure (p. 152) • QC recommendations (p. 153)
Table 3E-2. Zone Diameter Disk Diffusion Breakpoints for Enterobacterales Direct From Blood Culture (new table)	**Added:** • Enterobacterales disk diffusion breakpoints for antimicrobial agents approved for susceptibility testing directly from blood culture bottles and associated comments and references (pp. 154-155)

Overview of Changes (Continued)

Section/Table	Changes
Tables 3. (Continued)	
Table 3E-3. Zone Diameter Disk Diffusion Breakpoints for *Pseudomonas aeruginosa* Direct From Blood Culture (new table)	**Added:** • *P. aeruginosa* disk diffusion breakpoints for antimicrobial agents approved for susceptibility testing directly from blood culture bottles and associated comments and references (p. 156)
Table 3K. Test for Detecting High-Level Aminoglycoside Resistance in *Enterococcus* spp.	**Revised:** • Additional testing and reporting comments (p. 175)
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:** • Gepotidacin QC range for *Enterococcus faecalis* ATCC® 29212 • Colistin QC ranges – *E. coli* NCTC 13486 – *E. coli* ATCC® BAA-3170™ (formerly AR Bank #0349 *mcr-1*) **Revised:** • Imipenem QC range for *E. coli* ATCC® 25922 • Ozenoxacin QC range for *E. faecalis* ATCC® 29212 • Tebipenem QC range for *S. aureus* ATCC® 29213
Table 5A-2. MIC QC Ranges for Nonfastidious Organisms and β-Lactam Combination Agents	**Added:** • Ceftibuten QC ranges: – *E. coli* ATCC® 25922 – *E. coli* NCTC 13353 – *Klebsiella pneumoniae* ATCC® BAA-1705™ – *K. pneumoniae* ATCC® BAA-2814™ • Meropenem QC ranges: – *E. coli* NCTC 13353 – *Acinetobacter baumannii* NCTC 13304 **Revised:** • Imipenem QC ranges: – *E. coli* ATCC® 25922 – *K. pneumoniae* ATCC® 700603 • Imipenem-relebactam QC ranges: – *E. coli* ATCC® 25922 – *K. pneumoniae* ATCC® 700603 • Meropenem-nacubactam QC range for *E. coli* ATCC® 25922

Overview of Changes (Continued)

Section/Table	Changes
Tables 5. (Continued)	
Table 5B. MIC QC Ranges for Fastidious Organisms (Broth Dilution Methods)	**Revised:** • Grepafloxacin QC range for *H. influenzae* ATCC® 49247
Table 5C. MIC QC Ranges for *Neisseria gonorrhoeae* (Agar Dilution Method)	**Added:** • Gentamicin QC range for *Neisseria gonorrhoeae* ATCC® 49226
Table 5D. MIC QC Ranges for Anaerobes (Agar Dilution Method)	**Added:** • Tebipenem QC ranges: – *Bacteroides fragilis* ATCC® 25285 – *Bacteroides thetaiotaomicron* ATCC® 29741 – *Clostridioides difficile* ATCC® 700057 – *Eggerthella lenta* ATCC® 43055 **Revised:** • Fidaxomicin QC range for C. *difficile* ATCC® 700057
Appendixes	
Appendix B. Intrinsic Resistance; B1. Enterobacterales	**Added:** • Polymyxin B and colistin for *Hafnia alvei* (p. 249) • Footnote regarding intrinsic resistance for *Hafnia paralvei* (p. 249)
Appendix C. QC Strains for Antimicrobial Susceptibility Tests	**Added:** • QC strain *E. coli* NCTC 13486 (p. 257) **Revised:** • Nomenclature for *E. coli* ATCC® BAA-3170™ (formerly *E. coli* AR Bank #0349 *mcr-1*) (p. 257)

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Overview of Changes (Continued)

Section/Table	Changes
Appendixes (Continued)	
Appendix E. Dosage Regimens Used to Establish Susceptible or Susceptible-Dose Dependent Breakpoints	**Added:** • Enterobacterales – Ampicillin (parenteral and oral) (p. 268) – Amoxicillin-clavulanate (parenteral and oral) (p. 268) – Ampicillin-sulbactam (p. 268) – Indications for cefazolin (uncomplicated UTIs and infections other than uncomplicated UTIs) (p. 268) – Imipenem-relebactam exclusion for the family *Morganellaceae* (p. 269) – Piperacillin-tazobactam (p. 270) • *Staphylococcus* spp. – Dalbavancin, oritavancin, tedizolid, and televancin as applicable to *S. aureus* only (p. 271) • *Enterococcus* spp. – Ampicillin (parenteral and oral) (p. 271) – Dalbavancin as applicable to vancomycin-susceptible *E. faecalis* only (p. 271) • *H. influenzae* and *H. parainfluenzae* – Ampicillin (p. 272) – Ampicillin-sulbactam (p. 272) • *S. pneumoniae* – Amoxicillin (p. 272) – Amoxicillin-clavulanate (p. 272) • *Streptococcus* spp. ß-hemolytic group – Dalbavancin as applicable to *S. pyogenes*, *S. agalactiae*, and *S. dysgalactiae* only (p. 273) – Tedizolid as applicable to *S. pyogenes* and *S. agalactiae* only (p. 273) • *Streptococcus* spp. viridans group – Dalbavancin and tedizolid as applicable to *S. anginosus* group only (p. 273) • *Neisseria meningitis* – Ampicillin (p. 273) ***Deleted:*** • *P. aeruginosa* – Ticarcillin

Overview of Changes (Continued)

Section/Table	Changes
Glossaries	
Glossary II. Antimicrobial Agent Abbreviation(s), Route(s) of Administration, and Drug Class	**Added:** • Rifapentine **Corrected:** • Cefepime-nacubactam abbreviation • Rifaximin abbreviation • Sulbactam-durlobactam route of administration
Glossary III. List of Identical Abbreviations Used for More Than One Antimicrobial Agent in US Diagnostic Products	**Added:** • Cefdinir • Cefditoren • Clinafloxacin • Cloxacillin • Cefpirome • Cefprozil • Ceftolozane-tazobactam • Colistin • Tobramycin • Trimethoprim

Abbreviations: ATCC®, American Type Culture Collection; MIC, minimal inhibitory concentration; UTI, urinary tract infection.

Footnote

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

CLSI Breakpoint Additions/Revisions Since 2010

Previous breakpoints can be found in the edition of M100 that precedes the document listed in the column labeled "Date of Addition/Revision (M100 edition)." For example, previous breakpoints for aztreonam are listed in M100-S19 (January 2009).

Antimicrobial Agent	Date of Addition/Revision (M100 edition)	Disk Diffusion Breakpoints		MIC Breakpoints		Comments
		New[a]	Revised[b]	New[a]	Revised[b]	
Enterobacterales						
Azithromycin	January 2015 (M100-S25)	X		X		*S. enterica* ser. Typhi only
	March 2021 (M100-Ed31)	X		X		*Shigella* spp. Previously assigned an ECV
Aztreonam	January 2010 (M100-S20)		X		X	
Cefazolin (parenteral)	January 2010 (M100-S20)				X	Removed disk diffusion breakpoints January 2010 (M100-S20)
	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	January 2019 (M100, 29th ed.)			X		
	January 2020 (M100, 30th ed.)	X				
	February 2022 (M100-Ed32)		**X**			
Cefotaxime	January 2010 (M100-S20)		X		X	
Ceftaroline	January 2013 (M100-S23)	X		X		
Ceftazidime	January 2010 (M100-S20)		X		X	
Ceftazidime-avibactam	January 2018 (M100, 28th ed.)	X		X		
Ceftizoxime	January 2010 (M100-S20)		X		X	
Ceftolozane-tazobactam	January 2016 (M100-S26)			X		
	January 2018 (M100, 28th ed.)	X				
	February 2022 (M100-Ed32)		**X**			
Ceftriaxone	January 2010 (M100-S20)		X		X	

CLSI Breakpoint Additions/Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition/Revision (M100 edition)	Disk Diffusion Breakpoints		MIC Breakpoints		Comments
		New[a]	Revised[b]	New[a]	Revised[b]	
Enterobacterales (Continued)						
Ciprofloxacin	January 2012 (M100-S22)		X		X	***Salmonella* spp. (including *S. enterica* ser. Typhi)**
	January 2019 (M100, 29th ed.)		X		X	**Non-*Salmonella* spp.**
Colistin	January 2020 (M100, 30th ed.)			X		Previously assigned an ECV
Doripenem	June 2010 (M100-S20-U)	X		X		
Ertapenem	June 2010 (M100-S20-U)		X		X	
	January 2012 (M100-S22)		X		X	
Imipenem	June 2010 (M100-S20-U)		X		X	
Imipenem-relebactam	March 2021 (M100-Ed31)	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.**
Meropenem	June 2010 (M100-S20-U)		X		X	
Meropenem-vaborbactam	January 2019 (M100, 29th ed.)	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)
Pefloxacin	January 2015 (M100-S25)	X				*Salmonella* spp. (including *S. enterica* ser. Typhi) Surrogate test for ciprofloxacin
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**	
Polymyxin B	January 2020 (M100, 30th ed.)			X		

CLSI Breakpoint Additions/Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition/Revision (M100 edition)	Disk Diffusion Breakpoints		MIC Breakpoints		Comments
		New[a]	Revised[b]	New[a]	Revised[b]	
Pseudomonas aeruginosa						
Cefiderocol	January 2019 (M100, 29th ed.)			X		
	January 2020 (M100, 30th ed.)	X				
Ceftazidime-avibactam	January 2018 (M100, 28th ed.)	X		X		
Ciprofloxacin	January 2019 (M100, 29th ed.)		X		X	
Colistin	January 2017 (M100, 27th ed.)				X	
	January 2020 (M100, 30th ed.)				X	
Doripenem	January 2012 (M100-S22)	X		X		
Imipenem	January 2012 (M100-S22)		X		X	
Imipenem-relebactam	March 2021 (M100-Ed31)	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	
Piperacillin-tazobactam	January 2012 (M100-S22)		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	
***Acinetobacter* spp.**						
Cefiderocol	January 2019 (M100, 29th ed.)			X		
	January 2020 (M100, 30th ed.)	X				
	February 2022 (M100-Ed32)		**X**			
Colistin	January 2020 (M100, 30th ed.)				X	
Doripenem	January 2014 (M100-S24)	X		X		
Imipenem	January 2014 (M100-S24)		X		X	
Meropenem	January 2014 (M100-S24)		X		X	
Polymyxin B	January 2020 (M100, 30th ed.)				X	

CLSI Breakpoint Additions/Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition/Revision (M100 edition)	Disk Diffusion Breakpoints		MIC Breakpoints		Comments
		New[a]	Revised[b]	New[a]	Revised[b]	
Stenotrophomonas maltophilia						
Cefiderocol	January 2019 (M100, 29th ed.)			X		
	January 2020 (M100, 30th ed.)	X				
	February 2022 (M100-Ed32)		**X**		**X**	
Other Non-Enterobacterales						
Norfloxacin	January 2020 (M100, 30th ed.)	X		X		Reinstated breakpoints deleted from M100, 29th ed.
***Staphylococcus* spp.**						
Cefoxitin	January 2019 (M100, 29th ed.)		X			*S. epidermidis* Surrogate test for oxacillin
Ceftaroline	January 2013 (M100-S23)	X		X		
	January 2019 (M100, 29th ed.)		X		X	Revised breakpoints include SDD
Dalbavancin	January 2018 (M100, 28th ed.)			X		
Lefamulin	March 2021 (M100-Ed31)	X		X		
Norfloxacin	January 2020 (M100, 30th ed.)	X		X		Reinstated breakpoints deleted from M100, 29th ed.
Oritavancin	January 2016 (M100-S26)			X		
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*
Tedizolid	January 2016 (M100-S26)			X		
Telavancin	January 2016 (M100-S26)	X		X		
	January 2017 (M100, 27th ed.)					Removed disk diffusion breakpoints January 2017 (M100, 27th ed.)

CLSI Breakpoint Additions/Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition/Revision (M100 edition)	Disk Diffusion Breakpoints		MIC Breakpoints		Comments
		New[a]	Revised[b]	New[a]	Revised[b]	
Enterococcus spp.						
Dalbavancin	January 2018 (M100, 28th ed.)			X		
Daptomycin	January 2019 (M100, 29th ed.)				X	
	January 2020 (M100, 30th ed.)				X	Separated into two sets of breakpoints: • *Enterococcus* spp other than *Enterococcus faecium* • *E. faecium* (includes SDD)
Norfloxacin	January 2020 (M100, 30th ed.)	X		X		Reinstated breakpoints deleted from M100, 29th ed.
Oritavancin	January 2016 (M100-S26)			X		
Tedizolid	January 2016 (M100-S26)			X		
Telavancin	January 2016 (M100-S26)	X		X		
	January 2017 (M100, 27th ed.)					Removed disk diffusion breakpoints January 2017 (M100, 27th ed.)
Haemophilus influenzae and *Haemophilus parainfluenzae*						
Amoxicillin-clavulanate	**February 2022 (M100-Ed32)**				**X**	**Removed disk diffusion breakpoints February 2022 (M100-Ed32)**
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		
	February 2022 (M100-Ed32)		**X**			**For *H. influenzae* only**

CLSI Breakpoint Additions/Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition/Revision (M100 edition)	Disk Diffusion Breakpoints		MIC Breakpoints		Comments
		New[a]	Revised[b]	New[a]	Revised[b]	
Neisseria gonorrhoeae						
Azithromycin	January 2019 (M100, 29th ed.)			X		Previously assigned as ECV
	March 2021 (M100-Ed31)	X				
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		
	February 2022 (M100-Ed32)		**X**			
Tetracycline	January 2013 (M100-S23)		X		X	
***Streptococcus* spp. ß-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		
Telavancin	January 2016 (M100-S26)	X		X		
	January 2017 (M100, 27th ed.)					Removed disk diffusion breakpoints January 2017 (M100, 27th ed.)
***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		
Telavancin	January 2016 (M100-S26)	X		X		
	January 2017 (M100, 27th ed.)					Removed disk diffusion breakpoints January 2017 (M100, 27th ed.)

CLSI Breakpoint Additions/Revisions Since 2010 (Continued)

Antimicrobial Agent	Date of Addition/Revision (M100 edition)	Disk Diffusion Breakpoints		MIC Breakpoints		Comments
		New[a]	Revised[b]	New[a]	Revised[b]	
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; SDD, susceptible-dose-dependent; UTI, urinary tract infection.

Footnotes

a. "New" indicates the breakpoints are listed for the first time for a specific organism or organism group in the respective Table 2.
b. "Revised" indicates previously established breakpoints for a specific organism or organism group in the respective Table 2 have changed. 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 *S. enterica* ser. Typhi]" was previously grouped with Enterobacterales).

CLSI Archived Resources

Resource	Web Address for Archived Table
Breakpoints that have been eliminated from M100 since 2010 have been relocated to the CLSI website.	https://clsi.org/media/pqlom3b5/_m100_archived_drugs_table.pdf
Methods that have been eliminated from M100 have been relocated to the CLSI website.	https://clsi.org/media/nszl4tbc/_m100_archived_methods_table.pdf
QC ranges that have been eliminated from M100 since 2010 have been relocated to the CLSI website.	https://clsi.org/media/r31oari2/_m100_archived_qc_table.pdf
ECVs that have been replaced by breakpoints have been relocated to the CLSI website.	https://clsi.org/media/3mekwxft/_m100_archived_ecvs_table.pdf

Abbreviations: ECV, epidemiological cutoff value; QC, quality control.

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 Quality Control Ranges

The Clinical and Laboratory Standards Institute (CLSI) is an international, voluntary, not-for-profit, interdisciplinary, standards-developing, and educational organization accredited by the American National Standards Institute 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 document 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 this document are found in the meeting summary minutes of the Subcommittee on Antimicrobial Susceptibility Testing at https://clsi.org/meetings/ast-file-resources/.

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

It is important for users of M02,[1] M07,[2] and M100 to recognize that the standard methods described in CLSI documents are reference methods. These methods may be used for routine antimicrobial susceptibility testing of patient isolates, for evaluating commercial devices that will be used in medical laboratories, or by drug or device manufacturers for testing new agents or systems. 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 document 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.

Following discussions with appropriate stakeholders (eg, infectious diseases and pharmacy practitioners, the pharmacy and therapeutics and infection prevention committees of the medical staff, and the antimicrobial stewardship team), newly approved or revised breakpoints may be implemented by laboratories. Following verification, CLSI disk diffusion test breakpoints may be implemented as soon as they are published in M100. If a device includes antimicrobial test concentrations sufficient to allow interpretation of susceptibility and resistance to an agent using the CLSI breakpoints, a laboratory could choose to, after appropriate verification, interpret and report results using CLSI breakpoints.

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 and 1B:** suggested groupings of antimicrobial agents that should be considered for testing and reporting by microbiology laboratories. These guidelines are based on antimicrobial agents approved by the US Food and Drug Administration (FDA) for clinical use in the United States. In other countries, placement of antimicrobial agents in Tables 1A and 1B should be based on available drugs approved for clinical use by relevant regulatory 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
  - Suggested agents that should be considered for routine testing and reporting by medical microbiology laboratories, as specified in Tables 1A and 1B (test/report groups A, B, C, U)
  - Additional drugs that are appropriate for the respective organism group but would generally not warrant routine testing by a medical microbiology laboratory in the United States (test/report group O for "other"; test/report group Inv. for "investigational" [not yet FDA approved])
  - Zone diameter and minimal inhibitory concentration (MIC) breakpoints

- **Tables 1C 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 to 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 infectious diseases and pharmacy practitioners, the pharmacy and therapeutics and infection prevention committees of the medical staff, and the antimicrobial stewardship team. The recommendations for each organism group include agents of proven efficacy that show acceptable *in vitro* test performance. Considerations in the assignment of agents to specific test/report groups include clinical efficacy, prevalence of resistance, minimizing emergence of resistance, cost, FDA clinical indications for use, and current consensus recommendations for first-choice and alternative drugs. Tests on selected agents may be useful for infection prevention purposes.

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. Within each box, an "or" between agents indicates 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.

C. Test/Report Groups

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

2. **Group B** includes antimicrobial agents that may warrant primary testing, but they may be reported only selectively, such as when the organism is resistant to agents of the same antimicrobial class, as in group A. Other indications for reporting the result might include a selected specimen source (eg, a third-generation cephalosporin for Enterobacterales from CSF or

trimethoprim-sulfamethoxazole for urinary tract isolates); a polymicrobial infection; infections involving multiple sites; cases of patient allergy, intolerance, or failure to respond to an antimicrobial agent in group A; or for infection prevention.

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

4. **Group U ("urine")** includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating UTIs. These agents should not be routinely reported against pathogens recovered from other infection sites. An exception to this rule is for Enterobacterales in Table 1A, in which cefazolin is listed as a surrogate test agent for oral cephalosporins. Other antimicrobial agents with broader indications may be included in group U for specific urinary pathogens (eg, *Enterococcus* and ciprofloxacin).

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

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

D. Selective Reporting

Each laboratory should decide which agents in the tables to report routinely (group A) and which might be reported only selectively (from group B), in consultation with the infectious diseases and pharmacy practitioners, the pharmacy and therapeutics and infection prevention committees of the health care institution, and the antimicrobial stewardship team. Selective reporting should improve the clinical relevance of test reports and help minimize the selection of multiresistant, health care-associated strains by overusing broad-spectrum antimicrobial agents. Results for group B antimicrobial agents tested, but not reported routinely, should be available on request, or they may be reported for selected specimen types. Unexpected resistance, when confirmed, should be reported (eg, resistance to a secondary agent but susceptibility to a primary agent, such as a *P. aeruginosa* isolate resistant to amikacin but susceptible to tobramycin; as such, both drugs should be reported). In addition, each laboratory should develop a protocol to cover isolates that are confirmed as resistant to all agents on its routine test panels. This protocol should include options for testing additional agents in-house or sending the isolate to a referral laboratory.

II. Breakpoint and Interpretive Category Definitions

A. Breakpoint Definition

breakpoint - minimal inhibitory concentration (MIC) or zone diameter value used to categorize an organism as susceptible, susceptible-dose dependent, intermediate, resistant, or nonsusceptible; **NOTE 1:** MIC or zone diameter values generated by a susceptibility test can be interpreted based on established breakpoints; **NOTE 2:** Because breakpoints are **largely** based on pharmacologically and clinically rich datasets using *in vitro* and *in vivo* data, they are considered robust predictors of likely clinical outcome; **NOTE 3:** Also known as "clinical breakpoint"; **NOTE 4:** See **interpretive category.**

B. Interpretive Category Definition

interpretive category - category derived from microbiological characteristics, pharmacokinetic/pharmacodynamic parameters, and clinical outcome data, when available; **NOTE 1:** MIC or zone diameter values generated by a susceptibility test can be interpreted based on established breakpoints; **NOTE 2:** See **breakpoint.**

EXAMPLE:

Interpretive Category	Breakpoints	
	MIC, µg/mL	Zone Diameter, mm
Susceptible	≤4	≥20
Susceptible-dose dependent	8-16	15-19
Intermediate	8-16	15-19
Resistant	≥32	≤14
Nonsusceptible	>1	<17

MIC or zone diameter value breakpoints and interpretive categories are established per CLSI document M23[4] for categories of susceptible, intermediate, and resistant (and susceptible-dose dependent and nonsusceptible, when appropriate).

- **susceptible (S)** - a category defined by a breakpoint that implies that isolates with an MIC at or below or a zone diameter at or above the susceptible breakpoint are inhibited by the usually achievable concentrations of antimicrobial agent when the dosage recommended to treat the site of infection is used, resulting in likely clinical efficacy.

- **susceptible-dose dependent (SDD)** – a category defined by a breakpoint that implies that susceptibility of an isolate depends on the dosage regimen that is used in the patient. To achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either MICs or zone diameters) are in the SDD category, it is necessary to use a dosage regimen (ie, higher doses, more frequent doses, or both) that results in higher drug exposure than that achieved with the dose that was used to establish the susceptible breakpoint. Consideration should be given to the maximum, literature-supported dosage regimen, because higher exposure gives the highest probability of adequate coverage of an SDD isolate. Appendix E lists the doses used when establishing SDD categories. The drug label should be consulted for recommended doses and adjustment for organ function; **NOTE:** The SDD category may be assigned when doses well above those used to calculate the susceptible breakpoint are supported by the literature, widely used clinically, and/or approved and for which sufficient data to justify the designation exist and have been reviewed. This category also includes a buffer zone for inherent variability in test methods, which should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins. See Appendix F for additional information.

- **intermediate (I)** – a category defined by a breakpoint that includes isolates with MICs or zone diameters within the intermediate range that approach usually attainable blood and tissue levels and/or for which response rates may be lower than for susceptible isolates; **NOTE:** An I with a ^ in Tables 2 indicates agents that have the potential to concentrate in the urine. **The I^ is for informational use only. The decision to report I^ is best made by each laboratory based on institution-specific guidelines and in consultation with appropriate medical personnel.** The I category also includes a buffer zone for inherent variability in test methods, which should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins.

- **resistant (R)** – a category defined by a breakpoint that implies that isolates with an MIC at or above or a zone diameter at or below the resistant breakpoint are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules and/or that demonstrate MICs or zone diameters that fall in the range in which specific microbial resistance mechanisms are likely, and clinical efficacy of the agent against the isolate has not been reliably shown in treatment studies.

- **nonsusceptible (NS)** – a category used for isolates for which only a susceptible breakpoint is designated because of the absence or rare occurrence of resistant strains. Isolates for which the antimicrobial agent MICs are above or the zone diameters are below the value indicated for the susceptible breakpoint should be reported as nonsusceptible; **NOTE 1:** An isolate that is interpreted as nonsusceptible does not necessarily mean that the isolate has a resistance mechanism. It is possible that isolates with MICs above the susceptible breakpoint that lack resistance mechanisms may be encountered within the wild-type distribution after the time the susceptible-only breakpoint was set; **NOTE 2:** The term "nonsusceptible" should not be used when the text is describing an organism/drug category with intermediate

and resistant interpretive categories. Isolates that are in the categories of "intermediate" or "resistant" could be called "not susceptible" rather than "nonsusceptible."

C. Example of Breakpoints and Interpretive Categories as Used in Table 2

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL		
		S	I[a]	R	S	I[a]	R
X	30 µg	≥20	15-19	≤14	≤4	8-16	≥32
Y	-	-	-	-	≤1	2	≥4
Z	10 µg	≥16	-	-	≤1	-	-

[a] Or SDD, if appropriate.
Abbreviations: I, intermediate; R, resistant; S, susceptible; SDD, susceptible-dose dependent.

For antimicrobial agent X with breakpoints in the table above, the susceptible breakpoint is ≤ 4 µg/mL or ≥ 20 mm and the resistant breakpoint is ≥ 32 µg/mL or ≤ 14 mm. For some antimicrobial agents (eg, antimicrobial agent Y), only MIC breakpoints may be available. For these agents, the disk diffusion zone diameters do not correlate with MIC values or data have not been evaluated as described in CLSI document M23.[4] Technical issues may also preclude the use of the disk diffusion method for some agents. For some antimicrobial agents (eg, antimicrobial agent Z) only a "susceptible" category exists. For these agents, the absence or rare occurrence of resistant strains precludes defining any results categories other than "susceptible." For strains yielding results suggestive of a "nonsusceptible" category, organism identification and antimicrobial susceptibility test results should be confirmed (see Appendix A). In examples Y and Z, a dash mark (-) indicates a disk is not available or that breakpoints are not applicable.

III. Reporting Results

A. Organisms Included in Table 2

The MIC values determined as described in M07[2] may be reported directly to clinicians for patient care purposes. However, it is essential that an interpretive category result (S, SDD, I, R, or NS) also be provided routinely to facilitate understanding of the MIC report by clinicians. Zone diameter measurements without an interpretive category should not be reported. Recommended interpretive categories for various MIC and zone diameter values are included in tables for each organism group and are based on the evaluation of data as described in CLSI document M23.[4]

Laboratories should only report results for agents listed in Table 2 specific to the organism being tested. It is not appropriate to apply disk diffusion or MIC breakpoints borrowed from a table in which the organism is not listed. There may be rare cases for which an agent may be appropriate for an isolate but for which there are no CLSI breakpoints (eg, tigecycline). In these cases, the FDA Susceptibility Test Interpretive Criteria (STIC) website (https://www.fda.gov/drugs/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria) and the prescribing information document for the agent should be consulted.

For more information on reporting epidemiological cutoff values in the medical laboratory, see Appendix G.

B. Organisms Excluded From Table 2

For some organism groups excluded from Tables 2A through 2J, CLSI document M45[5] provides suggestions for standardized methods for AST, including information about drug selection, interpretation, and QC. The organism groups covered in that guideline are *Abiotrophia* and *Granulicatella* spp. (formerly known as nutritionally deficient or nutritionally variant streptococci); *Aerococcus* spp.; *Aeromonas* spp.; *Bacillus* spp. (not *Bacillus anthracis*); *Campylobacter jejuni/coli; Corynebacterium* spp. (including *Corynebacterium diphtheriae*); *Erysipelothrix rhusiopathiae; Gemella* spp.; the HACEK group: *Aggregatibacter* spp. (formerly *Haemophilus aphrophilus, Haemophilus paraphrophilus, Haemophilus segnis,* and *Actinobacillus actinomycetemcomitans*), *Cardiobacterium* spp., *Eikenella corrodens,* and *Kingella* spp.; *Helicobacter pylori; Lactobacillus* spp.; *Lactococcus* spp.; *Leuconostoc* spp.; *Listeria monocytogenes; Micrococcus* spp.; *Moraxella catarrhalis; Pasteurella* spp.; *Pediococcus* spp.; *Rothia mucilaginosa;* potential agents of bioterrorism; and *Vibrio* spp., including *Vibrio cholerae*.

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

C. Cumulative Antibiograms

Policies regarding the generation of cumulative antibiograms should be developed together with the infectious diseases service, infection prevention personnel, the pharmacy and therapeutics committee, and the antimicrobial stewardship team. See CLSI document M39[6] for detailed instructions on generating cumulative antibiograms.

D. MIC Reporting Concentrations

When serial twofold dilution MICs are being prepared and tested, the actual dilution scheme is, eg:

16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.0625, 0.03125 µg/mL, etc. (see Table 7 for additional dilutions).

For convenience only, not because these are the actual concentrations tested, it was decided to use the following values in M100: 16, 8, 4, 2, 1, 0.5, 0.25, 0.12, 0.06, 0.03 µg/mL, etc.

The values that appear in the tables are equivalent to the actual values tested, eg, 0.12 µg/mL = 0.125 µg/mL, and laboratories should report an MIC of ≤ 0.125 µg/mL as ≤ 0.12 µg/mL.

IV. Therapy-Related Comments and Dosage Regimens

Some comments in the tables relate to therapy concerns. These are denoted with an ***Rx*** symbol. It may be appropriate to include some of these comments (or modifications thereof) on the patient report. An example would be inclusion of a comment when rifampin is being reported stating that "Rifampin should not be used alone for antimicrobial therapy." Antimicrobial dosage regimens often vary widely among practitioners and institutions. In some cases, the MIC breakpoints rely on pharmacokinetic/pharmacodynamic (PK/PD) data, using specific human dosage regimens. In cases in which specific dosage regimens are important for properly applying breakpoints, the dosage regimen is listed. These dosage regimen comments are not generally intended for use on individual patient reports.

V. Confirmation of Patient Results

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

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

VI. Development of Resistance and Testing of Repeat Isolates

Isolates that are initially susceptible may become intermediate or resistant after therapy is initiated. Therefore, subsequent isolates of the same species from a similar anatomical site should be tested to detect resistance that may have developed. Development of resistance can occur within as little as three to four days and has been noted most frequently in *Enterobacter* (including *Klebsiella* [formerly *Enterobacter*] *aerogenes*), *Citrobacter*, and *Serratia* spp. with third-generation cephalosporins, in *P. aeruginosa* with all antimicrobial agents, and in staphylococci with fluoroquinolones. For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy.

In certain circumstances, the decision to perform susceptibility tests on subsequent isolates necessitates knowledge of the specific situation and the severity of the patient's condition (eg, an isolate of *E. cloacae* complex from a blood culture on a premature infant or methicillin (oxacillin)-resistant *S. aureus* [MRSA] from a patient with prolonged bacteremia). Laboratory guidelines on when to perform susceptibility testing on repeat isolates should be determined after consultation with the medical staff.

VII. Warning

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

Locations	Organisms	Antimicrobial Agents
"Warning": The following antimicrobial agent/organism combinations may appear active *in vitro* but are not effective clinically and must not be reported as susceptible.		
Table 2A	*Salmonella* spp., *Shigella* spp.	First- and second-generation cephalosporins, cephamycins, and aminoglycosides
Table 2D	*Enterococcus* spp.	Aminoglycosides (except for high-level resistance testing), cephalosporins, clindamycin, and trimethoprim-sulfamethoxazole
"Warning": Do not report the following antimicrobial agents for bacteria isolated from CSF. These are not the drugs of choice and may not be effective for treating CSF infections caused by the bacteria included in Tables 2A through 2J:		
Tables 2A through 2J	Bacteria isolated from CSF	Agents administered by oral route only, 1st- and 2nd-generation cephalosporins and cephamycins, doripenem, ertapenem, imipenem, lefamulin, clindamycin, macrolides, tetracyclines, and fluoroquinolones

Abbreviation: CSF, cerebrospinal fluid.

VIII. Routine, Supplemental, Screening, Surrogate Agent, and Equivalent Agent Testing to Determine Susceptibility and Resistance to Antimicrobial Agents

The testing categories are defined as follows:

- **Routine test:** disk diffusion or broth or agar dilution MIC tests for routine clinical testing
- **Supplemental (not routine) test:** test that detects susceptibility or resistance to a drug or drug class by method other than routine disk diffusion or broth or agar dilution MIC and does not need additional tests to confirm susceptibility or resistance
  - Some supplemental tests identify a specific resistance mechanism and may be required or optional for reporting specific clinical results.
- **Screening test:** test that provides presumptive results; additional testing typically only needed for a specific result (eg, only if screen is positive)
- **Surrogate agent test:** test performed with an agent that replaces a test performed with the antimicrobial agent of interest and is used when the agent of interest cannot be tested due to **unavailability of the agent** or performance issues (eg, surrogate agent performs better than the agent of interest)
- **Equivalent agent test:** test performed with an agent that predicts results of closely related agents of the same class and increases efficiency by limiting testing of multiple closely related agents. Equivalent agents are identified by:
  - Listing equivalent agents with an "or" in Tables 1 and 2. "Or" indicates cross-susceptibility and cross-resistance is nearly complete (very major error + major error < 3%; minor error < 10%) and only one agent needs to be tested.
  - Listing agents that are equivalent and results that can be deduced by testing the equivalent agent in a comment (see Tables 1 and 2).

The following tables include tests that fall into the supplemental, screening, surrogate agent, and equivalent agent test categories. The tables for supplemental, screening, and surrogate agent tests are comprehensive. The table for equivalent agent tests includes several examples, and many other equivalent agent tests are described throughout Tables 1 and 2.

Supplemental Tests (Required)

Supplemental Test	Organisms	Test Description	Required for:	Table Location
Inducible clindamycin resistance	• *Staphylococcus* spp. • *S. pneumoniae* • *Streptococcus* spp. Β-hemolytic group	Broth microdilution or disk diffusion with clindamycin and erythromycin tested together	Isolates that test erythromycin resistant and clindamycin susceptible or intermediate before reporting the isolate as clindamycin susceptible	3I
Β-lactamase	• *Staphylococcus* spp.	Chromogenic cephalosporin (all staphylococci), penicillin disk diffusion zone-edge test (*S. aureus* only)	Isolates that test penicillin susceptible before reporting the isolate as penicillin susceptible	3F

Supplemental Tests (Optional)

Supplemental Test	Organisms	Test Description	Optional for:	Table Locations
ESBL	• *E. coli* • *K. pneumoniae* • *Klebsiella oxytoca* • *Proteus mirabilis*	Broth microdilution or disk diffusion clavulanate inhibition test for ESBLs	Isolates demonstrating reduced susceptibility to cephalosporins Results that indicate presence or absence of ESBLs	3A
CarbaNP	• Enterobacterales • *P. aeruginosa*	Colorimetric assay for detecting carbapenem hydrolysis	Isolates demonstrating reduced susceptibility to carbapenems Results that indicate presence or absence of certain carbapenemases	3B, 3B-1
mCIM with or without eCIM	• mCIM only: Enterobacterales and *P. aeruginosa* • mCIM with eCIM: Enterobacterales only	Disk diffusion for detecting carbapenem hydrolysis (inactivation) eCIM add-on enables differentiation of metallo-ß-lactamases from serine carbapenemases in Enterobacterales isolates that are positive for mCIM	Isolates demonstrating reduced susceptibility to carbapenems Results that indicate presence or absence of certain carbapenemases	3C
Colistin agar test	• Enterobacterales • *P. aeruginosa*	Modified agar dilution	Determining the colistin MIC	3D
Colistin broth disk elution	• Enterobacterales • *P. aeruginosa*	Tube dilution using colistin disks as antimicrobial agent source	Determining the colistin MIC	3D
Oxacillin salt agar	• *S. aureus*	Agar dilution; MHA with 4% NaCl and 6 µg/mL oxacillin	Detecting MRSA; see cefoxitin surrogate agent tests, which are preferred	3G-1

Abbreviations: eCIM, EDTA-modified carbapenem inactivation method; ESBL, extended-spectrum ß-lactamase; mCIM, modified carbapenem inactivation method; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRSA, methicillin (oxacillin)-resistant *Staphylococcus aureus*.

Screening Tests

Screening Test	Organisms	Test Description	When to Perform Confirmatory Test	Confirmatory Test	Table Location
Vancomycin agar screen	• *S. aureus* • *Enterococcus* spp.	Agar dilution; BHI with 6 µg/mL vancomycin	If screen positive	Vancomycin MIC	3H
HLAR by disk diffusion	• *Enterococcus* spp.	Disk diffusion with gentamicin and streptomycin	If screen inconclusive	Broth microdilution, agar dilution MIC	3K

Abbreviations: BHI, brain heart infusion; HLAR, high-level aminoglycoside resistance; MIC, minimal inhibitory concentration.

