Volume 7, Issue 1, June 2022

CLSI Subcommittee on Antimicrobial Susceptibility Testing

CLSI AST News Update

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The CLSI **Outreach Working Group (ORWG)** is providing this News Update to highlight some recent issues related to antimicrobial susceptibility testing (AST) and reporting. We are listing links to some new educational materials and reminding you where you can find information about the CLSI AST Subcommittee (SC) proceedings.

Inside This Issue:

CLSI and the AST Subcommittee Meetings

Specific scheduling modifications for the AST SC include:

1. Winter 2021, Summer 2021, and Winter 2022 meetings were held virtually. Content from these meetings is available **here.**
2. June 25-28, 2022: Loews Chicago, Rosemont, IL (virtual option available) **register here.**
3. Save the date for the next meeting: January 19-24, 2023. Virtual option will be available.

What does the CLSI AST Subcommittee do?

The first edition of the CLSI AST News Update (Vol 1, Issue 1, Spring 2016) described details about the organization and operation of the CLSI AST Subcommittee.

- You can access that Newsletter **here.**
- To learn more about upcoming or past meetings, click **here.**
- CLSI posts meeting minutes and summaries for public access **here.**
- For a quick overview, you can check out a "New Attendee Orientation" video presentation **here.**

Interested in becoming a CLSI volunteer? Learn more here.

Please remember that CLSI AST Subcommittee welcomes suggestions from you about any aspect of CLSI documents, educational materials, or this News Update.

CLSI AST Subcommittee Partnerships

Representatives with expertise in antimicrobials from the following organizations attend and participate in CLSI AST Subcommittee meetings and aid in dissemination of information regarding CLSI decisions and AST issues.

American College of Clinical Pharmacy Infectious Diseases Practice and Research Network (ACCP INFD PRN)
American Society for Microbiology (ASM)
Association of Public Health Laboratories (APHL)
ASTM International
College of American Pathologists (CAP)
European Committee on Antimicrobial Susceptibility Testing (EUCAST)
Infectious Diseases Society of America (IDSA)
Pediatric Infectious Diseases Society (PIDS)
Society for Healthcare Epidemiology of America (SHEA)
Society of Infectious Diseases Pharmacists (SIDP)
Susceptibility Testing Manufacturers Association (STMA)

Instructions for Accessing Topics/Articles in Previous CLSI News Updates:

1. Access the searchable CLSI AST SC Files and Resources **here.**
2. Enter keyword (eg, *Candida auris*) in the "Search" box.
3. A listing will display items in which this keyword appears. In columns 2 (Document) and 4 (Details), the notation "AST News Update" identifies the News Update edition where the keyword appears.
4. Click on the link in column 2 ("Document") to access the specific News Update edition and retrieve the article.

Note that additional AST SC Files and Resources can be accessed by following these same steps.

Webinars

Registration will open mid-June. for information on upcoming webinars please visit the CLSI website **here.**

Upcoming Webinar

2022 CLSI Joint Webinar With SIDP-ACCP
The Laboratory—Stewardship Partnership: Putting Susceptibility Testing Results for Gram-Negative Organisms Into Practice

Thursday, July 14, 2022 | 1:00-2:30 pm Eastern (US) Time

Presenters:

Tanis Dingle, PhD, D(ABMM), FCCM
Clinical Microbiologist
Alberta Precision Laboratories–Public Health Laboratory
Edmonton, AB, Canada

Samuel L. Aitken, PharmD, MPH, BCIDP
Pharmacy Specialist, Infectious Diseases
University of Michigan
Ann Arbor, MI, USA

Archived and Free On-Demand Webinars:

Recently archived CLSI webinars can be accessed on demand (it is best to search by date) **here.** Archived on-demand webinars are available free of charge **six months** after the scheduled event for CLSI members. Some recent webinars are listed below:

- Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data (April 2022)
- CLSI 2022 Antimicrobial Susceptibility Testing Update (March 2022)
- Breakpoints Matter: Understanding CLSI Efforts and New CAP Requirements to Ensure Appropriate Antimicrobial Treatment for All Patients (January 2022)
- *CLSI-SIDP ACCP Annual Webinar: The Evolving Value of a Laboratory - Stewardship Partnership: Cases in Susceptibility Testing, Rapid Diagnostics and More! (September 2021)
- CLSI-CAP Annual Webinar: Ensuring Quality Beyond the Test: Reporting Antimicrobial Susceptibility Results (FREE January 2021)
- CLSI-CAP Annual Webinar: Incorporating the Newest CLSI Recommendations for Antimicrobial Susceptibility Testing Into Your Stewardship Activities (FREE January 2021)
- What's New in the 2020 Standards for Antimicrobial Susceptibility Testing (FREE February 2020)
- Understanding Breakpoint Decisions: CLSI Rationale Documents (FREE December 2019)
- CLSI-CAP Annual Webinar: Rational Approach to Antibacterial and Antifungal Breakpoints (FREE November 2019)
- Understanding Susceptibility Test Data as a Component of Antimicrobial Stewardship in Veterinary Settings (FREE July 2019)

*This webinar was not hosted by CLSI, but can be purchased on demand **here.**

CLSI Educational Workshops Held at CLSI Meetings

Upcoming Workshop (In Person, Virtual, and On Demand)

Updating Breakpoints—Challenges and Solutions for Various Stakeholders

Saturday, June 25, 2022, 5:00–7:00 PM CST
Loews Chicago O'Hare Hotel, Rosemont, IL

Presenters:

Natasha Griffin, PhD
Center for Devices and Radiological Health (CDRH)
US Food and Drug Administration
Silver Spring, MD

Romney M. Humphries, PhD, D(ABMM)
Medical Director, Clinical Microbiology
Vanderbilt University Medical Center
Nashville, TN

Jean B. Patel, PhD, D(ABMM)
Principal Scientist, Microbiology
Beckman Coulter
Sacramento, CA

Dimitri Iarikov, MD, PhD
Center for Drug Evaluation and Research (CDER)
US Food and Drug Administration
Silver Spring, MD

The slides presented for previous educational workshops can be found **here.**

Note: The last workshop was held in January 2020. Workshops will resume with the above-mentioned event.

2.0 P.A.C.E.® CE Credits will be provide

ASM Microbe 2022 (In Person and Virtual) Washington, DC

ORWG-Submitted Presentations (Available On Demand)

Symposium

Title: Antibiograms: What for?

Date/Time: Monday, June 13, 2022, 8:15-10:00 am EST

Presenters:

Patricia Simner, PhD, D(ABMM)
Johns Hopkins Medical Institute
Baltimore, MD

Kate Dzintars, PharmD, BCPS-AQ ID
Johns Hopkins Medical Institute
Baltimore, MD

Meet the Experts

Title: Piperacillin-Tazobactam: Clinical and Susceptibility Review

Date/Time: Sunday, June 12, 2022, 7:00-8:00 am EST

Presenter:

Pranita Tamma, MD
Johns Hopkins Medical Institute
Baltimore, MD

New Educational Resource for CLSI M100! FREE!

Using M100-Ed32

Using M100: Performance Standards for Antimicrobial Susceptibility Testing

Improve your lab's antimicrobial susceptibility testing (AST) by using this self-paced, online learning program. This interactive program will teach you how to navigate the many tables found in CLSI's document M100—Performance Standards for Antimicrobial Susceptibility Testing, 32nd Edition.

