Meeting Title:	**Subcommittee on Antimicrobial Susceptibility Testing (AST)**	**Contact:**	egomez@clsi.org
Meeting Location:	Rosemont (Chicago), Illinois, USA		
Meeting Dates and Times: All times are Central (US) time.	**Plenary 1:** Sunday, 26 June 2022, 2:00 - 5:00 PM **Plenary 2:** Monday, 27 June 2022, 7:30 – 11:30 AM **Plenary 3:** Monday, 27 June 2022, 1:00 – 6:00 PM **Plenary 4:** Tuesday, 28 June 2022, 7:30 AM – 12:00 PM		
Meeting Purpose:	The purpose of this meeting is to review and discuss AST WG and SC business in preparation for publication of the next edition of M100 (33rd).		
Requested Attendee(s):	SC Chairholder, Vice-Chairholder, Members, Advisors, and Reviewers; Expert Panel on Microbiology Chairholder and Vice-Chairholder; Other Interested Parties; CLSI Staff		

Attendee(s):	
James S. Lewis, PharmD, FIDSA AST Subcommittee Chairholder	**Oregon Health and Science University**
Melvin P. Weinstein, MD AST Subcommittee Vice-Chairholder	**Robert Wood Johnson University Hospital**
Jean B. Patel, PhD, D(ABMM) Expert Panel on Microbiology Chairholder	**Beckman Coulter, Inc.**
Members Present:	
Sharon K. Cullen, BS, RAC	Beckman Coulter, Inc. Microbiology Business
Tanis Dingle, PhD, D(ABMM), FCCM	Alberta Precision Laboratories
Marcelo F. Galas, BSc	Pan American Health Organization
Romney M. Humphries, PhD, D(ABMM), FIDSA	Vanderbilt University Medical Center
Thomas J. Kirn, MD, PhD	Rutgers Robert Wood Johnson Medical School
Brandi Limbago, PhD	Centers for Disease Control and Prevention
Amy J. Mathers, MD, D(ABMM)	University of Virginia Medical Center
Virginia M. Pierce, MD	Massachusetts General Hospital
Sandra S. Richter, MD, D(ABMM), FIDSA	Mayo Clinic (Jacksonville, FL)
Michael Satlin, MD	Weill Cornell Medicine
Audrey N. Schuetz, MD, MPH, D(ABMM)	Mayo Clinic (Rochester, MN)
Susan Sharp, PhD, D(ABMM), F(AAM)	Copan Diagnostics, Inc.
Patricia J. Simner, PhD, D(ABMM)	Johns Hopkins School of Medicine, Department of Pathology
Advisors Present:	
Tanaya Bhowmick, MD	Rutgers Robert Wood Johnson Medical School
April M. Bobenchik, PhD, D(ABMM), MT(ASCP)	Penn State Hershey Medical Center
Carey-Ann Burnham, PhD, D(ABMM)	Washington University School of Medicine
Shelley Campeau, PhD, D(ABMM)	Accelerate Diagnostics, Inc.
Mariana Castanheira, PhD	JMI Laboratories
Sanchita Das, MD, D(ABMM)	National Institutes of Health
German Esparza, MSc	Proasecal SAS
Christian G. Giske, MD, PhD	Karolinska University Hospital
Howard Gold, MD, FIDSA	Beth Israel Deaconess Medical Center
Janet A. Hindler, MCLS, MT(ASCP), F(AAM)	Los Angeles County Department of Public Health
Dmitri Iarikov, MD, PhD	FDA Center for Drug Evaluation and Research
Maria Karlsson, PhD	Centers for Disease Control and Prevention
Joseph Kuti, PharmD, FIDP, FCCP	Hartford Hospital
Joseph D. Lutgring, MD	Centers for Disease Control and Prevention
Linda A. Miller, PhD	CMID Pharma Consulting LLC
Stephanie L. Mitchell, PhD, D(ABMM)	Cepheid, Inc.

Greg Moeck, PhD	Venatorx Pharmaceuticals, Inc.
Navaneeth Narayanan, PharmD, MPH	Rutgers University
Robin Patel, MD	Mayo Clinic
Eric Wenzler, PharmD, BCPS, AAHIVP	University of Illinois at Chicago
Barbara L. Zimmer, PhD	Beckman Coulter
Reviewers and Guests (Non-SC-roster attendees): see Plenary Attendee List below	
Staff:	
Jennifer Adams, MT(ASCP), MSHA	CLSI
Kathy Castagna, MS, MT(ASCP)CT, MB	CLSI
Glen Fine, MS, MBA, CAE	CLSI
Emily Gomez, MS, MLS(ASCP)MB	CLSI
Barb Jones, PhD	CLSI
Christine Lam, MT(ASCP)	CLSI

Plenary Agendas

PLENARY AGENDA: Session 1 Sunday, 26 June 2022 (In-person/Hybrid) 2:00 PM – 5:00 PM All Times listed are Central (US) Time			
Time	**Item**	**Presenter**	**Page**
2:00 PM – 2:05 PM (5 min)	Opening Remarks	J. Lewis	7
2:05 PM – 2:10 PM (5 min)	Tribute to Jim Poupard	L. Miller	7
2:10 PM – 2:20 PM (10 min)	CLSI Update	G. Fine	7
2:20 PM – 2:30 PM (10 min)	VET AST Update	R. Bowden	8
2:30 PM – 2:40 PM (10 min)	M45 Update	R. Humphries T. Simner	9
2:40 PM – 3:10 PM (30 min)	Text and Tables WG	A. Bobenchik S. Campeau	10
3:10 PM – 3:30 PM (20 min)	Break		
3:30 PM – 5:00 PM (1 hr 30 min)	Table 1 AHWG	T. Simner	13

PLENARY AGENDA: Session 2 Monday, 27 June 2022 (In-person/Hybrid) 7:30 AM – 11:30 AM All Times listed are Central (US) Time			
Time	**Item**	**Presenter**	**Page**
7:30 AM – 7:40 AM (10 min)	EUCAST Update	C. Giske	25
7:40 AM – 7:45 AM (5 min)	M23 Update	M. Wikler	25
7:45 AM – 9:45 AM (2 hr)	Breakpoint WG: Part 1	A. Mathers M. Satlin	26
9:45 AM – 10:05 AM (20 min)	Break		

10:05 AM – 11:30 AM (1 hr 25 min)	Breakpoint WG: Part 2	A. Mathers M. Satlin	26

PLENARY AGENDA: Session 3
Monday, 27 June 2022 (In-person/Hybrid)
1:00 PM – 5:00 PM
All Times listed are Central (US) Time

Time	Item	Presenter	Page
1:00 PM – 2:00 PM (1 hr)	Breakpoint WG: Part 3	A. Mathers M. Satlin	38
2:00 PM – 3:00 PM (1 hr)	Quality Control WG	S. Cullen C. Pillar	44
3:00 PM – 3:20 PM (20 min)	Break		
3:20 PM – 5:00 PM (1 hr 40 min)	Methods Application and Interpretation WG	T. Kirn B. Limbago	60

PLENARY AGENDA: Session 4
Tuesday, 28 June 2022 (In-person/Hybrid)
8:00 AM – 12:00 PM
All Times listed are Central (US) Time

Time	Item	Presenter	Page
8:00 AM – 10:30 AM (2 hours 30 min)	Methods Development and Standardization WG	D. Hardy B. Zimmer	66
10:30 AM – 10:50 AM (20 min)	Break		
10:50 AM – 11:20 AM (30 min)	Outreach WG	J. Hindler A. Schuetz	75
11:20 AM – 11:40 AM (20 min)	Joint CLSI-EUCAST WG	J. Hindler E. Matuschek	77
11:40 AM – 11:45 AM (5 min)	Closing Remarks	J. Lewis	77

Summary of Voting Decisions and Action Items

Summary of Passing Votes			
#	**Motion Made and Seconded**	**Results[a]**	**Page[b]**
1.	To approve the removal of dosage comments from Tables 2 with an added general comment in Table 2 to refer user to Appendix E for this information.	11-2-0-0	10
2.	To remove piperacillin-tazobactam from the Table 1A e footnote.	9-4-0-0	13
3.	To approve Table 1A Enterobacterales (not including *Salmonella*/*Shigella*) and the proposed footnotes.	13-0-0-0	13
4.	To approve Table 1C *Salmonella* and *Shigella* spp. and the proposed footnotes.	11-1-1-0	15
5.	To add imipenem-relebactam to tier 4 in Table 1P Gram-Negative Anaerobes.	11-1-1-0	16
6.	To approve Table 1P Gram-Negative Anaerobes, with the removal of ceftizoxime, and the proposed footnotes.	13-0-0-0	16
7.	To approve Table 1Q Gram-Positive Anaerobes, with the removal of ceftizoxime and addition of imipenem-relebactam to tier 4, and the proposed footnotes.	12-1-0-0	18
8.	To remove Table 2 column 1 (Test/Report Groups) and to task the Text and Tables Working Group with designating the remaining drug test/report groups (investigational, urine only, and other).	9-4-0-0	20
9.	To approve gentamicin MIC BPs for Enterobacterales (S≤2, I 4, R≥8) with the proposed comment, pending disk correlation data, and rationale document.	12-0-0-1	26
10.	To approve tobramycin MIC BPs for Enterobacterales (S≤2, I 4, R≥8) with the proposed comments, pending disk correlation data, and rationale document.	12-0-1-0	27
11.	To approve amikacin MIC BPs for Enterobacterales (S≤4, I 8, R≥16) with the proposed comment, pending disk correlation data, and rationale document.	13-0-0-0	29
12.	To approve tobramycin MIC BPs for *Pseudomonas aeruginosa* (S≤1, I 2, R≥4) with the proposed comment, pending disk correlation data, and rationale document.	10-3-0-0	30
13.	To remove gentamicin MIC BPs for *Pseudomonas aeruginosa* with comment.	13-0-0-0	32
14.	To approve amikacin MIC BPs (S≤16, I 32, R≥64) for *Pseudomonas aeruginosa* with a comment stating for infections originating from the urinary tract (EUCAST comment).	12-1-0-0	38
15.	To keep levofloxacin MIC BPs for *Stenotrophomonas maltophilia* as S≤2, I 4, R≥8 with the addition of the proposed comment.	11-2-0-0	41
16.	To approve ceftibuten-ledaborbactam disk QC ranges for *E.coli* ATCC 25922, *E.coli* NCTC 13353, *K. pneumoniae* ATCC 700603, *K. pneumoniae* ATCC BAA-1705, and *K. pneumoniae* ATCC BAA-2814. Only publish *E.coli* NCTC 13353 QC ranges (24-29 mm).	13-0-0-0	44
17.	To approve ceftibuten disk QC ranges for *E.coli* ATCC 25922, *E.coli* NCTC 13353, *K. pneumoniae* ATCC 700603, *K. pneumoniae* ATCC BAA-1705, and *K. pneumoniae* ATCC BAA-2814. Only publish *E.coli* NCTC 13353 QC ranges (15-23 mm) in Table 4A-2 and highlight for QC integrity. Note: QC range for ceftibuten-ledaborbactam *E. coli* ATCC® 25922 (0.03/4 –0.12/4 µg/mL) in Table 5A-2 will be deleted for consistency.	13-0-0-0	45
18.	To approve gentamicin disk QC range for *N. gonorrhoeae* ATCC 49226 (15-20 mm).	13-0-0-0	46
19.	To approve piperacillin-tazobactam MIC QC range of 1/4 - 8/4 and piperacillin 1-4 for *E. coli* ATCC 25922.	13-0-0-0	51

Summary of Voting Decisions and Action Items (continued)

Summary of Passing Votes (continues)			
#	**Motion Made and Seconded**	**Results**[a]	**Page**[b]
20.	To approve proposed Table 5A-1 colistin MIC QC range footnote revisions, Table 5G Troubleshooting Guide additions and Table 3D colistin QC revisions changing "target" to "mode".	13-0-0-0	54
21.	To approve proposed Troubleshooting Guide additions for QC organism maintenance.	13-0-0-0	56
22.	To approve proposed revision to Table 3I for QC recommendations – in row for lot/shipment for disk diffusion indicate Perform QC according to standard disk diffusion QC procedures per M02 (eg, daily, weekly).	12-0-1-0	57
23.	To remove the referrals to M100 S20.	13-0-0-0	60
24.	To approve a Table 2A inducible AmpC comment with the Table 1A footnote and new proposed retesting statement.	10-2-0-1	61
25.	To approve proposed revision to Table 2A Enterobacterales and carbapenem comment and Tables 3B and 3C introduction.	12-0-0-1	62
26.	To approve proposed Mueller Hinton-Fastidious Media (MH-F) broth comment.	13-0-0-0	66
27.	To approve chloramphenicol disk QC range change (28-36 mm) and current clarithromycin disk QC range (11-17 mm) and retain the current amoxicillin-clavulanate disk QC range with MH-F Media for *Haemophilus influenzae* ATCC 49247.	13-0-0-0	66
28.	To approve proposed disk diffusion testing equivalency shown between HTM and MH-F for ampicillin, ceftriaxone, cefuroxime, clarithromycin, chloramphenicol, levofloxacin, and tetracycline.	13-0-0-0	68
29.	To approve recommendation of reading tedizolid disk diffusion zones of growth inhibition using reflected light with QC data for transmitted vs reflected light confirmation.	12-1-0-0	69
30.	To approve proposed recommendations for exebacase susceptibility testing.	13-0-0-0	71
31.	To approve tobramycin disk BPs for *Pseudomonas aeruginosa* (S≥19, I 13-18, R≤12) with future review.	11-0-1-1	42
32.	To approve tobramycin disk BPs for Enterobacterales (S≥17, I 13-16, R≤12) with future review.	11-0-1-1	42
33.	To approve gentamicin disk BPs for Enterobacterales (S≥18, I 15-17, R≤14) with future review.	11-0-1-1	42
34.	To approve amikacin disk BPs for Enterobacterales (S≥19, I 16-18, R≤15) with future review.	11-0-1-1	42

[a] Key for voting: X-X-X-X = For-against-abstention-absent

[b] Page links can be used to go directly to the related topic presentation and voting discussions.

2022 JUNE AST MEETING SUMMARY MINUTES PLENARY 1: Sunday, 26 June 2022 (In-person/Hybrid) 2:00 PM - 5:00 PM Central (US) Time	
#	**Description**
1.	**OPENING REMARKS (J. LEWIS)** Dr. Lewis opened the meeting at 2:00 PM Central (US) time by welcoming the participants to the first hybrid CLSI meeting in Rosemont (Chicago), IL.
2.	**TRIBUTE TO JIM POUPARD (J. HINDLER)** Ms. Hindler provided a tribute to Dr. Jim Poupard (1943-2022). A moment of silence was taken in honor of Dr. Poupard. A list of his accomplishments include: • Clinical Microbiologist (Clinical lab and Industry) • CLSI Advisor (1990's to 2015) • Served on ISO committee to standardize BMD (ISO20776-1) • > 50-year member of ASM National and Eastern PA Branch ASM • ASM National and EP ASM Branch Archivist
3.	**CLSI UPDATE (G. FINE)** Mr. Fine provided a brief update on the status of CLSI. The main points included: • Mr. Fine will retire as of 30 June 2022. • He expressed his gratitude to all the volunteers for the outstanding achievements to CLSI. • The state of CLSI is in fantastic shape: staffing, products, and finances. • He introduced CLSI's new CEO Barbara Jones. Dr. Lewis and the AST SC thanked Mr. Fine for his 17 years of service to CLSI and wished him the best with retirement. Ms. Jones shared a career story about the impact CLSI has on the medical community. She thanked the CLSI volunteers for the work completed for the mission of CLSI.

4. **VET SUBCOMMITTEE (VAST) UPDATE (R. BOWDEN)**

Mr. Bowden provided an update on the activities of the Subcommittee on Veterinary Antimicrobial Susceptibility testing. The following items are in progress:

- WG on Aquatic Animals
  - Develop ECVs for multiple agents for *Streptococcus iniae, Yersinia ruckeri,* and multiple *Aeromonas* spp., *Edwardsiella* spp., and *Vibrio* spp.
  - *Aeromonas salmonicida* MIC QC ranges were approved for conditions of 44-48 hours incubation at 28C. These conditions are necessary to support standardized testing of *Edwardsiella ictaluri*. Ranges were approved for ampicillin, enrofloxacin, erythromycin, florfenicol, flumequine, gentamicin, ormetoprim-sulfadimethoxine, oxolinic acid, oxytetracycline, and trimethoprim-sulfamethoxazole.
  - *A. salmonicida* ECVs (44-48 hr incubation @ 22C) were reanalyzed for florfenicol, oxolinic acid, and oxytet. Florfenicol and oxytetracycline ECVs were upheld, while oxolinic acid's ECV was lowered one dilution.
  - *A. salmonicida* disk ECVs were approved for ampicillin and revised for florfenicol, oxolinic acid, and oxytet
  - Additional ECVs are expected to be presented at the winter 2023 meeting, with a proposal to update VET04S
- Bovine Mastitis Interpretive Criteria WG (BMIC WG)
  - In January 2019, the process proposed by the BMIC WG and approved by the SC on VAST is a model in which the BMIC WG evaluates the data and makes a BP recommendation to the VAST SC for ratification on behalf of the sponsor rather than sponsors independently presenting and debating BP proposals with the VAST SC.
  - The process has met with challenges, as some recent proposals have been approved by the WG but are then rejected when brought to the VAST SC.
  - The 3 criteria typically used to set BPs (clinical data, MIC data, and PK/PD data) cannot always be applied
    - Some agents are administered as intramammary injections vs. systemic administration
    - Development of PD targets is complicated as milk residue data is typically the only PK data to investigate
    - Clinical outcomes data can be especially challenging to interpret due to the high rate of spontaneous cure, as well as differing regional regulations regarding study design and control groups
  - It was concluded that VET02 requires updating to provide further guidance on development of mastitis BPs
- WG on VAST Breakpoints/Editorial Tables (VET01S)
  - Creation of new tables for bovine mastitis BPs
  - Expansion of vet-specific BPs from single bacterial species into families. Changes will be incorporated into VET01S-Ed7 (2023).
  - Deletion of body site designation for BPs failed to meet consensus for approval and no changes will be made.
  - Oxacillin BP changes in M100 Table 2C vs VET01S Table 2C-1: M100S-Ed31 saw oxacillin MIC BPs for staphylococci other than *S. aureus* and *S. lugdunensis* change from <=0.25 "S" to <=0.5 "S". The VET01S WG's *Staphylococcus* subgroup is tasked with examining the issue and presenting its recommendation for/against adoption of <=0.5 "S" at the VAST winter 2023 meeting.
- VET05 WG (VET05 Generation, Presentation, and Application of AST Data for Bacteria of Animal Origin)
  - 1st edition published as X08-R in 2011 and was re-coded as VET05 when reaffirmed in 2016
  - Discussion occurred on M39's inclusion of a veterinary chapter and the need to avoid overlapping content
  - It was noted that M39 is primarily focused on the antibiogram and aiding empiric therapy decision making, while VET05 will have a greater focus on larger surveillance study design and incorporation of WGS data
  - Project proposal for a 2nd edition was approved at the winter 2022 plenary
- VET06 WG (VET06 Methods for AST of Infrequently Isolated or Fastidious Bacteria Isolated From Animals)
  - Major aim is to enable further studies of these organisms to be conducted in a standardized manner, generating data sufficient for the methods and BPs to be moved to the VET01 and VET01S documents

- There was discussion about differentiating VET06 BPs that are based on use of CLSI VAST SC-approved standard methods described in VET01 vs. BPs that require use of test methods described in VET06 that are derived from published studies but are not currently published by CLSI as a standard method in VET01
- Purpose of VET06 also includes providing cautions relating to recovery of and AST of sentinel agents
- Project proposal for 2nd edition was approved at the winter 2022 plenary
- Discussion occurred on the topic of adding AST methods for multiple species of *Mycoplasma*. It was suggested that this topic should perhaps be the focus of a joint AST-VAST WG to develop a new document.

- Other Activities
  - VET01 WG: Publication of the 7th edition is now scheduled to coincide with the release of VET01S-Ed7 in Fall 2023
  - WG on Understanding AST Data in Veterinary Settings (VET09): Work is underway on a 2nd edition, with revisions and the addition of two chapters
  - WG on PD Targets for Establishing Breakpoints (Subgroup of VET02 WG): Work is underway to review, revise, and expand the list of PK/PD targets for use in future BP analyses
  - Molecular AST
    - Great strides have been made in developing genotypic tools to predict resistance in foodborne pathogens
    - UN FAO is now promoting use of genotypic AST
    - M100 Appendix H has been reviewed by VAST but incorporation into VET01S is considered premature
    - It was agreed that several companies have emerged with products whose utility is considered questionable
    - A position paper by members of the SC on VAST will be developed and submitted to JAVMA or JVIM

5. **M45 UPDATE (T. SIMNER)**

Dr. Simner provided an update on the M45 Revision. The following items are in progress:

- Three teleconferences, fourth planned for Summer 2022
- Organism groups assigned to members
- Ongoing evaluation vs. EUCAST guidance, new clinical data, and testing issues
- Evaluate disk diffusion correlates:
  - Panels identified and to be manufactured in Summer 2022 (IHMA and ThermoFisher)
  - Studies will be conducted at 3 sites, Summer-Fall 2022
- New BPs and revision to existing BPs: Data in literature, clinical data and comparison to M100, EUCAST
- Testing considerations
  - Growth failures for *Aerococcus*
  - *H. pylori* gradient diffusion
- New organisms
  - *Campylobacter upsaliensis*, *C. lari*, *C. fetus*, *C. hyointestinalis*
  - *Actinomyces* split from *Corynebacterium* spp.
  - *Weissella* spp.
  - *Kocuria*, *Nesterkonia*, *Dermacoccus*, *Kytococcus* (split from *Micrococcus*)
  - *Bacillus cereus* serovar *anthracis*
- Consideration of intrinsic resistance tables for M45 organisms
- Ask: M45 needs to be available free on the CLSI website

6. **TEXT AND TABLES WG (TTWG) REPORT (S. CAMPEAU)**

Member Update: Suki Chandrasekaran is the new TTWG Secretary.

