Navigating CLSI Documents: M45 and M100

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OUTLINE

I. Navigating the M100 document

- A. Introductory sections do matter
- B. Comments, comments, comments
- C. Relevance of supplemental testing in Wisconsin
- D. Decisions (role playing) by the laboratory
- E. Additional resources in CLSI M100

II. M45 document for infrequently-isolated organisms

- A. Potential organisms to test
- B. How much testing can we really do?

The Small Roman Numerals

WHAT'S IN THERE?

- Overview of changes
- Processes for establishing breakpoints, quality control ranges
- CLSI reference vs. commercial methods
  CLSI reference vs. FDA breakpoints
- Breakpoint additions/revisions since 2010

CLSI M100-Ed32; 2022

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	

7 pages of this → audits of past laboratory reports antibiogram shifts

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BREAKPOINT REVISIONS FOR 2022

- Cefiderocol

  Disk diffusion *Enterobacterales* (only the I and R)
  Disk diffusion *Acinetobacter* spp. (S only)
  Both formats *Stenotrophomonas maltophilia* (S only)

- Piperacillin-tazobactam for *Enterobacterales*

  Disk diffusion, broth microdilution
  Intermediate → susceptible dose dependent

- Piperacillin for *Enterobacterales*

  Intermediate → susceptible dose dependent
  Broth microdilution; “lost” disk diffusion (for now)

SUSCEPTIBLE DOSE DEPENDENT

- Susceptible dose dependent (multiple regimens)
  - Implies that susceptibility of isolate is dependent on dosing regimen
  - Higher dose or more-frequent dosing results in higher drug exposure
- CLSI currently employs this for (Appendix F):

  Cefepime/*Enterobacterales*
  Ceftaroline/*Staphylococcus*
  (Piperacillin)-tazobactam/*Enterobacterales*
  Daptomycin/*Enterococcus*

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Instructions for Use of Tables

INSTRUCTIONS FOR USE (selected)

- Selecting antimicrobial agents for testing, reporting
- Breakpoint and interpretive category definitions
- Cumulative antibiograms (shout out to Ray)
- An “eye test” before reporting (then Appendix A)

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INSTRUCTIONS FOR USE (selected)

- Testing of repeat isolates (as little as 3-4 days)

3° cephems	*Klebsiella aerogenes* *Citrobacter* spp. *Serratia* spp.
All agents	*Pseudomonas aeruginosa*
Fluoroquinolones	Staphylococci

- Warning comments (examples)

  Active *in vitro*, not good *in vivo* (*Enterococcus* spp.)
  Don’t report from certain sites (stay tuned)

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BEYOND ROUTINE

- Supplemental

Supplemental Tests (Required)

Supplemental Test	Organisms	Test Description	Required for:	Table Location
Inducible clindamycin resistance	• *Staphylococcus* spp. • *S. pneumoniae* • *Streptococcus* spp. B-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
B-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

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BEYOND ROUTINE

- Screening

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.

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BEYOND ROUTINE

- Surrogate agent

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

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BEYOND ROUTINE

- Equivalent agent

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

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Joel Whitburn Presents
Billboard #1s: The '80s
Billboard

Table 1


#1
WE'RE #1

NON-FASTIDIOUS GROUPINGS (1A)

- Group A Primary test and report
- Group B Optional primary test, report selectively
- Group C Supplemental report selectively
- Group U Supplemental for urine only

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NON-FASTIDIOUS GROUPINGS (1A)

These exist for:

Enterobacterales
Pseudomonas aeruginosa (no group C or group U)
Acinetobacter spp. (no group C)
Burkholderia cepacia complex (no group U)
Stenotrophomonas maltophilia (no group U)
Other non-*Enterobacterales*
Staphylococcus spp.
Enterococcus spp.

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FASTIDIOUS GROUPINGS (1B)

- Group A Primary test and report
- Group B Optional primary test, report selectively
- Group C Supplemental report selectively

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FASTIDIOUS GROUPINGS (1B)

These exist for:

Haemophilus influenzae
Haemophilus parainfluenzae
Neisseria gonorrhoeae (no group B or no group C)
Streptococcus pneumoniae
β-hemolytic *Streptococcus*
viridans group *Streptococcus*

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EXAMPLE (and a promotion!!!)

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	
B-LACTAM COMBINATION AGENTS									
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	
Inv.	Cefiderocol	30 µg	≥15	11-14	≤10	≤4	8	≥16	(2) Breakpoints are based on a dosage regimen of 2 g every 8 h administered over 3 h.