During this online learning course, you will learn:

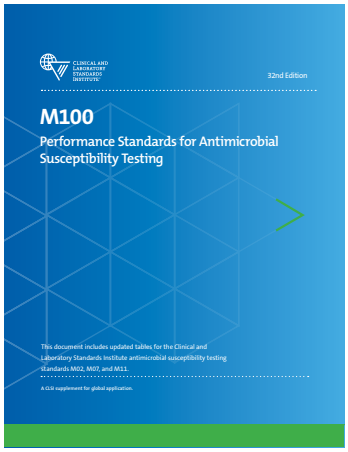
- More about CLSI and its role in AST.
- How to locate specific tables in M100 that can guide AST testing and reporting decisions, such as:
  - Selecting antimicrobial agents for testing and reporting.
  - Interpreting zone diameter and minimal inhibitory concentration (or MIC) measurements.
  - Choosing organisms for quality control of disk diffusion and MIC tests.

Cost: Free

Interested in getting 1.5 P.A.C.E.® CE Credits for completing this course? Simply purchase the add-on CE credits for $30 **here,** before or after you complete the course.

New/Updated CLSI AST Documents Are Here!

M100 | Performance Standards for Antimicrobial Susceptibility Testing, 32nd Edition



This new edition is available as a read-only version **here.**

Review the listing of all changes in the front of M100 32nd Edition "Overview of Changes" section.

Major changes include:

Revised Breakpoints:

- Cefiderocol
  - Disk diffusion breakpoints for Enterobacterales and *Acinetobacter* spp.
  - Disk diffusion and MIC breakpoints for *Stenotrophomonas maltophilia*
- Ceftolozane-tazobactam
  - Disk diffusion breakpoints for Enterobacterales
- Piperacillin-tazobactam
  - Disk diffusion and MIC breakpoints for Enterobacterales
- Ampicillin-clavulanate
  - MIC breakpoints for *Haemophilus influenzae*
- Lefamulin
  - Disk diffusion breakpoints for *H. influenzae* and *Streptococcus pneumoniae*

Deleted Breakpoints:

- Amoxicillin-clavulanate
  - Disk diffusion breakpoints for *H. influenzae*

Additional Information:

- New dosage regimen comments for existing antimicrobial agents and a variety of organisms/organism groups
- Activity of beta-lactam combination agent versus beta-lactam alone

Expanded Recommendations:

- Direct disk diffusion testing: Enterobacterales from positive blood culture broth
  - Added breakpoints for 8-10 h readings for:
    - Aztreonam
    - Ceftazidime
    - Ceftriaxone
    - Tobramycin
- Direct disk diffusion testing: *Pseudomonas aeruginosa* from positive blood culture broth
  - Added breakpoints for 8-10 h readings for:
    - Ciprofloxacin
    - Meropenem
  - Added breakpoints for 16-18 h readings for:
    - Ceftazidime
    - Ciprofloxacin
    - Meropenem
    - Tobramycin

M100-Ed32 Updates *(Continued)*

MIC QC ranges added:

- Colistin
  - *Escherichia coli* NCTC™ 13846
- Ceftibuten
  - *E. coli* ATCC® 13353
  - *Klebsiella pneumoniae* ATCC® BAA-1705
  - *K. pneumoniae* ATCC® BAA-2814
- Gentamicin
  - *Neisseria gonorrhoeae* ATCC® 49226
- Meropenem:
  - *E. coli* NCTC™ 13353
  - *Acinetobacter baumannii* NCTC™ 13304
- Tebipenem QC ranges:
  - *Bacteroides fragilis* ATCC® 25285
  - *Bacteroides thetaiotaomicron* ATCC® 29741
  - *Clostridioides difficile* ATCC® 700057
  - *Eggerthella lenta* ATCC® 43055

MIC QC ranges revised:

- Colistin
  - *E. coli* ATCC® BAA-3170 (formerly AR Bank #0349 *mcr-1*)
  - *P. aeruginosa* ATCC® 27853
- Imipenem
  - *E. coli* ATCC® 25922™
  - *K. pneumoniae* ATCC® 700603
- Imipenem-relebactam
  - *E. coli* ATCC® 25922™
  - *K. pneumoniae* ATCC® 700603
- Fidaxomicin
  - *C. difficile* ATCC® 700057

No additions/revisions to disk diffusion QC ranges

Rationale Documents

CLSI publishes rationale documents that provide the scientific reasons behind the subcommittee's decisions, along with documentation of the standardized data and methods used to determine breakpoints.

Piperacillin-tazobactam Breakpoints for Enterobacterales, 1st edition was published in February 2022 and is the latest addition to these documents. To access rationale documents, click **here.**

FDA-recognized breakpoints can be found **here.**

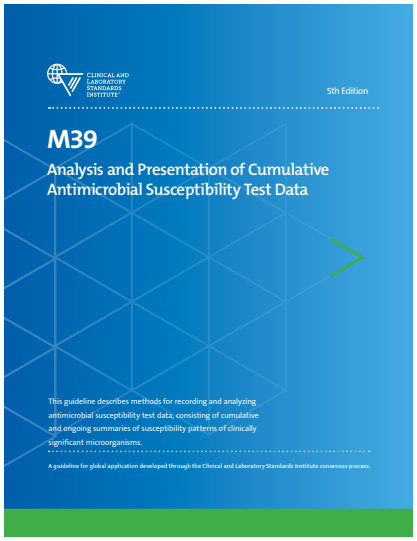
Archives of Retired Breakpoints and Methods

An archive of breakpoints removed from M100 since 2010 together with the rationale for their removal is available **here.**

Similarly, an archive of methods removed from M100 since 2017 is available **here.**

New/Updated CLSI AST Documents Are Here!

M39 | Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data, 5th Edition



This guideline describes methods for recording and analyzing antimicrobial susceptibility test data, consisting of cumulative and ongoing summaries of susceptibility patterns of clinically significant microorganisms.

New and expanded content includes:

- Refined definitions for "cumulative antimicrobial susceptibility test data report" and "antibiogram."
- Considerations for extracting data from different sources (eg, automated antimicrobial susceptibility testing instrument, LIS, electronic health record) for antibiogram preparation.
- Combining results from rapid diagnostics and antimicrobial resistance marker testing with the antibiogram.
- Developing antibiograms for yeast and antifungal agents.
- Developing antibiograms for multiple facilities, long-term care facilities, and veterinary practices.
- Use of antibiograms in antimicrobial stewardship programs.
- Considerations for preparing cumulative antimicrobial susceptibility test data reports for peer-reviewed publication.
- Using statistical analysis including percentiles, interquartile ranges, MIC_{50}, MIC_{90}, to evaluate antibiogram data.
- Including intermediate^ in antibiograms for applicable antimicrobial agents known to have the ability to concentrate in the urine.
- Defining antibiogram percent susceptible thresholds related to empirical therapy decisions.