TABLES 2 DOSAGE COMMENTS

- Systematic review of dosage comments within M100, with particular attention to consistency across Tables 2 and placement of dosage comments.
- To ensure language consistency the WG pulled all dosage comments from the document and organized by location, table, organism, and drug. Then, the dosage comments were grouped into similar themes.
- The main issues of inconsistency include:
  - Inclusion or exclusion of the drug name in the comment
  - Inclusion or exclusion of route of administration
  - Inclusion or exclusion of disease indication when it's relevant to establishment of the breakpoint (eg, ceftol/tazo with dosage regimen for 'pneumonia' and for 'other indications')
- Proposed dosage comment structure:

Basic structure:

Breakpoints are based on a dosage regimen of 2.5 g every 8 h administered over 2 h

Modifiable parts, as needed:

Breakpoints **for susceptible|susceptible dose dependent** are based on a dosage regimen of **X g|mg**
for pneumonia
for ciprofloxacin
every **X h** **parenterally|orally|intravenously** administered **over X h|min**

- Two options were proposed:
  - Option 1: Removal of dosage comments from Tables 2 with added general comment in each Table 2 to refer user to Appendix E for this information, and review Appendix E for completeness.
  - Option 2: Alternative placement and formatting of dosage comments within Tables 2. Includes removing numbering for dosage comments, keeping #s only for non-dosage comments.
- New proposed general comment for each Table 2 for Option 1: For breakpoints that are based on specific dosage regimens, the dosage regimens are listed in Appendix E.

SC DISCUSSION (MAIN POINTS)

- SC agreed with proposed dosage comment structure and language consistency.
- Suggestion for addition of quick links to dosage comments in M100 electronic version.

- Clarification was provided that a general dosage comment would be added at the beginning of Table 2. Suggestion was made to add a footnote to all relevant Appendix E referral locations.
- Concerns about SDDs and if the dosages should be in Table 2 or Appendix E. Also, with other organisms and antibiotics for which there are different dosing regiments based on the pathogen.
- Concerns that Appendix E will not be viewed because it is in the back of the document. Suggestion was made to list the dosages in the front of the document like EUCAST.
- Support to move the dosages to one location for the laboratory and ID physicians.
- There is an Rx comment option where the laboratory is suggested to put a therapy comment on the reports.
- Suggestion to add a dosage column in Table 2 along with Appendix E.
- VET01S already has a dosage table in place that can be used for an example.
- Changes would be made in M100 34th Edition.
- Suggestion to add an indication (symbol) that a dosage comment is in Appendix E. TTWG would make Appendix E complete with every drug whether there is a dosage regimen or not; therefore, an indication would not be needed. Also, further education to users is needed.
- Concern if there will be emphasis on when the dosage amounts change for breakpoints.

A motion to approve the removal of dosage comments from Tables 2 with an added general comment in Table 2 to refer user to Appendix E for this information was made and seconded. Vote: 11 for, 2 against, 0 abstain, 0 absent (Pass)

Against Vote Reasoning:
- Like having the dosages in Table 2 especially with SDD.

TABLES 2 TEST/REPORT COLUMN REMOVAL
- Allows expansion of comment column to create more room
- Would want to:
  - Expand on O and INV designations in Instructions for Use and/or Table 1 introduction
  - Address ”U” designation by adding new comments
  - Add General Comment to all Tables 2 to refer users to Table 1 for tiered testing/reporting information
- Definitions of “O” and “Inv” in Instructions for Use
  - O (“other”): antimicrobial agents with established clinical breakpoints in Tables 2 but are generally not candidates for testing and reporting in the United States.
  - Inv. (“investigational”**):** antimicrobial agents that are investigational for the organism group and have not yet been approved by the FDA for use in the United States.
- An option would be to edit IFU and possibly add to new Tables 1 something like:

“Some antimicrobial agents with breakpoints in Tables 2A-2J are not listed in Tables 1A-1Q have a clinical indication for the organism group but are generally not candidates for routine testing and reporting in the United States.

Other agents with breakpoints in Tables 2A-2J are not considered for inclusion in Tables 1A-1Q because they are investigational for the organism group and have not yet been approved by the FDA for use in the United States. These are denoted as “Inv.” by the antimicrobial agent name in Tables 2A-2J.”

	• New proposed general comment for each Table 2: Refer to Table 1 for antimicrobial agents that should be considered for testing and reporting by microbiology laboratories. **SC DISCUSSION (MAIN POINTS)** • Suggestion was made to review Inv. drugs and if they should remain in the table. • ORWG will need to help with further education for laboratories and pharmacies.

7. **TABLE 1 AHWG REPORT (T. SIMNER)**

TABLE 1A: ENTEROBACTERALES (NOT INCLUDING *SALMONELLA/SHIGELLA*)

Table 1A: Enterobacterales (not including ~~Inducible AmpC producers &~~ *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 may warrant routine testing or tested by request in institutions that serve patients at high risk for MDRO but should only be reported following cascade or selective reporting rules	**Tier 4:** Antimicrobial agents that may warrant testing and reporting by request if antimicrobial agents in other Tiers are not optimal because of various factors
Ampicillin			
Cefazolin	Cefuroxime		
Cefotaxime[e] or Ceftriaxone[e]	Cefepime[f]		
	Ertapenem Imipenem Meropenem	Cefiderocol Ceftazidime-Avibactam Imipenem-Relebactam Meropenem-Vaborbactam	
Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam			
Gentamicin	Tobramycin Amikacin		
Ciprofloxacin Levofloxacin			
Trimethoprim-Sulfamethoxazole			
	Cefotetan Cefoxitin		
	Tetracycline[b]		
			Aztreonam
			Ceftaroline[e]
			Ceftazidime[e]
			Ceftolozane-Tazobactam
Urine only			
Cefazolin (surrogate for uUTI)[c]			
Nitrofurantoin			
		Fosfomycin[d] (*Escherichia coli*)	

Abbreviations. MDRO, multi-drug resistant organism; uUTI, uncomplicated urinary tract infection

TABLE 1A FOOTNOTES

a) See Appendix B for species-specific intrinsic resistance profiles. If a specific antimicrobial agent/organism combination that is defined as intrinsically resistant is tested, the result for antimicrobial agent/organism combination should be reported as resistant. Consideration may be given to adding comments regarding intrinsic resistance of agents not tested. See Appendix A, footnote "a".
b) Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.
c) See cefazolin comments in Table 2A for using cefazolin as a surrogate test for oral cephalosporins and for reporting cefazolin when used for therapy in uUTIs.
d) For testing and reporting of *E. coli* urinary tract isolates only.
e) *Citrobacter freundii* complex, *Enterobacter cloacae* complex, *Hafnia alvei, Klebsiella* (formerly *Enterobacter) aerogenes*, *Morganella morganii, Providencia* species, *Serratia marcescens*, and *Yersinia enterocolitica* may test susceptible to ceftriaxone, cefotaxime, ceftazidime, ceftaroline and piperacillin-tazobactam but these agents may be ineffective against these genera due to derepression of inducible AmpC beta-lactamase. The risk of AmpC derepression during therapy is moderate to high with *E. cloacae, C. freundii* and *K. aerogenes* and appears to less frequent with *M. morganii, Providencia* species and *S. marcescens* (IDSA Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections: Version 2.0).
f) Cefepime should be considered as a Tier 1 agent for testing/reporting of *Citrobacter freundii* complex, *Enterobacter cloacae* complex, *Hafnia alvei, Klebsiella* (formerly *Enterobacter) aerogenes*, *Morganella morganii, Providencia* species, *Serratia marcescens*, and *Yersinia enterocolitica*. See footnote e. (IDSA Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections: Version 2.0).

SC DISCUSSION (MAIN POINTS)

- Concern with ceftazidime in tier 4 and not in tier 3. It was placed in tier 4 in order to avoid the anti-*Pseudomonas* activity in the Enterobacterales. The drugs are recommendations. If there is a unique need, the drugs can be tested. Ceftazidime was already voted on previously to be included in tier 4.
- Trimethoprim-sulfamethoxazole needs to be in a separate box.
- Concern that piperacillin-tazobactam should not be mentioned in the footnote since it has not been shown to select for AmpC derepression. Piperacillin-tazobactam was included because there is some contention on its derepression and to provide guidance for clinicians to consider. It is not saying that piperacillin-tazobactam causes derepression but that in a derepressed organism piperacillin-tazobactam may be less active.
- Concern that colistin is not in Table 1 for countries that do not have new drugs. Suggestion to add to tier 4. Table 1 focuses on United States laboratories and in the future other countries will be evaluated. The title of Table 1 is "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".
- Concern with referring to IDSA Guidance in the footnotes. M100 is not a treatment guide. Clarification was given that it will be in the normal citation format with the specific version in the bibliography not in the Table 1 footnote text.
- Suggestion to include norfloxacin. It is not used in the United States and therefore, is not include in Table 1. Norfloxacin is included in Table 2.

A motion to remove piperacillin-tazobactam from the Table 1A e footnote was made and seconded. Vote: 9 for, 4 against, 0 abstain, 0 absent (Pass)

Against Vote Reasoning:

- Agreed with footnote as proposed. There is data that piperacillin-tazobactam fails with organisms that are derepressed.

A motion to approve Table 1A Enterobacterales (not including *Salmonella/Shigella*) and the proposed footnotes was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

TABLE 1C. *SALMONELLA AND SHIGELLA* SPP.

Table 1C. *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 may warrant routine testing or tested by request in institutions that serve patients at high risk for MDRO but should only be reported following cascade or selective reporting rules	**Tier 4:** Antimicrobial agents that may warrant testing and reporting by request if antimicrobial agents in other Tiers are not optimal because of various factors
Ampicillin			
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
Cefotaxime or Ceftriaxone			Ertapenem Imipenem Meropenem
	Azithromycin[c]		
			Tetracycline[d]

Abbreviation. MDRO, multi-drug resistant organism

TABLE 1C. SALMONELLA AND SHIGELLA SPP. FOOTNOTES

a. Table 2A should be used for interpreting antimicrobial susceptibility testing results for *Salmonella* and *Shigella* species.
b. WARNING: For *Salmonella* spp. and *Shigella* spp., aminoglycosides, first- and second-generation cephalosporins, and cephamycins may appear active in vitro but are not effective clinically and should not be reported as susceptible.

   Routine susceptibility testing is not indicated for nontyphoidal *Salmonella* spp. isolated from intestinal sources. In contrast, susceptibility testing is indicated for all Shigella isolates.

   When fecal isolates of *Salmonella* and *Shigella* spp. are tested, only ampicillin, a fluoroquinolone, and trimethoprim-sulfamethoxazole should be reported routinely. In addition, for extraintestinal isolates of *Salmonella* spp., a third generation cephalosporin should be tested and reported. Azithromycin may be tested and reported per institutional guidelines. Ertapenem, imipenem and/or meropenem might be considered for testing/reporting for isolates resistant to all of these agents although there are limited clinical data suggesting their effectiveness for treating salmonellosis or shigellosis (CDC Health Advisory, CDCHAN-00439, 2021).

c. For reporting against *Salmonella enterica* ser. Typhi and *Shigella* spp. only.
d. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline. However, some organisms that are intermediate or resistant to tetracycline may be susceptible to doxycycline, minocycline, or both.

SC DISCUSSION (MAIN POINTS)

- Discussion on including ertapenem, imipenem, and meropenem in tier 4. The footnote states that there is limited clinical data. It at least provides some guidance to users.

A motion to approve Table 1C *Salmonella* and *Shigella* spp. and the proposed footnotes was made and seconded. Vote: 11 for, 1 against, 1 abstain, 0 absent (Pass)

Against Vote Reasoning:

- No carbapenem clinical data to provide a recommendation.

TABLE 1P. GRAM-NEGATIVE ANAEROBES AND FOOTNOTES

Table 1P. Gram-Negative Anaerobes

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 may warrant routine testing or tested by request in institutions that serve patients at high risk for MDRO but should only be reported following cascade or selective reporting rules	**Tier 4:** Antimicrobial agents that may warrant testing and reporting by request if antimicrobial agents in other Tiers are not optimal because of various factors
Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam			
Clindamycin			
Ertapenem Imipenem[a] Meropenem			
Metronidazole			
			Penicillin[b] Ampicillin
			Cefotetan Cefoxitin
			Ceftizoxime Ceftriaxone
			Moxifloxacin

Abbreviation. MDRO, multi-drug resistant organism

NOTE 1: Most anaerobic infections are polymicrobial, including both ß-lactamase-positive and ß-lactamase-negative strains. Testing may not be necessary for isolates associated with polymicrobial anaerobic infections. However, if susceptibility testing is requested, only the organism most likely to be resistant (eg, *Bacteroides* spp. and *Parabacteroides* spp.) should be tested and results reported (see Appendix D).

[a] Organisms that test susceptible to imipenem are also considered susceptible to imipenem-relebactam. However, organisms that test susceptible to imipenem-relebactam cannot be assumed to be susceptible to imipenem.

[b] Penicillin retains good *in vitro* activity against most *Fusobacterium* species and may be considered for primary testing and reporting with this genus.

SC DISCUSSION (MAIN POINTS)

- Anaerobe AHWG had concerns about imipenem-relebactam not being included in Table 1P and unanimously agreed that it was an appropriate inclusion in the table. It does not send out an encouraging message to pharmaceutical companies for it not to be included.
- Footnote a seems like a Table 2 footnote for laboratoriess that cannot pursue imipenem-relebactam testing. A general footnote is included in Table 2 but not this specific footnote. A similar footnote is included in Table 1A for tetracycline; therefore, footnote a is appropriate for Table 1P.

	• Imipenem-relebactam was previously tier 3, the sponsor prefers it to be included in tier 3. SC agreed it is better placed in tier 4 because of the rare occurrence. • Suggestion to move penicillin, imipenem-relebactam, and moxifloxacin to tier 3. • Question regarding what relebactam adds to imipenem for anaerobes. It is rare that the MIC decreases when relebactam is added to imipenem. There are occasions that it does provide additional activity. • Suggestion to move footnote a to Table 2. TTWG clarified that a combo drug comment that is already linked to Table 2. SC agreed to not move footnote to Table 2 in order to maintain comment consistency for combo drugs. • Suggestion to add the footnote b to the antibiogram table. • Question if ceftizoxime is available in the United States. Ceftizoxime is not available and will be removed from the table.
	A motion to add imipenem-relebactam to tier 4 in Table 1P Gram-Negative Anaerobes was made and seconded. Vote: 11 for, 1 against, 1 abstain, 0 absent (Pass)
	Against Vote Reasoning: • Wanted to have imipenem-relebactam in tier 3.
	A motion to approve Table 1P Gram-Negative Anaerobes, with the removal of ceftizoxime, and the proposed footnotes was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)
	TABLE 1Q. GRAM-POSITIVE ANAEROBES AND FOOTNOTES

Table 1Q. Gram-Positive Anaerobes

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 may warrant routine testing or tested by request in institutions that serve patients at high risk for MDRO but should only be reported following cascade or selective reporting rules	**Tier 4:** Antimicrobial agents that may warrant testing and reporting by request if antimicrobial agents in other Tiers are not optimal because of various factors
Ampicillin[b] Penicillin[b]			
Amoxicillin-clavulanate Ampicillin-sulbactam Piperacillin-tazobactam			
Clindamycin			
Ertapenem Imipenem[c] Meropenem			
Metronidazole[a]			
			Cefotetan Cefoxitin
			Ceftizoxime Ceftriaxone
			Moxifloxacin
			Tetracycline

Abbreviation. MDRO, multi-drug resistant organism

Footnotes

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

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

c. Organisms that test susceptible to imipenem are also considered susceptible to imipenem-relebactam. However, organisms that test susceptible to imipenem-relebactam cannot be assumed to be susceptible to imipenem.

NOTE 1: Most anaerobic infections are polymicrobial, including both ß-lactamase-positive and ß-lactamase-negative strains. Testing may not be necessary for isolates associated with polymicrobial anaerobic infections. However, if susceptibility testing is requested, only the organism most likely to be resistant (eg, *Bacteroides* spp. and *Parabacteroides* spp.) should be tested and results reported (see Appendix D).

NOTE 2: Specific *Clostridium* spp. (eg, *Clostridium septicum*, *Clostridium sordellii*) may be the singular cause of infection and are typically susceptible to penicillin and ampicillin. Penicillin and clindamycin resistance have been reported in *Clostridium perfringens*. Agents in group A of Table 1C should be tested and reported for *Clostridium* spp.

SC DISCUSSION (MAIN POINTS)

- Question if ceftizoxime is available in the United States. Ceftizoxime is not available and will be removed from the table.
- Add imipenem-relebactam to tier 4 for consistency with Table 1P.

A motion to approve Table 1Q Gram-Positive Anaerobes, with the removal of ceftizoxime and addition of imipenem-relebactam to tier 4, and the proposed footnotes was made and seconded. Vote: 12 for, 1 against, 0 abstain, 0 absent (Pass)

Against Vote Reasoning:

- No data on imipenem-relebactam for Gram-positive anaerobes.

NEXT STEPS

- Create resources to help laboratories with implementation
- Education
- Look at developing the tables for other geographic areas

TABLE 2 TEST/REPORT GROUP

- Do we need the Test/Report Group in Tables 2?

Pros to Removing	Cons to Removing
Repetitive to Table 1	Most users of M100 generally flip to Tables 2 and don't often use Tables 1
Reduces potential of errors to occur between Tables 1 and 2	Upon request for AST of infrequently tested agent for a particular organism it is nice have that information available in one place
More real-estate in Tables 2 for other information	
Tier numbers rather than previous group letters may add confusion	

SC DISCUSSION (MAIN POINTS)

- Concerns with removing important information included in Table 2 and making sure to clarify the designations (Inv., U, O).
- Important to consult with the international community.
- U and O designation in Table 2 is used by technologists.

A motion to remove Table 2 column 1 (Test/Report Group) and to task the Text and Tables Working Group with designating the remaining drug test/report groups (investigational, urine only, and other) was made and seconded. Vote: 9 for, 4 against, 0 abstain, 0 absent (Pass)

Against Vote Reasoning:

- Too premature to make edits for M100-33rd edition.

TTWG TABLE 2 EXAMPLE (PRESENTED AT PLENARY 3)

- Current:

Table 2A. Enterobacterales (Continued)

Test/Report Tier	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
			S	SDD	I	R	S	SDD	I	R	
PENICILLINS											
1	Ampicillin	10 µg	≥17	-	14-16^	≤13	≤8	-	16^	≥32	**(6)** Results of ampicillin testing can be used to predict results for amoxicillin. See general comment (2). 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. Breakpoints when oral ampicillin is used only for therapy of salmonellosis, shigellosis, or uncomplicated UTIs due to E. coli and P. mirabilis are based on an ampicillin dosage regimen of 500 mg orally administered every 6 h or an amoxicillin dosage regimen of 250 mg orally administered every 8 h or 500 mg every 12 h.
0	Piperacillin		-	-	-	-	≤8	16	-	≥32	**(9)** Disk diffusion breakpoints have been removed because no disk correlate data are available for the revised piperacillin MIC breakpoints. Disk diffusion breakpoints will be reassessed if data become available.
0	~~Mecillinam~~	10 µg	≥15	-	12-14^	≤11	≤8	-	16^	≥32	**(10)** For testing and reporting of *E. coli* urinary tract isolates only.
β-LACTAM COMBINATION AGENTS											
(11) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test SDD, intermediate, or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.											
1	Amoxicillin-clavulanate	20/10 µg	≥18	-	14-17^	≤13	≤ 8/4	-	16/8^	≥32/16	Breakpoints are based on a dosage regimen of 1.2 g IV administered every 6 h. Breakpoints when amoxicillin-clavulanate is used for therapy of uncomplicated UTIs or for completion of therapy for systemic infection are based on a dosage regimen of either 875/125

- Proposed:

Table 2A. Enterobacterales

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm				Interpretive Categories and MIC Breakpoints, µg/mL				Comments
		S	SDD	I	R	S	SDD	I	R	
PENICILLINS										
Ampicillin	10 µg	≥17	-	14-16^	≤13	≤8	-	16^	≥32	**(6)** Results of ampicillin testing can be used to predict results for amoxicillin. (7) Breakpoints are based on an ampicillin dosage regimen of 2 g parenterally administered every 4-6 h or an amoxicillin dosage regimen of 1-2 g parenterally administered every 6 h. (8) Breakpoints when oral ampicillin is used for therapy of uncomplicated UTIs due only to *E. coli*, *P. mirabilis*, *Shigella*, and *Salmonella* are based on an ampicillin dosage regimen of 500 mg orally administered every 6 h or an amoxicillin dosage regimen of 250 mg orally administered every 8 h or 500 mg every 12 h. See general comment (2).
Piperacillin		-	-	-	-	≤8	16	-	≥32	**(8)** Disk diffusion breakpoints have been removed because no disk correlate data are available for the revised piperacillin MIC breakpoints. Disk diffusion breakpoints will be reassessed if data become available.
Mecillinam	10 µg	≥15	-	12-14^	≤11	≤8	-	16^	≥32	**(9)** For testing and reporting of *E. coli* urinary tract isolates only.
β-LACTAM COMBINATION AGENTS										
(10) Organisms that test susceptible to the β-lactam agent alone are also considered susceptible to the β-lactam combination agent. However, organisms that test susceptible to the β-lactam combination agent cannot be assumed to be susceptible to the β-lactam agent alone. Similarly, organisms that test SDD, intermediate, or resistant to the β-lactam agent alone may be susceptible to the β-lactam combination agent.										
Amoxicillin-clavulanate	20/10 µg	≥18	-	14-17^	≤13	≤8/4	-	16/8^	≥32/16	**(12)** Breakpoints are based on a dosage regimen of 1.2 g IV administered every 6 h. (13) Breakpoints when amoxicillin-clavulanate is used for therapy of

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

- Abbreviations will be added for Inv. and U.
- A symbol * will be added and state “designation for ‘Other’ agents not included in Tables 1 but have established clinical breakpoints.”
- A comment will be added to all Tables 2 referring to the associated organism/organism group Tables 1. For example, a comment will be added to Table 2A stating: Refer to Table 1A-1C for antimicrobial agents that should be considered for testing and reporting by microbiology laboratories.
- The Test/Report tables in Instructions for Use will be updated (Tables X and Y).

SC DISCUSSION (MAIN POINTS)

- AST SC agreed with the proposed Table 2 changes.
- Discussion on the value of adding O instead of the *.
- Suggestion to add that the drugs may not need to be testing to the * comment.
- Suggestion to remove “designation for ‘Other’ agents not included” in the * comment. Thought that it will help users to understand the change.

