2023 Updates to CLSI M100

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The presenter states no conflict of interest and has no financial relationship to disclose relevant to the content of this presentation.

OUTLINE

I. Quick discussion(s) relative to major revisions

II. Objectives of webinar

Describe significant changes relevant to pre-existing antimicrobial susceptibility breakpoints…

Describe significant changes relevant to antimicrobial susceptibility testing methodology…

Identify (new) organism/antimicrobial combinations for which susceptibility breakpoints now exist…

as outlined in the CLSI M100-Ed33 document.

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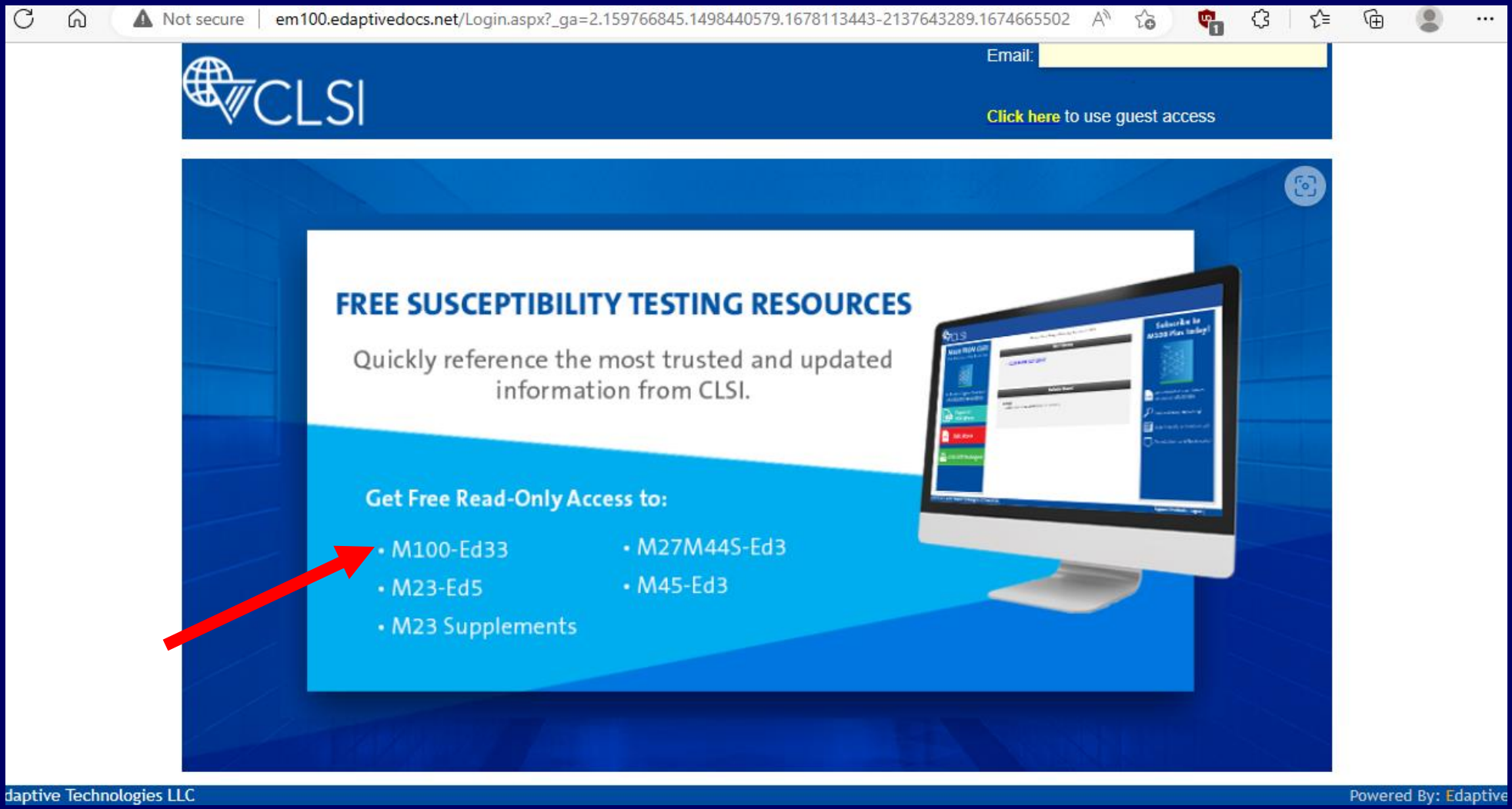
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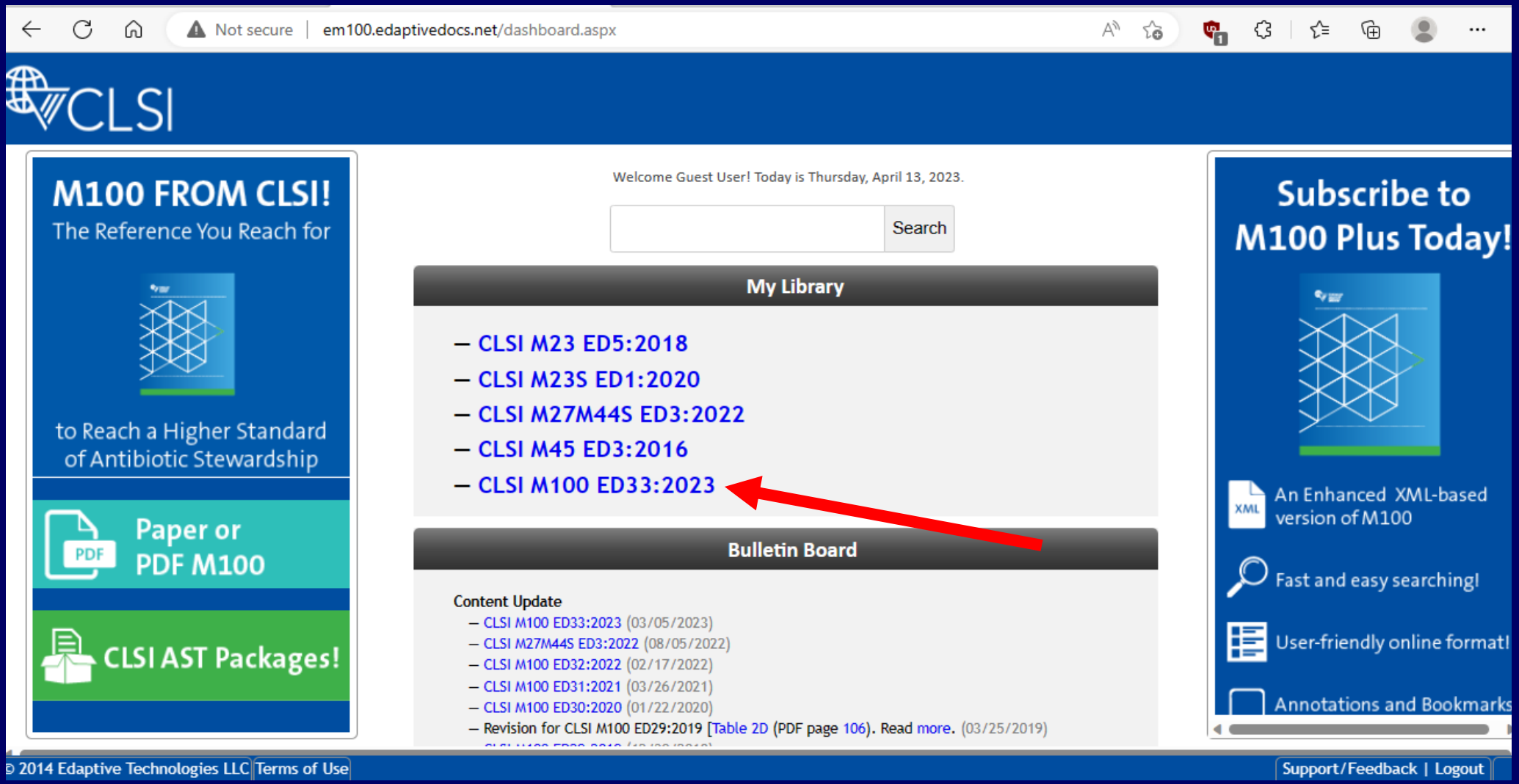
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Content Update
– CLSI M100 ED33:2023 (03/05/2023)
– CLSI M27M44S ED3:2022 (08/05/2022)
– CLSI M100 ED32:2022 (02/17/2022)
– CLSI M100 ED31:2021 (03/26/2021)
– CLSI M100 ED30:2020 (01/22/2020)
– Revision for CLSI M100 ED29:2019 [Table 2D (PDF page 106). Read more. (03/25/2019)
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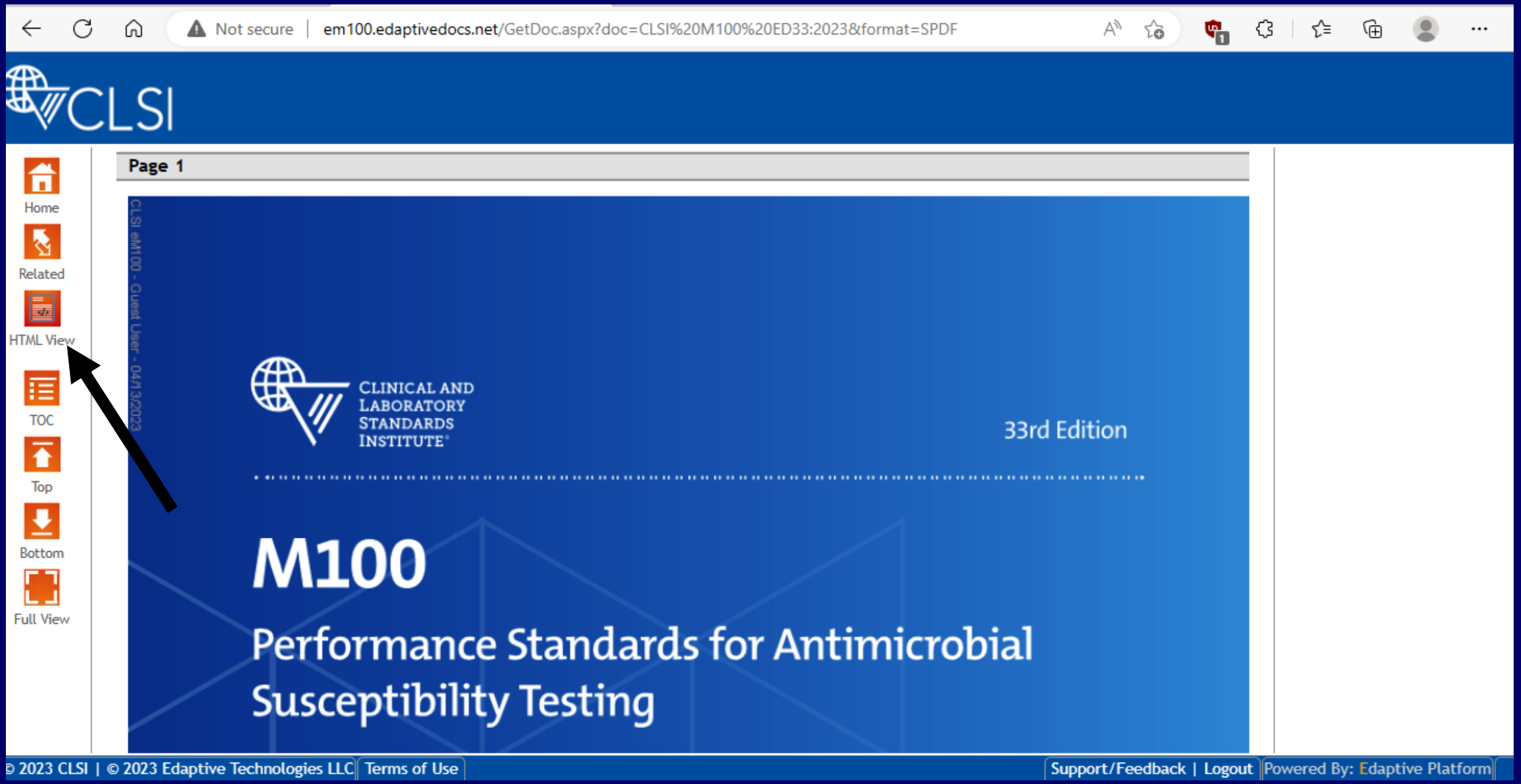