Table 1A
Suggested Nonfastidious Groupings
M02 and M07

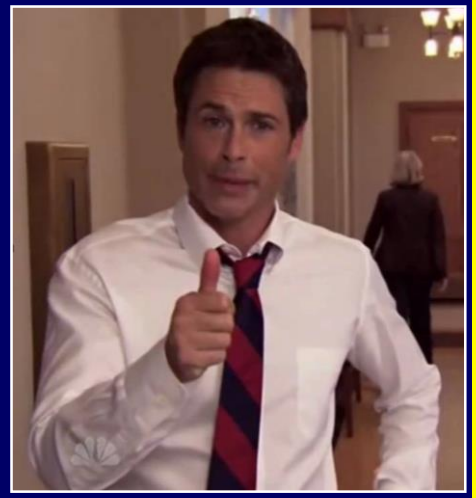

Table 1A. (Continued)

Acinetobacter spp.	*Burkholderia cepacia* complex	*Stenotrophomonas maltophilia*	Other Non-Enterobacterales[l,w]
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.			
Ampicillin-sulbactam	Levofloxacin[l]	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.[l]			
Amikacin	Ceftazidime	Ceftazidime[l]	Amikacin
Piperacillin-tazobactam	Minocycline		Aztreonam
Cefepime			Cefepime
Cefotaxime Ceftriaxone			Ciprofloxacin Levofloxacin
Cefiderocol		**Cefiderocol**	

CLSI M100-Ed31, 2021; CLSI M100-Ed32, 2022

ALSO ANAEROBES (1C)

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

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Table 2

APPROPRIATE MEDIUM

Table 2D
Enterococcus spp.
M02 and M07

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®a 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.

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APPROPRIATE INCUBATION

Table 2C
Staphylococcus spp.
M02 and M07

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®a 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.

(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.

CLSI M100-Ed32; 2022

TABLE 2

These exist for:

Enterobacterales
Pseudomonas aeruginosa
Acinetobacter spp.
Burkholderia cepacia complex
Stenotrophomonas maltophilia
Other non-*Enterobacterales*
Staphylococcus spp.
Enterococcus spp.

Haemophilus influenzae
Haemophilus parainfluenzae
Neisseria gonorrhoeae
Streptococcus pneumoniae
β-hemolytic *Streptococcus*
viridans group *Streptococcus*
Neisseria meningitidis
Anaerobes

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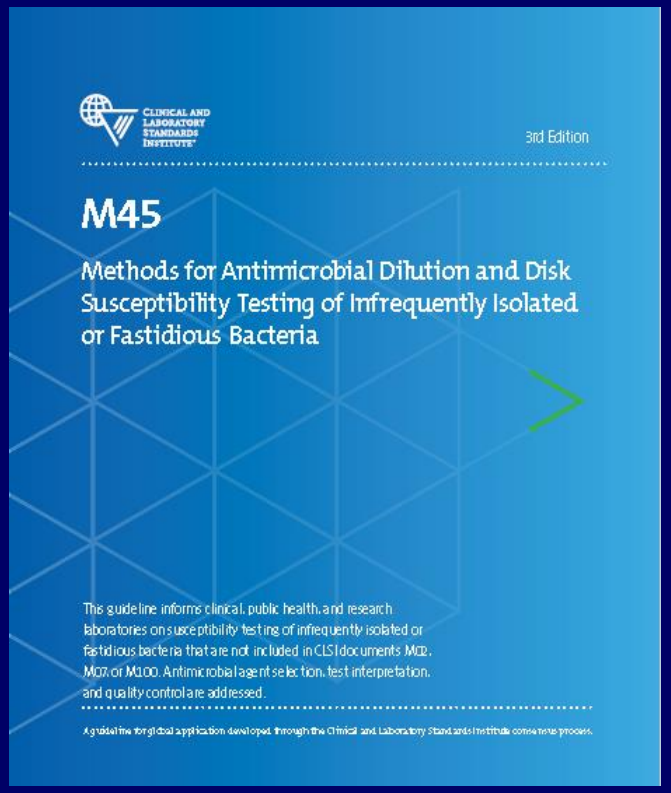
CAVEATS

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		
			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 a susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, or 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



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ASSISTS WITH *Staphylococcus* (2C)

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												

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ASSISTS WITH *Staphylococcus* (2C)

