Meeting Title:	**Subcommittee on Antimicrobial Susceptibility Testing (AST)**	**Contact:**	mhackenbrack@clsi.org
Meeting Dates and Start times:	**Plenary 1:** Wednesday, 3 February 2021, 3:00 – 6:00 PM Eastern (US) Time **Plenary 2:** Friday, 5 February 2021, 1:00 – 4:00 PM Eastern (US) Time **Plenary 3**: Friday, 12 February 2021, 1:00 – 4:00 PM Eastern (US) Time **Plenary 4:** Monday, 22 February 2021, 3:00 – 5:00 PM Eastern (US) Time		
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 (ed). Revision progress on M23 and M39 will also be discussed.		
Requested Attendee(s):	SC Chairholder, Vice-chairholder, Members, Advisors, and Reviewers; Expert Panel on Microbiology Chairholder and Vice-chairholder; Interested Parties; CLSI Staff (see SC roster)		

Attendee(s):	
James S. Lewis, PharmD, FIDSA AST Subcommittee Chairholder **Melvin P. Weinstein, MD** AST Subcommittee Vice-Chairholder **Jean B. Patel, PhD, D(ABMM)** Expert Panel on Microbiology Chairholder	**Oregon Health and Science University** **Rutgers Robert Wood Johnson Medical School** **Beckman Coulter**
Members Present:	
Sharon K. Cullen, BS, RAC Marcelo F. Galas Howard Gold, MD, FIDSA Romney M. Humphries, PhD, D(ABMM) Thomas J. Kirn, MD, PhD Brandi Limbago, PhD Amy J. Mathers, MD, D(ABMM) Tony Mazzulli, MD, FACP, FRCP(C) (Both) Sandra S. Richter, MD, D(ABMM), FCAP, FIDSA Michael Satlin, MD, MS Audrey N. Schuetz, MD, MPH, D(ABMM) Patricia J. Simner, PhD, D(ABMM)	Beckman Coulter, Inc. Microbiology Business Pan American Health Organization Beth Israel Deaconess Medical Center Vanderbilt University Medical Center Rutgers Robert Wood Johnson Medical School Centers for Disease Control and Prevention University of Virginia Medical Center Sinai Health System bioMérieux, Inc. New York Presbyterian Hospital Mayo Clinic Johns Hopkins School of Medicine, Department of Pathology
Members Absent	
3 February – Plenary 1 5 February – Plenary 2 12 February – Plenary 3 22 February – Plenary 4	None None None None
Advisors Present	
Tanaya Bhowmick, MD April M. Bobenchik, PhD, D(ABMM), MT(ASCP) Carey-Ann Burnham, PhD, D(ABMM) Shelley Campeau, PhD, D(ABMM) Mariana Castanheira, PhD Sanchita Das, MD, D(ABMM) Tanis Dingle, PhD, D(ABMM), FCCM George M. Eliopoulos, MD	Rutgers Robert Wood Johnson Medical School Lifespan Academic Medical Center Washington University School of Medicine Accelerate Diagnostics, Inc. JMI Laboratories National Institutes of Health Alberta Precision Laboratories Beth Israel Deaconess Medical Center

German Esparza, MSc	Proasecal SAS
Christian G. Giske, MD, PhD	Karolinska University Hospital
Janet A. Hindler, MCLS, MT(ASCP), F(AAM)	Los Angeles County Department of Public Health
Elizabeth Hirsch, PharmD	University of Minnesota College of Pharmacy
Maria Karlsson, PhD	Centers for Disease Control and Prevention
Joe Kuti, PharmD, FIDP	Hartford Hospital
Joseph D. Lutgring, MD	Centers for Disease Control and Prevention
Linda A. Miller, PhD	CMID Pharma Consulting LLC
Greg Moeck, PhD	Venatorx Pharmaceuticals, Inc.
Navaneeth Narayanan, PharmD, MPH	Rutgers University
Robin Patel, MD	Mayo Clinic
Samir Patel, PhD, FCCM, D(ABMM)	Public Health Ontario
Virginia M. Pierce, MD	Massachusetts General Hospital
Ribhi M. Shawar, PhD, D(ABMM), F(AAM)	FDA Center for Devices and Radiological Health
Barbara L. Zimmer, PhD	Beckman Coulter
Reviewers, and Guests: See the attached attendence list	
Staff:	
Kathy Castagna, MS, MT(ASCP)CT, MB	CLSI
Glen Fine, MS, MBA, CAE	CLSI
Emily Gomez, MS, MLS(ASCP)MB	CLSI
Marcy L. Hackenbrack, MCM, M(ASCP)	CLSI
Patrick McGinn, CAE	CLSI
Lori Moon, MS, MT(ASCP)	CLSI
Christine Lam, MT(ASCP)	CLSI

Plenary Virtual Meeting Time/Date	Length	Chairholder(s)	Objectives		Background Folder	Page
Plenary (Part 1) **Wednesday, 3 February 2021 at 3:00 PM**	3 hr.	**J. Lewis** (Chairholder) **M. Weinstein** (Vice -Chairholder)	**Opening Remarks:** Dr. Lewis	5 min.	N/A	4
			CLSI Update: Mr. Fine	10 min.	N/A	4
			Vet AST Update: Mr. Bowden	15 min.	N/A	5
			M23 Report: Dr. Wikler	15 min.	N/A	5-6
			M39 Report: Ms. Hindler and Dr. Simner	15 min.	N/A	6
			Methods Application and Interpretation WG Report: Dr. Kirn and Dr. Limbago	1 hour	F	6-9
			QC WG Report: Ms. Cullen and Ms. Traczewski	1 hour	I	9-16
Plenary (Part 2) **Friday, 5 February 2021 at 1:00 PM**	3 hr.		**EUCAST Update:** Dr. Giske	15 min.	N/A	17
			Joint CLSI-EUCAST WG Report: Ms. Hindler and Dr. Matuschek	20 min.	L	17-18
			Outreach WG Report: Ms. Hindler and Dr. Schuetz	15 min.	H	18-19
			Text and Tables WG Report: Dr. Bobenchik and Dr. Campeau	20 min.	J	19-22
			Methods Development and Standardization WG: Dr. Hardy and Dr. Zimmer	2 hours	G	22-27
Plenary (Part 3) **Friday, 12 February 2021 at 1:00 PM**	3 hr.		**Table 1 WG Report:** Dr. Simner and Dr. Eliopoulos	1 hour	M	29-31
			Breakpoint WG Report (Part 1): Dr. Mathers, Dr. Satlin, Dr. Eliopoulos	2 hours	E	32-47
Plenary (Part 4) **Monday, 22 February 2021 at 3:00 PM**	2 hr.		**Breakpoint WG Report (Part 2):** Dr. Mathers, Dr. Satlin, Dr. Eliopoulos	2 hours	E	32-47

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PLENARY 1: WEDNESDAY, 3 FEBRUARY 2021 **NOTE:** • **All presentations from the plenary sessions are now available on the CLSI Website (2021 Winter AST Plenary Presentations).** • **Summer 2020 Meeting Summary Minutes: Voted on electronically and approved October 2020 -** The approved summary minutes are included in the meeting background materials and have been posted on the CLSI website using the following link to the 2020 Summer AST Meeting Files • **Number of Voting Members present: 12 of 12**	
1.	**Opening Remarks: Dr. Lewis** **Dr. Lewis opened the meeting at 3:00 PM Eastern (US) time by thanking the participants for their time and attendance.** • He expressed his gratitude and appreciation to Dr. Mel Weinstein for his many years of service with CLSI and for his leadership as Chairholder during the previous four years.
2.	**CLSI Update: Mr. Fine** **Mr. Fine provided an update on the status of CLSI.** • He recognized the issues associated with the pandemic over the past year. He expressed his gratitude to the volunteers for their handling of the pandemic and their ability to continue making contributions to CLSI. • For CLSI, it has been a challenging year for standards production. Schedules have been adjusted to accommodate volunteers who have been deeply involved with fighting the pandemic. • Overall, with expense reductions (eg, all virtual meetings, telecommuting etc.), CLSI has been able to remain financially stable. • The June 2021 AST meeting is planned to be virtual; however, the current expectation is that the January 2022 will be in person (Ft. Lauderdale, 23-25 January 2022). This meeting might be held as in a hybrid format (in person and virtual). • Mr. Fine recognized Dr. Shelley Campeau and Dr. April Bobenchik by presenting each of them with the annual CLSI Excellence in Standards Development Award for their extensive work for the AST SC. Their many contributions included: – Leading the Text and Tables WG – Spending countless hours assisting the project manager with M100 draft reviews – Responding to reviewer comments – Discussing and forming revisions to M100 – Keeping M100 on schedule for publication – Individually working on 12 other WGs associated with M100

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3.	**<u>Subcommittee (SC) on Veterinary Antimicrobial Susceptibility Testing (VAST) Update</u>: Mr. Bowden** **Mr. Bowden provided an update on the activities of the VAST SC. The highlights included:** • The 2nd ed. of VET02, *Developing In-Vitro Susceptibility Testing Criteria and QC Data* (the equivalent to M23) published January 21, 2021. • The 2nd ed. of VET03, *Methods for Antimicrobial Disk Susceptibility Testing of Bacteria Isolated From Aquatic Animals* published May 2020. • The 3rd ed. of VET04S, *Methods for Broth Dilution Susceptibility Testing of Bacteria Isolated From Aquatic Animals*, published May 2020. • The WG on Bovine Mastitis Interpretive Criteria is expected to review proposals for kanamycin and cephalexin MIC and disk breakpoints (BPs) for various microorganisms. • The 5th ed. of VET01, *Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals* and its supplement (VET01S) published in October 2020. Various species-specific BPs for cats, dogs, and horses were added. • The WG on VAST Breakpoints and Editorial tables are working on several projects including (but not limited to): – Developing an animal-specific table similar to Tables 1 in M100 – Developing disk correlates for agents currently having only MIC breakpoints – Develop recommendations for the use of oxacillin/cefoxitin to predict ß-lactams – Revise VET09, *Understanding Susceptibility Test Data as a Component of Antimicrobial Stewardship in Veterinary Settings* • The WG on Education developed a webinar on VET01S revisions which was presented by Michael Sweeney. • The WG on Generic Drugs is reviewing BPs for amoxicillin-clavulanate, ampicillin, chloramphenicol, doxycycline, and marbofloxacin. • The WG on Infrequent/Fastidious Organisms is planning for the revision of VET06 (VAST version of M45). • The WG on Veterinary Breakpoint Rationale is in the process of developing VET-specific rationale documents based on the AST template. • SC Discussion: – Insight on how the VAST SC is handling the aminopenicillin BPs was requested (Response: The VAST SC was notified regarding the work by the Aminopenicillin Ad hoc WG (AHWG) and it was suggested that the two groups might work together). – It was noted that the VAST SC is has large amounts of supporting data for setting animal BPs. It was questioned how the data is being distributed. (Response: Rationale documents are planned. Currently, each BP includes a dosage regimen comment indicating the dosage on which the BP is modeled and indicates any other data used to set the BP).
4.	**<u>M23 WG Report</u>: Dr. Wikler [Folder K]** **WG Roster**: Avery Goodwin, Matt Wikler (Co-Chairholders); Romney Humphries (Recording Secretary); Timothy Bensman, Mariana Castanheira, Patricia Conville, Sharon Cullen, Linda Miller, Stephanie Mitchell, Greg Moeck, Margaret Ordoñez Smith de Danies, Mike Satlin, Simone Shurland (Members) **Dr. Wikler provided an update on the progress of the M23 revision project.** • The draft is in the final WG review stage. Comments are due for submission by February 24th. • Once all comments are resolved, the draft will be submitted to the editorial staff to prepare for the 60-day proposed draft review and vote (SC member, Expert Panel on Microbiology, CLSI delegate vote; SC advisor, reviewer, and M23 WG review and comment) (expected in June 2021). • 20-day final vote by the Consensus Council is projected for December 2021 with publication expected in April 2022.

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	• Dr. Wikler requested that the SC consider its commitment to the periodic BP review process as described in M23. The SC reached consensus on the following points: – The SC is committed to performing the periodic reviews and has done reviews for several drug groups (eg, fluoroquinolones, daptomycin, aminopenicillins, etc). – The procedure in M23 is acceptable and the process needs to be systematic. – A list of drugs and drug groups to be reviewed needs to be prioritized. – Older BPs were established using methods that are not used now and literature reviews require someone with medical expertise. – Investigators need to take advantage of the FDA grants to review drugs that need to be reviewed. – If a signal that a BP might be a problem, then the drug (or drug class) should be investigated. – It was agreed that the procedure will be endorsed and a list will be prioritized.
5.	**M39 WG Report: Ms. Hindler/Dr. Simner [Folders N, K]** **WG Roster:** Janet Hindler, Trish Simner (Co-Chairholders); April Abbott (Recording Secretary); Faiza Benahmed, Tanaya Bhowmick, Sanchita Das, Sharon Erdman, Andrea Ferrell, Kristie Johnson, Brian Lubbers, Ron Master, Jimish Mehta, Ian Morrissey, Mark Redell, Helio Sader, Dawn Sievert, Paula Snippes Vagnone, John Stelling **Dr. Simner provided an information-only update on the progress of the M39 revision project.** • The draft is currently with the editorial staff to prepare the draft for the 60-day proposed draft review and vote (SC member, Expert Panel on Microbiology, CLSI delegate vote; SC advisor, reviewer, and M23 WG review and comment) which is expected in late February or early March 2021. • The 20-day final vote by the Consensus council is projected for July/August 2021 with publication expected in October 2021. • Highlights of new information added to the new edition (5th) include: – Reorganizing, categorizing, and sectioning the topics into Parts (I through VIII) – Providing guidance for developing antibiograms for yeasts and antifungal agents, multiple facilities, long-term care facilities, and veterinary practices – Providing guidance for use of antibiogram data by antimicrobial stewardship programs – Providing guidance for using statistical analysis techniques – Outlining considerations for extracting data from different sources (eg, automated AST instruments, LIS, etc.) for preparing an antibiogram – Providing guidance for incorporating antimicrobial resistance marker test results with the antibiogram – Providing guidance to clinicians for selecting empiric therapy for initial infections when test results are not yet available. – Adding a new section on frequently asked questions. • **SC discussion:** – **Question:** Should I^ be included in the antibiogram? (**Response:** Guidance on using I^ has been included in M39). – **Comment:** In regard to the % susceptible cutoff to guide therapy: Factors other than the antibiogram should be considered when deciding on empiric therapy.

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6.	**<u>Methods Application and Interpretation WG (MAIWG) Report</u>: Dr. Kirn/Dr. Limbago [Folders F, K]** **WG Roster:** Tom Kirn, Brandi Limbago (Co-Chairholders); Kristie Johnson (Recording Secretary); Darcie Carpenter, Steve Jenkins, Joe Kuti, Samir Patel, Virginia Pierce, Sandy Richter, Susie Sharp, Trish Simner (Members) **Dr. Kirn reported on the activities of the MAIWG. All items were informational only with no votes needed.** **<u>Infectious Disease Society of America (IDSA) and CLSI guidance on β-lactamases</u>** • New IDSA guidance regarding detection of carbapenemase (CP) (either genotypically or phenotypically) for carbapenemase-resistant Enterobacterales (CRE) and *P. aeruginosa* appears to be in discordance with CLSI recommendations. • IDSA recommends using CP detection to guide therapy while CLSI recommends using CP detection for infection prevention and epidemiological purposes only (not for routine use). • The MAIWG expressed concerns that the range of antimicrobial agents has changed in recent years (potentially increasing the utility of carbapenemase detection for guiding therapy), about the accuracy of AST results for some β-lactams when testing CP positive organisms, and that guidance within M100 disagrees with IDSA recommendations. • The MAIWG requested that an Ad Hoc WG (AHWG) be formed to review current statements in M100 regarding testing and reporting of CPs only and make recommendations for revisions to Table 3A, 3B, and Appendix H (if necessary). • The SC agreed on the following points: – The newer agents were designed for specific enzymes. Knowing about the presence of a carbapenemase is important in prescribing. – CP testing is very important but users need to be wary of the test that is being used. Education is going to be extremely important for informing users. – ESBLs also need to be considered. – Some smaller laboratories don't have the capability to test some of the newest methods and this should be considered. – Testing should not be used just for epidemiological purposes and can be used in guiding treatment. – The genotype results can be reported more quickly than the phenotype in some cases, such as when genotypic tests are performed on samples from positive blood culture bottles. – An AHWG should be formed to review the CP testing comments. **Action Item: Form an AHWG to review carbapenemase testing/reporting comments and recommendations throughout M100 (including Tables 3A and 3B and Appendix H to provide harmonized guidance.** **<u>Revision of M100, Appendix H</u>** • The WG believes that Appendix H needs to be updated with new methods and data and harmonized with other areas of M100 (eg, Tables 3B, and 3C). • The WG recommended that the same AHWG (CP issue) review Appendix H to harmonize with recommendations regarding detecting and reporting CPs throughout M100.