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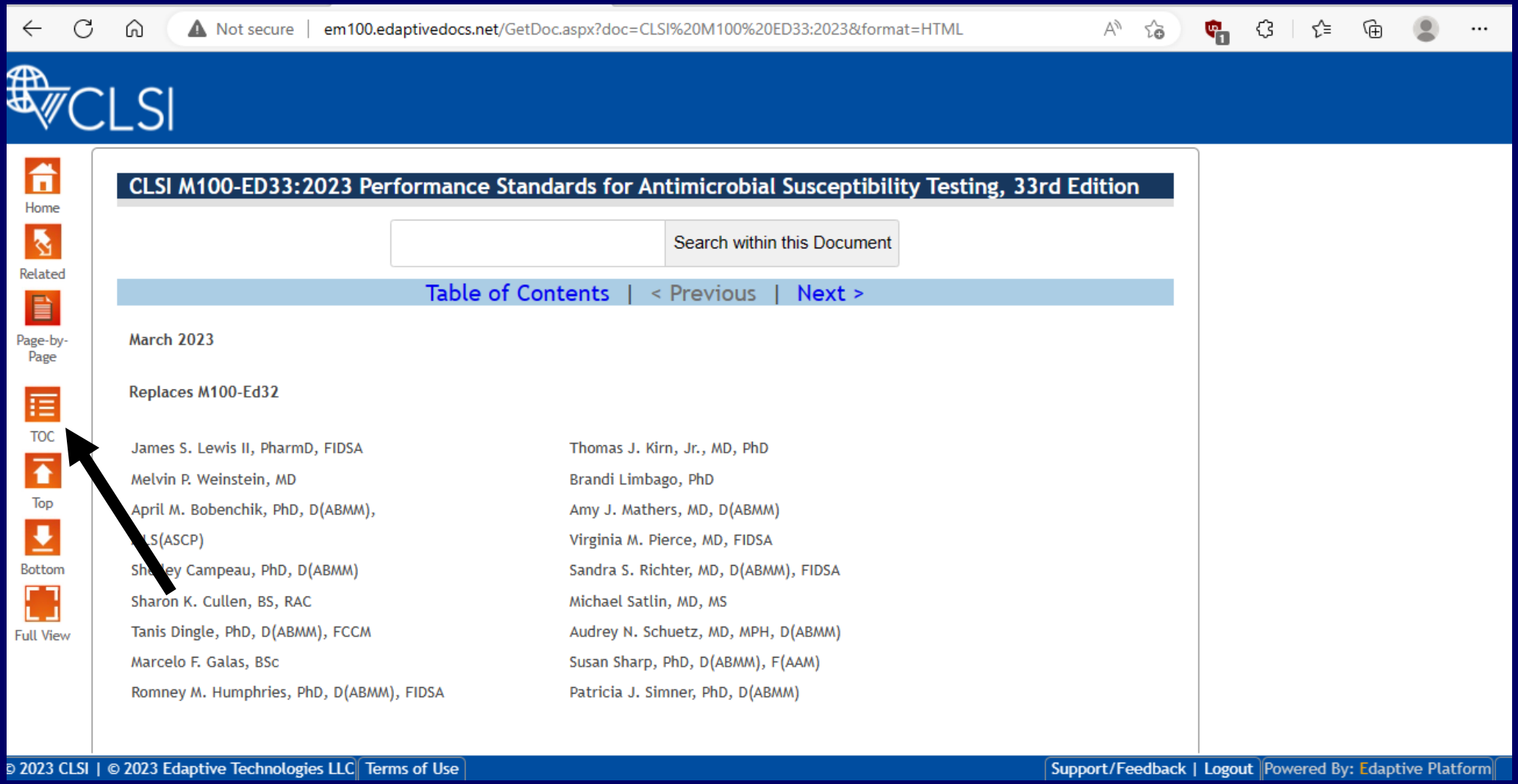

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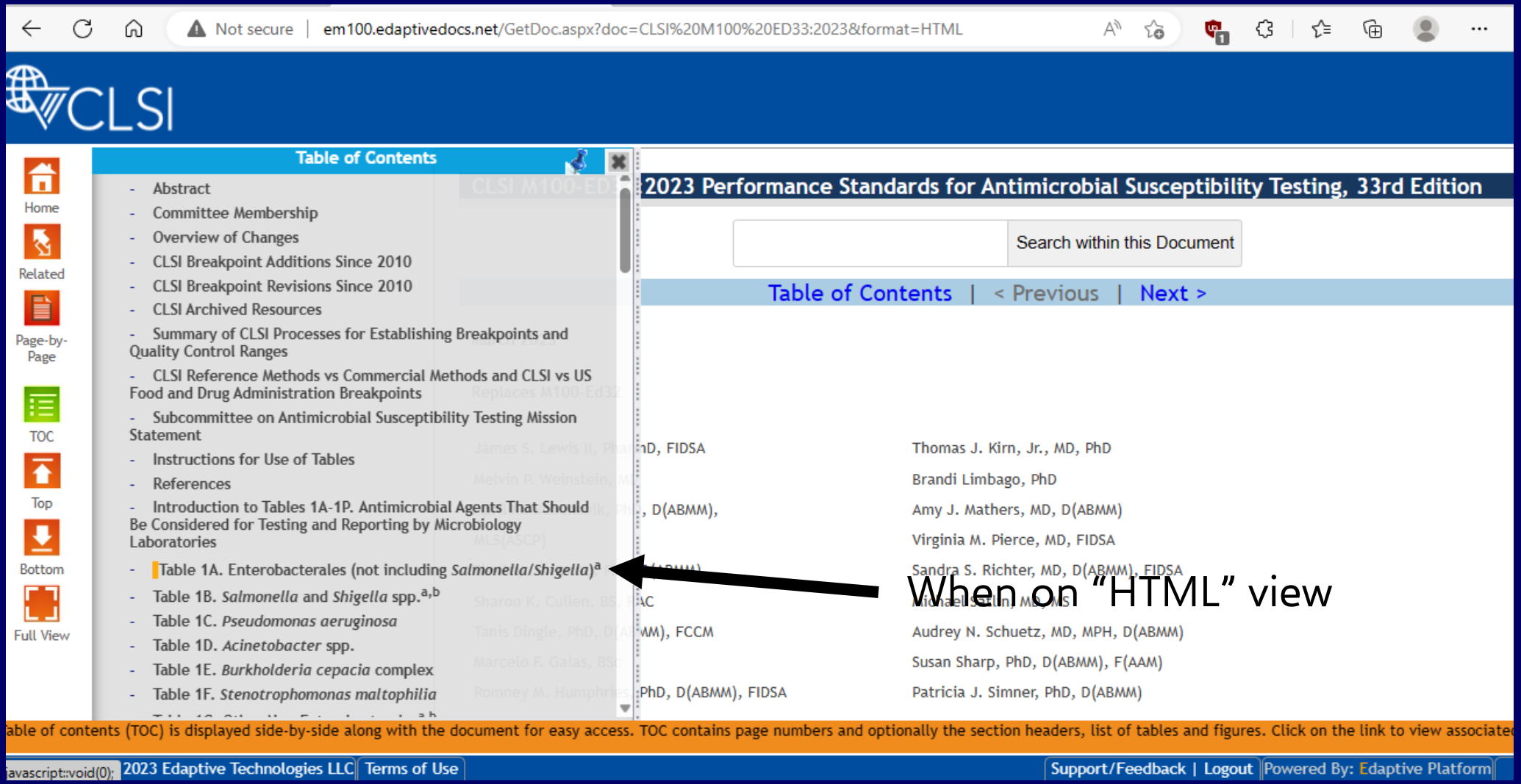

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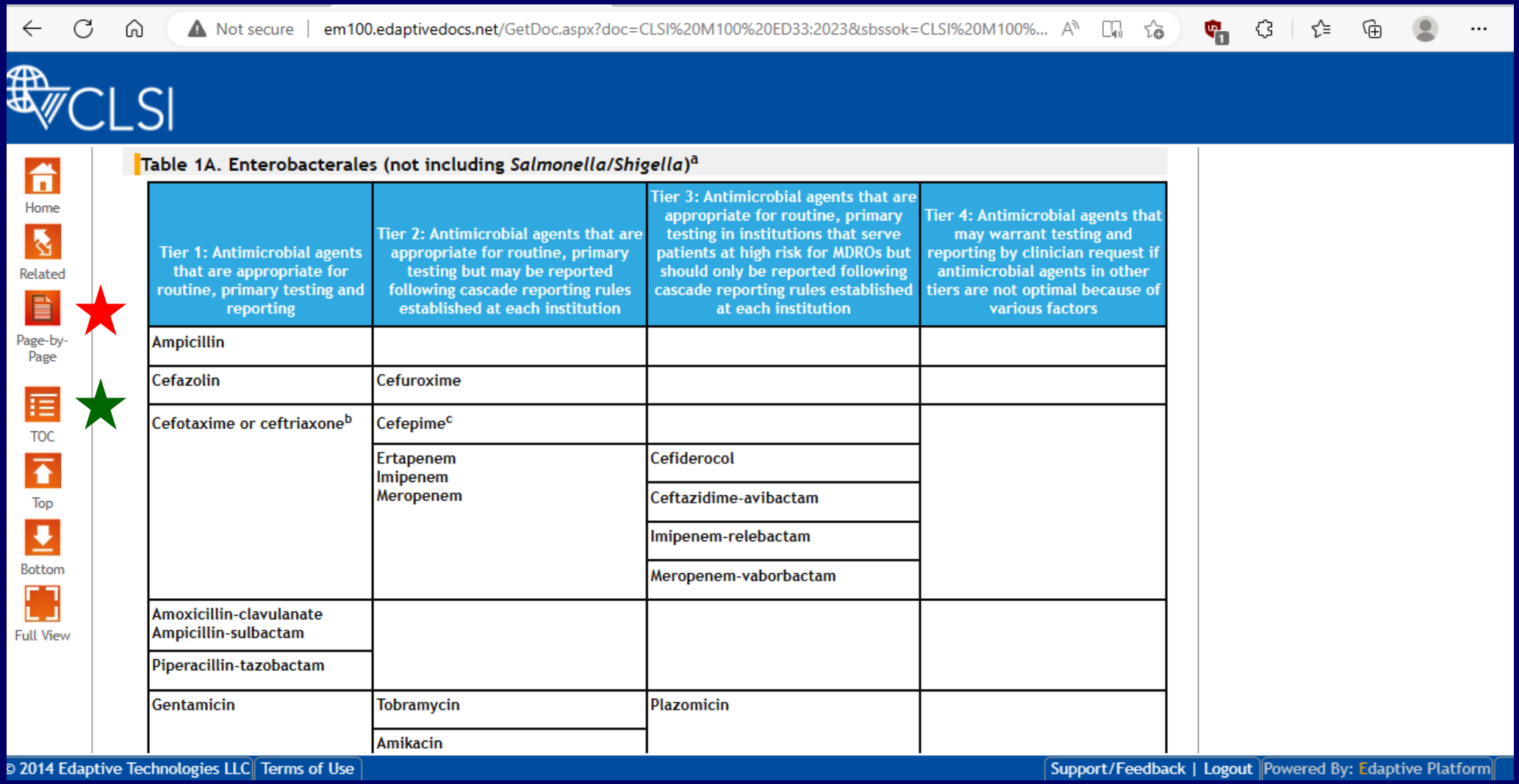
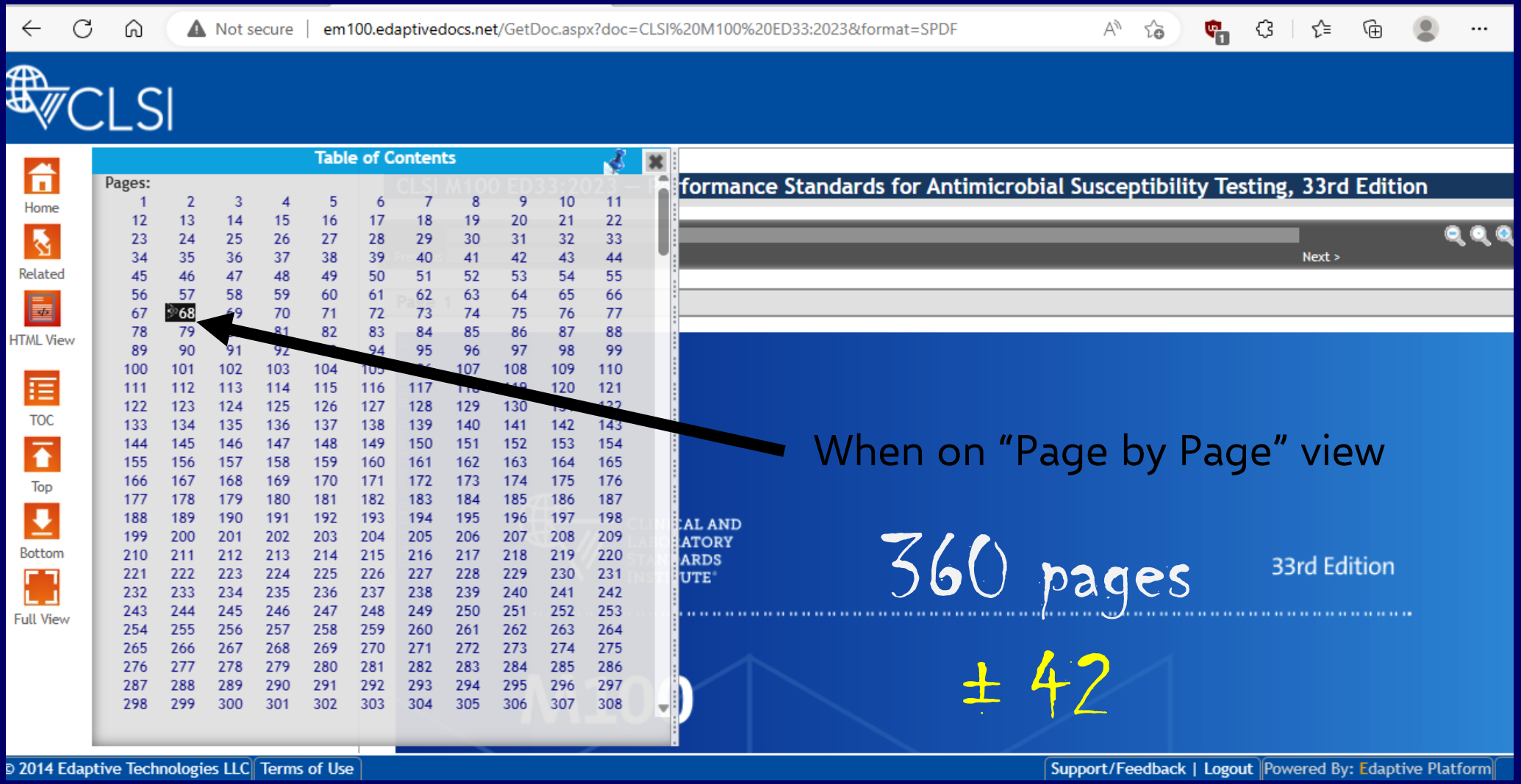