- *Staphylococcus aureus* and coagulase-negative staphylococci with MIC ≤ 0.12 (disk diffusion ≥ 29 mm) assessed for β-lactamase
- Positive nitrocefin-based results from induced growth (penicillin, cefoxitin) can be reported (resistant to penicillin, amino-, carboxy-, ureidopenicillins)
- Follow up negatives with zone-edge test (10 unit penicillin disk) or use zone-edge as primary assay (*S. aureus*)

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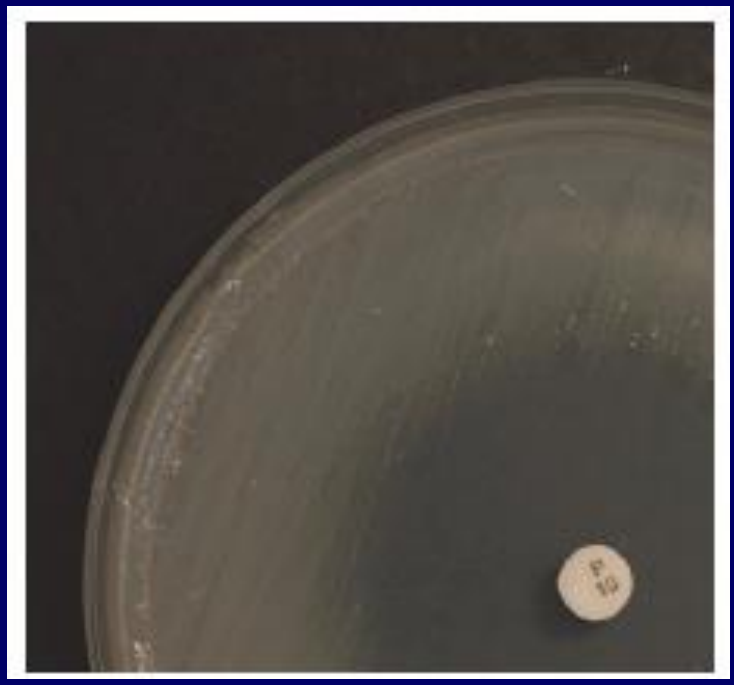
ZONE EDGE TEST (method in Table 3F)

Sharp
Cliff
β-lactamase-positive



Fuzzy
Beach
β-lactamase-negative

Perhaps not as pivotal with *S. lugdunensis* (β-lactamase promotes MIC > 0.12)

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ASSISTS WITH *Staphylococcus* (2C)

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]

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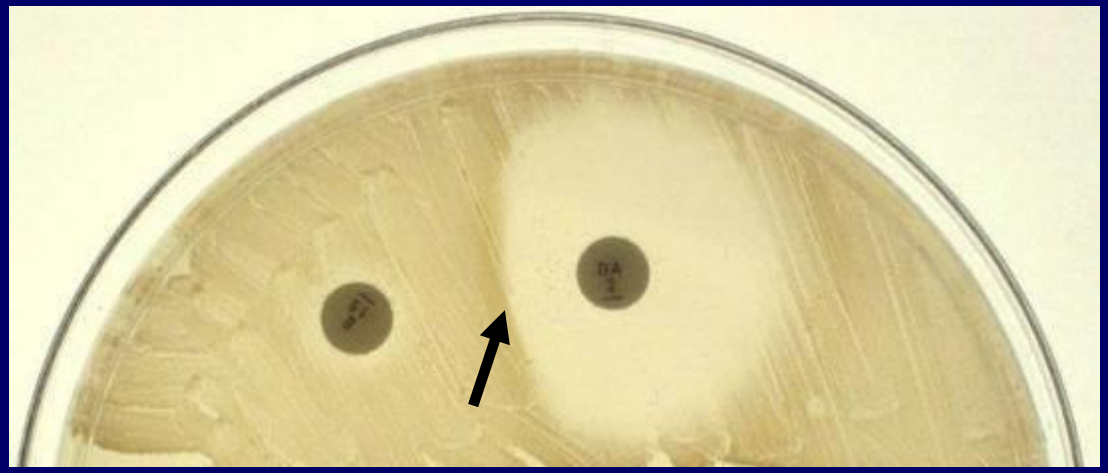
ASSISTS WITH *Staphylococcus* (2C)

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)**.



15-26 mm apart; Table 3I for method

"This isolate is presumed to be resistant based on the detection of ICR, as determined by testing clindamycin in combination with erythromycin."