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	AmpC ß-lactamases: Dr. Simner provided a review of AmpC ß-lactamases. • There are multiple types of AmpC ß-lactamases, some of which are chromosomal while others are plasmid-mediated, and some of which are inducible while others are not inducible. • There are no CLSI endorsed confirmatory methods and most MICs are reported as tested. • This has created confusion as to how to treat AmpC+ organisms (eg, ceftriaxone vs cefepime). • There is currently a comment in M100 that states: "*Enterobacter*, *Klebsiella* (formerly *Enterobacter*) *aerogenes*, *Citrobacter*, and *Serratia* may develop resistance during prolonged therapy with third-generation cephalosporins as a result of derepression of AmpC ß-lactamase. Therefore, isolates that are initially susceptible may become resistant within 3 to 4 days after initiation of therapy. Testing of repeat isolates may be warranted." • Dr. Simner questioned if CLSI should provide more guidance for reporting AmpC+ organism susceptibility results. • The SC Discussion (**Note:** Comments and questions may be paraphrased). – More guidance for reporting Amp C+ organisms is needed for 1st and subsequent isolates. – There was disagreement regarding suppressing results and additional guidance is needed. – Recommended comments need review and there was uncertainly whether suppressing certain results is the answer. – It needs to be clear if the recommendation's apply to all types of infections or just severe infections. – It was suggested to update the comment to provide the laboratory and the antimicrobial stewardship team the opportunity make their own decisions on suppression. – Historically, suppression of results has been discussed multiple times. The current comment was reached by consensus allowing use of 3rd - generation cephalosporins if treatment had not selected for derepressed mutants. Suppression of results was not favored unless there is an indication of clinical failure, including retesting of a later isolate. • Path forward: It was decided to revise the comment without a recommendation for result suppression.
	Action Item: The MAIWG will work on a revision of the comment for presentation at the June 2021 meeting.
	I^ (intermediate with accumulation in anatomic sites) • Since its inception and inclusion in M100, there has been confusion regarding reporting drugs with the I^. • It has been determined that urine is the only anatomic site where drugs accumulate. • The WG discussed possible solutions: – Eliminate I^ and indicate when drugs accumulate in the urine – Develop urine breakpoints for other drugs (eg, like for cefazolin) – Revise intermediate definition and comments • The WG agreed that the information is useful but it needs to be presented more clearly and that most clinicians will not use I^ drugs over susceptible drugs. • The WG recommendations included:

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	– Revise the definition for I^ to remove non-urine sites and clarify that I^ is for information only and consultation with ID and the stewardship team is needed. – Review each drug to ensure all are for urine only. – Dr. Bobenchik noted that in the 31st edition of M100, the I^ have only been added to drugs that accumulate in the urine and that the definition has also been revised to reflect urine only. • The SC agreed with the MAIWG plans. **Action Item: The MAIWG will revise the I^ definition to reflect that I^ is for information only and that infectious disease practitioners and the antimicrobial stewardship team needs to be consulted. All uses of I^ in M100 will be reviewed for the 32nd edition.** **Anaerobe AHWG update** • New data for metronidazole and rifampin has emerged that shows that resistance may be under called. The AHWG will follow up in June. • For *Cutibacterium* and rifampin, the location of a note in the antibiogram will be changed. • The AHWG is requesting data for updating the anaerobe antibiogram. Agar dilution and gradient diffusion results are acceptable and should be submitted by **15 March 2021**. • The QCWG has Tier 2 QC data to present to justify revising the QC ranges for fidaxomicin and *Clostridioides difficile*. • The AHWG will be exploring disk testing as performed by EUCAST.
7.	**Quality Control WG Report: Ms. Cullen/Ms. Traczewski [I, K]** **WG Roster:** Sharon Cullen, Maria Traczewski (Co-Chairholders); Mike Huband (Recording Secretary); Alexandra Bryson, Patricia Conville, Dana Dressel, Janet Hindler, David Lonsway, Erika Matuschek, Stephanie Mitchell, David Paisey, Elizabeth Palavecino, Chris Pillar, Susan Thomson, Katherine Young (Members) **Ms. Cullen reported on the activities of the QCWG.** **Tier 2 QC ranges were presented** • Gepotidacin

Drug: gepotidacin	**Abbreviation (Glossary II & III):** GEP	**Previous ID:** GSK2140944
Solvent (Table 6A): DMSO	**Diluent (Table 6A):** Water	**Preparation (Table 6C combination agents):** NA
Route of administration (Glossary II): PO, IV	**Class (Glossary I & II)** : Triazaacenaphthylene	**Subclass (Glossary I & II):** None Listed
Study Report by: JMI	**Pharma Co:** GlaxoSmithKline	**Control Drug**: Levofloxacin

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Additional Information (M23 requirements)	• **Tier 1 Impact Assessment** (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): Only very high inoculum had an impact. • **Equivalency of agar dilution to broth dilution**: Was established (GSK-03 report on file with sponsor) • **ISO/TS 16782 assessment of Tier 2 study materials**: Confirmed
Footnotes:	• **Recommendations for Troubleshooting Guide (Table 4D Disk or 5G MIC)**: None
Discussion	Only *E. faecalis* ATCC® 29212 was tested. Proposed QC range covers dilutions likely to be tested.

Drug Name:	gepotidacin (GSK2140944): GEP				Votes:		13/0/1/1 (For, Against, Absent, Abstain)			
QC Strain	Range	% In	Mode	Dil	Shoulder	Media Mode	Lab Mode	M23 Range	Range Finder	Comments
E. faecalis ATCC® 29212	1-4	97.7	2	3	52% @ 4	2 @ 2 1 @ 2 with 70% shoulder @ 4.	5 @ 2, 3 @ 1, 1 @ 1	1-4	1-4	Some lab and media variability.

Lab G

- Gepotidacin mode was 1 and data for Lot B was excluded due to no growth.
- Levofloxacin mean identified as a statistical outlier. Mode 0.25-5 (at the bottom of the current range 0.25-2 µg/ml).
- Levofloxacin control: Mode @ 1 for all labs/media. 100% within current range 0.25-2 µg/ml.

A motion to accept the Gepotidacin QC ranges of 1 – 4 µg/mL for *E. faecalis* ATCC® 29212 was made (P. Simner) and seconded (R. Humphries). Vote: 12 for; 0 against; 0 abstentions; 0 absent (Pass)

- **Ceftibuten**

Drug: ceftibuten	Abbreviation (Glossary II & III): CTB	**Previous ID:** NA
Solvent (Table 6A): 1/10 volume phosphate buffer pH 8.0 (0.1M).	**Diluent (Table 6A):** Water	**Preparation (Table 6C combination agents):** NA
Route of administration (Glossary II): Oral	**Class (Glossary I & II):** cephems (oral)	**Subclass (Glossary I & II):** cephalosporins
Study Report by: JMI	**Pharma Co:** Venatorx Pharmaceuticals	**Control Drug:** Piperacillin/tazobactam, *E. coli* ATCC® 25922 range previously approved

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Additional Information	• **Tier 1 Impact Assessment** (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): Only very high inoculum had an impact. • **Equivalency of agar dilution to broth dilution**: Established by Venatorx (on file with sponsor) • **ISO/TS 16782 assessment of Tier 2 study materials**: Confirmed
Footnotes:	• Recommendations for Troubleshooting Guide (Table 4D Disk or 5G MIC): None
Discussion	• **Considerations for Tier 3 assessment (from control drug data)**: – *E. coli* ATCC® 25922 with piperacillin/tazobactam: Range 1/4 – 4/4, mode at 4/4 µg/ml (2 media lots) – *E. coli* ATCC® 25922 with ceftibuten: Mode 0.25 µg/ml with 83% shoulder at 0.5 (top of range. Mode for one media at 0.5 (3 lots tested). Add to Tier 3 list to monitor.

Drug Name:	**ceftibuten**				**Votes:**		**13/0/1/1 (For, Against, Absent, Abstain)**			
QC Strain	**Range**	**% In**	**Mode**	**Dil**	**Shoulder**	**Media Mode**	**Lab Mode**	**M23 Range**	**Range Finder**	**Comments**
E. coli ATCC® 25922	0.12-0.5	100	0.25	3	83% @ 0.5	2 @ 0.25, 1 @ 0.5	5 @ 0.25 1 @ 0.25-0.5 2 @ 0.5	NA	NA	Currently approved QC range. Lab and media variability observed. One media at top of range.
E. coli NCTC 13353	16-64	100	32	3	43% @ 16	3 @ 32	6 @ 32, 1 @ 16-32	16-64	16-64	Lab H mode 128 – excluded as outlier QC integrity strain.
K. pneumoniae ATCC® BAA-1705	4-32	100	16	4	82% @ 8	1 @ 16, 2 @ 8-16	4 @ 8, 4 @ 16	4-32	4-32	Lab and media variability observed. QC integrity strain
K. pneumoniae ATCC® BAA-2814	8-32	99.6	16	3	46% @ 32	3 @ 16	6 @ 16, 2 @ 32	8-32	8-32	QC integrity strain (confirmation not routinely required for this QC strain)

Drug: ceftibuten/VNRX-5236 (fixed 4 µg/mL)	**Abbreviation (Glossary II & III):** CLB (tentative)	**Previous ID**: NA
Solvent: see ceftibuten, water for VNRX-5236	**Diluent:** see ceftibuten, water for VNRX-5236	**Preparation (Table 6c combination agents)**: Same as aztreonam-avibactam
Route of administration (Glossary II): Oral	**Class (Glossary I & II):** ß-lactam combination agents	**Subclass (Glossary I & II):** None listed
Study Report by: JMI	**Pharma Co:** Venatorx Pharmaceuticals	**Control Drug**: piperacillin/tazobactam

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Additional Information (M23 requirements)	• **Tier 1 Impact Assessment** (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): Only very high inoculum had an impact. • **Equivalency of agar dilution to broth dilution**: Established by Venatorx (on file with sponsor) • **ISO/TS 16782 assessment of Tier 2 study materials**: Confirmed
Footnotes:	• Recommendations for Troubleshooting Guide (Table 4D Disk or 5G MIC): None
Discussion	• The 3 QC organisms identified for routine QC all have relevant resistant mechanisms and QC ranges for ceftibuten alone don't overlap QC range for combination agent. • **Note:** *E. coli* NCTC 13353 QC range is 4 dilutions, while other 2 strains have 3 dilution QC ranges. • **Action:** Develop proposal for Tables 4A-2 and 5A-2, Appendix C: Stephanie M, Alexandra B, Janet H – Potential options: Footnote: Any of the routine QC strains can be used or preferred routine QC strain. New color or footnote for "alternative" QC strain for routine QC. • Future agenda topic: criteria for selection of routine QC for combination agents (e.g., avoid overlap with QC range for single agent, QC range closer to dilutions likely to be tested, 3 dil range vs 4 dil range).

Drug Name:	**ceftibuten/VNRX-5236 (fixed 4 µg/mL)**					**Votes:**	**13/0/1/1 (For, Against, Absent, Abstain)**			
QC Strain	**Range**	**% In**	**Mode**	**Dil**	**Shoulder**	**Media Mode**	**Lab Mode**	**M23 Range**	**Range Finder**	**Comments**
E. coli ATCC® 25922	0.03/4 - 0.12/4	99.5	0.06/4	3	43% @ 0.12/4	2 @ 0.06/4 1 @ 0.06/4, 79% shoulder @ 0.12/4	6 @ 0.12/4, 1 @ 0.12/4,	0.03/4 - 0.12/4	0.03/4 - 0.12/4	Media variability. Lab H mode 0.12/4-0.5/4- excluded as outlier
E. coli NCTC 13353	0.03/4 - 0.25/4	99.5	0.12/4	4	89% @ 0.06/4	2 @ 0.06/4 1 @ 0.12/4	4 @ 0.06/4, 3 @ 0.12/4,	0.03/4 - 0.25/4	0.03/4 - 0.25/4	Lab and media variability. Lab H mode 0.25/4 - excluded as outlier **Routine QC strain**
K. pneumoniae ATCC® BAA-1705	0.12/4 - 0.5/4	100	0.25/4	3	<30%	2 @ 0.12/4, 1 @ 0.12/4 - 0.25/4	7 @ 0.25/4, 1 @ 0.5/4	0.12/4 - 0.5/4	0.12/4 - 0.5/4	**Routine QC strain**
K. pneumoniae ATCC® BAA-2814	0.5/4 - 2/4	97.1	1/4	3	<30%	3 @ 1.4	7 @ 1/4	0.5/4 - 2/4	0.5/4 -2/4	Lab H mode 4/4 - excluded as outlier **Routine QC strain**

Ranges for ceftibuten alone : *E. coli* NCTC 13353 (16-64). *K. pneumoniae* ATCC® BAA-1705 (4-32) or *K. pneumoniae* ATCC® BAA-2814 (8-32). No overlap with QC range for β-lactam combination.

- **SC Discussion** (**Note:** Comments and questions may be paraphrased.)

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- Strains to be designated as routine QC strains will be clarified.
- Question: Is there is a way to document media and laboratory variability for future reference? (Response: The plan is to work with CLSI to have this information published on the CLSI website.

A motion to accept the QC ranges for ceftibuten for *E. coli* ATCC® 25922 (0.12-0.5 µg/mL), *E. coli* NCTC 13353 (16-64 µg/mL), *K. pneumoniae* ATCC® BAA-1705 (4-32 µg/mL), and *K. pneumoniae* ATCC® BAA-2814 (8-32 µg/mL) and for ceftibuten/VNRX-5236 for *E. coli* ATCC® 25922 (0.03/4 -0.12/4 µg/mL), *E. coli* NCTC 13353 (0.03/4 -0.25/4 µg/mL), *K. pneumoniae* ATCC® BAA-1705 (0.12/4 -0.5/4 µg/mL), and *K. pneumoniae* ATCC® BAA-2814 (0.5/4 -2/4 µg/mL) was made (A. Schuetz) and seconded (T. Kirn). Vote: 12 for; 0 against; 0 abstentions; 0 absent (Pass).

Tier 3 MIC Data were presented. Ms. Cullen noted that the range below will be further discussed at the June 2021 meeting

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern
E. coli ATCC® 25922	Imipenem	0.06-0.25	**Consider revision to include 0.5** **Corrected entry for Lab 2**. Potentially analyze with Rangefinder. Try to get Tier 2 data. Also evaluate IMR.	Tier 3 with >900 results from 5+ labs Mode 0.12 with shoulder 69% at 0.25 (varies by lab). <1% at 0.06, 3% out of range high at 0.5. If assessed per M23 would propose QC range 0.06-0.5 (4 dilutions).
E. coli ATCC® *25922*	Imipenem/ relebactam	0.06/4-0.25/4	**Request feedback.** Potentially analyze with Rangefinder.	Tier 3: 5 labs and >900 results. Mode 0.12 with 42% shoulder at 0.25. 4% out high at 0.5. Tier 2 mode 0.12 with 32% shoulder at 0.25. Overall only 2% at bottom of range at 0.06 Not a routine QC strain.
K. pneumoniae ATCC® *700603*	Imipenem/ relebactam	0.03/4-0.25/4	**Consider adjusting range to include 0.5/4.** Suggestions to analyze with Rangefinder, reassess IMR with other KPC orgs and *E. coli* 25922 with Imipenem	5% out high with multiple labs. Tier 2 and 3 mode is same but results shifted higher. **Note:** *K. pneumoniae* ATCC BAA-1705 or 2814 are recommended for routine QC

Ms. Cullen stated that a vote for fidaxomicin QC ranges with *C. difficile* ATCC® 700057 is being requested.

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern
E. coli NCTC ATCC® 13486 and/or CDC AR Bank #0349	Colistin	NA	**Need additional data** to meet M23 Tier 2 for CBDE and CAT and to approve a range for BMD	*E. coli* NCTC 13486: EUCAST target 4, with occasional 2 or 8 (based on limited data) *E. coli* CDC AR Bank #0349: CLSI target 2, range 1-4 for CBDE and AD (June 2019 with limited disk & media data). Need ranges for broth microdilution
S. pneumoniae ATCC® 49619	Levofloxacin	0.5-2	**Request additional 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.
K. pneumoniae ATCC® 700603	Ampicillin/ Sulbactam	8/4 – 32/16	**Request feedback**	Report from one lab with results at 64/32

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Item #	Description

C. difficile ATCC® 700057	Fidaxomicin	0.06-0.25	Propose 0.03-0.25. Per M23, reassess Tier 2. Combine with Tier 3 and adjust	Agar dilution, results out reporting MIC out on the low side, observing MIC at 0.03 (Anaerobe WG). Tier 2: mode 0.12, shoulder 53% @ 0.06 Tier 3: 53 results. mode 0.03-0.06
E. coli ATCC® 25922	Pip/Tazo	1/4 – 4/4	Monitor/request feedback (Added Jan 2021)	Control drug in Ceftibuten/VNRX-5236 Tier 2 Jan 21 Mode at 4/4 µg/ml (2 media lots) at top of range. 4% out high at 8/4
E. coli ATCC® 25922	Ceftibuten	0.12-0.5	Monitor/request feedback (Added Jan 2021)	Control drug ceftibuten/VNRX-5236 Tier 2 Jan 21 Mode 0.25 with 83% shoulder at 0.5, Mode for one media at 0.5 (3 lots). 100% in range.

- **SC discussion (Note: Comments or questions may be paraphrased).**
  - **Question:** Was the CLSI drug preparation protocol followed? (**Response:** The preparation was followed but additional study data will be presented in June 2021 and additional guidance will be added to M100).

A motion to accept the QC ranges for *C. difficile* ATCC® 700057 (0.03-0.25 µg/mL) with fidaxomicin was made (T. Simner) and seconded (T. Mazzulli). Vote: 12 for; 0 against; 0 against; 0 absent (Pass).

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern
H. influenzae ATCC 49247	Moxifloxacin	0.008-0.03	Monitor-request feedback	80.0% at upper extreme (0.03 µg/mL) of MIC range (results were from only one study, Table 3-29) Refer to USCAST Quinolone report V1.2.
E. faecalis ATCC 29212	Amikacin	64-256	Monitor-request feedback	CDC reported out low when testing gram-neg. panels, other strains in range.
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.
S. aureus ATCC 29213	Rifampin	0.004 to 0.016	Monitor-request feedback	One report of S. aureus out low
K. pneumoniae ATCC BAA-1705	Imipenem/ relebactam	0.03/4-0.25/4	Monitor-request feedback	Results at high end with one lab.

Tier 3 Disk QC Data was presented

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern
P. aeruginosa ATCC 27853	Cefiderocol	22-31	Collect additional data, preferably from non-European labs.	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.
E. coli ATCC 25922	Minocycline	19-25	Monitor. Collect additional data.	Values at top of range and above range from one lab.

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Item #	**Description**
	NOTE: The remainder of the QCWG report was presented at Plenary #2 held on **Friday, 5 February 2021** following the Joint CLSI-EUCAST WG report. ***K. pneumoniae* ATCC® 700603: Troubleshooting multiple colony types** • ATCC recognizes two colony types for *K. pneumoniae* ATCC® 700603. One colony type is dominant and cannot be distinguishe biochemically. • An investigation showed that both colony types yield same AST result and confirmed via sequencing. EUCAST has added a note to their QC table regarding including both colony types when subculturing and testing the strain. • The WG will propose additions to the Troubleshooting Guide, QC table footnote, and Appendix C.
	Action item: Propose language regarding the two colony types of *K. pneumoniae* ATCC® 700603 to the appropriate sections of M100.
	QC Process Improvements • An AHWG on QC Process Improvements will be formed. – Volunteers to be included: CLSI, EUCAST, and various other stakeholders – The AHWG will formally be under the CLSI-EUCAST WG but will also report to the QCWG. • **Other possible improvements** – Making QCWG summaries or data available on the CLSI website – Investigating other CLSI/EUCAST harmonization opportunities – Tier 2 media differences: Assess for outliers and consider these when setting QC ranges – Proactively assess control drug data in Tier 2 studies (add to Tier 3 list) – Clarify Table 2 Routine QC (eg, Table 2A: *E. coli* ATCC® 25922, *P. aeruginosa* ATCC® 27853- carbapenems) • **Targets or Median/Mode:** – Historically, CLSI (then NCCLS) documents included accuracy controls (means of 5 values or maximum zone diameters for 5 consecutive tests) and monitored those. However, these are no longer published in M100. – The WG suggested adding this information back to M100. • **EUCAST recommendations and examples for the following items were presented.** – Detection of disk variation between manufacturers and within cartridge – Determination of product accuracy vs day-to-day variation – Monitoring laboratory results – Monitoring QC ranges and targets – The WG suggested providing more guidance on optimal results

SUMMARY MINUTES	
Item #	**Description**
	• **QC improvements to the next edition of M23** – Report Tier 1 conclusions with Tier 2 report – Confirm agar and broth equivalency was established – Recommend confirming integrity of materials used in Tier 2 studies – Confirm Tier 2 study materials met ISO/TS 16782 requirements – Allow for alternative study designs and supplement testing, if needed – Include observations on variability in QCWG Summary – Proactively update troubleshooting guide with Tier 1 and Tier 2 observations – New recommendations for clinical isolate reproducibility • **Streamlining User QC** – Hope to reduce the burden of QC testing for the clinical laboratory but keep quality at a high level – Issues include: o QC of combination β-lactam agents: Currently need up to 8 QC strains to QC multiple agents o Provide better guidance on routine vs supplemental QC stains for single agents and update the Table 2 QC recommendations boxes – Ideas and possible approaches included: o Use quality system processes to identify most common failures, causes and impacts o Survey users/manufacturers to compile experiences o Identify critical indicators based on user and manufacturers responsibilities and common failures. o Propose reduced list of QC strains to test routinely vs each lot/shipment or supplemental (as needed). o Reinforce role/importance of Quality Assurance o Provide guidance to document streamlined QC decisions using Individualized Quality Control Plan (IQCP) to meet lab accreditation standards – Successful examples of streamlining QC included publication of M50 (streamlined QC for Identification), revisions to M02 and M07 to describe the responsibilities of the manufacturer vs the user and revisions to the QC tables and comment, addition of screening test tables, and the QC troubleshooting guide. – Ms. Cullen requested that interested volunteers contact her. She suggested that CMS representatives be included. • **SC Discussion** – It was noted that streamlining the number of strains to test with the combination agents will be very helpful.
8.	**Adjournment**: Dr. Lewis thanked the presenters and participants and adjourned the meeting at 6:05 PM Eastern (US) time.