8.	**ADJOURNMENT** Dr. Lewis thanked the participants for their attention. The meeting was adjourned at 5:15 PM Central (US) time.

2022 JUNE AST MEETING SUMMARY MINUTES PLENARY 2: Monday, 27 June 2022 (In-person/Hybrid) 7:30 AM – 11:30 AM Central (US) Time	
#	**Description**
1.	**OPENING** Dr. Lewis opened the meeting at 7:30 AM Central (US) time.
2.	**EUCAST UPDATE (C. GISKE)** Dr. Giske provided an update on the activities of EUCAST. The main points included: • Revision of fosfomycin MIC breakpoints for *E. coli* (S≤8 mg/L, R>8 mg/L) and bracketed *S. aureus* (S≤(32) mg/L, R>(32) mg/L) for the daily dose of at least 16g. (#) indicate that for systemic infections, fosfomycin IV should be used in combination with other active therapy. In this circumstance, the value in brackets can be used to distinguish wild type organisms and organisms with acquired resistance mechanisms. • Proposed revision of chloramphenicol MIC breakpoints for Enterobacterales, *Staphylococcus* spp., *Streptococcus* groups A, B, C, G, and *S. pneumoniae*. • Ongoing discussion for Cephs vs *S. aureus*.
3.	**M23 UPDATE (M. WIKLER)** Dr. Wikler provided an update on the M23 Revision. The following items are in progress: • The Proposed Draft comment resolutions were completed in June 2022. • Estimated publication is Q1 2023.

4. **BREAKPOINT WG (BPWG) REPORT (A. MATHERS AND M. SATLIN)**

GENTAMICIN ENTEROBACTERALES PROPOSED BREAKPOINTS

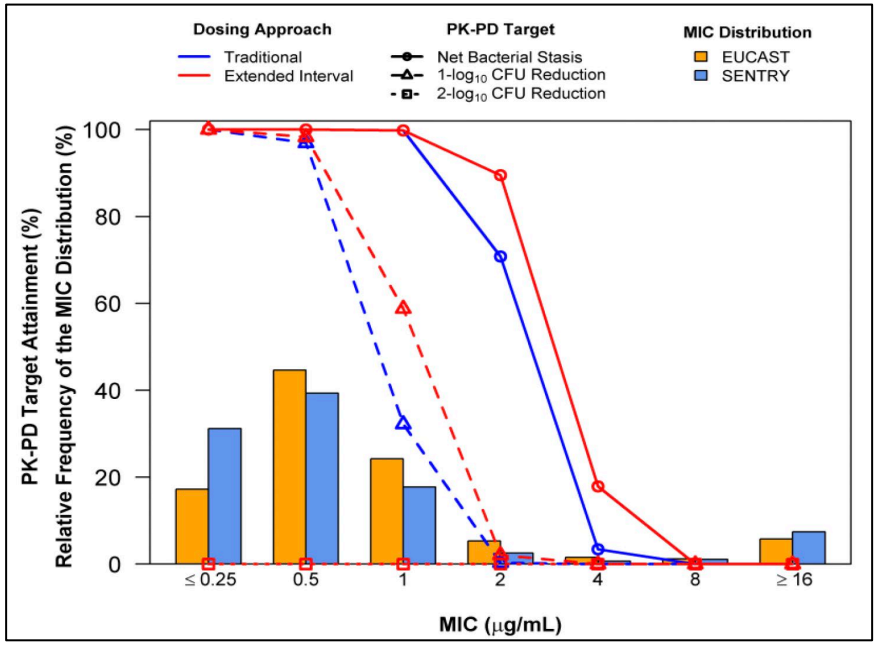
- Data:

ECV (JMI)	95%	97.5%	99%	EUCAST
E. coli	1	2	2	2
K. pneumo	0.5	0.5	0.5	2
E. cloacae	0.5	0.5	0.5	2
P. mirabilis	1	2	2	4
All	1	2	2	

Enterobacterales without AME or RMT: 96.4% inhibited at 2.
EUCAST: S≤2 (urine)

MIC	Traditional	7 mg/kg/day
1	99.8%	99.8%
2	**70.8%**	**89.5%**

PTA for stasis target from murine thigh model.



- Proposed Breakpoints:

	S	I	R
Gentamicin (NEW)	≤2	4	≥8
Gentamicin (OLD)	≤4	8	≥16

Breakpoints based on 7 mg/kg daily.

- Proposed Dosage Comment: Breakpoints are based on a dosage regimen of (7 or 15) mg/kg administered parenterally every 24 h. Gentamicin/tobramycin is 7 mg/kg and amikacin is 15 mg/kg.
- Proposed Comment (in addition to proposed dosage comment): Breakpoints for the aminoglycoside class are based on population distributions of various species, PK/PD target attainment analyses with an endpoint of net bacterial stasis, and limited clinical data. Clinical outcomes data for aminoglycosides as monotherapy for systemic infections are limited though have resulted in worse treatment outcomes (for infections outside of the urinary tract) when compared to other therapies. Consider combination therapy for most indications other than urinary tract infections. Consultation with an infectious diseases specialist is recommended.

SC DISCUSSION (MAIN POINTS)

- Concerns with changes in breakpoints and dosages will not be accepted with the FDA. FDA reassured CLSI to move forward in submitting a rationale document.
- Suggestion to have disk correlation before approving MIC breakpoints. EUCAST will share disk data with CLSI. JMI has gentamicin and amikacin disk correlate data.
- Question whether data was from United States only. The data was from the United States only. A wild type population is the same worldwide.
- Breakpoints based on ECOFF RangeFinder.
- Concern with laboratories reporting first sentence of proposed comment. Suggestion to move the first sentence to a rationale document and not include in M100.

A motion to approve gentamicin MIC BPs for Enterobacterales (S≤2, I 4, R≥8) with the proposed comment, pending disk correlation data, and rationale document was made and seconded. Vote: 12 for, 0 against, 0 abstain, 1 absent (Pass)

TOBRAMYCIN ENTEROBACTERALES PROPOSED BREAKPOINTS

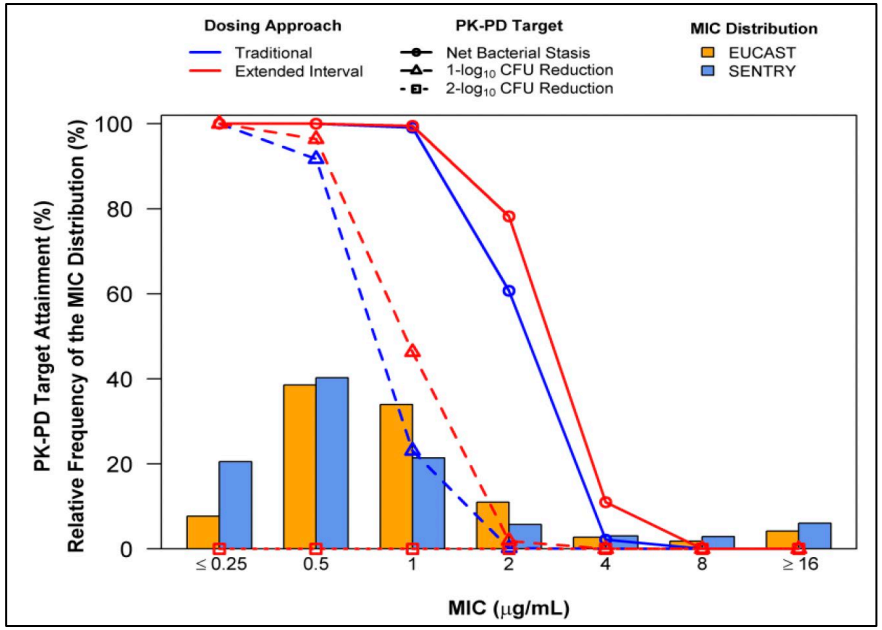
- Data:

ECV (JMI)	95%	97.5%	99%	EUCAST
E. coli	2	2	2	4
K. pneumo	0.5	0.5	1	2
E. cloacae	0.5	1	1	2
P. mirabilis	2	2	2	4
All	2	2	2	

Enterobacterales without AME or RMT: 96% inhibited at 2.
EUCAST: S≤2 (urine)

MIC	Traditional	7 mg/kg/day
1	99.1%	99.5%
2	**60.7%**	**78.2%**

PTA for stasis target from murine thigh model.



- Proposed Breakpoints:

	S	I	R
Tobramycin (NEW)	≤2	4	≥8
Tobramycin (OLD)	≤4	8	≥16

Breakpoints based on 7 mg/kg daily.
Excludes *Serratia marcescens* because of higher MICs (EUCAST ECOFF 8 µg/mL).

SC DISCUSSION (MAIN POINTS)

- Clarification was made that *Serratia* would not be called intrinsically resistant and would be excluded. If *Serratia* is excluded, device manufacturers would be unable to report an MIC for *Serratia*.
- Suggestion was made to include *Serratia* and include a comment similar to *Proteus*, *Providencia*, and *Morganella* with imipenem. SC agreed to include *Serratia marcescens* tobramycin MIC breakpoints with a comment.

A motion to approve tobramycin MIC BPs for Enterobacterales (S≤2, I 4, R≥8) with the proposed comments, pending disk correlation data, and rationale document was made and seconded. Vote: 12 for, 0 against, 1 abstain, 0 absent (Pass)

AMIKACIN ENTEROBACTERALES PROPOSED BREAKPOINTS

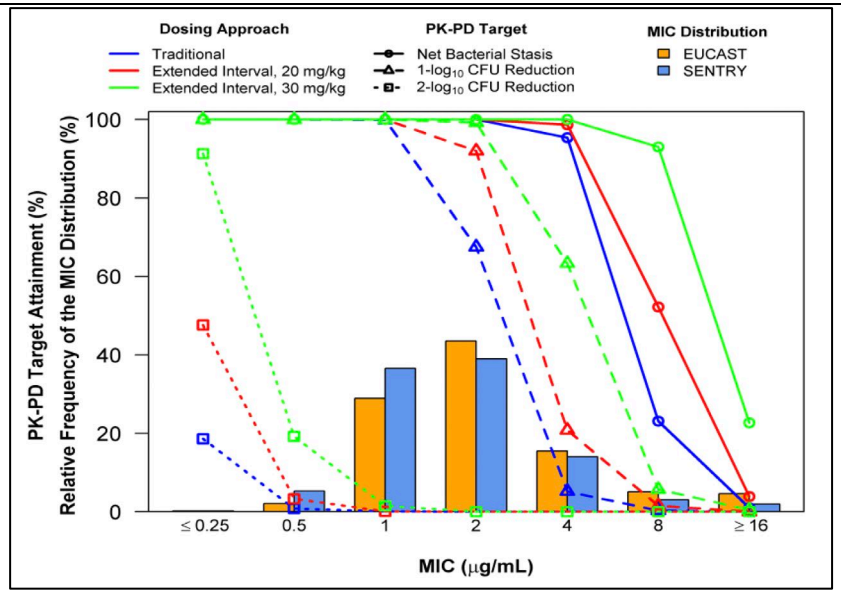
- Data:

ECV	95%	97.5%	99%	EUCAST
E. coli	8	8	8	8
K. pneumo	2	2	2	8
E. cloacae	2	2	2	8
P. mirabilis	8	8	8	16
All	4	8	8	

Enterobacterales without AME or RMT: 95.5% inhibited at 4.
EUCAST: S≤8 (urine)

MIC	Traditional	20 mg/kg	30 mg/kg
4	**95.4%**	**98.7%**	**100%**
8	23.1%	52.2%	93.0%

PTA for stasis target from murine thigh model.



- Proposed Breakpoints:

	S	I	R
Amikacin (NEW)	≤4	8	≥16
Amikacin (OLD)	≤16	32	≥64

Breakpoints based on 15 mg/kg daily.

SC DISCUSSION (MAIN POINTS)

- Clarification was made that the dosage is 15 mg/kg/day.

A motion to approve amikacin MIC BPs for Enterobacterales (S≤4, I 8, R≥16) with the proposed comment, pending disk correlation data, and rationale document was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

TOBRAMYCIN *PSEUDOMONAS AERUGINOSA* PROPOSED BREAKPOINTS

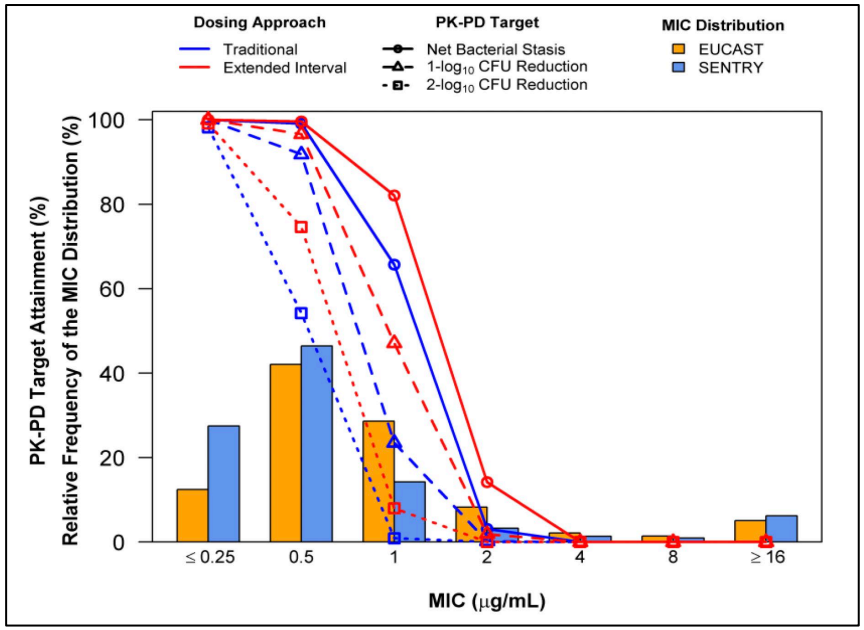
- Data:

ECV	95%	97.5%	99%
JMI	1	1	2
IHMA	2	2	2
EUCAST	2		

EUCAST: S≤2 (urine)

MIC	Traditional	7 mg/kg
1	**65.7%**	**82.1%**
2	3.1%	14.2%

PTA for stasis target from murine thigh model.



- Proposed Breakpoints:

	S	I	R
Tobramycin (NEW)	≤1	2	≥4
Tobramycin (OLD)	≤4	8	≥16

Breakpoints based on 7 mg/kg daily.

SC DISCUSSION (MAIN POINTS)

- A test that works is clinically needed. It is not great but the best that can be provided at this time.
- Cmax/MIC ≥10 is an alternative PD target and is supported by clinical data (although data less robust with *P. aeruginosa*). Using this PD target would lead to a PK-PD breakpoint of susceptible ≤2 µg/mL.
- The dosage proposal is 7 mg/kg/day. The exposure is no different than the recommended breakpoint. It is based on an alternative PD endpoint for efficacy. There is no issue with toxicity or patient safety. This is the standard dose in the majority of institutions.

A motion to approve tobramycin MIC BPs for *Pseudomonas aeruginosa* (S≤1, I 2, R≥4) with the proposed comment, pending disk correlation data, and rationale document was made and seconded. Vote: 10 for, 3 against, 0 abstain, 0 absent (Pass)

Against Vote Reasoning:

- Want to wait to see disk correlation data first.
- Swayed by clinical target of Cmax/MIC.

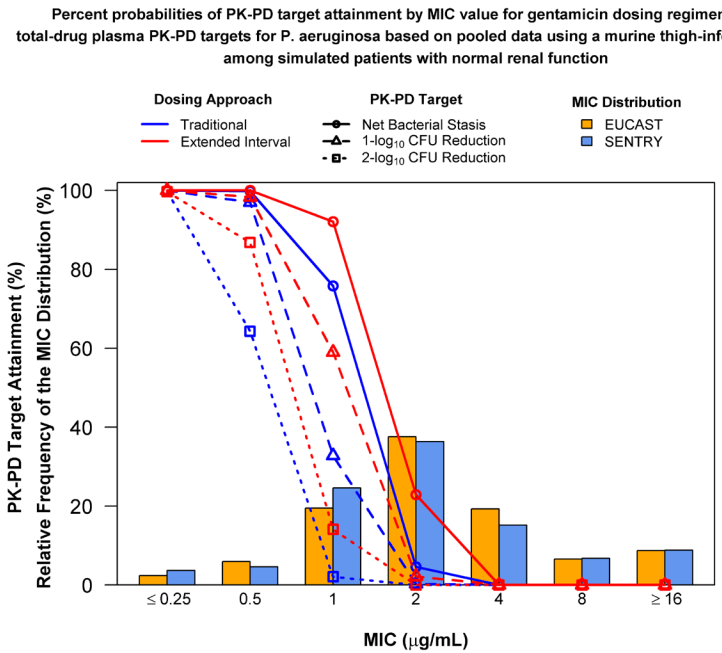
REMOVAL OF GENTAMICIN *PSEUDOMONAS AERUGINOSA* BREAKPOINTS

- Harmonizes with EUCAST and USCAST
- Data:

ECV: 8 mg/L
PK/PD cutoff (1-log kill): 0.5 mg/L
PK/PD cutoff (stasis): 1 mg/L

MIC (µg/mL)	Percent probabilities of PK-PD target attainment by MIC	
	Extended interval	
	Net bacterial stasis (58.3)	1-$\log_{10}$ CFU reduction from baseline (83.9)
0.5	100	98.3
1	92.1	59.0
2	22.9	2.20

a. Percent probabilities of PK-PD target attainment by MIC are shown for each bacterial reduction endpoint. The associated magnitude of the non-clinical total-drug plasma AUC:MIC ratio target for each endpoint based on a neutropenic murine thigh infection model is shown in parenthesis in each column header.



Percent probabilities of PK-PD target attainment by MIC are shown overlaid over MIC distributions from the SENTRY Antimicrobial Surveillance Program (2011-2016, USA) and EUCAST data (2017).

SC DISCUSSION (MAIN POINTS)

- Concerns with FDA not recognizing the removal of gentamicin and causing problems with device manufacturers. Once the breakpoint is removed, device manufacturers will not supply a MIC.
- Question if clinicians are using gentamicin. It is in the best interest to not use on patients.
- Education will be important for communicating this change.
- Suggestion to add comment to state removal of gentamicin and reasoning. Proposed comment: "Tobramycin does not predict susceptibility to gentamicin."

A motion to remove gentamicin MIC BPs for *Pseudomonas aeruginosa* with comment was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

AMIKACIN *PSEUDOMONAS AERUGINOSA* BREAKPOINTS (REMOVAL OPTION)

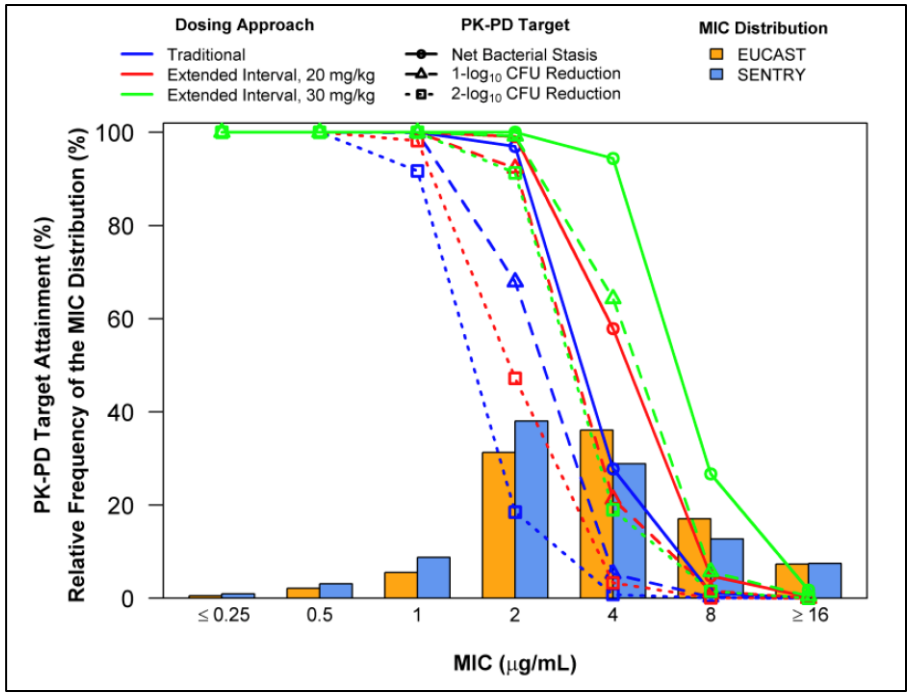
- Data:

ECV	95%	97.5%	99%
JMI	8	16	16
IHMA	8	8	8
EUCAST	16		

EUCAST: S≤16 (urine)

MIC	Traditional	20 mg/kg	30 mg/kg
2	**97.0%**	**99.1%**	**100%**
4	27.8%	57.9%	94.4%
8	1.2%	1.6%	26.7%

PTA for stasis target from murine thigh model.



SC DISCUSSION (MAIN POINTS)

- Concerns of amikacin use in other countries with tobramycin resistant organisms. Suggestion to have intermediate only breakpoint. Concerns with FDA approving intermediate only breakpoint.
- Suggestion to use the insufficient evidence like EUCAST. It would at least provide an option in combination therapy and help other countries.
- Concerns with not having two aminoglycosides available for combination treatment.
- Amikacin is used often for *P. aeruginosa* that were susceptible for tobramycin. Amikacin is no better than gentamicin.

- EUCAST clarified their MIC of 16 that they believed that it would be used in combination therapy and they did not want to split the wild-type.
- Suggestion for a urine only breakpoint. Clinical trials have supported success in UTI infections with *P. aeruginosa*.
- Suggestion to use an ECV instead of a breakpoint.

A motion to remove amikacin MIC BPs for *Pseudomonas aeruginosa* was made and seconded. Vote: 6 for, 7 against, 0 abstain, 0 absent (Fail)

Against Vote Reasoning:
- Prefer urine only breakpoint or intermediate only breakpoint.
- Concern for international use.
- Will never get MIC from a commercial system.

