Meeting Title:	**Subcommittee on Antimicrobial Susceptibility Testing (AST)**	**Contact:**	mhackenbrack@clsi.org
Meeting Dates and Start Times:	**Plenary Part 1:** Friday, 25 September 2020, 2:00 – 4:00 PM Eastern (US) Time **Plenary Part 2:** Tuesday, 29 September 2020, 12:00 – 3:00 PM Eastern (US) Time		
Virtual Meeting Access Information	Individual panelist information was sent by email. Attendee links are posted in the meeting document library in CLSI Exchange.		
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).		
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)	
Melvin P. Weinstein, MD AST Subcommittee Chairholder	**Rutgers Robert Wood Johnson Medical School**
James S. Lewis, PharmD, FIDSA AST Subcommittee Vice-chairholder	**Oregon Health and Science University**
Jean B. Patel, PhD, D(ABMM) Expert Panel on Microbiology Chairholder	Beckman Coulter
Members Present:	
Sharon K. Cullen, BS, RAC	Beckman Coulter, Inc. Microbiology Business
Marcelo F. Galas	Pan American Health Organization
Howard Gold, MD, FIDSA	Beth Israel Deaconess Medical Center
Romney M. Humphries, PhD, D(ABMM)	Vanderbilt University Medical Center
Thomas J. Kirn, MD, PhD	Rutgers Robert Wood Johnson Medical School
Brandi Limbago, PhD	Centers for Disease Control and Prevention
Amy J. Mathers, MD, D(ABMM)	University of Virginia Medical Center
Sandra S. Richter, MD, D(ABMM), FCAP, FIDSA	bioMérieux, Inc.
Michael Satlin, MD, MS	New York Presbyterian Hospital
Audrey N. Schuetz, MD, MPH, D(ABMM)	Mayo Clinic
Patricia J. Simner, PhD, D(ABMM)	Johns Hopkins School of Medicine, Department of Pathology
Members Absent	
Tony Mazzulli, MD, FACP, FRCP(C) (Both)	Sinai Health System
Advisors Present	
Tanaya Bhowmick, MD	Rutgers Robert Wood Johnson Medical School
April M. Bobenchik, PhD, D(ABMM), MT(ASCP)	Lifespan Academic Medical Center
Carey-Ann Burnham, PhD, D(ABMM)	Washington University School of Medicine
Mariana Castanheira, PhD	JMI Laboratories
George M. Eliopoulos, MD	Beth Israel Deaconess Medical Center
German Esparza, MSc	Proasecal SAS Colombia
Sheila Farnham, MT(ASCP)	bioMérieux, Inc.
Christian G. Giske, MD, PhD	Karolinska University Hospital, Solna
Janet A. Hindler, MCLS, MT(ASCP), F(AAM)	Los Angeles County Department of Health
Elizabeth Hirsch, PharmD	University of Minnesota College of Pharmacy
Maria Karlsson, PhD	Centers for Disease Control and Prevention
Joseph Kuti, PharmD	Hartford Hospital
Joseph Lutgring, MD	Centers for Disease Control and Prevention
Linda A. Miller, PhD	CMID Pharma Consulting, LLC.