SUMMARY MINUTES	
#	**Description**
PLENARY 2: FRIDAY, 5 FEBRUARY 2021 • **Number of Voting Members Present: 12 of 12**	
1.	Dr. Lewis opened the meeting at 1:00 PM Eastern (US) time. He noted that the agenda was reorganized to accommodate the Methods Development and Standardization WG (MDSWG). The Direct BC AST AHWG report was changed to follow the EUCAST update.
2.	**EUCAST Update: Dr. Giske [Folder K]** **Dr.Giske provided an update from EUCAST. The main points of the presentation are listed below.** • **The EUCAST standing and Ad Hoc subcommittees include**: – **Standing:** Antifungal, Veterinary, and Antimycobacterial – **Ad Hoc:** Intrinsic resistance and expert rules; MIC distributions and ECOFFs; Joint working group with CLSI on disk mass development and QC criteria; Relationship between WGS (NGS) and phenotypic susceptibility testing (new); Anaerobic AST (new) • **Breakpoint consultations for 2020 included**: – Fosfomycin oral breakpoints for *E. coli* were decided – Piperacillin-tazobactam and Enterobacterales – Meningitis breakpoints for all species. The main purpose was to remove all I-groups, as these are not logical given that high exposure is used already for the S-group – Breakpoints and methodology published for *Achromobacter* and *Bacillus* • **New Breakpoints Approved included:** – Cefiderocol (Enterobacterales, *P. aeruginosa*) – Lefamulin (*S. pneumoniae* and *S. aureus* in community acquired pneumonia) – Temocillin (*E. coli*, *Klebsiella* spp. [except *K. aerogenes*] and *P. mirabilis* [UTI only]). The wild type is in the I-group. – Pretomanid: There were insufficient data to set breakpoints. • **Activities planned for 2021 include:** – **Oral aminopenicillins and Enterobacterales**: ECOFF is 8 mg/L; PK-PD breakpoint for high exposure is 1 or 2 mg/L – **Fosfomycin IV:** Assessing PK-PD and clinical data beyond *E. coli* – **Colistin:** Potentially breakpoints in brackets (as for aminoglycosides) – **Endocarditis breakpoints**: Harmonize with endocarditis guidelines to avoid discordance
3.	**Joint CLSI-EUCAST WG Report: Ms. Hindler/Dr. Matuschek [Folders K, L]** **WG Roster:** Janet Hindler, Erika Matuschek (Co-Chairholders); Mariana Castanheira, Sharon Cullen, Christian Giske, Gunnar Kahlmeter, Laura Koeth, Maria Traczewski, John Turnidge, Mandy Wooton **Ms. Hindler reported on the activities of the Joint CLSI-EUCAST WG (Informational)** • In January 2021, the WG was redesignated as a "standing WG" that will report directly to the subcommittee. • 1st WG goal: To describe a method for disk content determination to be used in the drug development process was completed with the publication of M23S, *Procedure for Optimizing Disk Contents (Potencies) for Disk Diffusion Testing of Antimicrobial Agents Using Harmonized CLSI and EUCAST Criteria*, 1st Edition.

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#	Description
	– This document is freely available on the CLSI website. – The plan is for M23S to be revised to include a protocol for sponsors to work with the WG. – The protocol will provide guidance for effective ongoing discussions before and during the disk content data review. – It is expected that turnaround for data review from each phase will be completed within 2 weeks. – A checklist that follows recommendations published in M23S is being drafted. • 2nd WG goal: To harmonize QC between CLSI and EUCAST. More detailed information was presented during the QCWG report. – The plan for harmonization includes: o Determining the amount of data required o Determining the method for selecting QC range o Set criteria for identification and elimination of outlying data o Establishing target, media, and/or mode criteria in addition to acceptable QC range and when such additional criteria might be used o Develop additional measures to ensure disk diffusion (DD) "quality"
4.	**Outreach WG (ORWG) Report: Ms. Hindler/Dr. Schuetz (Note:** This report was presented during Plenary #3 on 12 February 2021)**[Folders K, N]** **WG Roster:** Janet Hindler, Audrey Schuetz (Co-Chairholders); Stella Antonara (Recording Secretary); April Abbott, April Bobenchik, Andrea Farrell (new), Romney Humphries, Graeme Forrest, Shawn Lockhart, Rianna Malherbe (new), Nicole Scangarella-Oman, Paula Snippes-Vagnone, Priyanka Uprety (new), Lars Westblade **Ms. Hindler reported on Outreach WG activities.** • **2020 Webinars** – CLSI 2020 Antimicrobial Susceptibility Testing Update (February 26-27, 2020): 716 sites joined – CLSI-SIDP ACCP Annual Webinar: Incorporating the Newest CLSI Recommendations for Antimicrobial Susceptibility Testing into Your Stewardship Activities (14 July 2020): 487 sites • **New Attendee Orientation** (13 January 2021 & and recording available at https://www.youtube.com/watch?v=x-RQqRbFVxw&feature=youtu.be) – Information on all three subcommittees provided o AST: Janet Hindler and Audrey Schuetz o Antifungal: Shawn Lockhart o Vet AST: Brian Lubbers – Introduced the timeline for first publication of major AST SC documents – Described the roles and responsibilities within the SC – Reviewed the current AST standing and ad Hoc WGs and their roles within the SC – Provided information for how to learn more about SCs and how to get involved • **2021 Webinars** – CAP/CLSI Joint Webinar: Ensuring Quality Beyond the Test: Reporting Antimicrobial Susceptibility Results (21 January 2021): 164 sites – CLSI 2021 Antimicrobial Susceptibility Testing Update (28-29 April 2021) – Practical advice for bench techs – how to recognize unusual AST patterns (Date TBD)

SUMMARY MINUTES	
#	Description
	• **ASM Virtual World Microbe Forum (20-24 June 2021)** – Modern Approaches to Antimicrobial Susceptibility Testing (Romney Humphries) – Antimicrobial Stewardship Practice and Personalized Medicine; Where's the Connection? (Navaneeth Narayanan) • **CLSI AST SC News Update** – July 2020 o COVID-19 and AMR and Pandemics o Case Study: Learning about Vet AST o Practical tips for applying susceptibility interpretations to C. parapsilosis complex o Hot topics: Cefiderocol and lefamulin o In Memoriam: Mary Jane Ferraro – Spring 2021 o Understanding S, I, I^, SDD, R, WT, NWT o Practical tips: ASTs that need attention and suggestions for how labs can determine what breakpoints they are using with their AST system o Hot topic on imipenem-relebactam and ARLN testing of aztreonam-avibactam o Updates on changes in the 31st edition of M100 • **New and Ongoing ORWG Projects** – Journal of Clinical Microbiology Mini-Review of M100, 31st edition – Interactive program for M100 – Develop list of AST optional "report comments" to augment AST reports – Pursue additional translations of News Update in various languages (Spanish, Portuguese, Chinese) – Continued suggestions on CLSI website pertaining to AST SC and SC on Antifungal Tests – Pursue social media to disseminate messages – Post / tweet / ? - select Q&As submitted to CLSI • **Chinese translation and distribution of M100** – Initiated by China Antimicrobial Resistance Surveillance System (1,500 clinical labs participate) – Prof. Wang Hui (CLSI AST SC Advisor) is senior translator and Prof. Hu Fupin as main translator – Sponsored by bioMérieux China - free hard copy of M100 to clinical laboratories – Free online and face-to-face education for M100
5.	**Text and Tables WG (TTWG) Report: Dr. Bobenchik/Dr. Campeau [Folders J, K]** **WG Roster**: April Bobenchik, Shelley Campeau (Co-Chairholders); Carey-Ann Burnham (Recording Secretary); Suki Chandrasekaran, Nicolyn Cole (new), Andrea Ferrell, Janet Hindler, Melissa Jones, Jean Patel, Barth Reller, Felicia Rice, Flavia Rossi, Dale Schwab, Maria Traczewski, Nancy Watz (Members); Darcie Carpenter, Sandy Richter, Barbara Zimmer (WG Liaisons) **Dr. Bobenchik reported on the Text and Tables WG activities. Issues raised primarily related to comments submitted during the SC review and voting period.**

SUMMARY MINUTES	
#	Description
	• **Surrogate Testing Comments** – Comments regarding surrogacy are inconsistent throughout M100. – WG is planning to harmonize the comments describing the use of surrogate agents to predict susceptibility for other agents. • **Consistency in Comment Reporting** ("For testing and reporting of _____ only" comments) – Wording of these comments is inconsistent throughout the document (eg, Tables 1, 2, and 3; Appendixes). – The TTWG needs to determine whether to refer back to similar comments in each table or repeat the comment with each instance. – **SC Discussion (Note: Comments and questions may be paraphrased).** o **Comment:** Laboratories may not refer back to a cited comment so it may be better state the comment with every instance. o **Comment:** By keeping the comment for combination agents, if the lab does not test the combination agent, and the parent agent is susceptible, the lab could notify the clinician that both the parent and the combination agent are susceptible without additional testing. o **Suggestion:** Include the same comment for all combination agents. o **Suggestion:** A general comment regarding the combination agents would cover the issue and keep the tables less cluttered. • **Formatting in Appendix E** – There is inconsistency in how select organisms are indicated for a particular agent. – M100 will be reviewed to harmonize language in Tables 2 and Appendix E. • **Tables 2A Cephems, Oral Predictions** – There is confusion about category mismatches between cefuroxime and cefazolin AST results to predict cefuroxime activity for treating UTIs. Cefuroxime can test resistant when cefazolin tests susceptible. – It was suggested that this discrepancy occurs because cefuroxime BPs are based on serum drug concentrations and the cefazolin is based upon urine levels. – All cephem comments and their placement in Tables 2 will be reviewed and edits will be proposed for review at the June meeting. Volunteers to review the comments has been requested. • **Definition of INV (investigational) in Tables 1 and Tables 2** – The current definition of INV states that INV is for agents that are investigational for the organism/group but have not been FDA approved for use in the US. – There are agents listed in Tables 2 as INV which are approved by the FDA (ie, cefiderocol). The TTWG questioned if the definition should be revised. – This issue was submitted to the Breakpoint WG for discussion. It was noted in the chat that the definition coordinates with what is presented in M23. • **Tables 2, Routine QC Recommendations Box** – When QC strains are recommended for QC of specific agents (eg, *P. aeruginosa* for carbapenemases), there is confusion regarding whether other listed agents (eg. *E. coli*) still needs to be tested.

#	Description
	– The new AHWG under the QCWG will be reviewing all routine QC recommendations for all drugs. Any revisions will be deferred until the QCWG has completed their review. • **Glossary III** (List of Identical Abbreviations Used for More than One Antimicrobial Agent in US Diagnostic Products) – Comments regarding abbreviations listed in Glossary II in comparison to Glossary III were submitted. – The TTWG questioned if Glossary III is being used routinely and if it needs to be updated. – The TTWG will work with Susceptibility Testing Manufacturers Association (STMA) to determine if Glossary III is being used and should be updated, as needed. • **TTWG Review Process: Suggestions for Improving Efficiency and Clarity** – The TTWG suggested that new comments or revised comments be drafted before they are inserted into M100. This will require interaction between the TTWG, sponsors, WGs, and CLSI staff before they are incorporated into M100. – The WG also requested that disk content information be included in all sponsor presentations. • **The revised Breakpoints Additions and Revisions Table was reviewed**. – The changes have been specified as new vs those that have been revised. – Definitions of "new" and "revised" are included with the table. • **Update on the Revision of M02 and M07** – The project proposal is ready for submission to the Expert Panel on Microbiology for review and endorsement but chairholder designates must be identified. – A call for volunteers was distributed to the SC. **NOTE:** A number of volunteer names have been submitted and the list will be reviewed by the TTWG Co-chairholders in the near future. – It is expected that if endorsed by the Expert Panel that the proposal will be submitted for Chairholders Council review in June 2021 with a project start in the Fall 2021. • **I^** – Several comments regarding the use of I^ in M100 were submitted. – The comments have been submitted to the MAIWG for further discussion and clarification is expected to be published in the 32nd edition. **NOTE:** I^ has only been designated for agents that accumulate in the urine in the upcoming 31st edition. • **Quinupristin-dalfopristin** – During the 2020 meetings, there was discussion regarding the removal of quinupristin-dalfopristin from Table 2D (Enterococcus) because it is no longer recommended by the FDA for treating *Enterococcus*. However, no vote to remove it from Table 2D was taken. Also, use of the agent outside of the US was not considered. – The removal has been deferred until it can be determined if the agent is still being used outside of the US. – A request has been submitted to the Breakpoint WG for consideration. • ***Enterococcus* high-level resistance language** – Comment edits regarding low-level resistance in Table 2D and Table 3K (HLAR in Enterococcus) are needed.

#	Description

– A request has been submitted to the Breakpoint WG for consideration.

Action Items:

- **Refine surrogate agent definition, including added clarity around text: "cannot be tested due to lack of availability"**
- **Create standard language for newer ß-lactam/ß-lactamase inhibitor compounds and prediction of newer agent based on susceptibility to parent agent**
- **For species-specific breakpoints (eg, for *H. influenzae* only), discuss referring back to similar comments or repeat the comment in each instance.**
- **Harmonize organism comment language between Tables 2 and Appendix E.**
- **Review all cephem comments and their placement in Tables 2 and propose edits**
- **Work with STMA to determine if Glossary III is being used and update it if needed.**
- **Interact with appropriate parties to develop and revised comments before they are inserted in M100.**
- **Identify potential Co-chairholders for the revision of M02 and M07.**

6. **Methods Development and Standardization WG (MDSWG) Report: Dr. Hardy/Dr. Zimmer [Folders G, K]**

WG Roster: Dwight Hardy, Barbara Zimmer (Co-Chairholders); Katherine Sei (Recording Secretary); Kevin Alby, Jennifer Dien Bard, Susan Butler-Wu, Tanis Dingle, German Esparza, Laura Koeth, Ribhi Shawar

Dr. Hardy reported on the activities of the MDSWG.

Tedizolid Disk Diffusion (DD) Method (Informational)

- Harmonization of the DD method for tedizolid between EUCAST and CLSI was discussed.
- Previous studies compared 20 µg tedizolid disks to broth microdilution (BMD) for *Staphylococcus* spp. and showed significant very major and minor errors.
  - A study was performed to evaluate 2 and 5 µg disks to determine if an alternative disk mass could be used.
  - EUCAST reviewed the data and agree that the 2 µg disk should be considered for QC and MIC correlation studies.
- Current Tedizolid 2 µg *S. aureus* QC ranges

S. aureus ATCC 25923	CLSI	18-24 mm (transmitted read)
S. aureus ATCC 29213	EUCAST	19-25 mm (target 22 mm; reflected read)

- The method and parameters for the EUCAST study were reviewed. The results were published in January 2020.
  - The study was performed to collect MIC and tedizolid disk diffusion (2 µg) data as per CLSI and EUCAST requirements for establishing tedizolid breakpoints for *Staphylococcus* spp.
  - The results for tedizolid DD (read with transmitted light) using a 2 µg disk vs MIC showed the following:

Error	Occurrences	
	Number	Percentage
ME	27	5.7
VME	21	4.4

- Additional studies on tedizolid and *Staphylococcus* spp. by JMI Laboratories and ACM Global Laboratories were reviewed.
  - The studies (2018 and 2020) used the 2 µg tedizolid disk and CLSI protocols, and were performed to generate MIC/DD correlation analyses for establishing tedizolid DD breakpoints against indicated species for proposal to CLSI.
  - The results from the studies (read at complete inhibition with transmitted light) using a 2 µg disk vs MIC showed the following:

Species (No. tested)	Breakpoints (mm)		Error rates		
	S (≥)	R (≤)	Very major (%)	Major (%)	Minor (%)
S. *aureus* (901)	15	11	2 (0.22)	0 (0.0)	14 (1.55)
	15	11	3 (0.38)	0 (0.0)	11 (1.39)
S. aureus (1,691)	15	11	3 (0.38)	0 (0.0)	25 (1.48)
S. aureus (1,691)	17	13	3 (0.38)	0 (0.0)	45 (2.66)
S. aureus (1,691)	18	14	0 (0.0)	0 (0.0)	191 (11.29)

- A comparison between the EUCAST and other studies was performed.
  - The tedizolid zone diameters obtained against both QC strains during the JMI/ACM studies were generally lower than those obtained at EDL/LSI.
  - Consequently, the proposed tedizolid DD breakpoint for *S. aureus* from JMI/ACM studies (≥15 mm or ≥17 mm for susceptible) were lower than EUCAST's (≥21 mm for susceptible).
  - Further studies are needed to resolve the discrepancies are needed before breakpoints are proposed to CLSI.

- A new study is being planned
  - 4 labs testing 25 susceptible and 25 resistant isolates
  - Analyzes will be performed using the best-fit disk criteria calculated with the dBETS software
  - A method needs to be developed before harmonization can happen.

- Conclusions
  - Using common QC strains between EUCAST and CLSI for validation of DD may be beneficial and facilitate the harmonization process.
  - Development of a DD method for tedizolid has gone through several iterations and harmonization between CLSI and EUCAST has been pursued; however, it has not been achieved yet due to the discrepant (lower) breakpoints obtained during studies performed at JMI/ACM.
  - Once breakpoint harmonization is achieved, breakpoints will be presented and proposed to the CLSI committee.

SUMMARY MINUTES	
#	Description
	Update on studies for performing AST for *H. influenzae* using Mueller Hinton-Fastidious Media (MHF)(Informational) • The study objective was to compare the performance of *Haemophilus* Test Media (HTM) and MHF using BMD and DD for assessing *H. influenzae* susceptibility. • The study was postponed due to the pandemic and related supply issues and will undergo some modifications. • 12 antimicrobial agents are being tested with three only being tested by MIC. • It is expected that the study will begin in April 2021. **Update from the Cefazolin High Inoculum AHWG (Informational)** • Background – Penicillinase-producing staphylococci have been shown to be able hydrolyze cefazolin resulting in clinical failures. – Methicillin-susceptible *S. aureus* (MSSA) isolates that fail therapy were found to have cefazolin MICs that increased in proportion with the number of bacteria in the inoculum, a phenomenon known as the cefazolin inoculum effect (CIE). – The AHWG's goal is to develop an accurate and reproducible rapid CIE assay. • The AHWG Objectives include: – PHASE 1: Assess the prevalence of CIE phenotype in methicillin-susceptible *S. aureus* (MSSA) isolates in contemporary US strains – PHASE 2: Evaluate a rapid CIE assay in a multi-center study. If assay performs well, develop CLSI guidance on testing CIE in clinical laboratories. – PHASE 3: Obtain funding to perform an outcome study in CIE positive vs CIE negative patients. • Phase 1 has been completed and showed that an average of 17% of isolates exhibit CIE. A manuscript is in preparation for publication. • Phase 2 is in planning and a protocol using a rapid disk method has been developed. The AHWG is looking for donations of materials for the study (eg, BHI broth, microcentrifuge tubes, 1 µL loops, ampicillin disks, nitrocefin stock, tubes, and DMSO). **Update from the Direct Blood Culture Disk Diffusion AHWG (Votes needed)** • **Goal:** Define DD breakpoints for applicable gram-negative rods direct from positive blood culture bottle broth using 16-18 hr (overnight) and 8-10 hr (early) reads. • Data from the Direct Susceptibility Testing of Gram Negative Rods from Blood Cultures (ARLG DISK Study) for the Enterobacterales and seeded isolate testing for *P. aeruginosa* reviewed. – An overview of the procedure and study parameters was provided. The procedure using overnight reads has been approved (Summer 2020) and will be published in the 31st edition of M100. – The MDSWG voted to use the standard DD method at the site as the main comparator. – QC strains: *E. coli* ATCC® 25922, *E. coli* ATCC® 35218, and *P. aeruginosa* ATCC® 27853 • The AHWG requested VOTES as shown below for: – 8-10 h direct reads, applying current Table 2A Enterobacterales breakpoints for aztreonam, ceftazidime, ceftriaxone, and tobramycin. – 16-18 h (overnight) direct reads, applying current Table 2B-1 *P. aeruginosa* breakpoints for ciprofloxacin and meropenem. • The study data for the 8-10 hr reads applying the current breakpoints for Enterobacterales direct blood culture DD was presented. The voting requests are listed below.