Surrogate Agent Tests

Surrogate Agent	Organisms	Test Description	Results	Table Locations
Cefazolin	• *E. coli* • *K. pneumoniae* • *P. mirabilis*	Broth microdilution or disk diffusion	When used for therapy of uncomplicated UTIs, predicts results for the following oral antimicrobial agents: cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, cephalexin, and loracarbef Cefazolin tested as a surrogate may overcall resistance to cefdinir, cefpodoxime, and cefuroxime. If cefazolin tests resistant, test these drugs individually if needed for therapy.	1A, 2A
Cefoxitin	• *S. aureus* • *S. lugdunensis* • *S. epidermidis* • Other *Staphylococcus* spp. (except *S. pseudintermedius* and *S. schleiferi*)	Broth microdilution: *S. aureus* *S. lugdunensis* Disk diffusion: *S. aureus* *S. lugdunensis* Other *Staphylococcus* spp., excluding *S. pseudintermedius* and *S. schleiferi*	Predicts results for *mecA*-mediated methicillin (oxacillin) resistance.	1A, 2C, 3G-1, 3G-2
Oxacillin	• *S. pneumoniae*	Disk diffusion	Predicts penicillin susceptibility if oxacillin zone is ≥ 20 mm. If oxacillin zone is ≤ 19 mm, penicillin MIC must be performed.	1B, 2G
Pefloxacin	• *Salmonella* spp.	Disk diffusion	Predicts reduced susceptibility to ciprofloxacin	2A

Abbreviations: MIC, minimal inhibitory concentration; PBP2a, penicillin-binding protein 2a; UTI, urinary tract infection.

Examples of Equivalent Agent Tests

Agents	Organisms	Identified by	Table Locations
Cefotaxime or ceftriaxone	Enterobacterales	"Or"	1A and 2A
Colistin or polymyxin B	Enterobacterales, *P. aeruginosa*, *Acinetobacter baumannii* complex	"Or"	2A, 2B-1, and 2B-2
Azithromycin or clarithromycin or erythromycin	*Staphylococcus* spp.	"Or"	1A and 2C
Penicillin-susceptible staphylococci are susceptible to other β-lactam agents with established clinical efficacy for staphylococcal infections (including both penicillinase-labile and penicillinase-stable agents; see Glossary I). Penicillin-resistant staphylococci are resistant to penicillinase-labile penicillins.	*Staphylococcus* spp.	Note listed	1A and 2C
The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin.	*Haemophilus* spp.	Note listed	1B and 2E
The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin.	Anaerobes	Note listed	2J

IX. Quality Control and Verification

Recommendations for QC are included in various tables and appendixes. Acceptable ranges for QC strains are provided in Tables 4A-1 through 4B for disk diffusion and Tables 5A-1 through 5E for MIC testing. Guidance for QC frequency and modifications of antimicrobial susceptibility testing (AST) systems is found in Table 4C for disk diffusion and Table 5F for MIC testing. Guidance for troubleshooting out-of-range results is included in Table 4D for disk diffusion and Table 5G for MIC testing. Additional information is available in Appendix C (eg, QC organism characteristics, QC testing recommendations).

Implementing any new diagnostic test requires verification.[7] Each laboratory that introduces a new AST system or adds a new antimicrobial agent to an existing AST system must verify or establish that, before reporting patient test results, the system meets performance specifications for that system. Verification generally involves testing patient isolates with the new AST system and comparing results to those obtained with an established reference method or a system that has been previously verified. Testing patient isolates may be done concurrently with the two systems. Alternatively, organisms with known MICs or zone sizes may be used for the verification. Guidance on verification studies is not included in this document. Other publications describe AST system verification (eg, CLSI document M52[8] and Patel J, et al.[9]).

X. Abbreviations and Acronyms

AST	antimicrobial susceptibility testing
ATCC®[a]	American Type Culture Collection
BHI	brain heart infusion
BLNAR	ß-lactamase negative, ampicillin-resistant
BMHA	blood Mueller-Hinton agar
BSC	biological safety cabinet
BSL-2	biosafety level 2
BSL-3	biosafety level 3
CAMHB	cation-adjusted Mueller-Hinton broth
CAT	colistin agar test
CBDE	colistin broth disk elution
CFU	colony-forming unit(s)
CMRNG	chromosomally mediated penicillin-resistant *Neisseria gonorrhoeae*
CSF	cerebrospinal fluid
DMSO	dimethyl sulfoxide
ECV	epidemiological cutoff value
eCIM	EDTA-modified carbapenem inactivation method
EDTA	ethylenediaminetetraacetic acid
ESBL	extended-spectrum ß-lactamase
FDA	US Food and Drug Administration
HLAR	high-level aminoglycoside resistance
HTM	*Haemophilus* test medium
I	intermediate
ICR	inducible clindamycin resistance
IM	intramuscular
ID	identification
LHB	lysed horse blood
mCIM	modified carbapenem inactivation method
MHA	Mueller-Hinton agar

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

MH-F agar	Mueller-Hinton fastidious agar
MHB	Mueller-Hinton broth
MIC	minimal inhibitory concentration
MRS	methicillin (oxacillin)-resistant staphylococci
MRSA	methicillin (oxacillin)-resistant *Staphylococcus aureus*
NAD	ß-nicotinamide adenine dinucleotide
NCTC	National Collection of Type Cultures
NS	nonsusceptible
NWT	non-wild-type
PBP2a	penicillin-binding protein 2a
PCR	polymerase chain reaction
PK/PD	pharmacokinetic/pharmacodynamic
pH	negative logarithm of hydrogen ion concentration
QC	quality control
R	resistant
S	susceptible
SDD	susceptible-dose dependent
TSA	tryptic soy agar
TSB	trypticase soy broth
UTI	urinary tract infection
WT	wild-type

Table 1A. Suggested Groupings of Antimicrobial Agents Approved by the US Food and Drug Administration for Clinical Use That Should Be Considered for Testing and Reporting on Nonfastidious Organisms by Microbiology Laboratories in the United States

Group A: Includes antimicrobial agents considered appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.			
Enterobacterales	*Pseudomonas aeruginosa*	*Staphylococcus* spp.	*Enterococcus* spp.[a]
Ampicillin[b]	Ceftazidime	Azithromycin[c] or clarithromycin[c] or erythromycin[c]	Ampicillin[d]
Cefazolin[f]	Gentamicin Tobramycin		Penicillin[e]
Gentamicin[b] Tobramycin[b]	Piperacillin-tazobactam	Clindamycin[c]	
		Oxacillin[g,h,i,j,k] Cefoxitin[g,h,j] (surrogate test for oxacillin)	
		Penicillin[g]	
		Trimethoprim-sulfamethoxazole	
Group B: Includes antimicrobial agents that may warrant primary testing but may be reported only selectively, such as when the organism is resistant to agents of the same antimicrobial class in Group A.[l]			
Amikacin[b]	Amikacin	Ceftaroline[m]	Daptomycin[l,n]
Amoxicillin-clavulanate Ampicillin-sulbactam	Aztreonam	Daptomycin[l,n]	Linezolid Tedizolid[o]
Azithromycin[p]			
Ceftazidime-avibactam	Cefepime	Linezolid Tedizolid[m]	Vancomycin
Ceftolozane-tazobactam	Ceftazidime-avibactam		
Imipenem-relebactam	Imipenem-relebactam		
Meropenem-vaborbactam	Ceftolozane-tazobactam		
Piperacillin-tazobactam			
Cefuroxime	Ciprofloxacin Levofloxacin	Doxycycline Minocycline[c] Tetracycline[q]	
Cefepime	Doripenem Imipenem Meropenem	Lefamulin[m]	
Cefotetan Cefoxitin		Vancomycin[l]	
Cefotaxime[b,f] or Ceftriaxone[b,f]			
Cefiderocol	**Cefiderocol**		
Ciprofloxacin[b] Levofloxacin[b]		Rifampin[r]	
Doripenem Ertapenem Imipenem Meropenem			
Trimethoprim-sulfamethoxazole[b]			

Table 1A. (Continued)

Group C: Includes alternative or supplemental antimicrobial agents that may require testing in institutions that harbor endemic or epidemic strains resistant to several of the primary drugs, for treatment of patients allergic to primary drugs, for treatment of unusual organisms, or for reporting to infection prevention as an epidemiological aid.			
Enterobacterales	*Pseudomonas aeruginosa*	*Staphylococcus* spp.	*Enterococcus* spp.[a]
Aztreonam Ceftazidime		Chloramphenicol[c]	Gentamicin (high-level resistance testing only)
Ceftaroline		Ciprofloxacin or levofloxacin Moxifloxacin	Streptomycin (high-level resistance testing only)
Chloramphenicol[b,c]			
Tetracycline[q]			Dalbavancin[l,s]
		Gentamicin[t]	Oritavancin[l,s]
		Dalbavancin[l,m]	Telavancin[l,s]
		Oritavancin[l,m]	
		Telavancin[l,m]	
Group U: Includes antimicrobial agents that are used only or primarily for treating UTIs.			
Cefazolin (surrogate test for uncomplicated UTI)[u]		Nitrofurantoin	Ciprofloxacin Levofloxacin
Fosfomycin[v]		Sulfisoxazole	
Nitrofurantoin		Trimethoprim	Fosfomycin[v]
Sulfisoxazole			Nitrofurantoin
Trimethoprim			Tetracycline[q]

Table 1A
Suggested Nonfastidious Groupings
M02 and M07

Page 56

Table 1A. (Continued)

Group A: Includes antimicrobial agents considered appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.			
Acinetobacter spp.	*Burkholderia cepacia* complex	*Stenotrophomonas maltophilia*	Other Non-Enterobacterales[f,w]
Ampicillin-sulbactam	Levofloxacin[i]	Levofloxacin	Ceftazidime
Ceftazidime	Meropenem	Minocycline	Gentamicin
Ciprofloxacin Levofloxacin	Trimethoprim-sulfamethoxazole	Trimethoprim-sulfamethoxazole	Tobramycin
Doripenem Imipenem Meropenem			
Gentamicin Tobramycin			
Group B: Includes antimicrobial agents that may warrant primary testing but may be reported only selectively, such as when the organism is resistant to agents of the same antimicrobial class in Group A.[i]			
Amikacin	Ceftazidime	Ceftazidime[i]	Amikacin
Piperacillin-tazobactam	Minocycline		Aztreonam
Cefepime			Cefepime
Cefotaxime Ceftriaxone			Ciprofloxacin Levofloxacin
Cefiderocol		**Cefiderocol**	
Doxycycline			Imipenem Meropenem
Minocycline			Piperacillin-tazobactam
Trimethoprim-sulfamethoxazole			Trimethoprim-sulfamethoxazole
Group C: Includes alternative or supplemental antimicrobial agents that may require testing in institutions that harbor endemic or epidemic strains resistant to several of the primary drugs, for treatment of patients allergic to primary drugs, for treatment of unusual organisms, or for reporting to infection prevention as an epidemiological aid.			
	Chloramphenicol[c,i]	Chloramphenicol[c,i]	Cefotaxime Ceftriaxone
			Chloramphenicol[c]
Group U: Includes antimicrobial agents that are used only or primarily for treating UTIs.			
Tetracycline[q]			Sulfisoxazole
			Tetracycline[q]

Abbreviations: CSF, cerebrospinal fluid; MIC, minimal inhibitory concentration; UTI, urinary tract infection.

Table 1A. (Continued)

"Warning": Do not report the following antimicrobial agents for bacteria isolated from CSF. These are not the drugs of choice and may not be effective for treating CSF infections caused by the bacteria included in Tables 2A through 2J:

- Agents administered by oral route only
- First- and second-generation cephalosporins and cephamycins
- Doripenem, ertapenem, and imipenem
- Clindamycin
- Lefamulin
- Macrolides
- Tetracyclines
- Fluoroquinolones

Refer to Glossary I for individual agents within the drug classes listed above.

Footnotes

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

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. In contrast, 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, and if requested, chloramphenicol and azithromycin may be tested and reported. Susceptibility testing is indicated for typhoidal *Salmonella* (*S. enterica* ser. Typhi and *Salmonella enterica* ser. Paratyphi A-C) isolated from extraintestinal and intestinal sources.

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

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

Table 1A. (Continued)

e. Enterococci susceptible to penicillin are predictably susceptible to ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, and piperacillin-tazobactam for non-ß-lactamase-producing enterococci. However, enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin. If penicillin results are needed, penicillin testing is required. ***Rx:*** Combination therapy with ampicillin, penicillin, or vancomycin (for susceptible strains) plus an aminoglycoside is usually indicated for serious enterococcal infections, such as endocarditis, unless high-level resistance to both gentamicin and streptomycin is documented; such combinations are predicted to result in synergistic killing of *Enterococcus*. For strains with low-level penicillin or ampicillin resistance when combination therapy with a ß-lactam is being considered, see additional testing and reporting information in Table 3K.[1]

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

g. Penicillin-susceptible staphylococci are also susceptible to other ß-lactam agents with established clinical efficacy for staphylococcal infections. Penicillin-resistant staphylococci are resistant to penicillinase-labile penicillins. Methicillin (oxacillin)-resistant staphylococci are resistant to all currently available ß-lactam antimicrobial agents, with the exception of ceftaroline. Thus, susceptibility or resistance to a wide array of ß-lactam antimicrobial agents may be deduced from testing only penicillin and either cefoxitin or oxacillin. Routine testing of other ß-lactam agents, except ceftaroline, is not advised.

h. If a penicillinase-stable penicillin is tested, oxacillin is the preferred agent, and results can be applied to the other penicillinase-stable penicillins (refer to Glossary I). Detection of methicillin (oxacillin) resistance in staphylococci is achieved by using specific methods as described in Tables 2C, 3G-1, and 3G-2.

i. MIC testing only; disk diffusion test is unreliable.

j. See oxacillin and cefoxitin comments in Table 2C for using cefoxitin as a surrogate test for oxacillin.

k. For *S. aureus*, *S. lugdunensis*, and other *Staphylococcus* spp. (except *S. epidermidis*, *S. pseudintermedius*, and *S. schleiferi*), only MIC testing, not disk diffusion testing, is acceptable; see exceptions in Table 2C.

l. Section I, C.2. in the Instructions for Use of Tables lists additional examples of when a Group B agent might be reported.

m. For *S. aureus* only, including methicillin (oxacillin)-resistant *S. aureus* (MRSA).

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

o. For testing and reporting of *E. faecalis* only.

Table 1A. (Continued)

p. For reporting against *Salmonella enterica* ser. Typhi and *Shigella* spp. only.

q. 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.

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

s. For testing and reporting of vancomycin-susceptible *E. faecalis* only.

t. For staphylococci that test susceptible, gentamicin is used only in combination with other active agents that test susceptible.

u. 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.

v. For testing and reporting of *E. coli* and *E. faecalis* urinary tract isolates only.

w. Other non-Enterobacterales include *Pseudomonas* spp. and other nonfastidious, glucose-nonfermenting, gram-negative bacilli but exclude *P. aeruginosa*, *Acinetobacter* spp., *B. cepacia* complex, and *S. maltophilia*. Refer to each respective organism column for suggested antimicrobial agents to test and report. Recommendations for testing and reporting *Aeromonas* spp., *Burkholderia mallei*, *Burkholderia pseudomallei*, and *Vibrio* spp. (including *V. cholerae*) are found in CLSI document M45.[2]

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

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

References for Table 1A

1 Murray BE, Arias CA, Nannini EC. Glycopeptides (vancomycin and teicoplanin) and lipoglycopeptides (telavancin, oritavancin, and dalbavancin). In: Bennett JE, Dolin R, Blaser MJ. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 9th ed. Elsevier; 2019: Chapter 30.

2 CLSI. *Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria*. 3rd ed. CLSI guideline M45. Clinical and Laboratory Standards Institute; 2016.

Table 1B. Suggested Groupings of Antimicrobial Agents Approved by the US Food and Drug Administration for Clinical Use That Should Be Considered for Testing and Reporting on Fastidious Organisms by Microbiology Laboratories in the United States

Group A: Includes antimicrobial agents considered appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.				
Haemophilus influenzae[a] and *Haemophilus parainfluenzae*	*Neisseria gonorrhoeae*[b]	*Streptococcus pneumoniae*[c]	*Streptococcus* spp. B-Hemolytic Group[d]	*Streptococcus* spp. Viridans Group[d]
Ampicillin[a,e]	Azithromycin[f,g]	Erythromycin[h,i]	Clindamycin[i,j]	Ampicillin [f,k] Penicillin[f,k]
	Ceftriaxone[g] Cefixime[g]			
	Ciprofloxacin[g]	Penicillin[l] (oxacillin disk)	Erythromycin [h,i,j]	
	Tetracycline[g]		Penicillin[g,m] or ampicillin[g,m]	
		Trimethoprim-sulfamethoxazole		
Group B: Includes antimicrobial agents that may warrant primary testing but may be reported only selectively, such as when the organism is resistant to agents of the same antimicrobial class, as in Group A.[n]				
Ampicillin-sulbactam		Cefepime[f] Cefotaxime[f,l] Ceftriaxone[f,l]	Cefepime or cefotaxime or ceftriaxone	Cefepime Cefotaxime Ceftriaxone
Cefotaxime[a] or ceftazidime[a] or ceftriaxone[a]		Clindamycin[i]	Vancomycin	Vancomycin
Ciprofloxacin or levofloxacin or moxifloxacin		Doxycycline		
		Lefamulin		
		Levofloxacin[c] Moxifloxacin[c]		
Meropenem[a]		Meropenem[f,l]		
		Tetracycline[o]		
		Vancomycin[l]		

Table 1B. (Continued)

Group C: Includes alternative or supplemental antimicrobial agents that may require testing in institutions that harbor endemic or epidemic strains resistant to several of the primary drugs, for treatment of patients allergic to primary drugs, for treatment of unusual organisms, or for reporting to infection prevention as an epidemiological aid.				
Haemophilus influenzae[a] and *Haemophilus parainfluenzae*	*Neisseria gonorrhoeae*[b]	*Streptococcus pneumoniae*[c]	*Streptococcus* spp. β-Hemolytic Group[d]	*Streptococcus* spp. Viridans Group[d]
Azithromycin[p] Clarithromycin[p]		Amoxicillin[f] Amoxicillin-clavulanate[f]	Ceftaroline	Ceftolozane-tazobactam
Aztreonam		Cefuroxime[f]	Chloramphenicol[i]	Chloramphenicol[i]
Amoxicillin-clavulanate[p]		Ceftaroline	Daptomycin[f,q]	Clindamycin[j]
Cefaclor[p] Cefprozil[p]		Chloramphenicol[i]	Levofloxacin	Erythromycin[h,l]
Cefdinir[p] or cefixime[p] or cefpodoxime[p]		Ertapenem[f] Imipenem[f]	Linezolid Tedizolid[r]	Linezolid Tedizolid[s]
		Linezolid	Dalbavancin[f,t] Oritavancin[f] Telavancin[f]	Dalbavancin[f,t] Oritavancin[f] Telavancin[f]
Ceftaroline[u]		Rifampin[v]		
Cefuroxime[p]				
Chloramphenicol[i]				
Ceftolozane-tazobactam[u]				
Ertapenem or imipenem				
Lefamulin[u]				
Rifampin[w]				
Tetracycline[o]				
Trimethoprim-sulfamethoxazole				

Abbreviations: CSF, cerebrospinal fluid; MIC, minimal inhibitory concentration.

Table 1B
Suggested Fastidious Groupings
M02 and M07

Table 1B. (Continued)

"Warning": Do not report the following antimicrobial agents for bacteria isolated from CSF. These are not the drugs of choice and may not be effective for treating CSF infections caused by the bacteria included in Tables 2A through 2J:

- Agents administered by oral route only
- First- and second-generation cephalosporins and cephamycins
- Doripenem, ertapenem, and imipenem
- Clindamycin
- Lefamulin
- Macrolides
- Tetracyclines
- Fluoroquinolones

Refer to Glossary I for individual agents within the drug classes listed above.

Footnotes

a. For isolates of *H. influenzae* from CSF, only results of testing with ampicillin, any of the third-generation cephalosporins listed, and meropenem are appropriate to report.

b. Culture and susceptibility testing of *N. gonorrhoeae* should be considered in cases of treatment failure. Antimicrobial agents recommended for testing include, at a minimum, the agents listed in group A. The most current guidelines for treatment and testing are available from the Centers for Disease Control and Prevention at https://www.cdc.gov/std/gonorrhea/stdfact-gonorrhea.htm.

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

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

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

f. MIC testing only; disk diffusion test is unreliable.

Table 1B. (Continued)

g. Routine testing is not necessary.

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

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

j. ***Rx:*** Recommendations for intrapartum prophylaxis for group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin. Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin but may be resistant to erythromycin and clindamycin. When group B Streptococcus is isolated from a pregnant woman with severe penicillin allergy (high risk for anaphylaxis), erythromycin and clindamycin (including inducible clindamycin resistance [ICR]) should be tested, and only clindamycin should be reported. Erythromycin, even when tested for determination of ICR, should not be reported. See Table 3I.

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

l. Penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method (such as that described in M07[1]) and reported routinely with CSF isolates of *S. pneumoniae*. Such isolates can also be tested against vancomycin using the MIC or disk diffusion method. With isolates from other sites, the oxacillin disk test may be used. If the oxacillin zone size is ≤ 19 mm, penicillin, cefotaxime, ceftriaxone, or meropenem MICs should be determined.

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

n. Section I, C.2. in the Instructions for Use of Tables lists additional examples of when a Group B agent might be reported.

Table 1B. (Continued)

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

p. Amoxicillin-clavulanate, azithromycin, cefaclor, cefdinir, cefixime, cefpodoxime, cefprozil, cefuroxime, and clarithromycin are used as empiric therapy for respiratory tract infections due to *Haemophilus* spp. The results of susceptibility tests with these antimicrobial agents are often not necessary for managing individual patients.

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

r. For reporting against *S. pyogenes* and *S. agalactiae* only.

s. For reporting against *S. anginosus* group (includes *S. anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*) only.

t. For reporting against *S. pyogenes*, *S. agalactiae*, *Streptococcus dysgalactiae*, and *S. anginosus* group.

u. For reporting against *H. influenzae* only.

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

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

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

Reference for Table 1B

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 1C. Suggested Groupings of Antimicrobial Agents Approved by the US Food and Drug Administration for Clinical Use That Should Be Considered for Testing and Reporting on Anaerobic Organisms by Microbiology Laboratories in the United States

Group A: Includes antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Gram-Negative Anaerobes	**Gram-Positive Anaerobes[a]**
Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam	Ampicillin[b] Penicillin[b]
	Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam
Clindamycin	Clindamycin
Doripenem Ertapenem Imipenem Imipenem-relebactam Meropenem	Doripenem Ertapenem Imipenem Imipenem-relebactam Meropenem
Metronidazole	Metronidazole
Group C: Includes alternative or supplemental antimicrobial agents that may require testing in institutions that harbor endemic or epidemic strains resistant to several of the primary drugs, for treatment of patients allergic to primary drugs, for treatment of unusual organisms, or for reporting to infection prevention as an epidemiological aid.	
Gram-Negative Anaerobes	**Gram-Positive Anaerobes[a]**
Penicillin[b] Ampicillin[b]	
Cefotetan Cefoxitin	Cefotetan Cefoxitin
Ceftizoxime Ceftriaxone	Ceftizoxime Ceftriaxone
Chloramphenicol	
Moxifloxacin	Moxifloxacin
	Tetracycline

Footnotes

a. Many non-spore-forming, gram-positive anaerobic rods are resistant to metronidazole (see Appendix D).

b. If ß-lactamase positive, report as resistant to penicillin and ampicillin. Be aware that ß-lactamase-negative isolates may be resistant to penicillin and ampicillin by other mechanisms.

Table 1C. (Continued)

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

NOTE 2: Most anaerobic infections are polymicrobial, including both β-lactamase-positive and β-lactamase-negative strains. Testing may not be necessary for isolates associated with polymicrobial anaerobic infections. However, if susceptibility testing is requested, only the organism most likely to be resistant (eg, *Bacteroides* spp. and *Parabacteroides* spp.) should be tested and results reported (see Appendix D).

NOTE 3: Specific *Clostridium* spp. (eg, *Clostridium septicum*, *Clostridium sordellii*) may be the singular cause of infection and are typically susceptible to penicillin and ampicillin. Penicillin and clindamycin resistance have been reported in *Clostridium perfringens*. Agents in group A of Table 1C should be tested and reported for *Clostridium* spp.

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 [5]).

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® 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) 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.

(2) 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 not be comparable to ampicillin, with poorer efficacy.** In addition, for extraintestinal isolates of *Salmonella* spp., a 3rd-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.

Table 2A. Enterobacterales (Continued)

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

(4) **An intermediate (I) with a ^ in Tables 2 indicates agents that have the potential to concentrate in the urine. The I^ is for informational use only. The decision to report I^ is best made by each laboratory based on institution-specific guidelines and in consultation with appropriate medical personnel.**

(5) Positive blood culture broth can be used as the inoculum for direct disk diffusion testing of select antimicrobial agents against Enterobacterales **(using methods described in Table 3E-1 and applying breakpoints in Table 3E-2).** For antimicrobial agents not listed **in Table 3E-2** for Enterobacterales, CLSI has not yet evaluated this direct disk diffusion method.

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

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
PENICILLINS											
A	Ampicillin	10 µg	≥17	-	14-16^	≤13	≤8	-	16^	≥32	(6) Results of ampicillin testing can be used to predict results for amoxicillin. **(7) Breakpoints are based on an ampicillin dosage regimen of 2 g parenterally administered every 4-6 h or an amoxicillin dosage regimen of 1-2 g parenterally administered every 6 h.** **(8) Breakpoints when oral ampicillin is used for therapy of uncomplicated UTIs due only to *E. coli*, *P. mirabilis*, *Shigella*, and *Salmonella* are based on an ampicillin dosage regimen of 500 mg orally administered every 6 h or an amoxicillin dosage regimen of 250 mg orally administered every 8 h or 500 mg every 12 h.** See general comment (2).
O	Piperacillin		-	-	-	-	**≤8**	**16**	-	**≥32**	**(9) Disk diffusion breakpoints have been removed because no disk correlate data are available for the revised piperacillin MIC breakpoints. Disk diffusion breakpoints will be reassessed if data become available.**
O	Mecillinam	10 µg	≥15	-	12-14^	≤11	≤8	-	16^	≥32	(10) For testing and reporting of *E. coli* urinary tract isolates only.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
β-LACTAM COMBINATION AGENTS											
(11) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test SDD, intermediate, or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.											
B	Amoxicillin-clavulanate	20/10 µg	≥18	-	14-17^	≤13	≤8/4	-	16/8^	≥32/16	**(12) Breakpoints are based on a dosage regimen of 1.2 g IV administered every 6 h.** **(13) Breakpoints when amoxicillin-clavulanate is used for therapy of uncomplicated UTIs or for completion of therapy for systemic infection are based on a dosage regimen of either 875/125 mg administered orally every 12 h or 500/125 mg every 8 h.**
B	Ampicillin-sulbactam	10/10 µg	≥15	-	12-14^	≤11	≤8/4	-	16/8^	≥32/16	**(14) Breakpoints are based on a dosage regimen of 3 g administered parenterally every 6 h.**
B	Ceftolozane-tazobactam	30/10 µg	**≥22**	-	**19-21^**	**≤18**	≤2/4	-	4/4^	≥8/4	(15) Breakpoints are based on a dosage regimen of **3 g administered every 8 h for pneumonia and 1.5 g administered every 8 h for other indications.**
B	Ceftazidime-avibactam	30/20 µg	≥21	-	-	≤20	≤8/4	-	-	≥16/4	(16) Breakpoints are based on a dosage regimen of 2.5 g every 8 h administered over 2 h. (17) Confirmatory MIC testing is indicated for isolates with zones of 20-22 mm to avoid reporting false-susceptible or false-resistant results.
B	Imipenem-relebactam	10/25 µg	≥25	-	21-24^	≤20	≤1/4	-	2/4^	≥4/4	(18) Breakpoints are based on a dosage regimen of 1.25 g administered every 6 h. (19) Breakpoints do not apply to the family *Morganellaceae*, which includes but is not limited to the genera *Morganella*, *Proteus*, and *Providencia*.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
β-LACTAM COMBINATION AGENTS (Continued)											
B	Meropenem-vaborbactam	20/10 µg	≥ 18	-	15-17^	≤ 14	≤ 4/8	-	8/8^	≥ 16/8	**(20)** Breakpoints are based on a dosage regimen of 4 g every 8 h administered over 3 h.
B	Piperacillin-tazobactam	100/10 µg	**≥ 25**	**21-24**		**≤ 20**	**≤ 8/4**	**16/4**		**≥ 32/4**	**(21) Breakpoints for susceptible are based on a dosage regimen of 3.375-4.5 g administered every 6 h as a 30-minute infusion. Breakpoints for SDD are based on a dosage regimen of 4.5 g administered every 6 h as a 3-h infusion or 4.5 g administered every 8 h as a 4-h infusion.**
O	Ticarcillin-clavulanate	75/10 µg	≥ 20	-	15-19^	≤ 14	≤ 16/2	-	32/2-64/2^	≥ 128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)											

(22) WARNING: For *Salmonella* spp. and *Shigella* spp., 1st- and 2nd-generation cephalosporins and cephamycins may appear active *in vitro* but are not effective clinically and should not be reported as susceptible.

(23) Following evaluation of PK/PD properties, limited clinical data, and MIC distributions, revised breakpoints for cephalosporins (cefazolin, cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone) and aztreonam were first published in January 2010 (M100-S20) and are listed in this table. Cefuroxime (parenteral) was also evaluated; however, no change in breakpoints was necessary for the dosage indicated below. When using the current breakpoints, routine ESBL testing is no longer necessary before reporting results (ie, it is no longer necessary to edit results for cephalosporins, aztreonam, or penicillins from susceptible to resistant). However, ESBL testing may still be useful for epidemiological or infection prevention purposes. For laboratories that have not implemented the current breakpoints, ESBL testing should be performed as described in Table 3A.

Breakpoints for drugs with limited availability in many countries (eg, moxalactam, cefonicid, cefamandole, and cefoperazone) were not evaluated. If considering use of these drugs for *E. coli*, *Klebsiella* spp., or *Proteus* spp., ESBL testing should be performed (see Table 3A). If isolates test ESBL positive, the results for moxalactam, cefonicid, cefamandole, and cefoperazone should be reported as resistant.

(24) *Enterobacter*, *Klebsiella* (formerly *Enterobacter*) *aerogenes*, *Citrobacter*, and *Serratia* may develop resistance during prolonged therapy with 3rd-generation cephalosporins as a result of derepression of AmpC β-lactamase. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing repeat isolates may be warranted.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)											
A	Cefazolin	30 µg	≥23	-	20-22	≤19	≤2	-	4	≥8	**(25)** Breakpoints when cefazolin is used for therapy of infections other than uncomplicated UTIs due to *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Breakpoints are based on a dosage regimen of 2 g administered every 8 h. See comment (23).
U	Cefazolin	30 µg	≥15	-	-	≤14	≤16	-	-	≥32	**(26)** Breakpoints when cefazolin is used for therapy of uncomplicated UTIs due to *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Breakpoints are based on a dosage regimen of 1 g administered every 12 h. See additional information in CEPHEMS (ORAL).
C	Ceftaroline	30 µg	≥23	-	20-22^	≤19	≤0.5	-	1^	≥2	**(27)** Breakpoints are based on a dosage regimen of 600 mg administered every 12 h.
B	Cefepime	30 µg	≥25	19-24	-	≤18	≤2	4-8	-	≥16	**(28)** The breakpoint for susceptible is based on a dosage regimen of 1 g administered every 12 h. The breakpoint for SDD is based on dosage regimens that result in higher cefepime exposure, either higher doses or more frequent doses or both, up to approved maximum dosage regimens. See Appendix E for more information about breakpoints and dosage regimens. Also see the definition of SDD in the Instructions for Use of Tables section.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
CEPHEMS (PARENTERAL) (including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)											
B B	Cefotaxime or ceftriaxone	30 µg 30 µg	≥ 26 ≥ 23	-	23-25^ 20-22^	≤ 22 ≤ 19	≤ 1 ≤ 1	-	2^ 2^	≥ 4 ≥ 4	**(29)** Breakpoints are based on a dosage regimen of 1 g administered every 24 h for ceftriaxone and 1 g administered every 8 h for cefotaxime. See comment (23).
B	Cefotetan	30 µg	≥ 16	-	13-15^	≤ 12	≤ 16	-	32^	≥ 64	
B	Cefoxitin	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	**(30)** Breakpoints are based on a dosage regimen of at least 8 g per day (eg, 2 g administered every 6 h).
B	Cefuroxime (parenteral)	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	**(31)** Breakpoints are based on a dosage regimen of 1.5 g administered every 8 h. See comment (23).
C	Ceftazidime	30 µg	≥ 21	-	18-20^	≤ 17	≤ 4	-	8^	≥ 16	**(32)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h. See comment (23).
O	Cefamandole	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	See comment (23).
O	Cefmetazole	30 µg	≥ 16	-	13-15^	≤ 12	≤ 16	-	32^	≥ 64	**(33)** Insufficient new data exist to reevaluate breakpoints listed here.
O	Cefonicid	30 µg	≥ 18	-	15-17^	≤ 14	≤ 8	-	16^	≥ 32	See comment (23).
O	Cefoperazone	75 µg	≥ 21	-	16-20	≤ 15	≤ 16	-	32	≥ 64	See comment (23).
O	Ceftizoxime	30 µg	≥ 25	-	22-24^	≤ 21	≤ 1	-	2^	≥ 4	**(34)** Breakpoints are based on a dosage regimen of 1 g administered every 12 h. See comment (23).
O	Moxalactam	30 µg	≥ 23	-	15-22^	≤ 14	≤ 8	-	16-32^	≥ 64	See comment (23).
B	Cefiderocol	30 µg	≥ 16	-	**9**-15^	**≤ 8**	≤ 4	-	8^	≥ 16	**(35)** Breakpoints are based on a dosage regimen of 2 g every 8 h administered over 3 h.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
CEPHEMS (ORAL)											
B	Cefuroxime **(oral)**	30 µg	≥23	-	15-22^	≤14	≤4		8-16^	≥32	See comment (36).
U	Cefazolin (surrogate test for oral cephalosporins and uncomplicated UTIs)	30 µg	≥15	-	-	≤14	≤16	-	-	≥32	**(36)** Breakpoints are for cefazolin when used as a surrogate test to predict results for the oral agents cefaclor, cefdinir, cefpodoxime, cefprozil, cefuroxime, cephalexin, and loracarbef when used for therapy of uncomplicated UTIs due to *E. coli*, *K. pneumoniae*, and *P. mirabilis*. Cefazolin tested as a surrogate may overcall resistance to cefdinir, cefpodoxime, and cefuroxime. If cefazolin tests resistant, test these drugs individually if needed for therapy.
O	Loracarbef	30 µg	≥18	-	15-17^	≤14	≤8	-	16^	≥32	**(37)** Do not test *Citrobacter*, *Providencia*, or *Enterobacter* spp. with cefdinir or loracarbef by disk diffusion because false-susceptible results have been reported. See comment (36).
O	Cefaclor	30 µg	≥18	-	15-17^	≤14	≤8	-	16^	≥32	See comment (36).
O	Cefdinir	5 µg	≥20	-	17-19^	≤16	≤1	-	2^	≥4	See comments (36) and (37).
O	Cefixime	5 µg	≥19	-	16-18^	≤15	≤1	-	2^	≥4	**(38)** Do not test *Morganella* spp. with cefixime, cefpodoxime, or cefetamet by disk diffusion.
O	Cefpodoxime	10 µg	≥21	-	18-20^	≤17	≤2	-	4^	≥8	See comments (36) and (38).
O	Cefprozil	30 µg	≥18	-	15-17^	≤14	≤8	-	16^	≥32	**(39)** Do not test *Providencia* spp. with cefprozil by disk diffusion because false-susceptible results have been reported. See comment (36).
Inv.	Cefetamet	10 µg	≥18	-	15-17^	≤14	≤4	-	8^	≥16	See comment (38).
Inv.	Ceftibuten	30 µg	≥21	-	18-20^	≤17	≤8	-	16^	≥32	**(40)** For testing and reporting of urinary tract isolates only.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
MONOBACTAMS											
C	Aztreonam	30 µg	≥21	-	18-20^	≤17	≤4	-	8^	≥16	**(41)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h. See comment (23).
CARBAPENEMS											
(42) Following evaluation of PK/PD properties, limited clinical data, and MIC distributions that include recently described carbapenemase-producing strains, revised breakpoints for carbapenems were first published in June 2010 (M100-S20-U) and are listed below. Because of limited treatment options for infections caused by organisms with carbapenem MICs or zone diameters in the intermediate range, clinicians may wish to design carbapenem dosage regimens that use maximum recommended doses and possibly prolonged intravenous infusion regimens, as has been reported in the literature.[4-7] Consultation with an infectious diseases practitioner is recommended for isolates for which the carbapenem MICs or zone diameter results from disk diffusion testing are in the intermediate or resistant ranges. Laboratories using Enterobacterales MIC breakpoints for carbapenems described in M100-S20 (January 2010) should perform the CarbaNP test, mCIM, eCIM, and/or a molecular assay (refer to Tables 3B and 3C for methods) when isolates of Enterobacterales are suspicious for carbapenemase production based on imipenem or meropenem MICs 2–4 µg/mL or ertapenem MIC 2 µg/mL (refer to Tables 3B-1 and 3C-1 for guidance on reporting). After implementing the current breakpoints, these additional tests may not need to be performed other than for epidemiological or infection prevention purposes (ie, it is no longer necessary to edit results for the carbapenems to resistant if a carbapenemase producer is detected). See Appendix H, Table H3 regarding suggestions for reporting when molecular and phenotypic methods are discordant. The following information is provided as background on carbapenemases in Enterobacterales that are largely responsible for MICs and zone diameters in the intermediate and resistant ranges, and thus the rationale for setting revised carbapenem breakpoints: • The clinical effectiveness of carbapenem treatment of infections produced by isolates for which the carbapenem MIC or disk diffusion test results are within the intermediate range is uncertain due to lack of controlled clinical studies. Imipenem MICs for *Proteus* spp., *Providencia* spp., and *Morganella morganii* tend to be higher (eg, MICs in the intermediate or resistant range) than meropenem or doripenem MICs. These isolates may have elevated imipenem MICs by mechanisms other than production of carbapenemases.										
B	Doripenem	10 µg	≥23	-	20-22^	≤19	≤1	-	2^	≥4	**(43)** Breakpoints are based on a dosage regimen of 500 mg administered every 8 h.
B	Ertapenem	10 µg	≥22	-	19-21^	≤18	≤0.5	-	1^	≥2	**(44)** Breakpoints are based on a dosage regimen of 1 g administered every 24 h.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
CARBAPENEMS (Continued)											
B	Imipenem	10 µg	≥ 23	-	20-22^	≤ 19	≤ 1	-	2^	≥ 4	**(45)** Breakpoints are based on a dosage regimen of 500 mg administered every 6 h or 1 g every 8 h.
B	Meropenem	10 µg	≥ 23	-	20-22^	≤ 19	≤ 1	-	2^	≥ 4	**(46)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h.
LIPOPEPTIDES											
(47) WARNING: Clinical and PK/PD data demonstrate colistin and polymyxin B have limited clinical efficacy, even if an intermediate result is obtained. Alternative agents are strongly preferred. Colistin and polymyxin B should be used in combination with one or more active antimicrobial agents. Consultation with an infectious diseases specialist is recommended. **(48)** Several species are intrinsically resistant to the lipopeptides (colistin and polymyxin B). Refer to Appendix B.											
O	Colistin or polymyxin B		- -	- -	- -	- -	- -	- -	≤ 2 ≤ 2	≥ 4 ≥ 4	**(49)** Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses (see International Consensus Guidelines[8]). **(50)** Polymyxin B should be given with a loading dose and maximum recommended doses (see International Consensus Guidelines[8]). **(51)** When colistin or polymyxin B is given systemically, neither is likely to be effective for pneumonia. **(52)** For colistin, broth microdilution, CBDE, and CAT MIC methods are acceptable. For polymyxin B, broth microdilution is the only approved method. Disk diffusion and gradient diffusion methods should not be performed (see Table 3D).