AMIKACIN *PSEUDOMONAS AERUGINOSA* BREAKPOINTS (I^ OPTION)
- I^ breakpoint (with comment) with no "susceptible" breakpoint based on ECVs, PK/PD, and clinical data
- *P. aeruginosa*
  - Tobramycin: I ≤ 1 mg/L, R ≥ 2 mg/L
  - Amikacin: I ≤ 4 mg/L, R ≥ 8 mg/L
- Proposed comment (in addition to dosage comment): Clinical and PK-PD data demonstrate aminoglycosides have limited clinical efficacy as monotherapy for systemic infections, even if an intermediate result is obtained. Alternative agents are strongly preferred. Aminoglycosides should be used in combination with one or more active antimicrobial agents. Consultation with an infectious diseases specialist is recommended.

ECV (95% - 99.5%)	Gentamicin	Tobramycin	Amikacin
Enterobacterales	1 - 2	2 - 2	4 - 8
P. aeruginosa	4 - 8	1 - 2	8 - 16

SC DISCUSSION (MAIN POINTS)
- Suggestion for intermediate only breakpoint of less than 16. Commercial panels do not provide amikacin concentrations below 16.
- Concern that laboratories will only be able to report breakpoints on urine specimens.
- A breakpoint at 16 would not cut into the wild-type distribution.
- Clinical trial data of amikacin for *P. aeruginosa* UTIs was provided.
- Suggestion to include a comment similar to colistin.
- Discussion on I vs I^. If the intention is to convey the idea that it is only going to be used for urinary tract infections then I^ is appropriate. The intent of the I^ is to say that if you use it in the urine you have high concentrations of drug that probably support the use at the high MIC. Support to use I^ to not be specific to urine.
- Question if the urine would be for complicated or uncomplicated infections. It would need to be for complicated UTIs.

A motion to approve amikacin MIC BPs for *Pseudomonas aeruginosa* (I^≤16, R≥32) with the proposed comment was made and seconded. Vote: 5 for, 8 against, 0 abstain, 0 absent (Fail)

Against Vote Reasoning:

- Not appropriate to have breakpoint at 16. Prefer lower breakpoint.

AMIKACIN *PSEUDOMONAS AERUGINOSA* BREAKPOINTS (URINE ONLY OPTION: VOTE #1)

- Urine breakpoint based on stasis PK/PD cutoff, ECVs, clinical data
- *P. aeruginosa*
  - Amikacin: S ≤ 16 mg/L, I = 32 mg/L, R ≥ 64 mg/L

ECV (95% - 99.5%)	Gentamicin	Tobramycin	Amikacin
Enterobacterales	1 - 2	2 - 2	4 - 8
P. aeruginosa	4 - 8	1 - 2	8 - 16

For	Against
Aligns with EUCAST breakpoints (minus part about brackets for systemic infxns)	Largely based on ECVs (true PK/PD cutoffs based on stasis are lower)
PK/PD stasis target is consistent with low bacterial burden infections; easier to tx	No urine-specific PK/PD data as basis (could breakpoints be higher?)
Clinical efficacy is most reliable for UTIs	Will labs only test from urine specimens?

SC DISCUSSION (MAIN POINTS)

- Concerns from international community to use as urine only. Suggestion to include comment that it can be used for combination therapy for other sources.
- Used for complicated UTIs.

A motion to approve amikacin urine only MIC BPs for *Pseudomonas aeruginosa* (S≤16, I 32, R≥64) was made and seconded. Vote: 4 for, 9 against, 0 abstain, 0 absent (Fail)

Against Vote Reasoning:

- Prefer to remove amikacin breakpoint.
- Prefer intermediate only breakpoint.

5. **ADJOURNMENT**

Dr. Lewis thanked the participants for their attention. The meeting was adjourned at 11:30 AM Central (US) time.

2022 JUNE AST MEETING SUMMARY MINUTES PLENARY 3: Monday, 27 June 2022 (In-person/Hybrid) 1:00 PM – 6:00 PM Central (US) Time	
#	**Description**
1.	**OPENING** Dr. Lewis opened the meeting at 1:00 PM Central (US) time.

2.	**BREAKPOINT WG (BPWG) REPORT CONTINUE (A. MATHERS AND M. SATLIN)** **AMIKACIN *PSEUDOMONAS AERUGINOSA* BREAKPOINTS (URINE ONLY OPTION: VOTE #2)** • Urine breakpoint based on stasis PK/PD cutoff, ECVs, clinical data • *P. aeruginosa* – Tobramycin: S ≤ 2 mg/L, I = 4 mg/L, R ≥ 8 mg/L – Amikacin: S ≤ 16 mg/L, I = 32 mg/L, R ≥ 64 mg/L • Proposed comment: The breakpoints no longer apply to systemic infections and are under review. **SC DISCUSSION (MAIN POINTS)** • Proposal to remove amikacin MIC breakpoints and reanalyze for a urine only breakpoint for next edition. Concern about the confusion that will be created from having no breakpoint for a year. • Question if a comment or explanation would be provided stating that the AST SC is reviewing urine only breakpoints. A comment similar to the gentamicin systemic breakpoint removal for *P. aeruginosa* could be provided. Or a comment that the use of amikacin for urine only is under review and to refer to M100 32nd edition for breakpoints. • Suggestion for gentamicin urine only breakpoints for *P. aeruginosa* to be reviewed. • Amikacin is IV and therefore, this would be for complicated UTI. • Concern about the effects on manufacturers. • Concern that the users in Latin America will use EUCAST data to test. • There needs to be discussion with the FDA on what a urine only breakpoint means. • Concern about what additional data is available. The AHWG provided the data already that was available. There is older data that could be reviewed.
	A motion to approve current amikacin MIC BPs for *Pseudomonas aeruginosa* (S≤16, I 32, R≥64) as urine only with proposed comment and future analysis of aminoglycoside urine only breakpoints was made and seconded. Vote: 8 for, 4 against, 1 abstain, 0 absent (Fail)
	Against Vote Reasoning: • Concern with FDA approval. • No guidance for systemic infections. • No additional review of urine only data prior to published breakpoints. • Too rushed. **AMIKACIN *PSEUDOMONAS AERUGINOSA* BREAKPOINTS (URINE ONLY OPTION: VOTE #3)** • Urine breakpoint based on stasis PK/PD cutoff, ECVs, clinical data • *P. aeruginosa* – Amikacin: S ≤ 16 mg/L, I = 32 mg/L, R ≥ 64 mg/L • Proposed comment similar to EUCAST regarding infections originating from the urinary tract.

SC DISCUSSION (MAIN POINTS)

- Will not review urine only for the other aminoglycosides.
- FDA already has the data regarding outcomes of UTIs treated with amikacin. The data is already FDA approved.
- Question as to why AHWG did not prefer the urine only option. There was concern about bisecting the wild-type distribution. The original recommended option to have a systemic breakpoint with a comment explaining the suboptimal nature of the drug is a better and more unifying breakpoint. It is better to have systemic use. Urine only or intermediate only are stepped down options from what is ideal.
- From the urine is a low risk source based on the clinical data. It is complicated urines from infections originating from the urinary tract.
- Question on how to report. The report would state the source as urine and the clinicians would need to make the decision. Urine result could be used for recovery in other sources.

A motion to approve amikacin urine only MIC BPs for *Pseudomonas aeruginosa* (S≤16, I 32, R≥64) with proposed comment was made and seconded. Vote: 12 for, 1 against, 0 abstain, 0 absent (Pass)

Against Vote Reasoning:

- Concern with laboratory confusion when there is a urine only breakpoint for sepsis.

STENOTROPHOMONAS MALTOPHILIA BREAKPOINT AHWG REPORT

- Differences in recognized breakpoints for *Stenotrophomonas maltophilia*

	CLSI			EUCAST		FDA	
	Category	MIC (µg/mL)	DD (mm)	MIC (mg/L)	DD (mm)	MIC (µg/mL)	DD (mm)
Ticarcillin-clavulanate	O	S ≤16/2, I 32/2-64/2, R ≥128/2	---	XX	XX	XX	XX
Ceftazidime	B	S ≤8, I 16, R≥32	---	XX	XX	S ≤8, I 16, R≥32	--
Cefiderocol[#]	B	S ≤1	S ≥15	S ≤ 0.001 mg/L "off scale" breakpoint (IE).	≥20 mm corresponds with MIC≤2	XX	XX
Minocycline	A	S ≤4, I 8 R ≥16	S ≥19, I 15-18, R ≤14	XX	XX	XX	XX
Levofloxacin	A	S ≤2 I 4 R ≥8	S ≥17, I 14-16, R ≤13	XX	XX	XX	XX
Trimethoprim-sulfamethoxazole	A	S ≤2/38, R≥4/76	S ≥16 I 11-15 R ≤10	S=0.001, I ≤2, R>4 mg/L*	S>50 mm* I16-50 R<16 mm	XX	XX
Chloramphenicol	C	S ≤8, I 16, R≥32	---	XX	XX	XX	XX

[#] Breakpoints are based on PK/PD properties, MIC distributions, and limited clinical data. *Reading guide provided trimethoprim component only. MICs ≤2 as intermediate, which requires the use of a higher dosing regimen, 240 mg (trimethoprim component) intravenously every 12 hours.

- In vivo PK/PD models
  - Three papers reviewed: 2 papers used neutropenic murine pneumonia model (Imoto - JGAR, Nakamura - AAC) and 1 paper used neutropenic murine thigh infection model (Fratoni - JAC)
  - Summary:
    - Only 3 in vivo PK/PD studies available
    - 2 of 3 studies used dosing that does not simulate clinically relevant LVX dosing
    - Fratoni/Kuti data suggest breakpoint of 0.5 mg/L (96% PTA) or 1 mg/L (72% PTA) would be appropriate
  - Discussion:
    - Fratoni model based on variable popPK averaging of population which would include non-healthy volunteers
    - Fit composite curve to give AUC:MIC for log kill ~40 stasis, 55 is 1-log kill.
    - Somewhere in between *P. aeruginosa* and Enterobacterales thresholds
    - Increased patient variability leads to lower PTA
    - Discussion about neutropenia model and thigh model---Lung model would be next body of work with ELF but thought would be that it should be 1:1
- Clinical Outcomes and Data Analysis
  - Results:
    - CLSI breakpoints did not discriminate patients based on risk-adjusted mortality outcome
    - For the levofloxacin cohort: within the susceptible range, lower MIC breakpoints are not associated with a lower mortality outcome (eg, ≤ 2, ≤1, ≤ 0.5)
  - Summary:
    - Retrospective studies with heterogenous patient populations, study goals, and outcomes
    - Very limited data on outcomes according to MICs
    - Clinical studies do not provide robust data for or against a change in the breakpoint
  - Discussion:
    - Current clinical data very challenging and compounded by colonization
    - Not a signal at MIC but the data is limited as several important patients (eg, patients who had change in therapy) were excluded from models
    - Data does indicate that there is quick emergence of levofloxacin resistance after exposure which was part of the reason dual therapy was suggested in the IDSA AMR guidance
- Microbiology Laboratory Data Analysis
  - Summary:
    - MIC mode = 1µg/mL
    - Known resistance mechanisms
    - BMD essential agreement is 89-92%
    - Essential agreement for commercial methods compared to BMD: 86-91% (Khan et al.)
    - Setting disk diffusion breakpoints corresponding to MIC values of ≤1 S; 2 I; ≥4 R requires the M23 6.3.2 Table 7 discrepancy rates
- Proposed Breakpoints:

Test/Report Group	Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
			S	I	R	S	I	R	
Fluoroquinolones									
A	Levofloxacin	5 µg	≥ 17	14-16^	≤ 13	≤ 2	4	≥ 8	

Keep Levofloxacin breakpoints as is with a comment regarding monotherapy for systemic infections, with no delay implementation.

SC DISCUSSION (MAIN POINTS)

- No persistence data was presented only mortality data. The clinical data looking at outcomes by MIC was inconclusive.
- Concern with PK/PD being in the middle of the distribution.
- Concern with adding the comment without changing the breakpoint is not enough to change practice. Preference for I only breakpoint of ≤2 and R≥4 with a comment about combination therapy for the I.
- Concern that there is not a good combination drug with levofloxacin.
- Based on PK/PD data, there is support for S, I, and R breakpoints.
- Currently not FDA recognized and not on device panels. No EUCAST breakpoints.
- Concerns with changing levofloxacin and not trimeth-sulf since the data is similar.

A motion to keep levofloxacin MIC BPs for *Stenotrophomonas maltophilia* as S≤2, I 4, R≥8 with the addition of the proposed comment was made and seconded. Vote: 8 for, 5 against, 0 abstain, 0 absent (Fail)

Against Vote Reasoning:

- Data outside of the MIC distribution suggests it is not the right target.
- Should wait to review all *Stenotrophomonas* drugs.
- In favor of I only breakpoint.

STENOTROPHOMONAS MALTOPHILIA BREAKPOINT (VOTE #2)

SC DISCUSSION (MAIN POINTS)

- There is a precedent to add a comment that you cannot use monotherapy to an organism drug combination that has a susceptible breakpoint (example, *Staphylococcus* and rifampin).
- Suggestion to keep breakpoints as is with proposed comment and future review of all *Stenotrophomonas* drugs. With a passing vote, levofloxacin breakpoints will continue to be re-evaluated along with the other *Stenotrophomonas* antibiotics for consistency across therapies.
- Confirmation that the FDA only recognizes ceftazidime.

A motion to keep levofloxacin MIC BPs for *Stenotrophomonas maltophilia* as S≤2, I 4, R≥8 with the addition of the proposed comment was made and seconded. Vote: 11 for, 2 against, 0 abstain, 0 absent (Pass)

AZITHROMYCIN AND NON-TYPHI *SALMONELLA* BREAKPOINTS (INFORMATIONAL ONLY)

- Summary:
  - Increasing resistance and shift of MICs as well as acquisition of resistance genes seen in NARMS surveillance
  - Several guidelines recommend using azithromycin as potential alternative treatment
  - Ongoing clinical trial looking at use of azithromycin for treatment in pediatrics and will include invasive disease
  - Request to revisit the current azithromycin breakpoints and perhaps expansion of azithromycin breakpoints to include non-Typhi Salmonella
    - Expand current *Salmonella typhi* MIC breakpoints to non-Typhi serotypes other than Paratyphi A OR
    - Add a comment indicating potential applicability to other *Salmonella* serotypes. "In vitro MIC data for azithromycin support potential utility of these interpretive criteria for non-Typhi serotypes other than Paratyphi A"
- Discussion:
  - Emerging resistance in this area is important and concerning and appreciate CDC raising issue
  - Additional treatment options are needed
  - *S. typhi* have clinical treatment data was central to assigning a BP without PK/PD data and would be critical for setting a breakpoint for NTS
  - Clinical data will be forthcoming in the Fall and potentially will have an update with additional data in 2023

AMINOGLYCOSIDE DISK:MIC (PRESENTED AT PLENARY 4)

- Proposed Breakpoints:

Organism	Antimicrobial	S	I	R	Errors (VME/ME/mE)
Enterobacterales	Gentamicin	≥18	15-17	≤14	0% / 0% / 2.7%
Enterobacterales	Tobramycin	≥17	13-16	≤12	0% / 0% / 4.5%
Enterobacterales	Amikacin	≥19	16-18	≤15	0% / 0% / 6.1%
Ps. aeruginosa	Tobramycin	≥19	13-18	≤12	0% / 0% / 2.8%

SC DISCUSSION (MAIN POINTS)

- Concern with data not presented in the agenda book and having time to review. Vote will be done today and revoted on prior to the January meeting.
- Question about how often routine statistics and how often error rate bound method is used. Error rate bound method is acceptable and often used.

A motion to approve tobramycin disk BPs for *Pseudomonas aeruginosa* (S≥19, I 13-18, R≤12) with future review was made and seconded. Vote: 11 for, 0 against, 1 abstain, 1 absent (Pass)

A motion to approve tobramycin disk BPs for Enterobacterales (S≥17, I 13-16, R≤12) with future review was made and seconded. Vote: 11 for, 0 against, 1 abstain, 1 absent (Pass)

	A motion to approve gentamicin disk BPs for Enterobacterales (S≥18, I 15-17, R≤14) with future review was made and seconded. Vote: 11 for, 0 against, 1 abstain, 1 absent (Pass)
	A motion to approve amikacin disk BPs for Enterobacterales (S≥19, I 16-18, R≤15) with future review was made and seconded. Vote: 11 for, 0 against, 1 abstain, 1 absent (Pass)

3. **QUALITY CONTROL WG (QCWG) REPORT (S. CULLEN)**

CLSI TIER 2 QC

CEFTIBUTEN-LEDABORBACTAM DISK QC

- Information:

Drug: Ceftibuten-ledaborbactam (formerly ceftibuten/VNRX-5236) 5/2.5 µg disk per CLSI M23S (2020) and CLSI/EUCAST WG	**Abbreviation (Glossary II & III)**: CLB (ceftibuten-ledaborbactam) 5/2.5 µg disks	**Previous ID**: NA
Solvent (Table 6A): Ceftibuten: Phosphate buffer pH 8.0 0.1 M, Ledaborbactam: sterile distilled water (previously established Jan, 2021)	**Diluent (Table 6A):** Ceftibuten: Phosphate buffer pH 8.0 0.1 M, Ledaborbactam: sterile distilled water	**Preparation(Table 6C combination agents):** Proposed addition: Ceftibuten-ledaborbactam. Prepare same as aztreonam-avibactam. (previously established Jan, 2021)
Route of administration (Glossary II): Oral	**Class (Glossary I & II):** β-lactam combination agents	**Subclass (Glossary I & II):** NA
Study Report by: JMI	**Pharma Co**: Venatorx	**Control Drug**: meropenem/vaborbactam, ceftibuten, cefepime

Additional Information (M23 requirements)	• **Tier 1 Impact Assessment** (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): • No significant issues, previously reported (Jan, 2021) • **Equivalency of agar dilution to broth dilution**: Yes, previously reported (Jan, 2021) • **ISO/TS 16782 assessment of Tier 2 study materials**: Confirmed
Footnotes:	• **Recommendations for Troubleshooting Guide (Table 4D Disk or 5G MIC):** No additional footnotes needed.
Discussion	• Study included 3 lots of Mueller-Hinton from 2 manufacturers (Remel, Hardy) and 2 disk manufacturers (Oxoid, MAST). Data from 2 other media manufacturers (BBL, Teknova) shared verbally from Disk mass studies and all were within the proposed ranges (no footnote regarding limited media data is proposed) -Refer to January 2020 MGDWG • Ceftibuten disks from 2 manufacturers (Liofilchem, Bio-Rad). • When making a 1.28 mg/mL stock, solution was still cloudy using 10% or 100% DMSO as solvent. Using 0.1 M pH 8.0 phosphate buffer, occasional flecks disappeared when sonicated. Recommend removing DMSO as solvent for ceftibuten. • Only publish QC range for *E. coli* NCTC 13353 in QC tables. Others don't adequately QC this beta lactamase inhibitor but may be useful for future compounds.

- Proposed QC:

Drug Name:	Ceftibuten-ledaborbactam (formerly Ceftibuten/VNRX-5236) 5/2.5 µg disk – CLB	**Votes:**	(For, Against, Absent, Abstain) 10/0/3/1 Approved all ranges. Only publish *E. coli* NCTC 13353 in tables

QC Strain	Range	% In	Median	mm	Media	Disk	Labs	Gavan	Range Finder	Comments
E. coli **ATCC 25922** (page 7)	27-33	99.8%	30	7	3@30	2@30	1@28,29 6@30 1@31	27-33, 7mm, 99.8%	27-33, 7mm, 99.8%	Ceftibuten range 27-35
E. coli **NCTC 13353** (page 10)	24-29	99.8%	26	6	2@26, 1@27	2@26	1@25 5@26 2@27 1@28	24-28, 5 mm, 96.7%	24-29, 6 mm, 99.8%	Some media and lab variability Routine QC strain: no overlap Ceftibuten range 15-23
K. pneumoniae **ATCC 700603** (page 13)	23-28	97.6%	25	6	2@25, 1@26	1@25 1@26	4@25 3@26 2@27	23-27, 5 mm, 92.6%	23-28, 6 mm, 97.6%	Some media, disk and lab variability. Lab D larger zones but not outlier. Ceftibuten range 24-32
K. pneumoniae **ATCC BAA-1705** (page 16)	20-27	100%	23	8	3@23	2@23	3@22 2@23 1@24,25 2@26	21-25, 5 mm, 83.7%	20-27, 8 mm, 100%	Large lab variability Lab D, G mode outliers. Only 1 result @20 Ceftibuten range 17-28
K. pneumoniae **ATCC BAA-2814** (page 19)	15-20	99.6%	17	6	3@17	2@17	1@16 5@17 1@18 2@19	15-19 5 mm 98.1%	15-20 6 mm 99.6%	Some lab variability Ceftibuten range 14-22

A motion to approve ceftibuten-ledaborbactam disk QC ranges for *E.coli* ATCC 25922, *E.coli* NCTC 13353, *K. pneumoniae* ATCC 700603, *K. pneumoniae* ATCC BAA-1705, and *K. pneumoniae* ATCC BAA-2814 and only publish *E.coli* NCTC 13353 QC ranges (24-29 mm) was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass). Note: See additional discussion from Plenary #4: QC range for ceftibuten-ledaborbactam *E. coli* ATCC® 25922 (0.03/4 -0.12/4 µg/mL) in Table 5A-2 will be deleted for consistency.

CEFTIBUTEN DISK QC

- Proposed QC:

Drug Name:	Ceftibuten 30 µg disk	**Votes:**	(For, Against, Absent, Abstain) 10/0/3/1 Approved all ranges. Only publish *E. coli* NCTC 13353 in Table 4A-2.Highlight for QC Integrity.

QC Strain	Range	% In	Median	mm	Media	Disk	Labs	Gavan	Range Finder	Comments
E. coli **ATCC 25922** (page 23)	27-35	98.9	32	9	3@32	1@31, 1@33	1@29, 31 4@32 1@32.5 2@33			Large disk and lab variability Current range 27-35
E. coli **NCTC 13353** (page 26)	15-23	95.7%	19	9	1@18 1@19 1@20	1@18, 1@20	2@17, 18 1@19 4@21	15-23 9 mm 95.7%	14-24 11 mm 99.3%	Large disk, lab, media variability Lab E, F mode outliers
K. pneumoniae **ATCC 700603** (page 29)	24-32	98.1%	28	9	3@28	1@27 1@29	4@27 1@27.5, 28, 28.5 2@30	24-32 9 mm 98.1	24-32 9 mm 98.1	Large disk, lab variability Labs A, C, I mode outliers
K. pneumoniae **ATCC BAA-1705** (page 32)	17-28	100%	22	12	3@22	1@20 1@23.5	1@20 2@20.5 1@ 21, 22 2@23 1@23.5, 25	18-26 9 mm 93.9%	17-28 12 mm 100%	Large disk, lab variability Labs D, G, H mode outliers Note shaded area for range doesn't include 17 – no results @17
K. pneumoniae **ATCC BAA-2814** (page 35)	14-22	100%	18	9	3@18	1@16 1@20	1@16, 3@17.5 1@18 2@18.5 1@19, 19.5	14-22 9 mm 99.8%	14-22 9 mm 99.8%	Large disk, lab variability Lab B, C, E, G, I mode outliers

Observed differences in zones between disk manufacturers, but only used for QC integrity and ranges cover data for both disks.