#	Description

– **Aztreonam** (MDSWG vote 8-1-1 was contingent upon recommendations/review for/of QC method at 8-10 hours; 1 vote against was for early QC recommendation inclusion)

	S	I	R
Aztreonam	≥21 mm	18-20 mm	≤17 mm

– **SC discussion** (**Note:** Comments and questions may be paraphrased).
  - **Question**: Was the 8-hour QC was performed during the study? (**Response:** The 8-hour QC was performed and data was collected but the data has not yet been reviewed or discussed).
  - **Question**: Is there any evidence that the QC will be different for the 8-hour reads? (**Response:** The AHWG was not able to provide a definitive answer but it was noted that the data were difficult to assess before this meeting).
  - **Question**: Was the same procedure used for the QC strains as for the clinical strains? (**Response:** The QC strains were picked from a plate while the clinical strains were taken from the positive blood culture bottle).
- **NOTE: If the additional QC data does not support the vote, the vote will be voided.** The AHWG will consult with the QCWG regarding the issues related to QC at 8-10 hrs.

A motion to accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for aztreonam (S = ≥21 mm; I = 18-20 mm; R = ≤17 mm) with the caveat that early QC recommendations (pending QC data review and addition) are to follow was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).

– **Ceftazidime** (MDSWG: 10-0-0)

	S	I	R
Ceftazidime	≥21	18-20	≤17

– **SC discussion** (**Note:** Comments and questions may be paraphrased).
  - **Question**: Will labs assume that if you can read DD results from a blood culture bottle at 8-10 hrs. that DD results from an isolated colony on a plate can also be read at 8-10 hrs.? (**Response:** This issue will need to be discussed and will need to be clearly stated that the early reads are not validated for DD from isolated colonies. The AHWG believed that the direct method will not need to be confirmed. The appropriate wording will be provided before the next edition of M100 (32nd) publishes).
  - **Question:** Were manual blood culture bottles tested or only those from automated methods? (**Response:** Only bottles from automated systems were tested).
  - **Suggestion:** The QC strains might be tested from the blood culture bottles.
  - **Question:** Does the AHWG have confidence that enough isolates of the less frequently isolated organisms were tested? (Response: This issue was discussed by the AHWG and it was agreed that not all mechanisms of resistance were included. Further studies will be performed using seeded blood culture bottles. These breakpoints are not intended to be species specific but for all Enterobacterales.
  - **Comment**: Regarding QC, the goal is to devise a practical method and it would be very difficult for labs to seed blood culture bottles with QC strains. It was noted that all materials (plates, drug disks etc.) are routinely QC' d.

- **Comment**: Questions performing the QC using a different methodology with different incubation period than with the clinical isolates. (**Response:** The QC is going to be reviewed before the information is published).
- **Question**: What will the procedure for validating the procedure be communicated? (**Response:** A plan is in process for the QC, validation etc.

A motion to accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for ceftazidime (S = ≥21 mm; I = 18-20 mm; R = ≤17 mm) with the caveat that early QC recommendations (pending QC data review and addition) are to follow was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).

– **Ceftriaxone** (MDSWG: 10-0-0 PASS)

	S	I	R
Ceftriaxone	≥23	20-22	≤19

– **SC discussion:** No discussion was needed.

A motion to accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for ceftriaxone (S = ≥23 mm; I = 20-22 mm; R = ≤19 mm) with the caveat that early QC recommendations (pending QC data review and addition) are to follow was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).

– **Tobramycin** (MDSWG: 10-0-0 PASS)

	S	I	R
Tobramycin	≥15	13-14	≤12

– **SC discussion:** No discussion was needed

A motion to accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for tobramycin (S = ≥15 mm; I = 13-14 mm; R = ≤12 mm) with the caveat that early QC recommendations (pending QC data review and addition) are to follow was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).

- The study data for the 16-18 hr (overnight) reads applying the current breakpoints for *P. aeruginosa* direct blood culture DD (patient supplemented with isolates from seeded cultures) was presented. The voting requests are listed below.

– **Ciprofloxacin** (MDSWG: 10-0-0 PASS)

	S	I	R
Ciprofloxacin	≥25	19-24	≤18

- **SC discussion** (**Note:** Comments and questions may be paraphrased).
  - **Question:** Labs won't know what the organism is when the test is being done. How will labs know when to perform the reading? (**Response:** This issue will be addressed when the information is published).

A motion to accept the 16-18 hour direct DD reads for *P. aeruginosa* applying the current breakpoints for ciprofloxacin in Table 2B-1 (S = ≥25 mm; I = 19-24 mm; R = ≤18 mm) was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).

- **Meropenem** (MDSWG: 10-0-0 PASS)

	S	I	R
Meropenem	≥19	16-18	≤15

- **SC discussion:** No discussion was needed.

A motion to accept the 16-18 hour direct DD reads for *P. aeruginosa* applying the current breakpoints for meropenem in Table 2B-1 (S = ≥19 mm; I = 16-18 mm; R = ≤15 mm) was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).

- The AHWG path forward was reviewed. The plan includes:
  - Assess breakpoints other than the current ones for various antimicrobial agents with Enterobacterales with early and overnight reads.
  - Assess breakpoints for various antimicrobial agents with *P. aeruginosa* with early and overnight reads.
  - Perform *Acinetobacter* seeding studies.
  - Discuss M100 placement, including new table consideration.

- **Issues with the direct method with Tobramycin and *P. aeruginosa***
  - DD testing with 16-18 hr reads showed good results (1 minor error)
  - When seeded isolate reads were compared to MIC, there was 1 very major error (S by DD; R by MIC)(3.6%).
  - Same issue when tested by standard DD.
  - Patient isolates showed no issues when compared to MIC. MDSWG agreed that the appropriate comparator is standard DD method.

	S	I	R
Tobramycin	≥15	13-14	≤12

- **SC discussion** (**Note:** Comments and questions may be paraphrased).
  - **Comment**: The FDA standards for acceptability were reviewed and it was questioned whether the FDA would accept the breakpoints.

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	○ **Comment**: It was noted that the FDA fixes VMEs at 2%; however, new methods are compared to the reference method. In this case, the same method (DD) is being performed with a new inoculum. MIC is generally used as a secondary analysis for commercial systems. Since this is comparing DD to DD and there are so few discrepancies, this should not be a problem. ○ **Suggestion**: It should be made clear that this method is not a reference method but is a standard method that should always be performed the same way. ○ **Comment**: Concern regarding the comparison with MIC was expressed. DD breakpoints are based on MIC correlates; therefore, how are the results going to correlate with the MIC. ○ **Comment**: The right message and education needs to be provided to the users to emphasize that this is not a reference method but an alternative method. It would also not be acceptable as comparison for a new method.
	A motion to accept the 16-18 hour direct DD reads for *P. aeruginosa* applying the current breakpoints for tobramycin in Table 2B-1 (S = ≥15 mm; I = 13-14 mm; R = ≤12 mm) was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).
7.	**Adjournment**: Dr. Lewis closed the meeting at 4:00 PM Eastern (US) time.

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#	**Description**
PLENARY 3: FRIDAY 12 FEBRUARY 2021 (Number of Voting Members Present: 12 of 12)	
1.	Dr. Lewis opened the meeting at 1:00 PM Eastern (US) time.
2.	**Table 1 WG Report: Dr. Eliopoulos/Dr. Simner** **WG Roster:** George Eliopoulos, Trish Simner (Co-Chairholders); Virginia Pierce (Recording Secretary); Tanaya Bhowmick, April Bobenchik, Carey-Ann Burnham, Barth Reller, Sandy Richter, Lauri Thrupp, Matt Wikler **Dr. Simner reported on the activities of the Table 1 WG.** • **A recap of discussions at the Fall plenary was provided.** – The concept of an additional "Group" passed AST SC vote (9-2-1) – The primary concern was the term "Group" and it was suggested to rethink the category concept. A functional classification vs groups was considered. It was suggested to add cascading "rules" within the categories. – The WG discussed whether M100 is the correct place for Table 1 since Table 1 is specific for FDA-approved agents and doesn't consider non-US agents. – A suggestion to create an adjunct document on use of Table 1 and to provide extensive education on its use was made. • **The goals for the winter WG meeting were reviewed.** – Finalize the "group" names and definitions, re-evaluate the definition of "panel", and investigate tiered/or cascade reporting. – Work on assignments for the organism "groups" – Review IDSA guidelines for multiple-drug resistant organisms • **The WG discussed replacing the term "group" with "tiers".** – **Tier 1 (Group A)** - Agents considered appropriate for routine, primary testing, as well as for routine reporting of results for the specific organism groups. – **Tier 2 (Group B1)** – Agents that warrant primary testing, but may be reported routinely or only selectively (eg. organism is resistant to agents of the same antimicrobial class, as in Tier 1 [Group A]). – **Tier 3 (NEW: Group B2)** – Agents that may warrant primary testing, especially in institutions that harbor endemic or epidemic strains resistant to several primary drugs in Tiers 1 and 2 (Groups A and B1). Report agents selectively on MDRO strains as defined by institutional specific guidelines. – **Tier 4 (Group C)** – Alternative or supplemental agents that may require testing and reporting for treatment of patients allergic to primary drugs; for treatment of unusual organisms; or for reporting to infection control as an epidemiological aid. • **Suggestions for providing more guidance for testing and reporting of tiered agents were reviewed.** – Testing: o Tiers 1, 2, and 3 agent should be available in the laboratory for testing o Tier 4 agents are tested by request only and can be offered through the laboratory or through send-out testing. – Reporting o Reporting based on institutional guidelines but recommendations for reporting are provided in Table 1 o Agents released in a tiered approach based on the susceptibility profile o If agents from the same class are encountered within a Tier, cascading strategies are provided.

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#	Description

– Example table (horizontal presentation)

Tier 1 (Group A) - Antimicrobial agents that are considered appropriate for routine, primary testing, as well as for routine reporting of results for the specific organism groups	**Tier 2 (Group B1)** – Antimicrobial agents that warrant primary testing, but they may be reported routinely or only selectively, such as when the organism is resistant to agents of the same antimicrobial class, as in Tier 1 (Group A).	**Tier 3 (NEW: Group B2)** – Antimicrobial agents that may warrant primary testing, especially in institutions that harbor endemic or epidemic strains resistant to several primary drugs in Tiers 1 and 2 (groups A and B1). These agents should be reported selectively on multidrug-resistant strains as defined by institutional specific guidelines.	**Tier 4 (Group C)** – Alternative or supplemental antimicrobial agents that may require testing and reporting for treatment of patients allergic to primary drugs; for treatment of unusual organisms; or for reporting to infection control as an epidemiological aid.
Amoxicillin-clavulanate Ampicillin-Sulbactam Piperacillin-tazobactam			
Ampicillin[c]			
Cefazolin[d]	Cefuroxime		
Cefotaxime[c,d] or ceftriaxone[c,d]	Cefepime, Ertapenem, Imipenem, Meropenem	Ceftazidime-Avibactam, Cefiderocol, Imipenem-Relebactam, Meropenem-Vaborbactam	
Ciprofloxain, Levofloxacin			
Gentamicin[c]	Tobramycin → Amikacin		
Trimethoprim-Sulfamethoxazole[c]			
	Cefotetan, Cefoxitin		
	Tetracycline → Minocycline, Doxycycline*		
			Aztreonam
			Ceftaroline
			Ceftazidime
			Ceftolozane-Tazobatam
			Chloramphenicol
			Colistin
			Ceftaroline
Urine			
Cefazolin (surrogate for uUTI)			
Nitrofurantoin			
		Fosfomycin	
Reporting Tiers and Cascading within Tiers			Sulfisoxazole
			Trimethoprim

- **The WG requested guidance on how the SC wants to present Table 1.**
  - Provide testing guidance and be less prescriptive about reporting, or
  - Build in cascade reporting recommendations

- **Input on layout was requested**: Vertical (current layout with Tier definitions) vs horizontal layout (as shown in the example above)
  - Either layout would include a table separate from Enterobacterales for *Salmonella* and *Shigella*.
  - It was also questioned whether guidance regarding intrinsic resistance should be included.
  - **SC Discussion (Note: Comments or questions may be paraphrased).**
    - A number of SC members/advisors supported the change to a horizontal format. Reasons included:
      - It forces the user to think of the table in a new way and also promotes interaction between the lab and others in the institution outside the lab.
      - The horizontal format provides some guidance on antimicrobial stewardship.
      - The horizontal format has been used by UCLA for many years and is instrumental in teaching.
      - The horizontal layout is much clearer.
      - This table will be more useful and the additional guidance is valuable.
      - The horizontal format is more amenable to cascading.
    - Other SC members/advisors preferred the current system. Reasons included:
      - Prefer the current system and have reservations about cascade reporting due to some organisms having resistance profiles different than the norm.
      - Believes the cascading guidance may be too prescriptive and may be difficult to follow. Clear instructions for how to use the new format would be needed or some labs could interpret the guidance incorrectly.
      - Table 1 is intended for laboratory directors and should also take patient care into consideration. Care needs to be taken when "demoting" some of the newer agents which might delay therapy in patients with more difficult-to-treat infections. The implementation needs to be accompanied by extensive education.
    - Other discussion.
      - Table 1 seems to be intended for smaller labs that have more limited access to experts to guide them than at large, teaching institutions .
      - It was suggested that feedback from smaller community hospital labs as to how they would interpret the revised table might be useful.
      - General guidance on prioritizing drugs by keeping the groups broad and not too prescriptive would be very helpful for many hospitals without robust stewardship teams.
      - System manufacturer's also use Table 1 and smaller labs tend to follow what manufacturer's provide.
  - Dr. Lewis noted that the SC members are leaning toward the horizontal option with guidance on cascading but to be careful on how prescriptive to be.

- **Next steps**
  - Hold 2-3 virtual meetings before June to finalize our recommendations and have an AHWG vote
  - Submit our finalized recommendations for review and vote by the AST SC for the June meeting

#	Description

3. **Breakpoint WG (BPWG) Report (Part 1): Dr. Eliopoulos/Dr. Mathers/ Dr. Satlin**

WG Roster: George Eliopoulos, Amy Mathers, Mike Satlin (Co-Chairholders); Karen Bush (Recording Secretary); Marcelo Galas, Romney Humphries, Navaneeth Narayanan, Robin Patel, Simone Shurland, Lauri Thrupp, Hui Wang, Barbara Zimmer (Members); Matt Wikler (Advisor)

Cefiderocol BPs (Dr. Satlin)

- **History of cefiderocol breakpoints (BPs)**
  - CLSI approved investigational MIC BPs for Enterobacterales, *P. aeruginosa*, *A. baumannii*, and *S. maltophilia* which were published in January 2019 (S: ≤4 µg/mL; I = 8 µg/mL; 16 µg/mL). Disk diffusion (DD) BPs were also established for each group.
  - CLSI also approved broth microdilution (BMD) testing using iron-depleted cation-adjusted Mueller-Hinton broth (CAMHB).
  - FDA approved cefiderocol for complicated UTI and BPs for Enterobacterales (S: ≤2; I: 4; R: 8 µg/mL) and *P. aeruginosa* (S: ≤1; I: 2; R: 4 µg/mL) (Nov. 2019).
  - EUCAST approved BPs for Enterobacterales and *P. aeruginosa* in May 2020 (S= ≤2; R= >2) and none for *A. baumannii*, and *S. maltophilia* (insufficient evidence).
  - FDA increased BPs for Enterobacterales (4/8/16 µg/mL) and added the BPs for *A. baumannii* (1/2/4 µg/mL) in Sept 2020 with the approval of cefiderocol for HABP/VABP. No change for *P. aeruginosa*.

Current MIC BPs (µg/mL)

	CLSI			FDA			EUCAST	
Organisms	S	I	R	S	I	R	S	R
Enterobacterales	≤4	8	≥16	≤4	8	≥16	≤2	>2
P. aeruginosa	≤4	8	≥16	≤1	2	≥4	≤2	>2
A. baumannii	≤4	8	≥16	≤1	2	≥4	-	-
S. maltophilia	≤4	8	≥16	-	-	-	-	-

Current DD BPs

	CLSI			FDA		
Organisms	S	I	R	S	I	R
Enterobacterales	≥16	12-15	≤11	≥16	9-15	≤8
P. aeruginosa	≥18	13-17	≤12	≥22	13-21	≤12
A. baumannii	≥15	11-14	≤10	≥19	12-18	≤11
S. maltophilia	≥17	13-16	≤12	-	-	-

- **EUCAST Assessment Criteria was reviewed.**
  - Used all clinical isolate data from APEKS-cUTI, CREDIBLE-CR, and APEKS-NP.

- Conducted disk zone correlation studies using 5, 10, 15 and 30 µg disk mass and agreed to use 30 µg disk mass.
- Tentative ECOFF for BMD and disk diffusion (DD) was determined using a limited number of isolates.
- PTA was 95% PTA for 100% fT>MIC.
- No intermediate BP was set.

- **Shionogi (sponsor) Assessment**
  - BPs (4/8/16 µg/mL) are appropriate for all species.
    - Preclinical infection models using human drug exposure support efficacy of at least 4 µg/mL for Enterobacterales and non-fermenters
    - Robust PK/PD and PoP PK including patient ELF support BPs of 4/8/16 even for 100% fT>MIC in plasma and ELF
    - Clinical trial data support 4/8/16 µg/mL for Enterobacterales. Lower BPs for non-fermenters due to is lack of patients enrolled in clinical trials with higher MIC pathogens and not due to lack of efficacy data.

- **MIC distribution and susceptibility rate data for the organisms from Year 1 to 4 SIDERO-WT studies were reviewed.**
  - For all Enterobacterales, what is considered S by CLSI and FDA (4 µg/mL) is considered R by EUCAST.
  - Among Enterobacterales not susceptible to carbapenems, carbapenemase producing (KPC and MBLs) Enterobacterales are often non-susceptible by old FDA and current EUCAST breakpoints.
  - For all *P. aeruginosa*, susceptible is either 1, 2 or 4 µg/mL and resistant is either 4 or 16 µg/mL.
  - For carbapenem non-susceptible *P. aeruginosa* (#1 pathogen for compassionate care cases), 60% have MICs >1 µg/mL. Metallo-carbapenemase (particularly IMP) producing *P. aeruginosa* would be considered NS or R by FDA or EUCAST BPs.
  - For *A. baumannii*, cefiderocol is the first novel agent to have *A. baumannii* complex included in the HABP/VABP indication (imipenem/relebactam grandfathered for imipenem-susceptible strains via 505 (b) 2 application.