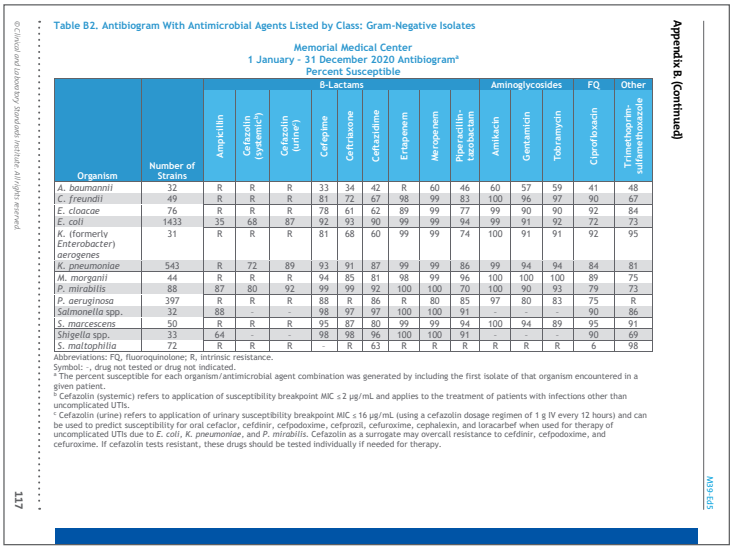


Table B2. Antibiogram With Antimicrobial Agents Listed by Class: Gram-Negative Isolates

Memorial Medical Center
1 January - 31 December 2020 Antibiogram[a]
Percent Susceptible

Organism	Number of Strains	β-Lactams								Aminoglycosides			FQ	Other
		Ampicillin	Cefazolin (systemic[b])	Cefazolin (urine[c])	Cefepime	Ceftriaxone	Ceftazidime	Ertapenem	Meropenem	Piperacillin-tazobactam	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Trimethoprim-sulfamethoxazole
A. baumannii	32	R	R	R	33	34	42	R	60	46	60	57	59	41	48
C. freundii	49	R	R	R	81	72	67	98	99	83	100	96	97	90	67
E. cloacae	76	R	R	R	78	61	62	89	99	77	99	90	90	92	84
E. coli	1433	35	68	87	92	93	90	99	99	94	99	91	92	72	73
K. (formerly *Enterobacter*) *aerogenes*	31	R	R	R	81	68	60	99	99	74	100	91	91	92	95
K. pneumoniae	543	R	72	89	93	91	87	99	99	86	99	94	94	84	81
M. morganii	44	R	R	R	94	85	81	98	99	96	100	100	100	89	75
P. mirabilis	88	87	80	92	99	99	92	100	100	70	100	90	93	79	73
P. aeruginosa	397	R	R	R	88	R	86	R	80	85	97	80	83	75	R
Salmonella spp.	32	88	-	-	98	97	97	100	100	91	-	-	-	90	86
S. marcescens	50	R	R	R	95	87	80	99	99	94	100	94	89	95	91
Shigella spp.	33	64	-	-	98	98	96	100	100	91	-	-	-	90	69
S. maltophilia	72	R	R	R	-	R	63	R	R	R	R	R	R	6	98

Abbreviations: FQ, fluoroquinolone; R, intrinsic resistance.
Symbol: -, drug not tested or drug not indicated.
[a] The percent susceptible for each organism/antimicrobial agent combination was generated by including the first isolate of that organism encountered in a given patient.
[b] Cefazolin (systemic) refers to application of susceptibility breakpoint MIC ≤ 2 µg/mL and applies to the treatment of patients with infections other than uncomplicated UTIs.
[c] Cefazolin (urine) refers to application of urinary susceptibility breakpoint MIC ≤ 16 µg/mL (using a cefazolin dosage regimen of 1 g IV every 12 hours) and can be used to predict susceptibility for oral 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 as a surrogate may overcall resistance to cefdinir, cefpodoxime, and cefuroxime. If cefazolin tests resistant, these drugs should be tested individually if needed for therapy.

Appendix B. (Continued)

M39-Appendix B, Table B2.

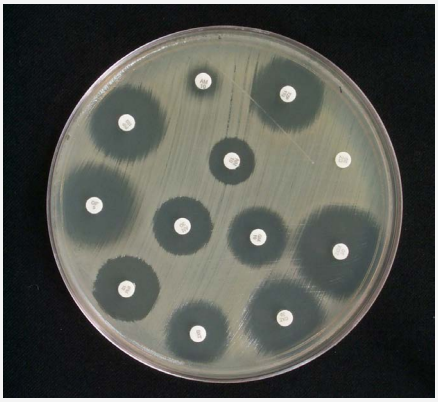
In addition, the recommendation to list percent intermediate in addition to percent susceptible for penicillin with viridans group streptococci was deleted.

Featured Article

Implementation of the CLSI Method for Direct Disk Diffusion Testing From Positive Blood Cultures

Audrey N. Schuetz, Mayo Clinic, Rochester, MN
April Bobenchik, Penn State Hershey Medical Center, Hershey, PA
Shelley Campeau, Microbiology Consultant, Tucson, AZ

The CLSI AST Subcommittee has developed and published breakpoints for direct blood culture disk diffusion (DD) testing of several antimicrobial agents for Enterobacterales and *Pseudomonas aeruginosa*.[1] This project was undertaken to provide antimicrobial susceptibility testing (AST) results earlier than traditional AST methods. Rapidity of susceptibility testing and reporting is particularly important for bloodstream infections. Studies have shown that mortality from sepsis increases every hour that the time to first appropriate antimicrobial is delayed.[2] CLSI developed this method to provide laboratories with a direct-from-blood culture testing approach which is both simple to perform and inexpensive.



An initial pilot study of direct DD from positive blood cultures demonstrated good performance, and the method has since been optimized.[3] To establish breakpoints, results from the direct DD method using positive blood culture broth as the inoculum with incubation of the DD test for 8-10 and 16-18 hours were compared to the standard DD method using isolated colonies with 16-18 hours incubation. For some agents, the standard breakpoints worked, while others needed adjustment. It is important to note that the breakpoints for *P. aeruginosa* for ciprofloxacin at the 8-10 hour read differ from the standard DD breakpoints for *P. aeruginosa* for that antimicrobial. Details of this method and DD breakpoints are provided in Tables 3E-1, -2, and -3 of the M100 document.

Recent M100 2022 breakpoint additions for direct blood culture DD include several antimicrobial agents for Enterobacterales and *P. aeruginosa*, including both early (8-10-hour reading) and overnight (16-18-hour reading) breakpoints for several antimicrobials (see Table 1).

Table 1. CLSI Breakpoints for Direct Blood Culture Disk Diffusion

Antimicrobial	Enterobacterales		*Pseudomonas aeruginosa*	
	8-10 hr read	16-18 hr read	8-10 hr read	16-18 hr read
Ampicillin		X		
Aztreonam	X[a]	X		
Ceftazidime	X[a]	X		X[a]
Ceftriaxone	X[a]	X		
Ciprofloxacin			X[a,b]	X[a]
Meropenem				X[a]
Tobramycin	X[a]	X	X[a]	X[a]
Trimethoprim-sulfamethoxazole		X		

[a] Antimicrobials with direct DD newly provided in M100 32nd edition.
[b] Antimicrobial for which direct DD breakpoints differ from the standard DD breakpoints.

Implementation of the CLSI Method for Direct Disk Diffusion Testing From Positive Blood Cultures (*Continued*)

Performance of the direct blood culture DD method must be paired with an identification method since breakpoints are specific to either Enterobacterales or *P. aeruginosa*. Laboratory workflows for this method vary based on whether or not the organism identification is available at the time of direct DD set up (see Figure 1). It is important to note that direct DD must be set up within 8 hours of the blood culture bottle flagging positive for gram-negative bacilli. If the organism identification is available at the time of direct DD set up, the applicable numbers of disks should be used (ie, if Enterobacterales, set up the six applicable disks for which breakpoints have been developed; if *P. aeruginosa*, set up the four applicable disks). However, if the identification is other than Enterobacterales or *P. aeruginosa*, direct DD should not be set up. On the other hand, if identification will be available after direct DD set up, the laboratory should set up all eight disks. Options for identification at the time of direct DD set up include rapid molecular tests or rapid (ie, early) matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).