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
CARBAPENEMS (Continued)											
B	Imipenem	10 µg	≥ 23	-	20-22^	≤ 19	≤ 1	-	2^	≥ 4	**(45)** Breakpoints are based on a dosage regimen of 500 mg administered every 6 h or 1 g every 8 h.
B	Meropenem	10 µg	≥ 23	-	20-22^	≤ 19	≤ 1	-	2^	≥ 4	**(46)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h.
LIPOPEPTIDES											
(47) WARNING: Clinical and PK/PD data demonstrate colistin and polymyxin B have limited clinical efficacy, even if an intermediate result is obtained. Alternative agents are strongly preferred. Colistin and polymyxin B should be used in combination with one or more active antimicrobial agents. Consultation with an infectious diseases specialist is recommended. **(48)** Several species are intrinsically resistant to the lipopeptides (colistin and polymyxin B). Refer to Appendix B.											
O	Colistin or polymyxin B		- -	- -	- -	- -	- -	- -	≤ 2 ≤ 2	≥ 4 ≥ 4	**(49)** Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses (see International Consensus Guidelines[8]). **(50)** Polymyxin B should be given with a loading dose and maximum recommended doses (see International Consensus Guidelines[8]). **(51)** When colistin or polymyxin B is given systemically, neither is likely to be effective for pneumonia. **(52)** For colistin, broth microdilution, CBDE, and CAT MIC methods are acceptable. For polymyxin B, broth microdilution is the only approved method. Disk diffusion and gradient diffusion methods should not be performed (see Table 3D).

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
AMINOGLYCOSIDES											
(53) WARNING: For *Salmonella* spp. and *Shigella* spp., aminoglycosides may appear active *in vitro* but are not effective clinically and should not be reported as susceptible.											
A	Gentamicin	10 µg	≥15	-	13-14^	≤12	≤4	-	8^	≥16	
A	Tobramycin	10 µg	≥15	-	13-14^	≤12	≤4	-	8^	≥16	
B	Amikacin	30 µg	≥17	-	15-16^	≤14	≤16	-	32^	≥64	
O	Kanamycin	30 µg	≥18	-	14-17^	≤13	≤16	-	32^	≥64	
O	Netilmicin	30 µg	≥15	-	13-14^	≤12	≤8	-	16^	≥32	
O	Streptomycin	10 µg	≥15	-	12-14^	≤11	-	-	-	-	
MACROLIDES											
B	Azithromycin	15 µg	≥13	-	-	≤12	≤16	-	-	≥32	**(54)** *S. enterica* ser. Typhi only: breakpoints are based on MIC distribution data and limited clinical data. **(55)** Breakpoints are based on a dosage regimen of 500 mg administered daily.
			≥16	-	11-15	≤10	≤8	-	16	≥32	**(56)** *Shigella* spp. only: azithromycin disk diffusion zones can be hazy and difficult to measure, especially *S. sonnei*. If an isolate has a zone of inhibition that is difficult to measure, an MIC method is recommended. Media source may affect the clarity of the end points for disk diffusion tests. See comment (55).
TETRACYCLINES											
(57) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.											
C	Tetracycline	30 µg	≥15	-	12-14	≤11	≤4	-	8	≥16	
O	Doxycycline	30 µg	≥14	-	11-13	≤10	≤4	-	8	≥16	
O	Minocycline	30 µg	≥16	-	13-15	≤12	≤4	-	8	≥16	

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
QUINOLONES AND FLUOROQUINOLONES for Enterobacterales except *Salmonella* spp. (Please refer to Glossary I.)											
B B	Ciprofloxacin Levofloxacin	5 µg 5 µg	≥ 26 ≥ 21	-	22-25^ 17-20^	≤ 21 ≤ 16	≤ 0.25 ≤ 0.5	-	0.5^ 1^	≥ 1 ≥ 2	**(58)** Breakpoints for ciprofloxacin are based on a dosage regimen of 400 mg IV or 500 mg orally administered every 12 h. **(59)** Breakpoints for levofloxacin are based on a dosage regimen of 750 mg administered every 24 h.
O	Cinoxacin	100 µg	≥ 19	-	15-18^	≤ 14	≤ 16	-	32^	≥ 64	See comment (40).
O	Enoxacin	10 µg	≥ 18	-	15-17^	≤ 14	≤ 2	-	4^	≥ 8	See comment (40).
O	Gatifloxacin	5 µg	≥ 18	-	15-17^	≤ 14	≤ 2	-	4^	≥ 8	
O	Gemifloxacin	5 µg	≥ 20	-	16-19	≤ 15	≤ 0.25	-	0.5	≥ 1	**(60)** For testing and reporting of *K. pneumoniae* only.
O	Grepafloxacin	5 µg	≥ 18	-	15-17	≤ 14	≤ 1	-	2	≥ 4	
O	Lomefloxacin	10 µg	≥ 22	-	19-21^	≤ 18	≤ 2	-	4^	≥ 8	
O	Nalidixic acid	30 µg	≥ 19	-	14-18	≤ 13	≤ 16	-	-	≥ 32	See comment (40).
O	Norfloxacin	10 µg	≥ 17	-	13-16	≤ 12	≤ 4	-	8	≥ 16	See comment (40).
O	Ofloxacin	5 µg	≥ 16	-	13-15^	≤ 12	≤ 2	-	4^	≥ 8	
Inv.	Fleroxacin	5 µg	≥ 19	-	16-18^	≤ 15	≤ 2	-	4^	≥ 8	
QUINOLONES AND FLUOROQUINOLONES for *Salmonella* spp. (Please refer to Glossary I.)											
(61) For testing and reporting of *Salmonella* spp. (including *S. enterica* ser. Typhi and *S. enterica* ser. Paratyphi A-C). Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources. **(62)** The preferred test for assessing fluoroquinolone susceptibility or resistance in *Salmonella* spp. is a ciprofloxacin MIC test. A levofloxacin or ofloxacin MIC test can be performed if either agent, respectively, is the fluoroquinolone of choice in a specific facility. If a ciprofloxacin, levofloxacin, or ofloxacin MIC or ciprofloxacin disk diffusion test cannot be done, pefloxacin disk diffusion may be used as surrogate test to predict ciprofloxacin susceptibility. **(63)** No single test detects resistance resulting from all possible fluoroquinolone resistance mechanisms that have been identified in *Salmonella* spp.										

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
QUINOLONES AND FLUOROQUINOLONES for *Salmonella* spp. (Please refer to Glossary I.) (Continued)											
B	Ciprofloxacin	5 µg	≥31	-	21-30^	≤20	≤0.06	-	0.12-0.5 ^	≥1	**(64)** Isolates of *Salmonella* spp. that test not susceptible to ciprofloxacin, levofloxacin, ofloxacin, or pefloxacin may be associated with clinical failure or delayed response in fluoroquinolone-treated patients with salmonellosis.
B	Levofloxacin	-	-	-	-	-	≤0.12	-	0.25-1^	≥2	
O	Ofloxacin	-	-	-	-	-	≤0.12	-	0.25-1^	≥2	
Inv.	Pefloxacin (surrogate test for ciprofloxacin)	5 µg	≥24	-	-	≤23	-	-	-	-	**(65)** Report results as ciprofloxacin susceptible or resistant based on the pefloxacin test result. Pefloxacin will not detect resistance in *Salmonella* spp. due to *aac(6')-Ib-cr*. Pefloxacin disks are not available in the United States. See comment (63).
FOLATE PATHWAY ANTAGONISTS											
B	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16	-	11-15	≤10	≤2/38	-	-	≥4/76	See general comment (2).
U	Sulfonamides	250 or 300 µg	≥17	-	13-16	≤12	≤256	-	-	≥512	**(66)** Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations.
U	Trimethoprim	5 µg	≥16	-	11-15	≤10	≤8	-	-	≥16	
PHENICOLS											
C	Chloramphenicol	30 µg	≥18	-	13-17	≤12	≤8	-	16	≥32	**(67)** Not routinely reported on isolates from the urinary tract.
FOSFOMYCINS											
U	Fosfomycin	200 µg	≥16	-	13-15	≤12	≤64	-	128	≥256	**(68)** Disk diffusion and MIC breakpoints apply only to *E. coli* urinary tract isolates and should not be extrapolated to other species of Enterobacterales. **(69)** The 200-µg fosfomycin disk contains 50 µg of glucose-6-phosphate. **(70)** The only approved MIC method for testing is agar dilution using agar media supplemented with 25 µg/mL of glucose-6-phosphate. Broth dilution MIC testing should not be performed.

Table 2A. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
NITROFURANS											
U	Nitrofurantoin	300 µg	≥17	-	15-16	≤14	≤32	-	64	≥128	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CAT, colistin agar test; CBDE, colistin broth disk elution; eCIM, EDTA-modified carbapenem inactivation method; ESBL, extended-spectrum β-lactamase; I, intermediate; IV, intravenous; mCIM, modified carbapenem inactivation method; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; PK/PD, pharmacokinetic/pharmacodynamic; QC, quality control; R, resistant; S, susceptible; SDD, susceptible-dose dependent; UTI, urinary tract infection.
Symbol: ^, designation for agents that have the potential to concentrate in the urine.

Footnote

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

References for Table 2A

1 Hackel MA, Tsuji M, Yamano Y, Echols R, Karlowsky JA, Sahm DF. Reproducibility of broth microdilution MICs for the novel siderophore cephalosporin, cefiderocol, determined using iron-depleted cation-adjusted Mueller-Hinton broth. *Diagn Microbiol Infect Dis*. 2019;94(4):321-325.

2 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

4 Perrott J, Mabasa VH, Ensom MH. Comparing outcomes of meropenem administration strategies based on pharmacokinetic and pharmacodynamic principles: a qualitative systematic review. *Ann Pharmacother*. 2010;44(3):557-564.

5 Cirillo I, Vaccaro N, Turner K, Solanki B, Natarajan J, Redman R. Pharmacokinetics, safety, and tolerability of doripenem after 0.5-, 1-, and 4-hour infusions in healthy volunteers. *J Clin Pharmacol*. 2009;49(7):798-806.

6 Sakka SG, Glauner AK, Bulitta JB, et al. Population pharmacokinetics and pharmacodynamics of continuous versus short-term infusion of imipenem-cilastatin in critically ill patients in a randomized, controlled trial. *Antimicrob Agents Chemother*. 2007;51(9):3304-3310.

7 Peleg AY, Hooper DC. Hospital-acquired infections due to gram-negative bacteria. *N Engl J Med*. 2010;362(19):1804-1813.

8 Tsuji BT, Pogue JM, Zavascki AP, et al. International consensus guidelines for the optimal use of the polymyxins: endorsed by the American College of Clinical Pharmacy (ACCP), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Society of America (IDSA), International Society for Anti-Infective Pharmacology (ISAP), Society of Critical Care Medicine (SCCM), and Society of Infectious Diseases Pharmacists (SIDP). *Pharmacotherapy*. 2019;39(1):10-39.

Table 2B-1. Zone Diameter and MIC Breakpoints for *Pseudomonas aeruginosa*

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)

Pseudomonas aeruginosa ATCC® 27853

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.

General Comments

(1) 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.

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

(3) *P. aeruginosa* may develop resistance during prolonged therapy with all antimicrobial agents. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted.

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

(5) **An intermediate (I) with a ^ in Tables 2 indicates agents that have the potential to concentrate in the urine. The I^ is for informational use only. The decision to report I^ is best made by each laboratory based on institution-specific guidelines and in consultation with appropriate medical personnel.**

Table 2B-1. *Pseudomonas aeruginosa* (Continued)

(6) Positive blood culture broth can be used as the inoculum for direct disk diffusion testing of select antimicrobial agents against *P. aeruginosa* (using methods described in Table 3E-1 and applying breakpoints in Table 3E-3). For antimicrobial agents not listed in Table 3E-3 for *P. aeruginosa*, CLSI has not yet evaluated this direct disk diffusion method.

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

Table 2B-1. *Pseudomonas aeruginosa* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
O	Piperacillin	100 µg	≥21	15-20^	≤14	≤16	32-64^	≥128	**(7)** Breakpoints for piperacillin (alone or with tazobactam) are based on a piperacillin dosage regimen of at least 3 g administered every 6 h.
β-LACTAM COMBINATION AGENTS									
(8) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test intermediate or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.									
A	Piperacillin-tazobactam	100/10 µg	≥21	15-20^	≤14	≤16/4	32/4-64/4^	≥128/4	**(9)** Breakpoints for piperacillin (alone or with tazobactam) are based on a piperacillin dosage regimen of at least 3 g administered every 6 h.
B	Ceftazidime-avibactam	30/20 µg	≥21	-	≤20	≤8/4	-	≥16/4	**(10)** Breakpoints are based on a dosage regimen of 2.5 g administered every 8 h over 2 h.
B	Ceftolozane-tazobactam	30/10 µg	≥21	17-20^	≤16	≤4/4	8/4^	≥16/4	**(11) Breakpoints are based on a dosage regimen of 3 g administered every 8 h for pneumonia and 1.5 g administered every 8 h for other indications.**
B	Imipenem-relebactam	10/25 µg	≥23	20-22^	≤19	≤2/4	4/4^	≥8/4	**(12)** Breakpoints are based on a dosage regimen of 1.25 g administered every 6 h.
O	Ticarcillin-clavulanate	75/10 µg	≥24	16-23^	≤15	≤16/2	32/2-64/2^	≥128/2	**(13)** Breakpoints for ticarcillin (alone or with clavulanate) are based on a ticarcillin dosage regimen of at least 3 g administered every 6 h.
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftazidime	30 µg	≥18	15-17^	≤14	≤8	16^	≥32	**(14)** Breakpoints are based on a dosage regimen of 1 g administered every 6 h or 2 g administered every 8 h.
B	Cefepime	30 µg	≥18	15-17^	≤14	≤8	16^	≥32	**(15)** Breakpoints are based on a dosage regimen of 1 g administered every 8 h or 2 g administered every 12 h.
B	Cefiderocol	30 µg	≥18	13-17^	≤12	≤4	8^	≥16	**(16)** Breakpoints are based on a dosage regimen of 2 g every 8 h administered over 3 h.
MONOBACTAMS									
B	Aztreonam	30 µg	≥22	16-21^	≤15	≤8	16^	≥32	**(17)** Breakpoints are based on a dosage regimen of 1 g administered every 6 h or 2 g administered every 8 h.

Table 2B-1. *Pseudomonas aeruginosa* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
CARBAPENEMS									
B	Doripenem	10 µg	≥19	16-18^	≤15	≤2	4^	≥8	**(18)** Breakpoints for doripenem are based on a dosage regimen of 500 mg administered every 8 h.
	Imipenem	10 µg	≥19	16-18^	≤15	≤2	4^	≥8	**(19)** Breakpoints for imipenem are based on a dosage regimen of 1 g administered every 8 h or 500 mg administered every 6 h.
	Meropenem	10 µg	≥19	16-18^	≤15	≤2	4^	≥8	**(20)** Breakpoints for meropenem are based on a dosage regimen of 1 g administered every 8 h.
LIPOPEPTIDES									
(21) WARNING: Clinical and PK/PD data demonstrate colistin and polymyxin B have limited clinical efficacy, even if an intermediate result is obtained. Alternative agents are strongly preferred. Colistin and polymyxin B should be used in combination with one or more active antimicrobial agents. Consultation with an infectious diseases specialist is recommended.									
O	Colistin or polymyxin B	-	-	-	-	-	≤2	≥4	**(22)** Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses (see International Consensus Guidelines[4]). **(23)** Polymyxin B should be given with a loading dose and maximum recommended doses (see International Consensus Guidelines[4]). **(24)** When colistin or polymyxin B is given systemically, neither is likely to be effective for pneumonia. **(25)** For colistin, broth microdilution, CBDE, and CAT MIC methods are acceptable. For polymyxin B, broth microdilution is the only approved method. Disk diffusion and gradient diffusion methods should not be performed (see Table 3D).

Table 2B-1. *Pseudomonas aeruginosa* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
AMINOGLYCOSIDES									
A	Gentamicin	10 µg	≥15	13-14^	≤12	≤4	8^	≥16	
A	Tobramycin	10 µg	≥15	13-14^	≤12	≤4	8^	≥16	
B	Amikacin	30 µg	≥17	15-16^	≤14	≤16	32^	≥64	
O	Netilmicin	30 µg	≥15	13-14^	≤12	≤8	16^	≥32	
FLUOROQUINOLONES									
B	Ciprofloxacin	5 µg	≥25	19-24^	≤18	≤0.5	1^	≥2	**(26)** Breakpoints are based on a dosage regimen of 400 mg IV administered every 8 h.
B	Levofloxacin	5 µg	≥22	15-21^	≤14	≤1	2^	≥4	**(27)** Breakpoints are based on a dosage regimen of 750 mg administered every 24 h.
O	Lomefloxacin	10 µg	≥22	19-21^	≤18	≤2	4^	≥8	**(28)** For testing and reporting of urinary tract isolates only.
O	Norfloxacin	10 µg	≥17	13-16	≤12	≤4	8	≥16	See comment (28).
O	Ofloxacin	5 µg	≥16	13-15^	≤12	≤2	4^	≥8	
O	Gatifloxacin	5 µg	≥18	15-17^	≤14	≤2	4^	≥8	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CAT, colistin agar test; CBDE, colistin broth disk elution; I, intermediate; IV, intravenous; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; PK/PD, pharmacokinetic/pharmacodynamic; QC, quality control; R, resistant; S, susceptible.
Symbol: ^, designation for agents that have the potential to concentrate in the urine.

Footnote

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

References for Table 2B-1

1 Hackel MA, Tsuji M, Yamano Y, Echols R, Karlowsky JA, Sahm DF. Reproducibility of broth microdilution MICs for the novel siderophore cephalosporin, cefiderocol, determined using iron-depleted cation-adjusted Mueller-Hinton broth. *Diagn Microbiol Infect Dis*. 2019;94(4):321-325.

2 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

4 Tsuji BT, Pogue JM, Zavascki AP, et al. International consensus guidelines for the optimal use of the polymyxins: endorsed by the American College of Clinical Pharmacy (ACCP), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Society of America (IDSA), International Society for Anti-Infective *Pharmacology* (ISAP), Society of Critical Care Medicine (SCCM), and Society of Infectious Diseases Pharmacists (SIDP). *Pharmacotherapy*. 2019;39(1):10-39.

Table 2B-2. Zone Diameter and MIC Breakpoints for *Acinetobacter* spp.

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
Incubation:	35°C±2°C; ambient air; 20-24 hours, all methods

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

Escherichia coli ATCC® 25922 (for tetracyclines and trimethoprim-sulfamethoxazole)
Pseudomonas aeruginosa ATCC® 27853

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.

General Comment

(1) 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. 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.

Table 2B-2. *Acinetobacter* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
O	Piperacillin	100 µg	≥21	18-20	≤17	≤16	32-64	≥128	
β-LACTAM COMBINATION AGENTS									
(2) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test intermediate or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.									
A	Ampicillin-sulbactam	10/10 µg	≥15	12-14	≤11	≤8/4	16/8	≥32/16	
B	Piperacillin-tazobactam	100/10 µg	≥21	18-20	≤17	≤16/4	32/4-64/4	≥128/4	
O	Ticarcillin-clavulanate	75/10 µg	≥20	15-19	≤14	≤16/2	32/2-64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftazidime	30 µg	≥18	15-17	≤14	≤8	16	≥32	
B	Cefepime	30 µg	≥18	15-17	≤14	≤8	16	≥32	
B	Cefotaxime	30 µg	≥23	15-22	≤14	≤8	16-32	≥64	
B	Ceftriaxone	30 µg	≥21	14-20	≤13	≤8	16-32	≥64	
B	Cefiderocol	30 µg	≥15	-	-	≤4	8	≥16	**(3)** Breakpoints are based on a dosage regimen of 2 g every 8 h administered over 3 h. **Disk diffusion zone diameters ≤ 14 mm should not be interpreted or reported because zone diameters ≤ 14 mm occur with resistant, intermediate, and susceptible isolates. For isolates with zone diameters ≤ 14 mm, do not report cefiderocol without performing an MIC test.** **(4) For testing and reporting against *Acinetobacter baumannii* complex only.**
CARBAPENEMS									
A	Doripenem	10 µg	≥18	15-17	≤14	≤2	4	≥8	**(5)** Breakpoints for doripenem are based on a dosage regimen of 500 mg administered every 8 h.
A	Imipenem	10 µg	≥22	19-21	≤18	≤2	4	≥8	**(6)** Breakpoints for imipenem are based on a dosage regimen of 500 mg administered every 6 h.
A	Meropenem	10 µg	≥18	15-17	≤14	≤2	4	≥8	**(7)** Breakpoints for meropenem are based on a dosage regimen of 1 g administered every 8 h or 500 mg administered every 6 h.

Table 2B-2. *Acinetobacter* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
LIPOPEPTIDES									
(8) WARNING: Clinical and PK/PD data demonstrate colistin and polymyxin B have limited clinical efficacy, even if an intermediate result is obtained. Alternative agents are strongly preferred. Colistin and polymyxin B should be used in combination with one or more active antimicrobial agents. Consultation with an infectious diseases specialist is recommended.									
O	Colistin or polymyxin B	- -	- -	- -	- -	- -	≤2 ≤2	≥4 ≥4	**(9)** Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses (see International Consensus Guidelines[4]). **(10)** Polymyxin B should be given with a loading dose and maximum recommended doses (see International Consensus Guidelines[4]). **(11)** When colistin or polymyxin B is given systemically, the drug is unlikely to be effective for pneumonia. **(12)** The only approved MIC method is broth microdilution. CBDE, CAT, disk diffusion, and gradient diffusion should not be performed. **(13)** See comment (4).
AMINOGLYCOSIDES									
A	Gentamicin	10 µg	≥15	13-14	≤12	≤4	8	≥16	
A	Tobramycin	10 µg	≥15	13-14	≤12	≤4	8	≥16	
B	Amikacin	30 µg	≥17	15-16	≤14	≤16	32	≥64	
O	Netilmicin	-	-	-	-	≤8	16	≥32	
TETRACYCLINES									
(14) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.									
B	Doxycycline	30 µg	≥13	10-12	≤9	≤4	8	≥16	
B	Minocycline	30 µg	≥16	13-15	≤12	≤4	8	≥16	
U	Tetracycline	30 µg	≥15	12-14	≤11	≤4	8	≥16	

Table 2B-2. *Acinetobacter* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
FLUOROQUINOLONES									
A	Ciprofloxacin	5 µg	≥21	16-20	≤15	≤1	2	≥4	
A	Levofloxacin	5 µg	≥17	14-16	≤13	≤2	4	≥8	
O	Gatifloxacin	5 µg	≥18	15-17	≤14	≤2	4	≥8	
FOLATE PATHWAY ANTAGONISTS									
B	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16	11-15	≤10	≤2/38	-	≥4/76	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CAT, colistin agar test; CBDE, colistin broth elution test; I, intermediate; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; PK/PD, pharmacokinetic/pharmacodynamic; QC, quality control; R, resistant; S, susceptible.

Footnote

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

References for Table 2B-2

1 Hackel MA, Tsuji M, Yamano Y, Echols R, Karlowsky JA, Sahm DF. Reproducibility of broth microdilution MICs for the novel siderophore cephalosporin, cefiderocol, determined using iron-depleted cation-adjusted Mueller-Hinton broth. *Diagn Microbiol Infect Dis*. 2019;94(4):321-325.

2 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

4 Tsuji BT, Pogue JM, Zavascki AP, et al. International consensus guidelines for the optimal use of the polymyxins: endorsed by the American College of Clinical Pharmacy (ACCP), European Society of Clinical Microbiology and Infectious Diseases (ESCMID), Infectious Diseases Society of America (IDSA), International Society for Anti-Infective Pharmacology (ISAP), Society of Critical Care Medicine (SCCM), and Society of Infectious Diseases Pharmacists (SIDP). *Pharmacotherapy*. 2019;39(1):10-39.

Table 2B-3. Zone Diameter and MIC Breakpoints for *Burkholderia cepacia* complex

Testing Conditions	
Medium:	Disk diffusion: MHA Broth dilution: CAMHB Agar dilution: MHA
Inoculum:	Broth culture method or colony suspension, equivalent to a 0.5 McFarland standard
Incubation:	35°C±2°C; ambient air; 20-24 hours, all methods

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

Escherichia coli ATCC® 25922 (for chloramphenicol, minocycline, and trimethoprim-sulfamethoxazole)
Pseudomonas aeruginosa ATCC® 27853

Refer to Tables 4A-2 and 5A-2 to select strains for routine QC of ß-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.

General Comment

(1) 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,[1] 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*[2]). Hold the Petri plate a few inches above a black background illuminated with reflected light. The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

Table 2B-3. *Burkholderia cepacia* complex (Continued)

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

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

Footnote

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

References for Table 2B-3

1 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

2 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

Table 2B-4. Zone Diameter and MIC Breakpoints for *Stenotrophomonas maltophilia*

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
Incubation:	35°C±2°C; ambient air; 20-24 hours, all methods

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

Escherichia coli ATCC®a 25922 (for chloramphenicol, minocycline, and trimethoprim-sulfamethoxazole)
Pseudomonas aeruginosa ATCC® 27853

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.

General Comment

(1) 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. 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.

Table 2B-4. *Stenotrophomonas maltophilia* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
B-LACTAM COMBINATION AGENTS									
O	Ticarcillin-clavulanate	-	-	-	-	≤16/2	32/2-64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
B	Ceftazidime	-	-	-	-	≤8	16	≥32	
B	**Cefiderocol**	30 µg	**≥15**	**-**	**-**	**≤1**	**-**	**-**	**(2)** Breakpoints are based on a dosage regimen of 2 g every 8 h administered over 3 h. **Breakpoints are based on PK/PD properties, MIC distributions, and limited clinical data.**
TETRACYCLINES									
A	Minocycline	30 µg	≥19	15-18	≤14	≤4	8	≥16	
FLUOROQUINOLONES									
A	Levofloxacin	5 µg	≥17	14-16	≤13	≤2	4	≥8	
FOLATE PATHWAY ANTAGONISTS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16	11-15	≤10	≤2/38	-	≥4/76	
PHENICOLS									
C	Chloramphenicol	-	-	-	-	≤8	16	≥32	**(3)** Not routinely reported on isolates from the urinary tract.

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

Footnote

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

References for Table 2B-4

1 Hackel MA, Tsuji M, Yamano Y, Echols R, Karlowsky JA, Sahm DF. Reproducibility of broth microdilution MICs for the novel siderophore cephalosporin, cefiderocol, determined using iron-depleted cation-adjusted Mueller-Hinton broth. *Diagn Microbiol Infect Dis*. 2019;94(4):321-325.

2 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

Table 2B-5. MIC Breakpoints for Other Non-Enterobacterales (Refer to General Comment 1)

Testing Conditions		Routine QC Recommendations (see Table 5A-1 for acceptable QC ranges)
Medium:	Broth dilution: CAMHB Agar dilution: MHA	*Escherichia coli* ATCC® 25922 (for chloramphenicol, tetracyclines, sulfonamides, and trimethoprim-sulfamethoxazole) *Pseudomonas aeruginosa* ATCC® 27853
Inoculum:	Broth culture method or colony suspension, equivalent to a 0.5 McFarland standard	Refer to Tables 4A-2 and 5A-2 to select strains for routine QC of β-lactam combination agents.
Incubation:	35°C ± 2°C; ambient air; 16–20 hours	When a commercial test system is used for susceptibility testing, refer to the manufacturer's instructions for QC test recommendations and QC ranges.

General Comments

(1) Other non-Enterobacterales include *Pseudomonas* spp. and other nonfastidious, glucose-nonfermenting, gram-negative bacilli but exclude *P. aeruginosa*, *Acinetobacter* spp., *B. cepacia* complex, and *S. maltophilia* (refer to Tables 2B-2, 2B-3, and 2B-4, respectively). Recommendations for testing and reporting *Aeromonas hydrophila* complex, *Burkholderia mallei*, *Burkholderia pseudomallei*, and *Vibrio* spp. (including *V. cholerae)* are found in CLSI document M45.[1]

(2) For other non-Enterobacterales, the disk diffusion method has not been systematically studied. Therefore, for this organism group, disk diffusion testing is not recommended.

Table 2B-5. Other Non-Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
O	Piperacillin	-	-	-	-	≤16	32-64	≥128	
β-LACTAM COMBINATION AGENTS									
(3) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test intermediate or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.									
B	Piperacillin-tazobactam	-	-	-	-	≤16/4	32/4-64/4	≥128/4	
O	Ticarcillin-clavulanate	-	-	-	-	≤16/2	32/2-64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftazidime	-	-	-	-	≤8	16	≥32	
B	Cefepime	-	-	-	-	≤8	16	≥32	
C	Cefotaxime	-	-	-	-	≤8	16-32	≥64	
C	Ceftriaxone	-	-	-	-	≤8	16-32	≥64	
O	Cefoperazone	-	-	-	-	≤16	32	≥64	
O	Ceftizoxime	-	-	-	-	≤8	16-32	≥64	
O	Moxalactam	-	-	-	-	≤8	16-32	≥64	
MONOBACTAMS									
B	Aztreonam	-	-	-	-	≤8	16	≥32	
CARBAPENEMS									
B	Imipenem	-	-	-	-	≤4	8	≥16	
B	Meropenem	-	-	-	-	≤4	8	≥16	
AMINOGLYCOSIDES									
A	Gentamicin	-	-	-	-	≤4	8	≥16	
A	Tobramycin	-	-	-	-	≤4	8	≥16	
B	Amikacin	-	-	-	-	≤16	32	≥64	
O	Netilmicin	-	-	-	-	≤8	16	≥32	
TETRACYCLINES									
(4) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.									
U	Tetracycline	-	-	-	-	≤4	8	≥16	
O	Doxycycline	-	-	-	-	≤4	8	≥16	
O	Minocycline	-	-	-	-	≤4	8	≥16	

Table 2B-5. Other Non-Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
FLUOROQUINOLONES									
B	Ciprofloxacin	-	-	-	-	≤1	2	≥4	
B	Levofloxacin	-	-			≤2	4	≥8	
O	Gatifloxacin	-	-	-	-	≤2	4	≥8	
O	Lomefloxacin	-	-	-	-	≤2	4	≥8	
O	Norfloxacin	-	-	-	-	≤4	8	≥16	**(5)** For testing and reporting of urinary tract isolates only.
O	Ofloxacin	-	-	-	-	≤2	4	≥8	
FOLATE PATHWAY ANTAGONISTS									
B	Trimethoprim-sulfamethoxazole	-	-	-	-	≤2/38	-	≥4/76	
U	Sulfonamides	-	-	-	-	≤256	-	≥512	**(6)** Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations.
PHENICOLS									
C	Chloramphenicol	-	-	-	-	≤8	16	≥32	**(7)** Not routinely reported on isolates from the urinary tract.

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

Footnote

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

Reference for Table 2B-5

1 CLSI. *Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria*. 3rd ed. CLSI guideline M45. Clinical and Laboratory Standards Institute; 2016.

Table 2C. Zone Diameter and MIC Breakpoints for *Staphylococcus* spp.

Testing Conditions

Medium: Disk diffusion: MHA
Broth dilution: CAMHB; CAMHB + 2% NaCl for oxacillin; CAMHB supplemented to 50 µg/mL calcium for daptomycin.
Agar dilution: MHA; MHA + 2% NaCl for oxacillin.
NOTE: Agar dilution has not been validated for daptomycin.

Inoculum: Colony suspension, equivalent to a 0.5 McFarland Standard

Incubation: 35°C ± 2°C; ambient air
Disk diffusion: 16–18 hours; 24 hours (for cefoxitin when testing *Staphylococcus* spp., except *S. aureus*, *S. lugdunensis*, *S. pseudintermedius*, and *S. schleiferi*)
Dilution methods: 16–20 hours; 24 hours for oxacillin and vancomycin
Testing at temperatures above 35°C may not detect methicillin (oxacillin)-resistant staphylococci (MRS).

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

Disk diffusion:
S. aureus ATCC® 25923

Dilution methods:
S. aureus ATCC® 29213

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.