Table 1A. Enterobacterales (not including *Salmonella/Shigella*)[a]

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ampicillin			
Cefazolin	Cefuroxime		
Cefotaxime or ceftriaxone[b]	Cefepime[c]		
	Ertapenem Imipenem Meropenem	Cefiderocol	
		Ceftazidime-avibactam	
		Imipenem-relebactam	
		Meropenem-vaborbactam	
Amoxicillin-clavulanate Ampicillin-sulbactam			
Piperacillin-tazobactam			
Gentamicin	Tobramycin	Plazomicin	
	Amikacin		

FUTZING WITH THIS…MORE



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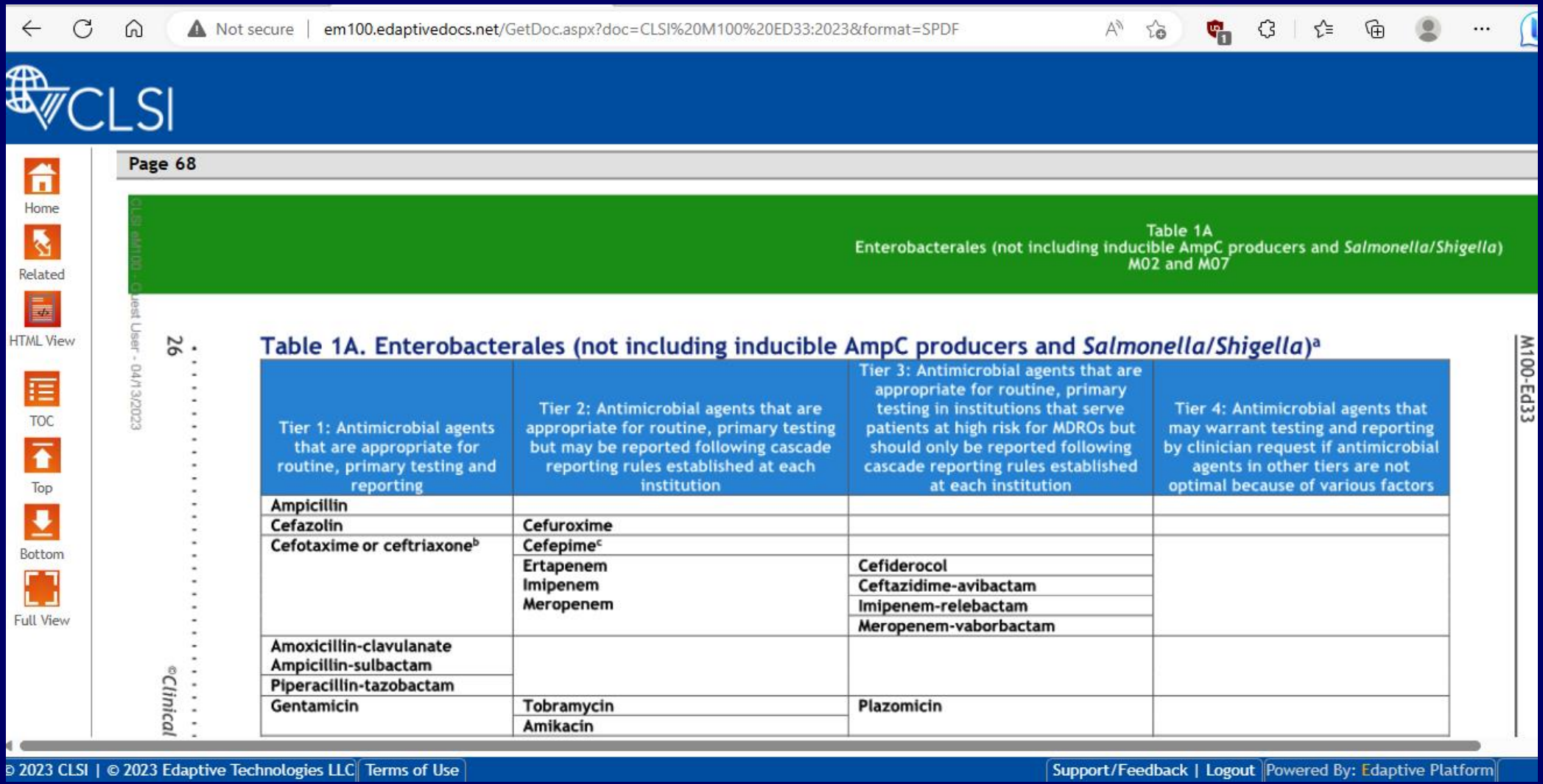

The Really Big Ones

THE REALLY BIG ONES #1

Table 1A
Suggested Nonfastidious Groupings
M02 and M07

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

	Enterobacteriaceae	*Pseudomonas aeruginosa*	*Staphylococcus* spp.	*Enterococcus* spp.[m]
GROUP A PRIMARY TEST AND REPORT	Ampicillin[c]	Ceftazidime	Azithromycin[b] or clarithromycin[b] or erythromycin[b]	Ampicillin[n] Penicillin[o]
	Cefazolin[d]	Gentamicin Tobramycin		
	Gentamicin[c] Tobramycin[c]	Piperacillin-tazobactam	Clindamycin[b]	
			Oxacillin[j,k,r,t] & Cefoxitin[j,k,t] (surrogate test for oxacillin)	
			Penicillin[l]	
			Trimethoprim-sulfamethoxazole	

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NON-FASTIDIOUS GROUPINGS

- 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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TABLES 1

Table 1A
Suggested Nonfastidious Groupings
M02 and M07

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

	Enterobacteriaceae	*Pseudomonas aeruginosa*	*Staphylococcus* spp.	*Enterococcus* spp.[m]

Table 1B
Suggested Fastidious Groupings
M02 and M07

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

	Haemophilus influenzae[d] and *Haemophilus parainfluenzae*	*Neisseria gonorrhoeae*[l]	*Streptococcus pneumoniae*[j]	*Streptococcus* spp. β-Hemolytic Group[p]	*Streptococcus* spp. Viridans Group[p]

Table 1C
Suggested Anaerobe Groupings
M11

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

	Gram-Negative Anaerobes	Gram-Positive Anaerobes[a]

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A HUGE FORMATTING CHANGE

Table 1C
Pseudomonas aeruginosa
M02 and M07

Table 1C. *Pseudomonas aeruginosa*

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution.	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ceftazidime	**Imipenem**	**Cefiderocol**	
Cefepime	**Meropenem**	**Ceftazidime-avibactam**	
Piperacillin-tazobactam		**Ceftolozane-tazobactam**	
		Imipenem-relebactam	
Tobramycin			
Ciprofloxacin **Levofloxacin**			
			Aztreonam
Urine Only			
	Amikacin		

Abbreviation: MDRO, multidrug-resistant organism.

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

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CRITERIA FOR INCLUSION

Agents of proven efficacy
Acceptable *in vitro* test performance

CRITERIA FOR ASSIGNMENT

Clinical efficacy
Prevalence of resistance
Minimizing emergence of resistance
FDA clinical indications for use
Current consensus recommendations for first-choice or alternative drugs
Co$t

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TABLE 1 GROUPINGS

- Tier 1 — Antimicrobial agents that are appropriate for routine, primary testing and reporting

- Tier 2 — Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution

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TABLE 1 GROUPINGS

- Tier 3

  Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution

- Tier 4

  Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors

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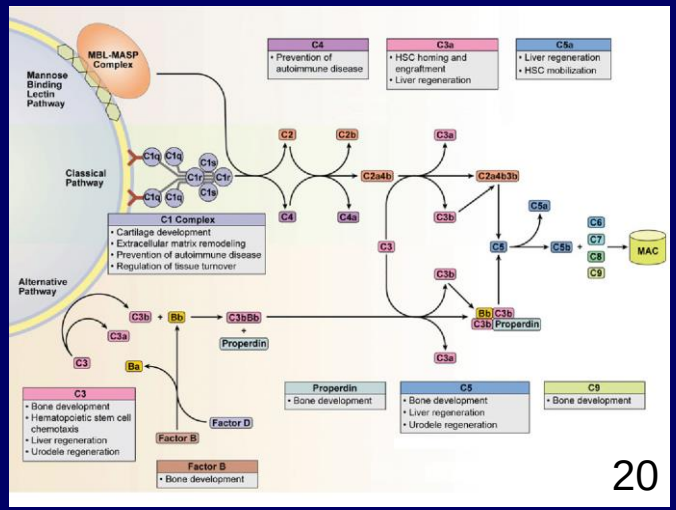
REPORTING

- **Selective** Based on defined criteria unrelated to susceptibility testing data

  Organism ID — Clinical setting
  Site of infection — Patient demographics

- **Cascade** Based on overall antimicrobial susceptibility profile of isolate



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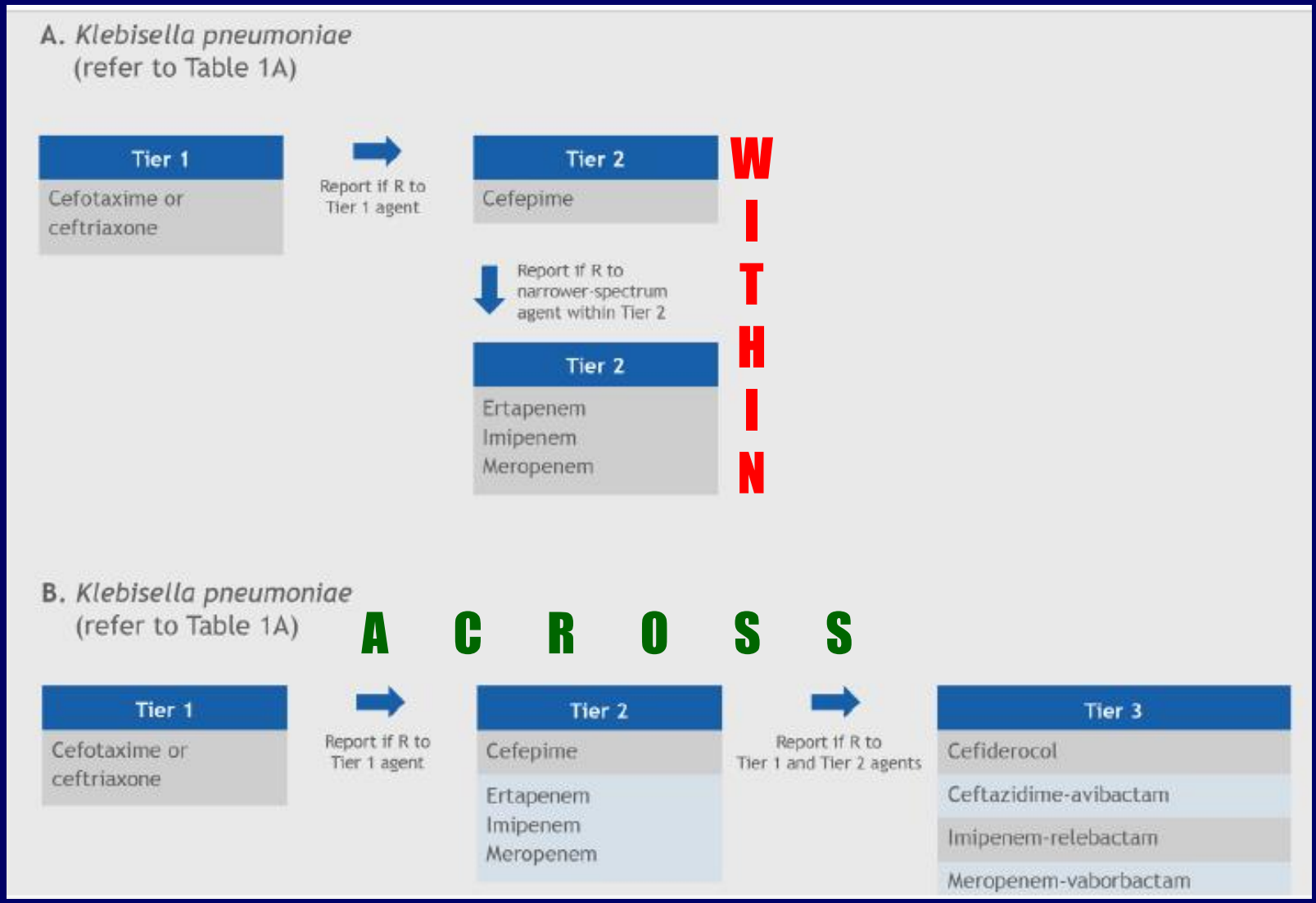
CASCADING



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MORE ON FOUR

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

Tier	Definition	Test	Report[a]	Additional Testing and Reporting Considerations
4	Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors	By request	By request	• Test and report by clinician request due to: – Unavailability of preferred drug for clinical use – Patient underlying condition, including allergies – Unusual susceptibility profile of the organism, including resistance to agents in Tiers 1, 2, and 3 – Polymicrobial infection • May also warrant testing as an epidemiological aid (eg, testing ceftazidime for Enterobacterales to indicate potential extended-spectrum β-lactamase production; see Table 3A).

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URINE OR YER OUT

Table 1C. *Pseudomonas aeruginosa*

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution.	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ceftazidime	**Imipenem**	**Cefiderocol**	
Cefepime	**Meropenem**	**Ceftazidime-avibactam**	
Piperacillin-tazobactam		**Ceftolozane-tazobactam**	
		Imipenem-relebactam	
Tobramycin			
Ciprofloxacin **Levofloxacin**			
			Aztreonam
Urine Only			
	Amikacin		

Abbreviation: MDRO, multidrug-resistant organism.