Greg Moeck, PhD	VenatoRx Pharmaceuticals
Sumathi Nambiar, MD	FDA Center for Drug Evaluations and Research
Navaneeth Narayanan, PharmD, MPH	Ernest Mario School of Pharmacy, 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)	FDA Center for Devices and Radiological Health
Barbara L. Zimmer, PhD	Beckman Coulter, Inc.
Reviewers Present	
Kevin Alby, PhD, D(ABMM)	University of North Carolina
Robert Bowden, BS	Beth Israel Deaconess Medical Center
Patricia Bradford, PhD	Antimicrobial Development Specialties, LLC.
Eileen Burd,	Emory University Hospital
Shelley Campeau, PhD, D(ABMM)	Accelerate Diagnostics
Darcie E. Carpenter, PhD	IHMA
Tanis Dingle, PhD, D(ABMM), FCCM	University of Alberta Hospital
Paul Edelstein, MD	Hospital of the University of Pennsylvania
Andrea L. Ferrell, MLScm(ASCP)	Becton Dickinson
Lawrence V. Friedrich, PharmD	Paratek Pharmaceutical
Beth P. Goldstein, PhD	Beth Goldstein Consultant
Dwight J. Hardy, PhD	University of Rochester Medical Center
Denise Holliday, MT(ASCP)	BD Diagnostic Systems
Melissa Jones, MT(ASCP), CKS	UNC Healthcare
James H. Jorgensen, PhD	University of Texas Health Science Center
Susan M. Kircher, MS, MT(ASCP)	BD Diagnostic Systems
Laura M. Koeth, BS, MT(ASCP) (	Laboratory Specialists, Inc.
Sarah B. Leppanen, MT(ASCP)	Blaine Healthcare Associates, Inc.
Niki Litchfield, MS	BD
Ron Master, SM(AAM)	Quest Diagnostics Nichols Institute
Sandra McCurdy, MS, M(ASCP)	Melinta Therapeutics Inc.
Sarah McLeod	Entasis Therapeutics Inc.
Rodrigo Mendes, PhD	JMI Laboratories
Stephanie L. Mitchell, PhD, D(ABMM)	UPMC/University of Pittsburgh
Mary R. Motyl, PhD, D(ABMM)	Merck & Company, Inc.
Susan O'Rourke, BS	BD Diagnostic Systems
Linda Otterson, BS	Faulkner Hospital
Mark A. Redell, PharmD	The Medicines Company
Marc H. Scheetz, PharmD, MSc	Midwestern University
Carole Schubert, MT	bioMérieux, Inc.
Dale A. Schwab, PhD, D(ABMM)cm	Quest Diagnostics Infectious Disease
Katherine Sei, BS	Beckman Coulter, Inc.
Susan Sharp, PhD	Copan Diagnostics
Dee Shortridge, PhD	JMI Labortories
Simone M. Shurland	FDA Center for Drug Evaluation and Research
Dawn M. Sievert, PhD, MS	Centers for Disease Control and Prevention
Pragya Singh, PhD	Specific Diagnostics
Maria Traczewski, BS, MT(ASCP)	Clinical Microbiology Institute
Lauri Thrupp, MD	University of California Irvine Medical Center
Nancy E. Watz, MS, MT(ASCP), CLS	Stanford Health Care
Matthew A, Wikler, MD, FIDSA, MBA	IDTD Consulting
Katherine Young, AB	Merck & Company, Inc.
Guests (Non-SC-roster attendees)	
Stephanie Abromaitis	California Department of Public Health

Amelia Bhatnagar	Centers for Disease Control and Prevention
Sandra Boyd	Centers for Disease Control and Prevention
Jennifer Boyer	BD
Davina Campbell	Centers for Disease Control and Prevention
Cecilia Carvalhaes	JMI Laboratories
Sukantha Chandrasekaran	UCLA
Susan Cusik	Venatorx
Elaine Duncan	Beckman Coulter
Hari Dwivedi	bioMérieux
John Farley, MD	FDA Center for Drug Evaluations and Research
Andrew Fuhrmeister	JMI Laboratories
Steve Gelone	Nabriva Therapeutics
Natasha Griffin	FDA
Kelly Harris	Merck Research Labs
David Hilbert	Merck
Danielle Hilligoss	BD
Nilia M. Robles Hernandez	bioMérieux
Rita Hoffard	Becton Dickenson
Sopheay Hun	AR Laboratory Network
Greg Inami	California Department of Public Health
Akiki Kimura	California Department of Public Health
Karen J. Kryaton	Beckman Coulter
Katherine Lambda	California Department of Public Health
Gar-Wei Lee	California Department of Public Health
Naeemah Logan	Centers for Disease Control and Prevention, NARMS
Mersedeh Miraliakbari	Nabriva Therapeutics
Suzanne Paukner	Nabriva Therapeutics
Antonieta Jimenez Pearson	Inciensa and Pan American Health
Carol Rauch	CDC AR Laboratory Network
Carmello E. Russo	Vanderbilt University Medical Center
Jennifer Schranz	Nabriva Therapeutics
Linda Schuemeyer	bioMérieux
Jennifer Smart	Basilea Pharmaceutica
Laura Stewart	BD
Masakatsu Tsuji, PhD	Shionogi & Co., Ltd.
Benjamin von Bradow	UCLA
Louise Francois Watkins	Centers for Disease Control and Prevention
Jean Whichard	Centers for Disease Control and Prevention
Tiffany Keepers White	Paratek Pharmaceuticals
Wolfgang Wicha	Nabriva Therapeutics
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
Lori Moon, MS, MT(ASCP)	CLSI
Christine Lam, MT(ASCP)	CLSI