- **New data were presented for cefiderocol and included (See BPWG presentation here):**
  - Phase 3 clinical trial outcomes by MIC and species (APEKS-NP, CREDIBLE-CR, compassionate use case data)
    - Wunderink et al. *Lancet Infectious Disease*, online October 2020
    - Bassetti et al. *Lancet Infectious Disease*, online October 2020
  - Updated clinical PK/PD analyses (PoP PK and ELF penetration/pneumonia)
  - Updated frequency distribution ECVs
  - Updated disk zone correlation by species

- **Conclusions**

	Enterobacterales	*P. aeruginosa*
ECV	**>2 µg/mL** (ECV: 0.06 to 4 µg/mL) • Only *K. pneumoniae* showed ECV of 4 µg/mL	**>1 µg/mL** (ECV: 1 µg/mL)
Non-clinical PK/PD cutoff	**4 µg/mL** • Target $fT_{>MIC}$ of 75% on average for 1 log kill in mouse thigh/lung infection models • >95% PTA achieved against the isolates with MIC of 4 µg/mL based on plasma concentration from population PK from Ph 2/3 studies and target $fT_{>MIC}$ of 100% • Effective against the isolates with MIC of ≤4 µg/mL in neutropenic mouse thigh infection models under human PK	**4 µg/mL**

Clinical exposure response cutoff	Unable to assess because almost all patients in Ph 2/3 studies achieved PK/PD targets	
Clinical cutoff	**4 μg/mL** • No clear relationship between efficacy and MIC • Clinical success (8/10) was observed for the isolates with MIC of 4 μg/mL (APEKS-cUTI: 4/4, APEKS-NP: 1/2, CREDIBLE-CR: 3/4)	**2 to 4 μg/mL** • No clear relationship between efficacy and MIC • Clinical success (3/4, 2/2, 2/2) was observed for the isolates with MIC of 1, 2, 4 μg/mL, respectively • In compassionate use, clinical response was observed for 16/20 isolates with MIC of >1 (2: 10/13 isolates, 4: 5/5 isolates)

	A. baumannii	*S. maltophilia*
ECV	**1 μg/mL**	**1 μg/mL**
Non-clinical PK/PD cutoff	**4 μg/mL** • Target $fT_{>MIC}$ of 75% on average (88% for *A. baumannii* and 54% for *S. maltophilia*) for 1 log kill in mouse lung infection models • >95% PTA achieved against the isolates with MIC of 4 μg/mL based on plasma concentration from population PK from Ph 2/3 studies and target $fT_{>MIC}$ of 100% • Effective against the isolates with MIC of ≤4 μg/mL (≤0.5 μg/mL for *S. maltophilia*) in neutropenic mouse thigh infection models under human PK	**4 μg/mL**
Clinical exposure response cutoff	• Unable to assess because almost all patients in Ph 2/3 studies achieved PK/PD targets	
Clinical cutoff	**Insufficient information** • No clear relationship between efficacy and MIC • Clinical studies: only 2 isolates with MIC 1 (1/2 eradication and 2/2 cure), and 3 isolates with MIC 2 (1/3 eradication, 1/3 cure) • Compassionate use: only 1 isolate with MIC 2 (1/1 responded)	**Insufficient information** • No clear relationship between efficacy and MIC • Clinical studies: APEKS-NP: 1 isolate with MIC 0.25 (1/1 eradication and 1/1 cure), CREDIBLE-CR: 5 isolates with MIC ≤0.03-0.25 (0/5 eradication and 0/5 cure) • Compassionate use: no information

  - BPs of 4/8/16 μg/mL are proposed for all species
    - Preclinical infection models with human drug exposure support efficacy at 4 μg/mL for Enterobacterales and non-fermenters
    - Robust PK/PD and PoP PK including ELF support BPs of 4/8/16 μg/mL
    - Clinical trial data support 4/8/16 μg/mL for Enterobacterales; reason for lower BPs for non-fermenters is absence of data, not data showing lack of efficacy.
  - Conservative BPs are not informative (R does not predict failure) and potentially deprive patients of meaningful treatment

- **BPWG Discussion on MIC BPs. Issues discussed included:**
  - Differences with EUCAST (S:≤ 2 μg/mL for Enterobacterales and *P. aeruginosa*)
  - Variability in MICs by CLSI-approved methods
  - Clarification that compassionate use cases may have received multiple therapies (obtained because there were no other options)
  - There was a lack of cases of *S. maltophilia* in clinical trials.
  - Differences in FDA BPs: Related to lack of clinical data at MICs of 2 and 4 μg/mL in clinical trials with Enterobacterales and *P. aeruginosa*

- Differences in EUCAST BPs: Related to different ECVx and 95% target attainment
- **WG Vote:** Keep current BPs for cefiderocol and Enterobacterales and *P. aeruginosa* (≤4/8/≥16 µg/mL) – **Pass** (6 yes, 0 no, 2 abstain, 4 absent)
- **WG Vote:** Keep current BPs for cefiderocol and *A. baumannii* (≤4/8/≥16 µg/mL) – **Fail** (3 yes, 2 no, 4 abstain, 3 absent)
  - No votes were related to insufficient clinical data
  - WG discussed possibility of expanding the intermediate range to account for uncertainty
  - It was noted that there was a mortality imbalance with *A. baumannii* in CREDIBLE-CR study
  - PK/PD data in neutropenic mouse model were comparable to trials
- **WG Vote:** Set S-only BP for *S. maltophilia* (≤1 µg/mL) – **Fail** (3 yes, 2 no, 3 abstain, 4 absent)
  - No votes were related to the lack of clinical data
  - WG discussed retaining as "INV" even though the drug is FDA approved
  - There was a suggestion to move *S. maltophilia* to M45, but it is not an uncommon or fastidious organism

- **SC Discussion (Enterobacterales and *P. aeruginosa*)(Note: Comments and questioned may be paraphrased)**
  - **Question**: Data seems to be based on 1-log kill. 2-log kill is usually preferred so could this have caused the difference with the FDA? (**Response:** The FDA primarily based their decision on lack of clinical outcome data. During studies it was difficult to reach a 2-log kill so a 1-log kill for calculations was used.)
  - **Question:** How will this drug be handled by automated system manufacturers? Responses and comments included:
    - The automated system manufacturers must follow the FDA STIC website for their information. With more harmonization between CLSI and FDA, the process is more streamlined for adding new drugs to AST systems. Rationale documents posted by CLSI help to alleviate discrepancies between FDA and CLSI.
    - Manufacturer's must use FDA BPs if there are discrepancies between FDA and CLSI unless FDA accepts CLSI rationale.
    - The data presented to CLSI are the same data reviewed by the FDA and EUCAST in 2020. It was noted that special media is needed to test the drug; therefore, it is difficult for manufacturers to add cefiderocol to automated devices.
    - Most labs will likely use DD to test cefiderocol and need to validate the results. Most will also go to CLSI for guidance and DD is the fallback when automated system can't be used.
    - It was noted that accreditation organizations in the US have no preference for using FDA over CLSI and vice versa.
    - It was noted that in one volunteer laboratory, the FDA BPs for DD were validated but with new data, the CLSI BPs seem more clinically significant. Specific guidance on what BPs to use was requested.
    - It was suggested that CLSI can help labs by providing a list of organisms and expected results to perform the verification. Some isolates may be available from the CDC AR bank.
  - The compassionate use data showed that many isolates were not susceptible using the FDA BPs. It was suggested that it may be worth setting BPs different from the FDA. The FDA may not approve a rationale document based on data they have already seen.
  - Concern was expressed that labs seem to be uneasy about testing new drugs that have the potential to treat MDR infections that don't respond to older drugs (eg, compassionate use of cefiderocol). The discovery of new antimicrobial agents with improved antibacterial properties should not be de-incentivized.
  - The sponsor noted that the FDA reviewed the compassionate use data but did not consider it. Other drugs were tested and most except cefiderocol tested resistant.
  - Based on the data, the BP of ≤4 for S appears to be confirmed.

SUMMARY MINUTES	
#	Description
	A motion to retain the cefiderocol MIC CLSI breakpoints (≤4/8/≥16 µg/mL) for Enterobacterales and *P. aeruginosa* was made and seconded. VOTE: 10 for, 0 against, 0 absent, 2 abstentions (Conflicts: Dr. Satlin, Dr. Simner). (Pass)
	• **SC Discussion (*A. baumannii*) (Note: Comments and questioned may be paraphrased.)** – **Question:** Is the intermediate range is wide enough to account for variability and will this cause issues during testing? The QC ranges for cefiderocol are published in M100, 30th ed. for *P. aeruginosa* ATCC® 27853 as 0.06-0.5 µg/mL for MIC and 22-31 mm for disks and for *E. coli* ATCC® 25922 at 0.06-0.5 µg/mL for MIC and 25-31 mm for disks. – Despite the lack of clinical outcome data, it was suggested that the clinical outcome data be put aside and the SC should consider establishing BPs based on PK/PD, MIC distributions, and the neutropenic mice model data. *Acinetobacter* and *Stenotrophomonas* are problematic but generally patients don't die from infections (infection vs colonization) and may depend on the status of the host. Believed that there is too much emphasis on the clinical outcome data. – If the BP is going to be based on data without clinical outcomes, it was suggested that a comment about the lack of clinical outcome data could be included with the BP. – It was noted that FDA-CDER's rule for setting the upper limit of susceptible BPs is the highest MIC that was successfully treated in the clinical trial.
	A motion to retain the cefiderocol MIC CLSI breakpoints (≤4/8/≥16 µg/mL) for *A. baumannii* was made and seconded. VOTE: 7 for, 1 against, 1 absent (Dr. Limbago), 3 abstentions (Dr. Satlin, Dr. Simner, Ms. Cullen). (Pass) – **Vote against** (Dr. Galas): Didn't believe there was enough clinical outcome data.
	• **SC Discussion (*S. maltophilia*) (Note: Comments and questions may be paraphrased.). Comments and suggestions included:** – There are limited BPs available for *S. maltophilia* and it can be challenging to find therapy even though there is a lack of clinical data. – *S. maltophilia* is not on the FDA drug label as an indication for cefiderocol and there is no FDA STIC BP. So, this will not facilitate availability for commercial devices. It is the responsibility of the lab to validate. – Additional PK studies were performed by Dr. Nicolau's group and the data have been published. Cefiderocol was effective against organisms with cefiderocol MICs of 1 µg/mL. – . – The data haven't shown that the CLSI BPs originally approved are incorrect except for the lack of clinical data. Guidance needs to be provided. – There does not appear to be enough data to keep the original breakpoints but, in some labs, many isolates tested had very low MICs. The BPs can be re-evaluated as more data become available. – Additional data presented for *S. maltophilia* with cefiderocol showed that cefiderocol MICs stayed below 0.5 µg/mL.
	A motion to approve a susceptible BP of ≤ 1 µg/mL and non-susceptible BP of >1 µg/mL for *S. maltophilia* with cefiderocol and including a comment regarding limited data was made and seconded. VOTE: 7 for, 2 against, 2 abstentions (Dr. Satlin, Dr. Simner), 1 absent (Dr. Limbago) (Pass) – **Vote against (Dr. Richter, Ms. Cullen):** o Ms. Cullen needed to see the comment to see if it will address concerns. o Dr. Richter was not comfortable with lack of clinical data.

SUMMARY MINUTES	
#	Description
	• **SC Discussion (DD BPs Enterobacterales):** No discussion was needed. **A motion to approve the current FDA DD breakpoints for cefiderocol with Enterobacterales (S ≥ 16 mm; I 9-15 mm; R ≤8 mm) was made and seconded. VOTE: 8 for, 1 against, 2 abstain (Dr. Satlin, Dr. Simner), 1 absent (Dr. Limbago). (Pass)** – **Vote against (Ms. Cullen from chat):** I struggle with the harmonization vs variability (concerns about disk performance) and prefer wider range. But can support the majority vote – **Dr. Weinstein:** Expressed concerned about the lower end of the range getting close to the disk. • **SC Discussion (DD BPs *P. aeruginosa*)** – BPWG vote to approve the disk correlates (6 yes, 0 no, 3 abstain, 3 absent) – There was concern regarding the lack of resistant isolates. – **Question:** How many compassionate use isolates are available and will the SC be able to see them against the disks? It would be helpful to see results from isolates with higher MICs. (**Response:** All MICs presented were sent to IHMA and should be available for additional susceptibility testing and zone size calibration. However, most did not have high MICs.) – **Question:** Are there any *P. aeruginosa* isolates from surveillance studies with higher MICs? (**Response:** Most did not have MICs above 8 µg/mL. They are very rare.) – **Question:** Were data presented to support an intermediate range of 13-15 mm? Seems an intermediate at 13-15 works. (**Response:** 3 mm I range might be too tight as per the QC ranges. – The current QC ranges for cefiderocol and *P. aeruginosa* in M100, 30th ed. are 22-31 mm. The intermediate range would then be 4-5 mm range. Variability with cefiderocol and *P. aeruginosa* is low. **A motion to approve the DD breakpoints for cefiderocol and *P. aeruginosa* (S: ≥18 mm, I: 13-17 mm, R: ≤12 mm) was made and seconded. VOTE: 10 for; 0 against; 2 abstain (Dr. Satlin, Dr. Simner); 0 absent. (Pass).** • **SC Discussion (DD BPs *A. baumannii*)** – BPWG vote to approve the disk correlates (6 yes, 0 no, 3 abstain, 3 absent). o It was noted that MIC BPs would need to be established. o There were VMEs (3%) and minor errors (mE) (25.4%) with the proposed intermediate range. – There was concern regarding the percentage of mEs. It was noted that the result could be confirmed using an MIC method; however, practically, this is not always available and *A. baumannii* is difficult to read. It was suggested a comment might be included. – It was agreed that a comment directed at the labs would be helpful with regards to the high mEs that may occur during verification. – **Comment:** Agree with the 'comment' idea, but it is difficult to determine where to draw the line. Perhaps there should be an S-only BP.The mEs will be a problem for labs that try to verify the BP. – The SC discussed the possibility of setting an S/NS-only DD BPs. o There was concern about what labs will be able to do with an S-only BP and an intermediate range would be preferred. o From the chat: Agree with the S-only BP at 15 mm. These data show that zones < 15 are either S, I or R (ie, no answer). Suspected that the variation in zones with some of the resistant isolates may be due to how the inner colonies are read. Also agree with comment that MIC and disk replicate testing of some of these strains is warranted and may be a good way to resolve the intermediate/resistant breakpoint in the future – A comment was suggested: “Correlation of disk to MIC was low for isolates characterized as resistant by MIC.”

SUMMARY MINUTES	
#	**Description**
	A motion to approve the susceptible-only DD breakpoint for cefiderocol and *A. baumannii* (S: ≥15 mm) (with MIC BPs as approved) and with a comment regarding evaluating zone sizes of 14 and below was made and seconded: VOTE: 8 for; 2 against (Dr. Humphries, Ms. Cullen); 2 abstain (Dr. Satlin, Dr. Simner); 0 absent. (Pass)
	– Votes against were due to issues related to the errors that will be generated during verification and an intermediate range is needed. – It was requested that additional data (triplicate disk data with some of the "problematic" strains) be generated (ideally for the June meeting) so that an intermediate BP be set. – It was noted that a guideline for reading the BMD would be helpful. (Note: A reviewer of this summary has noted that a guideline already exists for this in 2020 M100; see Appendix I3, pg. 275-276 Determining Broth Microdilution End Points. It includes 2 pictures for reading cefiderocol end points.) • **SC Discussion (DD BPs *S. maltophilia*)** – BPWG did not vote, as an MIC BP had not yet been set. – **Question:** What is known about reading/reproducibility with *S. maltophilia*? (**Response:** The zones are generally very large and easy to read.) – Data appear to be cleaner. – There was concern regarding the lack of clinical data.
	A motion to approve the S/NS DD breakpoints for cefiderocol and *S. maltophilia* (S: ≥15 mm, NS: ≤14 mm) was made and seconded. VOTE: 9 for, 1 against (Dr. Richter); 2 abstain (Dr. Satlin, Dr. Simner); 0 absent. (Pass).
	– Vote against was due to concern regarding the lack of clinical data. – Addition of a comment for *S. maltophilia* was discussed. o Comment would clarify the data used to set the S-only MIC BP. o It was suggested that the definition of NS be clarified in M100. **A motion to include a comment regarding the origin of the susceptible-only cefiderocol MIC BP for *S. maltophilia* (Suggested: The susceptible breakpoint is based on PK/PD, MIC distributions and limited clinical data.) was made and seconded. VOTE: 10 for; 0 against; 2 abstain (Dr. Satlin, Dr. Simner); 0 absent. (Pass)**
4.	**Adjournment**: Dr. Lewis closed the meeting at 4:00 PM Eastern (US) time by thanking the participants for their excellent work.

SUMMARY MINUTES	
#	**Description**
PLENARY 4: MONDAY, 22 FEBRUARY 2021 • **Number of Voting Members Present: 12 of 12**	
1.	Dr. Lewis opened the meeting at 3:00 PM Eastern (US) time.
2.	**Breakpoint WG Report (Part 2): Dr. Eliopoulos/Dr. Mathers/ Dr. Satlin** **WG Roster:** George Eliopoulos, Amy Mathers, Mike Satlin (Co-Chairholders); Karen Bush (Recording Secretary); Marcelo Galas, Romney Humphries, Navaneeth Narayanan, Robin Patel, Simone Shurland, Lauri Thrupp, Hui Wang, , Barbara Zimmer (Members); Matt Wikler (Advisor) **NOTE: See the summary for February 12th for the completion of the minutes for the Cefiderocol presentation.** **Lefamulin Breakpoints (Dr. Satlin)** • **History** – Lefamulin approved for treating community-acquired bacterial pneumonia (CABP) in August 2019. The following organisms are on List 1 in the FDA label: *S. pneumoniae*, *S. aureus* (methicillin susceptible), and *H. influenzae*. The following organisms are on List 2:, *S. aureus* (MRSA), *S. agalactiae*, *S. anginosus*, *S. mitis*, *S. pyogenes*, *S. salivarius, H. parainfluenzae*, and *M. catarrhalis*. – Summer 2020: AST SC approved susceptible-only FDA BPs for *S. aureus* (MSSA and MRSA) (MIC: ≤0.25 µg/mL; DD: ≥23 mm), *S. pneumoniae* (MIC: ≤0.5 µg/mL; DD: ≥17mm), and *H. influenzae* (MIC: ≤2 µg/mL ; DD: ≥17mm). o The BPWG noted that the challenge set of isolates for *S. aureus* used gradient diffusion, not BMD, for comparison with DD. o There were few isolates above the BPs for *S. pneumoniae* and *H. influenzae*. The sponsor was asked to provide more data at the Winter 2021 meeting. • **New data for DD BPs for *S. pneumoniae* were presented.** – DD BPs approved in Summer 2020: DD: S ≥17 mm; NS: ≤16 mm. o There were no non-susceptible isolates, preventing assessment for very major errors (VME) o Additional data were requested. – A challenge set of *S. pneumoniae* isolates with lefamulin MICs around the BP (2.2% NS isolates compared to 0.12% NS in surveillance) were tested using BMD and DD and additional data were pulled from studies completed since Summer 2020. o NS isolates at the end of the MIC WT distribution produces a VME rate of 15.9% in S+R MIC range when the current provisional BP (≥17 mm) was applied o dBETS suggested BPs of S: ≥19 mm; NS: ≤18 mm – 3 Options for setting *S. pneumoniae* DD BPs were presented by the BPWG. o **1A) Set S/NS disk BPs (S: ≥19 mm; NS: ≤18 mm);** New BPs are within M23 guidance for errors with challenge set o **1B) Set N/S disk BPs (same as #1) with a comment**: "Confirmatory MIC testing is indicated for isolates with zones of 17-18 mm to avoid reporting false-resistant results" given that 15/20 isolates with disk zones of 17-18 mm (NS by disk) were S by MIC. o **Assign S/I/R BPs** ▪ MIC BPs: S: ≤0.5 µg/mL; I: 1 µg/mL; R: ≥2 µg/mL ▪ DD BPs: S: ≥20 mm; I: 17-19 mm; R: ≤16 mm – BPWG Discussion o There were concerns regarding setting an "I" BP. These included:

- Dropoff in percent target attainment (PTA) at 1 µg/mL. (Note: the drop off is only in ELF PK/PD and in free-drug plasma PTA when evaluated using randomly assigned variation. There was no drop off using the standard Median plasma PK/PD targets)
- Unknowns regarding a new drug class and translation of animal models
- Appropriate PTA for an "I" category is unclear (Note: Although PTA using the standard median plasma PK/PD targets were > 97%)

  - Concern that adding a comment recommending MIC testing may make it difficult for labs that don't perform MIC testing
  - The data showed that MIC and DD results were very reproducible.