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

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NEW TABLES 1

Table 1A
Enterobacterales (not including inducible AmpC producers and *Salmonella/Shigella*)
M02 and M07

Table 1A. Enterobacterales (not including inducible AmpC producers and *Salmonella/Shigella*)[a]

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ampicillin			
Cefazolin	Cefuroxime		
Cefotaxime or ceftriaxone[b]	Cefepime[c]		
	Ertapenem Imipenem Meropenem	Cefiderocol	
		Ceftazidime-avibactam	
		Imipenem-relebactam	
		Meropenem-vaborbactam	
Amoxicillin-clavulanate Ampicillin-sulbactam			
Piperacillin-tazobactam			
Gentamicin	Tobramycin	Plazomicin	
	Amikacin		
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
	Cefotetan Cefoxitin		
	Tetracycline[d]		
			Aztreonam
			Ceftaroline[b]

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NEW TABLES 1

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

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Ampicillin			
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
Cefotaxime or ceftriaxone			Ertapenem[c] Imipenem[c] Meropenem[c]
	Azithromycin[d]		
			Tetracycline[e]

Abbreviation: MDRO, multidrug-resistant organism.

Footnotes

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

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

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HERE'S THE REST I

1C *Pseudomonas aeruginosa*
1D *Acinetobacter* spp.
1E *Burkholderia cepacia* complex
1F *Stenotrophomonas maltophilia*
1G Other non-Enterobacterales
1H *Staphylococcus* spp.
1I *Enterococcus* spp.

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HERE'S THE REST II

1J *Haemophilus influenzae* and *Haemophilus parainfluenzae*
1K *Neisseria gonorrhoeae*
1L *Streptococcus pneumoniae*
1M *Streptococcus* spp. β-hemolytic Group
1N *Streptococcus* spp. Viridans Group
1O Gram-Negative Anaerobes
1P Gram-Positive Anaerobes

no *N. meningitidis*

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NOT IN TABLES 1

Antimicrobial Agent Test and Report Designations and Additional Considerations for Agents Not Listed in Tables 1

Designation	Definition	Test	Report[a]	Additional Testing and Reporting Considerations
Other	Antimicrobial agents with established clinical breakpoints designated by an * in Tables 2 that are generally not candidates for testing and reporting in the United States	By request	By request	Test and report only by clinician request and only following consultation with the antimicrobial stewardship team and other relevant institutional stakeholders to ensure appropriateness of the request. Agents with an "Other" designation may not reflect current consensus recommendations for first-choice and alternative drugs for the specific organism or organism group.
Inv.	Antimicrobial agents that are investigational for the organism group designated by "Inv." in Tables 2 have not yet been approved by the FDA for use in the United States.	By request	By request	Test and report only by clinician request and only following consultation with the antimicrobial stewardship team and other relevant institutional stakeholders to ensure appropriateness of the request. These agents would likely be clinically available for compassionate use only.

Abbreviations: FDA, US Food and Drug Administration; UTI, urinary tract infection.

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THE REALLY BIG ONES #2

Organism	Method	Gentamicin Previous			Gentamicin New		
		S	I	R	S	I	R
Enterobacterales	BMD	≤ 4	8	≥ 16	≤ 2	4	≥ 8
	DD	≥ 15	13-14	≤ 12	≥ 18	15-17	≤ 14

Organism	Method	Tobramycin Previous			Tobramycin New		
		S	I	R	S	I	R
Enterobacterales	BMD	≤ 4	8	≥ 16	≤ 2	4	≥ 8
	DD	≥ 15	13-14	≤ 12	≥ 17	13-16	≤ 12

Organism	Method	Amikacin Previous			Amikacin New		
		S	I	R	S	I	R
Enterobacterales	BMD	≤ 16	32	≥ 64	≤ 4	8	≥ 16
	DD	≥ 17	15-16	≤ 14	≥ 20	17-19	≤ 16

CLSI M100-Ed32, 2022; M100-Ed33, 2023

WISCONSIN SURVEILLANCE DATA

- *Enterobacter cloacae*

Year	Percentage Susceptible	
	Gentamicin	Tobramycin
2018	99.3	99.3
2019	100	100

Previous

≤ 4	8	≥ 16

Cumulative frequency distribution

MIC	Number of Isolates by Agent	
	Gentamicin	Tobramycin
≤ 2	593	591
4	2	4
8		1
16	1	1
>16		
32		
>32	1	

"Red" shading indicates decreased susceptibility

WISCONSIN SURVEILLANCE DATA

- *Klebsiella pneumoniae*

Year	Percentage Susceptible	
	Gentamicin	Tobramycin
2018	97.7	97.7
2019	98.9	98.9

Previous

≤ 4	8	≥ 16

Cumulative frequency distribution

MIC	Number of Isolates by Agent	
	Gentamicin	Tobramycin
≤ 2	669	669
4	7	7
8		8
16	4	1
>16		2
32	5	
>32	2	

"Red" shading indicates decreased susceptibility

WISCONSIN SURVEILLANCE DATA

- *Proteus mirabilis*

Year	Percentage Susceptible	
	Gentamicin	Tobramycin
2016	91.4	92.1
2017	93.1	94.0
2018	92.4	92.7
2019	89.1	89.1
2020	94.4	95.5
2021	95.0	95.4
2022	95.8	96.2

Previous

≤ 4	8	≥ 16

MIC	Number of Isolates by Agent	
	Gentamicin	Tobramycin
≤ 2	1850	1843
4	5	23
8	27	46
16	38	53
>16		34
32	53	
>32	26	

Cumulative frequency distribution

"Red" shading indicates decreased susceptibility

WISCONSIN SURVEILLANCE DATA

- *Escherichia coli*

Year	Percentage Susceptible	
	Gentamicin	Tobramycin
2016	93.1	93.1
2017	93.4	94.6
2018	93.9	94.8
2019	91.9	93.5
2020	95.2	96.2
2021	94.2	96.9
2022	92.1	94.5

Previous

≤ 4	8	≥ 16

Cumulative frequency distribution

MIC	Number of Isolates by Agent	
	Gentamicin	Tobramycin
≤ 2	2329	2318
4	3	47
8	8	58
16	10	39
>16		34
32	40	
>32	106	

"Red" shading indicates decreased susceptibility

WISCONSIN SURVEILLANCE DATA

- Organism cumulative antibiogram before and after

Organism	Percentage Susceptible			
	Gentamicin		Tobramycin	
	Previous	New	Previous	New
Enterobacter cloacae	99.7	99.3	99.7	99.0
Klebsiella pneumoniae	98.4	97.4	98.4	97.4
Proteus mirabilis	92.8	92.5	93.3	92.2
Escherichia coli	93.4	93.3	94.8	92.9

Previous			New		
≤ 4	8	≥ 16	≤ 2	4	≥ 8

OVERCALLING SUSCEPTIBILITY?

Organism	Method	Ciprofloxacin Previous			Ciprofloxacin New		
		S	I	R	S	I	R
Enterobacterales	BMD	≤ 1	2	≥ 4	≤ 0.25	0.5	≥ 1
P. aeruginosa	BMD	≤ 1	2	≥ 4	≤ 0.5	1	≥ 2

Organism	Method	Levofloxacin Previous			Levofloxacin New		
		S	I	R	S	I	R
Enterobacterales	BMD	≤ 2	4	≥ 8	≤ 0.5	1	≥ 2
P. aeruginosa	BMD	≤ 2	4	≥ 8	≤ 1	2	≥ 4

CLSI M100 28th ed., 2018; M100 29th ed., 2019

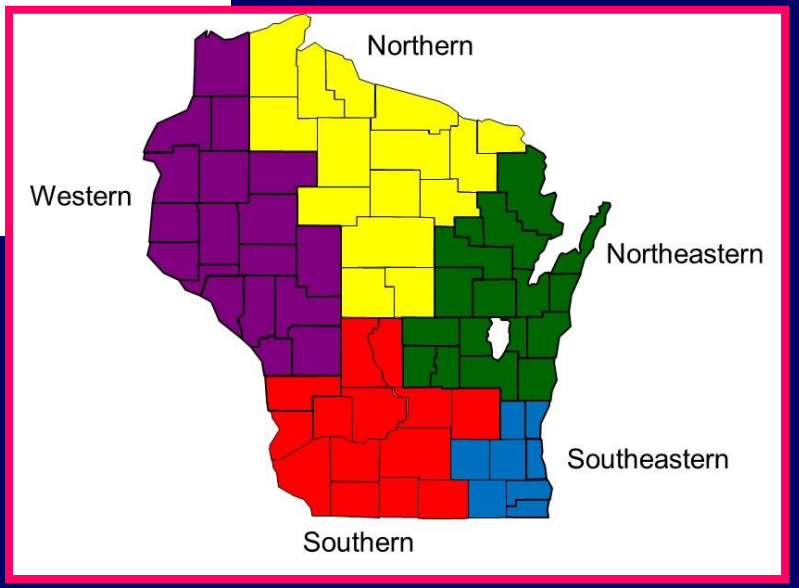
Clinical Medicine & Research
Volume 20, Number 2: 81-88

clinmedres.org

Original Research

Surveillance of Fluoroquinolone Resistance in Wisconsin: Geographic Variation and Impact of Revised CLSI Breakpoints

Giovanna Lazzerini; Stephen C. Lavey; Barry C. Fox, MD;



E. coli 1.5-3.2% reduced fluoroquinolone susceptibility
P. mirabilis 2.6-6.3% reduced fluoroquinolone susceptibility
P. aeruginosa 4.5-5.1% reduced fluoroquinolone susceptibility

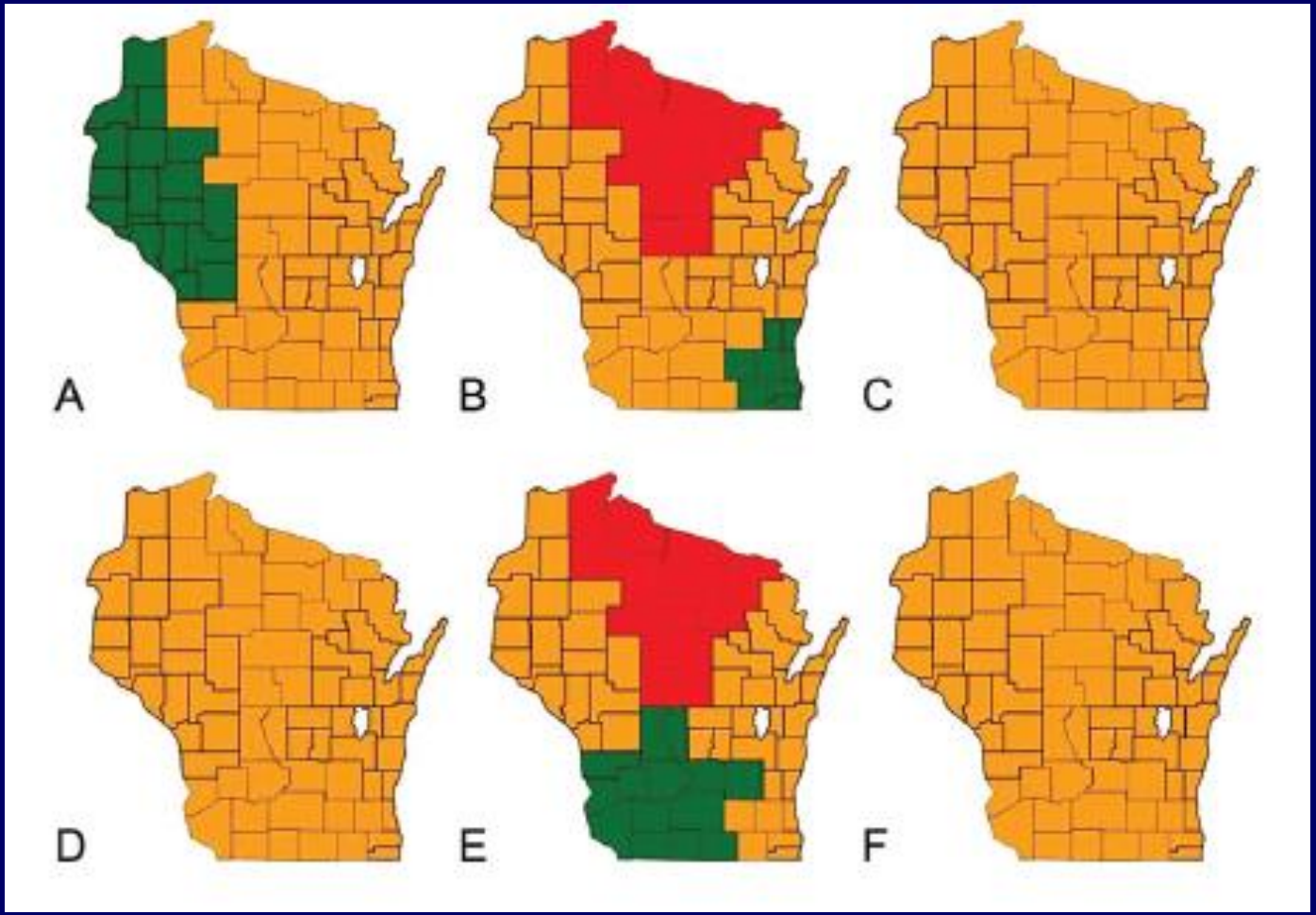
Clin Med Res. 20:81-88; 2022

CIPROFLOXACIN

E. coli *P. mirabilis* *P. aeruginosa*

CLSI previous →

CLSI new →



Clin Med Res. 20:81-88; 2022

WISCONSIN SURVEILLANCE DATA

- *Escherichia coli*

Region	Percentage Susceptible			
	Gentamicin		Tobramycin	
	Previous	New	Previous	New
Northern	95.2	95.2	96.7	95.5
Northeastern	94.6	94.5	96.2	93.4
Southern	92.5	92.3	93.3	91.8
Southeastern	91.3	91.1	91.5	90.7
Western	93.3	93.3	95.6	93.3
WISCONSIN	93.4	93.3	94.8	92.9