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CLSI STILL FOLLOWING CDC

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 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	
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.

BIG ONE

Digging deeper →

Recent clarification →

CLSI M100-Ed32, 2022; MMWR 59 (RR-10):1-32, 2010

"DON'T YOU…FORGET ABOUT ME"

Table 2H-1
Streptococcus spp. B-Hemolytic Group
M02 and M07

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									

not for viridans group *Streptococcus* spp.
12 mm between disks

Table 2G
Streptococcus pneumoniae
M02 and M07

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).

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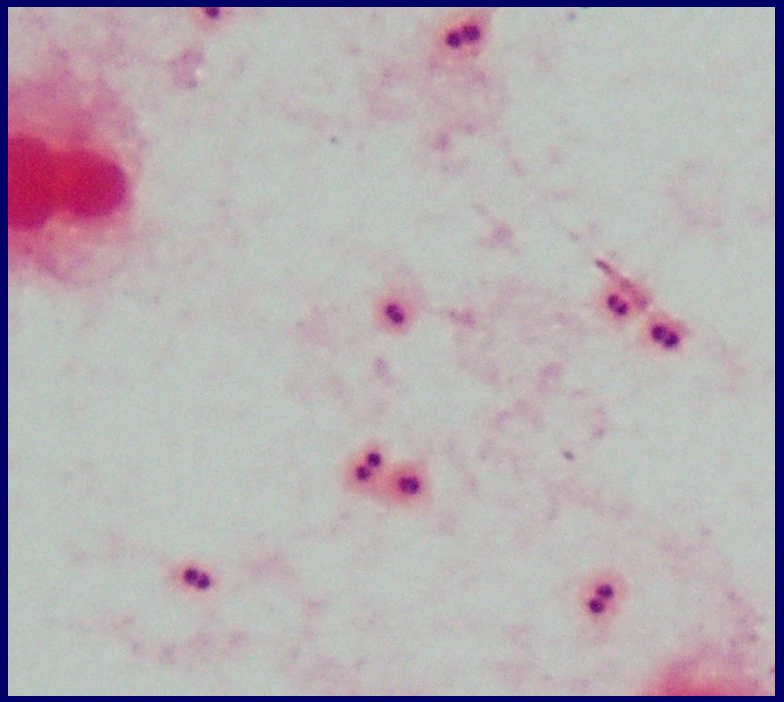
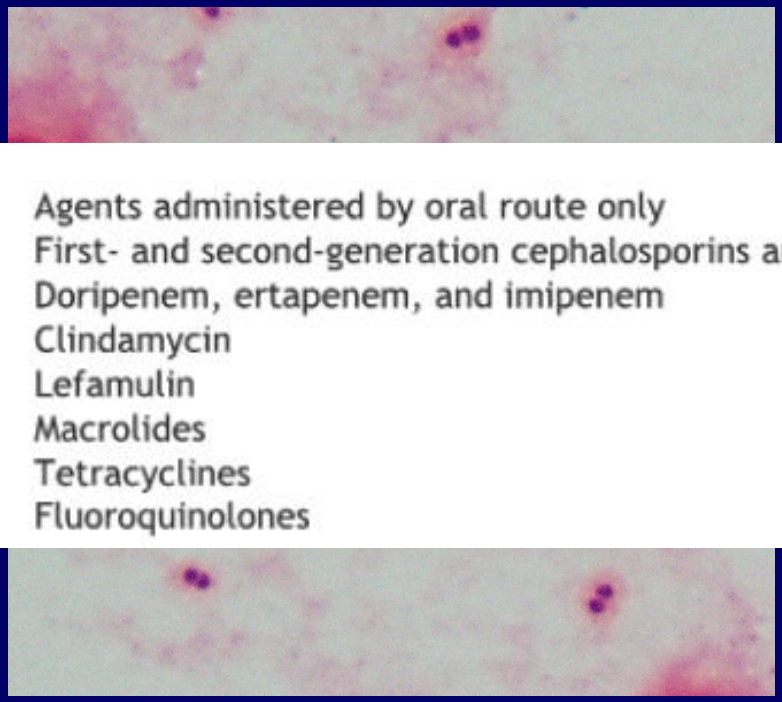
68-YEAR-OLD ALCOHOLIC WITH mucoid, alpha, bile-soluble colony



Penicillin	1	R
Ceftriaxone	1	I
Trimeth-sulfa	0.25	S
Vancomycin	0.5	S
Erythromycin	2	R
Clindamycin	0.12	S
Tetracycline	1	S
Levofloxacin	0.5	S