- BPWG Vote
  - Option 1: Set DD BP as S: ≥19 mm and NS: ≤18 mm with no comment.
  - Passed: Yes (10), No (0), Abstain (0), Absent (2)

- **New data for DD BPs for *S. aureus* were presented.**
  - DD BPs approved in Summer 2020: DD – S: ≥23 mm; NS: 22 mm
    - Applying susceptible BP of≤0.25 µg/mL (≥23 mm), 1 major error (ME)(false-resistant; 0.3%) occurred due to an MRSA isolate.
    - No very major or major errors with sponsor proposed susceptible BP of ≤0.25 µg/mL (≥22 mm)
  - Additional NS isolates with defined lefamulin resistance mechanisms and susceptible isolates were tested by BMD and DD after the summer meeting.
    - Disk zones and MICs correlated well and S isolates were separated well from NS isolates
    - Low rate of VME and no ME
    - Most VMEs are detected for isolates with a lefamulin MIC of 0.5 µg/mL, that may be genotypically WT or resistant
    - dBETS agreed with disk correlate approved in Summer 2020.
  - Options for setting DD BPs
    - Keep current disk breakpoints S: ≥23 mm; NS: ≤22 mm
    - Assign S/I/R BPs
      - MIC BPs: S: ≤0.25 µg/mL; I: 0.5 µg/mL; R: ≥1 µg/mL
      - DD BPs: S: ≥23 mm; I: 20-22 mm; R: ≤19 mm
  - BPWG: There was consensus that the provisional BPs worked well and no changes were needed.

- **New data for DD BPs for *H. influenzae* were presented.**
  - DD BPs approved in Summer 2020: S: ≥17 mm); NS: ≤16 mm
    - Only 1 NS isolate tested
    - No MEs detected when applying the approved BP of ≤2 µg/mL (≥17 mm)
    - Could not assess for VMEs due to lack of NS isolates
    - Additional data were requested
  - Challenge set of *H. influenzae* isolates tested with lefamulin MICs around the BP (8.1% NS isolates compared to 0.94% NS in surveillance) and additional data pulled from studies completed since Summer 2020
    - NS isolates at the end of the MIC WT distribution produced VME rate of 22.1% in S+R MIC range when applying the current BP of ≥17 mm
    - dBETS: Suggested BPs of S: ≥18 mm; NS: ≤17 mm
  - 4 Options for DD BPs for *H. influenzae*
    - 1A) **Set S/NS disk breakpoints**: S: ≥18 mm; NS: ≤17 mm
    - 1B) **Set N/S disk breakpoints (same as #1) with a comment**: "Confirmatory MIC testing is indicated for isolates with zones of 15-17 mm to avoid reporting false-susceptible or false-resistant results"

- 2A) **Assign S/I/R disk diffusion breakpoints and S/R for MICs**
  - MIC BPs: S: ≤2 µg/mL; R: ≥4 µg/mL
  - DD BPs: S: ≥21 mm; I: 18-20 mm; R: ≤17 mm
- 2B) **Assign S/I/R DD and MIC BPs**
  - MIC BPs: S: ≤2 µg/mL; I: 4 µg/mL; R: ≥8 µg/mL
  - DD BPs: S: ≥18 mm; I: 15-17 mm; R: ≤14 mm

– BPWG Discussion
- Concerns included:
  - High VME rate with Option 1
  - Applying an "I" category: Only 1 dosing option and no PK/PD models ("I" would only be assigned for technical uncertainties)
- It was agreed that there were no issues with reading disk zones

– BPWG Vote
- Option 1: S/NS DD BPs (S: ≥18 mm; NS: ≤17 mm) with no comment
- Passed: Yes (9), No (0), Abstain (0), Absent (3)

• **SC Discussion**

– Proposed Disk Breakpoints (Options 1 and 2)

Organism	FDA and Provisional CLSI S/NS Breakpoints		Option 1: Revision of Disk Breakpoints for S/NS		Option 2: Introduction of Intermediate Category for S/I/R Breakpoints	
	MIC (µg/mL)	Disk (mm)	MIC (µg/mL)	Disk (mm)	MIC (µg/mL)	Disk (mm)
	S/I/R	S/I/R	S/I/R	S/I/R	S/I/R	S/I/R
S. pneumoniae	≤0.5/-/-	≥17/-/-	≤0.5/-/-	≥19/-/-	≤0.5/1/≥2	≥20/17-19/≤16
S. aureus	≤0.25/-/-	≥23/-/-	≤0.25/-/-	≥23/-/-	≤0.25/0.5/≥1	≥23/20-22/≤19
H. influenzae	≤2/-/-	≥17/-/-	≤2/-/-	≥18/-/-	Opt. 2A: ≤2/-/≥4 (Opt. 2B: ≤2/4/≥8)	Opt. 2A: ≥21/18-20/≤17 (Opt. 2B: ≥18/15-17/≤14)

– SC Discussion
- It was noted that S/NS BPs were approved for MIC and that the preference was to keep S/NS BPs for DD.
- **Question:** Why wasn't a comment pursued for *S. pneumoniae*? **Response:** The BPWG thought the performance was reasonable and a comment could put the laboratory in a difficult spot. These types of isolates are relatively rare.

#	Description

A motion to approve the DD correlate BPs from Option 1 for lefamulin for *S. pneumoniae* (S: ≥19 mm; NS: ≤18 mm), *S. aureus* (S: ≥23 mm; NS: ≤22 mm), and *H. influenzae* (S: ≥18 mm; NS: ≤17 mm) was made and seconded. VOTE: 11 for; 0 against; 0 abstain; 1 absent (Dr. Gold). (Pass)

Sponsor request for lefamulin BPs for List 2 organisms

- **Proposal for *Streptococcus* BPs**
  - ß-hemolytic streptococci can rarely cause CABP, and may be severe.
  - Proposed MIC BPs and DD correlates: S: ≤0.25 µg/mL (≥19 mm); NS: ≥0.5 µg/mL (≤18 mm)
  - ECV was 0.06 µg/mL
  - *S. pneumoniae* PK/PD cut-offs were proposed as a surrogate.
  - The number of cultured clinical isolates at baseline in the Phase 3 CABP studies and in the Phase 2 ABSSI trial was small
  - Requested BPs - S: ≤0.25 µg/mL (≥19 mm); NS: ≥0.5 µg/mL (≤18 mm)
  - Viridans group streptococci can rarely cause pneumonia with empyema or parapneumonic effusion (FDA-recognized as a cause of CABP)
    - Isolates include *S. mitis*, *S. anginosus*, and *S. salivarius* (included on FDA label)
    - ECVs were between 0.5 and 1 µg/mL
    - *S. pneumoniae* PK/PD cutoffs were proposed as a surrogate
    - Requested BPs - S: ≤0.5 µg/mL (≥18 mm); NS: ≥1 µg/mL (≤17 mm)
  - BPWG Discussion
    - AHWG: Some members thought BPs for ß-hemolytic strep reasonable because of clinical outcomes in Phase 2 skin and soft tissue study and 2 isolates in LEAP trials
    - Concern due to lack of PK/PD data for ß-hemolytic strep and assumptions from *S. pneumoniae*
    - Concern about applying clinical data from skin and soft tissue infections to pneumonia although the infections due to ß-hemolytic streptococci were severe and the clinical success rate was high
    - Concern that viridans group strep not usually a respiratory pathogen
    - BPWG Vote for lefamulin and ß-hemolytic strep BPs

Pathogen	MIC (µg/mL)			Disk diffusion (mm)		
	S	I	R	S	I	R
Beta-hemolytic streptococci	≤0.25	-	-	≥19	-	-

    - **5 for; 5 against; 0 abstain; 2 absent (Did not pass).** Objections due to lack of clinical data in community-acquired bacterial pneumonia or PK/PD and difficulty in getting commercial systems approved without FDA BPs.
    - No motion was made for viridans group strep

  - **SC Discussion**
    - **Comment:** The lack of clinical data should be kept separate from the issue of the difficulty getting commercial systems approved without FDA BPs.
    - There was concern about the using the *S. pneumoniae* PK/PD surrogate.
    - There was concern that a decision about ECVs is not a clinical one. ECVs are confusing for labs and there was concern for applying the ECV as a BP.

- It was noted that there are many alternatives for treatment of ß-hemolytic streptococci and it was questioned if the drug would even be used for this organism. However, it was also noted that potential use of a new drug is generally not be taken into account for setting BPs; and Table 1 provides guidance for testing and reporting.

A motion to approve an ECV for lefamulin for ß-hemolytic streptococci (S: ≤0.06 µg/mL) was made and seconded. VOTE: 3 for, 8 against, 0 abstain, 1 absent (Dr. Gold). (Fail)

- No votes taken
  - Lack of clinical and PK/PD data for ß-hemolytic streptococci in community-acquired bacterial pneumonia
  - The Subcommittee believed that there was little value in setting an ECV or BP at the present time.

- **Proposal for *M. catarrhalis*: Request for BPs to be added to M45**
  - *M. catarrhalis* primarily diagnosed by PCR applying a conservative cut-off value corresponding to ≥0.5x10^6 CFU/mL in sputum
  - Assumed that the MICs of most *M. catarrhalis* pathogens identified by PCR-only would be below the ECV. Therefore, the good clinical success for *M. catarrhalis* in these patients supports an S/NS BP for the WT population set at the ECV.
  - Proposed BPs
    - Option 1: ≤ 0.5 µg/mL (≥19 mm)
    - Option 2: ≤ 0.25 µg/mL (≥19 mm)
  - BPWG Discussion
    - AHWG was comfortable with S at ≤ 0.5 µg/mL (≥19 mm) (for M45)
    - Concern for lack of PK/PD model
    - BPWG vote for lefamulin and *M. catarrhalis* (9 for; 0 against; 1 abstain; 2 absent)

Pathogen	MIC (µg/mL)		Disk diffusion (mm)	
	S	NS	S	NS
Moraxella catarrhalis	≤0.5	≥1	≥19	≤18 mm

A motion to accept S/NS BPs for lefamulin with *M. catarrhalis* (MIC-S: 0.5 µg/mL and NS: ≥1 µg/mL; DD-S: ≥19mm and NS: ≤18 mm) to be added to M45 was made and seconded. VOTE: 12 for, 0 against, 0 abstain, 0 absent. (Pass)

Aminopenicillin (A4) AHWG Report

- **Background**
  - AHWG was charged with reviewing the validity of the current aminopenicillin BPs.
  - BPs for streptococci, *N. meningitidis* and *Haemophilus* with ampicillin, amoxicillin, amoxicillin/clavulanate, and ampicillin/sulbactam were reviewed.
  - BPs were also compared to those for EUCAST to determine if harmonization is possible.
  - The review of the following BPs was presented.

Table	Organism	Ampicillin	Amoxicillin	Amox/clavulanate	Amp/Sulbactam
2E	*Haemophilus*	1/2/4	amp surrogate	4/8	2/4

2G	*S. pneumoniae*	none	2/4/8	2/4/8	none
2H-1	B-streptococci	0.25/	penicillin surrogate		
2H-2	viridans strep.	0.25/	none		
2I	*N. meningitidis*	0.125/	none		

- The current CLSI and EUCAST BPs were reviewed.

Table	Organism	Ampicillin	Amoxicillin	Amox/clavulanate	Amp/Sulbactam
CLSI	*S. pneumoniae* (non-CSF)	none	2/4/8	2/4/8	none
EUCAST		0.5/4	0.5/2 (PO)*	0.5/2 (PO)*	amp surrogate
CLSI	B streptococci	0.25/	penicillin surrogate		
EUCAST		penicillin surrogate			
CLSI	Viridans streptococci	0.25/0.5-4/8	none		
EUCAST		0.5/4	0.5/4	penicillin surrogate	
CLSI	*N. meningitidis*	0.125/0.25-1/2	none		
EUCAST	non-CSF;CSF	0.125/2;none	0.125/2;none	none	
CLSI	*H. influenzae, H. parafluenzae*	1/2/4	amp surrogate	4/8	2:1/4:2
EUCAST		1/2	2/4 or 0.001/4 (IV or PO)	2/4 or 0.001/4 (IV or PO)	1/2

- **Ampicillin-sulbactam (Amp-Sul) for *Haemophilus* spp.**
  - PK
    - Variable results: Study dependent
    - Some show easy achievement of S-BP with 1.5 g Q8h at Ft>MIC of 40% but others indicate 3g q6hr may be needed
    - Good achievement of T>MIC with PK data shown
  - Clinical data
    - Community acquired pneumoniae: All treated with a dosage of 1.5g to 3g q 6h (based on renal function) showed were cured or improved
    - Otitis media in children: Oral Amp/Sul 50 mg/kg/d showed 100% success rate with completed therapy
  - AHWG recommendation: Retain the current BP but add dosage comment to M100
    - Suggested: The susceptible BP is based on a dosage regimen of 3g administered intravenously every 6 to 8 hrs.
    - BPWG vote: 10 for, 0 against, 0 abstain, 2 absent
  - **SC Discussion**
    - The time associated with administration was questioned (every 6 vs every 8 hrs). It was recommended that 6 hr. intervals as it has a better time above the MIC exposure.
    - It was questioned if all drugs in M100 should include a dosage regimen for each BP.
      - It was noted that new drugs added to M100 do include the dosage regimen on which the BP is based.
      - For older drugs, it was suggested that the dosage regimen be added if there are data that are supportive. For older drugs, it might be difficult to find the appropriate data.

- This is provided to indicate that the BP is based on the dosage regimen and that most of the data is based on 6 hrs.

A motion to add a dosage regimen comment for *Haemophilus* spp. with the current BP for ampicillin-sulbactam that states (or with similar language as determined by the Text and Tables WG), "BP dosage is based on dosage regimen of 3g IV administered every 6 hrs." was made and seconded. VOTE: 12 for; 0 against, 0 abstain, 0 absent. (Pass).

- **Amoxicillin and Amoxicillin-clavulanate (Amox-Clav) for non-CSF *S. pneumoniae***
  - History
    - BPs of S ≤2, I = 4, R ≥8 µg/mL adopted (1999) with a comment: "Data on clinical and microbiologic outcomes of pneumococcal infections due to penicillin resistant strains treated with various oral ß-lactam agents are limited. In some cases, breakpoints have been based primarily on pharmaco-kinetic and pharmacodynamic considerations" and no specified dosage regimen.
    - Review of publications showed:
      - PTA for various amoxicillin dosing regimens shown to reach the PD target 40% *f*T>MIC for a range of MICs.
      - Monte Carlo simulations from oral amoxicillin regimens in healthy volunteers indicated 95% PTA for the population reached the PD target 40% f>MIC
      - Neutropenic murine thigh model using a dosage equivalent to human 500 mg of amoxicillin q8h showed that there was a 3-4 log drop in S. pneumoniae numbers with an amoxicillin MIC ≤ 2 µg/mL while treatment was ineffective at MIC ≥ 4 µg/mL.
      - Clinical data for otitis media and pneumonia showed that there was ≥ 90% efficacy against otitis media in children for MIC ≤ 2 µg/mL and good evidence that amoxicillin 500 tid to 875 bid is effective for pneumococcal pneumonia at current BP.
  - **AHWG Recommendation**: Retain the current BPs and add a dosage regimen comment
    - Suggested: The susceptible breakpoint is based on an orally administered amoxicillin component dosage of 500 mg given every 8 hours or 875 mg given twice daily.
    - BPWG vote: 11 for, 0 against, 0 abstain, 1 absent
  - **SC Discussion**: No discussion was needed.

A motion to add a dosage regimen comment in Table 2G for *S. pneumoniae* with the current BP for amoxicillin and amoxicillin-clavulanate (non-meningitis) that states (or with similar language as determined by the Text and Tables WG): "The susceptible breakpoint is based on an orally administered amoxicillin component dosage of 500 mg administered every 8 hrs. or 875 mg administered every 12 hrs." was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).

- **Ampicillin for ß-hemolytic *Streptococcus***
  - History
    - 1995: Penicillin (S: ≤0.12; I – 0.25-1; R ≥ 2 µg/mL) and ampicillin (S: ≤0.25; I – 0.5-2; R ≥ 4 µg/mL) BPs for non-pneumococcal streptococci approved without supporting clinical data.
    - 2002: Non-pneumococcal streptococci separated into beta- and alpha- tables, no change in the S BP and elimination of non-S categories for ß
    - Review of publications showed:
      - PTA for various amoxicillin dosage regimens reach the PD target 40% $fT_{>MIC}$ for a range of MICs
      - Clinical studies for ß-strep infection showed:
        - Ampicillin dosage of 125 to 250 mg oral tid highly effective for Grp. A streptococcal pharyngitis

- Ampicillin dosage of 500 mg IV intrapartum stops neonatal colonization with GBS in colonized women 0% vs. 50% (amp vs control), and decreases group B streptococcus neonatal sepsis rate
- Amoxicillin dosage showed 250 mg to 500 mg PO tid cured almost all cases of otitis media, pneumonia, and skin and soft tissue infections

– AHWG Recommendation
  - No BP changes
  - PTA/PK seems to be sufficient
  - Few clinical data are available.
  - No clinical signals have been observed.
  - Retain comment regarding the lack of clinical data
– SC Discussion: No discussion or change to the document was needed.

- **Ampicillin and amoxicillin for Viridans streptococci**
  – Review of publications showed:
    - PTA for various amoxicillin dosing regimens reach the PD target 40% $fT_{>MIC}$ for a range of MICs
    - Clinical and PD data
      - Uninformative reports of mixed infections without MIC data
      - No available UTI studies with sufficient # isolates or MICs
      - Stepdown oral therapy in POET trial for streptococci with MIC<1 mg/L1 (Note: Treatment was in combination with other agents)
      - Successful treatment 1 case of endocarditis adult 750 mg PO QID x 21d
  – AHWG Recommendations: No suggested changes
    - PTA/PK seems to be sufficient
    - Few clinical data are available.
    - No clinical signals have been observed.
    - No BP changes were recommended.
    - Retain Current note: “Breakpoints …based on population distributions, PK, literature, clinical experience. Systemically collected clinical data …not available”
  – **SC Discussion:**
    - There were insufficient data to determine a dosage regimen comment could be added.
    - No vote was needed.