General Comments

(1) 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,[1] 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*[2]). Hold the Petri plate a few inches above a black background illuminated with reflected light, except for linezolid, which should be read with transmitted light (plate held up to light source). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter. For linezolid, any discernible growth within the zone of inhibition is indicative of resistance to the respective agent.

(2) *S. aureus* complex consists of the coagulase-positive species *S. aureus*, *Staphylococcus argenteus*, and *Staphylococcus schweitzeri*. If *S. argenteus* is identified by MALDI-TOF MS or sequencing, it is recommended that it be reported as "*S. aureus* complex (*S. argenteus*)," and *S. aureus* phenotypic testing method recommendations, breakpoints, and interpretive categories should be used. Human infections with *S. schweitzeri* have yet to be reported.[3]

Table 2C. Staphylococcus spp. (Continued)

(3) For staphylococci when testing chloramphenicol, clindamycin, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored (see M07,[4] Figures 3 and 4). With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, read the end point at the concentration in which there is ≥ 80% reduction in growth compared with the control (see M07,[4] Figure 5).

(4) Routine testing of urine isolates of *Staphylococcus saprophyticus* is not advised, because infections respond to concentrations achieved in urine of antimicrobial agents commonly used to treat acute, uncomplicated UTIs (eg, nitrofurantoin, trimethoprim - sulfamethoxazole, or a fluoroquinolone).

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

(6) Most methicillin (oxacillin) resistance is mediated by *mecA*, encoding PBP2a (also called PBP2'). Testing for *mecA* and PBP2a are the most definitive tests for detection of methicillin (oxacillin) resistance for *Staphylococcus* spp. Isolates that test positive for *mecA* or PBP2a or resistant by any of the recommended phenotypic methods should be reported as methicillin (oxacillin) resistant (see Appendix H and the table below).

Detection of methicillin (oxacillin) resistance in staphylococci is achieved by using specific methods as listed in Table 2C and further described in Tables 3G-1 and 3G-2.

Organism	Phenotypic Methods for Detection of Methicillin (Oxacillin)-Resistant *Staphylococcus* spp.				
	Cefoxitin MIC	Cefoxitin disk diffusion	Oxacillin MIC	Oxacillin disk diffusion	Oxacillin salt agar
S. aureus	Yes (16–20 h)	Yes (16–18 h)	Yes (24 h)	No	Yes (24 h)
S. lugdunensis	Yes (16–20 h)	Yes (16–18 h)	Yes (24 h)	No	No
S. epidermidis	No	Yes (24 h)	Yes (24 h)	Yes (16–18 h)	No
S. pseudintermedius	No	No	Yes (24 h)	Yes (16–18 h)	No
S. schleiferi	No	No	Yes (24 h)	Yes (16–18 h)	No
Staphylococcus spp. (not listed above or not identified to the species level)	No	Yes[a] (24 h)	Yes[a] (24 h)	No	No

Abbreviations: h, hour(s); MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant staphylococci; PBP2a, penicillin-binding protein 2a.
[a] For isolates that fall into the category of *Staphylococcus* spp (not listed above or not identified to the species level) from serious infections for which the oxacillin MICs are 1-2 µg/mL, testing for *mecA* or PBP2a should be considered, because these are the most definitive tests for detection of methicillin (oxacillin) resistance (see comment [18]). Recent data suggest that the cefoxitin disk diffusion test may not perform reliably for all species (eg, *S. haemolyticus*) that fall into the category of "*Staphylococcus* spp. (not listed above or not identified to the species level)."[5]

Table 2C. *Staphylococcus* spp. (Continued)

Mechanisms of methicillin (oxacillin) resistance other than *mecA* are rare and include a novel *mecA* homologue, *mecC*.[6] MICs for strains with *mecC* are typically cefoxitin resistant and oxacillin susceptible; *mecC* resistance cannot be detected by tests directed at *mecA* or PBP2a.

(7) MRS, as defined by cefoxitin or oxacillin testing, as appropriate to the species, are considered resistant to other β-lactam agents, ie, penicillins, β-lactam combination agents, cephems (with the exception of ceftaroline), and carbapenems. This is because most cases of documented MRS infections have responded poorly to β-lactam therapy or because convincing clinical data that document clinical efficacy for those agents have not been presented.

(8) For tests for β-lactamase production, methicillin (oxacillin) resistance and *mecA*-mediated methicillin (oxacillin) resistance using cefoxitin, reduced susceptibility to vancomycin, ICR, and high-level mupirocin resistance (*S. aureus* only), refer to Tables 3F, 3G-1, 3G-2, 3H, and 3J, respectively.

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

Table 2C. *Staphylococcus* spp. (Continued)

Test/Report Group	Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
				S	SDD	I	R	S	SDD	I	R	
PENICILLINASE-LABILE PENICILLINS												
(9) Penicillin-susceptible staphylococci are susceptible to other β-lactam agents with established clinical efficacy for staphylococcal infections (including both penicillinase-labile and penicillinase-stable agents; see Glossary I). Penicillin-resistant staphylococci are resistant to penicillinase-labile penicillins. **(10)** Penicillin should be used to test the susceptibility of all staphylococci to penicillinase-labile penicillins (see Glossary I). Penicillin-resistant strains of staphylococci produce β-lactamase. Perform a test(s) to detect β-lactamase production on staphylococci for which the penicillin MICs are ≤ 0.12 µg/mL or zone diameters ≥ 29 mm before reporting the isolate as penicillin susceptible. Rare isolates of staphylococci that contain genes for β-lactamase production may appear negative by β-lactamase tests. Consequently, for serious infections requiring penicillin therapy, laboratories should perform MIC tests and β-lactamase testing on all subsequent isolates from the same patient. PCR testing of the isolate for the *blaZ* β-lactamase gene may be considered. See Table 3F.												
A	Penicillin	All staphylococci	10 units	≥29	-	-	≤28	≤0.12		-	≥0.25	**(11)** For methicillin (oxacillin)-resistant staphylococci, report penicillin as resistant or do not report.
PENICILLINASE-STABLE PENICILLINS												
(12) Cefoxitin is tested as a surrogate for oxacillin for some species of *Staphylococcus*. Isolates that test resistant by cefoxitin or oxacillin, when using the appropriate test method for the species, should be reported as methicillin (oxacillin) resistant. If testing only cefoxitin, report as methicillin (oxacillin) susceptible or resistant based on the cefoxitin result. **(13)** Oxacillin (or cefoxitin) results can be applied to the other penicillinase-stable penicillins (cloxacillin, dicloxacillin, methicillin, and nafcillin). For agents with established clinical efficacy and considering site of infection and appropriate dosing, methicillin (oxacillin)-susceptible staphylococci can be considered susceptible to: • β-lactam combination agents (amoxicillin-clavulanate, ampicillin-sulbactam, piperacillin-tazobactam) • Oral cephems (cefaclor, cefdinir, cephalexin, cefpodoxime, cefprozil, cefuroxime, loracarbef) • Parenteral cephems including cephalosporins I, II, III, and IV (cefamandole, cefazolin, cefepime, cefmetazole, cefonicid, cefoperazone, cefotaxime, cefotetan, ceftizoxime, ceftriaxone, cefuroxime, ceftaroline, moxalactam) • Carbapenems (doripenem, ertapenem, imipenem, meropenem) Methicillin (oxacillin)-resistant staphylococci are resistant to all currently available β-lactam antimicrobial agents, with the exception of ceftaroline. Thus, susceptibility or resistance to a wide array of β-lactam antimicrobial agents may be deduced from testing only penicillin and either cefoxitin or oxacillin. Testing of other β-lactam agents, except ceftaroline, is not advised. See general comments (6) and (7). Additional explanation on the use of cefoxitin for prediction of *mecA*-mediated methicillin (oxacillin) resistance can be found in Subchapter 3.12 of M07[4] and Subchapter 3.9 of M02.[1]											

Table 2C. *Staphylococcus* spp. (Continued)

Test/ Report Group	Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
				S	SDD	I	R	S	SDD	I	R	
PENICILLINASE-STABLE PENICILLINS (Continued)												
A	Oxacillin	*S. aureus* and *S. lugdunensis*	-	-	-	-	-	≤2 (oxacillin)	-	-	≥4 (oxacillin)	**(14)** Oxacillin disk testing is not reliable for *S. aureus* and *S. lugdunensis*. **(15)** For isolates of S. *aureus* that do not grow well on CAMHB or unsupplemented MHA (eg, small-colony variants), testing on other media (eg, BMHA) does not reliably detect *mecA*-mediated resistance. Testing for PBP2a using induced growth (ie, growth taken from the zone margin surrounding a cefoxitin disk on either BMHA or a blood agar plate after 24 hours incubation in 5% CO_2) or *mecA* should be done. See general comments (6) and (7) and comments (9), (12), and (13).
			30 µg cefoxitin (surrogate test for oxacillin)	≥22	-	-	≤21	≤4 (cefoxitin)	-	-	≥8 (cefoxitin)	
A	Oxacillin	*S. epidermidis*	1 µg oxacillin	≥18 (oxacillin)	–	–	≤17 (oxacillin)	≤0.5 (oxacillin)	–	–	≥1 (oxacillin)	See general comments (6) and (7) and comments (9), (12), and (13). **(16)** Cefoxitin MIC testing is not reliable for detecting *mecA*-mediated resistance in *S. epidermidis*.
			30 µg cefoxitin (surrogate test for oxacillin)	≥25 (cefoxitin)	–	–	≤24 (cefoxitin)	–	–	–	–	
		S. pseudintermedius and *S. schleiferi*	1 µg oxacillin	≥18	–	-	≤17	≤0.5	–	-	≥1	**(17)** Neither cefoxitin MIC nor cefoxitin disk tests are reliable for detecting *mecA*-mediated resistance in *S. pseudintermedius* and *S. schleiferi*. See general comments (6) and (7) and comments (9), (12), and (13).

Table 2C. *Staphylococcus* spp. (Continued)

Test/ Report Group	Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
				S	SDD	I	R	S	SDD	I	R	
PENICILLINASE-STABLE PENICILLINS (Continued)												
A	Oxacillin	*Staphylococcus* spp., except: *S. aureus* *S. lugdunensis* *S. epidermidis* *S. pseudintermedius* *S. schleiferi*	30 µg cefoxitin (surrogate test for oxacillin)	≥ 25 (cefoxitin)	–	-	≤ 24 (cefoxitin)	≤ 0.5 (oxacillin)	–	-	≥ 1 (oxacillin)	**(18)** Oxacillin MIC breakpoints may overcall resistance, and some isolates for which the oxacillin MICs are 1-2 µg/mL may be *mecA* negative. Isolates from serious infections for which oxacillin MICs are 1-2 µg/mL may be tested for *mecA* or for PBP2a. Isolates that test *mecA* or PBP2a negative should be reported as methicillin (oxacillin) susceptible. See general comments (6) and (7) and comments (9), (12), and (13).
CEPHEMS (PARENTERAL)												
B	Ceftaroline	*S. aureus*, including MRSA	30 µg	≥ 25	20-24		≤ 19	≤ 1	2-4	–	≥ 8	**(19)** The breakpoint for susceptible is based on a dosage regimen of 600 mg administered every 12 h. **(20)** The breakpoint for SDD is based on a dosage of 600 mg every 8 h administered over 2 h.

Table 2C. *Staphylococcus* spp. (Continued)

Test/Report Group	Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
				S	SDD	I	R	S	SDD	I	R	
GLYCOPEPTIDES												
(21) MIC tests should be performed to determine the susceptibility of all isolates of staphylococci to vancomycin. The disk test does not differentiate vancomycin-susceptible isolates of *S. aureus* from vancomycin-intermediate isolates, nor does the test differentiate among vancomycin-susceptible, -intermediate, and -resistant isolates of *Staphylococcus* spp. other than *S. aureus*, all of which give similar size zones of inhibition.												
B	Vancomycin	*S. aureus*, **including MRSA**	-	-	-	-	-	≤2	-	4-8	≥16	**(22)** For *S. aureus*, vancomycin-susceptible isolates may become vancomycin intermediate during the course of prolonged therapy. **(23)** Send any *S. aureus* for which the vancomycin is ≥8 µg/mL to a referral laboratory. See Appendix A. Also refer to Table 3G-1 for *S. aureus*, Subchapter 3.12 in M07,[4] and Subchapter 3.9 in M02.[1]
		Staphylococcus spp. other than *S. aureus*	-	-	-	-	-	≤4	-	8-16	≥32	See comment (20). **(24)** Send any *Staphylococcus* spp. other than *S. aureus* for which the vancomycin MIC is ≥32 µg/mL to a referral laboratory. See Appendix A. See also Subchapter 3.12 in M07[4] and Subchapter 3.9 in M02.[1]
LIPOGLYCOPEPTIDES												
C	Dalbavancin	*S. aureus*, including MRSA	-	-	-	-	-	≤0.25	-	-	-	**(25) Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes.**
C	Oritavancin		-	-	-	-	-	≤0.12	-	-	-	**(26) Breakpoints are based on a dosage regimen of 1200 mg IV administered once.**
C	Telavancin		-	-	-	-	-	≤0.12	-	-	-	**(27) Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h.**
Inv.	Teicoplanin	All staphylococci	-	-	-	-	-	≤8	-	16	≥32	

Table 2C. *Staphylococcus* spp. (Continued)

Test/ Report Group	Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
				S	SDD	I	R	S	SDD	I	R	
LIPOPEPTIDES												
B	Daptomycin	All staphylococci	-	-	-	-	-	≤1	-	-	-	**(28)** Daptomycin should not be reported for isolates from the respiratory tract.
AMINOGLYCOSIDES												
(29) For staphylococci that test susceptible, gentamicin is used only in combination with other active agents that test susceptible.												
C	Gentamicin	All staphylococci	10 µg	≥15	-	13-14	≤12	≤4	-	8	≥16	
MACROLIDES												
(30) Not routinely reported on organisms isolated from the urinary tract.												
A	Azithromycin	All staphylococci	15 µg	≥18	-	14-17	≤13	≤2	-	4	≥8	
A	or clarithromycin		15 µg	≥18		14-17	≤13	≤2		4	≥8	
A	or erythromycin		15 µg	≥23		14-22	≤13	≤0.5		1-4	≥8	
	Dirithromycin		15 µg	≥19	-	16-18	≤15	≤2	-	4	≥8	
TETRACYCLINES												
(31) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.												
B	Tetracycline	All staphylococci	30 µg	≥19	-	15-18	≤14	≤4	-	8	≥16	
B	Doxycycline		30 µg	≥16	-	13-15	≤12	≤4	-	8	≥16	
B	Minocycline		30 µg	≥19	-	15-18	≤14	≤4	-	8	≥16	See comment (30).
FLUOROQUINOLONES												
(32) *Staphylococcus* spp. may develop resistance during prolonged therapy with quinolones. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted.												
C	Ciprofloxacin	All staphylococci	5 µg	≥21	-	16-20	≤15	≤1	-	2	≥4	
C	or levofloxacin		5 µg	≥19	-	16-18	≤15	≤1	-	2	≥4	
C	Moxifloxacin		5 µg	≥24	-	21-23	≤20	≤0.5	-	1	≥2	
O	Enoxacin		10 µg	≥18	-	15-17	≤14	≤2	-	4	≥8	**(33)** For testing and reporting of urinary tract isolates only.
O	Gatifloxacin		5 µg	≥23	-	20-22	≤19	≤0.5	-	1	≥2	
O	Grepafloxacin		5 µg	≥18	-	15-17	≤14	≤1	-	2	≥4	
O	Lomefloxacin		10 µg	≥22	-	19-21	≤18	≤2	-	4	≥8	
O	Norfloxacin		10 µg	≥17	-	13-16	≤12	≤4	-	8	≥16	See comment (33).
O	Ofloxacin		5 µg	≥18	-	15-17	≤14	≤1	-	2	≥4	
O	Sparfloxacin		5 µg	≥19	-	16-18	≤15	≤0.5	-	1	≥2	
Inv.	Fleroxacin		5 µg	≥19	-	16-18	≤15	≤2	-	4	≥8	

Table 2C. *Staphylococcus* spp. (Continued)

Test/ Report Group	Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
				S	SDD	I	R	S	SDD	I	R	
NITROFURANS												
U	Nitrofurantoin	All staphylococci	300 µg	≥17	-	15-16	≤14	≤32	-	64	≥128	
LINCOSAMIDES												
A	Clindamycin	All staphylococci	2 µg	≥21	-	15-20	≤14	≤0.5	-	1-2	≥4	**(34)** For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for ICR by disk diffusion using the D-zone test or by broth microdilution is required before reporting clindamycin (see Table 3I, Subchapter 3.9 in M02,[1] and Subchapter 3.12 in M07[4]). See comment **(30)**.
FOLATE PATHWAY ANTAGONISTS												
A	Trimethoprim-sulfamethoxazole	All staphylococci	1.25/23.75 µg	≥16	-	11-15	≤10	≤2/38	-	-	≥4/76	
U	Sulfonamides	All staphylococci	250 or 300 µg	≥17	-	13-16	≤12	≤256	-	-	≥512	**(35)** Sulfisoxazole can be used to represent any of the currently available sulfonamide preparations.
U	Trimethoprim	All staphylococci	5 µg	≥16	-	11-15	≤10	≤8	-	-	≥16	
PHENICOLS												
C	Chloramphenicol	All staphylococci	30 µg	≥18	-	13-17	≤12	≤8	-	16	≥32	See comment **(30)**.
ANSAMYCINS												
B	Rifampin	All staphylococci	5 µg	≥20	-	17-19	≤16	≤1	-	2	≥4	**(36)** ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.
STREPTOGRAMINS												
O	Quinupristin-dalfopristin	*S. aureus*	15 µg	≥19	-	16-18	≤15	≤1	-	2	≥4	**(37)** For reporting against methicillin (oxacillin)-susceptible *S. aureus*.

Table 2C. *Staphylococcus* spp. (Continued)

Test/ Report Group	Antimicrobial Agent	*Staphylococcus* spp. Indications	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
				S	SDD	I	R	S	SDD	I	R	
OXAZOLIDINONES												
(38) *S. aureus* that test susceptible to linezolid by MIC are also considered susceptible to tedizolid. However, some organisms that test resistant to linezolid may be susceptible to tedizolid.												
B	Linezolid	All staphylococci	30 µg	≥21	-	-	≤20	≤4	-	-	≥8	**(39)** When testing linezolid, disk diffusion zones should be examined using transmitted light. Organisms with resistant results by disk diffusion should be confirmed using an MIC method.
B	Tedizolid	*S. aureus*, including MRSA	-	-	-	-	-	≤0.5	-	1	≥2	**(40) Breakpoints are based on a dosage regimen of 200 mg administered every 24 h.**
PLEUROMUTILINS												
B	Lefamulin	*S. aureus*, **including MRSA**	20 µg	≥23	-	-	-	≤0.25	-	-	-	**(41)** The breakpoints for susceptible are based on a dosage regimen of 150 mg IV or 600 mg orally administered every 12 h. **(42)** Not routinely reported on organisms isolated from the urinary tract.

Abbreviations: ATCC®, American Type Culture Collection; BMHA, blood Mueller-Hinton agar; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; ICR, inducible clindamycin resistance; IV, intravenous; MALDI-TOF MS; matrix-assisted laser-desorption/ionization time-of-flight mass spectrometry; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant staphylococci; MRSA, methicillin (oxacillin)-resistant *S. aureus;* PBP2a, penicillin-binding protein 2a; PCR, polymerase chain reaction; QC, quality control; R, resistant; S, susceptible; SDD, susceptible-dose dependent; UTI, urinary tract infection.

Footnote

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

Table 2C. *Staphylococcus* spp. (Continued)

References for Table 2C

1. CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.
2. CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.
3. Becker K, Schaumburg F, Kearns A, et al. Implications of Identifying the recently defined members of the *Staphylococcus aureus* complex S. *argenteus* and S. *schweitzeri*: a position paper of members of the ESCMID Study Group for Staphylococci and Staphylococcal Diseases (ESGS). *Clin Microbiol Infect*. 2019;25(9):1064-1070.
4. CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.
5. Humphries RM, Magnano P, Burnham CA, et al. Evaluation of surrogate tests for the presence of *mecA*-mediated methicillin resistance in *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Staphylococcus capitis* and *Staphylococcus warneri*. *J. Clin Microbiol*. 2020;59(1):e02290-20.
6. García-Álvarez L, Holden MT, Lindsay H, et al. Methicillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study. *Lancet Infect Dis*. 2011;11(8):595-603.

Table 2D. Zone Diameter and MIC Breakpoints for *Enterococcus* spp.

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

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

Disk diffusion:
S. aureus ATCC® 25923

Dilution methods:
E. faecalis ATCC® 29212

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 3H and 3K for additional testing recommendations, reporting suggestions, and QC.

General Comments

(1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and 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,[1] 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*[2]). Hold the Petri plate a few inches above a black background illuminated with reflected light, except for vancomycin, which should be read with transmitted light (plate held up to light source). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. Any discernible growth within the zone of inhibition indicates vancomycin resistance.

(2) For enterococci when testing chloramphenicol, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored (see M07,[3] Figures 3 and 4).

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

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

(5) An intermediate (I) with a ^ in Tables 2 indicates agents that have the potential to concentrate in the urine. The I^ is for informational use only. The decision to report I^ is best made by each laboratory based on institution-specific guidelines and in consultation with appropriate medical personnel.

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

Table 2D. *Enterococcus* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	I	R	S	SDD	I	R	
PENICILLINS										
A	Penicillin	10 units	≥15	-	≤14	≤8	-	-	≥16	**(6)** The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. Ampicillin results may be used to predict susceptibility to amoxicillin-clavulanate, ampicillin-sulbactam, and piperacillin-tazobactam among non-ß-lactamase-producing enterococci. Ampicillin susceptibility can be used to predict imipenem susceptibility, providing the species is confirmed to be *E. faecalis*. **(7)** Enterococci susceptible to penicillin are predictably susceptible to ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, and piperacillin-tazobactam for non-ß-lactamase-producing enterococci. However, enterococci susceptible to ampicillin cannot be assumed to be susceptible to penicillin. If penicillin results are needed, testing of penicillin is required. **(8)** *Rx:* Combination therapy with **high-dosage parenteral** ampicillin, **amoxicillin,** penicillin, or vancomycin (for susceptible strains only), plus an aminoglycoside, is usually indicated for serious enterococcal infections, such as endocarditis, unless high-level resistance to both gentamicin and streptomycin is documented; such combinations are predicted to result in synergistic killing of enterococci. **(9) Breakpoints are based on an ampicillin dosage regimen of 2 g parenterally administered every 4-6 h or an amoxicillin dosage regimen of 1-2 g parenterally administered every 6 h.** **(10) Breakpoints when oral ampicillin is used for therapy of uncomplicated UTIs only are based on an ampicillin dosage regimen of 500 mg orally administered every 6 h or amoxicillin dosage regimen of 250 mg orally administered every 8 h or 500 mg every 12 h.**
A	Ampicillin	10 µg	≥17	-	≤16	≤8	-	-	≥16	

Table 2D
Enterococcus spp.
M02 and M07

Table 2D. *Enterococcus* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	I	R	S	SDD	I	R	
PENICILLINS (Continued)										
A	Penicillin	10 units	≥15	-	≤14	≤8	-	-	≥16	**(11)** Penicillin or ampicillin resistance among enterococci due to β-lactamase production has been reported very rarely. Penicillin or ampicillin resistance due to β-lactamase production is not reliably detected with routine disk or dilution methods but is detected using a direct, nitrocefin-based β-lactamase test. Because of the rarity of β-lactamase–positive enterococci, this test does not need to be performed routinely but can be used in selected cases. A positive β-lactamase test predicts resistance to penicillin as well as amino- and ureidopenicillins (see Glossary I).
A	Ampicillin	10 µg	≥17	-	≤16	≤8	-	-	≥16	
GLYCOPEPTIDES										
B	Vancomycin	30 µg	≥17	15-16	≤14	≤4	-	8-16	≥32	**(12)** When testing vancomycin against enterococci, plates should be held a full 24 hours for accurate detection of resistance. Zones should be examined using transmitted light; the presence of a haze or any growth within the zone of inhibition indicates resistance. Organisms with intermediate zones should be tested by an MIC method as described in M07.[3] For isolates for which the vancomycin MICs are 8–16 µg/mL, perform biochemical tests for identification as listed under the "Vancomycin MIC ≥ 8 µg/mL" test found in Table 3H. See general comment (4) and comment (8).

Table 2D. *Enterococcus* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	I	R	S	SDD	I	R	
LIPOGLYCOPEPTIDES										
C	Dalbavancin	-	-	-	-	≤0.25	-	-	-	**(13)** For reporting against vancomycin-susceptible *E. faecalis*. **(14) Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes.**
C	Oritavancin	-	-	-	-	≤0.12	-	-	-	**(15) Breakpoints are based on a dosage regimen of 1200 mg administered IV once.** See comment (13).
C	Telavancin	-	-	-	-	≤0.25	-	-	-	**(16) Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h.** See comment (13).
Inv.	Teicoplanin	30 µg	≥14	11-13	≤10	≤8	-	16	≥32	
LIPOPEPTIDES										
B	Daptomycin *E. faecium* only	-	-	-	-	-	≤4	-	≥8	**(17)** Daptomycin should not be reported for isolates from the respiratory tract. **(18)** The breakpoint for SDD is based on a dosage regimen of 8-12 mg/kg administered every 24 h and is intended for serious infections due to *E. faecium*. Consultation with an infectious diseases specialist is recommended.
B	Daptomycin *Enterococcus* spp. other than *E. faecium*	-	-	-	-	≤2	-	4	≥8	**(19)** The breakpoint for susceptible is based on a dosage regimen of 6 mg/kg administered every 24 h. See comment (17).

Table 2D. *Enterococcus* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	I	R	S	SDD	I	R	
MACROLIDES										
O	Erythromycin	15 µg	≥23	14-22	≤13	≤0.5	-	1-4	≥8	**(20)** Not routinely reported on isolates from the urinary tract.
TETRACYCLINES										
(21) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.										
U	Tetracycline	30 µg	≥19	15-18	≤14	≤4	-	8	≥16	
O	Doxycycline	30 µg	≥16	13-15	≤12	≤4	-	8	≥16	
O	Minocycline	30 µg	≥19	15-18	≤14	≤4	-	8	≥16	
FLUOROQUINOLONES										
U	Ciprofloxacin	5 µg	≥21	16-20^	≤15	≤1	-	2^	≥4	
U	Levofloxacin	5 µg	≥17	14-16^	≤13	≤2		4^	≥8	
O	Gatifloxacin	5 µg	≥18	15-17^	≤14	≤2	-	4^	≥8	
O	Norfloxacin	10 µg	≥17	13-16	≤12	≤4	-	8	≥16	**(22)** For testing and reporting of urinary tract isolates only.
NITROFURANS										
U	Nitrofurantoin	300 µg	≥17	15-16	≤14	≤32	-	64	≥128	
ANSAMYCINS										
O	Rifampin	5 µg	≥20	17-19	≤16	≤1	-	2	≥4	**(23)** ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.

Table 2D. *Enterococcus* spp. (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	I	R	S	SDD	I	R	
FOSFOMYCINS										
U	Fosfomycin	200 µg	≥16	13-15	≤12	≤64	-	128	≥256	**(24)** For testing and reporting of *E. faecalis* urinary tract isolates only. **(25)** The approved MIC testing method is agar dilution. Agar media should be supplemented with 25 µg/mL of glucose-6-phosphate. Broth dilution testing should not be performed. **(26)** The 200-µg fosfomycin disk contains 50 µg glucose-6-phosphate.
PHENICOLS										
O	Chloramphenicol	30 µg	≥18	13-17	≤12	≤8	-	16	≥32	See comment (20).
STREPTOGRAMINS										
O	Quinupristin-dalfopristin	15 µg	≥19	16-18	≤15	≤1	-	2	≥4	**(27)** For reporting against vancomycin-resistant *Enterococcus faecium*.
OXAZOLIDINONES										
(28) *E. faecalis* that test susceptible to linezolid by MIC are also considered susceptible to tedizolid. However, some organisms that are intermediate or resistant to linezolid may be susceptible to tedizolid.										
B	Linezolid	30 µg	≥23	21-22	≤20	≤2	-	4	≥8	
B	Tedizolid	-	-	-	-	≤0.5	-	-	-	**(29)** For reporting against *E. faecalis* only. **(30) Breakpoints are based on a dosage regimen of 200 mg administered every 24 h.**

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; I, intermediate; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible; SDD, susceptible-dose dependent**; UTI, urinary tract infection**. Symbol: ^, designation for agents that have the potential to concentrate in the urine.

Footnote

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

References for Table 2D

1 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

2 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 2E. Zone Diameter and MIC Breakpoints for *Haemophilus influenzae* and *Haemophilus parainfluenzae*

Testing Conditions	
Medium:	Disk diffusion: HTM Broth dilution: HTM broth
Inoculum:	Colony suspension, equivalent to a 0.5 McFarland standard prepared using colonies from an overnight (preferably 20- to 24-hour) chocolate agar plate (see general comment [2])
Incubation:	35°C ± 2°C Disk diffusion: 5% CO_2; 16–18 hours Broth dilution: ambient air; 20–24 hours

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

H. influenzae ATCC®[a] 49247
H. influenzae ATCC® 49766

Use either *H. influenzae* ATCC® 49247 or *H. influenzae* ATCC® 49766 or both of these strains, based on the antimicrobial agents to be tested. Neither strain has QC ranges for all agents that might be tested against *H. influenzae* or *H. parainfluenzae*.

E. coli ATCC® 35218 (when testing amoxicillin-clavulanate)

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

General Comments

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

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

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

(4) For isolates of *H. influenzae* from CSF, only results of testing with ampicillin, any of the 3rd-generation cephalosporins listed below, chloramphenicol, and meropenem are appropriate to report.

(5) Amoxicillin-clavulanate, azithromycin, cefaclor, cefdinir, cefixime, cefpodoxime, cefprozil, cefuroxime, and clarithromycin are used as empiric therapy for respiratory tract infections due to *Haemophilus* spp. The results of susceptibility tests with these antimicrobial agents are often not necessary for management of individual patients.

Table 2E. *Haemophilus influenzae* and *Haemophilus parainfluenzae* (Continued)

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

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

Table 2E. *Haemophilus influenzae* and *Haemophilus parainfluenzae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
A	Ampicillin	10 µg	≥22	19-21	≤18	≤1	2	≥4	See general comment (4). **(7) Breakpoints when ampicillin is used for therapy of meningitis are based on a dosage regimen of 2 g IV administered every 4 h.** **(8)** The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. The majority of isolates of *H. influenzae* that are resistant to ampicillin and amoxicillin produce a TEM-type β-lactamase. In most cases, a direct β-lactamase test can provide a rapid means of detecting resistance to ampicillin and amoxicillin. **(9)** Rare BLNAR strains of *H. influenzae* should be considered resistant to amoxicillin-clavulanate, ampicillin-sulbactam, cefaclor, cefamandole, cefetamet, cefonicid, cefprozil, cefuroxime, loracarbef, and piperacillin-tazobactam, despite apparent *in vitro* susceptibility of some BLNAR strains to these agents.

Table 2E. *Haemophilus influenzae* and *Haemophilus parainfluenzae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
β-LACTAM COMBINATION AGENTS									
(10) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test intermediate or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.									
B	Ampicillin-sulbactam	10/10 µg	≥20	-	≤19	≤2/1	-	≥4/2	See comment (9). **(11) Breakpoints are based on a dosage regimen of 3 g IV administered every 6 h.**
C	Amoxicillin-clavulanate	20/10 µg	-	-	-	**≤2/1**	**4/2**	≥8/4	**(12) Breakpoints are based on a dosage regimen of 875/125 mg orally administered every 12 h or 500/125 mg every 8 h. Additional disk correlate data are pending before disk diffusion breakpoints with this dosage regimen can be established.** See general comment (5) and comment (9).
C	Ceftolozane-tazobactam	-	-	-	-	≤ 0.5/4	-	-	**(13) Breakpoints are based on a dosage regimen of 3 g IV administered every 8 h.** (14) For testing and reporting of *H. influenzae* only.
O	Piperacillin-tazobactam	100/10 µg	≥21	-	-	≤1/4	-	≥2/4	See comment (9).
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
B B B	Cefotaxime or ceftazidime or ceftriaxone	30 µg 30 µg 30 µg	≥26 ≥26 ≥26	- - -	- - -	≤2 ≤2 ≤2	- - -	- - -	See general comment (4).
C	Cefuroxime	30 µg	≥20	17-19	≤16	≤4	8	≥16	See general comment (5) and comment (9).
C	Ceftaroline	30 µg	≥30	-	-	≤0.5	-	-	**(15)** See comment (14). **(16)** Breakpoints are based on a dosage regimen of 600 mg administered every 12 h.
O	Cefonicid	30 µg	≥20	17-19	≤16	≤4	8	≥16	See comment (9).

Table 2E. *Haemophilus influenzae* and *Haemophilus parainfluenzae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)									
O	Cefamandole	-	-	-	-	≤4	8	≥16	See comment (9).
O	Cefepime	30 µg	≥26	-	-	≤2	-	-	
O	Ceftizoxime	30 µg	≥26	-	-	≤2	-	-	See general comment (4).
CEPHEMS (ORAL)									
C	Cefaclor	30 µg	≥20	17-19	≤16	≤8	16	≥32	See general comment (5) and comment (9).
C	Cefprozil	30 µg	≥18	15-17	≤14	≤8	16	≥32	
C	Cefdinir or	5 µg	≥20	-	-	≤1	-	-	See general comment (5).
C	cefixime or	5 µg	≥21	-	-	≤1	-	-	
C	cefpodoxime	10 µg	≥21	-	-	≤2	-	-	
C	Cefuroxime	30 µg	≥20	17-19	≤16	≤4	8	≥16	See general comment (5) and comment (9).
O	Loracarbef	30 µg	≥19	16-18	≤15	≤8	16	≥32	See general comment (5) and comment (9).
O	Ceftibuten	30 µg	≥28	-	-	≤2	-	-	
Inv.	Cefetamet	10 µg	≥18	15-17	≤14	≤4	8	≥16	See comment (9).
MONOBACTAMS									
C	Aztreonam	30 µg	≥26	-	-	≤2	-	-	
CARBAPENEMS									
B	Meropenem	10 µg	≥20	-	-	≤0.5	-	-	See general comment (4).
C	Ertapenem or	10 µg	≥19	-	-	≤0.5	-	-	
C	imipenem	10 µg	≥16	-	-	≤4	-	-	
O	Doripenem	10 µg	≥16	-	-	≤1	-	-	
MACROLIDES									
C	Azithromycin	15 µg	≥12	-	-	≤4	-	-	See general comment (5).
C	Clarithromycin	15 µg	≥13	11-12	≤10	≤8	16	≥32	
TETRACYCLINES									
(17) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, resistance to doxycycline and minocycline cannot be inferred from tetracycline resistance.									
C	Tetracycline	30 µg	≥29	26-28	≤25	≤2	4	≥8	
FLUOROQUINOLONES									
B	Ciprofloxacin or	5 µg	≥21	-	-	≤1	-	-	
B	levofloxacin or	5 µg	≥17	-	-	≤2	-	-	
B	moxifloxacin	5 µg	≥18	-	-	≤1	-	-	
O	Gemifloxacin	5 µg	≥18	-	-	≤0.12	-	-	
O	Gatifloxacin	5 µg	≥18	-	-	≤1	-	-	
O	Grepafloxacin	5 µg	≥24	-	-	≤0.5	-	-	
O	Lomefloxacin	10 µg	≥22	-	-	≤2	-	-	
O	Ofloxacin	5 µg	≥16	-	-	≤2	-	-	
O	Sparfloxacin	-	-	-	-	≤0.25	-	-	

Table 2E. *Haemophilus influenzae* and *Haemophilus parainfluenzae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
FLUOROQUINOLONES (Continued)									
O	Trovafloxacin	10 µg	≥22	-	-	≤1	-	-	
Inv.	Fleroxacin	5 µg	≥19	-	-	≤2	-	-	
FOLATE PATHWAY ANTAGONISTS									
C	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥16	11-15	≤10	≤0.5/9.5	1/19-2/38	≥4/76	
PHENICOLS									
C	Chloramphenicol	30 µg	≥29	26-28	≤25	≤2	4	≥8	See general comment (4). **(18)** Not routinely reported on organisms isolated from the urinary tract.
ANSAMYCINS									
C	Rifampin	5 µg	≥20	17-19	≤16	≤1	2	≥4	**(19)** May be appropriate only for prophylaxis of case contacts. These breakpoints do not apply to therapy of patients with invasive *H. influenzae* disease.
PLEUROMUTILINS									
C	Lefamulin	20 µg	**≥18**	-	-	≤2	-	-	**(20)** The breakpoints for susceptible are based on a dosage regimen of 150 mg IV or 600 mg orally administered every 12 h. See comments (14) and (18).