68-YEAR-OLD ALCOHOLIC WITH MENINGITIS

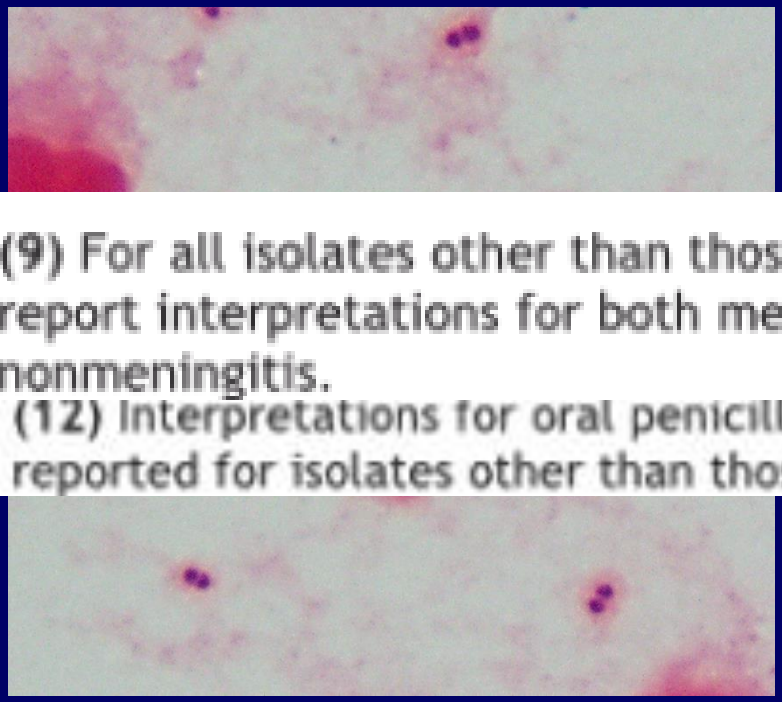


Agents administered by oral route only
First- and second-generation cephalosporins and cephamycins
Doripenem, ertapenem, and imipenem
Clindamycin
Lefamulin
Macrolides
Tetracyclines
Fluoroquinolones

Penicillin	1	R
Ceftriaxone	1	I
Trimeth-sulfa	0.25	S
Vancomycin	0.5	S

CLSI M100-Ed32; 2022

68-YEAR-OLD ALCOHOLIC WITH PNEUMONIA



(9) For all isolates other than those from CSF, report interpretations for both meningitis and nonmeningitis.

(12) Interpretations for oral penicillin may be reported for isolates other than those from CSF.

Penicillin	1	R (CSF) S (non-CSF) I (oral)
Ceftriaxone	1	I (CSF) S (non-CSF)
Trimeth-sulfa	0.25	S
Vancomycin	0.5	S
Erythromycin	2	R
Clindamycin	0.12	S
Tetracycline	1	S
Levofloxacin	0.5	S

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MORE SPECIAL REPORTING

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.

CLSI M100-Ed32; 2022

Table 3

AS A REMINDER…

Table 3A
Tests for ESBLs

Tables 3B and 3B-1
CarbaNP Test for Suspected Carbapenemase Production and Modifications When Using MIC Breakpoints Described in M100-S20 (January 2010)

Tables 3C and 3C-1
Modified Carbapenem Inactivation Methods and Modifications When Using MIC Breakpoints Described in M100-S20 (January 2010)

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

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

Table 3F
Test for β-Lactamase Production in *Staphylococcus* spp.

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

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

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

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

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

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

CLSI M100-Ed31; 2021

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

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	

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

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

CLSI M100-Ed32; 2022

Additional Tables

OTHER TABLES

- Table 4: Disk diffusion quality control ranges
  Disk diffusion troubleshooting
- Table 5: MIC quality control ranges
  MIC troubleshooting
- Tables 6, 7, 8: DIY susceptibility testing

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Appendices

APPENDIX B

B4. Enterococcus spp.

Organism \ Antimicrobial Agent	Cephalosporins	Vancomycin	Teicoplanin	Aminoglycosides	Clindamycin	Quinupristin-dalfopristin	Trimethoprim	Trimethoprim-sulfamethoxazole	Fusidic Acid
E. faecalis	R[a]			R[a]	R[a]	R	R	R[a]	R
E. faecium	R[a]			R[a]	R[a]		R	R[a]	R
E. gallinarum/E. casseliflavus	R[a]	R		R[a]	R[a]	R	R	R[a]	R

Abbreviation: R, resistant.