SC DISCUSSION (MAIN POINTS)

- Question if NCTC organisms were still hard to obtain. Answer is that they are easier to obtain now.

A motion to approve ceftibuten disk QC ranges for *E.coli* ATCC 25922, *E.coli* NCTC 13353, *K. pneumoniae* ATCC 700603, *K. pneumoniae* ATCC BAA-1705, and *K. pneumoniae* ATCC BAA-2814. Only publish E.coli NCTC 13353 QC ranges (15-23 mm) in Table 4A-2 and highlight for QC integrity was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

GENTAMICIN AND SPECTINOMYCIN FOR *NEISSERIA GONORRHOEAE* DISK QC

- Information:

Drug: Gentamcin and Spectinomycin (for testing GC)	**Abbreviation (Glossary II & III)**:	**Previous ID**: NA
Solvent (Table 6A): No change	**Diluent (Table 6A): No change**	**Preparation(Table 6C combination agents):** No change Per Table 4B.
Route of administration (Glossary II): NA	**Class (Glossary I & II):** NA	**Subclass (Glossary I & II): NA**
Study Report by: CDC	**Pharma Co**: NA	**Control Drug**: Spectinomycin QC range 23-29

Additional Information (M23 requirements)	• **Tier 1 Impact Assessment** (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): • No significant issues • **Equivalency of agar dilution to broth dilution**: NA (broth microdilution isn't approved method for GC). • **ISO/TS 16782 assessment of Tier 2 study materials**: NA
Footnotes:	• **Recommendations for Troubleshooting Guide (Table 4D Disk or 5G MIC):** None
Discussion	• Included 9 labs, 3 different media manufacturers and 2 different disk manufacturers per M23 • Per Table 4B: GC Agar based and 1% defined growth supplement. The use of cysteine-free growth supplement is not required for diffusion testing. • Incubation Conditions: 5% CO_2. 20-24 hours, 35˚C • Inconsistencies in Tables: Table 4B says 35˚C, Presentation Methods overview says 36 +/-1˚C, Table 2 says 36 +/- 1˚C (do not exceed 37˚C). o Recommend to Text and Tables to revise Table 4B to be consistent with Table 2. • Discussed potential to reassess Spectinomycin QC range, however this is not frequently tested and issues appear to be media related. Add to Tier 3 list to monitor/reassess if needed.

- Proposed QC:

Drug Name:	Gentamycin for testing GC Note: No EUCAST QC ranges	**Votes:**	(For, Against, Absent, Abstain) 11/0/3/0 for gentamicin No Change for Spectinomycin at this time

N. gonorrhoeae ATCC 49226	Range	% In	Median	mm	Media Median	Disk Median	Labs Median	Gavan	Range Finder	Comments
Gentamcin 10 µg disks	15-20	99.2%	18	6mm	17.5	2@18,	3@17, 5@18, 1@20 (Lab 8 median outlier)	16-20, 5mm, 94.4% 16-19, 4 mm, 95.2% w/o Lab 8	15-21, 7mm, 97.8% 15-20, 6 mm, 99.2% w/o Lab 8	Media lot 1: wider spread and 5.6% out (mostly high). Lab 8 had 8 out of range (high). Lab 8 colony counts were lowest and widest range. Exclude Lab 8 due to outliers (median for gentamicin, mean and mode for control drug) Note: agar dilution range 4-16
Spectinomycin 100 µg disks	23-29 current range	79.9% w/Lab 8 87.5% w/o Lab 8 96.7% with range 23-30 w/o Lab 8		6						Current range: 23-29 Control drug (one disk Mfg, 3 media lots) Outliers: Lab 8 median and mode. Lab 5 mode. 62 results out with current range and all labs. 9.7% (26) out at 30mm. 10% (27) out with Lab 8. Media lot 3: 10.8% out high (26) Add to Tier 3 list.

A motion to approve gentamicin disk QC range for *N. gonorrhoeae* ATCC 49226 (15-20 mm) was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

CLSI TIER 3 QC MIC

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern	Reported
K. pneumoniae ATCC BAA-1705	Imipenem/ relebactam	0.03/4-0.25/4	Request data.	Results at high end with one lab Dec 2021: Added 1 lab with limited 2021 data. Only 2% out high @ 0.5/4 µg/ml for all Tier 3 (n=1147 results).	19-Jan
S. pneumoniae ATCC 49619	Levofloxacin	0.5-2	Request data, consider expanding to include 0.25	Mode 0.5 USCAST data (86% of 1,520). Tier 3: 120 results, mode 0.5, 4% out at 0.25. Dec 2021: no new data	18-Jan
E. coli ATCC 25922	Aztreonam/ avibactam	0.03/4-0.12/4	Request data	Additional data from only 1 lab (multiple years). Tier 3 bimodal 0.06/4-0./12/4, with 5% out high Dec 2021: added data but still only 2 labs	Jun-21
K. pneumoniae ATCC 700603	Pip/Tazo	8/4-32/4	Request feedback	Tier 2 data. Report from 3 labs. Limited data, one lab with mode at low end of range, one lab bimodal, other lab and Tier 2 with mode in middle. June 2022: data from one additional lab added	Jun-21
K. pneumoniae ATCC 700603	Ampicillin/ sulbactam	8/4-32/16	Request data	Tier 3: 2% out high, mode 8/4 with 78% shoulder at 16/4 Dec 2021: data from one additional lab	Jun-21
S. aureus ATCC 29213	Exebacase	0.25-2	Request feedback	According to sponsor, additional media data suggests a potential to narrow range	Jun-22

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern	Reported
E. coli ATCC 25922	Colistin	0.25-2	Request additional data	Mode at bottom of range in 2 studies (control drug for QPX9003 (1 media lot) and MRX-8 (full 3 lot study) Tier 2 control data from 2 studies plus data from 4 labs: Mode 0.5 with 51% shoulder at 1. None out low. (See excel file) Consider use for identification with proposed changes	21-Jun
P. aeruginosa ATCC 27853	Colistin	0.5-4	Request additional data	Mode at bottom of range in 2 studies (control drug for QPX9003 (1 media lot) and MRX-8 (full 3 lot study) Tier 2 control data from 2 studies plus data from 4 labs: Mode 1 with 46% shoulder at 0.5. None out low. (See excel file). Consider use for identification with proposed changes	21-Jun

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern	Reported
E. faecalis ATCC 29212	Amikacin	64-256	Monitor-request feedback	CDC reported out low when testing gram-neg. panels, other strains in range. Dec 2021: no new data	18-Jan
S. aureus ATCC 29213	Rifampin	0.004 to 0.016	Monitor-request feedback	One report of *S. aureus* out low Dec 2021: no new data	19-Dec
E. coli ATCC 25922	Pip/Tazo	1/4 – 4/4	QCWG 8 yes, 2 no, 3 absent, 1 abstain – expand to 1/4 - 8/4 Comments: Mode and shoulder support range change although <5% out of range. Only used as QC integrity strain. Piperacillin should have same range, but not frequently tested.	Control drug in Ceftibuten/ledaborbactam (formerly VNRX-5236) Tier 2 Jan 21, results from 3 other labs Mode at 4/4 µg/ml (2 media lots) at top of range. 4% out high at 8/4; remaining labs with mode in middle of range June 2022: data from one additional lab EUCAST range 1/4 – 4/4 with target 2/4. Piperacillin QC range 1-4	Jan-21
S. aureus ATCC 29213	Ciprofloxacin	0.12-0.5	Monitor/request feedback	"bi-modal" MIC distribution noted from three studies. Consider revising range to 0.12-1. (Table 3-28). Refer to USCAST Quinolone report V1.2. Dec 2021: no new data	18-Jan

PIPERACILLIN-TAZOBACTAM *E.COLI* MIC QC

- Information:
  - Tier 3 data is more than sufficient: 657 total results from 12 labs and multiple days, multiple media
  - Shoulder (71%) at 4/4 support range change although <5% out of range
  - Only used as QC integrity strain
  - Piperacillin should have same range (currently 1-4), but not frequently tested
- Proposed QC: Expand the piperacillin-tazobactam *E.coli* ATCC 25922 MIC QC range from 1/4 - 4/4 to 1/4 - 8/4 and have a piperacillin MIC QC range of 1-4.

A motion to approve piperacillin-tazobactam MIC QC range of 1/4 - 8/4 and piperacillin 1-4 **for *E. coli* ATCC 25922 was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)**

CLSI TIER 3 QC DISK DIFFUSION

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recmd	Concern	Update	Date Reported
S. aureus ATCC 25923	Ciprofloxacin 5 µg Levofloxacin 5 µg Moxifloxacin 5 µg Ofloxacin 5 µg Norfloxacin 10 µg	22-30 25-30 28-35 24-28 17-28	Request data. Potentially revise range or harmonize reading instructions with EUCAST	Fuzzy zone edges results in too small zones (also observed for S. aureus ATCC 29213).	June 2022: Additional data added, but all data from BD. Small zones for one data set.	May-21
P. aeruginosa ATCC 27853	Cefiderocol 30 µg	22-31	Collect additional data, preferably from non-European labs. Potentially revise to 23-29 or 23-30. No change now. Review Jan 2022	Major media differences observed in M23 study, which resulted in a 10 mm range. EUCAST QC range is set to 23-29 mm. New data from European labs fit with the EUCAST range.	June 2022: Little data added. Hardy is planning media adjustments and data falls within proposed ranges. Remel Tier 3 data at high end (23-31, also verbal report some at 32 mm) compared to Tier 2 results at low end (21-28). Jan 2022 plans: Review EUCAST media/clinical isolate study, investigate and pursue troubleshooting to address results at high end. Additional Tier 2 study data available in Jan 2022 (compile plastic & media used, assay drug).	Jan-21
E. coli ATCC 25922	Minocycline 30 µg	19-25	Monitor. Collect additional data.	One lab at top of range and above range.	June 2022: No additional data.	Jan-21
N. gonorrhoeae ATCC 49226	Spectinomycin	23-29	Request feedback/data	QC study out high	Observations in Gentamicin QC study especially with one lab and media.	Jun-22

CEFIDEROCOL AND *P. AERUGINOSA* ATCC 27853 DISK QC STUDY

- Tier 2 cefiderocol QC study summary:
  - Results <23 were primarily from one Lab (Lab C)
  - All result >29 are from Media Lot C
  - No zones <23 in Tier 3 data
  - If Hardy is excluded, 95.3% in range with both 23-29 and 23-30 and would need to combine with Tier 3 data to meet M23 or add a footnote about limited media manufacturers
  - Current CLSI QC range 22-31 mm
  - EUCAST QC range 23-29 mm

Table G. Media lot, disk lot, and inter- and intra-laboratory comparisons of cefiderocol disk diffusion results versus *P. aeruginosa* ATCC 27853.

Zone	Occurrences By Media Lot			Occurrences by disk lot		Laboratory Code (Occurrences)								Total N
(mm)	A	B	C	A	B	A	B	C	D	E	F	H	I	
19														0
20		4		1	3			4						4
21	4	9		8	5	1		12						13
22	4	7		5	6			9					2	11
23	8	22	2	18	14	1		11		3			17	32
24	13	41	4	27	31	6	7	9	1	12	13	3	7	58
25	29	65	10	56	48	19	13	11	16	4	10	18	13	104
26	45	11	1	23	34	7	7	1	12	13	4	12	1	57
27	42	1	3	27	19	5	13	3	3	8	7	7		46
28	14		21	17	18	5			9		5	2	14	35
29	1		35	17	19	6	7		1	3	7	7	5	36
30			62	31	31	10	13		11	7	9	11	1	62
31			21	9	12				7	9	5			21
32			1	1						1				1
33														0
Total	160	160	160	240	240	60	60	60	60	60	60	60	60	480
Median	26	24	30	26	26	26	27	23	27	26	27	26	25	26
Mode	26	25	30	25	25	25	27	21	25	26	24	25	23	25
GeoMean	25.7	24.0	29.0	26.1	26.2	26.5	26.9	22.9	27.3	26.9	26.9	26.8	25.2	26.1
Range	9	8	10	13	12	10	7	8	8	10	8	7	9	

*Laboratory G was excluded because QC was out of range.

Gavan Statistic	
All lab median	26
Median of ranges {MR}	8
1/2 MR rounded up {R}	4
All lab median +/- R	22-30

Summary	Range (mm)	Size of Range	% in range	
Gavan Statistic	22-30	9	96.5	(463/480)
Rangefinder	21-32	12	99.2	(476/480)
Proposed Range:	22-30	9	96.5	(463/480)

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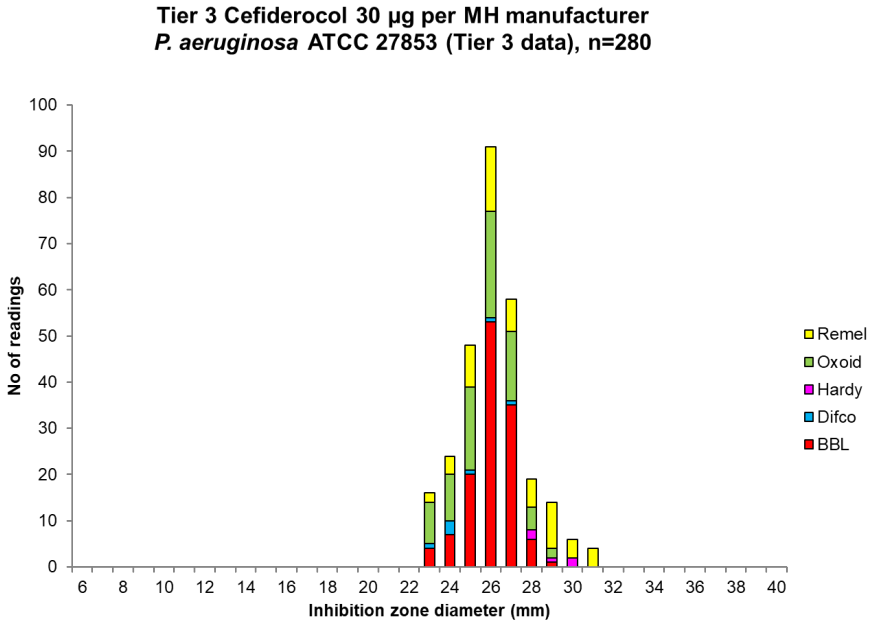
- Tier 3 cefiderocol study summary:
  - 280 total results, 14 labs, 5 media manufacturers
  - No results <23mm
  - Hardy results (n=11) at high end but none >30.
  - Additional Hardy data (next slides) - adjusted media in range
  - Small number of Remel results at 31 (one lab also verbally indicated additional data with some at 32). Original Tier 2 data 22-29. Investigate shift and results at high end.



- Summary:
  - Potential to revise from 22-31 (10mm) to either
    - 23-30, 8mm, (98.6% Tier 3, 89.6% Tier 2)
    - 23-29, 9mm, (96.4% Tier 3, 83.7% Tier 2), EUCAST range
- Tier 3 additional Hardy data cefiderocol:
  - Current media 29-32
  - Adjusted media 24-28 (all within proposed ranges)
  - All indicator drugs per ISO/TS 16782 within range
  - Small operator variability (within 1-2 mm)

COLISTIN QC FOLLOW UP

- Summary:
  - CLSI QC ranges were updated in January 2022 for *E. coli* NCTC 13486 and *E. coli* ATCC BAA-3170 (AR Bank #0349) both of which are mcr-1 strains.
  - Additional discussion points/follow up
    - Potentially add to troubleshooting guide and/or preparation of materials. – Addressed in Troubleshooting Guide and Table 5A-1 footnote

  - What do we mean by “investigate” and “occurs frequently”? What actions should be taken and when? - Addressed in Table 5A-1 footnote
  - Whether or not we should provide guidance on strains to test for routine QC. –Addressed in Table 5A-1 footnote.
  - For Table 3D, should we change “target” to “mode” to be more consistent with other CLSI QC information – Addressed in Table 3D
- Suggested improvements to CLSI M07
  - Comment about 3 or 4 dilution QC ranges and need to observe for trending with 4 dilution range
  - Reference MIC method QC versus QC of other commercial methods
  - Strains for routine QC versus supplemental QC
  - Recommend including supplemental QC strains for production lots of MIC reference panels

- Proposed Table 5A-1 Footnote Revisions:
  - New footnote: Colistin results are significantly impacted by preparation and handling of testing materials including stock solutions, test medium, composition of testing tube/plate (eg, glass, polystyrene, polypropylene). QC results may fall outside the established CLSI QC ranges if methods other than CLSI reference methods described in M07 and M100 are used.
  - Revised footnote h: *P. aeruginosa* ATCC 27853 is recommended for routine QC. *E. coli* ATCC 25922 is provided as a supplemental QC strain. Additional ranges for colistin are also provided as supplemental QC (eg, confirm quality of production lots, validation studies).

	MIC QC ranges µg/mL	Mode µg/mL	Comments
E. coli NCTC 13486	1-8	2-4	Results of 1 µg/mL or 8 µg/mL were infrequent (<5%) during Tier 2 studies to establish colistin QC ranges. Investigate if MIC results trend at the low or high end of the range (1 µg/mL or 8 µg/mL). See Troubleshooting Guide.
E. coli ATCC BAA-3170	1-4	2	

- Proposed Table 3D Colistin QC Revisions:
  - Change “target” to “mode” to be more consistent with other CLSI QC information.
  - January 2022: Request feedback on QC data from users of BDE and agar screen.
    - Consider editing ≤1 to >4 (nothing would be out of range with dilutions tested) to 1 to 4 for E. coli ATCC BAA 3170. Alternatively provide additional guidance if frequent results at either edge of range.
    - Consider *E. coli* BAA 3170 for lot/shipment and *P. aeruginosa* ATCC 27853 for routine QC.
- Propoosed Table 5G Troubleshooting Guide: Colistin MIC:

Antimicrobial Agent	QC Strains	Observation	Probable Cause	Comments/Suggested Actions
Colistin [a]	*E. coli* ATCC® 25922 *P. aeruginosa* ATCC® 27853 *E. coli* NCTC 13486 *E. coli* ATCC® BAA-3170™	MIC too high	Inadequate concentration of drug available in test medium due to drug adherence to surfaces (e.g., tubes, plates).	Check composition of containers (e.g., tubes, plates) used for production of test reagents and performance of MIC tests. Use tubes/plates made of untreated polystyrene. Prepare colistin stock solution on the day of use in production of tubes or panels for MIC testing. Use only the sulphate salts of polymyxins; the methanesulfonate derivative of colistin must not be used (it is an inactive pro-drug that breaks down slowly in solution).
Colistin [a]	*E. coli* ATCC® 25922 *P. aeruginosa* ATCC® 27853 *E. coli* NCTC 13486 *E. coli* ATCC® BAA-3170™	MIC too low	Surfactant added to test broth or inoculum diluent	Check to ensure surfactant (e.g., polysorbate-80) was not added to test medium or inoculum diluent.

[a]Colistin results are significantly impacted by preparation and handling of reagents / testing materials including stock solutions, test medium, composition of testing tube/plate (e.g., glass, polystyrene, polypropylene), etc. QC results may fall outside the established CLSI QC ranges if methods other than CLSI reference methods described in M07 and M100 are used.

SC DISCUSSION (MAIN POINTS)

- Clarification that with a single organism, *P. aeruginosa*, recommended for QC that would also be available to do weekly QC after the verification (3 by 5 or 20 to 30 days) for single QC organism for that drug combination. This is correct.
- Concerns about 5% trending comment. Do not need to worry until a higher percentage. 5% was added to address infrequent and what infrequent means. It is based on the Tier 2 studies.
- Suggestion to remove last two sentences in comment. Not an issue since it is supplemental and not routine. Keep only "Results of 1 ug/ml or 8 ug/ml were infrequent (<5% during Tier 2 studies to establish colistin QC ranges" and remove the remaining sentences. AST SC agreed to keep the comment as originally proposed by the QCWG and not remove the sentences.

A motion to approve proposed Table 5A-1 colistin MIC QC range footnote revisions, Table 5G Troubleshooting Guide additions for colistin and Table 3D colistin QC revisions (change "target" to "mode") was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

TROUBLESHOOTING GUIDE ADDITIONS TO QC ORGANISM MAINTENANCE

- Proposed Revisions

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
Carbenicillin	*P aeruginosa* ATCC 27853	MIC too high	QC strain develops resistance after repeated subculture	See general comment (1) on QC organism maintenance. Prepare new F1 subculture every two weeks
Ceftriaxone	*P aeruginosa* ATCC 27853	MIC too high	QC strain develops resistance after repeated subculture	See general comment (1) on QC organism maintenance. Prepare new F1 subculture every two weeks
ALL Agents				
Various	*S. pneumoniae* ATCC 49619	MIC too low Light growth	Inoculum source plate too old and contains too many nonviable cells. ~~Plate used to prepare inoculum should be incubated 18-20 hours~~	See general comment (1) on QC organism maintenance. Prepare new F1 subculture every two weeks to prevent loss of viability. Subculture QC strain and repeat QC, or retrieve new QC strain from stock. Plate used to prepare inoculum should be incubated 18-20 hours.
Various	*E. faecalis* ATCC 51299	MIC too low	QC strain loses resistance after repeated subculture	See general comment (1) on QC organism maintenance. Prepare new F1 subculture every two weeks to prevent loss of viability

A motion to approve proposed Troubleshooting Guide additions for QC organism maintenance was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

CUSTOMER SERVICE QUESTIONS

- Why there are no QC strains listed in the "QC recommendations – lot shipment" for disk diffusion?
- Does footnote imply that positive/growth QC strain should be tested for both MIC and disk diffusion D-zone test?
- Note: Negative/no growth is listed as routine for many Table 3 tests, with positive/growth added for lot/shipment
- There are no disk QC zones for BAA-976 and BAA-977 for erythromycin and clindamycin, although both usually no zone (6 mm).
- Conclusion: Additional disk diffusion QC is not needed since disks are already tested for routine disk diffusion.