OPENING PLENARY AGENDA Friday, 25 September 2020, 2:00 – 4:00 PM Eastern (US) Time								
Item #	**Item Title**	**Start**	**End**	**Length (Min)**	**Category**	**Presenter**	**Folder(s)**	**Page**
1.	Opening Remarks	2:00 PM	2:05 PM	5	Remarks	M. Weinstein	N/A	5
2.	Vote on January Summary/Disclosure updates	2:05 PM	2:10 PM	5	Vote/Update	M. Weinstein	B, C	5
3.	CLSI Update	2:10 PM	2:20 PM	10	Remarks	G. Fine	N/A	5
4.	Methods Development WG Report • Direct Blood Culture AST	2:20 PM	2:50 PM	30	Report/Vote	B. Zimmer D. Hardy	G, J	6-9
5.	Quality Control WG Report • Tier 2 QC ranges	2:50 PM	3:30 PM	40	Report/Vote	S. Cullen M. Traczewski	H, J	9-15
6.	Text and Tables WG Report • Table and comment revisions	3:30 PM	4:00 PM	30	Report/Vote	A. Bobenchik S. Campeau	I, J	15-17
7.	Adjournment	4:00 PM						

CLOSING PLENARY AGENDA Tuesday, 29 September 2020, 12:00 – 3:00 PM Eastern (US) Time								
Item #	**Item Title**	**Start**	**End**	**Length (Min)**	**Category**	**Presenter**	**Folder(s)**	**Page**
1.	Opening Remarks	12:00 PM	12:05 PM	5	Remarks	M. Weinstein	N/A	18
2.	New: FDA Update	Added	N/A					18
3.	New: M45 Revision Overview	Added	N/A					18-19
4.	Breakpoint WG Report • Lefamulin breakpoints • Azithromycin breakpoints/*Shigella* • Tedizolid comment	12:05 PM	2:00 PM	115	Votes	J. Lewis M. Satlin	E, F, K	19-27
5.	Table 1 Revision Review and Discussion Note: Item rescheduled for a later date	2:00 PM	3:00 PM	60	Information	T. Simner	K	27-33
6.	Adjournment	3:00 PM						

NOTE: The information contained in these minutes represents a summary of the discussions from a CLSI committee meeting, and do not represent approved current or future CLSI document content. These summary minutes and their content are considered property of and proprietary to CLSI, and as such, are not to be quoted, reproduced, or referenced without the expressed permission of CLSI. Thank you for your cooperation.

SUMMARY MINUTES	
Item #	**Description**
Friday, 25 September 2020 **(NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2020 Summer AST Plenary Presentations).**	
1.	**Opening Remarks** • Dr. Weinstein welcomed the panelists and attendees to the virtual plenary meeting. He commented that it was a pleasure to "see" the participants. • He recognized and congratulated Dr. Carey Ann Burnham for receiving the American Society for Microbiology (ASM) Award for Research and Leadership in Clinical Microbiology.
2.	**Vote on January 2020 Summary/Updates on Disclosures of Interest (DOI)** • **January 2020 Summary Minutes Vote** – There were no additional revisions to the January minutes. **A motion to accept the summary minutes from the January 2020 subcommittee meeting was made and seconded. VOTE: 11 for; 0 against; 1 absent (Pass).** – The approved summary minutes have been posted on the CLSI website using the following link to the 2020 January AST Meeting Files. • **DOI Updates:** There were no updates to any disclosures of interest.
3.	**CLSI Update: Mr. Fine** Mr. Fine provided a brief CLSI update. • The staff office has been virtual since March due to the pandemic. The staff offices have been sold and rental of new office space has been delayed due to the pandemic for at least six months; therefore, all employees are working virtually until further notice. • The COVID package of CLSI standards has been created (see link on top of web home page) and many are freely available. • Grant funding decisions for the Global Health Partnerships arm of CLSI (its training department) has been delayed by the US Government but are expected imminently. • New and revised consensus standards in development have been affected due to volunteer's priorities in addressing the pandemic. He noted the microbiology area has the largest number of standards in CLSI's library, including M100. He thanked the Subcommittee on Antimicrobial Susceptibility Testing (AST SC) members for their continued dedication, time and talents to publish M100 within the fiscal year. • Overall, CLSI's mission has never been more important than in these uncertain times of the global public health crises.