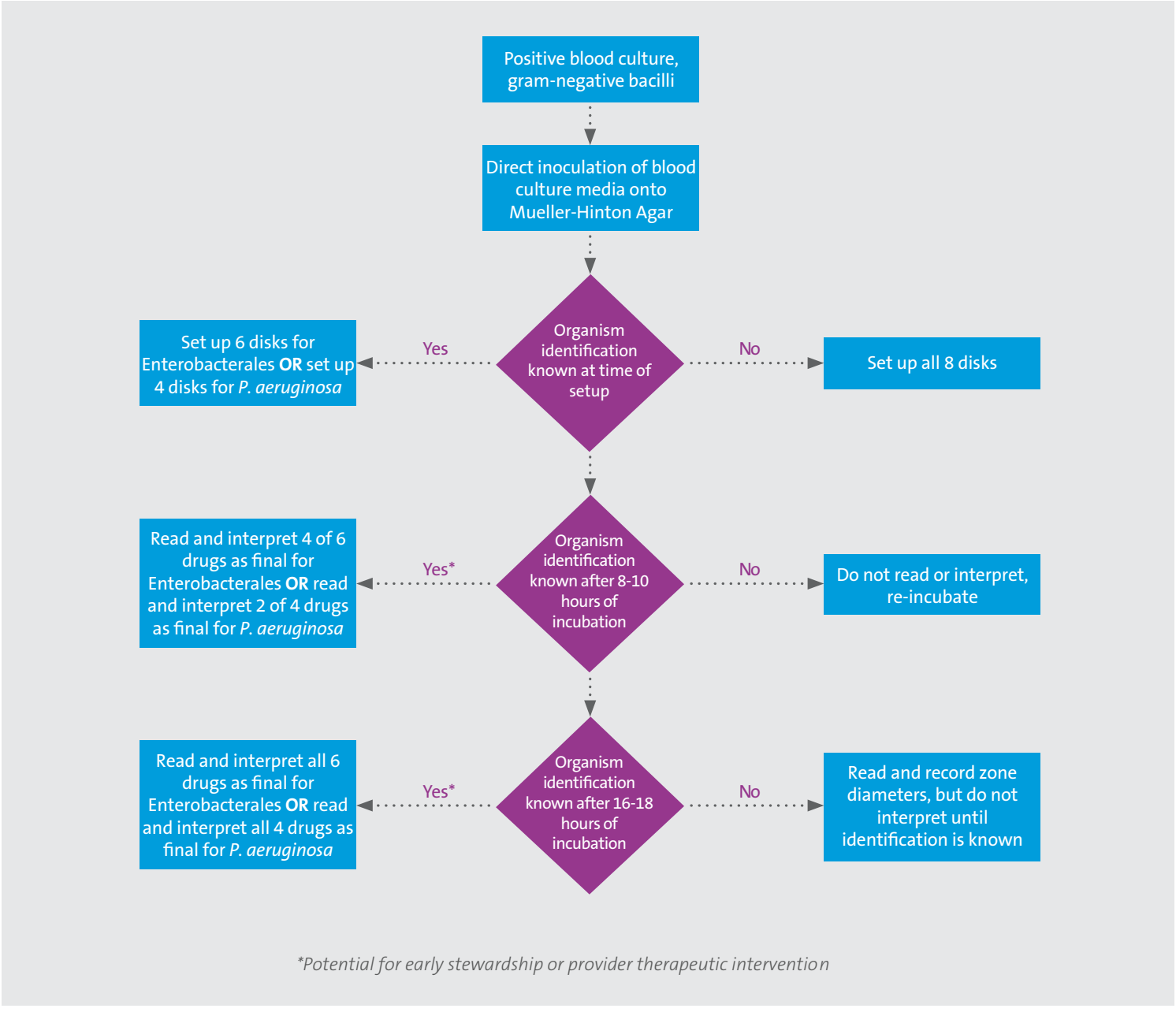


Figure 1. Workflow for direct blood culture disk diffusion testing

Implementation of the CLSI Method for Direct Disk Diffusion Testing From Positive Blood Cultures (*Continued*)

When reporting and interpreting antimicrobial DD results, follow intrinsic resistance rules provided in Appendix B of M100. Direct DD results are considered final and do not need to be confirmed or repeated; however, routine AST may be necessary to provide additional antimicrobial results. Laboratories should consider who will be notified of the early and overnight direct DD results and develop a notification system with actionable pieces of information regarding direct DD results. Some laboratories may choose to notify the primary patient-facing clinical team and/or they may notify the antimicrobial stewardship team with the direct DD results.

CLSI continues to evaluate additional antimicrobials for direct DD method breakpoints for Enterobacterales and *P. aeruginosa*. Direct DD breakpoints are still under evaluation for piperacillin-tazobactam and cefepime, which typically play a large role in therapy of bloodstream infections. Data on direct DD antimicrobials for *Acinetobacter* are also being assessed. Publication of the data leading to establishment of these breakpoints is underway, and guidance on initial verification and adoption of this method will also follow in an upcoming CLSI publication (pending).

In summary, consider adoption of the direct blood culture DD method regardless of which routine AST system is used in your laboratory. Paired organism identifications are necessary for appropriate result interpretation. As more breakpoints are developed for this method over time, it is important to highlight that those breakpoints listed in Tables 3E of M100 may differ from the standard breakpoints in Tables 2. QC should be performed following routine DD QC protocols.

References

1. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing.* 32nd ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2022.
2. Ferrer R, Martin-Loeches I, Phillips G, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: Results from a guideline-based performance improvement program. *Crit Care Med.* 2014:42(8):1749-1755.
3. Chandrasekaran S, Abbott A, Campeau S, et al. Direct-from-blood-culture disk diffusion to determine antimicrobial susceptibility of gram-negative bacteria: Preliminary report from the Clinical and Laboratory Standards Institute Methods Development and Standardization Working Group. *J Clin Microbiol.* 2018;56(3):e01678-17.

Case Studies

What's Wrong with This Picture? Case 1

Stella Antonara, OhioHealth, Columbus, OH
Lars F. Westblade, Weill Cornell Medicine, New York, NY

Case 1: Coagulase-negative *Staphylococcus* spp. An 86-year-old man with low blood pressure and elevated heart and respiratory rates presented to the emergency department with complaints of painful urination, fever, and chills. His white blood cell count was 1,000/mm^3 and he had elevated lactic acid levels. The patient was diagnosed with urosepsis, urine and blood cultures were ordered, and the patient was admitted. The urine culture was positive with >100,000 CFU/mL coagulase-negative staphylococci (CoNS) (pure culture) with antimicrobial susceptibility test (AST) results obtained from a commercial AST device (see Table 1).

Table 1. Coagulase-negative *Staphylococcus* - Urine Culture (Released Results)

Antimicrobial Agent	MIC (µg/mL)	Interpretation
Doxycycline	≤0.5	S
Nitrofurantoin	≤16	S
Oxacillin	**0.5**	**R[a]**
Trimethoprim-sulfamethoxazole	≤2/38	S
Vancomycin	1	S

Abbreviations: R, resistant; S, susceptible.
[a]Oxacillin-resistant staphylococci are resistant to cefazolin and all other beta-lactams.