- Proposed Revision to Table 3I, add to Disk Diffusion column in QC recommendations-lot/shipment row: Perform QC according to standard disk diffusion QC procedures per M02 (eg, daily or weekly)

Table 3I. (Continued)

Test	ICR			
Test method	**Disk Diffusion (D-zone test)**		**Broth Microdilution**	
Organism group (applies only to organisms resistant to erythromycin and susceptible or intermediate to clindamycin)	All *Staphylococcus* spp.	*S. pneumoniae* and β-hemolytic *Streptococcus* spp.	All *Staphylococcus* spp.[c]	*S. pneumoniae* and β-hemolytic *Streptococcus* spp.
Additional testing and reporting	Report isolates with ICR as "clindamycin resistant." The following comment may be included with the report: "This isolate is presumed to be resistant based on detection of ICR, as determined by testing clindamycin in combination with erythromycin."			
QC recommendations - routine[c]	*S. aureus* ATCC®[d] 25923 for routine QC of erythromycin and clindamycin disks	*S. pneumoniae* ATCC® 49619 for routine QC of erythromycin and clindamycin disks	*S. aureus* ATCC® BAA-976™ or *S. aureus* ATCC® 29213 - no growth	*S. pneumoniae* ATCC® 49619 or *S. aureus* ATCC® BAA-976™ - no growth
QC recommendations - lot/shipment[e]	Perform QC according to standard disk diffusion QC procedures per M02 (e.g., daily or weekly)		*S. aureus* ATCC® BAA-977™ - growth	
QC recommendations - supplemental[f]	*S. aureus* ATCC® BAA-976™ (D-zone test negative) *S. aureus* ATCC® BAA-977™ (D-zone test positive) Use of unsupplemented MHA is acceptable for these strains.		*S. aureus* ATCC® BAA-976™ (no growth) *S. aureus* ATCC® BAA-977™ (growth)	

A motion to approve proposed revision to Table 3I for QC recommendations - in row for lot/shipment for disk diffusion to indicate "Perform QC according to standard disk diffusion QC procedures per M02 (eg, daily, weekly)" **was made and seconded. Vote: 12 for, 0 against, 1 abstain, 0 absent (Pass)**

ROUTINE/STREAMLINED QC (INFORMATIONAL ONLY)

- Define members of Ad Hoc group and kick off meetings 2022. Susie Sharp to co-lead.
- Questions regarding Table 2s QC recommendations to be addressed in future meetings
- Questions regarding Table 4A-2 and 5A-2 for combination beta lactams
  - Explore options to streamline
  - Address confusion about testing strains not listed as "routine QC". Potential issue if user assumes drug potency is OK when other QC strains are "in range" but these strains don't assess potency of the beta lactamase inhibitor.
- See Additional Information/Back Up slides from troubleshooting guides

ADDITIONAL QC NOTIFICATIONS (PRESENTED AT PLENARY 4)

- Tedizolid Disk QC Range
  - S. aureus 25923 transmitted light range is 18-24 mm
  - S. aureus 25923 reflected light range is 18-25 or 19-25 mm
  - Greater than the needed 95%. No issues with tedizolid reflected light method with QC.
  - Will review linezolid data.

	• Ceftibuten-ledaborbactam Disk Clarification – Only approved to published *E. coli* NCTC 13353 disk ranges and not to publish *E. coli* ATCC 25922 disk ranges. – *E. coli* ATCC 25922 MIC ranges as well as MIC QC ranges for ceftibuten-ledaborbactam against *E. coli* NCTC 13353, *K. pneumoniae* ATCC® BAA-1705, and *K. pneumoniae* ATCC® BAA-2814) were approved previously (Winter 2021). – Request to not publish *E. coli* ATCC 25922 MIC ranges for ceftibuten-ledaborbactam since not publishing disk ranges to avoid confusion. Request granted by AST SC. – *E. coli* ATCC 25922 is not a routine QC strain for either broth microdilution or disk diffusion.

4. **METHODS APPLICATION AND INTERPRETATION WG (MAIWG) REPORT (T.KIRN)**

MDRO GUIDANCE IN M100

- CLSI and IDSA treatment guidance for MDRO do not align.
  - CLSI: Apply current breakpoints and report MIC as tested. Testing to define mechanisms of resistance can be performed for epidemiologic or infection control purposes only.
  - IDSA: Treatment guidance based on whether mechanism testing is performed or not. Recommended treatment will differ based on the mechanisms mediating resistance.
- NEW CAP Checklist Item Addressing the Application of Updated Breakpoints
  - CLSI and CAP in agreement that labs should apply updated breakpoints.
  - CLSI still references outdated (2010) cephalosporin and carbapenem breakpoints in current M100-S32 document and provides guidance to labs on how to handle testing and reporting when applying outdated breakpoints.

SC DISCUSSION (MAIN POINTS)

- Concern that laboratories do not have a good way to test for ESBL and adds extra work to laboratories.
- Question if removal will affect pip-tazo guidance. The only comment made in the latest version is that routine ESBL testing is not performed by most clinical microbiology laboratories. Agreement that the phenotypic testing is not great.
- Genotypic methods are common especially for blood cultures.
- Concerns with laboratories thinking it is ok to report ESBL tests from commercial assays that can often times be erroneous.

A motion to remove referral to M100 S20 was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

ESBL TESTING

- Proposed Enterobacterales and Cephem Comment: When using current breakpoints, routine ESBL testing is not necessary before reporting results. However, in consultation with the antimicrobial stewardship team and infection prevention committee, laboratories may decide to perform phenotypic or genotypic testing for ESBLs and the results may be used to guide therapeutic management or for epidemiological or infection prevention purposes. Limitations of phenotypic and genotypic methods must be considered (see Table 3A introduction). [ref: IDSA guidance] Removal of "For laboratories that have not implemented the current breakpoints, ESBL testing should be performed as described in the archived M100 S20 document Table 3A."
- Proposed Table 3A Introduction: Following evaluation of PK/PD properties, limited clinical data, and MIC distributions, revised breakpoints for cefazolin, cefotaxime, ceftazidime, ceftizoxime, ceftriaxone, and aztreonam were published in January 2010 (M100-S20) and are listed in Table 2A. Cefuroxime (parenteral) was also evaluated; however, no change in breakpoints was necessary with the dosage. When using the current breakpoints, routine ESBL testing is not necessary before reporting results. If ESBL testing is performed at your institution the results may be used to guide therapeutic management, or for epidemiological or infection prevention purposes.

  Certain phenotypic ESBL tests have known limitations that impact sensitivity (eg, false-negatives due to the co-production of an AmpC ß-lactamase) and specificity (e.g., false-positivity due to hyperproduction of narrower-spectrum ß-lactamases combined with altered permeability). Genotypic methods are limited by the targets included in the assay (eg, most FDA-cleared ESBL assays only target bla_{CTX-M}). Limitations of phenotypic and genotypic methods must be considered.

SC DISCUSSION (MAIN POINTS)

- Suggestion to remove the first sentence referencing M100 S20 in the Table 3A introduction.
- Suggestion to remove ESBL testing and Table 3A. Concern with removing is that some laboratories are testing and reporting results in some cases for therapeutic decisions.
- Further concerns with using ESBL results from commercial devices.
- Comments will be reviewed and revised by the MAIWG.

INDUCIBLE AMPC COMMENT

- Current Table 2A comment: *Enterobacter*, *Klebsiella* (formally *Enterobacter*) *aerogenes*, *Citrobacter*, and *Serratia* may develop resistance during prolonged therapy with 3rd-generation cephalosporins as a result of derepression of AmpC B-lactamase. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing repeat isolates may be warranted.
- Proposed Table 2A comment: Some Enterobacterales may develop resistance during therapy with 3rd generation cephalosporins as a result of derepression of AmpC beta-lactamase. This is most commonly seen with *Enterobacter cloacae* complex, *Klebsiella aerogenes*, and *Citrobacter freundii*. Isolates that are initially susceptible may become resistant within a few days after initiation of therapy. Testing subsequent isolates may be warranted if clinically indicated. The approach to reporting AST results for these organisms should be determined in consultation with ASP. See Table 1A footnote e. [ref: IDSA guidance]
- Table 1A footnote e: *Citrobacter freundii* complex, *Enterobacter cloacae* complex, *Hafnia alvei, Klebsiella* (formerly *Enterobacter) aerogenes*, *Morganella morganii, Providencia* species, *Serratia marcescens*, and *Yersinia enterocolitica* may test susceptible to ceftriaxone, cefotaxime, ceftazidime, ceftaroline and piperacillin-tazobactam but these agents may be ineffective against these genera due to derepression of inducible AmpC beta-lactamase. The risk of AmpC derepression during therapy is moderate to high with *E. cloacae, C. freundii* and *K. aerogenes* and appears to less frequent with *M. morganii, Providencia* species and *S. marcescens* (IDSA Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections: Version 2.0).

SC DISCUSSION (MAIN POINTS)

- Concern with not including all the organisms and drugs listed in the Table 1A footnote in the Table 2A footnote.
- Suggestion to not use the term "3rd generation cephalosporins".
- Question about retesting. It is guidance to laboratories to make sure the same organism is being recovered. The comment states that isolates may become resistant within a few days.
- Suggestion to readd the number of days for resistance after therapy. Issue was coming up with an accurate time frame. Suggestion to add "testing subsequent isolates is warranted" instead of a time frame. Suggestion to state "resistance may develop in little as one day".
- Concern that this implies that the laboratory will need to check which agents the patient is receiving before retesting.
- New proposed comment: Table 1A e footnote with "Therefore, isolates that are initially susceptible may become resistant. Testing repeat isolates may be warranted."

A motion to approve a Table 2A inducible AmpC comment with Table 1A footnote and new proposed retesting statement was made and seconded. Vote: 10 for, 2 against, 0 abstain, 1 absent (Pass)

Against Vote Reasoning:

- Prefer the original MAIWG proposed comment.
- Want to provide a time frame for the laboratories for retesting.

ENTEROBACTERALES AND CARBAPENEMS COMMENTS

- Current Table 2A comment: Laboratories using Enterobacterales MIC breakpoints for carbapenems described in M100-S20 (January 2010) should perform the CarbaNP test, mCIM, eCIM, and/or a molecular assay (refer to Tables 3B and 3C for methods) when isolates of Enterobacterales are suspicious for carbapenemase production based on imipenem or meropenem MICs 2–4 µg/mL or ertapenem MIC 2 µg/mL (refer to Tables 3B-1 and 3C-1 for guidance on reporting). After implementing the current breakpoints, these additional tests may not need to be performed other than for epidemiological or infection prevention purposes (ie, it is no longer necessary to edit results for the carbapenems to resistant if a carbapenemase producer is detected). See Appendix H, Table H3 regarding suggestions for reporting when molecular and phenotypic methods are discordant.
- Proposed Table 2A comment: Institutional treatment guidelines, infection prevention procedures or epidemiological investigations may necessitate identification of carbapenemase-producing Enterobacterales. Isolates with elevated carbapenem MICs (intermediate or resistant) can be tested for carbapenemase-production by a phenotypic and/or a molecular assay (refer to Tables 3B and 3C for methods). See Appendix H, Table H3 regarding suggestions for reporting when mechanism of resistance-based testing (molecular and phenotypic methods) are discordant with phenotypic AST.
- Current Tables 3B and 3C Introduction: Institutional infection prevention procedures or epidemiological investigations may necessitate identification of carbapenemase-producing Enterobacterales and *P. aeruginosa*. Such testing is not currently recommended for routine use.

  Laboratories using Enterobacterales MIC breakpoints for carbapenems described in M100-S20 (January 2010) should perform the CarbaNP test, mCIM, eCIM, and/or a molecular assay when isolates of Enterobacterales are suspicious for carbapenemase production based on imipenem or meropenem MICs 2–4 µg/mL or ertapenem MIC 2 µg/mL. Refer to the archived M100-S20 for reporting guidance. (refer to Tables 3B-1 and 3C-1 for guidance on reporting). After implementing the current breakpoints, these additional tests may not need to be performed other than for epidemiological or infection prevention purposes (ie, it is no longer necessary to edit results for the carbapenems to resistant if a carbapenemase producer is detected).
- Proposed Tables 3B and 3C Introduction: Institutional treatment guidelines, infection prevention procedures or epidemiological investigations may necessitate identification of carbapenemase-producing Enterobacterales and *P. aeruginosa* [ref: IDSA guidance].
- Tables 3B-1 and 3C-1 will be removed. The tables below 3B for Instructions for Preparing Test Components will not be removed.

A motion to approve proposed revision to Table 2A Enterobacterales and carbapenem comment and Tables 3B and 3C introduction was made and seconded. Vote: 12 for, 0 against, 0 abstain, 1 absent (Pass)

TABLE H3 MODIFICATIONS

- Confirm Table H3 guidance and terminology is consistent
- Clarify Table H3 phenotypic is referring to AST vs mechanism of resistance testing

ANTIMICROBIAL SUSCEPTIBILITY OF *ACHROMOBACTER* SPP. (INFORMATIONAL ONLY) (PRESENTED AT PLENARY 4)

- Data presented from the NIH showed possible intrinsic resistance to aztreonam in *Achromobacter* spp.
- M45 WG and MDWG will continue work on this topic.

AZTREONAM AND CEFTAZIDIME-AVIBACTAM DISK BROTH ELUTION DATA SUMMARY (INFORMATIONAL ONLY)

- Three testing sites compared aztreonam and ceftazidime-avibactam disk broth elution (DBE) test to reference broth microdilution (BMD) aztreonam and ceftazidime-avibactam AST results.
  - Phase 1: 61 Enterobacterales from the CDC AR Bank
  - Phase 2: 147 MBL-producing Enterobacterales, *P. aeruginosa,* or *S. maltophilia* clinical isolates at each site
  - Phase 1 data analysis: Categorical agreement = 172/175 results (98.3%), Major errors = 1.8%, Very major errors = 0%
  - Phase 2 data analysis: Categorical agreement = 144/147 results (97.9%), Major errors = 2.4%, Very major errors = 0%
- Manufacturer comparison study to determine if discrepancies in DBE results dependent on the manufacturer. Various manufacturers of disks and broths evaluated in multiple permutations.
- Conclusions
  - DBE is a precise and accurate methodology to determine susceptibility to the combination ATM-CZA
  - Recommend to confirm not susceptible results by BMD method
  - Manufacturer of CZA disks and CA-MHB important for test efficacy
- Next steps
  - Complete and compile the multicenter study data
  - Define the QC studies required
  - Compare disks and broths from multiple manufacturers
  - Zinc?
  - More *P. aeruginosa* data?
  - Lot to lot comparisons

ANAEROBE AHWG REPORT (INFORMATIONAL ONLY)

The following items are in progress:

- Breakpoint discussion
  - Metronidazole MIC Data Discussion – plan to present at January 2023 meeting
- Table 1 – Removal of Imipenem/Relebactam
  - The anaerobe working group strongly recommends revisiting this item.
  - The working group feels that this is setting a bad precedent since imi/rel has indications for anaerobes.
  - Since this is a new compound with indications, would it cause confusion if it is not listed.
  - The working group feels that not being able to be listed in the Table 1 for anaerobes could discourage pharmaceutical companies to pursue anaerobe indications going forward.
- Agar dilution as a reference method
  - This was discussed at the January meeting – since agar dilution is the only reference method for most anaerobes, the working group feels strongly that agar dilution needs to be kept as a reference method.
- Request – Future M23 Anaerobe studies
  - The working group is requesting if any agar dilution M23 studies for anaerobes are being done to consider adding the following antibiotics: trimethoprim/sulfamethoxazole, doxycycline, and levofloxacin.
- Disk testing – EUCAST efforts
  - EUCAST has released a guidance document and publication of the data. These documents have been shared with the working group and will be discussed at our next teleconference this fall.

	• Antibiogram – Appendix D – Received data from several sites, now compiling to update the antibiogram. • Membership – Still looking for new members
5.	**ADJOURNMENT** Dr. Lewis thanked the participants for their attention. The meeting was adjourned at 6:00 PM Central (US) time.

2022 June AST MEETING SUMMARY MINUTES PLENARY 4: Tuesday, 28 June 2022 (In-person/Hybrid) 7:30 AM – 12:00 PM Central (US) Time	
#	**Description**
1.	**OPENING** Dr. Lewis opened the meeting at 7:30 AM Central (US) time.

2. **METHODS DEVELOPMENT AND STANDARDIZATION WG (MDSWG) REPORT (B. ZIMMER AND D. HARDY)**

***HAEMOPHILUS INFLUENZAE* ANTIMICROBIAL SUSCEPTIBILITY TESTING USING MUELLER HINTON-FASTIDIOUS MEDIA**

- Study objectives and conclusions from January 2022
  - Compare the performance of HTM and MH-F using broth microdilution (BMD) and disk diffusion (DD) for assessing *H. influenzae* susceptibility.
    - Conclusions: MICs determined in MH-F and HTM broth correlate very well for both QC organisms and clinical isolates. MICs in MH-F broth are often much easier to read than MICs in HTM. Approved with request for bias calculations for two drugs.
  - Assess the possible need for changes in the approved CLSI Quality Control (QC) ranges for the designated QC organisms on MH-F agar and MH-F broth.
    - Conclusion: Approved. The CLSI-approved MIC QC ranges for HTM are acceptable for MH-F broth.
  - Assess the potential need for guidance regarding a "substantially inhibited growth phenotype" when interpreting β-lactam MICs on *H. influenzae* BMD panels.
  - Conclusions: Approved. Recommendation for users of HTM to disregard trailing growth and where endpoints should be selected. Recommend the addition of pictures.
- Broth Microdilution: Trend Analysis for HTM vs MH-F media
  - Conclusion: Overall, there is no bias exceeding 30% (average bias at 6.6%).
    - 22/24 drug/broth comparisons had bias numbers <30%.
    - There were two cases related to a drug and one of the two brands of broth where the bias was >30% (CXM with MHF-BBL, and RIF with MHF-Difco)
    - However, the essential agreement was >90%.
  - Recommendation to add note stating: MICs obtained for cefuroxime and rifampin using MH-F broth may show a one-dilution bias towards more resistance when compared to HTM broth. The comparative study showed ≥90% essential agreement between MH-F and HTM media.

SC DISCUSSION (MAIN POINTS)

- Clarification was asked about the bias calculation. It is a simple bias calculation. Takes the percentage of results below the diagonal and subtracting the number of results above the diagonal. Divide by the total number to get the percentage and then subtract one from the other. A positive number means a higher MIC and a negative number mean a lower MIC.
- Question about where the comment will be placed. It would be placed where the MH-F broth is discussed, which is not added to M100 yet. It will probably be added in multiple places.
- The comment to be included is the recommended broth microdilution note: MICs obtained for cefuroxime and rifampin using MH-F broth may show a one-dilution bias towards more resistance when compared to HTM broth. The comparative study showed ≥90% essential agreement between MH-F and HTM media.

A motion to approve proposed Mueller Hinton-Fastidious Media (MH-F) broth comment was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

***HAEMOPHILUS INFLUENZAE* ANTIMICROBIAL SUSCEPTIBILITY TESTING USING MUELLER HINTON-FASTIDIOUS MEDIA CONTINUE**

- Disk Diffusion Results: HTM vs MH-F media
  - Disk QC Overall Summary

Hflu ATCC 49247	HTM	MHF	Comment
Ampicillin	100%	>90%	Ok, E. coli 35218 – (6mm) – some 7mm readings at CDC
Amoxicillin-clavulanate (2:1)	100%	>95%	OK
Ceftriaxone	100%	>95%; 75% at CDC with 1 media	OK, At beginning of study, reader effect
Cefuroxime	100%, 1 set 83%	Generally >90%, some sets a little less	OK, (MHF may fit better with EUCAST QC range, not examined here)
Clarithromycin	100%	>95%	OK, Excludes Hardy disk, confirmed defective by manufacturer
Levofloxacin	100%	100% JMI, INS; some sets <90% CDC	OK
Tetracycline	100%	100%	OK
Chloramphenicol	100%	<90%	Range change proposed
Trimethoprim-Sulfamethoxazole	57-100%	0-100%	Further analysis

- Chloramphenicol Disk Diffusion Results

Antimicrobial agent: Chloramphenicol			Reference Result Frequency (HTM)				MH-F Hardy				MH-F BBL				
			Hardy Disk		BBL Disk		Hardy Disk		BBL Disk		Hardy Disk		BBL Disk		
QC Organism	Acceptable Ranges	MIC	CDC*	JMI	CDC*	INS	CDC*	JMI	CDC*	INS	CDC*	JMI	CDC*	INS	
H. influenzae ATCC 49247	CLSI: 31-40 EUCAST: None	Above Range	0	0	0	0	0	0	0	0	0	0	0	0	
		In Range	20	23	20	20	13	20	15	20	16	19	16	20	
		Below Range	0	0	0	0	7	3	5	0	4	4	4	0	
		Range	32-36	32-38	33-37	31-36	27-33	30-34	28-39	31-32	26-34	30-35	28-36	31-34	
		% In	100%	100%	100%	100%	65%	87%	75%	100%	80%	83%	80%	100%	
		Shoulder	33	34	33	36	33	31	33	32	33	32	33	32	
		Mode (by lab)	34	33	36	35	32	32	32	31	31	31	34	31	
		Mode (by media)				34								31	
		Mode (Overall)													31

QC Range Finder Results: 28 – 36 mm

- Clarithromycin Disk Diffusion Results

Antimicrobial agent: Clarithromycin			Reference Result Frequency (HTM)				MH-F Hardy				MH-F BBL				
			Hardy Disk		BBL Disk		Hardy Disk		BBL Disk		Hardy Disk		BBL Disk		
QC Organism	Acceptable Ranges	MIC	CDC*	JMI	CDC*	INS	CDC*	JMI	CDC*	INS	CDC*	JMI	CDC*	INS	
H. influenzae ATCC 49247	CLSI: 11-17 EUCAST: None	Above Range	0	0	0	0	0	0	1	0	0	0	1	0	
		In Range	15	11	20	20	20	23	19	20	20	23	19	20	
		Below Range	5	12	0	0	0	0	0	0	0	0	0	0	
		Range	9-12	8-12	11-17	11-14	12-14	11-14	13-21	11-14	11-14	12-14	13-19	12-16	
		% In	75%	48%	100%	100%	100%	100%	95%	100%	100%	100%	95%	100%	
		Shoulder	12	11	14	11	13	12	14	12	13	14	14	14	
		Mode (by lab)	11	9	13	13	14	13	15	13	12	13	15	13	
		Mode (by media)				11								13	
		Mode (Overall)													13

- Recommendations: The CLSI-approved disk QC ranges with *H. influenzae* 29247 for HTM are acceptable for disk diffusion testing with MH-F medium except: Range change for Chloramphenicol with MH-F only to 28-36 mm.