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APPENDIX D

NOTE: Isolates collected from selected US hospitals from 1 January 2013 to 31 December 2016.[a]

D1. *Bacteroides* spp. and *Parabacteroides* spp.

Anaerobic Organisms	Number of Strains	Ampicillin-sulbactam		Number of Strains	Piperacillin-tazobactam		Number of Strains	Cefoxitin		Number of Strains	Ertapenem		Number of Strains	Imipenem		Number of Strains	Meropenem	
Percent susceptible (%S) and percent resistant (%R)[b]		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R		%S	%R
Breakpoints, µg/mL		≤ 8/4	≥ 32/16		≤16/4	≥ 128/4		≤ 16	≥ 64		≤ 4	≥ 16		≤ 4	≥ 16		≤ 4	≥ 16
B. fragilis	129	84	2	1030	96	1	830	100	0	133	82	14	189	97	1	1505	93	5
B. thetaiotaomicron	76	82	5	252	87	0	258	13	54	-	-	-	70	100	0	328	99	0
B. ovatus	30	80	3	206	94	0	177	20	34	19[c]	84[c]	16[c]	49	100	0	236	95	1
B. vulgatus	20[c]	45[c]	15[c]	168	92	0	153	73	14	—	—	—	35	97	0	171	96	4
B. uniformis	19[c]	84[c]	0[c]	78	96	0	72	85	10	—	—	—	19[c]	100[c]	0[c]	93	100	0
Parabacteroides distasonis	27[c]	59[c]	19[c]	92	95	1	82	29	43	—	—	—	26[c]	100[c]	0	119	97	2

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OTHER APPENDICES

- A: Confirming AST results/organism identification
- C: QC strains for susceptibility testing
- E: Dosage regimens susceptible, susceptible DD
- F: Susceptible dose dependent
- G: Epidemiological cutoff values
- H: Molecular resistance detection
- I: Cefiderocol

CLSI M100-Ed32; 2022

Corynebacterium spp.; CORYNEFORMS

Format	Broth microdilution	Disk Diffusion
Medium	Cation-adjusted Mueller-Hinton broth with 2.5-5.0% (v/v) lysed horse blood; daptomycin caveat	
Inoculum	20-24 h direct colony suspension equivalent to 0.5 McFarland	
Incubation	35°C ambient air 24-48 hours	
Agents to consider for primary testing	Penicillin Vancomycin Gentamicin Erythromycin	

NOTES

- All *Corynebacterium* spp.
  Arcanobacterium spp.
  Arthrobacter spp.
  Brevibacterium spp.
  Cellulomonas spp.
  Cellulosimicrobium spp.
  Dermabacter spp.
  Leifsonia spp.
  Microbacterium spp.
  Oerskovia spp.
  Rothia spp.
  (not *Rothia mucilaginosa*)
  Trueperella spp.
  Turicella spp.
- Testing of isolates from normally-sterile sources may be warranted, especially in immunodeficient patients
- Some *Corynebacterium* spp. resistant to multiple drug classes

CLSI M45, 3rd ed.; 2015

MORE NOTES

- Interpretations of “resistant” may be reported at 24 hours; isolates appearing “susceptible” to β-lactam agents are re-incubated to be read @ 48h

- Derivations of interpretive criteria (CLSI M100)

  Cephems from *Streptococcus* spp.
  Linezolid from *Enterococcus* spp.
  Penicillin, erythromycin from population distributions
  Rest from *Staphylococcus* spp.

CLSI M45, 3rd ed.; 2015

OTHER POTENTIAL GENERA

Abiotrophia/Granulicatella spp.
Aerococcus spp.
Aeromonas spp.
Bacillus spp. (not *B. anthracis*)
Campylobacter jejuni/coli
Erysipelothrix rhusiopathiae
Gemella spp.
(H)ACEK group
Lactobacillus spp.
Lactococcus spp.
Leuconostoc spp.
Listeria monocytogenes
Micrococcus spp.
Moraxella catarrhalis
Pasteurella spp.
Pediococcus spp.
Rothia mucilaginosa
Vibrio spp.
BIOTERRORISM AGENTS

Most via broth microdilution (CAMHB with lysed horse blood)
Many bioterrorism agents with CAMHB

CLSI M45, 3rd ed.; 2015