Both blood culture sets were positive with gram-positive cocci in clusters within 24 hours of collection. A molecular test was performed on the positive blood culture broth from one of the aerobic bottles and was positive for *Staphylococcus* species and negative for the *mecA* gene. Subcultures from both sets of blood cultures revealed CoNS, based upon spot tests, and identified as *Staphylococcus hominis*. The blood isolate was preliminarily reported as "methicillin (oxacillin)-susceptible *S. hominis,* further susceptibilities to follow."

AST was performed on the isolate recovered from the blood culture bottle used for molecular testing, again using the commercial AST device. Results are shown in Table 2.

Table 2. *Staphylococcus hominis* - Blood Culture (Unconfirmed Results)

Antimicrobial Agent	MIC (µg/mL)	Interpretation
Clindamycin	≥4	R
Doxycycline	≤0.5	S
Erythromycin	≥8	R
Oxacillin	**0.5**	**R[a]**
Trimethoprim- sulfamethoxazole	≤2/38	S
Vancomycin	1	S

Abbreviations: R, resistant; S, susceptible.
[a]Oxacillin-resistant staphylococci are resistant to cefazolin and all other beta-lactams.

The technologist reviewing the results noticed that the oxacillin MIC interpretation of "Resistant" from the blood isolate did not agree with the negative result for *mecA* on the molecular panel performed on the positive blood culture broth. ***What's wrong with this picture?***

What's Wrong with This Picture? Case 1 (*Continued*)

Solution to Case 1: The urine culture isolate was identified as *S. hominis* using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), but, according to current laboratory practice, CoNS other than *Staphylococcus saprophyticus* are not reported to the species level. Instead, the isolate was initially reported as "coagulase-negative *Staphylococcus* spp." but was subsequently reported to the species level, given the clinical picture of urosepsis and the presence of the isolate in pure culture. In contrast, CoNS isolated from blood cultures are identified and reported to the species level. The blood culture isolate was identified as *S. hominis*.

The AST results for the blood culture and urine culture isolates were identical. These included clindamycin and erythromycin susceptibility results that were suppressed on the urine AST report. These agents should not be routinely reported on urine isolates as they are not effective in treating urinary tract infections. However, the oxacillin MIC interpretation for the blood isolate was inconsistent with the molecular panel results for which the *mecA* gene was not detected.

The following steps were taken to troubleshoot the discrepancy between the oxacillin AST and *mecA* results:

1. All subculture plates (including the AST purity plate) from the positive blood culture were reviewed for the presence of additional colony morphologies.
   - Subcultures were pure and only one colony type was noted, which was confirmed by MALDI-TOF MS to be *S. hominis*.
2. The molecular panel was run again on the positive blood culture broth (within the manufacturer-approved time after positive signal).
   - Identical results were obtained: *Staphylococcus* species detected, *mecA* not detected.

Subsequently, one of the technologists recalled that oxacillin MIC breakpoints were recently updated by CLSI in the M100 31st edition published in 2021.[1] The oxacillin susceptible breakpoint for all *Staphylococcus* species, except *Staphylococcus aureus* and *Staphylococcus lugdunensis,* was changed from ≤0.25 µg/mL to ≤0.5 µg/mL (see Table 3). This update was based on recent studies that demonstrated an oxacillin breakpoint of ≤0.5 µg/mL for susceptible correlated better with the absence of the *mecA* gene, especially for *Staphylococcus capitis, Staphylococcus haemolyticus, S. hominis,* and *Staphylococcus warneri* isolates. Consequently, there are fewer false resistant results (major errors) with these updated breakpoints.[2]

Table 3. Oxacillin Breakpoints for *Staphylococcus* Species Other Than *Staphylococcus aureus* and *Staphylococcus lugdunensis*

Organism Group	Old Oxacillin MIC Breakpoints (µg/mL)[a]			Current Oxacillin MIC Breakpoints (µg/mL)[b]		
	S	I	R	S	I	R
S. epidermidis	≤0.25	-	≥0.5	≤0.5	-	≥1
S. pseudintermedius and *S. schleiferi*	≤0.25	-	≥0.5	≤0.5	-	≥1
Staphylococcus spp., **except:** *S. aureus* *S. lugdunensis* *S. epidermidis* *S. pseudintermedius* *S. schleiferi*	≤0.25	-	≥0.5	≤0.5	-	≥1

Abbreviations: I, Intermediate; R, Resistant; S, Susceptible.
[a]CLSI M100 30th edition[3]
[b]CLSI M100 32nd edition[1]

The updated oxacillin breakpoints improve performance of oxacillin MIC tests with *Staphylococcus* spp. other than *S. aureus* and *S. lugdunensis,* however they are not perfect. This is particularly true for those species for which species-specific oxacillin breakpoints have not been set (ie, *Staphylococcus* spp. excluding the following: *S. aureus, S. lugdunensis, Staphylococcus epidermidis, Staphylococcus pseudintermedius,* and *Staphylococcus schleiferi;* OR, coagulase-negative *Staphylococcus* spp., which have not been identified to the species level). In fact, no phenotypic test is highly reliable for these species when oxacillin MICs are 1-2 µg/mL. Therefore, CLSI suggests testing for *mecA* or PBP2a for isolates with oxacillin MICs of 1-2 µg/mL from serious infections included in the category *Staphylococcus* spp., **except**: *S. aureus, S. lugdunensis, S. epidermidis, S. pseudintermedius,* and *S. schleiferi.* "Isolates that test *mecA* or PBP2a negative should be reported as methicillin (oxacillin) susceptible."[1]

What's Wrong with This Picture? Case 1 (*Continued*)

As part of the troubleshooting process, the urine and blood isolates were tested with PBP2a and results were negative, confirming the lack of *mecA* previously obtained by molecular testing of blood. Considering the updated breakpoints, and the negative *mecA* and PBP2a results, both the blood and urine isolates were reported as oxacillin susceptible (see Table 4).

Table 4. *Staphylococcus hominis* - Blood Culture (Released Results) and Urine Culture (Corrected Results)

Antimicrobial Agent	Blood Isolate		Urine Isolate	
	MIC (µg/mL)	Interpretation	MIC (µg/mL)	Interpretation
Clindamycin	≥4	R		
Doxycycline	≤0.5	S	≤0.5	S
Erythromycin	≥8	R		
Nitrofurantoin			≤16	S
Oxacillin		**S**[a,b]		**S**[a,b]
Trimethoprim- sulfamethoxazole	≤2/38	S	≤2/38	S
Vancomycin	1	S	1	S

Abbreviations: S, Susceptible; R, Resistant.
[a]Oxacillin-susceptible staphylococci are susceptible to cefazolin and all other beta-lactams
[b]PBP2a negative

Upon review of the breakpoints applied by the commercial AST device, the laboratory discovered that the system followed the prior CLSI oxacillin MIC breakpoints (ie, M100 30th Ed). Therefore, oxacillin MIC results were not released, as the laboratory had not yet officially validated the updated breakpoints. At this point, FDA has not approved the updated oxacillin breakpoints recommended by CLSI (FDA oxacillin breakpoints can be found on the FDA website[4]). It is important to remember that commercial manufacturers must use FDA breakpoints in their AST systems. However, laboratories can implement updated CLSI breakpoints, including the new oxacillin breakpoints, on their commercial AST system following performance of a validation.