SC DISCUSSION (MAIN POINTS)

- Concern with not having amoxicillin-clavulanate disk diffusion breakpoints.
- Question about the implications of changing the QC range if you are using media to media in terms of the breakpoint. There are no differences in the testing only the media. CLSI methodology was used. It would be appropriate to have a comment to indicate the media used.
- Question about the reasoning for MH-F. MH-F is recommended by EUCAST for *S. pneumoniae* and *H. influenzae*. The CLSI equivalency study was already completed for *S. pneumoniae* and the medias were equivalent. MH-F is slightly easier to read.
- Question if MH-F media is readily available in the United States. It is not. If CLSI starts approving it, it will be more readily available.
- Question if the CLSI QC ranges could be compared to EUCAST QC ranges. QC in general yes; however, EUCAST uses an additional organism and different method.

A motion to approve chloramphenicol disk QC range change (28-36 mm) and current clarithromycin disk QC range (11-17 mm) and retain the current amoxicillin-clavulanate disk QC range with MH-F Media for *Haemophilus influenzae* ATCC 49247 was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

HAEMOPHILUS INFLUENZAE ANTIMICROBIAL SUSCEPTIBILITY TESTING USING MUELLER HINTON-FASTIDIOUS MEDIA CONTINUE

- Disk Diffusion Isolate Reproducibility Summary: Consensus HTM vs MH-F

Drug	Isolates with same HTM/MH-F reference value CA	Minor Errors	Major/Very Major Errors	Isolates that could not have an HTM or MH-F Reference Value assigned
Ampicillin	92/96 (96%)	4/96 (4%)	0/96 (0%)	4/100 (4%)
Amox/Clav (old BPs)	95/97 (98%)	N/A	2/97 (2%)	3/100 (3%)
Ceftriaxone	100/100 (100%)	N/A	0/100 (0%)	0/100 (0%)
Cefuroxime	98/98 (100%)	0/98 (0%)	0/98 (0%)	2/100 (2%)
Clarithromycin*	63/65 (97%)	2/65 (3%)	0/65 (0%)	35/100 (35%)
Chloramphenicol	98/100 (98%)	2/100 (2%)	0/100 (0%)	0/100 (0%)
Levofloxacin	100/100 (100%)	0/100 (0%)	0/100 (0%)	0/100 (0%)
Tetracycline	98/99 (99%)	1/99 (1%)	0/99 (0%)	1/100 (1%)
Trim/Sulfa	99/99 (100%)	0/99 (0%)	0/99 (0%)	1/100 (1%)

*Hardy disks are excluded from the Clarithromycin analysis, as they were determined to be bad, and a new lot was not obtainable within the necessary time frame.

- Conclusions: MH-F replicated HTM results for clinical isolates very well. Four drugs were 100% in agreement. Five drugs had 95% or better agreement. Agar change requires reading plates from front vs back.
- Recommendations: To approve the disk diffusion testing equivalency shown between HTM and MH-F for ampicillin, ceftriaxone, cefuroxime, clarithromycin, chloramphenicol, levofloxacin, and tetracycline. There was no equivalency for amoxicillin-clavulanate. Since there are no current disk diffusion breakpints for amoxicillin-clavulanate, T/S was not further analyzed because of QC issues and reproducibility.

SC DISCUSSION (MAIN POINTS)

- Question if there are concerns with T/S with the disk diffusion breakpoints because of the lack of QC that works. In the study, the data was all over the place. Need to review EUCAST data.
- Concerns with not having amoxicillin-clavulanate.

A motion to approve proposed disk diffusion testing equivalency shown between HTM and MH-F for ampicillin, ceftriaxone, cefuroxime, clarithromycin, chloramphenicol, levofloxacin, and tetracycline was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

TEDIZOLID AND LINEZOLID DISK DIFFUSION AND CLSI/EUCAST HARMONIZATION

- CLSI has published MIC breakpoints for tedizolid against *S. aureus*, *Enterococcus* and Beta-Strep, but does not have disk diffusion breakpoints. CLSI does have published QC ranges for disk diffusion testing with *S. aureus* 25923.
- EUCAST published disk diffusion breakpoints for tedizolid in 2020 using reflected light.
  - *S. aureus* (S≥ 21 mm, R< 21 mm)
  - Changed in 2022 to S≥ 20 mm, R< 20 mm, with an ATU of 19 mm)
  - Enterococci (no MIC or DD breakpoints)

- *S. pneumoniae* (no MIC or DD breakpoints)
- *Streptococcus* group A, B, C and G (S≥ 18 mm, R< 18 mm)
- *S. anginosus* group (S≥ 18 mm, R< 18 mm)

- Merck reached out to JMI to generate MIC/DD correlation data to present and propose DD breakpoints to CLSI using CLSI methodology of transmitted light.
- Same tedizolid disk diffusion mass as EUCAST (2 µg).
- Four lab study with tedizolid and *S. aureus* was conducted.
- Conclusions:
  - Recommendation: Read tedizolid zones of growth inhibition using reflected light.
  - Evaluate recent data with linezolid to determine whether zones of growth inhibition should be read with reflected light rather than transmitted light.
  - Provide guidance to users regarding reading of zones of growth inhibition.
  - Potential addition of resistant QC strain
- Linezolid Issues
  - Challenges with the disk diffusion method for oxazolidinones, including linezolid, are not new and this has been presented/discussed in previous meetings.
  - Possible scenarios/solutions for linezolid to be further discussed at June 2022 meeting
    - Read zones of linezolid for *Staphylococcus* using reflected light
    - Update breakpoints of linezolid for *Staphylococcus* to include S, I and R breakpoints using recent data
  - Additional Comments:
    - Based on results for proficiency programs, the disk diffusion method does not have any issues generating/reporting results for linezolid susceptible isolates.
    - Most (>99%) Gram-positive clinical isolates are susceptible to linezolid/tedizolid.
    - Only 4.7% of labs surveyed by CAP in 2021 reported disk diffusion results for linezolid; the disk diffusion method is more likely to be used out side of the United States.

SC DISCUSSION (MAIN POINTS)

- In 2019, the QCWG reviewed transmitted light vs reflected light and did not see a large difference. Want to double check the QC data.
- Agreement that in concept standardizing the reading and not having special instructions is a positive.
- 29212 is listed in both the Troubleshooting Guide and as a footnote in the QC table that the strain can help in calibrating the reading.
- If you are reading multiple disks on a plate, there may some confusion and misreading of those zones that need to be read using reflected light.
- Question on what the rationale for reading linezolid with transmitted light. The presence of a haze or growth within the zone is more visible with transmitted light. More equipped to pick up resistant isolates with the transmitted light vs reflected light.
- Question if EUCAST suggests reflected light for linezolid and tedizolid. Answer is yes.
- Question if there is a need to redo QC ranges if the reading method is changed. Data showed that QC still fell within range using reflected light. A recommendation was made to review and confirm the QC data for the two methods. This can be confirmed after the vote.
- Suggestion to review reflected reading with linezolid. MDSWG will review the linezolid data and provide a recommendation prior to the January meeting.

A motion to approve recommendation of reading tedizolid disk diffusion zones of growth inhibition using reflected light with QC data for transmitted vs reflected light confirmation was made and seconded. Vote: 12 for, 1 against, 0 abstain, 0 absent (Pass)

Against Vote Reasoning:

- Against changing reading method for tedizolid and not linezolid.

EXEBACASE PRESENTATION

- Background
  - CF-301 (exebacase for injection) is a lysin (cell wall hydrolase) currently in Phase 3 of clinical development for the treatment of *Staphylococcus aureus* bacteremia, including right-sided infective endocarditis (ClinicalTrials.gov Identifier: NCT04160468).
  - The exebacase MIC method for *S. aureus* broth microdilution (BMD) MIC was approved by CLSI Subcommittee for AST in 2017[1] and Tier 2 QC[2] approved and subsequently published in 2020 (CLSI M100 30ed).
  - The media used for testing exebacase against *S. aureus* is cation-adjusted Mueller-Hinton broth (CAMHB) supplemented with 25% horse serum + 0.5 mM DL-dithiothreitol (CAMHB-HSD)[1].
  - Exebacase is a first-in-class, anti-staphylococcal lysin (Glossary 1 [Part 2], CLSI M100 31ed); as such it is the first lysin to be reviewed by CLSI.
  - To date extensive MIC testing to evaluate *in vitro* activity against *S. aureus* has been conducted at multiple laboratories.
  - MIC testing against other pathogens commonly causing bloodstream infection and infective endocarditis has also been conducted.
- Recommendations:
  - The Positive control (Growth control) well is the CAMHB Horse Serum (25%v/v) and 0.5 mM DTT. Recommend adding pictures and reading instructions to marked reduction of growth to M100 and M07.
  - Minor edits of media description to footnote text in to Tables 5A-1 and 6A (CAMHB with horse serum (25% v/v) and 0.5 mM DL-dithiothreitol):
    - [X]Exebacase is an enzyme that requires special handling. Thaw frozen stock solution in a 25ºC water bath, gently mix every 30 seconds until thawed (not longer than 5 minutes). Transfer the stock solution and dilutions to an ice bucket or refrigerate prior to use (within 1 hour). Discard unused stock solution. Freeze MIC panels (-60 to -80˚C) within 15 minutes of preparation.
    - [Y]CAMHB is prepared according to manufacturer's instructions. To prepare 1 liter of CAMHB-HSD, 250 mL of horse serum is added to 750 mL of CAMHB, 500 µL is removed and 500 µL of 1 M DTT is added.
  - For Streptococci, it is not necessary to add 2.5%-5% Lysed Horse Blood. Text to be added to M100 and M07.
  - Agar dilution Is not recommended for testing Exebacase susceptibility. Text to be added to M100 and M07.

SC DISCUSSION (MAIN POINTS)

- Question regarding *S. aureus* QC. As long as nothing is needed to make sure the growth supports the streps, then the ATCC 29213 would be sufficient.

A motion to approve proposed recommendations for exebacase susceptibility testing was made and seconded. Vote: 13 for, 0 against, 0 abstain, 0 absent (Pass)

OPTIMIZING BASELINE REFERENCE METHOD FOR CEFIDEROCOL AST TESTING (INFORMATIONAL ONLY)

- Study Objectives:
  - Optimize methodology for production of ID-CAMHB

- Reduce variability in depletion of Fe(III) between base MHB from major media manufacturers and inter-batch variation
- Further standardize ID-CAMHB reference for AST developers by defining parameters such as iron-binding resin, chelation period, cation supplementation
- Confirm reproducibility of MIC in optimized ID-CAMHB against isolates for which MIC has been validated through *in vivo* PK/PD studies

- Identify additional QC isolates to verify low iron levels in media
  - Identify strains with a large difference in MIC values determined in ID-CAMHB versus CAMHB

NEW ROCHE ANTIMICROBIAL AGENT RG6006 (INFORMATIONAL ONLY)

- RG6006 is a novel chemical class, pathogen-focused antibiotic. It has a narrow spectrum of activity restricted to *Acinetobacter* spp. Currently in Phase I clinical studies.
- Aberrant broth MIC readings pose a technical and interpretative challenge for RG6006.
- Following a systematic search for additives, 20% Horse serum was identified as a methodological fix for broth AST.
- MIC values obtained in CAMHB + 20% Horse serum correlate with in vivo efficacy studies (MIC obtained in CAMHB alone do not).
- Supplementing CAMHB with 20% Horse serum is suggested for RG6006 broth AST method development.

SC DISCUSSION (MAIN POINTS)

- There have been QC discussions regarding confirmation of quality of testing reagents and how to test.
- Question if horse serum concentrations (20% vs 25%) could be consistent for manufacturers. The sponsor did look at different percentages of horse serum and did not see any differences between 20% and 25%. They are open to the possibility of using 25%.
- Question if animal studies are being conducted to show correlation to PK/PD. Sponsor is looking into this.

CORRELATION OF BMD MIC WITH AGAR DISK DILUTION FOR SELECTED NONFERMENTATIVE GRAM-NEGATIVE BACILLI (INFORMATIONAL ONLY)

- Background: Prior discussions of the *ad hoc* WG on AST of NFGNB identified the following organisms currently included in Table 2B-5 as the most frequently encountered in clinical labs:
  - *Achromobacter xylosoxidans*
  - *Pseudomonas putida*
  - *Pseudomonas stutzeri*
- Purpose: Pilot study to determine correlation of BMD MICs with Agar Disk Diffusion Test results for the above organisms which are currently included in Table 2B-5.
- Organisms: Isolates were cultured from clinical specimens (preferentially sterile site specimens) submitted to UR Medicine Labs in 2019, 2020, 2021, and 2022. Isolates were identified by MALDI-TOF or 16S rRNA sequencing.
- Methods: BMD MICs were determined using CLSI M7, 11th ed. Agar Disk Diffusion was performed using CLSI M2, 13th ed. Scatterplots are analyzed with breakpoints for *Enterobacterales* and *P. aeruginosa* as in CLSI M100, 32nd ed. Representative drugs from Table 2B-5 were tested. Testing was performed at one experienced clinical laboratory by one experienced clinical microbiology technologist (UR Medicine Labs).
- Important to note that MIC breakpoints currently in Table 2B-5:
  - Pip/Tazo – same as current bkpts for *P. aeruginosa*
  - Ceftazidime - same as current bkpts for *P. aeruginosa*
  - Cefepime - same as current bkpts for *P. aeruginosa*
  - **Meropenem – do not match bkpts for *P. aeruginosa* or *Enterobacterales***

- Gentamicin – same as current bkpts for *P. aeruginosa* and *Enterobacterales*
- Doxycycline - same as current bkpts for *Enterobacterales*
- **Ciprofloxacin – do not match bkpts for *P. aeruginosa* or *Enterobacterales***
- Trim/Sulfa – same as current bkpts for *Enterobacterales*

CEFAZOLIN HIGH INOCULUM AHWG REPORT (INFORMATIONAL ONLY)

- Background
  - Cefazolin clinical failures have been reported for deep-seated methicillin susceptible *Staphylococcus aureus* (MSSA) infections, particularly infective endocarditis
  - Cefazolin failure observed in isolates with inoculum effect (CzIE)
  - Phenotype NOT detected by routine susceptibility testing
    - Gold standard assay: BMD at standard inoculum (10^5 CFU/mL) and high inoculum (10^7 CFU/mL)
    - An increase in cefazolin MIC to ≥16µg/mL with the high inoculum is considered positive for CIE
  - Availability of a rapid test for the CzIE phenotype could positivity impact treatment decisions for CzIE-positive MSSA in select clinically appropriate scenarios (i.e. high inoculum infections such as endocarditis)
  - Prevalence of CzIE was previously not well-defined in N. America
  - A rapid method for CzIE detection was published in 2021, but is not practical for most clinical laboratories
- Objectives
  - **PHASE 1:** Assess the prevalence of CzIE phenotype in MSSA isolates in contemporary US strains
  - **PHASE 2:** Evaluate a rapid CzIE assay. If assay performs well, develop CLSI guidance on testing CzIE in clinical laboratories.
    - Two methods: Optimized rapid CzIE nitrocefin test and CzlE broth disk elution screen
    - Methods and results were described.
    - Next Steps Rapid Nitrocefin Test:
      - Repeat a subset of samples with a second lot of Oxoid and BD Broth
      - Check recipes and test other BHI manufacturers
      - Calculate performance metrics according to BlaZ types
    - Next Steps CzIE Broth Disk Elution Screen:
      - Perform test with characterized clinical MSSA isolates
      - Reduce O/N incubation for inoculum to 4 hours
  - **PHASE 3:** Obtain funding to perform an outcome study in CzIE positive vs CzIE negative patients

M100 TABLE 6A (INFORMATIONAL ONLY)

- Proposal of an ad hoc working group tasked to ensure the accuracy and usability of Table 6A in M100, Solvents and Diluents for Preparing Stock Solutions of Antimicrobial Agents.
- Need for additional “helpful hints”.
- Some suggestions that came up for this table are to
  - Add the formulation of the powder that is known to dissolve with the solvents/diluents listed in CLSI
  - Make sure the solvent listed is correct and the one generally used
  - Add any special notes to get the "difficult" powders into solution

	– Beef up any additional tips for stock solution preparation • MDSWG is looking for volunteers to chair or participate on this short term WG

3.	**OUTREACH WG (ORWG) REPORT (J. HINDLER)** **2022 WEBINARS** • CLSI Annual Update (19th): What's New in the 2022 CLSI Standards for Antimicrobial Susceptibility Testing (AST)? – March 22 and 23, 2022 – Romney Humphries and Audrey Schuetz – March 22: 383 Attendees, March 23: 381 Attendees • M39 Antibiograms – April 28, 2022 – Trish Simner and Kate Dzintars • CLSI-SIDP ACCP Annual Webinar: The Laboratory- Stewardship Partnership: Putting Susceptibility Testing Results for Gram-Negative Organisms into Practice – July 14, 2022 – Tanis Dingle and Samuel Aitken • CAP-CLSI Annual Webinar: Mycobacterial AST – Fall 2022 (Date TBD) • Upcoming CLSI Webinar: AST Implications of Updated Taxonomy (M64) • New Attendee Orientation Susceptibility Testing Meetings is available on demand. • ASM Microbe 2022 Presentations – The Status of Antibiograms in 2022 by Trish Simner – Antibiograms in Healthcare: What they tell us and what they don't by Kate Dzintars – Piperacillin-tazobactam Clinical and Susceptibility Review by Pranita Tamma **M100 EDUCATIONAL PROGRAM** • No fee. • Provides 1.5 hour CEU ($30). • Currently 32nd edition but will be updated to the 33rd edition. **CLSI AST SC NEWS UPDATE** • Most recent published in June 2022. • Future Content: – Highlight cefiderocol testing issues using case examples – Other topics discussed during the plenary sessions ○ Table 1 ○ Dosage comment removal from M100 Tables 2 ○ Gentamicin, tobramycin, and amikacin BP changes **OTHER PUBLICATIONS** • What's New in Antibiograms? Updating CLSI M39 Guidance with Current Trends

- JCM June 2022
- Authors: Patricia Simner, Janet Hindler, Tanaya Bhowmick, Sanchita Das, Kristie Johnson, Brian Lubers, Mark Redell, John Stelling, and Sharon Erdman

AST SC MEETING WORKSHOPS

- June 2022: Updating Breakpoints – Challenges and Solutions for Various Stakeholders
- Tentative 2023:
  - Antimicrobial Reporting: to include Table 1 updates, selective and cascade reporting, reporting strategies and partnerships with key stakeholders
  - Standardization of Reference Standard AST Methods: to include discussions of global standardization of reference methods; variations of reference methods to accommodate various agents and organisms

NEW ORWG PROJECTS

- Reassess format/distribution of educational materials
- Breakpoint Implementation ad hoc WG

BREAKPOINT IMPLEMENTATION AHWG REPORT

- Goals:
  - Identify needs of clinical laboratories to ensure they are using current CLSI, FDA and/or EUCAST breakpoints (BPs)
  - Provide resources to assist clinical laboratories to determine:
    - What BPs are currently used in their laboratory at the AST instrument, LIS and EHR levels
    - Which BPs require updating
    - A plan for updating BPs
  - Develop ongoing mechanism for communicating with clinical laboratories any new information about BPs.
- Projects completed:
  - M100-33rd Edition Breakpoint Addition/Revision Table review
  - June 2022 CLSI AST News Update article
  - Development of spreadsheet to assist laboratories in recording breakpoints in use
- CLSI FDA AR Bank Isolates for Breakpoint Update Validations
  - Interact with CDC (Maria Machado)
  - Identify isolates for use in specific validations
    - Enterobacterales- piperacillin-tazobactam
  - Help identify opportunities to enhance access and usability
    - Alternatives to -70°C storage?
    - Test isolates in AST systems in use in clinical laboratories to confirm “reference” results reproduce in all systems
- Purpose is to develop consensus recommendations

4.	**JOINT CLSI-EUCAST WG REPORT (J. HINDLER)** **WG GOALS** • 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. • Discuss differences between CLSI and EUCAST QC criteria, methods for establishing QC criteria and the possibility of harmonizing CLSI and EUCAST QC criteria. **EVALUATION OF OPTIMAL DISK POTENCIES FOR CEFTIBUTEN-AVIBACTAM AGAINST ENTEROBACTERALES ISOLATES** • Two method phases were described. • Summary: The 10/4 µg disk was selected based on: – Best discrimination between supposedly susceptible and supposedly resistant strains, as there were lower error rates when applying tentative breakpoints; – Inhibition zones between 15 and 35 mm for supposedly susceptible isolates, as the susceptible breakpoint was >15 mm; – Desire to avoid false susceptible results due to elevated amount of inhibitor since avibactam (and most inhibitors) have antibacterial activity at high concentrations. **NEW PROTOCOL: CONFIRMING THE ACCEPTABILITY OF THE MUELLER-HINTON AGAR SOURCES FOR SUBSEQUENT USE IN CLSI AND/OR EUCAST STUDIES TO ESTABLISH DISK DIFFUSION QC RANGES** • Goals: – Confirm that the MHA sources selected are acceptable prior to performance of a full QC study (Tier 2) to avoid problems when establishing QC ranges. – Testing procedure is designed to minimize factors (eg, inoculum, incubation, measuring zones) other than the MHA source that might affect the results. • Remaining for Pre Tier-2 MHA QC Protocol – Provide examples of “acceptable” and “unacceptable” MHA – Define “process” (how/when to submit/review data) – Finalize SOP – Determine where to “post” **FUTURE WG PROJECTS** • Review CLSI vs. EUCAST QC range differences – For many EUCAST MIC QC ranges, EUCAST performs limited testing to confirm CLSI ranges • EUCAST to determine how much additional data would be needed (beyond CLSI data) to establish a EUCAST QC range • Compare QC ranges determined using both CLSI and EUCAST analysis procedures on a single data set • Summarize CLSI use/investigations into MH-F
5.	**ADJOURNMENT** Dr. Lewis thanked the participants for their attention. The meeting was adjourned at 12:00 PM Central (US) time.