- **Ampicillin for *N. meningitidis***
  – History
    - No breakpoint before 2005
    - MIC distributions presented 2004
    - Ampicillin breakpoints S ≤0.125, I = 0.25 to 1, R≥2 µg/mL adopted 2005, based on MIC distribution, and in silico estimation of CSF PK/PD
    - No clinical, animal data, or CSF-simulation experimental PD data presented
    - New Table 2I in 2006 or 2007
  – Review of publications showed:
    - BP based on *penA* (PBP2) penicillin resistance genotype frequency
    - Meningococcal meningitis outcomes with IV ampicillin treatment 200 mg/kg/d/6 doses

#	Description
	– Discussion and recommendations o BP was reasonable for meningitis based on MIC distributions, clinical trial results, and drug concentration in CSF at high dosage o AHWG suggested BPs for meningitis (S ≤ 0.125, R ≥ 0.25 with I eliminated) and non-meningitis (keep current) ▪ Eliminating the intermediate would be problematic for testing, lack of dosing strategy for meningitis (most cases) vs non-meningitis, and need to change penicillin if intermediate eliminated. o BPWG: ▪ Retain the current Ampicillin BPs of <0.12, 0.25 - 1, >2 µg/mL (S/I/R) for *N. meningitidis* ▪ Add comment "The susceptible breakpoint is based on an intravenously administered ampicillin dosage of 2 g given every 4 hours." ▪ Vote: 11 in favor, 0 opposed (0 abstain, 1 absent) – **SC Discussion**: o **Question:** It was noted that 60-70% of isolates in Central America test intermediate to ampicillin. Does this mean that *N. meningitis* can't be treated with ampicillin? ▪ It appears that by giving the highest dose, the treatment still works. In most cases, another agent will be given if ampicillin tests intermediate.
	A motion to retain the BPs for *N. meningitidis* and to add a dosage regimen comment: "Susceptible breakpoint is based on 2 g IV ampicillin administered every 4 hours" was made and seconded. VOTE: 12 for; 0 against; 0 abstain; 0 absent (Pass).
	• **Next steps:** Aminopenicillin BPs to be presented in June 2021 include Enterobacterales, *Acinetobacter*, *Enterococcus*, and *Haemophilus*. <u>Other BPWG Issues</u> • **Text and Tables WG follow-up issues** – Removal of quinupristin/dalfopristin from Table 2D (Enterococci) for *E. faecium* o Initially discussed in January and June 2020 but there was no discussion and no vote was taken o Rationale for removal: Revoked by the FDA for vancomycin-resistant *Enterococcus* because it there were no supportive data that it worked. o EUCAST has retained the BP but is not thought to be widely used o It has been suggested that it may need to be retained for use outside the United States o A formal review would be needed to formally remove the BP o SC Discussion ▪ Comment: The drug is still requested for testing on occasion so it was suggested it be retained. ▪ It was noted that, historically, drugs that are not cleared by the FDA are retained in Tables 2 and 3 (QC) but not in Table 1 for potential use outside the US. – Definition of Investigational (INV) designation o As per the definition in M100, INV includes antimicrobial agents that are investigational for the organism group and have not yet been approved by the FDA for use in the United States. o Cefiderocol BPs were approved by CLSI and the FDA and are listed in M100 as INV. As per M23, INV BPs should not be listed in M100. o It was suggested that the definition may need to be revised. o SC Discussion ▪ It was suggested that this issue be discussed with the M23 WG. It was noted that currently, the definition in the M23 draft has not changed. ▪ It was noted that in M100, new information is in bold to designate that the information is new and is tentative for one year. It was questioned if cefiderocol should have been published before FDA approval.

SUMMARY MINUTES	
#	**Description**
	▪ Historically, sponsors came to CLSI and FDA at the same time. CLSI published BPs without knowing if FDA would approve it. ▪ It was suggested that the SC consider how drugs are designated when FDA approval is pending. • **Repeat testing for new agents to monitor resistance on therapy** – A request was submitted to add a comment for repeat testing of ceftazidime-avibactam and ceftolozane-tazobactam susceptibilities because resistance can arise during treatment – M100 currently has guidance in Section IV of the Instructions for Use of tables. – There was concern that adding one agent might inappropriately single out a scenario unfairly as this can occur with many organism-drug combinations. – It was decided that no action is needed at this time. • **BPWG priorities were reviewed** – Review piperacillin/tazobactam reporting for ceftriaxone nonsusceptible *E. coli* and *K. pneumoniae* from MERINO – Form a plazomicin AHWG and initiate an aminoglycoside review – Consider adding a BP for tigecycline
3.	**Adjournment**: Dr. Lewis thanked the participants for their time and tremendous work. The meeting was adjourned at 6:00 PM Eastern (US) time.

Upcoming AST Meetings:

- **June 2021:** To be held virtually throughout June 2021.
  - All AHWGs and standing WG Chairholders: Please provide an estimation of time needed for a meeting by **Monday, 22 March 2021**. (**Note:** AHWG are expected to meet in May with standing WGs and the plenaries being held throughout June).
  - Polls will be distributed in late March and early April 2021.
  - Background materials for AHWG meetings are due for submission by **Monday, 1 May 2021**.
  - Background materials for Standing WG meetings are due for submission by **Monday, 24 May 2021**.

- **January 2022**: **In person (as allowed), Sunday – Tuesday, 23-25 January 2022**
  - St. Bonaventure Hotel, Ft. Lauderdale, Florida
  - All ad Hoc WG meetings to be held virtually in December 2021 and early January 2022.
  - Agenda requests and background material due for submission by **Monday, 13 December 2021**.

	ACTION ITEMS	Responsible
1.	Form an AHWG to review carbapenemase testing/reporting comments and recommendations throughout M100 (including Tables 3A and 3B and Appendix H to provide harmonized guidance.	MAIWG
2.	Revise the comment regarding AmpC ß-lactamases for presentation at the June 2021 meeting.	MAIWG
3.	Revise the I^ definition to reflect that I^ is for information only and that infectious disease practitioners and the antimicrobial stewardship team needs to be consulted and review all uses of I^ in M100 for the 32nd edition.	MAIWG
4.	Propose language regarding the two colony types of *K. pneumoniae* ATCC® 700603 to the appropriate sections of M100.	QCWG
5.	• Refine surrogate agent definition, including added clarity around text: "cannot be tested due to lack of availability" • Create standard language for newer ß-lactam/ß-lactamase inhibitor compounds and prediction of newer agent based on susceptibility to parent agent • For species-specific breakpoints (eg, for *H. influenzae* only), discuss referring back to similar comments or repeat the comment in each instance. • Harmonize organism comment language between Tables 2 and Appendix E. • Review all cephem comments and their placement in Tables 2 and propose edits • Work with STMA to determine if Glossary III is being used and update it if needed. • Interact with appropriate parties to develop and revised comments before they are inserted in M100. • Identify potential Co-chairholders for the revision of M02 and M07.	TTWG

Summary of Passing Votes			
#	**Motion Made and Seconded**	**Results***	**Page**
1.	To accept the Gepotidacin QC ranges of 1 – 4 µg/mL for *E. faecalis* ATCC® 29212	12-0-0-0	10
2.	To accept the QC ranges for ceftibuten: • *E. coli* ATCC® 25922 (0.12-0.5 µg/mL), • *E. coli* NCTC 13353 (16-64 µg/mL), • *K. pneumoniae* ATCC® BAA-1705 (4-32 µg/mL) • *K. pneumoniae* ATCC® BAA-2814 (8-32 µg/mL) To accept the QC ranges for ceftibuten/VNRX-5236: • *E. coli* ATCC® 25922 (0.03/4 –0.12/4 µg/mL) • *E. coli* NCTC 13353 (0.03/4 –0.25/4 µg/mL) • *K. pneumoniae* ATCC® BAA-1705 (0.12/4 –0.5/4 µg/mL) • *K. pneumoniae* ATCC® BAA-2814 (0.5/4 –2/4 µg/mL)	12-0-0-0	13
3.	To accept the QC ranges for *C. difficile* ATCC® 700057 (0.03-0.25 µg/mL) with fidaxomicin.	12-0-0-0	14
4.	To accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for aztreonam (S = ≥21 mm; I = 18-20 mm; R = ≤17 mm) pending QC data review and addition.	12-0-0-0	25
5.	To accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for ceftazidime (S = ≥21 mm; I = 18-20 mm; R = ≤17 mm) pending QC data review and addition.	12-0-0-0	26
6.	To accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for ceftriaxone (S = ≥23 mm; I = 20-22 mm; R = ≤19 mm) pending QC data review and addition.	12-0-0-0	26
7.	To accept the 8-10 hour direct DD reads for Enterobacterales applying the current breakpoints for tobramycin (S = ≥15 mm; I = 13-14 mm; R = ≤12 mm) pending QC data review and addition.	12-0-0-0	26

Summary of Passing Votes			
#	**Motion Made and Seconded**	**Results***	**Page**
8.	To accept the 16-18 hour direct DD reads for *P. aeruginosa* applying the current breakpoints for ciprofloxacin in Table 2B-1 (S = ≥25 mm; I = 19-24 mm; R = ≤18 mm).	12-0-0-0	27
9.	To accept the 16-18 hour direct DD reads for *P. aeruginosa* applying the current breakpoints for meropenem in Table 2B-1 (S = ≥19 mm; I = 16-18 mm; R = ≤15 mm)	12-0-0-0	27
10.	To accept the 16-18 hour direct DD reads for *P. aeruginosa* applying the current breakpoints for tobramycin in Table 2B-1 (S = ≥15 mm; I = 13-14 mm; R = ≤12 mm).	12-0-0-0	28
11.	To retain the MIC CLSI cefiderocol BPs (≤4/8/≥16 µg/mL) for both Enterobacterales and *P. aeruginosa*.	10-0-2-0	36
12.	To retain the MIC CLSI cefiderocol BPs (≤4/8/≥16 µg/mL) for *A. baumannii*.	7-1-3-1	36
13.	To approve a susceptible BP of ≤ 1 µg/mL and non-susceptible BP of >1 µg/mL for *S. maltophilia* with cefiderocol and including a comment regarding limited data.	7-2-2-1	37
14.	To approve the DD breakpoints for cefiderocol and *P. aeruginosa* (S: ≥18 mm, I: 13-17 mm, R: ≤12 mm).	10-0-2-0	37
15.	To approve the susceptible-only DD breakpoint for cefiderocol and *A. baumannii* (S: ≥15 mm) (with MIC BPs as approved) and with a comment regarding evaluating zone sizes of 14 and below.	8-2-2-0	38
16.	To approve the S/NS DD breakpoints for cefiderocol and *S. maltophilia* (S: ≥15 mm, NS: ≤14 mm).	9-1-2-0	38
17.	To include a comment regarding the origin of the S-only cefiderocol MIC BP for *S. maltophilia* (Suggested: The susceptible breakpoint is based on PK/PD, MIC distributions and limited clinical data.)	10-0-2-0	38
18.	To approve the DD correlate BPs from Option 1 for lefamulin and *S. pneumoniae* (S: ≥19 mm; NS: ≤18 mm), *S. aureus* (S: ≥23 mm; NS: ≤22 mm), and *H. influenzae* (S: ≥18 mm; NS: ≤17 mm).	11-0-0-1	41
19.	To accept S/NS BPs for lefamulin with *M. catarrhalis* (MIC-S: 0.5 µg/mL and NS: ≥1 µg/mL; DD-S: ≥19 mm and NS: ≤18 mm) to be added to M45.	12-0-0-0	43
20.	To add a dosage regimen comment for *Haemophilus* spp. with the current BP for ampicillin-sulbactam that states (or with similar language as determined by the Text and Tables WG), "BP dosage is based on dosage regimen of 3g IV administered every 6 hrs.".	12-0-0-0	44
21.	To add a dosage regimen comment in Table 2G for *S. pneumoniae* with the current BP for amoxicillin and amoxicillin-clavulanate (non-meningitis) that states (or with similar language as determined by the Text and Tables WG): "The susceptible breakpoint is based on an orally administered amoxicillin component dosage of 500 mg administered every 8 hrs. or 875 mg administered every 12 hrs.	12-0-0-0	45
22.	To retain the BPs for *N. meningitidis* and to add a dosage regimen comment: "Susceptible breakpoint is based on 2 g IV ampicillin administered every 4 hours"	12-0-0-0	47

* Key for voting: X-X-X-X = For-against-abstention-absent

Respectfully submitted,

Marcy L. Hackenbrack, MCM, M(ASCP)
Senior Project Manager

SC Reviewers and Guests (non-SC roster attendees) Present (Attendance recorded via link)

Full Name	Organization/Company Name	Meeting Attended
Darcie Carpenter	IHMA	AST SC Plenary (Part 1)
Gina Ewald-Saldana	Beckman Coulter MicroScan	AST SC Plenary (Part 1)
Jekia Cox	BD	AST SC Plenary (Part 1)
John Turnidge	University of Adelaide	AST SC Plenary (Part 1)
Karen Bush	Indiana University	AST SC Plenary (Part 1)
Katherine Young	Merck	AST SC Plenary (Part 1)
Masakatsu Tsuji	SHIONOGI & Co., Ltd.	AST SC Plenary (Part 1)
Matthew A. Wikler	Infectious Diseases Development Technology Consulting	AST SC Plenary (Part 1)
Michael D. Huband	JMI Laboratories	AST SC Plenary (Part 1)
Nancy Watz	Stanford Health Care	AST SC Plenary (Part 1)
Nicole Scangarella-Oman	GlaxoSmithKline	AST SC Plenary (Part 1)
Nydia Alejandra Castillo-Martinez	Universidad Autonoma de Baja California	AST SC Plenary (Part 1)
Paul Edelstein	Univ of Penn	AST SC Plenary (Part 1)
Robert Bowden	Beth Israel Deaconess Medical Center	AST SC Plenary (Part 1)
Stephanie Mitchell	University of Pittsburgh/UPMC	AST SC Plenary (Part 1)
Susan Butler-Wu	USC	AST SC Plenary (Part 1)
Susan Sharp	Copan Diagnostics	AST SC Plenary (Part 1)
Susan Thomson	Mast Group	AST SC Plenary (Part 1)
Tiffany Keepers White	Paratek	AST SC Plenary (Part 1)
Wayne Wang	Grady Health System	AST SC Plenary (Part 1)
Adam Belley	Allecra Therapeutics SAS	AST SC Plenary (Part 2)
Alex Lepak	UW Madison	AST SC Plenary (Part 2)
Alisa Serio	Paratek Pharma	AST SC Plenary (Part 2)
Amanda Kuperus	Microbiologics	AST SC Plenary (Part 2)
Andrea Ferrell	BD	AST SC Plenary (Part 2)
Beth Goldstein	Beth Goldstein Consultant	AST SC Plenary (Part 2)
Carol Rauch	CDC	AST SC Plenary (Part 2)
Claire Burbick	Washington State University	AST SC Plenary (Part 2)
Danielle Hilligoss	Becton Dickinson	AST SC Plenary (Part 2)
DARCIE CARPENTER	IHMA	AST SC Plenary (Part 2)
Davina Campbell	CDC	AST SC Plenary (Part 2)

Full Name	Organization/Company Name	Meeting Attended
Dee Shortridge	JMI Labs	AST SC Plenary (Part 2)
Diane Anastasiou	Paratek Pharmaceuticals	AST SC Plenary (Part 2)
Dwight Hardy	university of rochester medical center	AST SC Plenary (Part 2)
Elizabeth Palavecino	Wake Forest Baptist Medical Center	AST SC Plenary (Part 2)
Gina Ewald-Saldana	Beckman Coulter MicroScan	AST SC Plenary (Part 2)
Jekia Cox	BD	AST SC Plenary (Part 2)
Karen Anderson	Centers for Disease Control and Prevention	AST SC Plenary (Part 2)
Karen Bush	Indiana University	AST SC Plenary (Part 2)
Katherine Sei	Beckman Coulter	AST SC Plenary (Part 2)
Katherine Young	Merck & Co., Inc.	AST SC Plenary (Part 2)
Kelly Harris	Merck Research Labs	AST SC Plenary (Part 2)
Kevin Alby	UNC Health	AST SC Plenary (Part 2)
Laura Koeth	Laboratory Specialists, Inc.	AST SC Plenary (Part 2)
Laura Stewart	BD	AST SC Plenary (Part 2)
Linda Schuermeyer	bioMérieux	AST SC Plenary (Part 2)
Mark Fisher	University of Utah - ARUP	AST SC Plenary (Part 2)
Masakatsu Tsuji	SHIONOGI & Co., Ltd.	AST SC Plenary (Part 2)
Matthew A. Wikler, MD, FIDSA	Infectious Diseases Technology Development Consulting	AST SC Plenary (Part 2)
Megan Burgess	Thermo Fisher Scientific	AST SC Plenary (Part 2)
Melissa Boddicker	Merck & Co.	AST SC Plenary (Part 2)
MELISSA JONES	UNC HEALTHCARE	AST SC Plenary (Part 2)
Michael D. Huband	JMI Laboratories	AST SC Plenary (Part 2)
MORGAN PENCE	Cook Children's Medical Center	AST SC Plenary (Part 2)
Nancy Watz	Stanford Health Care	AST SC Plenary (Part 2)
Natasha Griffin	FDA	AST SC Plenary (Part 2)
Nicole Scangarella-Oman	GlaxoSmithKline	AST SC Plenary (Part 2)
Niki Litchfield	BD	AST SC Plenary (Part 2)
Nydia Alejandra Castillo-Martinez	Universidad Autonoma de Baja California	AST SC Plenary (Part 2)
Patricia Conville	FDA	AST SC Plenary (Part 2)
Paul Edelstein	univ penn	AST SC Plenary (Part 2)
Pragya Singh	Specific Diagnostics	AST SC Plenary (Part 2)
Rafael Canton	Hospital Ramón y Cajal / EUCAST	AST SC Plenary (Part 2)