This article describes a case wherein the laboratory applied the term "coagulase-negative *Staphylococcus* spp.," but determination of oxacillin resistance relied on species level identification of the organism. If phenotypic susceptibility testing and reporting are undertaken for oxacillin and/or cefoxitin, species level identification of CoNS must be performed. The decision to implement the updated staphylococcal oxacillin breakpoints should be made with the antimicrobial stewardship team. Laboratories should consider including *mecA* or PBP2a testing on all isolates of coagulase-negative staphylococci from serious infections (eg, prosthetic joints, blood cultures) for those isolates with oxacillin MICs of 1-2 µg/mL.

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Case Studies

What's Wrong with This Picture? Case 2

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Case 2: *Serratia marcescens*. Direct specimen Gram stain of a tracheal aspirate revealed a moderate quantity of gram-negative bacilli and rare polymorphonuclear cells. In culture, many *Stenotrophomonas maltophilia, Pseudomonas aeruginosa,* and *Serratia marcescens* were recovered and antimicrobial susceptibility testing (AST) was performed using an automated system. The AST results for the *S. maltophilia* and *P. aeruginosa* isolates were unremarkable. The *S. marcescens* AST profile is tabulated below (see Table 1). ***What's wrong with this picture?***

Table 1. *Serratia marcescens*

Antimicrobial Agent	MIC (µg/mL)	Interpretation
Ampicillin	>32	R
Ampicillin-sulbactam	>32/16	R
Cefazolin	>64	R
Cefoxitin	>64	R
Ceftriaxone	≤1	S
Ceftazidime	≤1	S
Cefepime	1	S
Aztreonam	>16	R
Ertapenem	**>8**	**R**
Meropenem	**>16**	**R**
Ciprofloxacin	≤0.25	S
Trimethoprim-sulfamethoxazole	≤1/19	S
Tetracycline	≤4	S
Gentamicin	≤1	S

Abbreviations: R, resistant; S, susceptible.

Solution to Case 2: The *S. marcescens* isolate's observed susceptibility to extended-spectrum cephalosporins (ceftriaxone, ceftazidime, and cefepime) in the setting of carbapenem (ertapenem and meropenem) resistance is unusual. Possible explanations for this observation are listed below:

1. Contamination of the AST panel. In this scenario, contamination of the AST panel with a meropenem-resistant isolate.
2. Technical error during AST panel set up.
3. Unusual or rare resistance mechanism. In this case, an unusual or rare β-lactam resistance mechanism.

The points listed above serve as a good starting framework to explain possible AST problems. Due to the unusual AST results, they were not released, and the case was raised to the AST technical specialist for further counsel. They suggested the following steps to investigate the root cause of the unusual AST profile. First, the purity plate was closely examined. It was pure for a single organism and the identity of the isolate was confirmed to be *S. marcescens* by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), demonstrating the AST panel was unlikely contaminated with a carbapenem-resistant species. Second, the results were discussed with the technologist who performed the testing. The technologist did not recall any issues with the automated instrument or the panels the previous day and had many years of experience with the automated AST system, suggesting technical error was unlikely on the part of the technologist. Furthermore, no issues with QC or the platform itself had been recorded for the past month implying instrument and/or panel error was improbable. Finally, given observed resistance to meropenem, the isolate was assayed using a commercial immunoassay for IMP, KPC, NDM, OXA-48-type, and VIM enzymes. It was negative for all five targets. Based on the performing laboratory's testing algorithm, all carbapenem-resistant isolates that test negative using the carbapenemase detection immunoassay are tested using a phenotypic (enzymatic) carbapenemase detection test (CDT) (Carba NP), which was positive.

What's Wrong with This Picture? Case 2 (*Continued*)

It was determined the *S. marcescens* isolate was likely producing an *S. marcescens* enzyme (SME). The AST was repeated using the same method and the initial results were confirmed. The AST results were released as they tested, as is recommended by the Clinical and Laboratory Standards Institute (CLSI).[1] SMEs are chromosomally-encoded serine carbapenemases that have only been observed in *S. marcescens*.[2,3] Four SME variants (SME-1 to SME-4) have been described, and they are resistant to carbapenems but susceptible to extended-spectrum cephalosporins,[2,3] as observed in our case. Of note, a similar AST profile (susceptible to extended-spectrum cephalosporins and resistant to carbapenems) can be observed for OXA-48-type-producing Enterobacterales.[3] The first description of SME-producing *S. marcescens* was from England in 1982 and they have remained relatively uncommon since that initial report, with most cases observed in the United States.[3,4] Due to their location on the chromosome, transmission of bla_{SME} (the gene encoding SME carbapenemases) is considered to be less of an infection control risk compared to other carbapenemases (eg, IMP, KPC, NDM, OXA-48-type, and VIM) where mobile genetic element (eg, plasmid)-mediated transmission is possible. Nevertheless, measures must be taken to contain SME-producing *S. marcescens* to prevent outbreaks resulting from clonal dissemination.[2] Interestingly, mobilization of bla_{SME} between *S. marcescens* isolates has been proposed via an excised circular intermediate of a cryptic prophage genomic island: *S. marcescens* genomic isolate 1-1, suggesting horizontal transfer between *S. marcescens* isolates is possible and that isolates harboring bla_{SME} could be more of an infection control risk than previously appreciated.[4]

The detection of SME-producing *S. marcescens* isolates can be difficult because of their susceptibility to extended-spectrum cephalosporins and the omission of bla_{SME} from CDTs designed to detect carbapenemase genes.[2,5] With the exception of the modified Hodge test, which is no longer endorsed by CLSI, most phenotypic CDTs readily detect SME-mediated carbapenemase activity.[1,4,5,6] It has been proposed that genotypic CDTs include bla_{SME} to promote the use of extended-spectrum cephalosporins when bla_{SME} is detected.[2] *S. marcescens* has been presumed to be at risk for the development of AmpC production, and thus cephalosporin resistance, although *in vitro* and clinical studies indicate clinically significant *ampC* expression in *S. marcescens* is unlikely.[7] Therefore, while data are limited, it has been suggested extended-spectrum cephalosporins can be considered for treatment of SME-producing isolates if they test susceptible.[2] Further, the clinical microbiology laboratory could append a comment that highlights the presence of a carbapenemase (SME)-producing isolate and counsels an infectious diseases consultation to determine the possibility of prescribing an extended-spectrum cephalosporin.

Clinical microbiology laboratories should have a high index of suspicion for SME-producing *S. marcescens* isolates when extended-spectrum cephalosporins test susceptible and carbapenems test resistant. For best practice, AST results should be confirmed and a test for enzymatic carbapenemase activity considered (currently, there are no US Food and Drug Administration-authorized diagnostic assays available that specifically identify SME). In our case, the laboratory's algorithm is to reflex *S. marcescens* isolates that yield an AST profile suspicious for SME production immediately to a CDT. While awaiting confirmatory and supplemental test results, to avoid delays in reporting, clinical microbiology laboratories may want to report the isolate as a presumptive carbapenem-resistant Enterobacterales. For infection control and epidemiologic purposes, ruling out an OXA-48-like enzyme (which can generate a similar AST profile to SME producers) and other carbapenemases (IMP, KPC, NDM, and VIM) using a targeted genotypic or immunoassay could be performed.[8,9] For SME-producing *S. marcescens* isolates, AST results should be reported as tested without modification of the interpretation of extended-spectrum cephalosporins.[1] A comment recommending an infectious diseases consultation could be appended to the report. For those clinical microbiology laboratories that use cascade reporting protocols, unusual AST results, as observed in this case, must be confirmed and reported in full so providers do not assume that susceptibility to narrow-spectrum agents (eg, extended-spectrum cephalosporins) implies susceptibility to broader-spectrum agents (eg, carbapenems).[1]

In summary, SME-producing *S. marcescens* isolates can be presumed when an *S. marcescens* isolate tests susceptible to extended-spectrum cephalosporins and resistant to carbapenems, is negative for IMP, KPC, NDM, OXA-48-type, and VIM carbapenemases; and displays enzymatic carbapenemase activity. SME-producing isolates can be sent to a public health laboratory for further characterization, and many locales require that carbapenemase-producing Enterobacterales, including SME-producing *S. marcescens*, are submitted.