Previous			New		
≤ 4	8	≥ 16	≤ 2	4	≥ 8

WISCONSIN SURVEILLANCE DATA

- *Proteus mirabilis*

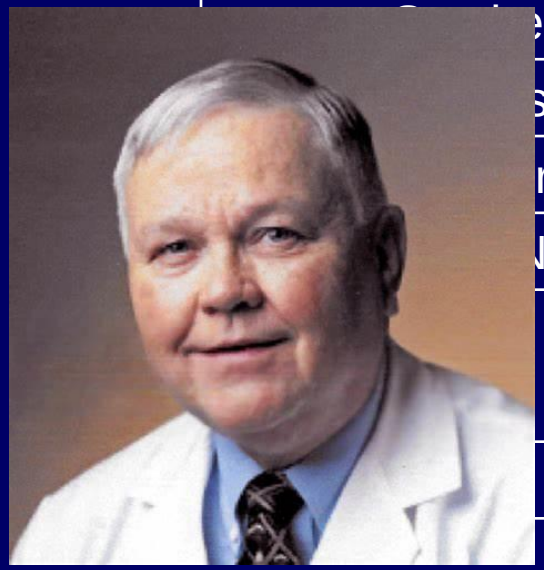
Region	Percentage Susceptible			
	Gentamicin		Tobramycin	
	Previous	New	Previous	New
Northern	90.4	90.0	90.4	89.3
Northeastern	94.1	93.6	94.8	92.6
Southern	90.1	89.8	90.9	90.1
Southeastern	96.3	96.3	96.8	96.3
Western	90.8	90.8	91.5	90.8
WISCONSIN	92.8	92.5	93.3	92.2

Previous			New		
≤ 4	8	≥ 16	≤ 2	4	≥ 8

WISCONSIN SURVEILLANCE DATA

- *Proteus mirabilis*

Region	Percentage Susceptible			
	Gentamicin		Tobramycin	
	Previous	New	Previous	New
Northern	90.4	90.0	90.4	89.3
Northeastern	94.1	93.6	94.8	92.6
rn	90.1	89.8	90.9	90.1
stern	96.3	96.3	96.8	96.3
rn	90.8	90.8	91.5	90.8
NSIN	92.8	92.5	93.3	92.2



Previous			New		
4	8	≥ 16	≤ 2	4	≥ 8

WHY???

Piperacillin-Tazobactam Breakpoints for Enterobacterales

CLSI

CLSI rationale document MR14
February 2022

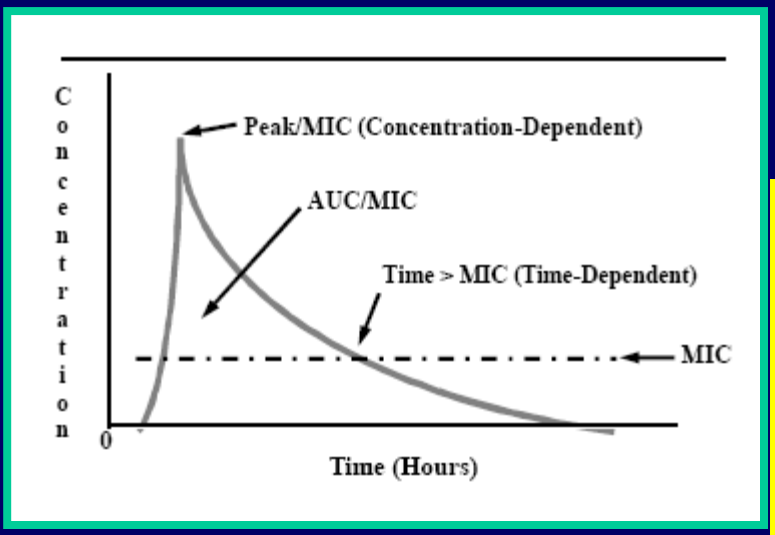
Romney M. Humphries, PhD, D(ABMM), FIDSA
Vanderbilt University Medical Center
USA

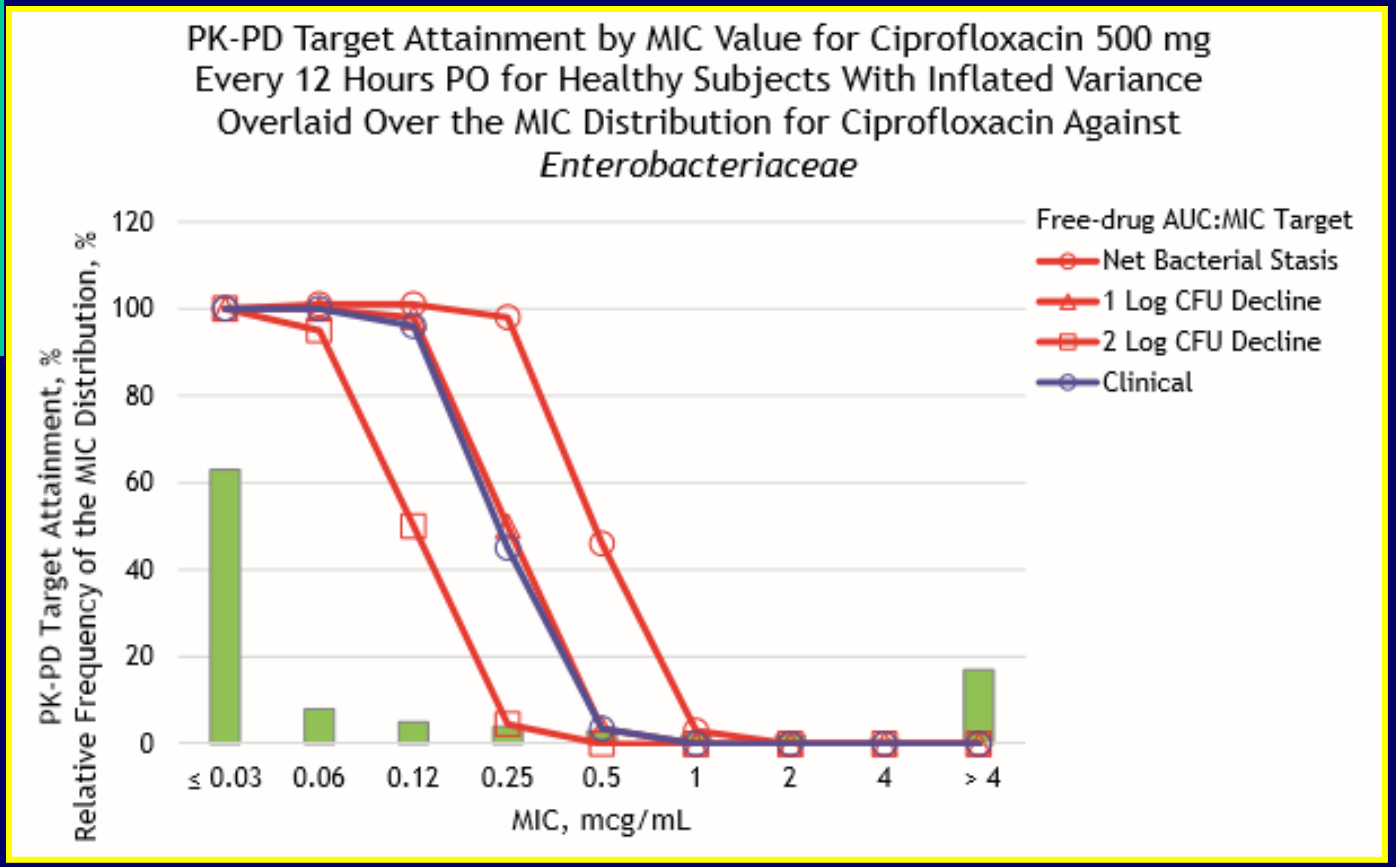
Table 2A. Enterobacterales (Continued)

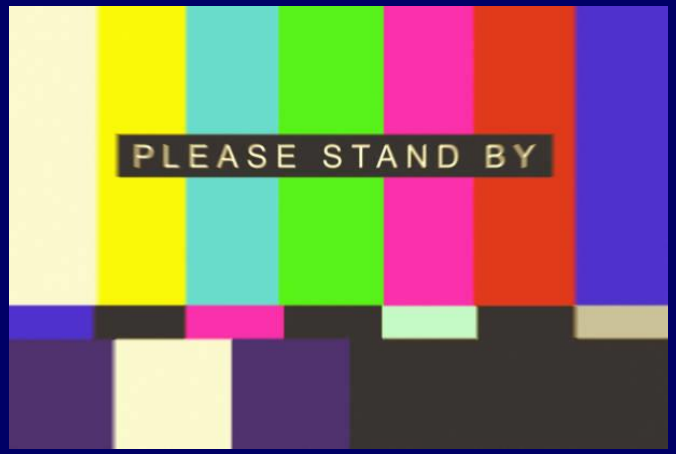
Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
AMINOGLYCOSIDES										
(54) WARNING: For *Salmonella* spp. and *Shigella* spp., aminoglycosides may appear active *in vitro* but are not effective clinically and should not be reported as susceptible. (55) Breakpoints for gentamicin, tobramycin, and amikacin are based on population distributions of various species, PK/PD target attainment analyses with an end point of net bacterial stasis and limited clinical data. Clinical outcomes data for aminoglycosides as monotherapy for systemic infections are limited and have resulted in worse treatment outcomes (for infections outside of the urinary tract) compared with other therapies. Combination therapy for most indications other than UTIs should be considered. Consultation with an infectious diseases specialist is recommended.									

CLSI M100-Ed33, 2023

MORE-SOPHISTICATED MODELING







CLSI MR02; 2019

PLAZOMICIN IV

- FDA approval in 2018
- Complicated UTI (including pyelonephritis) when limited options available

Escherichia coli
Klebsiella pneumoniae
Enterobacter cloacae
Proteus mirabilis

- Stable to hydrolysis by majority of aminoglycoside-modifying enzymes (AME)
- Isolates carrying 16S rRNA methyltransferases exhibit high MIC for plazomicin

Open Forum Infect Dis. 10:ofad058; 2023

PLAZOMICIN IV

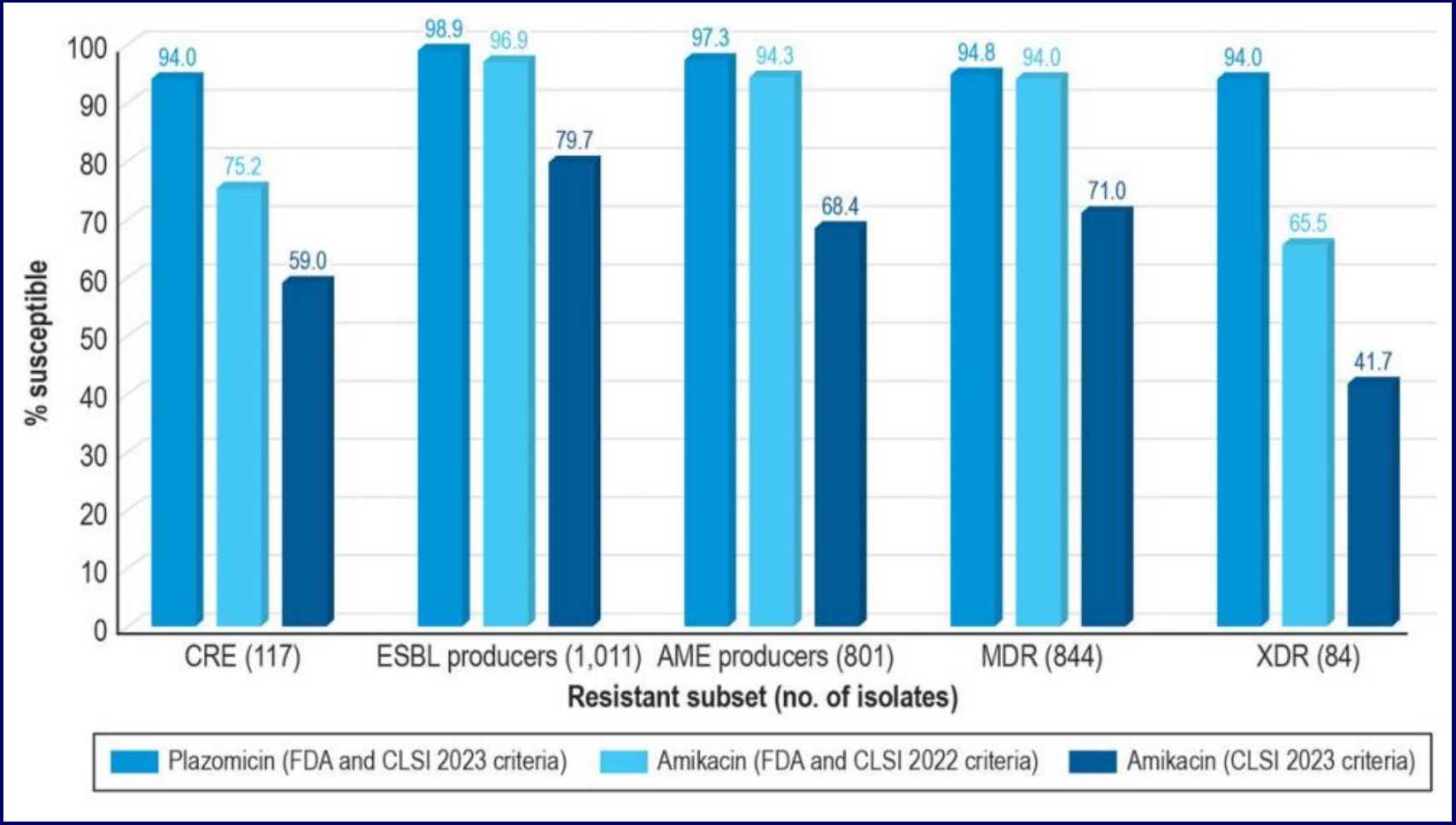
Table 2A. Enterobacterales (Continued)

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										
Gentamicin	10 µg	≥ 18	- -	15-17^	≤ 14	≤2	- -	4^	≥8	(56) Breakpoints are based on a dosage regimen of 7 mg/kg parenterally administered every 24 h.
Tobramycin	10 µg	≥ 17	-	13-16^	≤ 12	≤2	-	4^	≥8	(57) Breakpoints are based on a dosage regimen of 7 mg/kg parenterally administered every 24 h.
Amikacin	30 µg	≥ 20	-	17-19^	≤ 16	≤4	-	8^	≥16	(58) Breakpoints are based on a dosage regimen of 15 mg/kg parenterally administered every 24 h.
Plazomicin	**30 µg**	≥ 18	-	15-17^	≤ 14	≤ 2	-	4^	≥ 8	(59) Breakpoints are based on a dosage regimen of 15 mg/kg every 24 h over 30 minutes.