SUMMARY MINUTES	
Item #	**Description**
4.	**<u>Methods Development and Standardization Working Group (MDSWG) Report</u>: Dr. Zimmer (Folders G, J)** **WG Roster:** Dwight Hardy, Barbara Zimmer (Co-Chairholders); Katherine Sei (Secretary); Kevin Alby, Susan Butler-Wu, Jennifer Dien Bard, Tanis Dingle, German Esparza, Laura Koeth, Ribhi Shawar **<u>Direct Susceptibility Testing of Gram-Negative Bacilli from Blood Cultures (Antimicrobial Resistance Leadership Group [ARLG] Disk Study)</u>: Direct Blood Culture [DBC] Disk Diffusion Working Group [WG])** **Direct BC AST WG Roster:** Shelley Campeau, Audrey Schuetz (Co-Chairholders); April Abbott (Recording Secretary); Eileen Burd, Dwight Hardy, Romney Humphries, Kristie John, Ton Kirn, Niki Litchfield, Robin Patel, Susan Sharp, Lauri Thrupp, Mel Weinstein, Barbara Zimmer (Members). • An overview of the DBC susceptibility testing study was provided. Parameters included: – Five clinical sites and three BC systems were included in the study. – 500 total isolates were collected with 377 Enterobacterales isolates being tested. – The disk diffusion method was set up within 8 hrs. of the culture flagging as positive. – Four drops of the positive BC broth were inoculated to Mueller-Hinton agar (MHA). – A total of 12 antimicrobial agents were tested. – Comparator methods included standard disk diffusion on isolated colonies (on-site) and broth microdilution (BMD) and reference disk diffusion (referral site). – Standard QC strains recommended for disk diffusion on MHA were tested each day of testing. – The study's main objective was to evaluate direct disk diffusion's test performance with positive BC broth with reads after 16–18 hours (overnight) of incubation at 35°C. • The study data results on the gram-negative bacilli tested was presented. – Resistance was overcalled for Enterobacterales with ciprofloxacin, piperacillin-tazobactam, and cefepime. – Seeding bottles studies will be performed for *Acinetobacter*, *Pseudomonas aeruginosa*, additional Enterobacterales (resistant isolates) – Aztreonam: 97% category agreement (CA), 0 very major errors (VME), 0.31% major errors (ME), 2.7% minor errors (mE) – Ampicillin: 93.7% CA, 0 VME, 1.5% ME, 5.7% mE – Ceftazidime: 93.4% CA, 0 VME, 0.62% ME, 5.9% mE – Ceftriaxone: 94.3% CA, 0 VME, 0.315%, 5.4% mE – Tobramycin: 96.2% CA, 3.0% VME (1 VME with one outlier on the standard DD test), 1.2% ME, 2.4% mE – Trimethoprim-Sulfamethoxazole: 97.0% CA, 2.7% VME (3 VME with outer zones noted on S read for standard DD), 0% ME, 2.1% mE. • Based on the study data, the MDSWG proposed and unanimously approved: – The direct method for testing and reporting all Enterobacterales (not individual species) and interpreted using the breakpoints listed in Table 2A. – Direct test for testing six antimicrobial agents with Enterobacterales.

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	– A vote was requested for aztreonam, ampicillin, ceftazidime, ceftriaxone, tobramycin, and trimethoprim-sulfamethoxazole. • Questions and comments raised at the MDSWG meeting were reviewed. – In new Table 3E: ○ Comments regarding examining test plates to ensure confluent growth and other growth characteristics based on M02 will be included to cover questions regarding inoculum density. A journal article that lists the BC systems used in the study will be published. ○ The general comment regarding reference to Appendix B for intrinsic resistance will be included. – The ad Hoc WG (AHWG) is still working on determining the appropriate needle size. – Selection of appropriate drugs of choice is covered in Tables 1. – The testing will apply to all Enterobacterales and not individual species. • SC discussion (**Note:** Comments and questions may be paraphrased) – **Dr. Thrupp**: Suggested that a point be made regarding clinical relevance and mEs. mE tend to overcall false intermediate and are in the direction of clinical safety. – **Dr. Humphries**: For the inoculum issue, she indicated that she thought of it as an alternative inoculum. Perhaps a reference to a published journal article that provided data on colony counts from a seeding study could be added. A laboratory might need to perform a colony count study from their BC instrument. Dr. Zimmer agreed that a reference to the paper should be added. – **Dr. Hardy**: Noted that the inoculum issue was discussed at length and it was decided to follow as outlined in M02 rather than recommending colony counts. – **Dr. Schuetz**: Agreed with giving users an idea of the density of the inoculum. During the study, there were few growth issues seen with the BC systems studied. – **Dr. Satlin**: Questioned how this testing would be correlated a with the organism identification. – **Dr. Zimmer**: Noted that a Gram stain would be performed, the testing would only be performed on Enterobacterales (ie, gram-negative bacilli only) etc. Since it is an overnight read, most identification systems provide identifications within ≤ 24 hours. – **Dr. Mathers**: The species would need to be identified before the susceptibilities are reported. – **Dr. Weinstein**: If the assay can't be validated for *Pseudomonas* or other non-fermenters, since they are gram-negative bacilli as well, you would be setting up the direct susceptibility before the identification is known. If the test can be validated for more than just Enterobacterales, the test will become more useful. – **Dr. Zimmer**: Suggested adding more information regarding identification and to include the reference regarding inoculum. – **Dr. Miller:** Questioned if these will be preliminary results and will need to be repeated or is this result be final. – **Dr. Zimmer and Dr. Hardy**: Noted that the studies were compared to the standard methodology and there was agreement. Therefore the result is intended to be final and should not need to be repeated. – **Dr. Schuetz:** Agreed that this testing would be definitive and will not need to be repeated.