Abbreviations: ATCC®, American Type Culture Collection; BLNAR, β-lactamase negative, ampicillin-resistant; CFU, colony-forming unit(s); CSF, cerebrospinal fluid; HTM, *Haemophilus* test medium; I, intermediate; IV, intravenous; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; NAD, β-nicotinamide adenine dinucleotide; QC, quality control; R, resistant; S, susceptible.

Footnote

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

Reference for Table 2E

1 CLSI. *Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria*. 3rd ed. CLSI guideline M45. Clinical and Laboratory Standards Institute; 2016.

Table 2F. Zone Diameter and MIC Breakpoints for *Neisseria gonorrhoeae*

Testing Conditions	
Medium:	Disk diffusion: GC agar base and 1% defined growth supplement. (The use of a cysteine-free growth supplement is not required for disk diffusion testing.) Agar dilution: GC agar base and 1% defined growth supplement. (The use of a cysteine-free growth supplement is required for agar dilution tests with carbapenems and clavulanate. Cysteine-containing defined growth supplement does not significantly alter dilution test results with other drugs.)
Inoculum:	Colony suspension, equivalent to a 0.5 McFarland standard prepared in MHB or 0.9% phosphate-buffered saline, pH 7, using colonies from an overnight (20- to 24-hour) chocolate agar plate incubated in 5% CO_2
Incubation:	36°C ± 1°C (do not exceed 37°C); 5% CO_2; all methods, 20-24 hours

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

N. gonorrhoeae ATCC® 49226

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

General Comments

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

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

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

(4) The recommended medium for testing *N. gonorrhoeae* consists of GC agar to which a 1% defined growth supplement (1.1 g L-cystine, 0.03 g guanine HCl, 0.003 g thiamine HCl, 0.013 g para-aminobenzoic acid, 0.01 g B12, 0.1 g cocarboxylase, 0.25 g NAD, 1 g adenine, 10 g L-glutamine, 100 g glucose, 0.02 g ferric nitrate, 25.9 g L-cysteine HCl [in 1 L H_2O]) is added after autoclaving.

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

Table 2F. *Neisseria gonorrhoeae* (Continued)

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

Table 2F. *Neisseria gonorrhoeae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
MACROLIDES									
A	Azithromycin	15 µg	≥ 30	-	-	≤ 1	-	-	**(8)** This breakpoint presumes that azithromycin (1 g single dose) is used in an approved regimen that includes an additional antimicrobial agent (ie, ceftriaxone 250 mg IM single dose).
TETRACYCLINES									
(9) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.									
A	Tetracycline	30 µg	≥38	31-37	≤30	≤0.25	0.5-1	≥2	**(10) Isolates with disk zone diameters ≤ 19 mm usually indicate plasmid-mediated tetracycline resistance.** Resistance in these strains should be confirmed by a dilution test (MIC ≥ 16 µg/mL).
FLUOROQUINOLONES									
See general comment (3).									
A	Ciprofloxacin	5 µg	≥41	28-40	≤27	≤ 0.06	0.12-0.5	≥1	
AMINOCYCLITOLS									
O	Spectinomycin	100 µg	≥18	15-17	≤14	≤ 32	64	≥128	See general comment (2).

Abbreviations: ATCC®, American Type Culture Collection; I, intermediate; IM, intramuscular; MHB, Mueller-Hinton broth; MIC, minimal inhibitory concentration; NAD, ß-nicotinamide adenine dinucleotide; pH, negative logarithm of hydrogen ion concentration; QC, quality control; R, resistant; S, susceptible.

Footnote

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

Table 2G. Zone Diameter and MIC Breakpoints for *Streptococcus pneumoniae*

Testing Conditions

Medium: Disk diffusion: MHA with 5% sheep blood or MH-F agar (MHA with 5% defibrinated horse blood and 20 µg/mL NAD)
Broth dilution: CAMHB with LHB (2.5% to 5% v/v) (see M07[1] for instructions for preparation of LHB)
Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.

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

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

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

S. pneumoniae ATCC® 49619

Disk diffusion: deterioration of oxacillin disk content is best assessed with *S. aureus* ATCC® 25923, with an acceptable range of 18-24 mm on unsupplemented MHA.

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

General Comments

(1) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk (see the *M02 Disk Diffusion Reading Guide*[2]). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Do not measure the zone of inhibition of hemolysis. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth. With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, disregard slight growth (20% or less of the lawn of growth) and measure the more obvious margin to determine the zone diameter.

(2) For pneumococci when testing chloramphenicol, clindamycin, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored (see M07,[1] Figures 3 and 4). With trimethoprim and the sulfonamides, antagonists in the medium may allow some slight growth; therefore, read the end point at the concentration in which there is ≥ 80% reduction in growth compared with the control (see M07,[1] Figure 5).

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

(4) For *S. pneumoniae* isolated from CSF, penicillin and cefotaxime, ceftriaxone, or meropenem should be tested by a reliable MIC method (such as that described in M07[1]) and reported routinely. Such isolates can also be tested against vancomycin using the MIC or disk diffusion method.

(5) For disk diffusion, results using MHA with 5% sheep blood and MH-F agar were equivalent when disk contents, testing conditions, and zone diameter breakpoints in Table 2G were used. Disk diffusion QC ranges for *S. pneumoniae* ATCC® 49619 in Table 4B apply to testing using either MHA with 5% sheep blood or MH-F agar.

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
(6) For nonmeningitis isolates, a penicillin MIC of ≤ 0.06 µg/mL (or oxacillin zone ≥ 20 mm) can predict susceptibility to the following β-lactams: ampicillin (oral or parenteral), ampicillin-sulbactam, amoxicillin, amoxicillin-clavulanate, cefaclor, cefdinir, cefditoren, cefepime, cefotaxime, cefpodoxime, cefprozil, ceftaroline, ceftizoxime, ceftriaxone, cefuroxime, doripenem, ertapenem, imipenem, loracarbef, meropenem. See general comment (4).									
A	Penicillin	1 µg oxacillin	≥ 20	-	-	-	-	-	**(7)** Isolates of pneumococci with oxacillin zone sizes ≥ 20 mm are susceptible (MIC ≤ 0.06 µg/mL) to penicillin. Penicillin and cefotaxime, ceftriaxone, or meropenem MICs should be determined for isolates with oxacillin zone diameters ≤ 19 mm, because zones ≤ 19 mm occur with penicillin-resistant, -intermediate, or certain -susceptible strains. For isolates with oxacillin zones ≤ 19 mm, do not report penicillin as resistant without performing a penicillin MIC test.
A	Penicillin parenteral (nonmeningitis)	-	-	-	-	≤ 2	4	≥ 8	**(8)** ***Rx:*** Doses of intravenous penicillin of at least 2 million units every 4 hours in adults with normal renal function (12 million units per day) can be used to treat nonmeningeal pneumococcal infections due to strains with penicillin MICs ≤ 2 µg/mL. Strains with an intermediate MIC of 4 µg/mL may necessitate penicillin doses of 18-24 million units per day. **(9)** For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.
A	Penicillin parenteral (meningitis)	-	-	-	-	≤ 0.06	-	≥ 0.12	**(10)** ***Rx:*** Use of penicillin in meningitis requires therapy with maximum doses of intravenous penicillin (eg, at least 3 million units every 4 hours in adults with normal renal function). **(11)** For CSF isolates, report only meningitis interpretations. See general comment (4).

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS (Continued)									
A	Penicillin (oral penicillin V)	-	-	-	-	≤0.06	0.12-1	≥2	**(12)** Interpretations for oral penicillin may be reported for isolates other than those from CSF.
C	Amoxicillin (nonmeningitis)	-	-	-	-	≤2	4	≥8	**(13) Breakpoints for amoxicillin (alone or with clavulanate) are based on an oral amoxicillin dosage regimen of 500 mg administered every 8 h or 875 mg administered every 12 h.**
C	Amoxicillin-clavulanate (nonmeningitis)					≤2/1	4/2	≥8/4	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
See comment (6).									
O	Cefepime (meningitis)	-	-	-	-	≤0.5	1	≥2	**(14)** In the United States, for CSF isolates, report only nonmeningitis interpretations. There is not an FDA-approved indication for the use of cefepime for meningitis in the United States.
B	Cefepime (nonmeningitis)	-	-	-	-	≤1	2	≥4	**(15)** In the United States, report only interpretations for nonmeningitis and include the nonmeningitis notation on the report.
B	Cefotaxime (meningitis)	-	-	-	-	≤0.5	1	≥2	**(16)** For CSF isolates, report only meningitis interpretations. **(17)** ***Rx:*** Use of cefotaxime or ceftriaxone in meningitis requires therapy with maximum doses. See general comment (4).
B	Ceftriaxone (meningitis)	-	-	-	-	≤0.5	1	≥2	

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.) (Continued)									
B	Cefotaxime	-	-	-	-	≤1	2	≥4	**(18)** For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.
B	(nonmeningitis)	-	-	-	-	≤1	2	≥4	
	Ceftriaxone (nonmeningitis)								
C	Ceftaroline (nonmeningitis)	30 µg	≥26	-	-	≤0.5	-	-	**(19)** Breakpoints are based on a dosage regimen of 600 mg administered every 12 h.
C	Cefuroxime (parenteral)	-	-	-	-	≤0.5	1	≥2	
CEPHEMS (ORAL)									
See comment (6).									
C	Cefuroxime (oral)	-	-	-	-	≤1	2	≥4	**(20)** Interpretations for oral cefuroxime may be reported for isolates other than those from CSF.
O	Cefaclor	-	-	-	-	≤1	2	≥4	
O	Cefdinir	-	-	-	-	≤0.5	1	≥2	
O	Cefpodoxime	-	-	-	-	≤0.5	1	≥2	
O	Cefprozil	-	-	-	-	≤2	4	≥8	
O	Loracarbef	-	-	-	-	≤2	4	≥8	
CARBAPENEMS									
See comment (6).									
B	Meropenem	-	-	-	-	≤0.25	0.5	≥1	See general comment (4) and comment (7).
C	Ertapenem	-	-	-	-	≤1	2	≥4	
C	Imipenem	-	-	-	-	≤0.12	0.25-0.5	≥1	
O	Doripenem	-	-	-	-	≤1	-	-	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	-	-	≤1	-	-	See general comment (4).
MACROLIDES									
(21) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. **(22)** Not routinely reported for organisms isolated from the urinary tract.									
A	Erythromycin	15 µg	≥21	16-20	≤15	≤0.25	0.5	≥1	
O	Azithromycin	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
O	Clarithromycin	15 µg	≥21	17-20	≤16	≤0.25	0.5	≥1	
O	Dirithromycin	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
TETRACYCLINES									
(23) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline. However, resistance to doxycycline cannot be inferred from tetracycline resistance.									
B	Tetracycline	30 µg	≥28	25-27	≤24	≤1	2	≥4	
B	Doxycycline	30 µg	≥28	25-27	≤24	≤0.25	0.5	≥1	

Table 2G. *Streptococcus pneumoniae* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
FLUOROQUINOLONES									
B	Gemifloxacin	5 µg	≥23	20-22	≤19	≤0.12	0.25	≥0.5	**(24)** *S. pneumoniae* isolates susceptible to levofloxacin are predictably susceptible to gemifloxacin and moxifloxacin. However, *S. pneumoniae* susceptible to gemifloxacin or moxifloxacin cannot be assumed to be susceptible to levofloxacin.
B	Levofloxacin	5 µg	≥17	14-16	≤13	≤2	4	≥8	
B	Moxifloxacin	5 µg	≥18	15-17	≤14	≤1	2	≥4	
O	Gatifloxacin	5 µg	≥21	18-20	≤17	≤1	2	≥4	
O	Ofloxacin	5 µg	≥16	13-15	≤12	≤2	4	≥8	
O	Sparfloxacin	5 µg	≥19	16-18	≤15	≤0.5	1	≥2	
FOLATE PATHWAY ANTAGONISTS									
A	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥19	16-18	≤15	≤0.5/9.5	1/19-2/38	≥4/76	
PHENICOLS									
C	Chloramphenicol	30 µg	≥21	-	≤20	≤4	-	≥8	See comment (22).
ANSAMYCINS									
C	Rifampin	5 µg	≥19	17-18	≤16	≤1	2	≥4	**(25)** ***Rx:*** Rifampin should not be used alone for antimicrobial therapy.
LINCOSAMIDES									
B	Clindamycin	2 µg	≥19	16-18	≤15	≤0.25	0.5	≥1	**(26)** For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for ICR by disk diffusion using the D-zone test or by broth microdilution is required before reporting clindamycin (see Table 3I, Subchapter 3.9 in M02,[3] and Subchapter 3.12 in M07[1]). See comment (22).
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16-18	≤15	≤1	2	≥4	
OXAZOLIDINONES									
C	Linezolid	30 µg	≥21	-	-	≤2	-	-	
PLEUROMUTILINS									
B	Lefamulin	20 µg	**≥19**	-		≤0.5	-	-	**(27)** The susceptible breakpoints are based on a dosage regimen of 150 mg IV or 600 mg orally administered every 12 h. **(28)** Not routinely reported on organisms isolated from the urinary tract.

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CSF, cerebrospinal fluid; FDA, US Food and Drug Administration; I, intermediate; ICR, inducible clindamycin resistance; IV, intravenous; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MH-F agar, Mueller-Hinton fastidious agar; MIC, minimal inhibitory concentration; NAD, ß-nicotinamide adenine dinucleotide; QC, quality control; R, resistant; S, susceptible.

Table 2G. *Streptococcus pneumoniae* (Continued)

Footnote

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

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

References for Table 2G

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

2 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

Table 2H-1. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. ß-Hemolytic Group

Testing Conditions	
Medium:	Disk diffusion: MHA with 5% sheep blood Broth dilution: CAMHB with LHB (2.5% to 5% v/v); the CAMHB should be supplemented to 50 µg/mL calcium for daptomycin (see M07[1] for instructions for preparation of LHB) Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.
Inoculum:	Colony suspension, equivalent to a 0.5 McFarland standard, using colonies from an overnight (18- to 20-hour) sheep blood agar plate
Incubation:	35°C ± 2°C Disk diffusion: 5% CO_2; 20-24 hours Dilution methods: ambient air; 20-24 hours (CO_2 if necessary, for growth with agar dilution)

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

S. pneumoniae ATCC®a 49619

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 Table 3I for additional testing recommendations, reporting suggestions, and QC.

General Comments

(1) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk (see the *M02 Disk Diffusion Reading Guide*[2]). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Do not measure the zone of inhibition of hemolysis. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth.

(2) For ß-hemolytic streptococci when testing chloramphenicol, clindamycin, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored (see M07,[1] Figures 3 and 4).

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

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

Table 2H-1. *Streptococcus* spp. ß-Hemolytic Group (Continued)

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

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

Table 2H-1. *Streptococcus* spp. ß-Hemolytic Group (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
(6) An organism that is susceptible to penicillin can be considered susceptible to antimicrobial agents listed here when used for approved indications and does not need to be tested against those agents. For groups A, B, C, and G ß-hemolytic streptococci, penicillin is tested as a surrogate for ampicillin, amoxicillin, amoxicillin-clavulanate, ampicillin-sulbactam, cefazolin, cefepime, ceftaroline, cephradine, cephalothin, cefotaxime, ceftriaxone, ceftizoxime, imipenem, ertapenem, and meropenem. For group A ß-hemolytic streptococci, penicillin is also a surrogate for cefaclor, cefdinir, cefprozil, ceftibuten, cefuroxime, and cefpodoxime.									
A	Penicillin or	10 units	≥24	-	-	≤0.12	-	-	See general comment (4).
A	ampicillin	10 µg	≥24	-	-	≤0.25	-	-	
CEPHEMS (PARENTERAL) (including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
See comment (6).									
B	Cefepime or	30 µg	≥24	-	-	≤0.5	-	-	
B	cefotaxime or	30 µg	≥24	-	-	≤0.5	-	-	
B	ceftriaxone	30 µg	≥24	-	-	≤0.5	-	-	
C	Ceftaroline	30 µg	≥26	-	-	≤0.5	-	-	**(7)** Breakpoints are based on a dosage regimen of 600 mg administered every 12 h.
CARBAPENEMS									
See comment (6).									
O	Doripenem	-	-	-	-	≤0.12	-	-	
O	Ertapenem	-	-	-	-	≤1	-	-	
O	Meropenem	-	-	-	-	≤0.5	-	-	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	-	-	≤1	-	-	
LIPOGLYCOPEPTIDES									
C	Dalbavancin	-	-	-	-	≤0.25	-	-	**(8)** For reporting against *S. pyogenes*, *S. agalactiae*, and *S. dysgalactiae*. **(9) Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes.**
C	Oritavancin	-	-	-	-	≤0.25	-	-	**(10) Breakpoints are based on a dosage regimen of 1200 mg IV administered once.**
C	Telavancin	-	-	-	-	≤0.12	-	-	**(11) Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h.**
LIPOPEPTIDES									
C	Daptomycin	-	-	-	-	≤1	-	-	**(12)** Daptomycin should not be reported for isolates from the respiratory tract.

Table 2H-1. *Streptococcus* spp. β-Hemolytic Group (Continued)

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

Table 2H-1. *Streptococcus* spp. ß-Hemolytic Group (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
LINCOSAMIDES									
A	Clindamycin	2 µg	≥19	16-18	≤15	≤0.25	0.5	≥1	See comments (14) and (15). **(17)** For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for ICR by disk diffusion using the D-zone test or by broth microdilution is required before reporting clindamycin. See Table **3I**, Subchapter 3.9 in M02,[3] and Subchapter 3.12 in M07.[1]
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16-18	≤15	≤1	2	≥4	**(18)** For reporting against *S. pyogenes* only.
OXAZOLIDINONES									
(19) *S. agalactiae* and *S. pyogenes* that test susceptible to linezolid by MIC are also considered susceptible to tedizolid. However, some organisms that are nonsusceptible to linezolid may be susceptible to tedizolid.									
C	Linezolid	30 µg	≥21	-	-	≤2	-	-	
C	Tedizolid	-	-	-	-	≤0.5	-	-	**(20)** For reporting against *S. pyogenes* and *S. agalactiae* only. **(21) Breakpoints are based on a dosage regimen of 200 mg administered every 24 h.**

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

Footnote

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

References for Table 2H-1

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

2 CLSI. *M02 Disk Diffusion Reading Guide*. 1st ed. CLSI quick guide M02QG. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

Table 2H-2. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. Viridans Group

Testing Conditions	
Medium:	Disk diffusion: MHA with 5% sheep blood Broth dilution: CAMHB with LHB (2.5% to 5% v/v); the CAMHB should be supplemented to 50 µg/mL calcium for daptomycin (see M07[1] for instructions for preparation of LHB) Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.
Inoculum:	Colony suspension, equivalent to a 0.5 McFarland standard using colonies from an overnight (18- to 20-hour) sheep blood agar plate
Incubation:	35°C ± 2°C Disk diffusion: 5% CO_2; 20-24 hours Dilution methods: ambient air; 20-24 hours (CO_2 if necessary for growth with agar dilution)

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

S. pneumoniae ATCC® 49619

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

General Comments

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

(2) For viridans streptococci when testing chloramphenicol, clindamycin, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored (see M07,[1] Figures 3 and 4).

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

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

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

Table 2H-2. *Streptococcus* spp. Viridans Group (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
A	Penicillin	-	-	-	-	≤0.12	0.25-2	≥4	**(5)** Viridans streptococci isolated from normally sterile anatomical sites (eg, CSF, blood, bone) should be tested for penicillin susceptibility using an MIC method. **(6)** A penicillin MIC of ≤0.125 µg/mL is the same as a penicillin MIC of ≤0.12 µg/mL and both should be interpreted as susceptible. Laboratories should report an MIC of ≤0.125 µg/mL as ≤0.12 µg/mL. **(7)** *Rx:* Penicillin- or ampicillin-intermediate isolates may necessitate combined therapy with an aminoglycoside for bactericidal action.
A	Ampicillin	-	-	-	-	≤0.25	0.5-4	≥8	
β-LACTAM COMBINATION AGENTS									
C	Ceftolozane-tazobactam	-	-	-	-	≤8/4	16/4	≥32/4	**(8)** Breakpoints are based on a dosage regimen of 1.5 g administered every 8 h.
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
B	Cefepime	30 µg	≥24	22-23	≤21	≤1	2	≥4	
B	Cefotaxime	30 µg	≥28	26-27	≤25	≤1	2	≥4	
B	Ceftriaxone	30 µg	≥27	25-26	≤24	≤1	2	≥4	
CARBAPENEMS									
O	Doripenem	-	-	-	-	≤1	-	-	
O	Ertapenem	-	-	-	-	≤1	-	-	
O	Meropenem	-	-	-	-	≤0.5	-	-	
GLYCOPEPTIDES									
B	Vancomycin	30 µg	≥17	-	-	≤1	-	-	
LIPOGLYCOPEPTIDES									
C	Dalbavancin	-	-	-	-	≤0.25	-	-	**(9) Breakpoints are based on a dosage regimen of 1500 mg (single dose) or 1000 mg (two doses) IV administered over 30 minutes followed one week later by 500 mg IV administered over 30 minutes.** **(10)** For reporting against *S. anginosus* group (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*) only.

Table 2H-2. *Streptococcus* spp. Viridans Group (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
LIPOGLYCOPEPTIDES (Continued)									
C	Oritavancin	-	-	-	-	≤0.25	-	-	**(11) Breakpoints are based on a dosage regimen of 1200 mg IV administered once.**
C	Telavancin	-	-	-	-	≤0.06	-	-	**(12) Breakpoints are based on a dosage regimen of 10 mg/kg administered every 24 h.**
LIPOPEPTIDES									
O	Daptomycin	-	-	-	-	≤1	-	-	(13) Daptomycin should not be reported for isolates from the respiratory tract.
MACROLIDES									
(14) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. (15) Not routinely reported on isolates from the urinary tract.									
C	Erythromycin	15 µg	≥21	16-20	≤15	≤0.25	0.5	≥1	
O	Azithromycin	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
O	Clarithromycin	15 µg	≥21	17-20	≤16	≤0.25	0.5	≥1	
O	Dirithromycin	15 µg	≥18	14-17	≤13	≤0.5	1	≥2	
TETRACYCLINES									
(16) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, resistance to doxycycline and minocycline cannot be inferred from tetracycline resistance.									
O	Tetracycline	30 µg	≥23	19-22	≤18	≤2	4	≥8	
FLUOROQUINOLONES									
O	Levofloxacin	5 µg	≥17	14-16	≤13	≤2	4	≥8	
O	Ofloxacin	5 µg	≥16	13-15	≤12	≤2	4	≥8	
O	Gatifloxacin	5 µg	≥21	18-20	≤17	≤1	2	≥4	
O	Grepafloxacin	5 µg	≥19	16-18	≤15	≤0.5	1	≥2	
O	Trovafloxacin	10 µg	≥19	16-18	≤15	≤1	2	≥4	
PHENICOLS									
C	Chloramphenicol	30 µg	≥21	18-20	≤17	≤4	8	≥16	See comment (15).

Table 2H-2. *Streptococcus* spp. Viridans Group (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
LINCOSAMIDES									
C	Clindamycin	2 µg	≥19	16-18	≤15	≤0.25	0.5	≥1	See comment (15).
STREPTOGRAMINS									
O	Quinupristin-dalfopristin	15 µg	≥19	16-18	≤15	≤1	2	≥4	
OXAZOLIDINONES									
(17) *S. anginosus* group that test susceptible to linezolid by MIC are also considered susceptible to tedizolid. However, some organisms that are nonsusceptible to linezolid may be susceptible to tedizolid.									
C	Linezolid	30 µg	≥21	-	-	≤2	-	-	
C	Tedizolid	-	-	-	-	≤0.25	-	-	**(18) Breakpoints are based on a dosage regimen of 200 mg administered every 24 h.** See comment (10).

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

Footnote

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

Reference for Table 2H-2

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 2I. Zone Diameter and MIC Breakpoints for *Neisseria meningitidis*

Testing Conditions

Medium: Disk diffusion: MHA with 5% sheep blood
Broth microdilution: CAMHB supplemented with LHB (2.5% to 5% v/v) (see M07[1] for preparation of LHB)
Agar dilution: MHA supplemented with sheep blood (5% v/v)

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

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

Routine QC Recommendations (See Tables 4A-1, 4B, 5A-1, and 5B for acceptable QC ranges.)

Streptococcus pneumoniae ATCC®[a] 49619:

Disk diffusion: incubate in 5% CO_2.

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

E. coli ATCC® 25922

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

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

General Comments

Important: For complete information on safety precautions, see *Biosafety in Microbiological and Biomedical Laboratories*. 6th ed. Washington, DC: US Department of Health and Human Services; 2020. http://www.cdc.gov/biosafety/publications/bmbl5/. Accessed 7 January 2022.

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

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

(3) Laboratorians who are exposed routinely to potential aerosols of *N. meningitidis* should consider vaccination according to the current recommendations of the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices. http://www.cdc.gov/vaccines/acip/index.html. Accessed 7 January 2022.

Table 2I. *Neisseria meningitidis* (Continued)

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

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

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

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

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
PENICILLINS									
C	Penicillin		-	-	-	≤0.06	0.12-0.25	≥0.5	**(7) Breakpoints for ampicillin are based on a dosage regimen of 2 g administered every 4 h.**
C	Ampicillin		-	-	-	≤0.12	0.25-1	≥2	
CEPHEMS									
C	Cefotaxime or	30 µg	≥34	-	-	≤0.12	-	-	
C	ceftriaxone	30 µg	≥34	-	-	≤0.12	-	-	
CARBAPENEMS									
C	Meropenem	10 µg	≥30	-	-	≤0.25	-	-	
MACROLIDES									
C	Azithromycin	15 µg	≥20	-	-	≤2	-	-	See general comment (6). **(8)** May be appropriate only for prophylaxis of meningococcal case contacts. These breakpoints do not apply to therapy of patients with invasive meningococcal disease.
TETRACYCLINES									
C	Minocycline	30 µg	≥26	-	-	≤2	-	-	See comment (8).
FLUOROQUINOLONES									
(9) For surveillance purposes, a nalidixic acid MIC ≥8 µg/mL or a zone ≤25 mm may correlate with diminished fluoroquinolone susceptibility.									
C	Ciprofloxacin	5 µg	≥35	33-34	≤32	≤0.03	0.06	≥0.12	See comment (8).
C	Levofloxacin	-	-	-	-	≤0.03	0.06	≥0.12	

Table 2I. *Neisseria meningitidis* (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
FOLATE PATHWAY ANTAGONISTS									
C	Sulfisoxazole	-	-	-	-	≤2	4	≥8	See comment (8).
C	Trimethoprim-sulfamethoxazole	1.25/23.75 µg	≥30	26-29	≤25	≤0.12/2.4	0.25/4.75	≥ 0.5/9.5	**(10)** Trimethoprim-sulfamethoxazole is the preferred disk for detection of sulfonamide resistance. Trimethoprim-sulfamethoxazole testing predicts susceptibility and resistance to trimethoprim-sulfamethoxazole and sulfonamides. Sulfonamides may be appropriate only for prophylaxis of meningococcal case contacts.
PHENICOLS									
C	Chloramphenicol	30 µg	≥26	20-25	≤19	≤2	4	≥8	**(11)** Not routinely reported on isolates from the urinary tract.
ANSAMYCINS									
C	Rifampin	5 µg	≥25	20-24	≤19	≤0.5	1	≥2	See comment (8).

Abbreviations: AST, antimicrobial susceptibility testing; ATCC®, American Type Culture Collection; BSC, biological safety cabinet; BSL-2, biosafety level 2; BSL-3, biosafety level 3; CAMHB, cation-adjusted Mueller-Hinton broth; CFU, colony-forming unit(s); I, intermediate; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Footnote

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

Reference for Table 2I

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 2J. MIC Breakpoints for Anaerobes

Testing Conditions

Medium: Agar dilution (for all anaerobes): Brucella agar supplemented with hemin (5 µg/mL), vitamin K_1 (1 µg/mL), and laked sheep blood (5% v/v)
Broth microdilution (for *Bacteroides* spp. and *Parabacteroides* spp. only): Brucella broth supplemented with hemin (5 µg/mL), vitamin K_1 (1 µg/mL), and LHB (5% v/v)

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

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

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

Test one or more of the following organisms. The choice and number of QC strains tested should be based on obtaining on-scale end points for the antimicrobial agent tested.

B. fragilis ATCC®a 25285
Bacteroides thetaiotaomicron ATCC® 29741
Clostridioides (formerly *Clostridium*) *difficile* ATCC® 700057
Eggerthella lenta (formerly *Eubacterium lentum*) ATCC® 43055

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

General Comments

(1) For isolates for which the antimicrobial agent MICs fall within the intermediate category, maximum dosages, along with proper ancillary therapy, should be used to achieve the best possible levels of drug in abscesses and/or poorly perfused tissues. If this approach is taken, organisms for which the antimicrobial agent MICs fall within the susceptible range are generally amenable to therapy. Organisms for which the antimicrobial agent MICs are in the intermediate range may respond, but in such cases, efficacy as measured by patient clinical response should be carefully monitored. Ancillary therapy, such as drainage procedures and debridement, are of great importance for proper management of anaerobic infections.

(2) Refer to Figures 3 and 4 in CLSI document M11[1] for examples of reading end points.

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

(4) Broth microdilution is recommended only for testing *Bacteroides* spp. and *Parabacteroides* spp. MIC values for agar or broth microdilution are considered equivalent for those species.

(5) Until additional studies are performed to validate broth microdilution for testing other organisms, it should be used only for testing members of *Bacteroides* spp. and *Parabacteroides* spp.

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

Table 2J. Anaerobes (Continued)

Test/Report Group	Antimicrobial Agent	Interpretive Categories and MIC Breakpoints, µg/mL S	I	R	Comments
PENICILLINS					
A/C	Ampicillin[b]	≤0.5	1	≥2	**(6)** Ampicillin and penicillin are recommended for primary testing and reporting for gram-positive organisms (group A) because most of them are ß-lactamase negative, but not for gram-negative organisms (group C) because many are ß-lactamase positive. **(7)** *Bacteroides* spp. are intrinsically resistant to penicillin and ampicillin. *Parabacteroides* spp. are presumed to be resistant to penicillin and ampicillin. Other gram-negative and gram-positive anaerobes may be screened for ß-lactamase activity with a chromogenic cephalosporin; if ß-lactamase positive, report as resistant to penicillin, ampicillin, and amoxicillin. Be aware that ß-lactamase-negative isolates may be resistant to ß-lactams by other mechanisms. Because higher blood levels are achievable with these antimicrobial agents, infection with non-ß-lactamase-producing organisms with higher MICs (2-4 µg/mL) with adequate dosage regimen might be treatable. **(8)** Results of ampicillin testing can be used to predict results for amoxicillin.
A/C	Penicillin[b]	≤0.5	1	≥2	
ß-LACTAM COMBINATION AGENTS					
(9) Organisms that test susceptible to the ß-lactam agent alone are also considered susceptible to the ß-lactam combination agent. However, organisms that test susceptible to the ß-lactam combination agent cannot be assumed to be susceptible to the ß-lactam agent alone. Similarly, organisms that test intermediate or resistant to the ß-lactam agent alone may be susceptible to the ß-lactam combination agent.					
A	Amoxicillin-clavulanate	≤4/2	8/4	≥16/8	
A	Ampicillin-sulbactam	≤8/4	16/8	≥32/16	
A	Piperacillin-tazobactam	≤16/4	32/4-64/4	≥128/4	
A	Imipenem-relebactam	≤4/4	8/4	≥16/4	**(10)** Breakpoints are based on a dosage regimen of 1.25 g administered every 6 h.
O	Ticarcillin-clavulanate	≤32/2	64/2	≥128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)					
C	Cefotetan	≤16	32	≥64	
C	Cefoxitin	≤16	32	≥64	
C	Ceftizoxime	≤32	64	≥128	
C	Ceftriaxone	≤16	32	≥64	
O	Cefmetazole	≤16	32	≥64	
O	Cefoperazone	≤16	32	≥64	
O	Cefotaxime	≤16	32	≥64	

Table 2J. Anaerobes (Continued)

Test/Report Group	Antimicrobial Agent	Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	
CARBAPENEMS					
A	Doripenem	≤2	4	≥8	
A	Ertapenem	≤4	8	≥16	
A	Imipenem	≤4	8	≥16	
A	Meropenem	≤4	8	≥16	
TETRACYCLINES					
C	Tetracycline	≤4	8	≥16	
FLUOROQUINOLONES					
C	Moxifloxacin	≤2	4	≥8	
LINCOSAMIDES					
A	Clindamycin	≤2	4	≥8	
PHENICOLS					
C	Chloramphenicol	≤8	16	≥32	
NITROIMIDAZOLES					
A	Metronidazole	≤8	16	≥32	**(11)** Many non-spore-forming, gram-positive anaerobic rods are resistant to metronidazole.

Abbreviations: ATCC®, American Type Culture Collection; CFU, colony-forming unit(s); I, intermediate; LHB, lysed horse blood; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.

Footnotes

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

b. A/C: Group A for gram-positive anaerobes and group C for gram-negative organisms. Refer to Table 1C.

Reference for Table 2J

1 CLSI. *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria*. 9th ed. CLSI standard M11. Clinical and Laboratory Standards Institute; 2018.

Table 3A. Tests for Extended-Spectrum ß-Lactamases in *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Escherichia coli*, and *Proteus mirabilis*

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

Breakpoints for drugs with limited availability in many countries (eg, moxalactam, cefonicid, cefamandole, and cefoperazone) were not evaluated. If considering use of these drugs for *E. coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, or *Proteus mirabilis*, ESBL testing should be performed. If isolates test ESBL positive, the results for moxalactam, cefonicid, cefamandole, and cefoperazone should be reported as resistant.

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

Table 3A. (Continued)

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

Table 3A. (Continued)

Test	Criteria for Performance of ESBL Test		ESBL Test	
Test method	Disk diffusion	Broth microdilution	Disk diffusion	Broth microdilution
QC recommendations	When testing antimicrobial agents used for ESBL detection, *K. pneumoniae* ATCC®[b] 700603 is provided as a supplemental QC strain (eg, for training, competence assessment, or test evaluation). Either strain, *K. pneumoniae* ATCC® 700603 or *E. coli* ATCC® 25922, may then be used for routine QC (eg, weekly or daily).	When testing antimicrobial agents used for ESBL detection, *K. pneumoniae* ATCC® 700603 is provided as a supplemental QC strain (eg, for training, competence assessment, or test evaluation). Either strain, *K. pneumoniae* ATCC® 700603 or *E. coli* ATCC® 25922, may then be used for routine QC (eg, weekly or daily).	When performing the ESBL test, *K. pneumoniae* ATCC® 700603 and *E. coli* ATCC® 25922 should be used for routine QC (eg, weekly or daily).	When performing the ESBL test, *K. pneumoniae* ATCC® 700603 and *E. coli* ATCC® 25922 should be tested routinely (eg, weekly or daily).
	E. coli ATCC® 25922 (see acceptable QC ranges in Table 4A-1)	*E. coli* ATCC® 25922 = no growth (see acceptable QC ranges listed in Table 5A-1)	**Acceptable QC:** *E. coli* ATCC® 25922: ≤ 2-mm increase in zone diameter for antimicrobial agent tested in combination with clavulanate vs the zone diameter when tested alone.	**Acceptable QC:** *E. coli* ATCC® 25922: < 3 2-fold concentration decrease in MIC for antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone.
	K. pneumoniae ATCC® 700603: Cefpodoxime zone 9-16 mm Ceftazidime zone 10-18 mm Aztreonam zone 10-16 mm Cefotaxime zone 17-25 mm Ceftriaxone zone 16-24 mm	*K. pneumoniae* ATCC® 700603 = Growth: Cefpodoxime MIC ≥ 8 µg/mL Ceftazidime MIC ≥ 2 µg/mL Aztreonam MIC ≥ 2 µg/mL Cefotaxime MIC ≥ 2 µg/mL Ceftriaxone MIC ≥ 2 µg/mL	*K. pneumoniae* ATCC® 700603: ≥ 5-mm increase in zone diameter of ceftazidime-clavulanate vs ceftazidime alone; ≥ 3-mm increase in zone diameter of cefotaxime-clavulanate vs cefotaxime alone.	*K. pneumoniae* ATCC® 700603: ≥ 3 2-fold concentration decrease in MIC for an antimicrobial agent tested in combination with clavulanate vs the MIC of the agent when tested alone.