…but not for *Morganellaceae*

CLSI M100-Ed33, 2023

PLAZOMICIN IV



MDR: non-susceptible to at least 1 drug from ≥ 3 classes

XDR: susceptible to ≤ 2 classes

Open Forum Infect Dis. 10:ofad058; 2023

THE REALLY BIG ONES #3

Organism	Method	Tobramycin Previous			Tobramycin New		
		S	I	R	S	I	R
P. aeruginosa	BMD	≤ 4	8	≥ 16	≤ 1	2	≥ 4
	DD	≥ 15	13-14	≤ 12	≥ 19	13-18	≤ 12

Organism	Method	Amikacin Previous			Amikacin New		
		S	I	R	S	I	R
P. aeruginosa	BMD	NO	C	H	A	N	GE
	DD	NO	C	H	A	N	GE

CLSI M100-Ed32, 2022; M100-Ed33, 2023

WISCONSIN SURVEILLANCE DATA

- *Pseudomonas aeruginosa*

Year	Percentage Susceptible	
	Gentamicin	Tobramycin
2016	99.1	99.5
2017	97.2	97.2
2018	99.3	99.0
2019	97.2	98.9
2020	98.6	99.4
2021	99.2	99.2
2022	98.0	98.8

Previous for both

≤ 4	8	≥ 16

Cumulative frequency distribution

MIC	Number of Isolates by Agent	
	Gentamicin	Tobramycin
≤ 2	1888	1942
4	51	7
8	13	6
16	6	4
>16		13
32	1	
>32	13	

WHY???

Piperacillin-Tazobactam Breakpoints for Enterobacterales

CLSI

CLSI rationale document MR14
February 2022

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

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								
(28) Breakpoints for tobramycin and amikacin are based on population distributions of various species, PK/PD target attainment analyses with an end point of net bacterial stasis, and limited clinical data. Clinical outcomes data for aminoglycosides as monotherapy for systemic infections are limited and have resulted in worse treatment outcomes (for infections outside of the urinary tract) compared with other therapies. Combination therapy for most indications other than urinary tract infections should be considered. Consultation with an infectious diseases specialist is recommended.								
Tobramycin	10 µg	≥19	13-18^	≤12	≤1	2^	≥4	(29) Breakpoints are based on a dosage regimen of 7 mg/kg parenterally administered every 24 h. (30) Tobramycin does not predict susceptibility to gentamicin.
Amikacin (U)[b]	30 µg	≥17	15-16^	≤14	≤16	32^	≥64	(31) Breakpoints are based on a dosage regimen of 15 mg/kg parenterally administered every 24 h.

CLSI M100-Ed33, 2023

THE REALLY BIG ONES #3

Organism	Method	Pip/tazo Previous			Pip/tazo New		
		S	I	R	S	I	R
P. aeruginosa	BMD	≤ 16	32-64	≥ 128	≤ 16	32	≥ 64
	DD	≥ 21	15-20	≤ 14	≥ 22	18-21	≤ 17

Organism	Method	Tobramycin Previous			Tobramycin New		
		S	I	R	S	I	R
P. aeruginosa	BMD	≤ 4	8	≥ 16	≤ 1	2	≥ 4
	DD	≥ 15	13-14	≤ 12	≥ 19	13-18	≤ 12

Organism	Method	Amikacin Previous			Amikacin New		
		S	I	R	S	I	R
P. aeruginosa	BMD	NO	C	H	A	N	GE
	DD	NO	C	H	A	N	GE

CLSI M100-Ed32, 2022; M100-Ed33, 2023

WISCONSIN SURVEILLANCE DATA

- *Pseudomonas aeruginosa*

Year	Percentage Susceptible
	Piperacillin/tazobactam
2016	93.4
2017	92.7
2018	88.1
2019	92.5
2020	93.4
2021	90.2
2022	91.4

Previous

≤ 16	32-64	≥ 128

MIC	Number of Isolates by Agent
	Piperacillin-tazobactam
≤ 8	1650
16	157
32	68
64	26
128	29
256	26
>256	16

Cumulative frequency distribution

"Red" shading indicates resistance

WISCONSIN SURVEILLANCE DATA

- *Pseudomonas aeruginosa*, piperacillin/tazobactam

Parameter	Previous	New
% susceptible	91.6	91.6
% intermediate	4.8	3.4
% resistant	3.6	4.9

Region	Percentage Resistance	
	Previous	New
Northern	2.7	2.7
Northeastern	3.5	4.3
Southern	3.8	4.9
Southeastern	5.5	8.5
Western	1.8	3.3

Previous			New		
≤ 16	32-64	≥ 128	≤ 16	32	≥ 64

PROBABILITY OF TARGET ATTAINMENT

- Modern methods of PK/PD evaluation determined low PTA for piperacillin-tazobactam when utilizing current CLSI breakpoints (normal renal function)
- No studies revealed high PTA with MIC > 16 μg/mL

Table 5. Summary of Studies Investigating Piperacillin-Tazobactam PK and PD Data

Dosage	Infusion Time	MIC With ≥ 90% PTA[a]
3.375 g every 6 h	30 min	≤ 8 μg/mL[10-12]
4.5 g every 6 h	30 min	≤8 μg/mL[12-15]
3.375 g every 8 h	4 h	≤8 μg/mL[14-17]
[illegible] h	4 h	≤8 μg/mL[12-15]
[illegible] h	4 h	≤16 μg/mL[12,14,17,18]
[illegible] h	3 h	≤16 μg/mL[12,13,18,19]

CLSI MR14, 2022

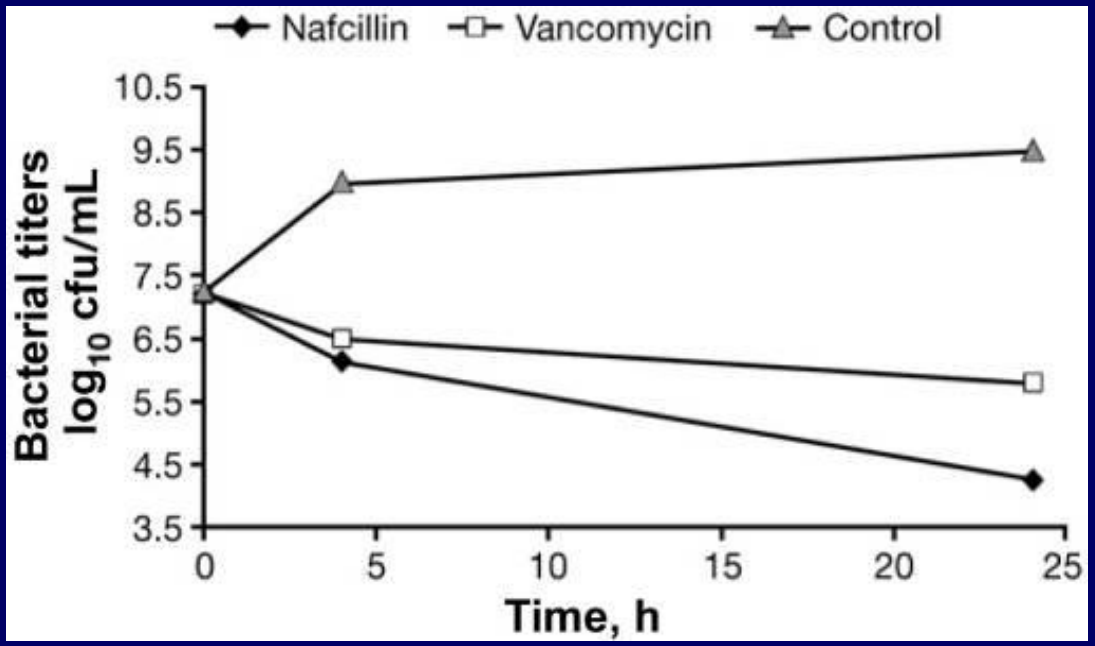
Old Business

WE ARE ON A ROLL

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, tests for *mecA* or PBP2a should be considered, because these are the most definitive tests for detection of methicillin (oxacillin) resistance (see comment [19]). 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]

CLSI M100-Ed33, 2023



AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

COMMENTARY

Use of Rapid Diagnostics To Manage Pediatric Bloodstream Infections? You Bet Your ASP!

Mark D. Gonzalez,[a] Melanie L. Yarbrough[b]

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POSITIVE BLOOD CULTURE BOTTLE

- Resistance in GNR can be multi-factorial; full phenotypic approach may be desirable
- Little standardization; very few laboratories report

J Clin Microbiol. 56:e01678-17; 2018

THEY'VE BEEN TRYING THIS…I

JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 1979, p. 347–350
0095-1137/79/03-0347/04$02.00/0

Vol. 9, No. 3

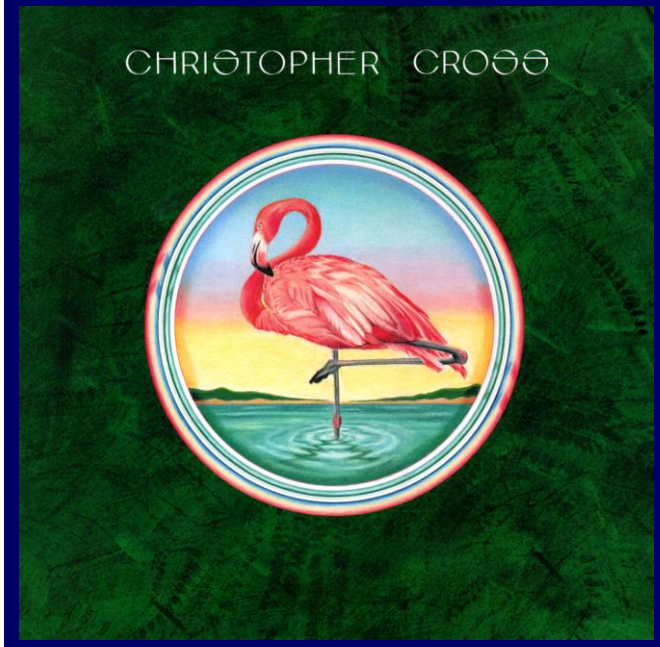
Standardization of Direct Susceptibility Test for Blood Cultures

DALE FAY†* AND JEAN E. OLDFATHER

Riverside Methodist Hospital, Columbus, Ohio 43214

Received for publication 17 December 1978

Insufficient data are available to establish the reliability of direct disk diffusion susceptibility tests performed utilizing positive blood culture broth as inoculum. When *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were used, 0.03 ml of turbid overnight blood culture broth was found to produce zone diameters closely approximating the size of diameters obtained by a standardized method. Results of direct (0.03 ml of inoculum) and standardized susceptibility tests were then compared for 116 positive blood cultures (1,069 individual disk comparisons). There were 1,011 test agreements (94.6%). There were also 48 (4.5%) minor discrepancies (change between sensitive and intermediate or between intermediate and resistant) and 10 (0.9%) major discrepancies (change between sensitive and resistant). The major discrepancies were randomly distributed among several organisms and antibiotics. Discrepancies occurred most frequently in the more clinically acceptable direction; i.e., in 79.3% the direct test indicted greater resistance than the standardized test. These data establish that 0.03 ml of turbid overnight blood culture broth produces results which compare closely to those obtained with standard methods, and in practice yield direct susceptibility results with a clinically acceptable level of reliability.