PLENARY ATTENDEES

Plenary 1	Plenary 2	Plenary 3	Plenary 4
Ahmed Abdul Azim	Ahmed Abdul Azim	Ahmed Abdul Azim	Ahmed Abdul Azim
Kevin Alby	Kevin Alby	Kevin Alby	Kevin Alby
Jeff Alder	Jeff Alder	Jeff Alder	Jeff Alder
Vanessa Allen	Vanessa Allen	Vanessa Allen	Vanessa Allen
Diane Anastasiou	Jane Ambler	Jane Ambler	Jane Ambler
Stella Antonara	Diane Anastasiou	Diane Anastasiou	Diane Anastasiou
Sophie Arbefeville	Stella Antonara	Stella Antonara	Stella Antonara
Francis Arhin	Sophie Arbefeville	Sophie Arbefeville	Sophie Arbefeville
Mari Ariyasu	Francis Arhin	Francis Arhin	Francis Arhin
Rocio Balbuena	Mari Ariyasu	Mari Ariyasu	Mari Ariyasu
Katie Barnett	Rocio Balbuena	Rocio Balbuena	Rocio Balbuena
Timothy Bensman	Katie Barnett	Katie Barnett	Katie Barnett
Amira Bhalodi	Timothy Bensman	Timothy Bensman	Timothy Bensman
Amelia Bhatnagar	Amira Bhalodi	Amira Bhalodi	Amira Bhalodi
Sujata Bhavnani	Amrita Bharat	Amrita Bharat	Amrita Bharat
Tanaya Bhowmick	Amelia Bhatnagar	Amelia Bhatnagar	Amelia Bhatnagar
April Bobenchik	Sujata Bhavnani	Sujata Bhavnani	Sujata Bhavnani
Melissa Boddicker	Tanaya Bhowmick	Tanaya Bhowmick	Tanaya Bhowmick
Robert Bowden	April Bobenchik	April Bobenchik	April Bobenchik
Jennifer Boyer	Melissa Boddicker	Melissa Boddicker	Melissa Boddicker
Patricia Bradford	Robert Bowden	Robert Bowden	Robert Bowden

Makena Brand	Jennifer Boyer	Jennifer Boyer	Jennifer Boyer
William Brasso	Patricia Bradford	Patricia Bradford	Patricia Bradford
John Breton	Makena Brand	Makena Brand	Makena Brand
Carson Brockbank	William Brasso	William Brasso	William Brasso
Alexandra Bryson	John Breton	John Breton	John Breton
Claire Burbick	Carson Brockbank	Carson Brockbank	Carson Brockbank
Karen Bush	Alexandra Bryson	Alexandra Bryson	Alexandra Bryson
Deborah Butler	Claire Burbick	Claire Burbick	Claire Burbick
Susan Butler-Wu	Carey-Ann Burnham	Carey-Ann Burnham	Carey-Ann Burnham
Davina Campbell	Karen Bush	Karen Bush	Karen Bush
Shelley Campeau	Deborah Butler	Deborah Butler	Deborah Butler
Rafael Canton	Susan Butler-Wu	Susan Butler-Wu	Susan Butler-Wu
Gerald Capraro	Hayat Caidi	Hayat Caidi	Hayat Caidi
Darcie Carpenter	Davina Campbell	Davina Campbell	Davina Campbell
Cecilia Carvalhaes	Shelley Campeau	Shelley Campeau	Shelley Campeau
Katharine Castagna	Rafael Canton	Rafael Canton	Rafael Canton
Mariana Castanheira	Gerald Capraro	Gerald Capraro	Gerald Capraro
Nydia Alejandra Castillo-Martinez	Darcie Carpenter	Darcie Carpenter	Darcie Carpenter
Suki Chandrasekaran	Cecilia Carvalhaes	Cecilia Carvalhaes	Cecilia Carvalhaes
Sudha Chaturvedi	Katharine Castagna	Katharine Castagna	Katharine Castagna
Jennifer Chau	Mariana Castanheira	Mariana Castanheira	Mariana Castanheira
YAMIN CHEN	Nydia Alejandra Castillo-Martinez	Nydia Alejandra Castillo-Martinez	Nydia Alejandra Castillo-Martinez
Jessica Chumaceiro	Suki Chandrasekaran	Suki Chandrasekaran	Suki Chandrasekaran
Katherine Cicala	Sudha Chaturvedi	Sudha Chaturvedi	Sudha Chaturvedi

Melvili Cintron	Jennifer Chau	Jennifer Chau	Jennifer Chau
Nicolynn Cole	YAMIN CHEN	YAMIN CHEN	YAMIN CHEN
Patricia Conville	Jessica Chumaceiro	Elizabeth Church	Elizabeth Church
Jekia Cox	Elizabeth Church	Katherine Cicala	Katherine Cicala
Arryn Craney	Katherine Cicala	Melvili Cintron	Melvili Cintron
Hannah Creager	Melvili Cintron	Nicolynn Cole	Nicolynn Cole
Sharon Cullen	Nicolynn Cole	Patricia Conville	Patricia Conville
Sanchita Das	Patricia Conville	Jekia Cox	Jekia Cox
Dmitri Debabov	Jekia Cox	Hannah Creager	Hannah Creager
Boudewijn DeJonge	Hannah Creager	Sharon Cullen	Sharon Cullen
Jennifer Dien Bard	Sharon Cullen	Sanchita Das	Sanchita Das
Tanis Dingle	Sanchita Das	Dmitri Debabov	Dmitri Debabov
Lindsay Donohue	Dmitri Debabov	Boudewijn DeJonge	Boudewijn DeJonge
Dana Dressel	Boudewijn DeJonge	Jennifer Dien Bard	Jennifer Dien Bard
Elaine Duncan	Jennifer Dien Bard	Tanis Dingle	Tanis Dingle
Allison Eberly	Tanis Dingle	Lindsay Donohue	Lindsay Donohue
Paul Edelstein	Lindsay Donohue	Dana Dressel	Dana Dressel
mervat elanany	Dana Dressel	Elaine Duncan	Elaine Duncan
German Esparza	Elaine Duncan	Allison Eberly	Allison Eberly
Gina Ewald-Saldana	Allison Eberly	Paul Edelstein	Paul Edelstein
John Farley	Paul Edelstein	mervat elanany	mervat elanany
Laura Filkins	mervat elanany	German Esparza	German Esparza
Glen Fine	German Esparza	Gina Ewald-Saldana	Gina Ewald-Saldana
Mark Fisher	Gina Ewald-Saldana	John Farley	John Farley

Laurie Flemming	John Farley	erica fernandez	erica fernandez
Kelly Flentie	erica fernandez	Laura Filkins	Laura Filkins
Graeme Forrest	Laura Filkins	Glen Fine	Glen Fine
Louise Francois Watkins	Glen Fine	Mark Fisher	Mark Fisher
Andrew Fratoni	Mark Fisher	Laurie Flemming	Laurie Flemming
Lawrence Friedrich	Laurie Flemming	Kelly Flentie	Kelly Flentie
Andrew Fuhrmeister	Kelly Flentie	Graeme Forrest	Graeme Forrest
Marcelo Galas	Graeme Forrest	Louise Francois Watkins	Louise Francois Watkins
Barb Gancarz	Louise Francois Watkins	Andrew Fratoni	Andrew Fratoni
Christian Giske	Andrew Fratoni	Lawrence Friedrich	Lawrence Friedrich
Melissa Gitman	Lawrence Friedrich	Andrew Fuhrmeister	Andrew Fuhrmeister
Howard Gold	Andrew Fuhrmeister	Marcelo Galas	Marcelo Galas
Beth Goldstein	Marcelo Galas	Barb Gancarz	Barb Gancarz
Emily Gomez	Barb Gancarz	Christian Giske	Christian Giske
Thomas GOMMÉ	Christian Giske	Melissa Gitman	Melissa Gitman
Kerian Grande Roche	Melissa Gitman	Howard Gold	Howard Gold
Natasha Griffin	Howard Gold	Beth Goldstein	Beth Goldstein
Meredith Hackel	Beth Goldstein	Emily Gomez	Emily Gomez
Lauren Hamilton	Emily Gomez	Thomas GOMMÉ	Thomas GOMMÉ
Camille Hamula	Thomas GOMMÉ	Kerian Grande Roche	Kerian Grande Roche
Liselotte Hardy	Kerian Grande Roche	Alice Gray	Alice Gray
Sarah Hepler	Alice Gray	Natasha Griffin	Natasha Griffin
Megan Hickey	Natasha Griffin	Meredith Hackel	Meredith Hackel
Megan Hickey	Meredith Hackel	Lauren Hamilton	Lauren Hamilton

David Hilbert	Lauren Hamilton	Camille Hamula	Camille Hamula
Danielle Hilligoss	Camille Hamula	Liselotte Hardy	Liselotte Hardy
Evann E. Hilt	Liselotte Hardy	Sarah Hepler	Sarah Hepler
Janet Hindler	Sarah Hepler	Megan Hickey	Megan Hickey
Elizabeth Hirsch	Megan Hickey	David Hilbert	David Hilbert
Rita Hoffard	David Hilbert	Danielle Hilligoss	Danielle Hilligoss
Denise Holliday	Danielle Hilligoss	Evann E. Hilt	Evann E. Hilt
Michael Huband	Evann E. Hilt	Janet Hindler	Janet Hindler
Romney Humphries	Janet Hindler	Elizabeth Hirsch	Elizabeth Hirsch
Antonieta Jimenez	Elizabeth Hirsch	Rita Hoffard	Rita Hoffard
Brian Johnson	Rita Hoffard	Denise Holliday	Denise Holliday
Kristie Johnson	Denise Holliday	Michael Huband	Michael Huband
Barb Jones	Michael Huband	Romney Humphries	Romney Humphries
Melissa Jones	Romney Humphries	Antonieta Jimenez	Antonieta Jimenez
James Jorgensen	Antonieta Jimenez	Brian Johnson	Brian Johnson
Diane Kawa	Brian Johnson	Kristie Johnson	Kristie Johnson
Michelle Kielar	Kristie Johnson	Barb Jones	Barb Jones
Susan Kircher	Barb Jones	Melissa Jones	Melissa Jones
Thomas Kirn	Melissa Jones	James Jorgensen	James Jorgensen
Anna Klavins	James Jorgensen	Maria Karlsson	Maria Karlsson
Laura Koeth	Maria Karlsson	Diane Kawa	Diane Kawa
Barbara Kostecki	Diane Kawa	Ellen Kersh	Ellen Kersh
Joseph Kuti	Ellen Kersh	Michelle Kielar	Michelle Kielar
Chris Lam	Michelle Kielar	Susan Kircher	Susan Kircher

Stephen LaVoie	Susan Kircher	Thomas Kirn	Thomas Kirn
Sarah Leppanen	Thomas Kirn	Anna Klavins	Anna Klavins
Autumn Lewis	Anna Klavins	Laura Koeth	Laura Koeth
James Lewis	Laura Koeth	Barbara Kostecki	Barbara Kostecki
Xian-Zhi Li	Barbara Kostecki	Joseph Kuti	Joseph Kuti
Rachael Liesman	Joseph Kuti	Chris Lam	Chris Lam
Brandi Limbago	Chris Lam	Stephen LaVoie	Stephen LaVoie
Luiz Lisboa	Stephen LaVoie	Sarah Leppanen	Sarah Leppanen
Niki Litchfield	Sarah Leppanen	Autumn Lewis	Autumn Lewis
Zabrina Lockett	Autumn Lewis	James Lewis	James Lewis
Naeemah Logan	James Lewis	Xian-Zhi Li	Xian-Zhi Li
David Lonsway	Xian-Zhi Li	Rachael Liesman	Rachael Liesman
Maria Machado	Rachael Liesman	Brandi Limbago	Brandi Limbago
Rianna Malherbe	Brandi Limbago	Luiz Lisboa	Luiz Lisboa
Rianna Malherbe	Luiz Lisboa	Niki Litchfield	Niki Litchfield
Allie Malmberg	Niki Litchfield	Zabrina Lockett	Zabrina Lockett
Ron Master	Zabrina Lockett	Naeemah Logan	Naeemah Logan
Amy Mathers	Naeemah Logan	David Lonsway	David Lonsway
Sandra McCurdy	David Lonsway	Joseph Lutgring	Joseph Lutgring
Pat McGinn	Joseph Lutgring	Maria Machado	Maria Machado
Sarah McLeod	Maria Machado	Rianna Malherbe	Rianna Malherbe
Felicita Medalla	Rianna Malherbe	Rianna Malherbe	Rianna Malherbe
Rod Mendes	Rianna Malherbe	Allie Malmberg	Allie Malmberg
Lisa Meyers	Allie Malmberg	Isabella Martin	Isabella Martin

Alita Miller	Isabella Martin	Ron Master	Ron Master
William Miller	Ron Master	Amy Mathers	Amy Mathers
Susan Mindel	Amy Mathers	Sandra McCurdy	Sandra McCurdy
Stephanie Mitchell	Sandra McCurdy	Sarah McLeod	Sarah McLeod
Greg Moeck	Sarah McLeod	Felicita Medalla	Felicita Medalla
Justin Moore	Felicita Medalla	Rod Mendes	Rod Mendes
Nicholas Moore	Rod Mendes	Lisa Meyers	Lisa Meyers
Yesenia Morales	Lisa Meyers	Alita Miller	Alita Miller
Ian Morrissey	Alita Miller	Linda Miller	Linda Miller
Mary Motyl	Linda Miller	William Miller	William Miller
Besarta Mullalli	William Miller	Susan Mindel	Susan Mindel
Samia Naccache	Susan Mindel	Stephanie Mitchell	Stephanie Mitchell
Navaneeth Narayanan	Stephanie Mitchell	Greg Moeck	Greg Moeck
Susan O'Rourke	Greg Moeck	Justin Moore	Justin Moore
Chie Ohno	Justin Moore	Nicholas Moore	Nicholas Moore
Margaret Ordonez Smith de Danies	Nicholas Moore	Yesenia Morales	Yesenia Morales
John Otero	Yesenia Morales	Ian Morrissey	Ian Morrissey
Linda Otterson	Ian Morrissey	Mary Motyl	Mary Motyl
Samantha Pacha	Mary Motyl	Besarta Mullalli	Besarta Mullalli
Elizabeth Palavecino	Besarta Mullalli	Samia Naccache	Samia Naccache
Harley Parker	Samia Naccache	Navaneeth Narayanan	Navaneeth Narayanan
Jean Patel	Navaneeth Narayanan	Susan O'Rourke	Susan O'Rourke
Robin Patel	Susan O'Rourke	Chie Ohno	Chie Ohno
Jeffrey Pearson	Chie Ohno	Margaret Ordonez Smith de Danies	Margaret Ordonez Smith de Danies

Morgan Pence	Margaret Ordonez Smith de Danies	John Otero	John Otero
Katherine Perez	John Otero	Linda Otterson	Linda Otterson
Virginia Pierce	Linda Otterson	Samantha Pacha	Samantha Pacha
Chris Pillar	Samantha Pacha	Elizabeth Palavecino	Elizabeth Palavecino
Dakota Poirrier	Elizabeth Palavecino	Nick Pankau	Nick Pankau
Eleanor Powell	Nick Pankau	Harley Parker	Harley Parker
Mimi Precit	Harley Parker	Jean Patel	Jean Patel
Lara Rajeev	Jean Patel	Robin Patel	Robin Patel
Karl Anthony Ramos	Robin Patel	Jeffrey Pearson	Jeffrey Pearson
Dev Ranjit	Jeffrey Pearson	Morgan Pence	Morgan Pence
Eric Ransom	Morgan Pence	Katherine Perez	Katherine Perez
Mark Redell	Katherine Perez	Victoria Phucas	Victoria Phucas
L. Barth Reller	Virginia Pierce	Virginia Pierce	Virginia Pierce
Jean-Yves RESSOT	Chris Pillar	Chris Pillar	Chris Pillar
Felicia Rice	Dakota Poirrier	Dakota Poirrier	Dakota Poirrier
Sandra Richter	Eleanor Powell	Eleanor Powell	Eleanor Powell
james roberts	Mimi Precit	Mimi Precit	Mimi Precit
Flavia Rossi	Lara Rajeev	Lara Rajeev	Lara Rajeev
Sarah Sabour	Karl Anthony Ramos	Karl Anthony Ramos	Karl Anthony Ramos
Helio Sader	Dev Ranjit	Dev Ranjit	Dev Ranjit
Michael Satlin	Eric Ransom	Eric Ransom	Eric Ransom
Nicole Scangarella-Oman	Mark Redell	Mark Redell	Mark Redell
Linda Schuermeyer	L. Barth Reller	L. Barth Reller	L. Barth Reller
Audrey Schuetz	Jean-Yves RESSOT	Jean-Yves RESSOT	Jean-Yves RESSOT

Dale Schwab	Felicia Rice	Felicia Rice	Felicia Rice
Katherine Sei	Sandra Richter	Sandra Richter	Sandra Richter
Alisa Serio	james roberts	james roberts	james roberts
Seyed Mojtaba Seyed Mousavi Tasieh	Flavia Rossi	Flavia Rossi	Flavia Rossi
Maroun Sfeir	Sarah Sabour	Sarah Sabour	Sarah Sabour
Samantha Shannon	Helio Sader	Helio Sader	Helio Sader
Susan Sharp	Michael Satlin	Michael Satlin	Michael Satlin
Ribhi Shawar	Nicole Scangarella-Oman	Nicole Scangarella-Oman	Nicole Scangarella-Oman
Amanda Sheets	Linda Schuermeyer	Linda Schuermeyer	Linda Schuermeyer
may sherif	Audrey Schuetz	Audrey Schuetz	Audrey Schuetz
Jingzi Sherman	Dale Schwab	Dale Schwab	Dale Schwab
Dee Shortridge	Katherine Sei	Katherine Sei	Katherine Sei
Simone Shurland	Alisa Serio	Alisa Serio	Alisa Serio
Sherry Siegert	Seyed Mojtaba Seyed Mousavi Tasieh	Seyed Mojtaba Seyed Mousavi Tasieh	Seyed Mojtaba Seyed Mousavi Tasieh
Patricia Simner	Maroun Sfeir	Maroun Sfeir	Maroun Sfeir
Pragya Singh	Samantha Shannon	Samantha Shannon	Samantha Shannon
Jennifer Slaughter	Susan Sharp	Susan Sharp	Susan Sharp
Jennifer Smart	Ribhi Shawar	Ribhi Shawar	Ribhi Shawar
Emily Snavely	Amanda Sheets	Amanda Sheets	Amanda Sheets
Paula Snippes Vagnone	may sherif	may sherif	may sherif
Judith Steenbergen	Jingzi Sherman	Jingzi Sherman	Jingzi Sherman
Eric Stern	Dee Shortridge	Dee Shortridge	Dee Shortridge
Laura Stewart	Simone Shurland	Simone Shurland	Simone Shurland

Gregory Stone	Michael Sidlak	Michael Sidlak	Michael Sidlak
Victoria Stone	Patricia Simner	Patricia Simner	Patricia Simner
Mira Suseno	Pragya Singh	Pragya Singh	Pragya Singh
Bieke Tack	Jennifer Slaughter	Jennifer Slaughter	Jennifer Slaughter
Pranita Tamma	Jennifer Smart	Jennifer Smart	Jennifer Smart
Yi-Wei Tang	Emily Snavely	Emily Snavely	Emily Snavely
Jolyn Tenllado	Paula Snippes Vagnone	Paula Snippes Vagnone	Paula Snippes Vagnone
Susan Thomson	Judith Steenbergen	Judith Steenbergen	Judith Steenbergen
Allison Tsan	Eric Stern	Eric Stern	Eric Stern
Valentine Usongo	Laura Stewart	Laura Stewart	Laura Stewart
Tam Van	Gregory Stone	Gregory Stone	Gregory Stone
Tam Van	Victoria Stone	Victoria Stone	Victoria Stone
Alani Vasquez	Bieke Tack	Bieke Tack	Bieke Tack
Wayne Wang	Pranita Tamma	Pranita Tamma	Pranita Tamma
Nancy Watz	Yi-Wei Tang	Yi-Wei Tang	Yi-Wei Tang
Rebecca Weingarten	Jolyn Tenllado	Jolyn Tenllado	Jolyn Tenllado
Melvin Weinstein	Susan Thomson	Susan Thomson	Susan Thomson
Eric Wenzler	Allison Tsan	Allison Tsan	Allison Tsan
Jean Whichard	Valentine Usongo	Valentine Usongo	Valentine Usongo
Matthew Wikler	Tam Van	Tam Van	Tam Van
Christine Yang	Tam Van	Tam Van	Tam Van
Lynn-Yao Lin	Alani Vasquez	Alani Vasquez	Alani Vasquez
Cheung Yee	Wayne Wang	Wayne Wang	Wayne Wang
Rebecca Yee	Nancy Watz	Nancy Watz	Nancy Watz

Katherine Young	Collette Wehr	Collette Wehr	Collette Wehr
Claudia Zampaloni	Chase Weikel	Chase Weikel	Chase Weikel
Barbara Zimmer	Rebecca Weingarten	Rebecca Weingarten	Rebecca Weingarten
	Melvin Weinstein	Melvin Weinstein	Melvin Weinstein
	Susan Weir	Susan Weir	Susan Weir
	Eric Wenzler	Eric Wenzler	Eric Wenzler
	Jean Whichard	Jean Whichard	Jean Whichard
	Matthew Wikler	Matthew Wikler	Matthew Wikler
	Christine Yang	Christine Yang	Christine Yang
	Lynn-Yao Lin	Lynn-Yao Lin	Lynn-Yao Lin
	Cheung Yee	Cheung Yee	Cheung Yee
	Rebecca Yee	Rebecca Yee	Rebecca Yee
	Katherine Young	Katherine Young	Katherine Young
	Claudia Zampaloni	Barbara Zimmer	Barbara Zimmer
	Barbara Zimmer		