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

Table 3A. (Continued)

Footnotes

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

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

Introduction to Tables 3B and 3C. Tests for Carbapenemases in Enterobacterales and *Pseudomonas aeruginosa*

Institutional infection prevention procedures or epidemiological investigations may necessitate identification of carbapenemase-producing Enterobacterales and *P. aeruginosa*. Such testing is not currently recommended for routine use.

Carbapenemase-producing isolates of Enterobacterales usually test intermediate or resistant to one or more carbapenems using the current breakpoints as listed in Table 2A (**NOTE:** Testing not susceptible to ertapenem is often the most sensitive indicator of carbapenemase production) and usually test resistant to one or more agents in cephalosporin subclass III (eg, cefoperazone, cefotaxime, ceftazidime, ceftizoxime, and ceftriaxone). However, some isolates that produce carbapenemases such as SME or IMI often test susceptible to these cephalosporins.

Laboratories using Enterobacterales MIC breakpoints for carbapenems described in M100-S20 (January 2010) should perform the CarbaNP test, mCIM, eCIM, and/or a molecular assay (refer to Tables 3B and 3C for methods) when isolates of Enterobacterales are suspicious for carbapenemase production based on imipenem or meropenem MICs 2–4 µg/mL or ertapenem MIC 2 µg/mL (refer to Tables 3B-1 and 3C-1 for guidance on reporting). After implementing the current breakpoints, these additional tests may not need to be performed other than for epidemiological or infection prevention purposes (ie, it is no longer necessary to edit results for the carbapenems to resistant if a carbapenemase producer is detected).

Introduction to Tables 3B and 3C. (Continued)

	Tests Used for Epidemiological or Infection Prevention-Related Testing			
	CarbaNP (Table 3B)	mCIM (Table 3C)	mCIM With eCIM (Table 3C)	Other (eg, molecular assays)
Organisms	Enterobacterales and *P. aeruginosa* that are not susceptible to one or more carbapenems	Enterobacterales and *P. aeruginosa* that are not susceptible to one or more carbapenems	Enterobacterales that are positive by mCIM	Enterobacterales and *P. aeruginosa* that are not susceptible to one or more carbapenems to determine the presence of a carbapenemase, or to determine carbapenemase type in isolates positive by CarbaNP or mCIM.
Strengths	Rapid	No special reagents or media necessary	No special reagents or media necessary	Determines type of carbapenemase in addition to absence or presence of the enzyme
Limitations	Special reagents are needed, some of which necessitate in-house preparation (and have a short shelf life). Invalid results occur with some isolates. Certain carbapenemase types (eg, OXA-type, chromosomally encoded) are not consistently detected.	Requires overnight incubation	Requires overnight incubation	Special reagents and equipment are needed. Specific to targeted genes; false-negative result if specific carbapenemase gene present is not targeted.

Abbreviations: eCIM, EDTA-modified carbapenem inactivation method; mCIM, modified carbapenem inactivation method, MIC, minimal inhibitory concentration.

Table 3B. CarbaNP Test for Suspected Carbapenemase Production in Enterobacterales and *Pseudomonas aeruginosa*[1-7]

NOTE: If using FORMER MIC breakpoints for carbapenems described in M100-S20 (January 2010), please refer to modifications in Table 3B-1.

Test	CarbaNP Test
When to perform this test	For epidemiological or infection prevention purposes. **NOTE:** No change in the interpretation of carbapenem susceptibility test results is necessary for CarbaNP-positive isolates. Such testing is not currently recommended for routine use.
Test method	Colorimetric microtube assay
Test reagents and materials	• Clinical laboratory reagent water • Imipenem reference standard powder • Commercially available bacterial protein extraction reagent in Tris HCl buffer, pH 7.4 • Zinc sulfate heptahydrate • Phenol red powder • 1 N NaOH solution • 10% HCl solution • Microcentrifuge tubes 1.5 mL, clear • 1-µL inoculation loops • Containers to store prepared solutions Use reagents above to prepare the following solutions (instructions for preparation are provided below this table): • 10 mM zinc sulfate heptahydrate solution • 0.5% phenol red solution • 0.1 N sodium hydroxide solution • CarbaNP Solution A • CarbaNP Solution B (solution A + imipenem)
Test procedure	1. Label two microcentrifuge tubes (one "a" and one "b") for each patient isolate, QC organism, and uninoculated reagent control. 2. Add 100 µL of bacterial protein extraction reagent to each tube. 3. For each isolate to be tested, emulsify a 1-µL loopful of bacteria from an overnight blood agar plate in both tubes "a" and "b." Vortex each tube for 5 seconds. (Uninoculated reagent control tubes should contain only bacterial protein extraction reagent, no organism.) **NOTE:** Do not use growth from selective media or plates containing antibiotics or other agents that select for certain bacteria. 4. Add 100 µL of solution A to tube "a." 5. Add 100 µL of solution B to tube "b." 6. Vortex tubes well. 7. Incubate at 35°C ± 2°C for up to 2 hours. Isolates that demonstrate positive results before 2 hours can be reported as carbapenemase producers.

Table 3B. (Continued)

Test	CarbaNP Test
Test interpretation	Strategy for reading (see Figure 1, below): 1. Read uninoculated reagent control tubes "a" and "b" (ie, "blanks"). • Both tubes must be red or red-orange. • If either tube is any other color, the test is invalid. 2. Read inoculated tube "a." • Tube "a" must be red or red-orange. • If tube "a" is any other color, the test is invalid. 3. Read inoculated tube "b." • Red or red-orange = negative • Light orange, dark yellow, or yellow = positive • Orange = invalid 4. Interpret results as follows:

Results for Patient and QC Tubes		
Tube "a": Solution A (serves as internal control)	Tube "b": Solution B	Interpretation
Red or red-orange	Red or red-orange	Negative, no carbapenemase detected
Red or red-orange	Light orange, dark yellow, or yellow	Positive, carbapenemase producer
Red or red-orange	Orange	Invalid
Orange, light orange, dark yellow, or yellow	Any color	Invalid

Table 3B. (Continued)

Test	CarbaNP Test
Test interpretation (Continued)	**NOTES:** A slight color change may be observed with the addition of imipenem to solution A. Compare patient tubes to the uninoculated reagent control tubes when interpreting questionable results. For invalid results: • Check reagents for QC strains and uninoculated reagent controls. Reagent deterioration can cause invalid results. An invalid result for an uninoculated reagent control test indicates a problem with solution A and/or solution B. Check the pH of solution A. If pH is < 7.8, prepare fresh solution A and solution B. • Repeat the test, including the uninoculated reagent controls. • If the repeat test is invalid, perform molecular assay.
Reporting	Report positive as "Carbapenemase producer." Report negative as "No carbapenemase detected."
QC recommendations	Test positive and negative QC strains and uninoculated reagent control tubes each day of testing. *K. pneumoniae* ATCC®[a] BAA-1705™—carbapenemase positive *K. pneumoniae* ATCC® BAA-1706™—carbapenemase negative Results for uninoculated reagent control tubes "a" and "b" must be negative (ie, red or red-orange). Any other result invalidates all tests performed on that day with the same lot of reagents. The addition of imipenem to tube "b" might cause tube "b" to appear red-orange when tube "a" is red.

Abbreviations: ATCC®, American Type Culture Collection; MIC, minimal inhibitory concentration; pH, negative logarithm of hydrogen ion concentration; QC, quality control.

Table 3D. Tests for Colistin Resistance for Enterobacterales and *Pseudomonas aeruginosa*

The polymyxins (colistin and polymyxin B) are antimicrobial agents of last resort for treating multidrug-resistant infections. Clinical and PK/PD data suggest that these agents have limited clinical efficacy. Alternative agents are strongly preferred. If these agents are not available, knowledge of the colistin MIC may be helpful to inform treatment decisions.

For colistin, broth microdilution, broth disk elution and agar dilution MIC methods are acceptable. Broth microdilution is the only approved method for polymyxin B. Disk diffusion and gradient diffusion methods should not be performed.

Colistin and polymyxin B are considered equivalent agents, so MICs obtained from testing colistin predict MICs to polymyxin B and vice versa. At this time, CLSI has not evaluated polymyxin B testing methods, and the procedures below should not be adapted to polymyxin B. The methods below were evaluated for *Acinetobacter* spp. by CLSI and found to yield inaccurate results.

These methods were established with limited disk and/or media manufacturers and are considered provisional until additional data are evaluated by CLSI and shown to meet CLSI document M23[1] guidelines.

Test	Colistin Broth Disk Elution	Colistin Agar Test
Approved organisms	Enterobacterales and *Pseudomonas aeruginosa*	Enterobacterales and *P. aeruginosa*
Strengths	No special reagents or media necessary	Ability to test up to 10 isolates at one time
Limitations	Hands-on time and cost	Requires special media (colistin agar plate)
When to perform this test	Testing multidrug-resistant isolates for clinical or infection prevention purposes	Testing multidrug-resistant isolates for clinical or infection prevention purposes
Test method	Tube dilution using colistin disk as the colistin source	Agar dilution: slight variation of method described in M07[2] (ie, different inoculum and different approach to interpreting results)
Organism group	Enterobacterales and *P. aeruginosa*	Enterobacterales and *P. aeruginosa*
Medium	CAMHB (10-mL tubes)	MHA (20 mL in 100-mm Petri plate)[a]
Antimicrobial concentration	10-µg colistin **sulfate** disks Final concentration: 0 µg/mL (growth control), 1 µg/mL, 2 µg/mL, and 4 µg/mL colistin	Colistin sulfate Final concentration: 0 µg/mL (growth control), 1 µg/mL, 2 µg/mL, and 4 µg/mL colistin[a]
Inoculum	1. Using a loop or swab, pick 3-5 colonies from a fresh (18-24 hours) nonselective agar plate and transfer to sterile saline (4-5 mL). 2. Adjust turbidity to equivalent of a 0.5 McFarland turbidity standard.	1. Using a loop or swab, pick 3-5 colonies from a fresh (18-24 hours) nonselective agar plate and transfer to sterile saline (4-5 mL). 2. Adjust turbidity to equivalent of a 0.5 McFarland turbidity standard. 3. Dilute the standardized inoculum 1:10 in saline.

Table 3D. (Continued)

Test	Colistin Broth Disk Elution	Colistin Agar Test
Test procedure	1. Let the CAMHB tubes (10 mL) and colistin disks warm to room temperature. 2. Label 4 tubes of CAMHB for each isolate to be tested with 1, 2, and 4 µg/mL and control (see Figure 1). 3. Using aseptic technique, carefully add: • 1 colistin disk to the tube labeled "1 µg/mL" • 2 colistin disks to tube labeled "2 µg/mL" • 4 colistin disks to the tube labeled "4 µg/mL" 4. Gently vortex the tubes with the added disk and let the colistin elute from the disks for at least 30 minutes but no longer than 60 minutes at room temperature. 5. Prepare the standardized inoculum. 6. Add 50 µL standardized inoculum to the control and 1-, 2-, and 4-µg/mL tubes to attain a final inoculum concentration of approximately 7.5×10^5 CFU/mL. 7. Using a 10-µL loop, subculture from the original inoculum tube to a blood agar plate as a purity check. 8. Cap the tubes tightly and vortex each inoculated tube on slow speed to mix. Slow speed is suggested to prevent colistin from sticking to the cap and glass surface above the meniscus of liquid. 9. Loosen the caps slightly before incubation. 10. Incubate the tubes and purity plate.	1. Divide each colistin agar plate with increasingly doubled dilutions of colistin in up to 10 parts, with a marker to test up to 10 isolates per plate. Label each part with the appropriate isolate number (see Figure 2). 2. Using a pipette or a 10-µL loop, streak 10 µL of the 1:10 dilution onto the appropriate part of each colistin agar plate. 3. Using a 10-µL loop, subculture from the original inoculum tube to a blood agar plate as a purity check. 4. Incubate the colistin agar plates and purity plate.
Incubation conditions	33 to 35°C; ambient air	33 to 35°C; ambient air
Incubation length	16-20 hours	16-20 hours

Table 3D
Tests for Colistin Resistance for
Enterobacterales and *Pseudomonas aeruginosa*

Table 3D. (Continued)

Test	Colistin Broth Disk Elution	Colistin Agar Test
Results	1. Examine the purity plate to ensure inoculum was pure. 2. Examine the growth control tube, which must demonstrate obvious turbidity for the test to be valid. NOTE: Some *P. aeruginosa* isolates may grow only near the meniscus. 3. Read the MIC as the lowest concentration that completely inhibits growth of the test isolate. (See Figure 1 for examples.) For Enterobacterales and *P. aeruginosa:* • ≤ 2 µg/mL = intermediate • ≥ 4 µg/mL = resistant	1. Examine the purity plate to ensure inoculum was pure. 2. Examine the growth control plate, which must demonstrate confluent growth for the test to be valid. 3. Examine the colistin plates carefully with transmitted light for colony or light film of growth. 4. Read the MIC as the lowest colistin agar plate concentration that completely inhibits growth of the test isolate (eg, even 1 colony would be considered growth). See Figure 2 for examples. For Enterobacterales and *P. aeruginosa:* • ≤ 2 µg/mL = intermediate • ≥ 4 µg/mL = resistant
Additional testing and reporting	If there is an inconsistent growth pattern (eg, no growth in 2 µg/mL but growth at 1 µg/mL and 4 µg/mL), repeat the test. An inconsistent growth pattern may occur as a result of: • Contamination at higher dilutions • Heteroresistance • Improper concentrations of antimicrobial agent in the tubes • Error inoculating the tubes	If there is an inconsistent growth pattern (eg, no growth in 2 µg/mL but growth at 1 µg/mL and 4 µg/mL), repeat the test. An inconsistent growth pattern may occur as a result of: • Contamination at higher dilutions • Heteroresistance • Improper concentrations of antimicrobial agent in the colistin agar plates • Error inoculating the plates
QC recommendations - routine[b]	*Escherichia coli* **ATCC® BAA-3170™ (formerly AR Bank #0349 *mcr-1*)** (≤ 1–**> 4 µg/mL**, with a target of 2 µg/mL)[c] and *P. aeruginosa* ATCC® 27853 (**1**–4 µg/mL)	*E. coli* **ATCC® BAA-3170™ (formerly AR Bank #0349 *mcr-1*)** (≤ 1–**> 4 µg/mL**, with a target of 2 µg/mL)[c] and *P. aeruginosa* ATCC® 27853 (**1**–4 µg/mL)

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; CFU, colony-forming unit(s); MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; PK/PD, pharmacokinetic/pharmacodynamic; QC, quality control.

Table 3D. (Continued)

Footnotes

a. Refer to M07[2] for preparation of media and antimicrobial agents.

b. QC recommendations – routine

Test recommended routine QC strains:

- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[3] and M07[2]) and the individualized QC plan is complete
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

Perform QC of colistin disks and test media daily or weekly following the routine disk diffusion QC procedure and handle disks as described in M02.[3]

c. The QC ranges were established with disks (colistin broth disk elution) and media from a limited number of manufacturers and are considered provisional until additional data are evaluated by CLSI and shown to meet CLSI document M23[1] guidelines.

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

Table 3E-1. Test for Performing Disk Diffusion Directly From Positive Blood Culture Broth

Test	Direct Disk Diffusion
Test method	Disk diffusion using positive blood culture broth
Organism group	Enterobacterales **and *Pseudomonas aeruginosa***
Medium	MHA
Antimicrobial concentration	Standard disk contents for the antimicrobials **are detailed in Table 3E-2 (Enterobacterales) and Table 3E-3 (*P. aeruginosa*)**
Inoculum	Positive blood culture broth with gram-negative bacilli, used within 8 hours of flagging positive by the blood culture system
Test procedure	1. Invert blood culture bottle 5-10 times to thoroughly mix. 2. Sterilize the top of the bottle with an alcohol wipe (allow to dry) and insert 20-gauge venting needle into the blood culture bottle. 3. Dispense 4 drops of blood culture broth onto an MHA plate. As a purity check, use an inoculated blood agar plate streaked for isolation. 4. Spread blood culture broth across the entire surface of the MHA plate using a sterile cotton swab. 5. Repeat this procedure by streaking twice more, rotating the plate approximately 60 degrees each time to ensure an even distribution of inoculum. 6. Leave the lid ajar for 3-5 minutes (ideally) but no more than 15 minutes. 7. Dispense antimicrobial disks onto the surface of the inoculated MHA plate. 8. Press each disk down to ensure complete contact with the agar surface. 9. Invert the plate and place in the incubator within 15 minutes of disks being applied.
Incubation conditions	35°C ± 2°C; ambient air
Incubation length	**8-10 hours or** 16-18 hours
Results	1. Examine the blood agar purity plate to ensure pure growth. 2. Examine the test plate to ensure confluent lawn of growth appropriate to read disk zone tests per M02.[1] 3. Measure the zone diameters according to routine disk diffusion recommendations in M02.[1] 4. Report results using the interpretive categories and zone diameter breakpoints in **Table 3E-2 or Table 3E-3** if the gram-negative bacillus tested is confirmed to be an Enterobacterales **or *P. aeruginosa*, respectively.** If species is identified as another organism, do not interpret or report results.

Table 3E-1. (Continued)

Test	Direct Disk Diffusion
Additional testing and reporting	• If there is an inconsistent growth pattern on the plate (eg, mixed inoculum, nonconfluent growth, growth is too faint to read), do not interpret or report results from the direct disk diffusion test, and perform standard susceptibility testing from pure colony growth. • Antimicrobial agents to which the organism is intrinsically resistant (see Appendix B) should be reported as resistant, regardless of measured zone size. • If two zones of growth inhibition are observed, measure the inner zone diameter. In case of colonies present within zones, or presence of both inner and outer zones, check the purity plate and, if pure, record the inner zone diameter.
QC recommendations	• **Perform QC according to the standard disk diffusion QC procedures per M021 (eg, daily or weekly).** • **See Tables 4A-1 and 4A-2 for acceptable QC ranges.** • ***E. coli* ATCC®[a] 25922, *P. aeruginosa* ATCC® 27853** • **Refer to Table 4A-2 to select strains for routine QC of β-lactam combination agents.**

Abbreviations: ATCC®, American Type Culture Collection; MHA, Mueller-Hinton agar; QC, quality control.

Footnote

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

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

Reference for Table 3E-1

1 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

Table 3E-1
Test for Performing Disk Diffusion Directly From Positive Blood Culture Broth

Table 3E-2. Zone Diameter Disk Diffusion Breakpoints for Enterobacterales Direct From Blood Culture

General Comments

(1) The dosage regimens shown in the Comments column below are needed to achieve plasma drug exposure (in adults with normal renal and hepatic function) on which breakpoints were based. When new breakpoints are implemented, it is strongly recommended that laboratories share this information with infectious diseases practitioners, pharmacists, pharmacy and therapeutics committees, infection prevention committees, and the antimicrobial stewardship team.

(2) For additional testing and reporting recommendations, refer to Table 2A.

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

Table 3E-2. Enterobacterales (Continued)

Test/Report Group	Antimicrobial Agent	Disk Content	Read Times, hours	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Comments
				S	SDD	I	R	
PENICILLINS								
A	Ampicillin	10 µg	8-10	-	-	-	-	(3) Results of ampicillin testing can be used to predict results for amoxicillin. (4) Breakpoints are based on an ampicillin dosage regimen of 2 g parenterally administered every 4-6 h or an amoxicillin dosage regimen of 1-2 g parenterally administered every 6 h.
			16-18	≥ 17	-	14-16	≤ 13	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)								
B	Ceftriaxone	30 µg	8-10	≥ 23	-	20-22	≤ 19	(5) Breakpoints are based on a dosage regimen of 1 g administered every 24 h.
			16-18	≥ 23	-	20-22	≤ 19	
C	Ceftazidime	30 µg	8-10	≥ 21	-	18-20	≤ 17	(6) Breakpoints are based on a dosage regimen of 1 g administered every 8 h.
			16-18	≥ 21	-	18-20	≤ 17	
MONOBACTAMS								
C	Aztreonam	30 µg	8-10	≥ 21	-	18-20	≤ 17	(7) Breakpoints are based on a dosage regimen of 1 g administered every 8 h.
			16-18	≥ 21	-	18-20	≤ 17	
AMINOGLYCOSIDES								
A	Tobramycin	10 µg	8-10	≥ 15	-	13-14	≤ 12	
			16-18	≥ 15	-	13-14	≤ 12	
FOLATE PATHWAY ANTAGONISTS								
B	Trimethoprim-sulfamethoxazole	1.25/ 23.75 µg	8-10	-	-	-	-	
			16-18	≤ 16	-	11-15	≤ 10	

Abbreviations: I, intermediate; MIC, minimal inhibitory concentration; R, resistant; S, susceptible; SDD, susceptible-dose dependent.

Table 3E-3. Zone Diameter Disk Diffusion Breakpoints for *Pseudomonas aeruginosa* Direct From Blood Culture

General Comments

(1) The dosage regimens shown in the Comments column below are necessary to achieve plasma drug exposure (in adults with normal renal and hepatic function) on which breakpoints were derived. When new breakpoints are implemented, it is strongly recommended that laboratories share this information with infectious diseases practitioners, pharmacists, pharmacy and therapeutics committees, infection prevention committees, and the antimicrobial stewardship team.

(2) For additional testing and reporting recommendations, refer to Table 2B-1.

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

Test/Report Group	Antimicrobial Agent	Disk Content	Read Times, hours	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Comments
				S	SDD	I	R	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)								
A	Ceftazidime	30 µg	8-10	-	-	-	-	(3) Breakpoints are based on a dosage regimen of 1 g administered every 6 h or 2 g administered every 8 h.
			16-18	≥ 18	-	15-17	≤ 14	
CARBAPENEMS								
B	Meropenem	10 µg	8-10	-	-	-	-	(4) Breakpoints are based on a dosage regimen of 1 g administered every 8 h.
			16-18	≥ 19	-	16-18	≤ 15	
AMINOGLYCOSIDES								
A	Tobramycin	10 µg	8-10	≥ 15	-	13-14	≤ 12	
			16-18	≥ 15	-	13-14	≤ 12	
FLUOROQUINOLONES								
B	Ciprofloxacin	5 µg	8-10	≥ 23	-	18-22	≤ 17	(5) Breakpoints are based on a dosage regimen of 400 mg administered parenterally every 8 h.
			16-18	≥ 25	-	19-24	≤ 18	

Abbreviations: I, intermediate; R, resistant; S, susceptible; SDD, susceptible-dose dependent.

Table 3F. Test for Detection of ß-Lactamase Production in *Staphylococcus* spp.

Test	ß-Lactamase Production	
Test method	Disk diffusion (penicillin zone-edge test)	Nitrocefin-based test
Organism group	*S. aureus* with penicillin MICs ≤ 0.12 µg/mL or zones ≥ 29 mm[a]	*Staphylococcus* spp.[a,b] with penicillin MICs ≤ 0.12 µg/mL or zones ≥ 29 mm
Medium	MHA	N/A
Antimicrobial concentration	10 units penicillin disk	N/A
Inoculum	Standard disk diffusion procedure	Induced growth (ie, growth taken from the zone margin surrounding a penicillin or cefoxitin disk test on either MHA or a blood agar plate after 16-18 hours of incubation)
Incubation conditions	35°C ± 2°C; ambient air	Room temperature
Incubation length	16-18 hours	Up to 1 hour for nitrocefin-based test or follow manufacturer's directions
Results	Sharp zone edge ("cliff") = ß-lactamase positive (see Figure 1 below this table) Fuzzy zone edge ("beach") = ß-lactamase negative (see Figure 2 below this table)	Nitrocefin-based test: conversion from yellow to red/pink = ß-lactamase positive.
Additional testing and reporting	ß-lactamase-positive staphylococci are resistant to penicillin, amino-, carboxy-, and ureidopenicillins.	Nitrocefin-based tests can be used for *S. aureus*, but negative results should be confirmed with the penicillin zone-edge test before reporting penicillin as susceptible. ß-lactamase-positive staphylococci are resistant to penicillin, amino-, carboxy-, and ureidopenicillins.
QC recommendations - routine[c]	*S. aureus* ATCC®[d] 25923 for routine QC of penicillin disk to include examination of zone-edge test (fuzzy edge = "beach")	
QC recommendations - lot/shipment[e]		*S. aureus* ATCC® 29213 - positive *S. aureus* ATCC® 25923 - negative (or see local regulations and manufacturers' recommendations)
QC recommendations - supplemental[f]	*S. aureus* ATCC® 29213 - positive penicillin zone-edge test (sharp edge = "cliff")	

Abbreviations: ATCC®, American Type Culture Collection; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; N/A, not applicable; QC, quality control.

Table 3F. (Continued)

Footnotes

a. The penicillin disk diffusion zone-edge test was shown to be more sensitive than nitrocefin-based tests for detection of β-lactamase production in *S. aureus*. The penicillin zone-edge test is recommended if only one test is used for β-lactamase detection. However, some laboratories may choose to perform a nitrocefin-based test first and, if this test is positive, report the results as positive for β-lactamase (or penicillin resistant). If the nitrocefin test is negative, the penicillin zone-edge test should be performed before reporting the isolate as penicillin susceptible in cases in which penicillin may be used for therapy (eg, endocarditis).[1,2]

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

c. QC recommendations – routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[3] and M07[4])
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

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

e. QC recommendations – lot/shipment

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

f. QC recommendations – supplemental

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

Table 3F. (Continued)

References for Table 3F

1. Kaase M, Lenga S, Friedrich S, et al. Comparison of phenotypic methods for penicillinase detection in *Staphylococcus aureus*. *Clin Microbiol Infect*. 2008;14(6):614-616.
2. Gill VJ, Manning CB, Ingalls CM. Correlation of penicillin minimum inhibitory concentrations and penicillin zone edge appearance with staphylococcal beta-lactamase production. *J Clin Microbiol*. 1981;14(4):437-440.
3. CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.
4. CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 3G-1. Test for Detecting Methicillin (Oxacillin) Resistance in *Staphylococcus aureus*[a] and *Staphylococcus lugdunensis*

Test	Detecting *mecA*-Mediated Resistance Using Cefoxitin[b]		Detecting *mecA*-Mediated Resistance Using Oxacillin	Detecting *mecA*-mediated Resistance Using Oxacillin Salt Agar for *S. aureus* Only
Test method	Disk diffusion	Broth microdilution	Broth microdilution and agar dilution	Agar dilution for *S. aureus*
Medium	MHA	CAMHB	CAMHB with 2% NaCl (broth microdilution) MHA with 2% NaCl (agar dilution)	MHA with 4% NaCl
Antimicrobial concentration	30-µg cefoxitin disk	4 µg/mL cefoxitin	2 µg/mL oxacillin	6 µg/mL oxacillin
Inoculum	Standard disk diffusion procedure	Standard broth microdilution procedure	Standard broth microdilution procedure or standard agar dilution procedure	Colony suspension to obtain 0.5 McFarland turbidity Using a 1-µL loop that was dipped in the suspension, spot an area 10–15 mm in diameter. Alternatively, using a swab dipped in the suspension and the excess liquid expressed, spot a similar area or streak an entire quadrant.
Incubation conditions	33 to 35°C; ambient air[c]			
Incubation length	16–18 hours	16–20 hours	24 hours (may be reported after 18 hours, if resistant)	24 hours; read with transmitted light
Results	≤ 21 mm = positive for *mecA*-mediated resistance ≥ 22 mm = negative for *mecA*-mediated resistance	≥ 8 µg/mL = positive for *mecA*-mediated resistance ≤ 4 µg/mL = negative for *mecA*-mediated resistance	≥4 µg/mL = positive for *mecA*-mediated resistance ≤ 2 µg/mL = negative for *mecA*-mediated resistance	Examine carefully with transmitted light for > 1 colony or light film of growth. > 1 colony = positive for *mecA*-mediated resistance
Additional testing and reporting	Isolates that test positive for *mecA*-mediated resistance should be reported as methicillin (oxacillin) (not cefoxitin) resistant; other β-lactam agents, except ceftaroline, should be reported as resistant or should not be reported.[d]			
QC recommendations - routine[e,f]	*S. aureus* ATCC®[g] 25923 - *mecA* negative (zone 23–29 mm)	*S. aureus* ATCC® 29213 - *mecA* negative (MIC 1–4 µg/mL)	*S. aureus* ATCC® 29213 - *mecA* negative (MIC 0.12–0.5 µg/mL)	*S. aureus* ATCC®[c] 29213 - susceptible (≤ 1 colony; with each test day)
QC recommendations - lot/shipment[h]	N/A	*S. aureus* ATCC® 43300 - *mecA* positive (MIC ≥ 8 µg/mL)	*S. aureus* ATCC® 43300 - *mecA* positive (MIC ≥ 8 µg/mL)	*S. aureus* ATCC® 43300 - *mecA* positive (>1 colony)

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant *Staphylococcus* spp.; N/A, not applicable.

Table 3G-1. (Continued)

Footnotes

a. Including members of the *S. aureus* complex (see Table 2C, comment 2).

b. Cefoxitin is used as a surrogate test for detecting *mecA*-mediated methicillin (oxacillin) resistance.

c. Testing at temperatures above 35°C may not detect MRS.

d. Testing of other β-lactam agents, except ceftaroline, is not advised.

e. QC recommendations - routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[1] and M07[2])

f. Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

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

h. QC Recommendations - lot/shipment

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

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

References for Table 3G-1

1 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

2 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 3G-2. Test for Detecting Methicillin (Oxacillin) Resistance in *Staphylococcus* spp. Except *Staphylococcus aureus*[a] and *Staphylococcus lugdunensis*

Test	Detecting *mecA*-Mediated Resistance Using Cefoxitin[b]	Detecting *mecA*-Mediated Resistance Using Oxacillin	
Test method	Disk diffusion	Disk diffusion	Broth microdilution and agar dilution
Organism group	*Staphylococcus* spp. except: *S. aureus* (refer to Table 3G-1) *S. lugdunensis* (refer to Table 3G-1) *S. pseudintermedius* (not recommended) *S. schleiferi* (not recommended)	Testing is only indicated for the species listed below: *S. epidermidis* *S. pseudintermedius* *S. schleiferi*	*Staphylococcus* spp. except: *S. aureus* (refer to Table 3G-1) *S. lugdunensis* (refer to Table 3G-1)
Medium	MHA	MHA	CAMHB with 2% NaCl (broth microdilution) MHA with 2% NaCl (agar dilution)
Antimicrobial concentration	30 µg cefoxitin disk	1-µg oxacillin disk	0.5 µg/mL oxacillin
Inoculum	Standard disk diffusion procedure	Standard disk diffusion procedure	Standard broth microdilution procedure or standard agar dilution procedure
Incubation conditions	33 to 35°C; ambient air[c]		
Incubation length	24 hours (may be reported after 18 hours, if resistant)	16-18 hours	24 hours (may be reported after 18 hours, if resistant)
Results	≤ 24 mm = positive for *mecA*-mediated resistance ≥ 25 mm = negative for *mecA*-mediated resistance	≤ 17 mm = positive for *mecA*-mediated resistance ≥ 18 mm = negative for *mecA*-mediated resistance	≥ 1 µg/mL = positive for *mecA*-mediated resistance ≤ 0.5 µg/mL = negative for *mecA*-mediated resistance
Additional testing and reporting	Isolates that test positive for *mecA*-mediated resistance should be reported as methicillin (oxacillin) (not cefoxitin) resistant; other β-lactam agents, except ceftaroline, should be reported as resistant or should not be reported.[d]		
			For *Staphylococcus* spp., excluding *S. aureus*, *S. lugdunensis*, *S. epidermidis*, *S. pseudintermedius*, and *S. schleiferi*, oxacillin MIC breakpoints may overcall resistance, and some isolates for which the oxacillin MICs are 1-2 µg/mL may be *mecA* negative. Isolates from serious infections for which oxacillin MICs are 1-2 µg/mL may be tested for *mecA* or for PBP2a. Isolates that test *mecA* or PBP2a negative should be reported as methicillin (oxacillin) susceptible.
QC recommendations - routine[e]	*S. aureus* ATCC®[ef] 25923 - *mecA* negative (zone 23-29 mm)	*S. aureus* ATCC® 25923 - *mecA* negative (zone 18-24 mm)	*S. aureus* ATCC® 29213 - *mecA* negative (MIC 0.12-0.5 µg/mL)
QC recommendations - lot/shipment[g]	N/A	*S. aureus* ATCC® 43300 - *mecA* positive (zone ≤ 24 mm)	*S. aureus* ATCC® 43300 - *mecA* positive (MIC ≥ 8 µg/mL)

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; MRS, methicillin (oxacillin)-resistant *Staphylococcus* spp.; N/A, not applicable.

Table 3G-2. (Continued)

Footnotes

a. Including members of the *S. aureus* complex (see Table 2C, general comment [2]).

b. Cefoxitin is tested as a surrogate for detecting *mecA*-mediated methicillin (oxacillin) resistance; however, recent data suggest that the cefoxitin disk diffusion test may not perform reliably for all species (eg, *S. haemolyticus*).[1]

c. Testing at temperatures above 35°C may not detect MRS.

d. Testing of other β-lactam agents, except ceftaroline, is not advised.

e. QC recommendations – routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[2] and M07[3])
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

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

g. QC Recommendations – lot/shipment

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

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

References for Table 3G-2

1 Humphries RM, Magnano P, Burnham CA, et al. Evaluation of surrogate tests for the presence of *mecA*-mediated methicillin resistance in *Staphylococcus haemolyticus*, *Staphylococcus hominis*, *Staphylococcus capitis* and *Staphylococcus warneri*. *J Clin Microbiol*. 2020;59(1):e02290-20.

2 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 3H. Vancomycin Agar Screen for *Staphylococcus aureus* and *Enterococcus* spp.

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

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

Table 3H. (Continued)

Footnotes

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

b. QC recommendations – routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[1] and M07[2])
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

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

d. QC recommendations – lot/shipment

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

References for Table 3H

1 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

2 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 3I. Test for Detecting Inducible Clindamycin Resistance in *Staphylococcus* spp., *Streptococcus pneumoniae*, and *Streptococcus* spp. B-Hemolytic Group[a,b]

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

Table 3I. (Continued)

Test	ICR			
Test method	Disk Diffusion (D-zone test)		Broth Microdilution	
Organism group (applies only to organisms resistant to erythromycin and susceptible or intermediate to clindamycin)	All *Staphylococcus* spp.	*S. pneumoniae* and β-hemolytic *Streptococcus* spp.	All *Staphylococcus* spp.[c]	*S. pneumoniae* and β-hemolytic *Streptococcus* spp.
Additional testing and reporting	Report isolates with ICR as "clindamycin resistant." The following comment may be included with the report: "This isolate is presumed to be resistant based on detection of ICR, as determined by testing clindamycin in combination with erythromycin."			
QC recommendations - routine[c]	*S. aureus* ATCC®[d] 25923 for routine QC of erythromycin and clindamycin disks	*S. pneumoniae* ATCC® 49619 for routine QC of erythromycin and clindamycin disks	*S. aureus* ATCC® BAA-976™ or *S. aureus* ATCC® 29213 – no growth	*S. pneumoniae* ATCC® 49619 or *S. aureus* ATCC® BAA-976™ - no growth
QC recommendations - lot/shipment[e]			*S. aureus* ATCC® BAA-977™ – growth	
QC recommendations - supplemental[f]	*S. aureus* ATCC® BAA-976™ (D-zone test negative) *S. aureus* ATCC® BAA-977™ (D-zone test positive) Use of unsupplemented MHA is acceptable for these strains.		*S. aureus* ATCC® BAA-976™ (no growth) *S. aureus* ATCC® BAA-977™ (growth)	

Abbreviations: ATCC®, American Type Culture Collection; CAMHB, cation-adjusted Mueller-Hinton broth; ICR, inducible clindamycin resistance; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; TSA, tryptic soy agar.