J Clin Microbiol. 9:347-350; 1979

TWO DROPS

TABLE 2. *Organisms included in the clinical comparison of the direct and standardized susceptibility tests*

Organism	No. of strains tested	Discrepancies		Agreements
		Major	Minor	
E. coli	46	2	22	390
Klebsiella	16	2	12	130
Proteus mirabilis	8	2	3	67
Providencia stuartii	1	0	1	8
Citrobacter diversus	1	0	0	9
Citrobacter freundii	1	0	1	8
Enterobacter aerogenes	3	0	1	26
Enterobacter cloacae	3	2	1	24
Enterobacter agglomerans	1	0	0	9
Serratia marcescens	3	0	0	27
P. aeruginosa	4	0	0	36
Pseudomonas species	2	0	2	16
Bordetella parapertussis	1	0	0	9
Acinetobacter calcoaceticus	1	0	0	9
S. aureus	12	0	0	120
Staphylococcus epidermidis	8	2	4	74
Enterococcus	3	0	1	29
Group D *Streptococcus* (not Enterococcus)	1	0	0	10
Viridans *Streptococcus*	1	0	0	10

TABLE 3. *Distribution of discrepancies between direct and standardized susceptibility tests by antibiotic*

Antibiotic	No. of comparisons	Discrepancies		
		Total	Major	Minor
Ampicillin	116	4 (3.8)[a]	1	3
Carbenicillin	91	4 (4.3)	0	4
Cephalothin	116	16 (13.8)	2	14
Chloramphenicol	116	6 (5.2)	3	3
Clindamycin	25	0	0	0
Colistin	91	6 (6.6)	2	4
Erythromycin	25	0	0	0
Gentamicin	116	0	0	0
Kanamycin	116	1 (0.8)	0	1
Methicillin	25	1 (4.0)	0	1
Penicillin	25	3 (12.0)	1	2
Streptomycin	91	9 (9.9)	0	9
Tetracycline	116	8 (6.9)	1	7

Major (0.9%): shift between sensitive and resistant

Minor (4.5%): shift between sensitive and intermediate
shift between intermediate and resistant

J Clin Microbiol. 9:347-350; 1979

THEY'VE BEEN TRYING THIS…II

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Nov. 1981, p. 696–698
0066-4804/81/110696-03$02.00/0
Vol. 20, No. 5

Evaluation of a Direct Blood Culture Disk Diffusion Antimicrobial Susceptibility Test

GARY V. DOERN,†* DAVID R. SCOTT,‡ ABDEL L. RASHAD, AND KENNETH S. KIM

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Received 10 April 1981/Accepted 6 August 1981

A total of 556 unique blood culture isolates of nonfastidious aerobic and facultatively anaerobic bacteria were examined by direct and standardized disk susceptibility test methods (4,234 antibiotic-organism comparisons). When discrepancies which could be accounted for by the variability inherent in disk diffusion susceptibility tests were excluded, the direct method demonstrated 96.8% overall agreement with the standardized method. A total of 1.6% minor, 1.5% major, and 0.1% very major discrepancies were noted.

Antimicrob Agents Chemother. 20:696-698; 1981

SIX DROPS

TABLE 1. *Comparison of direct blood culture disk susceptibility test results with standardized disk susceptibility test results*

Antibiotic	No. of discrepancies[a] for: Gram-negative bacilli[b] n = 171		Streptococci[c] n = 166		Staphylococci and micrococci[d] n = 219		Totals	
Kanamycin	0, 8, 66	(56.7)	NT		NT		0, 8, 66	(56.7)
Gentamicin	0, 1, 3	(97.7)	NT		NT		0, 1, 3	(97.7)
Tobramycin	0, 1, 5	(96.5)	NT		NT		0, 1, 5	(96.5)
Amikacin	0, 4, 17	(87.7)	NT		NT		0, 4, 17	(87.7)
Carbenicillin	0, 6, 14	(88.3)	NT		NT		0, 6, 14	(88.3)
Ampicillin	1, 3, 12	(90.6)	0, 2, 11	(92.2)	NT		1, 5, 23	(91.4)
Cephalothin	0, 4, 50	(68.5)	0, 0, 6	(96.4)	0, 0, 0	(100)	0, 4, 56	(89.2)
Tetracycline	0, 1, 43	(74.3)	1, 5, 15	(87.4)	1, 2, 2	(97.7)	2, 8, 60	(87.4)
Chloramphenicol	0, 1, 13	(91.8)	0, 0, 9	(94.6)	0, 3, 3	(97.2)	0, 4, 25	(94.8)
Erythromycin	NT		1, 1, 9	(93.4)	0, 2, 3	(97.7)	1, 3, 12	(95.8)
Clindamycin	NT		0, 0, 6	(96.4)	0, 2, 0	(99.1)	0, 2, 6	(97.9)
Penicillin	NT		0, 2, 14	(90.4)	0, 5, 25	(96.3)	0, 7, 39	(88.1)
Methicillin	NT		NT		1, 11, 6	(91.8)	1, 11, 6	(91.8)
Totals	1, 29, 223	(83.6)	2, 10, 70	(92.9)	2, 25, 39	(95.7)	5, 64, 332	(90.5)

Very Major Error; Major Error; Minor Error; (percentage concordance)

Antimicrob Agents Chemother. 20:696-698; 1981

THEY'VE BEEN TRYING THIS…III

JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 1984, p. 473–477
0095-1137/84/090473-05$02.00/0

Vol. 20, No. 3

Rapid Antimicrobial Susceptibility Testing of Isolates from Blood Cultures by Direct Inoculation and Early Reading of Disk Diffusion Tests

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Clinical Microbiology Division, University of Washington,[1] and University Hospital,[3] Seattle, Washington 98195; Harborview Medical Center, Seattle, Washington 98104;[2] Seattle Veterans Administration Medical Center, Seattle, Washington 98108;[4] and Childrens Orthopedic Hospital and Medical Center, Seattle, Washington 98105[5]

Received 13 January 1984/Accepted 24 May 1984

Disk diffusion tests, inoculated directly from positive blood cultures, were evaluated for accuracy of reading zone diameters after 4- and 6-h and overnight incubation. In comparisons with results from standard disk diffusion tests, the 4-h results were in agreement for 83% of tests with gram-positive organisms and 64% of tests with gram-negative organisms. When minor discrepancies were ignored, the 4-h readings were in agreement for 98% of the tests with gram-positive organisms and 95% of the tests with gram-negative organisms. After 6 h of incubation, 91% of the tests with gram-positive organisms and 86% of the tests with gram-negative organisms agreed with standard results. The agreement was 99% for tests with both gram-positive and gram-negative organisms when minor discrepancies were excluded. Very major discrepancies occurred in two tests (0.1%) with gram-positive organisms and were not observed in tests with gram-negative organisms. The frequencies of major discrepancies were 3.5% after 4 h, 0.6% after 6 h, and 0.7% after overnight incubation. Ampicillin and cephalothin tests with *Escherichia coli* and *Klebsiella* spp. accounted for 81% of the major discrepancies in tests with gram-negative organisms. Oxacillin tests accounted for more than half of the major discrepancies in tests with staphylococci. The results of this study, which did not include the newer antibiotics, indicate that direct susceptibility tests from blood cultures read after 6 h of incubation are more reliable than 4-h results and produce less than 1% major errors in comparisons with standard susceptibility tests.

J Clin Microbiol. 20:473-477; 1984

READING 'EM EARLY

TABLE 1. Percentage of isolates with direct tests read after 4 or 6 h

Blood culture isolate	No. of isolates	% Read after: 4 h	% Read after: 6 h[a]
Gram positive			
S. aureus	60	22	63
Coagulase-negative staphylococci	87	3	21
Beta-hemolytic streptococci	30	37	87
Enterococci	21	19	52
Pneumococci	21	10	38
Viridans streptococci	14	0	0
Total for gram positive	233	14	44
Gram negative			
E. coli	84	52	85
Klebsiella spp.	38	40	76
Enterobacter spp.	12	42	92
P. aeruginosa	11	0	64
Others[b]	25	36	60
Total for gram negative	170	43	78

TABLE 2. Discrepancies from direct tests compared with standardized tests

Isolate type, time incubated	No. of tests	No. of discrepancies: Very major (%)	Major (%)	Minor (%)	Overall agreement (%)
Gram positive					
4 h	216	1 (0.5)	3 (1.4)	32 (14.8)	83.3
6 h	494	0	3 (0.6)	39 (7.9)	91.4
Overnight	1,307	1 (0.07)	8 (0.6)	65 (5.0)	94.3
Gram negative					
4 h	361	0	17 (4.7)	114 (31.6)	63.7
6 h	438	0	3 (0.7)	59 (13.5)	85.8
Overnight	762	0	6 (0.8)	73 (9.6)	89.6

J Clin Microbiol. 20:473-477; 1984

RESULTS

TABLE 3 Resolved performance of direct-from-blood-culture disk diffusion method at 18 h, by antibiotic

Drug	No. of isolates		% CA	No. (%) of:		
	S	R		VME	ME	mE
Amikacin	45	13	96.7	0 (0)	0 (0)	2 (3.3)
Amoxicillin-clavulanate	9	17	88.9	0 (0)	1 (11.1)	2 (7.4)
Ampicillin	6	9	93.3	0 (0)	0 (0)	1 (6.7)
Aztreonam	21	28	94.3	0 (0)	0 (0)	3 (5.7)
Cefazolin	5	18	73.1	0 (0)	2 (40.0)	5 (19.2)
Cefepime	41	17	91.7	0 (0)	0 (0)	5 (8.3)
Cefoxitin	10	15	85.2	0 (0)	1 (10.0)	3 (11.1)
Ceftazidime	25	31	89.8	0 (0)	0 (0)	6 (10.2)
Ceftriaxone	16	29	87.5	0 (0)	2 (12.5)	4 (8.3)
Ciprofloxacin	26	27	96.6	0 (0)	0 (0)	1 (1.7)
Ertapenem	22	12	83.3	0 (0)	0 (0)	7 (16.7)
Gentamicin	39	18	95.0	0 (0)	1 (2.6)	2 (3.3)
Imipenem	34	21	68.3	0 (0)	3 (8.8)	15 (25.0)
Levofloxacin	33	25	91.7	0 (0)	1 (3.0)	3 (5.0)
Meropenem	37	19	84.7	0 (0)	1 (2.7)	8 (13.6)
Minocycline	29	11	80.0	0 (0)	0 (0)	9 (20.0)
Piperacillin-tazobactam	23	30	83.3	0 (0)	0 (0)	10 (16.7)
Tigecycline	35	3	87.2	0 (0)	0 (0)	5 (12.8)
Tobramycin	39	17	93.2	0 (0)	0 (0)	4 (6.8)
Trimethoprim-sulfamethoxazole	17	30	95.8	0 (0)	0 (0)	2 (4.2)

J Clin Microbiol. 56:e01678-17; 2018

RESULTS

TABLE 3 Resolved performancod-culture disk diffusion met 18 h, by antibiotic

Drug	% CA	No. (%) of: VME	ME
Amikacin	96.7	0 (0)	0 (0)
Amoxicillin-clavulanate	88.9	0 (0)	1 (11.1)
Ampicillin	93.3	0 (0)	0 (0)
Aztreonam	94.3	0 (0)	0 (0)
Cefazolin	73.1	0 (0)	2 (40.0)
Cefepime	91.7	0 (0)	0 (0)
Cefoxitin	85.2	0 (0)	1 (10.0)
Ceftazidime	89.8	0 (0)	0 (0)
Ceftriaxone	87.5	0 (0)	2 (12.5)
Ciprofloxacin	96.6	0 (0)	0 (0)
Ertapenem	83.3	0 (0)	0 (0)
Gentamicin	95.0	0 (0)	1 (2.6)
Imipenem	68.3	0 (0)	3 (8.8)
Levofloxacin	91.7	0 (0)	1 (3.0)
Meropenem	84.7	0 (0)	1 (2.7)
Minocycline	80.0	0 (0)	0 (0)
Piperacillin-tazobactam	83.3	0 (0)	0 (0)
Tigecycline	87.2	0 (0)	0 (0)
Tobramycin	93.2	0 (0)	0 (0)
Trimethoprim-sulfamethoxazole	95.8	0 (0)	0 (0)

TABLE 5 Resolved performance of direct-from-blood-culture disk diffusion method at 6 h, by antibiotic

Drug	No. of isolates S	R	% CA	No. (%) of: VME	ME	mE
Amikacin	45	13	62.2	3 (23.1)	2 (4.4)	12 (26.7)
Amoxicillin-clavulanate	9	17	60.0	0 (0)	1 (11.1)	9 (36.0)
Ampicillin	6	9	69.2	0 (0)	1 (16.7)	3 (23.1)
Aztreonam	21	28	84.2	0 (0)	1 (4.8)	5 (13.2)
Cefazolin	5	18	66.7	1 (5.6)	2 (40.0)	6 (25.0)
Cefepime	41	17	75.6	0 (0)	4 (9.8)	6 (13.3)
Cefoxitin	10	15	68.0	0 (0)	1 (10.0)	7 (28.0)
Ceftazidime	25	31	65.9	0 (0)	4 (16.0)	11 (25.0)
Ceftriaxone	16	29	77.3	0 (0)	3 (18.8)	7 (15.9)
Ciprofloxacin	24	27	57.1	0 (0)	1 (4.2)	16 (39.0)
Ertapenem	22	12	73.7	0 (0)	2 (9.1)	8 (21.1)
Gentamicin	39	18	95.6	0 (0)	0	2 (4.4)
Imipenem	34	21	46.7	0 (0)	6 (17.6)	18 (40.0)
Levofloxacin	33	25	75.6	0 (0)	1 (3.0)	10 (22.2)
Meropenem	36	19	52.3	0 (0)	9 (25.0)	11 (25.6)
Minocycline	29	11	65.9	0 (0)	0	12 (29.3)
Piperacillin-tazobactam	22	30	64.4	2 (6.7)	4 (18.2)	11 (25.0)
Tigecycline	35	3	45.7	0 (0)	3 (8.6)	16 (45.7)
Tobramycin	39	17	95.6	0 (0)	0	2 (4.4)
Trimethoprim-sulfamethoxazole	17	30	86.4	1 (3.3)	2 (11.8)	3 (6.8)

J Clin Microbiol. 56:e01678-17; 2018

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 **(refer to Tables 3E-2 and 3E-3 for antimicrobial agent-specific incubation lengths)**
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.

Daily or weekly QC; *E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853

CLSI M100-Ed33, 2023

TABLE 3E-2

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								
	Ampicillin	10 µg	8-10	≥ 16	-	12-15	≤11	(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.)								
	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	
	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								
	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								
	Tobramycin	10 µg	8-10	≥ 15	-	13-14	≤ 12	
			16-18	≥ 15	-	13-14	≤ 12	
FOLATE PATHWAY ANTAGONISTS								
	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.