What's Wrong with This Picture? Case 2 (*Continued*)

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Practical Tips

Updating Breakpoints–New Developments from CAP

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The College of American Pathologists (CAP) is introducing two new requirements for clinical laboratories to use updated breakpoints (BPs) when interpreting antimicrobial susceptibility testing (AST) results. CAP has recognized that some laboratories are using obsolete breakpoints,[1,2] even when devices have achieved US Food and Drug Administration (FDA) clearance for updates, which could lead to adverse consequences in managing patients.

In brief, laboratories will be required to:

Step 1
Determine and document which BPs are used in their laboratory for minimal inhibitory concentration (MIC) and/or disk diffusion tests. This involves checking all places where BPs are applied including the AST instrument, laboratory information system (LIS) and electronic health records (EHR). This new requirement is effective now.

Step 2
Identify obsolete BPs in use and make a plan to update BPs to current BPs that were updated prior to 2021. Labs will have 3 years to update BPs following FDA publication of BPs update. This new requirement will be effective January 2024.

The CAP Checklist Items Describing the New Breakpoint Requirements[3]

"Revised MIC.11380 9/22/2021 Antimicrobial Susceptibility Test Interpretation Criteria
(Previously MIC.21930 (Susceptibility Test Endpoint Determination)
For antimicrobial susceptibility testing systems, there are written criteria for determining and interpreting minimal inhibitory concentration (MIC) or zone diameter sizes as susceptible, intermediate, resistant, non-susceptible, or susceptible dose-dependent. These criteria are reviewed annually."

What this means:

- Laboratories must know what BPs are in use in their laboratory.
- Laboratories must review and document the BPs applied in their laboratory annually.
- Laboratories should discuss breakpoints in use with their antimicrobial stewardship team, as appropriate.

"New MIC.11385 9/22/2021 Current Antimicrobial Susceptibility Test Interpretation Breakpoints
Effective January 1, 2024, the laboratory uses current breakpoints for interpretation of antimicrobial minimum inhibitory concentration (MIC) and disk diffusion test results, and implements new breakpoints within three years of the date of official publication by the FDA or other standards development organization (SDO) used by the laboratory."

What this means:

- Effective January 1, 2024 laboratories must use current BPs for MIC and disk diffusion tests.
- At minimum, US laboratories must use current FDA BPs, but laboratories may choose to use current CLSI or EUCAST BPs.
- It will be **UNACCEPTABLE** for laboratories to use BPs that are no longer recognized by either FDA, CLSI, or EUCAST.
- In rare cases, a laboratory can use alternative BPs (including old breakpoints), if justified. This would require documentation that would optimally include input from the institution's antimicrobial stewardship team.

To learn more, an archived version of the January 2022 CAP-CLSI webinar can be accessed and purchased **here.**

Updating Breakpoints – New Developments from CAP (*Continued*)

Additional Resources to Get Started!

CLSI ORWG has developed an optional spreadsheet that laboratories can use to record breakpoints in use; this can be found **here.**

Please note that CAP is not prescriptive on the method used to document BPs in use.

The Association of Public Health Laboratories provides a Breakpoint Implementation Toolkit for updating carbapenem breakpoints which can be found **here.**

CLSI and other organizations are in the process of preparing additional tools to help laboratories with the task of updating breakpoints on their AST systems.

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Hot Topic

Candida auris Update: Method Variability with Amphotericin B Susceptibility Testing

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Candida auris is an emerging yeast that is causing numerous outbreaks in health care settings, and life-threatening infections in patients worldwide.[1] Most isolates of *C. auris* are multidrug resistant. In the United States, 85% of isolates have fluconazole minimal inhibitory concentration (MIC) values >64 µg/mL, 33% have amphotericin B MIC values >1 µg/mL, and 1-3% have FKS mutations indicating echinocandin resistance (CDC, unpublished data). Although an echinocandin is the Infectious Diseases Society of America (IDSA)-recommended initial therapy for *Candida* bloodstream infections, echinocandin resistance is increasing in *C. auris*[2] (CDC, unpublished data). Treatment with liposomal amphotericin B could be considered when an isolate has both fluconazole MIC >32 µg/mL and an echinocandin MIC >2 µg/mL.

There are several challenges with amphotericin B susceptibility testing of *Candida* species but especially for *C. auris*. Firstly, there are no CLSI or US Food and Drug Administration (FDA) breakpoints for amphotericin B and any species of *Candida*. Based on a single small study, clinicians use the MIC value of ≥2 µg/mL as the resistant breakpoint for all *Candida* species despite the paucity of scientific data to support it.[3,4] There has been little problem with this cutoff as the majority of *Candida* species have MIC values <1 µg/mL.[5] In 14,000 *Candida* bloodstream isolates collected during US candidemia surveillance 2008-2018, fewer than 10 isolates of all species combined had an MIC value >1 µg/mL (CDC, unpublished data). This has not been the case for *C. auris* as up to a third of US isolates have an MIC value of >1 µg/mL. With only a suggested susceptible breakpoint and no intermediate breakpoint, the margin of error of ± 1 doubling dilution leads to "essential agreement" but "categorical disagreement" for isolates with MIC values of 1 µg/mL (susceptible) and 2 µg/mL (resistant). The second challenge in amphotericin B testing is the difference in MIC distributions across testing methodologies. Broth microdilution (BMD), including Sensititre YeastOne, produces a narrow range of amphotericin MIC values (0.125-1 µg/mL), while gradient diffusion gives a wider range and lower MIC values (MIC_{50} and mode 0.6 µg/mL).[3,6] (CDC, unpublished data). Again, for most *Candida* species, since amphotericin B values are typically <1 µg/mL by both methodologies, the two methods achieve high "categorical agreement." But because so few isolates with MICs >1 µg/mL have been tested using different methodologies, it is not clear which methodology provides the more accurate detection of "resistance." In M27-Ed4 CLSI states for amphotericin B, "Some research has suggested that commercially available methods may provide a more accurate interpretation of the *in vitro* MIC."[6,7] This not-so-subtle hint from the CLSI Subcommittee on Antifungal Susceptibility Tests subcommittee suggests Etest, at least in studies reported nearly 30 years ago, was more reliable for testing *Candida* species and calls into question which is the more accurate methodology for amphotericin B antifungal susceptibility testing. For *C. auris*, the other widely used commercial method for susceptibility testing of amphotericin B, the VITEK 2®, is more likely to report isolates having amphotericin B MIC values >2 µg/mL when compared to both agar gradient diffusion and the CLSI BMD method.[8,9]

In summary, as stated above, amphotericin B MIC determination for *Candida* species has never been a clinical laboratory conundrum because there were so few isolates with MIC values so close to the suggested susceptible breakpoint, independent of the testing methodology. Now that *C. auris* has emerged, amphotericin B testing has jumped into the spotlight. There is significant variability in MIC values for *C. auris* and amphotericin B depending on the test method used. While both the CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) promote BMD as the reference methodology, only EUCAST has developed breakpoints for some *Candida* species. These are ≤1 µg/mL for susceptible and >1 µg/mL for resistant.[10] However, there are no breakpoints (for any antifungals) specifically for *C. auris*. Furthermore, there are no studies that show a direct correlation between MIC values and clinical outcomes for amphotericin B and any species of *Candida*. Hence, amphotericin B susceptibility results for *C. auris* should be interpreted with caution, particularly for treatment of multidrug-resistant *C. auris* infections, and laboratories should share this note of caution with providers when reporting amphotericin B.