Footnotes

a. Antimicrobial susceptibility testing of β-hemolytic streptococci does not need to be performed routinely (see general comment [4] in Table 2H-1). When susceptibility testing is clinically indicated, test for ICR in strains that are erythromycin resistant and clindamycin susceptible or intermediate.

b. In accordance with 2010 guidance from the Centers for Disease Control and Prevention, colonizing isolates of group B streptococci from penicillin-allergic pregnant women should be tested for clindamycin (including ICR) (see comment [12] in Table 2H-1).[1] For isolates that test susceptible to clindamycin (with erythromycin induction), consider adding the following comment to the patient's report: "This group B *Streptococcus* does not demonstrate inducible clindamycin resistance as determined by testing clindamycin in combination with erythromycin."

Table 3I
Test for Inducible Clindamycin Resistance in *Staphylococcus* spp., *Streptococcus pneumoniae*, and *Streptococcus* spp. β-Hemolytic Group

Table 3I. (Continued)

c. QC recommendations – routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[2] and M07[3])
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

d. ATCC® is a registered trademark of the American Type Culture Collection. Per ATCC® convention, the trademark symbol is used after "BAA" in each catalog number, in conjunction with the registered ATCC® name.

e. QC recommendations – lot/shipment

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

f. QC recommendations – supplemental

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

References for Table 3I

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

2 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

3 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 3J. Test for Detecting High-Level Mupirocin Resistance in *Staphylococcus aureus*

Test	High-Level Mupirocin Resistance[a,1-3]	
Test method	Disk diffusion	Broth microdilution
Organism group	*S. aureus*	
Medium	MHA	CAMHB
Antimicrobial concentration	200-µg mupirocin disk	Single mupirocin 256-µg/mL well
Inoculum	Standard disk diffusion procedure	Standard broth microdilution procedure
Incubation conditions	35°C ± 2°C; ambient air	35°C ± 2°C; ambient air
Incubation length	24 hours; read with transmitted light	24 hours
Results	Examine carefully with transmitted light for light growth within the zone of inhibition. No zone = high-level mupirocin resistance. Any zone = the absence of high-level mupirocin resistance.	For single 256-µg/mL well: Growth = high-level mupirocin resistance. No growth = the absence of high-level mupirocin resistance.
Additional testing and reporting	Report isolates with no zone as high-level mupirocin resistant. Report any zone of inhibition as the absence of high-level resistance.	Report growth in the 256-µg/mL well as high-level mupirocin resistant. Report no growth in the 256-µg/mL well as the absence of high-level resistance.
QC recommendations - routine[b]	*S. aureus* ATCC®[c] 25923 (200-µg disk) - *mupA* negative (zone 29–38 mm)	*S. aureus* ATCC® 29213 - *mupA* negative (MIC 0.06–0.5 µg/mL) or *E. faecalis* ATCC® 29212 - *mupA* negative (MIC 16–128 µg/mL)
QC recommendations - lot/shipment[d]	*S. aureus* ATCC® BAA-1708™ - *mupA* positive (no zone)	*S. aureus* ATCC® BAA-1708™ - *mupA* positive (growth in 256-µg/mL well)

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

Footnotes

a. Although not formally validated by CLSI document M23[1]-based analyses, some studies have linked a lack of response to mupirocin-based decolonization regimens with isolates for which the mupirocin MICs are ≥ 512 µg/mL.[2-4] Although this document does not provide guidance on breakpoints for mupirocin, disk-based testing and the MIC test described here identify isolates for which the mupirocin MICs are ≥ 512 µg/mL.

Table 3J. (Continued)

b. QC recommendations - routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[5] and M07[6])
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

c. ATCC® is a registered trademark of the American Type Culture Collection. Per ATCC® convention, the trademark symbol is used after "BAA" in each catalog number, in conjunction with the registered ATCC® name.

d. QC recommendations - lot/shipment

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

References for Table 3J

1 CLSI. *Development of* In Vitro *Susceptibility Testing Criteria and Quality Control Parameters*. 5th ed. CLSI guideline M23. Clinical and Laboratory Standards Institute; 2018.

2 Simor AE, Phillips E, McGeer A, et al. Randomized controlled trial of chlorhexidine gluconate for washing, intranasal mupirocin, and rifampin and doxycycline versus no treatment for the eradication of methicillin-resistant *Staphylococcus aureus* colonization. *Clin Infect Dis*. 2007;44(2):178-185.

3 Harbarth S, Dharan S, Liassine N, Herrault P, Auckenthaler R, Pittet D. Randomized, placebo-controlled, double-blind trial to evaluate the efficacy of mupirocin for eradicating carriage of methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother*. 1999;43(6):1412-1416.

4 Walker ES, Vasquez JE, Dula R, Bullock H, Sarubbi FA. Mupirocin-resistant, methicillin-resistant *Staphylococcus aureus*; does mupirocin remain effective? *Infect Control Hosp Epidemiol*. 2003;24(5):342-346.

5 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

6 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

Table 3K. Test for Detecting High-Level Aminoglycoside Resistance in *Enterococcus* spp.[a] (Includes Disk Diffusion)

Test	Gentamicin HLAR			Streptomycin HLAR		
Test method	Disk diffusion	Broth microdilution	Agar dilution	Disk diffusion	Broth microdilution	Agar dilution
Medium	MHA	BHI[b] broth	BHI[b] agar	MHA	BHI[b] broth	BHI[b] agar
Antimicrobial concentration	120-µg gentamicin disk	Gentamicin, 500 µg/mL	Gentamicin, 500 µg/mL	300-µg streptomycin disk	Streptomycin, 1000 µg/mL	Streptomycin, 2000 µg/mL
Inoculum	Standard disk diffusion procedure	Standard broth dilution procedure	10 µL of a 0.5 McFarland suspension spotted onto agar surface	Standard disk diffusion procedure	Standard broth dilution procedure	10 µL of a 0.5 McFarland suspension spotted onto agar surface
Incubation conditions	35°C ± 2°C; ambient air	35°C ± 2°C; ambient air	35°C ± 2°C; ambient air	35°C ± 2°C; ambient air	35°C ± 2°C; ambient air	35°C ± 2°C; ambient air
Incubation length	16–18 hours	24 hours	24 hours	16–18 hours	24–48 hours (if susceptible at 24 hours, reincubate)	24–48 hours (if susceptible at 24 hours, reincubate)
Results	6 mm = resistant 7–9 mm = inconclusive ≥ 10 mm = susceptible MIC correlates: R = > 500 µg/mL S = ≤ 500 µg/mL	Any growth = resistant	> 1 colony = resistant	6 mm = resistant 7–9 mm = inconclusive ≥ 10 mm = susceptible MIC correlates: R = > 1000 µg/mL (broth) and > 2000 µg/mL (agar) S = ≤ 1000 µg/mL (broth) and ≤ 2000 µg/mL (agar)	Any growth = resistant	> 1 colony = resistant

Table 3K. (Continued)

Test	Gentamicin HLAR			Streptomycin HLAR		
Additional testing and reporting	Resistant: is not synergistic with cell wall-active agent (eg, ampicillin, penicillin, and vancomycin). Susceptible: is synergistic with cell wall-active agent (eg, ampicillin, penicillin, and vancomycin) that is also susceptible. If disk diffusion result is inconclusive: perform an agar dilution or broth dilution MIC test to confirm. Strains of enterococci with ampicillin and penicillin MICs ≥ 16 µg/mL are categorized as resistant. However, enterococci with penicillin **MICs ≤ 64 µg/mL** or ampicillin MICs **≤ 32 µg/mL** may be susceptible to synergistic killing by these penicillins in combination with gentamicin or streptomycin (in the absence of high-level resistance to gentamicin or streptomycin, see Subchapter 3.12.2.3 in M07[1]) if high doses of penicillin or ampicillin are used. Enterococci possessing higher levels of penicillin (MICs ≥ 128 µg/mL) or ampicillin (MICs ≥ 64 µg/mL) resistance may not be susceptible to the synergistic effect.[2,3] Physicians' requests to determine the actual MIC of penicillin or ampicillin for blood and CSF isolates of enterococci should be considered.					
QC recommendations - routine[c]	*E. faecalis* ATCC®[d] 29212: 16-23 mm	*E. faecalis* ATCC® 29212 - susceptible	*E. faecalis* ATCC® 29212 - susceptible	*E. faecalis* ATCC® 29212: 14-20 mm	*E. faecalis* ATCC® 29212 - susceptible	*E. faecalis* ATCC® 29212 - susceptible
QC recommendations - lot/shipment[c]		*E. faecalis* ATCC® 51299 - resistant	*E. faecalis* ATCC® 51299 - resistant		*E. faecalis* ATCC® 51299 - resistant	*E. faecalis* ATCC® 51299 - resistant

Abbreviations: ATCC®, American Type Culture Collection; BHI, brain heart infusion; CSF, cerebrospinal fluid; HLAR, high-level aminoglycoside resistance; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control.

Footnotes

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

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

c. QC recommendations - routine

Test negative (susceptible) QC strain:

- With each new lot/shipment of testing materials
- Weekly if the test is performed at least once a week and criteria for converting from daily to weekly QC testing have been met (see Subchapter 4.7.2.3 in M02[4] and M07[1])
- Daily if the test is performed less than once per week and/or if criteria for converting from daily to weekly QC testing have not been met

Table 3K
Test for High-Level Aminoglycoside Resistance in *Enterococcus* spp.

Table 3K. (Continued)

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

e. QC recommendations – lot/shipment

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

References for Table 3K

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2018.

2 Torres C, Tenorio C, Lantero M, Gastañares MJ, Baquero F. High-level penicillin resistance and penicillin-gentamicin synergy in *Enterococcus faecium*. *Antimicrob Agents Chemother*. 1993;37(11):2427-2431.

3 Murray BE. Vancomycin-resistant enterococci. *Am J Med*. 1997;102(3):284-293.

4 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

Table 4A-1. Disk Diffusion QC Ranges for Nonfastidious Organisms and Antimicrobial Agents Excluding β-Lactam Combination Agents[a]

Antimicrobial Agent	Disk Content	Disk Diffusion QC Ranges, mm		
		Escherichia coli ATCC®[b] 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 25923
Amikacin	30 µg	19-26	20-26	20-26
Ampicillin	10 µg	15-22	-	27-35
Azithromycin	15 µg	-	-	21-26
Azlocillin	75 µg	-	24-30	-
Aztreonam	30 µg	28-36	23-29	-
Carbenicillin	100 µg	23-29	18-24	-
Cefaclor	30 µg	23-27	-	27-31
Cefamandole	30 µg	26-32	-	26-34
Cefazolin	30 µg	21-27	-	29-35
Cefdinir	5 µg	24-28	-	25-32
Cefditoren	5 µg	22-28	-	20-28
Cefepime	30 µg	31-37	25-31	23-29
Cefetamet	10 µg	24-29	-	-
Cefiderocol	30 µg	25-31	22-31	-
Cefixime	5 µg	20-26	-	-
Cefmetazole	30 µg	26-32	-	25-34
Cefonicid	30 µg	25-29	-	22-28
Cefoperazone	75 µg	28-34	23-29	24-33
Cefotaxime	30 µg	29-35	18-22	25-31
Cefotetan	30 µg	28-34	-	17-23
Cefoxitin	30 µg	23-29	-	23-29
Cefpodoxime	10 µg	23-28	-	19-25
Cefprozil	30 µg	21-27	-	27-33
Ceftaroline	30 µg	26-34	-	26-35
Ceftazidime	30 µg	25-32	22-29	16-20
Ceftibuten	30 µg	27-35	-	-
Ceftizoxime	30 µg	30-36	12-17	27-35
Ceftobiprole	5 µg	25-31	-	20-27
Ceftriaxone	30 µg	29-35	17-23	22-28
Cefuroxime	30 µg	20-26	-	27-35
Cephalothin	30 µg	15-21	-	29-37
Chloramphenicol	30 µg	21-27	-	19-26
Cinoxacin	100 µg	26-32	-	-

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Table 4A-1. (Continued)

Antimicrobial Agent	Disk Content	Disk Diffusion QC Ranges, mm		
		Escherichia coli ATCC[®b] 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 25923
Ciprofloxacin	5 µg	29-38	25-33	22-30
Clarithromycin	15 µg	-	-	26-32
Clinafloxacin	5 µg	31-40	27-35	28-37
Clindamycin[c]	2 µg	-	-	24-30
Colistin	10 µg	11-17	11-17	-
Delafloxacin[d]	5 µg	28–35	23–29	32–40
Dirithromycin	15 µg	-	-	18-26
Doripenem	10 µg	27-35	28-35	33-42
Doxycycline	30 µg	18-24	-	23-29
Enoxacin	10 µg	28-36	22-28	22-28
Eravacycline	20 µg	17-24	-	19-26
Ertapenem	10 µg	29-36	13-21	24-31
Erythromycin[c]	15 µg	-	-	22-30
Faropenem	5 µg	20-26	-	27-34
Fleroxacin	5 µg	28-34	12-20	21-27
Fosfomycin[e]	200 µg	22-30	-	25-33
Fusidic acid	10 µg	-	-	24-32
Garenoxacin	5 µg	28-35	19-25	30-36
Gatifloxacin	5 µg	30-37	20-28	27-33
Gemifloxacin	5 µg	29-36	19-25	27-33
Gentamicin[f]	10 µg	19-26	17-23	19-27
Gepotidacin	10 µg	18-26	-	23-29
Grepafloxacin	5 µg	28-36	20-27	26-31
Iclaprim	5 µg	14-22	-	25-33
Imipenem[g]	10 µg	26-32	20-28	-
Kanamycin	30 µg	17-25	-	19-26
Lefamulin	20 µg	-	-	26-32
Levofloxacin	5 µg	29-37	19-26	25-30
Levonadifloxacin	10 µg	27-33[d]	17-23[d]	32-39[d]
Linezolid	30 µg	-	-	25-32[h]
Lomefloxacin	10 µg	27-33	22-28	23-29
Loracarbef	30 µg	23-29	-	23-31
Mecillinam	10 µg	24-30	-	-
Meropenem	10 µg	28-35	27-33	29-37
Minocycline	30 µg	19-25	-	25-30
Moxalactam	30 µg	28-35	17-25	18-24

Table 4A-1
Nonfastidious Disk Diffusion QC Excluding β-Lactam Combination Agents
M02

Table 4A-1. (Continued)

Antimicrobial Agent	Disk Content	Disk Diffusion QC Ranges, mm		
		Escherichia coli ATCC®[b] 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 25923
Moxifloxacin	5 µg	28-35	17-25	28-35
Nafcillin	1 µg	-	-	16-22
Nafithromycin	15 µg	-	-	25-31[d]
Nalidixic acid	30 µg	22-28	-	-
Netilmicin	30 µg	22-30	17-23	22-31
Nitrofurantoin	300 µg	20-25	-	18-22
Norfloxacin	10 µg	28-35	22-29	17-28
Ofloxacin	5 µg	29-33	17-21	24-28
Omadacycline	30 µg	22-28	-	22-30
Oxacillin	1 µg	-	-	18-24
Pefloxacin	5 µg	25-33	-	-
Penicillin	10 units	-	-	26-37
Piperacillin	100 µg	24-30	25-33	-
Plazomicin	30 µg	21-27	15-21	19-25
Polymyxin B	300 units	13-19	14-18	-
Quinupristin-dalfopristin	15 µg	-	-	21-28
Razupenem	10 µg	21-26	-	-[l]
Rifampin	5 µg	8-10	-	26-34
Solithromycin	15 µg	-	-	22-30
Sparfloxacin	5 µg	30-38	21-29	27-33
Streptomycin[f]	10 µg	12-20	-	14-22
Sulfisoxazole[j]	250 µg or 300 µg	15-23	-	24-34
Sulopenem	2 µg	24-30[d]	-	-
Tebipenem[g]	10 µg	30-37	20-26	-
Tedizolid[k]	2 µg	-	-	18-24[h]
Teicoplanin	30 µg	-	-	15-21
Telithromycin	15 µg	-	-	24-30
Tetracycline	30 µg	18-25	-	24-30
Ticarcillin	75 µg	24-30	21-27	-
Tigecycline	15 µg	20-27	9-13	20-25
Tobramycin	10 µg	18-26	20-26	19-29
Trimethoprim[j]	5 µg	21-28	-	19-26
Trimethoprim-sulfamethoxazole[j]	1.25/23.75 µg	23-29	-	24-32
Trospectomycin	30 µg	10-16	-	15-20
Trovafloxacin	10 µg	29-36	21-27	29-35
Ulifloxacin (prulifloxacin)[l]	5 µg	32-38	27-33	20-26
Vancomycin	30 µg	-	-	17-21

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

Table 4A-1. (Continued)

Footnotes

a. Refer to Table 4A-2 for QC of β-lactam combination agents.

b. ATCC® is a registered trademark of the American Type Culture Collection. Per ATCC® convention, the trademark symbol is used after "BAA" in each catalog number, in conjunction with the registered ATCC® name.

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

d. QC ranges were established using data from only one disk manufacturer. Disks from other manufacturers were not available at the time of testing.

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

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

g. *Klebsiella pneumoniae* ATCC® 700603 is a supplemental QC strain for testing QC of imipenem (25-33 mm) and tebipenem (26-32 mm).

h. Zones of inhibition for linezolid and tedizolid with *S. aureus* ATCC® 25923 should be read using transmitted light.

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

j. These agents can be affected by excess levels of thymidine and thymine. See M02,[1] Subchapter 3.1.1.2 for guidance, should a problem with QC occur.

k. *E. faecalis* ATCC® 29212 is a supplemental QC strain for testing QC of tedizolid (14-21 mm) to assist with reading.

l. Ulifloxacin is the active metabolite of the prodrug prulifloxacin. Only ulifloxacin should be used for antimicrobial susceptibility testing.

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

Reference for Table 4A-1

[1] CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

Table 4B. Disk Diffusion QC Ranges for Fastidious Organisms

Antimicrobial Agent	Disk Content	Disk Diffusion QC Ranges, mm			
		Haemophilus influenzae ATCC® 49247	*Haemophilus influenzae* ATCC® 49766	*Neisseria gonorrhoeae* ATCC® 49226	*Streptococcus pneumoniae* ATCC® 49619[b]
Amoxicillin-clavulanate[c]	20/10 µg	15-23	-	-	-
Ampicillin	10 µg	13-21	-	-	30-36
Ampicillin-sulbactam	10/10 µg	14-22	-	-	-
Azithromycin	15 µg	13-21	-	30-38	19-25
Aztreonam	30 µg	30-38	-	-	-
Cefaclor	30 µg	-	25-31	-	24-32
Cefdinir	5 µg	-	24-31	40-49	26-31
Cefditoren	5 µg	25-34	-	-	27-35
Cefepime	30 µg	25-31	-	37-46	28-35
Cefetamet	10 µg	23-28	-	35-43	-
Cefixime	5 µg	25-33	-	37-45	16-23
Cefmetazole	30 µg	16-21	-	31-36	-
Cefonicid	30 µg	-	30-38	-	-
Cefotaxime	30 µg	31-39	-	38-48	31-39
Cefotetan	30 µg	-	-	30-36	-
Cefoxitin	30 µg	-	-	33-41	-
Cefpodoxime	10 µg	25-31	-	35-43	28-34
Cefprozil	30 µg	-	20-27	-	25-32
Ceftaroline	30 µg	29-39	-	-	31-41
Ceftaroline-avibactam[d]	30/15 µg	30-38	-	-	-
Ceftazidime	30 µg	27-35	-	35-43	-
Ceftazidime-avibactam[d]	30/20 µg	28-34	-	-	23-31
Ceftibuten	30 µg	29-36	-	-	-
Ceftizoxime	30 µg	29-39	-	42-51	28-34
Ceftobiprole[e]	30 µg	28-36	30-38	-	33-39
Ceftolozane-tazobactam[d]	30/10 µg	23-29	-	-	21-29
Ceftriaxone	30 µg	31-39	-	39-51	30-35
Cefuroxime	30 µg	-	28-36	33-41	-
Cephalothin	30 µg	-	-	-	26-32
Chloramphenicol	30 µg	31-40	-	-	23-27
Ciprofloxacin	5 µg	34-42	-	48-58	-
Clarithromycin	15 µg	11-17	-	-	25-31
Clinafloxacin	5 µg	34-43	-	-	27-34
Clindamycin	2 µg	-	-	-	19-25
Delafloxacin	5 µg	40–51	-	-	28-36[f]
Dirithromycin	15 µg	-	-	-	18-25
Doripenem	10 µg	21-31	-	-	30-38
Doxycycline	30 µg	-	-	-	25-34
Enoxacin	10 µg	-	-	43-51	-
Eravacycline	20 µg	-	-	-	23-30
Ertapenem[e]	10 µg	20-28	27-33	-	28-35

Table 4B. (Continued)

Antimicrobial Agent	Disk Content	Disk Diffusion QC Ranges, mm			
		Haemophilus influenzae ATCC[aa] 49247	*Haemophilus influenzae* ATCC® 49766	*Neisseria gonorrhoeae* ATCC® 49226	*Streptococcus pneumoniae* ATCC® 49619[b]
Erythromycin	15 µg	-	-	-	25-30
Faropenem	5 µg	15-22	-	-	27-35
Fleroxacin	5 µg	30-38	-	43-51	-
Fusidic acid	10 µg	-	-	-	9-16
Garenoxacin	5 µg	33-41	-	-	26-33
Gatifloxacin	5 µg	33-41	-	45-56	24-31
Gemifloxacin	5 µg	30-37	-	-	28-34
Gepotidacin	10 µg	-	-	32-40	22-28
Grepafloxacin	5 µg	32-39	-	44-52	21-28
Iclaprim	5 µg	24-33	-	-	21-29
Imipenem	10 µg	21-29	-	-	-
Lefamulin	20 µg	22-28	-	-	19-27
Levofloxacin	5 µg	32-40	-	-	20-25
Levonadifloxacin	10 µg	33-41[f]	-	-	24-31[f]
Linezolid	30 µg	-	-	-	25-34
Lomefloxacin	10 µg	33-41	-	45-54	-
Loracarbef	30 µg	-	26-32	-	22-28
Meropenem	10 µg	20-28	-	-	28-35
Moxifloxacin	5 µg	31-39	-	-	25-31
Nafithromycin	15 µg	16-20[f]	-	-	25-31[f]
Nitrofurantoin	300 µg	-	-	-	23-29
Norfloxacin	10 µg	-	-	-	15-21
Ofloxacin	5 µg	31-40	-	43-51	16-21
Omadacycline	30 µg	21-29	-	-	24-32
Oxacillin	1 µg	-	-	-	≤12[g]
Penicillin	10 units	-	-	26-34	24-30
Piperacillin-tazobactam	100/10 µg	33-38	-	-	-
Quinupristin-dalfopristin	15 µg	15-21	-	-	19-24
Razupenem	10 µg	24-30	-	-	29-36
Rifampin	5 µg	22-30	-	-	25-30
Solithromycin	15 µg	16-23	-	33-43	25-33
Sparfloxacin	5 µg	32-40	-	43-51	21-27
Spectinomycin	100 µg	-	-	23-29	-
Tedizolid	2 µg	-	-	-	18-25
Telithromycin	15 µg	17-23	-	-	27-33
Tetracycline	30 µg	14-22	-	30-42	27-31
Tigecycline	15 µg	23-31	-	30-40	23-29
Trimethoprim-sulfamethoxazole	1.25/23.75 µg	24-32	-	-	20-28
Trospectomycin	30 µg	22-29	-	28-35	-
Trovafloxacin	10 µg	32-39	-	42-55	25-32
Vancomycin	30 µg	-	-	-	20-27

Table 4B
Fastidious Disk Diffusion QC
M02

Table 4B. (Continued)

Disk Diffusion Testing Conditions for Clinical Isolates and Performance of QC

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

Abbreviations: ATCC®, American Type Culture Collection; HTM, *Haemophilus* test medium; MHA, Mueller-Hinton agar; MH-F agar, Mueller-Hinton fastidious agar; QC, quality control.

Footnotes

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

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

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

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

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

f. QC ranges for delafloxacin, levonadifloxacin, and nafithromycin were established using data from only one disk manufacturer. Disks from other manufacturers were not available at the time of testing.

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

Table 4C. Disk Diffusion Reference Guide to QC Frequency

This table summarizes the suggested QC frequency when modifications are made to antimicrobial susceptibility test systems (refer to CLSI document EP23™[1]). It applies only to antimicrobial agents for which satisfactory results have been obtained with either the 15-replicate (3- × 5-day) plan or 20 or 30 consecutive test day plan. Otherwise QC is required each test day.

Test Modification	Recommended QC Frequency			Comments
	1 Day	5 Days	15-Replicate Plan or 20- or 30-Day Plan	
Disks				
Use new shipment or lot number.	X			
Use new manufacturer.	X			
Addition of new antimicrobial agent to existing system.			X	In addition, perform in-house verification studies.
Media (prepared agar plates)				
Use new shipment or lot number.	X			
Use new manufacturer.		X		
Inoculum preparation				
Convert inoculum preparation/ standardization to use of a device that has its own QC protocol.		X		**Example:** Convert from visual adjustment of turbidity to use of a photometric device for which a QC procedure is provided.
Convert inoculum preparation/ standardization to a method that depends on user technique.			X	**Example:** Convert from visual adjustment of turbidity to another method that is not based on a photometric device.
Measuring zones				
Change method of measuring zones.			X	**Example:** Convert from manual zone measurements to automated zone reader. In addition, perform in-house verification studies.
Instrument/software (eg, automated zone reader)				
Software update that affects AST results		X		Monitor all drugs, not just those implicated in software modification.
Repair of instrument that affects AST results	X			Depending on extent of repair (eg, critical component such as the photographic device), additional testing may be appropriate (eg, 5 days).

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

Table 4C. (Continued)

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

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

NOTE 3: For troubleshooting out-of-range results, refer to M02,[2] Subchapter 4.8 and M100 Table 4D. Additional information is available in Appendix C (eg, QC organism characteristics, QC testing recommendations).

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

References for Table 4C

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

2 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

Table 4C
Disk Diffusion QC Testing Frequency
M02

Table 4D. Disk Diffusion Troubleshooting Guide

This table provides guidance for troubleshooting and corrective action for out-of-range QC, primarily using antimicrobial susceptibility tests with MHA. Refer to M02,[1] Chapter 4, for additional information. Out-of-range QC tests are often the result of contamination or the use of an incorrect QC strain; corrective action should first include repeating the test with a pure culture of a freshly subcultured QC strain. If the issue is unresolved, this troubleshooting guide should be consulted regarding additional suggestions for troubleshooting out-of-range QC results and unusual clinical isolate results. In addition, see general corrective action outlined in M02[1] and notify manufacturers of potential product problems.

General Comment

(1) QC organism maintenance: Avoid repeated subcultures. Retrieve new QC strain from stock (refer to M02,[1] Subchapter 4.4). If using lyophilized strains, follow the maintenance recommendations of the manufacturer.

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
β-LACTAMS				
β-lactam combination agents	*A. baumannii* ATCC® 13304 *E. coli* ATCC® 35218 *E. coli* ATCC® 13353 *K. pneumoniae* ATCC® 700603 *K. pneumoniae* ATCC® BAA-1705™	Zone too large or susceptible for single β-lactam agent; in range for combination β-lactam agent	Spontaneous loss of the plasmid encoding the β-lactamase	Obtain new frozen or lyophilized stock culture. Use other routine QC strains (if available). These strains should be stored at −60°C or below, and frequent subcultures should be avoided. **NOTE:** *K. pneumoniae* BAA-2814™ is stable and does not require QC integrity check.
β-lactam combination agents	*A. baumannii* ATCC® 13304 *E. coli* ATCC® 35218 *E. coli* ATCC® 13353 *K. pneumoniae* ATCC® 700603 *K. pneumoniae* ATCC® BAA-1705™ *K. pneumoniae* ATCC® BAA-2814™	Zone too small or resistant for both the single β-lactam agent and the combination β-lactam agent	Antimicrobial agent is degrading.	Use alternative lot of test materials. Check storage and package integrity. Imipenem and clavulanate are especially labile.
Carbenicillin	*P. aeruginosa* ATCC® 27853	Zone too small	QC strain develops resistance after repeated subculture.	See general comment (1) on QC strain maintenance.
Cefepime	*A. baumannii* NCTC 13304 *E. coli* NCTC 13353	QC strain integrity test	Discrete colonies may grow within the zone of inhibition when this organism is tested with cefepime 30-µg disk.	If this occurs, measure the colony-free inner zone.
Imipenem	*K. pneumoniae* ATCC® BAA-1705™ *K. pneumoniae* ATCC® BAA-2814™	QC strain integrity test	Discrete colonies may grow within the zone of inhibition when this organism is tested with cefepime. 30-µg disk.	If this occurs, measure the colony-free inner zone.
Penicillins	Any	Zone too large	pH of media too low	Acceptable pH range = 7.2-7.4 Avoid CO_2 incubation, which lowers pH.
Penicillins	Any	Zone too small	pH of media too high	Acceptable pH range = 7.2-7.4

Table 4D. (Continued)

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
NON-β-LACTAMS				
β-lactam group	Any	Zone initially acceptable, but decreases to possibly be out of range over time	Imipenem, clavulanate, and cefaclor are especially labile. Disks have lost potency.	Use alternative lot of disks. Check storage conditions and package integrity.
Aminoglycosides Quinolones	Any	Zone too small	pH of media too low	Acceptable pH range = 7.2-7.4 Avoid CO_2 incubation, which lowers pH.
	Any	Zone too large	pH of media too high	Acceptable pH range = 7.2-7.4
Aminoglycosides	*P. aeruginosa* ATCC® 27853	Zone too small	Ca++ and/or Mg++ content too high	Use alternative lot of media.
Aminoglycosides	*P. aeruginosa* ATCC® 27853	Zone too large	Ca++ and/or Mg++ content too low	Use alternative lot of media.
Clindamycin Macrolides	*S. aureus* ATCC® 25923	Zone too small	pH of media too low	Acceptable pH range = 7.2-7.4 Avoid CO_2 incubation, which lowers pH.
	S. aureus ATCC® 25923	Zone too large	pH of media too high	Acceptable pH range = 7.2-7.4
Quinolones	Any	Zone too small	pH of media too low	Acceptable pH range = 7.2-7.4 Avoid CO_2 incubation, which lowers pH.
Quinolones	Any	Zone too large	pH of media too high	Acceptable pH range = 7.2-7.4
Tedizolid	*E. faecalis* ATCC® 29212	Zone with *Enterococcus* spp. is difficult to read	Light growth on MHA	*E. faecalis* ATCC® 29212 is provided as supplemental QC to assist in personnel training and assessment of proper reading. Measure zone edge where there is a significant decrease in density of growth when using transmitted light as illustrated in the photographs.[b]
Tetracyclines	Any	Zone too large	pH of media too low	Acceptable pH range = 7.2-7.4 Avoid CO_2 incubation, which lowers pH.
Tetracyclines	Any	Zone too small	pH of media too high	Acceptable pH range = 7.2-7.4
Tetracyclines	Any	Zone too small	Ca++ and/or Mg++ content too high	Use alternative lot of media.
Tetracyclines	Any	Zone too large	Ca++ and/or Mg++ content too low	Use alternative lot of media.
Sulfonamides Trimethoprim Trimethoprim-sulfamethoxazole	*E. faecalis* ATCC® 29212	Zone ≤ 20 mm	Media too high in thymidine content	Use alternative lot of media.

Table 4D. (Continued)

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
ALL AGENTS				
Various	*S. pneumoniae* ATCC® 49619	Zones too large Lawn of growth scanty	Inoculum source plate too old and contains too many nonviable cells. Plate used to prepare inoculum should be 18-20 hours.	Subculture QC strain and repeat QC test or retrieve new QC strain from stock.
Various	Various	Zone too small	Contamination Use of magnification to read zones	Measure zone edge with visible growth detected with unaided eye. Subculture to determine purity and repeat if necessary.
Various	Any	Many zones too small	Inoculum too heavy Error in inoculum preparation Media depth too thick	Repeat using McFarland 0.5 turbidity standard or standardizing device. Check expiration date and proper storage if using barium sulfate or latex standards. Use agar with depth approximately 4 mm. Recheck alternate lots of MHA.
Various	Any	One or more zones too small or too large	Measurement error Transcription error Random defective disk Disk not pressed firmly against agar	Recheck readings for measurement or transcription errors. Retest. If retest results are out of range and no errors are detected, initiate corrective action.
Various	Various	Zone too large	Did not include lighter growth in zone measurement (eg, double zone, fuzzy zone edge)	Measure zone edge with visible growth detected with unaided eye.
Various	Any	QC results from one strain are out of range, but results from other QC strain(s) is in range with the same antimicrobial agent.	One QC strain may be a better indicator of a QC problem.	Retest this strain to confirm reproducibility of acceptable results. Evaluate with alternative strains with known MICs. Initiate corrective action with problem QC strain/antimicrobial agent(s).
Various	Any	QC results from two strains are out of range with the same antimicrobial agent.	A problem with the disk	Use alternative lot of disks. Check storage conditions and package integrity.
Various	Any	Zones overlap.	Too many disks per plate	Place no more than 12 disks on a 150-mm plate and 5 disks on a 100-mm plate; for some fastidious bacteria that produce large zones, use fewer.

Abbreviations: ATCC®, American Type Culture Collection; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; NCTC, National Collection of Type Cultures; pH, negative logarithm of hydrogen ion concentration; QC, quality control.