CLSI M100-Ed32, 2022; addendum from Ed33, 2023

NEWBIES

Agent	Concentration	Incubation time (hours)	Zone Diameters (mm)		
			S	I	R
Meropenem	10 μg	8-10	≥ 22	20-21	≤ 19
		16-18	≥ 22	19-21	≤ 18

Agent	Concentration	Incubation time (hours)	Zone Diameters (mm)		
			S	I	R
Ciprofloxacin*	5 μg	8-10	≥ 21	18-20	≤ 17
		16-18	≥ 21	18-20	≤ 17

* not for *Salmonella* spp.

CLSI M100-Ed33, 2023

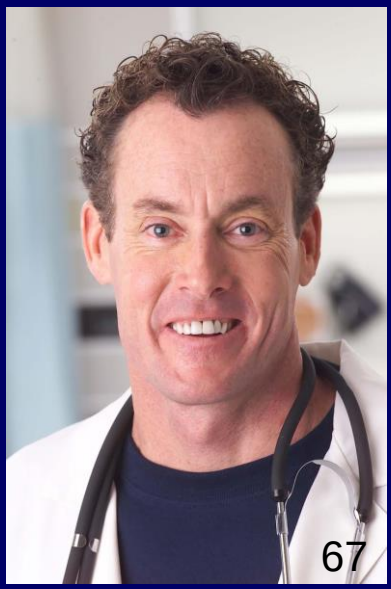

Table 3E-3. Zone Diameter Disk Diffusion Breakpoints for *Pseudomonas aeruginosa* Direct From Blood Culture

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.)								
	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								
	Meropenem	10 µg	8-10	**≥ 19**	-	**16-18**	**≤15**	(4) Breakpoints are based on a dosage regimen of 1 g administered every 8 h.
			16-18	≥ 19	-	16-18	≤ 15	
AMINOGLYCOSIDES								
	Tobramycin	10 µg	8-10	≥ 15	-	13-14	≤ 12	
			16-18	≥ 15	-	13-14	≤ 12	
FLUOROQUINOLONES								
	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.

CLSI M100-Ed32, 2022; addendum from Ed33, 2023


GET WILD UNO
UNO
NOW WITH CUSTOMIZABLE WILD CARDS!
2
3
4
WILD
2–10
7+

Table 1


one
BEE GEES

AmpC DEREPRESSION DURING Rx

Serratia spp.
Providencia spp.
Indole-positive *Proteus*
Citrobacter spp.
Enterobacter spp.

CLSI M100-Ed33, 2023

Serratia spp.	++
Providencia spp.	++
Morganella spp.	++
Citrobacter freundii	+++
Enterobacter cloacae	+++
yes, *Klebsiella aerogenes*	+++
Yersinia spp.	

Table 2

SELECTED THOUGHTS I

- Accuracy and reproducibility of cefiderocol susceptibility testing affected by Fe concentration and inoculum preparation (mfg. variability)

  Broth microdilution
  Disk diffusion

- Poor efficacy of amoxicillin vs. ampicillin; *Shigella*
- Clinical partners may request identification of ESBL or carbapenemase
- Gemifloxacin tested only on *K. pneumoniae*

CLSI M100-Ed33, 2023

SELECTED THOUGHTS II

- Discourage levofloxacin monotherapy for *Stenotrophomonas maltophilia*

- *Haemophilus parainfluenzae* HTM (and broth)

  Haemophilus influenzae HTM (and broth)
  MH-F agar/broth

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SELECTED THOUGHTS III

- *Streptococcus pneumoniae* from CSF:

Penicillin	MIC method
Ceftriaxone	MIC method
Cefotaxime	MIC method
Meropenem	MIC method
Vancomycin	MIC or disk diffusion method

- *Streptococcus pneumoniae* from other sites:

  Oxacillin disk diffusion method
  Follow with β-lactam MIC method if ≤ 19 mm

- Levofloxacin susceptibility can predict moxi, gemifloxacin susceptibility

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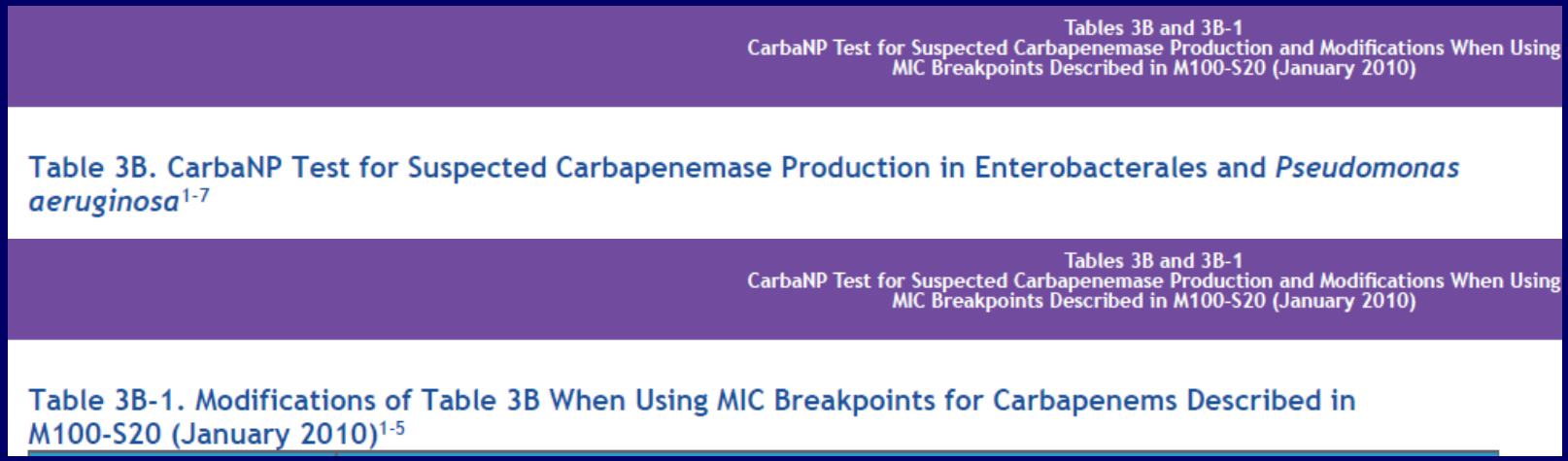
Table 3

TABLE 3B



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

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

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

Table 3B-1. Modifications of Table 3B When Using MIC Breakpoints for Carbapenems Described in M100-S20 (January 2010)[1-5]

Table 3B
CarbaNP Test for Suspected Carbapenemase Production

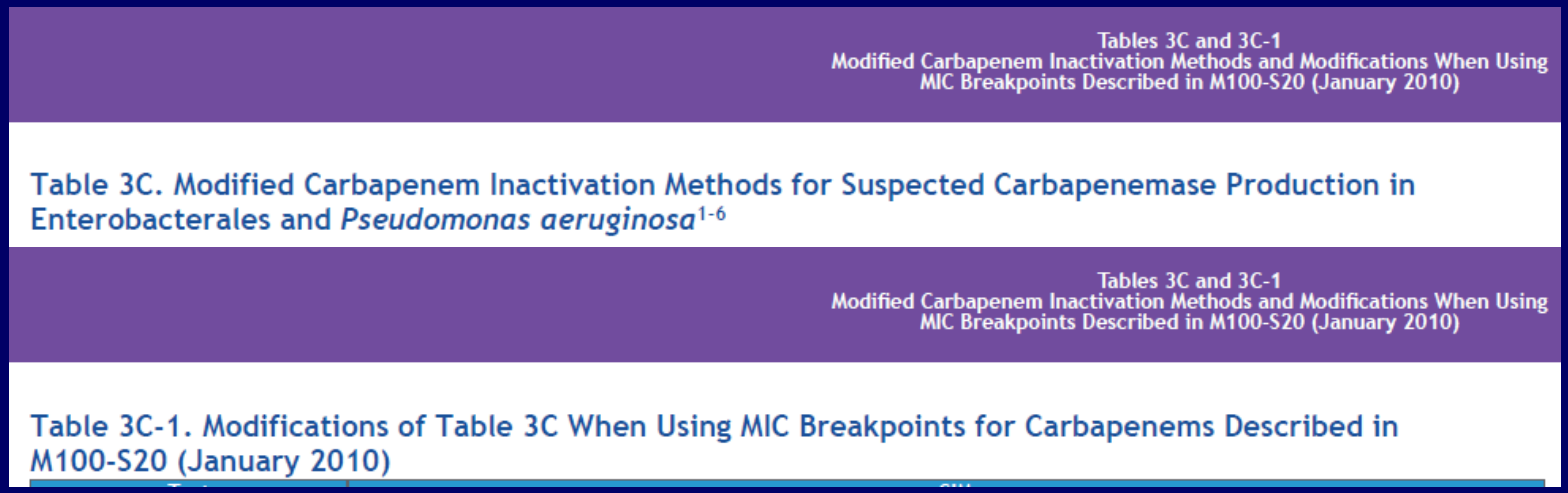
Table 3B. CarbaNP Test for Suspected Carbapenemase Production in Enterobacterales and *Pseudomonas aeruginosa*[1-7]

M100-E

"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."

CLSI M100-Ed31, 2021; Ed33, 2023

TABLE 3C



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

Table 3C. Modified Carbapenem Inactivation Methods for Suspected Carbapenemase Production in Enterobacterales and *Pseudomonas aeruginosa*[1-6]

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

Table 3C-1. Modifications of Table 3C When Using MIC Breakpoints for Carbapenems Described in M100-S20 (January 2010)

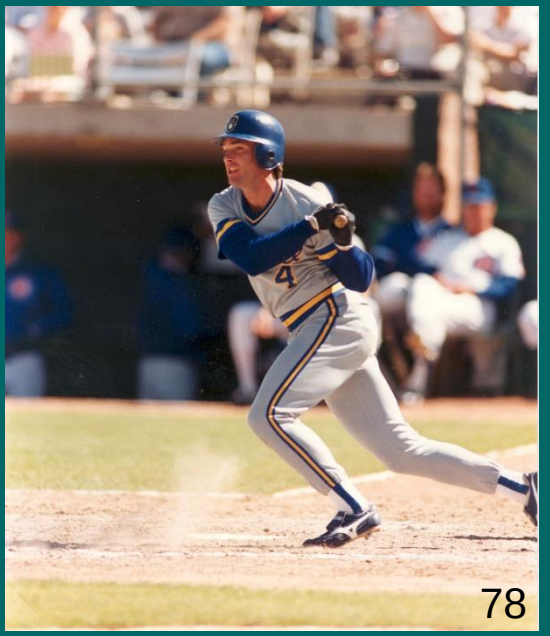
Table 3C
Modified Carbapenem Inactivation Methods

Table 3C. Modified Carbapenem Inactivation Methods for Suspected Carbapenemase Production in Enterobacterales and *Pseudomonas aeruginosa*[1-6]

"No change in the interpretation of carbapenem susceptibility test results is necessary for mCIM positive and/or eCIM results. mCIM with or without eCIM testing is not currently recommended for routine use."

CLSI M100-Ed31, 2021; Ed33, 2023

Table 4



SOME DD QC ADDITIONS/REVISIONS

E. coli NCTC 13353	ceftibuten-ledaborbactam ceftibuten
N. gonorrhoeae ATCC 49226	gentamicin

CLSI M100-Ed33, 2023

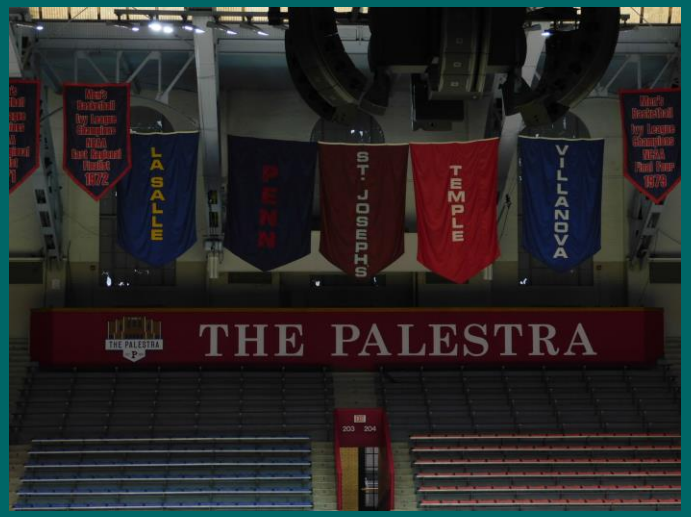

LA SALLE
PENN
ST. JOSEPHS
TEMPLE
VILLANOVA
THE PALESTRA

Table 5


FIVE GUYS
BURGERS and FRIES

SOME MIC QC ADDITIONS/REVISIONS

E. coli ATCC 25922	ceftibuten ceftibuten-avibactam piperacillin-tazobactam
E. coli NCTC 13353	ceftazidime-avibactam ceftibuten-avibactam ceftibuten-ledaborbactam
K. pneumoniae ATCC BAA-2814	ceftazidime-avibactam ceftibuten-avibactam ceftibuten-ledaborbactam meropenem-xeruborbactam
K. pneumoniae ATCC BAA-1705	ceftazidime-avibactam ceftibuten-avibactam ceftibuten-ledaborbactam
K. pneumoniae ATCC 700603	ceftibuten ceftibuten-avibactam
P. aeruginosa ATCC 27853	meropenem-xeruborbactam

CLSI M100-Ed33, 2023

MORE MIC QC ADDITIONS/REVISIONS

tebipenem	*H. influenzae* ATCC 49766 *S. pneumoniae* ATCC 49619

CLSI M100-Ed33, 2023


Thank you for your attention.
Have a better 2023.