Full Name	Organization/Company Name	Meeting Attended
Robert Bowden	Beth Israel Deaconess Medical Center	AST SC Plenary (Part 2)
Robin Patel	Mayo Clinic	AST SC Plenary (Part 2)
Ruel Mirasol	UCLA Health	AST SC Plenary (Part 2)
Sandra McCurdy	Melinta Therapeutics	AST SC Plenary (Part 2)
Sarah McLeod	Entasis Therapeutics	AST SC Plenary (Part 2)
Scott Killian	Thermo Fisher	AST SC Plenary (Part 2)
Shabbir Simjee	Elanco Animal Health	AST SC Plenary (Part 2)
Stephanie Mitchell	University of Pittsburgh/UPMC	AST SC Plenary (Part 2)
Sukantha Chandrasekaran	UCLA	AST SC Plenary (Part 2)
Susan Butler-Wu	USC	AST SC Plenary (Part 2)
Susan Sharp	Copan Diagnostics	AST SC Plenary (Part 2)
Susan Thomson	Mast group	AST SC Plenary (Part 2)
Susan Weir	PhAST Diagnostics, Inc.	AST SC Plenary (Part 2)
Tam T. Van	Kaiser Permanente	AST SC Plenary (Part 2)
Tiffany Keepers White	Paratek	AST SC Plenary (Part 2)
Wayne Wang	Grady Health System	AST SC Plenary (Part 2)
Andrew DeRyke	Merck	AST SC Plenary (Part 3)
Antonieta Jimenez	Inciensa Costa Rica	AST SC Plenary (Part 3)
Beth Goldstein	Beth Goldstein Consultant	AST SC Plenary (Part 3)
Dawn Sievert	CDC	AST SC Plenary (Part 3)
Gina Ewald-Saldana	Beckman Coulter MicroScan	AST SC Plenary (Part 3)
Karen (Kitty) Anderson	Centers for Disease Control and Preventions	AST SC Plenary (Part 3)
Katherine Young	Merck & Co., Inc.	AST SC Plenary (Part 3)
Masakatsu Tsuji	Shionogi & Co., Ltd.	AST SC Plenary (Part 3)
Matthew A. Wikler, MD, FIDSA	Infectious Diseases Technology Development Consulting	AST SC Plenary (Part 3)
Nicholas M Moore	Rush University Medical Center	AST SC Plenary (Part 3)
Nicole Scangarella-Oman	GlaxoSmithKline	AST SC Plenary (Part 3)
Nydia Alejandra Castillo-Martinez	Universidad Autonoma de Baja California	AST SC Plenary (Part 3)
Patricia Conville	FDA	AST SC Plenary (Part 3)
Paul Edelstein	Univ Penn	AST SC Plenary (Part 3)
Robert Bowden	Beth Israel Deaconess Medical Center	AST SC Plenary (Part 3)
Stephanie Mitchell	University of Pittsburgh/UPMC	AST SC Plenary (Part 3)

Full Name	Organization/Company Name	Meeting Attended
Susan Sharp	Copan Diagnostics	AST SC Plenary (Part 3)
Tiffany Keepers White	Paratek	AST SC Plenary (Part 3)
Wayne Wang	Grady Health System	AST SC Plenary (Part 3)
Antonieta Jimenez	Inciensa and PAHO	AST SC Plenary (Part 4)
Beth P Goldstein	Beth Goldstein Consultant	AST SC Plenary (Part 4)
Chris Lewis	Thermo Fisher	AST SC Plenary (Part 4)
DARCIE CARPENTER	IHMA	AST SC Plenary (Part 4)
Dee Shortridge	JMI Labs	AST SC Plenary (Part 4)
Elizabeth Palavecino	Wake Forest Baptist Medical Center	AST SC Plenary (Part 4)
Jane Ambler	ContraFect Corp	AST SC Plenary (Part 4)
Jennifer Ann Schranz	Nabriva	AST SC Plenary (Part 4)
Karen Bush	Indiana University	AST SC Plenary (Part 4)
Kelly Harris	Merck Research Labs	AST SC Plenary (Part 4)
Kerian Grande Roche	FDA/CDER	AST SC Plenary (Part 4)
Kevin Alby	UNC Health	AST SC Plenary (Part 4)
Lauri Thrupp, MD	Univ Calif Irvine Medical Center	AST SC Plenary (Part 4)
Lawrence Friedrich	Spero Therapeutics	AST SC Plenary (Part 4)
Marc H Scheetz	Midwestern University	AST SC Plenary (Part 4)
Mark Fisher	ARUP Labs	AST SC Plenary (Part 4)
Matthew A. Wikler, MD, FIDSA	Infectious Diseases Technology Development Consulting	AST SC Plenary (Part 4)
Nicole Scangarella-Oman	GlaxoSmithKline	AST SC Plenary (Part 4)
Nydia Alejandra Castillo-Martinez	Universidad Autonoma de Baja California	AST SC Plenary (Part 4)
Patricia Bradford	Antimicrobial Development Specialists, LLC	AST SC Plenary (Part 4)
Patricia Conville	FDA	AST SC Plenary (Part 4)
Paul Edelstein	Univ Penn	AST SC Plenary (Part 4)
Robert Bowden	Beth Israel Deaconess Medical Center	AST SC Plenary (Part 4)
Stephanie Mitchell	University of Pittsburgh/UPMC	AST SC Plenary (Part 4)
Susanne Paukner	Nabriva Therapeutics	AST SC Plenary (Part 4)
Valentine Usongo	Health Canada	AST SC Plenary (Part 4)
Wolfgang Wicha	Nabriva Therapeutics GmbH	AST SC Plenary (Part 4)

SC Reviewers and Guests (non-SC roster attendees) Present (Attendance recorded via Whova)

Attendees at "AST Plenary (Part 1)"	
Name	**Company**
Adam Belley	Allecra Therapeutics SAS
Alexandra Bryson	Virginia Commonwealth University Health System
Alice Gray	BioMérieux
Alita Miller	Entasis Therapeutics
Allison Tsan	UCLA
Amanda Kuperus	Microbiologics
Amanda Needham	Wadley Regional Medical Center
Amelia Bhatnagar	Centers for Disease Control and Prevention
Amrita Bharat	Public Health Agency of Canada
Andrea Ferrell	BD
Andrew Fuhrmeister	JMI Laboratories
Anne Butler	ThermoFisher Scientific
Audie Perniciaro	bioMérieux
Beth Goldstein	Beth Goldstein Consultant
Carmella Russo	Vanderbilt University Medical Center
Carol Rauch	Centers for Disease Control & Prevention
Carole Shubert	bioMérieux, Inc.
Carrine Brown	Thermo Fisher Scientific
Cecilia Carvalhaes	JMI Laboratories
Charles Jakielaszek	GlaxoSmithKline
Christian Gill	Center for Anti-Infective Research and Development, Hartford Hospital
Claire Burbick	Washington State University
Collette Wehr	Beckman Coulter Microbiology
Craig Bross	CDFA
Dale Schwab	Quest Diagnostics
Danielle Hilligoss	Becton Dickinson and Company
Davina Campbell	CDC
Dawn Sievert	Centers for Disease Control and Prevention
Deborah Butler	GlaxoSmithKline
Dee Shortridge	JMI Labs
Diane Anastasiou	Self employed

Attendees at "AST Plenary (Part 1)"	
Name	**Company**
Dylan Staats	Thermo Fisher Scientific
Elaine Duncan	Beckman Coulter, Inc.
Elizabeth Palavecino	Wake Forest Baptist Medical Center
Greg Stone	Pfizer, Inc.
Gregory Tyson	U.S. Food and Drug Administration
Hari Dwivedi	bioMérieux
Helio Sader	JMI Laboratories
Holly Huse	Harbor-UCLA
James Jorgensen	University of Texas Health Center
James Karlowsky	Shared Health Manitoba/University of Manitoba
Jekia Cox	BD
Jenn Dien Bard	Children's Hospital Los Angeles; University of Southern California
Jennifer Boyer	Becton Dickinson
Jennifer Chau	Beckman Coulter
Jennifer Hoover	GlaxoSmithKline
Jennifer Slaughter	bioMérieux, Inc.
John Breton	GlaxoSmithKline
John Turnidge	University of Adelaide
June Chan	NYSDOH/Wadsworth Center
Karen Anderson	Centers for Disease Control and Prevention
Karen Ingraham	GSK
Karri Sutter	Merck Research Labs
Katherine Young	Merck & Co., Inc.
Kelly Harris	Merck Research Labs
Kelsey Pischel	bioMérieux
Kenneth Klinker	Merck & Co, Inc
Kevin Alby	UNC Medical Center
Kristie Johnson	University of Maryland School of Medicine
Larry Friedrich	Spero Therapeutics
Laura Koeth	Laboratory Specialists, Inc.
Laura Stewart	BD

Attendees at "AST Plenary (Part 1)"	
Name	**Company**
Laurie K. Flemming, SM, MT(ASCP)	National Institutes of Health
Linda Otterson	BWFH, Atrius
Linda Schuermeyer	bioMérieux
Lynn McCloskey	GlaxoSmithKline
Lynn Yaolin	AbbVie Inc.
Marc Scheetz	Midwestern University
Mari Ariyasu	Shionogi & Co. Ltd.
Mark Lee	Duke University Health System
Mark Redell	Melinta Therapeutics
Maryann Brandt	Norman Regional Health System
Masakatsu Tsuji	Shionogi & Co. Ltd.
Matthew Wikler	Infectious Diseases Technology Development Consulting
Megan Burgess	Thermo Fisher Scientific
Melissa Boddicker	Merck & Co.
Melissa Johnson	Duke University Medical Center/DASON
Meredith Hackel	IHMA
Mike Huband	Associate Director
Morgan Pence	Cook Children's Medical Center
Nancy Watz	Stanford Health Care
Natalie Whitfield	GenMark Dx
Natasha Griffin	FDA
Nicholas Moore	Rush University Medical Center
Nicole Holliday	Thermo Fisher Scientific
Nicolynn Cole	Mayo Clinic
Niki Litchfield	BD
Nilia Robles Hernandez	BioMérieux
Patricia Conville	FDA
Patricia Bradford	Antimicrobial Dev. Specialists
Pragya Singh	Specific Diagnostics
Pranita Tamma	Johns Hopkins
Pritty Patel	Covance
Rafael Canton	Hospital Universitario Ramón y Cajal

Attendees at "AST Plenary (Part 1)"	
Name	**Company**
Rebekah Dumm	Hospital of the University of Pennsylvania - Children's Hospital of Philadelphia
Rita Hoffard	Becton Dickinson
Rodrigo Mendes	JMI Laboratories
Ruel Mirasol	UCLA Health
Samantha Shannon	Mayo Clinic
Sandra McCurdy	Melinta Therapeutics
Sarah Leppanen	Blaine Healthcare
Sarah McLeod	Entasis Therapeutics
Scott Killian	Thermo Fisher Scientific
Sharon Min	GlaxoSmithKline
Silvio Tsukuda	BD
Simone Shurland	FDA-CDER
Sopheay Hun	West Region - Washington State Department of Health
Sophie Arbefeville	bioMérieux
Stephanie Mitchell	UPMC/University of Pittsburgh
Stephen LaVoie	CDC
Steve Yan	FDA-CVM
Sukantha Chandrasekaran	University of California - Los Angeles
Susan Cusick	Venatorx Pharmaceuticals, Inc.
Susan Kircher	BD
Susan Weir	PhAST Diagnostics, Inc.
Tessa LeCuyer	Virginia Tech
Tsigereda Tekle	Johns Hopkins Hospital
Valentine Usongo	Health Canada
Victoria Stone	TN Department of Health
Xian-Zhi Li	Veterinary Drugs Directorate, Health Canada
Zabrina Lockett, PhD, MPH, MT(AAB)	Beckman Coulter Diagnostics

Attendees at "AST Plenary (Part 2)"	
Name	**Company**
Allison Eberly	Mayo Clinic
Amelia Bhatnagar	Centers for Disease Control and Prevention
Carrine Brown	Thermo Fisher Scientific
Chris Lewis	Thermo Fisher
Christian Gill	Center for Anti-Infective Research and Development, Hartford Hospital
Claire Burbick	Washington State University
Dale Schwab	Quest Diagnostics
Dylan Staats	Thermo Fisher Scientific
Jekia Cox	BD
Jennifer Hoover	GlaxoSmithKline
John Breton	GlaxoSmithKline
Kelsey Pischel	bioMerieux
Kenneth Klinker	Merck & Co, Inc
Laurie Flemming	National Institutes of Health
Linda Otterson	BWFH, Atrius
Marc Scheetz	Northwestern Medicine
Mark Redell	Melinta Therapeutics
Masakatsu Tsuji	Shionogi & Co., Ltd
Melvili Cintron	Memorial Sloan Kettering Cancer Center
Michael Urban	Beckman Coulter
Natalie Whitfield	GenMark Dx
Nicole Scangarella-Oman	GSK
Nicolynn Cole	Mayo Clinic
Nydia Alejandra Castillo-Martinez	Universidad Autonoma de Baja California
Patricia Conville	FDA
Pragya Singh	Specific Diagnostics
Pranita Tamma	Johns Hopkins
Pritty Patel	Covance
Simone Shurland	FDA-CDER
Sopheay Hun	West Region - Washington State Department of Health
Tsigereda Tekle	Johns Hopkins Hospital

Attendees at "AST Plenary (Part 2)"	
Name	**Company**
Victoria Stone	TN Department of Health

Attendees at "AST Plenary (Part 3)"	
Name	**Company**
Alice Gray	bioMérieux
Alisa Serio	Paratek Pharmaceuticals
Alita Miller	Entasis Therapeutics
Allison Tsan	UCLA
Amanda Kuperus	Microbiologics
Amelia Bhatnagar	Centers for Disease Control and Prevention
Andrew DeRyke	Merck
Andrew Fuhrmeister	JMI Laboratories
Carole Shubert	bioMérieux, Inc.
Carrine Brown	Thermo Fisher Scientific
Cecilia Carvalhaes	JMI Laboratories
Charles Jakielaszek	GlaxoSmithKline
Chris Lewis	Thermo Fisher
Christian Gill	Center for Anti-Infective Research and Development, Hartford Hospital
Collette Wehr	Beckman Coulter Microbiology
Dale Schwab	Quest Diagnostics
Danielle Hilligoss	Becton, Dickinson and Company
Darcie Carpenter	IHMA, Inc.
David Fam	Shionogi Inc.
Davina Campbell	CDC
Deborah Butler	GlaxoSmithKline
Dee Shortridge	JMI Labs
Diane Anastasiou	self employed
Elaine Duncan	Beckman Coulter, Inc.
Elizabeth Palavecino	Wake Forest Baptist Medical Center
Felicia Rice	Mayo Clinic Hospital
Frank Kung	Shionogi Inc.

Attendees at "AST Plenary (Part 3)"	
Name	**Company**
Hari Dwivedi	bioMérieux
Helio Sader	JMI Laboratories
Holly Huse	Harbor-UCLA
J West	GSK
James Karlowsky	Shared Health Manitoba/University of Manitoba
Janet Ehlert	Shionogi Inc.
Jekia Cox	BD
Jennifer Boyer	Becton Dickinson
Jennifer Slaughter	bioMérieux, Inc.
John Breton	GlaxoSmithKline
Kamisha Gray	Becton Dickinson
Karen Anderson	Centers for Disease Control and Prevention
Karen Bush	Indiana University
Karen Ingraham	GSK
Karri Sutter	Merck Research Labs
Katherine Young	Merck & Co., Inc.
Kelly Harris	Merck Research Labs
Kelsey Pischel	bioMérieux
Kenneth Klinker	Merck & Co, Inc
Kristie Johnson	University of Maryland School of Medicine
Larry Friedrich	Spero Therapeutics
Laura Koeth	Laboratory Specialists, Inc.
Laura Stewart	BD
Laurie K. Flemming, SM, MT(ASCP)	National Institutes of Health
Linda Otterson	BWFH, Atrius
Linda Schuermeyer	bioMerieux
Lynn McCloskey	GlaxoSmithKline
Marc Scheetz	Midwestern University
Mari Ariyasu	Shionogi & Co. Ltd.
Mark Fisher	University of Utah - ARUP
Mark Redell	Melinta Therapeutics

Attendees at "AST Plenary (Part 3)"	
Name	**Company**
Maryann Brandt	Norman Regional Health System
Megan Burgess	Thermo Fisher Scientific
Melvili Cintron	Memorial Sloan Kettering Cancer Center
Meredith Hackel	IHMA
Miki Takemura	
Morgan Pence	Cook Children's Medical Center
Natasha Griffin	FDA
Nicholas Moore	Rush University Medical Center
Nicole Holliday	Thermo Fisher Scientific
Nicole Scangarella-Oman	GSK
Nicolynn Cole	Mayo Clinic
Nilia Robles Hernandez	BioMérieux
Nydia Alejandra Castillo-Martinez	Universidad Autonoma de Baja California
Patricia Bradford	Antimicrobial Dev. Specialists
Pranita Tamma	Johns Hopkins
Ramona Azore	Becton Dickinson
Robert Badal	Robert Badal Consulting
Rodrigo Mendes	JMI Laboratories
Ron Master	Quest Diagnostics
Samantha Stephens	Shionogi
Sandra McCurdy	Melinta Therapeutics
Sarah Leppanen	Blaine Healthcare
Sarah McLeod	Entasis Therapeutics
Scott Killian	Thermo Fisher Scientific
Sharon Min	GlaxoSmithKline
Simone Shurland	FDA-CDER
Sopheay Hun	West Region - Washington State Department of Health
Steve Yan	FDA-CVM
Sukantha Chandrasekaran	University of California - Los Angeles
Susan Butler-Wu	University of Southern California
Susan Cusick	Venatorx Pharmaceuticals, Inc.

Attendees at "AST Plenary (Part 3)"	
Name	**Company**
Susan Kircher	BD
Susan Sharp	Copan Diagnostics
Susan Weir	PhAST Diagnostics, Inc.
Tsigereda Tekle	Johns Hopkins Hospital
Xian-Zhi Li	Veterinary Drugs Directorate, Health Canada
Zabrina Lockett, PhD, MPH, MT(AAB)	Beckman Coulter Diagnostics
yoshinori Yamano	Shionogi & Co., Ltd.

Attendees at "AST Plenary (Part 4)"	
Name	**Company**
Amanda Kuperus	Microbiologics
Amanda Needham	Wadley Regional Medical Center
Amelia Bhatnagar	Centers for Disease Control and Prevention
Carole Shubert	bioMérieux, Inc.
Cecilia Carvalhaes	JMI Laboratories
Christian Gill	Center for Anti-Infective Research and Development, Hartford Hospital
Collette Wehr	Beckman Coulter Microbiology
Davina Campbell	Cdc
Dawn Sievert	Centers for Disease Control and Prevention
Diane Anastasiou	self employed
Dylan Staats	Thermo Fisher Scientific
Elaine Duncan	Beckman Coulter, Inc.
Jekia Cox	BD
Jennifer Boyer	Becton Dickinson
Jennifer Slaughter	bioMérieux, Inc.
Joshua Chen	LAC USC
Karen Anderson	Centers for Disease Control and Prevention
Kelsey Pischel	bioMérieux
Larry Friedrich	Spero Therapeutics
Laura Koeth	Laboratory Specialists, Inc.
Laura Stewart	BD

Attendees at "AST Plenary (Part 4)"	
Name	**Company**
Linda Otterson	BWFH, Atrius
Linda Schuermeyer	bioMérieux
Lynn McCloskey	GlaxoSmithKline
Marc Scheetz	Midwestern University
Mari Ariyasu	Shionogi & Co. Ltd.
Mark Redell	Melinta Therapeutics
Megan Burgess	Thermo Fisher Scientific
Meredith Hackel	IHMA
Miki Takemura	
Natasha Griffin	FDA
Nilia Robles Hernandez	bioMérieux
Patrici Conville	FDA
Sarah McLeod	Entasis Therapeutics
Scott Killian	Thermo Fisher Scientific
Simone Shurland	FDA-CDER
Sopheay Hun	West Region - Washington State Department of Health
Sukantha Chandrasekaran	University of California - Los Angeles
Susan Cusick	Venatorx Pharmaceuticals, Inc.
Susan Sharp	Copan Diagnostics
Susan Weir	PhAST Diagnostics, Inc.
Tsigereda Tekle	Johns Hopkins Hospital
Wayne Wang	Grady Health System
Xian-Zhi Li	Veterinary Drugs Directorate, Health Canada
Zabrina Lockett, PhD, MPH, MT(AAB)	Beckman Coulter Diagnostics