Table 5A-1. MIC QC Ranges for Nonfastidious Organisms and Antimicrobial Agents Excluding β-Lactam Combination Agents[a]

Antimicrobial Agent	MIC QC Ranges, µg/mL			
	Escherichia coli ATCC[ab] 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 29213	*Enterococcus faecalis* ATCC® 29212
Amikacin	0.5-4	1-4	1-4	64-256
Amikacin-fosfomycin (5:2)[c]	0.25/0.1–2/0.8	1/0.4–8/3.2	0.5/0.2–4/1.6	32/12.8–128/51.2
Amoxicillin	-	-	-	-
Ampicillin	2-8	-	0.5-2	0.5-2
Azithromycin	-	-	0.5-2	-
Azlocillin	8-32	2-8	2-8	1-4
Aztreonam	0.06-0.25	2-8	-	-
Besifloxacin	0.06-0.25	1-4	0.016-0.06	0.06-0.25
Biapenem	0.03-0.12	0.5-2	0.03-0.12	-
Cadazolid	-	-	0.06–0.5	0.06–0.25
Carbenicillin	4-16	16-64	2-8	16-64
Cefaclor	1-4	-	1-4	-
Cefamandole	0.25-1	-	0.25-1	-
Cefazolin	1-4	-	0.25-1	-
Cefdinir	0.12-0.5	-	0.12-0.5	-
Cefditoren	0.12-1	-	0.25-2	-
Cefepime	0.016-0.12	0.5-4	1-4	-
Cefetamet	0.25-1	-	-	-
Cefiderocol[d]	0.06-0.5	0.06-0.5	-	-
Cefixime	0.25-1	-	8-32	-
Cefmetazole	0.25-1	> 32	0.5-2	-
Cefonicid	0.25-1	-	1-4	-
Cefoperazone	0.12-0.5	2-8	1-4	-
Cefotaxime	0.03-0.12	8-32	1-4	-
Cefotetan	0.06-0.25	-	4-16	-
Cefoxitin	2-8	-	1-4	-
Cefpodoxime	0.25-1	-	1-8	-
Cefprozil	1-4	-	0.25-1	-
Ceftaroline	0.03-0.12	-	0.12-0.5	0.25-2[e]
Ceftazidime	0.06-0.5	1-4	4-16	-
Ceftibuten	0.12-0.5	-	-	-
Ceftizoxime	0.03-0.12	16-64	2-8	-
Ceftobiprole	0.03-0.12	1-4	0.12-1	0.06-0.5
Ceftriaxone	0.03-0.12	8-64	1-8	-
Cefuroxime	2-8	-	0.5-2	-
Cephalothin	4-16	-	0.12-0.5	-

Table 5A-1. (Continued)

Antimicrobial Agent	MIC QC Ranges, µg/mL			
	Escherichia coli ATCC[ab] 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 29213	*Enterococcus faecalis* ATCC® 29212
Chloramphenicol	2-8	-	2-16	4-16
Cinoxacin	2-8	-	-	-
Ciprofloxacin[f]	0.004-0.016	0.12-1	0.12-0.5	0.25-2
Clarithromycin	-	-	0.12-0.5	-
Clinafloxacin	0.002-0.016	0.06-0.5	0.008-0.06	0.03-0.25
Clindamycin[g]	-	-	0.06-0.25	4-16
Colistin[h]	0.25-2	0.5-4	-	-
Dalbavancin[i]	-	-	0.03-0.12	0.03-0.12
Daptomycin[j]	-	-	0.12-1	1-4
Delafloxacin	0.008–0.03	0.12–0.5	0.001–0.008	0.016–0.12
Dirithromycin	-	-	1-4	-
Doripenem	0.016-0.06	0.12-0.5	0.016-0.06	1-4
Doxycycline	0.5-2	-	0.12-0.5	2-8
Enoxacin	0.06-0.25	2-8	0.5-2	2-16
Eravacycline	0.016-0.12	2-16	0.016-0.12	0.016-0.06
Ertapenem	0.004-0.016	2-8	0.06-0.25	4-16
Erythromycin[g]	-	-	0.25-1	1-4
Exebacase[k]	-	-	0.25-2	8-64
Faropenem	0.25-1	-	0.03-0.12	-
Fidaxomicin	-	-	2-16	1-4
Finafloxacin	0.004-0.03	1-8	0.03-0.25	0.25-1
Fleroxacin	0.03-0.12	1-4	0.25-1	2-8
Fosfomycin[l]	0.5-2	2-8	0.5-4	32-128
Fusidic acid	-	-	0.06-0.25	-
Garenoxacin	0.004-0.03	0.5-2	0.004-0.03	0.03-0.25
Gatifloxacin	0.008-0.03	0.5-2	0.03-0.12	0.12-1.0
Gemifloxacin	0.004-0.016	0.25-1	0.008-0.03	0.016-0.12
Gentamicin[m]	0.25-1	0.5-2	0.12-1	4-16
Gepotidacin	1-4	-	0.12-1	**1-4**
Grepafloxacin	0.004-0.03	0.25-2.0	0.03-0.12	0.12-0.5
Iclaprim	1-4	-	0.06-0.25	0.004-0.03
Imipenem	0.06-0.**5**	1-4	0.016-0.06	0.5-2
Kanamycin	1-4	-	1-4	16-64
Lefamulin	–	–	0.06-0.25	–
Levofloxacin	0.008-0.06	0.5-4	0.06-0.5	0.25-2
Levonadifloxacin	0.03–0.25	0.5–4	0.008–0.03	-
Linezolid[n]	-	-	1-4	1-4
Lomefloxacin	0.03-0.12	1-4	0.25-2	2-8
Loracarbef	0.5-2	> 8	0.5-2	-

Table 5A-1. (Continued)

Antimicrobial Agent	MIC QC Ranges, µg/mL			
	Escherichia coli ATCC[®b] 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 29213	*Enterococcus faecalis* ATCC® 29212
Mecillinam	0.03-0.25[o]	-	-	-
Meropenem	0.008-0.06	0.12-1	0.03-0.12	2-8
Minocycline[f]	0.25-1	-	0.06-0.5	1-4
Moxalactam	0.12-0.5	8-32	4-16	-
Moxifloxacin	0.008-0.06	1-8	0.016-0.12	0.06-0.5
Nafcillin	-	-	0.12-0.5	2-8
Nafithromycin	-	-	0.06-0.25	0.016-0.12
Nalidixic acid[f]	1-4	-	-	-
Netilmicin	≤0.5-1	0.5-8	≤0.25	4-16
Nitrofurantoin	4-16	-	8-32	4-16
Norfloxacin	0.03-0.12	1-4	0.5-2	2-8
Ofloxacin	0.016-0.12	1-8	0.12-1	1-4
Omadacycline[p]	0.25-2	-	0.12-1	0.06-0.5
Oritavancin[l]	-	-	0.016-0.12	0.008-0.03
Oxacillin	-	-	0.12-0.5	8-32
Ozenoxacin	-	-	0.001-0.004	**0.016**-0.06
Penicillin	-	-	0.25-2	1-4
Pexiganan	2-8	2-16	8-32	16-64
Piperacillin	1-4	1-8	1-4	1-4
Plazomicin	0.25-2	1-4	0.25-2	-
Polymyxin B	0.25-2	0.5-2	-	-
Quinupristin-dalfopristin	-	-	0.25-1	2-8
Razupenem	0.06-0.5	-	0.008-0.03	0.25-1
Rifampin	4-16	16-64	0.004-0.016	0.5-4
Solithromycin	-	-	0.03-0.12	0.016-0.06
Sparfloxacin	0.004-0.016	0.5-2	0.03-0.12	0.12-0.5
Sulfisoxazole[f,q]	8-32	-	32-128	32-128
Sulopenem	0.016-0.06	-	0.016-0.12	2-8
Tebipenem	0.008-0.03	1-8	0.01**6**-0.06	0.25-1
Tedizolid[r]	-	-	0.12-1	0.25-1
Teicoplanin	-	-	0.25-1	0.25-1
Telavancin[l]	-	-	0.03-0.12	0.03-0.12
Telithromycin	-	-	0.06-0.25	0.016-0.12
Tetracycline	0.5-2	8-32	0.12-1	8-32
Ticarcillin	4-16	8-32	2-8	16-64
Tigecycline[p]	0.03-0.25	-	0.03-0.25	0.03-0.12
Tobramycin	0.25-1	0.25-1	0.12-1	8-32

Table 5A-1. (Continued)

Antimicrobial Agent	MIC QC Ranges, µg/mL			
	Escherichia coli ATCC[ab] 25922	*Pseudomonas aeruginosa* ATCC® 27853	*Staphylococcus aureus* ATCC® 29213	*Enterococcus faecalis* ATCC® 29212
Trimethoprim[q]	0.5-2	>64	1-4	0.12-0.5
Trimethoprim-sulfamethoxazole[q] (1:19)	≤0.5/9.5	8/152-32/608	≤0.5/9.5	≤0.5/9.5
Trospectomycin	8-32	-	2-16	2-8
Trovafloxacin	0.004-0.016	0.25-2	0.008-0.03	0.06-0.25
Ulifloxacin (prulifloxacin)[s]	0.004-0.016	0.12-0.5	-	-
Vancomycin[t]	-	-	0.5-2	1-4
Zidebactam	0.06-0.25	1-8	-	-
Zoliflodacin	1-4	-	0.12-0.5	0.25-2

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

Footnotes

a. Refer to Table 5A-2 for QC of β-lactam combination agents.

b. ATCC® is a registered trademark of the American Type Culture Collection. Per ATCC® convention, the trademark symbol is used after "BAA" in each catalog number, in conjunction with the registered ATCC® name.

c. QC ranges reflect MICs obtained when medium is supplemented with 25 µg/mL of glucose-6-phosphate.

d. QC ranges reflect MICs obtained when CAMHB is iron depleted. Chelation is used for iron depletion, which also removes other cations (ie, calcium, magnesium, and zinc). Following this process, cations are added back to concentrations of calcium 20-25 mg/L, magnesium 10-12.5 mg/L, and zinc 0.5-1.0 mg/L.

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

f. QC limits for *E. coli* ATCC® 25922 with ciprofloxacin, nalidixic acid, minocycline, and sulfisoxazole when tested in CAMHB with 2.5% to 5% lysed horse blood incubated either in ambient air or 5% CO_2 (when testing *N. meningitidis*) are the same as those listed in Table 5A-1.

g. When the erythromycin/clindamycin combination well for detecting inducible clindamycin resistance (ICR) is used, *S. aureus* ATCC® BAA-977™ (containing inducible *erm*A-mediated resistance) and *S. aureus* ATCC® 29213 or *S. aureus* ATCC® BAA-976™ (containing *msr*A-mediated macrolide-only efflux) are recommended for QC purposes. *S. aureus* ATCC® BAA-977™ should demonstrate ICR (ie, growth in the well), whereas *S. aureus* ATCC® 29213 and *S. aureus* ATCC® BAA-976™ should not demonstrate ICR (ie, no growth in the well).

Table 5A-1. (Continued)

h. Additional QC strains and ranges for colistin include *E. coli* NCTC 13486 (1-4 µg/mL, mode 2) and *E. coli* ATCC® BAA-3170™ (formerly AR Bank #0349 *mcr-1*) (1-4 µg/mL, mode 2).

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

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

k. Exebacase QC ranges reflect MICs obtained when CAMHB is supplemented with 25% horse serum plus 0.5 mM DL-dithiothreitol (pH 7.2-7.4).

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

m. For control organisms for gentamicin and streptomycin high-level aminoglycoside tests for enterococci, see Table 3K.

n. QC range for *S. aureus* ATCC® 25923 with linezolid is 1-4 µg/mL; this strain exhibits less trailing, and MIC end points are easier to interpret. *S. aureus* ATCC® 25923 is considered a supplemental QC strain and is not required for routine QC of linezolid MIC tests.

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

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

q. Very medium-dependent, especially with enterococci.

r. QC range for *S. aureus* ATCC® 25923 with tedizolid is 0.12-0.5 µg/mL; this strain exhibits less trailing, and MIC end points are easier to interpret. *S. aureus* ATCC® 25923 is considered a supplemental QC strain and is not required for routine QC of tedizolid MIC tests.

s. Ulifloxacin is the active metabolite of the prodrug prulifloxacin. Only ulifloxacin should be used for antimicrobial susceptibility testing.

t. For QC organisms for vancomycin screen test for enterococci, see Table 3H.

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

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

Appendix F. Susceptible-Dose Dependent Interpretive Category

Abbreviations for Appendix F

AST	antimicrobial susceptibility testing
FDA	US Food and Drug Administration
MIC	minimal inhibitory concentration
QC	quality control
SDD	susceptible-dose dependent

Susceptible-dose dependent (SDD) is recommended instead of "intermediate" for several drug and organism combinations for which there are multiple approved or routinely used dosing options:

- Enterobacterales: cefepime, **piperacillin, and piperacillin-tazobactam**
- *Staphylococcus aureus*: ceftaroline
- *Enterococcus faecium*: daptomycin

SDD highlights the option of using higher doses or alternative dosing regimens by which to achieve a higher dose exposure for the treatment of infections caused by isolates when the minimal inhibitory concentration (MIC) or the zone diameter is in the SDD range.

What does SDD mean?

SDD is a category defined by a breakpoint that implies that susceptibility of an isolate depends on the dosing regimen that is used in the patient. To achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either MICs or zone diameters) are in the SDD category, it is necessary to use a dosing regimen (ie, higher doses, more frequent doses, or both) that results in higher drug exposure than that achieved with the dose that was used to establish the susceptible breakpoint. Consideration should be given to the maximum, literature-supported dosage regimens, because higher exposure gives the highest probability of adequate coverage of an SDD isolate. Appendix E lists the doses used when establishing SDD categories. The drug label should be consulted for recommended doses and adjustment for organ function.

NOTE: The concept of SDD has been included within the intermediate category definition for antimicrobial agents. However, this is often overlooked or not understood by clinicians and microbiologists when an intermediate result is reported. The SDD category may be assigned when doses well above those used to calculate the susceptible breakpoint are supported by the literature, widely used clinically, and/or approved and for which sufficient data to justify the designation exist and have been reviewed. When the intermediate category is used, its definition remains unchanged.

Glossary I (Part 1). β-Lactams: Class and Subclass Designations and Generic Names

In the late 1990s, several authorities were consulted to construct the glossary. The intention was to include all agents that appeared in M100, along with related agents available for human use. Since that time, agents have been added to the glossary as they were introduced to CLSI, and they do not need to be FDA cleared to be included. It cannot be assumed that the list is exhaustive, and some agents are no longer available for human use.

Antimicrobial Class	Antimicrobial Subclasses		Agents Included; Generic Names
Penicillins	Penicillinase-labile penicillins[a]	Penicillin	Penicillin
		Aminopenicillins	Amoxicillin Ampicillin
		Carboxypenicillins	Carbenicillin Ticarcillin
		Ureidopenicillins	Azlocillin Piperacillin
	Penicillinase-stable penicillins[b]		Cloxacillin Dicloxacillin Nafcillin Oxacillin
	Amdinocillin		Mecillinam
β-lactam combination agents			Amoxicillin-clavulanate Ampicillin-sulbactam Aztreonam-avibactam Aztreonam-nacubactam (1:1) Cefepime-enmetazobactam (4:1) Cefepime-nacubactam (1:1) Cefepime-taniborbactam Cefepime-tazobactam (1:1) Cefepime-zidebactam Ceftaroline-avibactam Ceftazidime-avibactam Ceftolozane-tazobactam Imipenem-relebactam Meropenem-nacubactam (1:1) Meropenem-vaborbactam Piperacillin-tazobactam Sulbactam-durlobactam Ticarcillin-clavulanate

Glossary I (Part 1). (Continued)

Antimicrobial Class	Antimicrobial Subclasses	Agents Included; Generic Names
Cephems (parenteral)	Cephalosporins I[c]	Cefazolin Cephalothin Cephapirin Cephradine
	Cephalosporins II[c]	Cefamandole Cefonicid Cefuroxime (parenteral)
	Cephalosporins III[c]	Cefoperazone Cefotaxime Ceftazidime Ceftizoxime Ceftriaxone
	Cephalosporins IV[c]	Cefepime Cefpirome
	Cephalosporins with anti-MRSA activity	Ceftaroline Ceftobiprole
	Cephamycins	Cefmetazole Cefotetan Cefoxitin
	Oxacephem	Moxalactam
	Siderophore cephalosporin	Cefiderocol
Cephems (oral)	Cephalosporins	Cefaclor Cefadroxil Cefdinir Cefditoren Cefetamet Cefixime Cefpodoxime Cefprozil Ceftibuten Cefuroxime (oral) Cephalexin Cephradine
	Carbacephem	Loracarbef
Monobactams		Aztreonam
Penems	Carbapenems	Biapenem Doripenem Ertapenem Imipenem Meropenem Razupenem Tebipenem
	Penems	Faropenem Sulopenem

Abbreviations: MRSA, methicillin (oxacillin)-resistant *Staphylococcus aureus*; FDA, US Food and Drug Administration.

Glossary I (Part 1). (Continued)

Footnotes

a. Hydrolyzed by staphylococcal penicillinase.

b. Not hydrolyzed by staphylococcal penicillinase.

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

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

Glossary I (Part 2). Non-β-Lactams: Class and Subclass Designations and Generic Names

In the late 1990s, several authorities were consulted to construct the glossary. The intention was to include all agents that appeared in M100, along with related agents available for human use. Since that time, agents have been added to the glossary as they were introduced to CLSI, and they do not need to be FDA cleared to be included. It cannot be assumed that the list is exhaustive, and some agents are no longer available for human use.

Antimicrobial Class	Antimicrobial Subclasses	Agents Included; Generic Names
Aminocyclitols		Spectinomycin
Aminoglycosides		Amikacin Gentamicin Kanamycin Netilmicin Plazomicin Streptomycin Tobramycin
Aminoglycoside-fosfomycin		Amikacin-fosfomycin
Ansamycins	Rifamycins	Rifabutin Rifapentine Rifampin Rifaximin
Lysins	Lysin with antistaphylococcal activity	Exebacase
Folate pathway antagonists	Dihydrofolate reductase inhibitors	Iclaprim Sulfonamides Trimethoprim Trimethoprim-sulfamethoxazole
	Sulfonamides	Sulfamethoxazole Sulfisoxazole
	Combination	Trimethoprim-sulfamethoxazole
Fosfomycins		Fosfomycin
Glycopeptides	Glycopeptide	Vancomycin
	Lipoglycopeptides	Dalbavancin Oritavancin Teicoplanin Telavancin
	Lipoglycodepsipeptide	Ramoplanin
Lincosamides		Clindamycin Lincomycin
Lipopeptides		Daptomycin Surotomycin
	Polymyxins	Colistin Polymyxin B
Macrocyclic lactone		Fidaxomicin

Glossary I (Part 2). (Continued)

Antimicrobial Class	Antimicrobial Subclasses	Agents Included; Generic Names
Macrolides		Azithromycin Clarithromycin Dirithromycin Erythromycin
	Fluoroketolide	Solithromycin
	Ketolides	Nafithromycin Telithromycin
Nitroheterocyclics	Nitrofuran	Nitrofurantoin
	Nitroimidazoles	Metronidazole Secnidazole Tinidazole
	Thiazolides	Nitazoxanide Tizoxanide
Oxazolidinones		Linezolid Tedizolid
Peptide	Magainin	Pexiganan
Phenicols		Chloramphenicol Thiamphenicol
Pleuromutilins		Lefamulin Retapamulin
Pseudomonic acid		Mupirocin
Quinolones		Cinoxacin Garenoxacin Nalidixic acid
	Benzoquinolizine	Levonadifloxacin
	Fluoroquinolones	Besifloxacin Ciprofloxacin Clinafloxacin Delafloxacin Enoxacin Finafloxacin Fleroxacin Gatifloxacin Gemifloxacin Grepafloxacin Levofloxacin Lomefloxacin Moxifloxacin Norfloxacin Ofloxacin Ozenoxacin Pefloxacin Sparfloxacin Trovafloxacin Ulifloxacin (prulifloxacin)

Glossary I (Part 2). (Continued)

Antimicrobial Class	Antimicrobial Subclasses	Agents Included; Generic Names
Quinolonyl oxazolidinone		Cadazolid
Spiropyrimidinetrione		Zoliflodacin
Steroid	Fusidane	Fusidic acid
Streptogramins		Quinupristin-dalfopristin
Tetracyclines		Doxycycline Minocycline Tetracycline
	Fluorocycline	Eravacycline
	Glycylcycline	Tigecycline
	Aminomethylcycline	Omadacycline
Triazaacenaphthylene		Gepotidacin

Abbreviation: FDA, US Food and Drug Administration.

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

Glossary II. Antimicrobial Agent Abbreviations, Routes of Administration, and Drug Class

In the late 1990s, several authorities were consulted to construct the glossary. The intention was to include all agents that appeared in M100, along with related agents available for human use. Since that time, agents have been added to the glossary as they were introduced to CLSI, and they do not need to be FDA cleared to be included. It cannot be assumed that the list is exhaustive, and some agents are no longer available for human use.

Antimicrobial Agent	Abbreviations[a,b]		Routes of Administration[c]				Drug Class or Subclass
	CLSI Recommended	In Use	PO	IM	IV	Topical	
Amikacin	AN	AN, AK, Ak, AMI, AMK, AKN		X	X		Aminoglycoside
Amikacin-fosfomycin	AKF	AKF	X[d]				Aminoglycoside-fosfomycin
Amoxicillin	AMX	AMX, Amx, AMOX, AC, AML, A	X				Penicillin
Amoxicillin-clavulanate	AMC	AMC, Amc, A/C, AUG, Aug, XL, AML	X				ß-lactam combination agent
Ampicillin	AM	AM, Am, AMP, AP	X	X	X		Penicillin
Ampicillin-sulbactam	SAM	SAM, A/S, AMS, AB			X		ß-lactam combination agent
Azithromycin	AZM	AZM, Azi, AZI, AZ, ATH	X		X		Macrolide
Azlocillin	AZL	AZ, Az, AZL		X	X		Penicillin
Aztreonam	ATM	ATM, AZT, Azt, AT, AZM			X		Monobactam
Aztreonam-avibactam	AZA	AZA			X		ß-lactam combination agent
Aztreonam-nacubactam	ANC	ANC			X		ß-lactam combination agent
Besifloxacin	BES	BES				X	Fluoroquinolone
Biapenem	BPM	BPM			X		Carbapenem
Cadazolid	CDZ	CDZ	X				Quinolonyl oxazolidinone
Carbenicillin (indanyl salt) Carbenicillin	CB	CB, Cb, BAR, CAR, CRB, PY	X	X	X		Penicillin
Cefaclor	CEC	CEC, CCL, Cfr, FAC, CF, CFC	X				Cephem
Cefadroxil	CFR	CFR, FAD, CDX	X				Cephem
Cefamandole	MA	MA, CM, Cfm, FAM, CMD		X	X		Cephem

Glossary II. (Continued)

Antimicrobial Agent	Abbreviations[a,b]		Routes of Administration[c]				Drug Class or Subclass
	CLSI Recommended	In Use	PO	IM	IV	Topical	
Cefazolin	CZ	CZ, CFZ, Cfz, FAZ, KZ, CZN		X	X		Cephem
Cefdinir	CDR	CDR, Cdn, DIN, CD, CFD	X				Cephem
Cefditoren	CDN	CDN, DIT, FD	X				Cephem
Cefepime	FEP	FEP, Cpe, PM, CPM		X	X		Cephem
Cefepime-enmetazobactam	FPE	FPE			X		β-lactam combination agent
Cefepime-nacubactam	**FNC**	**FNC**			X		β-lactam combination agent
Cefepime-taniborbactam	FTB	FTB			X		β-lactam combination agent
Cefepime-tazobactam	FPT	FPT			X		β-lactam combination agent
Cefepime-zidebactam	FPZ	FPZ			X		β-lactam combination agent
Cefetamet	CAT	CAT, FET	X				Cephem
Cefiderocol	FDC	FDC			X		Siderophore β-lactam
Cefixime	CFM	CFM, FIX, Cfe, IX	X				Cephem
Cefmetazole	CMZ	CMZ, CMZS, CMT, Cmz		X	X		Cephem
Cefonicid	CID	CID, Cfc, FON, CPO		X	X		Cephem
Cefoperazone	CFP	CFP, Cfp, CPZ, PER, FOP, CP		X	X		Cephem
Cefotaxime	CTX	CTX, TAX, Cft, FOT, CT		X	X		Cephem
Cefotetan	CTT	CTT, CTN, Ctn, CTE, TANS, CN		X	X		Cephem
Cefoxitin	FOX	FOX, CX, Cfx, FX		X	X		Cephem
Cefpirome	CPO	CPO, CPR, CR		X	X		Cephem
Cefpodoxime	CPD	CPD, Cpd, POD, PX	X				Cephem
Cefprozil	CPR	CPR, CPZ, FP	X				Cephem
Ceftaroline	CPT	CPT, Cpt, CTR			X		Cephem
Ceftaroline-avibactam	CPA	CPA			X		β-lactam combination agent
Ceftazidime	CAZ	CAZ, Caz, TAZ, TZ		X	X		Cephem
Ceftazidime-avibactam	CZA	CZA			X		β-lactam combination agent

Glossary II. (Continued)

Antimicrobial Agent	Abbreviations[a,b]		Routes of Administration[c]				Drug Class or Subclass
	CLSI Recommended	In Use	PO	IM	IV	Topical	
Ceftibuten	CTB	CTB, TIB, CB, CFB, CFT	X				Cephem
Ceftizoxime	ZOX	ZOX, CZX, CZ, Cz, CTZ, TIZ		X	X		Cephem
Ceftobiprole	BPR	BPR			X		Cephem
Ceftolozane-tazobactam	CT	CT, C/T, CXT, CLT			X		β-lactam combination agent
Ceftriaxone	CRO	CRO, CTR, FRX, Cax, AXO, TX		X	X		Cephem
Cefuroxime (oral) Cefuroxime (parenteral)	CXM	CXM, CFX, ROX, Crm, FUR, XM	X	X	X		Cephem
Cephalexin	CN	CN, LEX, CFL, CL, CFX	X				Cephem
Cephalothin	CF	CF, Cf, CR, CL, CEP, CE, KF, CEF			X		Cephem
Cephapirin	CP	CP, HAP		X	X		Cephem
Cephradine	RAD	RAD, CH, CED, CE	X				Cephem
Chloramphenicol	C	C, CHL, CL	X		X		Phenicol
Cinoxacin	CIN	CIN, Cn	X				Quinolone
Ciprofloxacin	CIP	CIP, Cp, CI	X		X		Fluoroquinolone
Clarithromycin	CLR	CLR, CLM, CLA, Cla, CH	X				Macrolide
Clinafloxacin	CLX	CFN, CLX, LF, CFL	X		X		Fluoroquinolone
Clindamycin	CM	CC, CM, CD, Cd, CLI, DA	X	X	X		Lincosamide
Cloxacillin	CLO	CX, Clx, CLO, OB, OX	X	X	X		Penicillin
Colistin	CL	CL, CS, CT, CI, CO, COL			X		Lipopeptide
Dalbavancin	DAL	DAL			X		Lipoglycopeptide
Daptomycin	DAP	DAP, Dap, DPC			X		Lipopeptide
Delafloxacin	DLX	DLX, DFX	X		X		Fluoroquinolone
Dicloxacillin	DX	DX, DIC	X				Penicillin
Dirithromycin	DTM	DTM, DT, DIR	X				Macrolide
Doripenem	DOR	DOR, Dor			X		Carbapenem
Doxycycline	DO	DO, DOX, DC, DOXY, D, DX, Dox, DXT	X		X		Tetracycline

Glossary II. (Continued)

Antimicrobial Agent	Abbreviations[a,b]		Routes of Administration[c]				Drug Class or Subclass
	CLSI Recommended	In Use	PO	IM	IV	Topical	
Enoxacin	ENX	ENX, Enx, ENO, ENOX, ENO(F)	X				Fluoroquinolone
Ertapenem	ETP	ETP, Etp		X	X		Carbapenem
Eravacycline	ERV	ERV	X		X		Fluorocycline
Erythromycin	E	E, ERY, EM	X		X		Macrolide
Exebacase	EXE	EXE			X		Antistaphylococcal lysin
Faropenem	FPM	FAR, FARO, FPM, Faro	X				Penem
Fidaxomicin	FDX	FDX	X				Macrocyclic
Finafloxacin	FIN	FIN	X		X	X	Fluoroquinolone
Fleroxacin	FLE	FLE, Fle	X		X		Fluoroquinolone
Fosfomycin	FOS	FOS, FF, FO, FM, Fos	X				Fosfomycin
Fusidic acid	FA	FA, FC, FUS, FD, FU, FAD	X		X	X	Steroidal
Garenoxacin	GRN	GRN, Grn	X		X		Quinolone
Gatifloxacin	GAT	GAT, Gat, GA, GFLX	X		X		Fluoroquinolone
Gemifloxacin	GEM	GEM, Gem	X				Fluoroquinolone
Gentamicin Gentamicin synergy	GM	GM, Gm, CN, GEN GM500, HLG, Gms, GHLR, GMS		X	X		Aminoglycoside
Gepotidacin	GEP	GEP	X		X		Triazaacenaphthylene
Grepafloxacin	GRX	GRX, Grx, GRE, GP	X				Fluoroquinolone
Iclaprim	ICL	ICL, IP			X		Folate pathway antagonist
Imipenem	IPM	IPM, IMI, Imp, IP			X		Carbapenem
Imipenem-relebactam	IMR	IMR, IPR, I/R			X		β-lactam combination agents
Kanamycin	K	K, KAN, HLK, KM		X	X		Aminoglycoside
Lefamulin	LMU	LMU	X		X		Pleuromutilin
Levofloxacin	LVX	LVX, Lvx, LEV, LEVO, LE	X		X		Fluoroquinolone
Levonadifloxacin	LND	LND			X		Benzoquinolizine
Lincomycin	LIN	L, Lin, LIN, MY		X	X		Lincosamide
Linezolid	LZD	LNZ, LZ, LZD, Lzd	X		X		Oxazolidinone
Lomefloxacin	LOM	LOM, Lmf, LFLX, LOMX	X				Fluoroquinolone
Loracarbef	LOR	LOR, Lor	X				Cephem

Glossary II. (Continued)

Antimicrobial Agent	Abbreviations[a,b]		Routes of Administration[c]				Drug Class or Subclass
	CLSI Recommended	In Use	PO	IM	IV	Topical	
Mecillinam	MEC	MEC, Mec, MM, MEL	X				Penicillin
Meropenem	MEM	MEM, Mer, MERO, MRP, MP			X		Carbapenem
Meropenem-nacubactam	MNC	MNC			X		ß-lactam combination agent
Meropenem-vaborbactam	MEV	MEV			X		ß-lactam combination agent
Methicillin	ME	ME, MET, DP		X	X		Penicillin
Metronidazole	MET	MET, MTZ, MZ, MRD, MTR	X		X		Nitroimidazole
Minocycline	MI	MI, MIN, Min, MN, MNO, MC, MH	X		X		Tetracycline
Moxalactam	MOX	MOX, Mox		X	X		Cephem
Moxifloxacin	MXF	MXF, Mxf, MX	X		X		Fluoroquinolone
Mupirocin	MUP	MUP, MOP, MU, Mup, PUM				X	Pseudomonic acid
Nafcillin	NF	NF, NAF, Naf		X	X		Penicillin
Nafithromycin	ZMK	ZMK, ZWK	X				Ketolide
Nalidixic acid	NA	NA, NAL	X				Quinolone
Netilmicin	NET	NET, Nt, NC		X	X		Aminoglycoside
Nitazoxanide	NIT	NIT	X				Thiazolide
Nitrofurantoin	FM	FM, F/M, FD, Fd, FT, NIT, NI, F	X				Nitrofuran
Norfloxacin	NX	NX, NOV, NV, NO	X				Fluoroquinolone
Novobiocin	NB	NB				X	Aminocoumarin
Ofloxacin	OFL	OFL, OFX, Ofl, OF	X	X	X		Fluoroquinolone
Omadacycline	OMC	OMC	X		X		Tetracycline
Oritavancin	ORI	ORI			X		Lipoglycopeptide
Oxacillin	OX	OX, Ox, OXS, OXA	X	X	X		Penicillin
Ozenoxacin	OZN	OZN				X	Fluoroquinolone
Pefloxacin	PEF	PEF, PF, Pef, PE					Fluoroquinolone
Penicillin	P	P, PEN, PV, PG	X	X	X		Penicillin
Pexiganan	PEX	PEX, P/N				X	Peptide

Glossary II. (Continued)

Antimicrobial Agent	Abbreviations[a,b]		Routes of Administration[c]				Drug Class or Subclass
	CLSI Recommended	In Use	PO	IM	IV	Topical	
Piperacillin	PIP	PIP, PI, PP, Pi, PRL		X	X		Penicillin
Piperacillin-tazobactam	TZP	TZP, PTZ, P/T, PTc			X		ß-lactam combination agent
Plazomicin	PLZ	PLZ			X		Aminoglycoside
Polymyxin B	PB	PB, POL, PO			X		Lipopeptide
Quinupristin-dalfopristin	SYN	SYN, Syn, QDA, RP, QDF			X		Streptogramin
Ramoplanin	RAM	RAM	X				Lipoglycodepsipeptide
Razupenem	RZM	RZ, RZM			X		Carbapenem
Rifampin	RA	RA, RIF, Rif, RI, RD, RP, RFP	X		X		Ansamycin
Rifamycin	RIF	RF, RIF	X		X		Ansamycin
Rifapentine	**RPT**	**RPT**				**X**	**Pleuromutilin**
Rifaximin	**RFX**	**RFX**	X				Ansamycin
Secnidazole	SEC	SEC	X				Nitroimidazole
Solithromycin	SOL	SOL	X		X	X	Fluoroketolide
Sparfloxacin	SPX	SPX, Sfx, SPX, SO, SPFX	X				Fluoroquinolone
Spectinomycin	SPT	SPT, SPE, SC, SP, SH, SPC		X	X		Aminocyclitol
Streptomycin Streptomycin synergy	STS	STS, S, STR, StS, SM, ST2000, HLS, SHLR		X	X		Aminoglycoside
Sulbactam-durlobactam	SUD	SUD, SUL			**X**		ß-lactam combination agent
Sulfonamides	SSS	G, SSS, S3	X		X		Folate pathway antagonist (some PO only)
Sulopenem	SLP	SLP, SPM	X		X		Penem
Surotomycin	SUR	SUR	X				Lipopeptide
Tebipenem	TBP	TBP	X				Carbapenem
Tedizolid	TZD	TZD	X		X		Oxazolidinone
Teicoplanin	TEC	TEC, TPN, Tei, TEI, TP, TPL		X	X		Lipoglycopeptide
Telavancin	TLV	TLV, TLA			X		Lipoglycopeptide
Telithromycin	TEL	TEL	X				Ketolide
Tetracycline	TE	TE, Te, TET, TC	X		X		Tetracycline

Glossary II. (Continued)

Antimicrobial Agent	Abbreviations[a,b]		Routes of Administration[c]				Drug Class or Subclass
	CLSI Recommended	In Use	PO	IM	IV	Topical	
Thiamphenicol	TP	TP	X	X	X		Phenicol
Ticarcillin	TIC	TIC, TC, TI, Ti		X	X		Penicillin
Ticarcillin-clavulanate	TIM	TIM, Tim, T/C, TCC, TLc, TTC			X		ß-lactam combination agent
Tigecycline	TGC	TGC, Tgc			X		Glycylcycline
Tinidazole	TNZ	TNZ	X				Nitroimidazoles
Tinoxanide	TIN	TIN	X				Thiazolide
Tobramycin	TM	TM, NN, TO, To, TOB, TN		X	X		Aminoglycoside
Trimethoprim	TMP	TMP, T, TR, W,TM	X				Folate pathway antagonist
Trimethoprim-sulfamethoxazole	SXT	SXT, SxT, T/S, TS, COT	X		X		Folate pathway antagonist
Trospectomycin	TBR	TBR		X	X		Aminocyclitol
Trovafloxacin	TRO	TVA, Tva, TRV, TV, TRO	X		X		Fluoroquinolone
Ulifloxacin (prulifloxacin)	PRU	PRU, ULI	X				Fluoroquinolone
Vancomycin	VA	VA, Va, VAN, VCM	X		X		Glycopeptide
Zoliflodacin	ZFD	ZFD	X				Spiropyriminetrione

Abbreviations: FDA, US Food and Drug Administration; IM, intramuscular; IV, intravenous; PO, oral.

Footnotes

a. Abbreviations assigned to one or more diagnostic products in the United States. If no diagnostic product is available, abbreviation is that of the manufacturer.

b. Abbreviations used by antimicrobial susceptibility testing device manufacturers may differ from those recommended by CLSI.

c. As available in the United States.

d. Amikacin-fosfomycin is aerosolized and inhaled.

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

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

In the late 1990s, several authorities were consulted to construct the glossary. The intention was to include all agents that appeared in M100, along with related agents available for human use. Since that time, agents have been added to the glossary as they were introduced to CLSI, and they do not need to be FDA cleared to be included. It cannot be assumed that the list is exhaustive, and some agents are no longer available for human use.

Abbreviations	Antimicrobial Agents for Which Respective Abbreviations Are Used
AZ	Azithromycin, azlocillin
AZM	Azithromycin, aztreonam
CB, Cb	Ceftibuten, carbenicillin
CD, Cd	Clindamycin, cefdinir
CDN, Cdn	**Cefdinir, cefditoren**
CF, Cf	Cefaclor, cephalothin
CFM, Cfm	Cefixime, cefamandole
CFR, Cfr	Cefaclor, cefadroxil
CFX, Cfx	Cefoxitin, cefuroxime
CH	Clarithromycin, cephradine
CL	Cephalothin, chloramphenicol
CLX, Clx	**Clinafloxacin, cloxacillin**
CM	Clindamycin, cefamandole
CN, Cn	Cephalexin, cefotetan, cinoxacin, gentamicin
CP, Cp	Cephapirin, cefoperazone, ciprofloxacin
CPR	**Cefpirome, cefprozil**
CPZ	Cefprozil, cefoperazone
CT	**Ceftolozane-tazobactam, colistin**
CZ, Cz	Ceftizoxime, cefazolin
DX	Doxycycline, dicloxacillin
FO	Fleroxacin, fosfomycin
NIT	Nitazoxanide, nitrofurantoin
TC	Tetracycline, ticarcillin
TM	**Tobramycin, trimethoprim**

Abbreviation: FDA, US Food and Drug Administration.

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