Candida auris Update: Method Variability with Amphotericin B Susceptibility Testing (*Continued*)

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More News!

American Society for Microbiology Updates IQCP Guidance

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The American Society for Microbiology (ASM), in collaboration with CLSI and the College of American Pathologists (CAP), has updated individualized quality control plan (IQCP) resources previously posted on ASM's Clinical Microbiology Portal and added a new IQCP template for molecular test systems.

The updated IQCP templates for AST are:

- IQCP for Disk Diffusion AST
- IQCP for Minimal Inhibitory Concentration (MIC)-based AST System

These two templates have been updated to include further guidance on how to conduct risk assessment including, for example, a redesign of the risk assessment section by organizing the information into five categories. Updates and changes to these templates are noted in red font for ease of comparison with the previous versions. Laboratories that are updating or revising their IQCPs may consider adopting these updated templates or may continue to use the original templates.

The "NEW" IQCP template is:

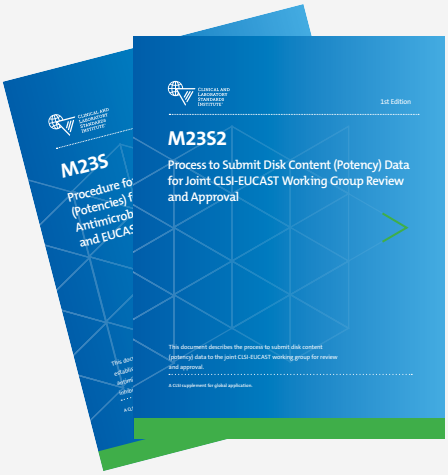
- IQCP for QC of molecular test system.

This newly developed template can be used to prepare and organize an IQCP for QC of a commercial cartridge-based molecular test system for detection of a single or multiple targets. For ease of use, it follows the same format as the other IQCP templates but addresses risk acceptability assignments that apply specifically to molecular test systems, such as extraction failures, cross contamination, and change in pathogen target sequences.

These IQCP templates are available **here.**

The Joint CLSI-EUCAST Working Group

Janet Hindler, LA County Department of Health, Los Angeles, CA
Erika Matuschek, EUCAST Development Laboratory, Stockholm, Sweden



The Joint CLSI-EUCAST Working Group (WG) was organized in 2018 and members include representatives from both CLSI and EUCAST. There are two main goals for this WG which are to:

1. Describe a method for disk content determination which can be used early in the drug development process to avoid having different disk contents in the CLSI and EUCAST standards.

2. Discuss differences between CLSI and EUCAST QC criteria, methods for establishing QC criteria and the possibility of harmonizing CLSI and EUCAST QC criteria.

To date, two freely available **guidelines** have been published to support Goal 1, which include the following:

CLSI M23-S 1st Ed. Procedure for Optimizing Disk Contents (Potencies) for Disk Diffusion Testing of Antimicrobial Agents Using Harmonized CLSI and EUCAST Criteria

CLSI M23-S2 1st Ed. Process to Submit Disk Content (Potency) Data for Joint CLSI-EUCAST Working Group Review and Approval

Pharmaceutical representatives with questions about disk content submissions can contact CLSI through a dedicated **webpage** or EUCAST **here.**

The Joint CLSI EUCAST WG is now addressing opportunities to harmonize recommendations for development of QC processes and QC ranges.

In Memoriam

In Memoriam: James A. Poupard, PhD (1943-2022)

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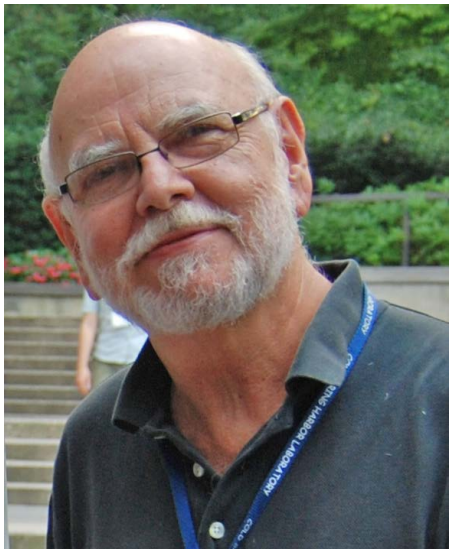
Janet Hindler, LA County Department of Health, Los Angeles, CA

James A. Poupard, PhD, microbiologist and lifelong Philadelphian, died on May 22, 2022, after a long illness. Dr. Poupard served several terms as an Advisor to the CLSI Subcommittee on Antimicrobial Susceptibility Testing (AST) before his retirement. He spent 13 years at GlaxoSmithKline Pharmaceuticals (GSK) where he was the Director of Clinical Microbiology and led the Anti-Infective Drug Discovery/Screening Group and a Scientific Product Support Group. In that role he co-coordinated worldwide clinical microbiology activities involving the life-cycle management of an extensive anti-infective portfolio. Following his retirement from GSK, Dr. Poupard became President of the Pharma Institute of Philadelphia, a network of specialists that served the needs of the pharmaceutical, biotechnology, and laboratory instrumentation industries. Prior to transitioning to a career in industry, Dr. Poupard was the Director of Microbiology at The Bryn Mawr Hospital and later became Associate Professor of Laboratory Medicine, Pathology, and Medicine at the Medical College of Pennsylvania. Jim's background in clinical microbiology and industry gave him a unique vantage point from which he provided CLSI with many valuable insights, including his contributions to the development of the ISO standard "Reference methods for testing the *in vitro* activity of antimicrobial agents against bacteria involved in infectious diseases" (ISO 20776-1) that resulted in global harmonization of the broth microdilution testing method.



James A. Poupard, PhD

Dr. Poupard was active in the American Society for Microbiology (ASM) and the Eastern PA Branch of ASM and was instrumental in creating the Center for the History of Microbiology /ASM Archives (CHOMA). With over 100 scientific publications, Dr. Poupard was a recognized expert in clinical microbiology, antibacterial drug development and factors for determining AST breakpoints. Dr. Poupard was a Fellow of the American Academy of Microbiology.

Jim leaves behind his wife of 60 years, three children and their partners, four grandchildren, two great grandchildren and many friends and colleagues. His insatiable passion for microbiology, educating others about microbiology, the history of science, quantum science, and his love of life were a gift to those who knew him. In his book, A History of Microbiology in Philadelphia: 1880 to 2010, Jim expressed his confidence that today's microbiologists can "live up to the many new challenges of a changing science." His contributions helped show us the way.