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	– **Dr. Shawar: N**oted that even with the standard systems, the identification is not known when the test is set up. At the end of the incubation, checking the growth is normal procedure check on the inoculum. He suggested that the length of time between positive and set could be shortened. – **Dr. Simner:** Since so few drugs have been studied so far, most laboratories will be setting up a broader panel anyway which would include these drugs. If there is discordance, it should be noted how to handle the situation. – **Dr. Limbago**: Agreed that her questions have been addressed and implementation is the next step. It should be clearly stated that if the identification shows to not be an Enterobacterales that the results should not be reported. **A motion to approve the direct BC susceptibility testing method for aztreonam, ampicillin, ceftazidime, ceftriaxone, tobramycin, and trimethoprim-sulfamethoxazole with Enterobacterales using the breakpoints listed in Table 2A (with implementation process to follow) was made and seconded. VOTE: 11 for; 0 against; 0 abstain; 1 absent (Pass)** • **Mock-ups of additions to Table 2A and the new Table 3E were presented.** – A notation will be placed in the Testing Conditions box in Table 2A under Inoculum that would refer to Comment (5) for positive blood culture broths. The comment will state: **"Positive blood culture broth can be used as the inoculum for direct disk diffusion testing of select antimicrobials (see below) against Enterobacterales as described in Table 3E with a standard incubation of 16-18 hours, using current disk diffusion breakpoints in Table 2A.** **For antimicrobials not listed below against Enterobacterales, for other genera, and for shorter direct incubation times, e.g. 8-10 hrs, CLSI has not yet evaluated this direct disk diffusion method or breakpoints; therefore, a standard antimicrobial susceptibility method from colony suspension should be used.** **Antimicrobial** **Ampicillin** **Aztreonam** **Ceftazidime** **Ceftriaxone** **Tobramycin** **Trimethoprim-sulfamethoxazole** – A new table designated as Table 3E (Test Method for Performing Disk Diffusion Directly from Positive Blood Culture Broth) will also be added to M100. – SC Discussion (**Note:** Comments and questions may be paraphrased.)

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<tr><th colspan="2">SUMMARY MINUTES</th></tr>
<tr><th>Item #</th><th>Description</th></tr>
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○ Dr. Mathers: Suggested that guidance on resolving on what susceptibility test data (ie, direct test vs a full panel for other than Enterobacterales) is correct should be added.
○ Dr. Simner: Asked what the plan is for the future (ie, shorter incubation) and perhaps, different breakpoints.
○ Dr. Zimmer: There are plans to address these issues once the studies have been done.
○ Dr. Kirn: Suggested using reference methods when there is discrepancy between two methods.
○ Dr. Schuetz: It is meant to be a definitive method.
○ Dr. Hardy: There should be a distinction between a definitive method and a reference method.
○ Ms. Cullen: (from chat) Sounds like we would be concluding and stating the CLSI documents would indicate this is an alternative that has been shown to be "equivalent" to the reference method. The reference method (eg, MIC or disk from isolated colonies) would be used when further evaluation is needed.
○ Ms. Koeth: (from chat): I agree that this method should be described as a method that was validated against the reference method.
○ Dr. Weinstein: Suggested that the reference method should be used to resolve discrepancies. This is a standardized method but is not equivalent to a reference method.
○ Dr. Shawar: Reminded the group that reference methods are used for validating other methods and this method would not be used to validate a new method. Therefore, it is not a reference method. The data has showed that it works and can be used as other methods in M100 are used.

– The SC members agreed to move forward with the revisions to M100 as presented with some additional guidance on resolving discrepancies with full panels.
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<u>Quality Control WG Report</u>: Ms. Cullen/Ms. Traczewski (Folders H, J)
WG Roster: Sharon Cullen, Maria Traczewski (Co-Chairholders); Mike Huband (Secretary); Alexandra Bryson, Patricia Conville, Dana Dressel, Janet Hindler, David Lonsway, Erika Matuschek, Stephanie Mitchell, David Paisey, Elizabeth Palavecino, Chris Pillar, Susan Thompson, Katherine Young

• <u>Tier 2 QC Studies</u>
– Ceftobiprole (5 µg) Disk Diffusion QC ranges
<table>
<tr><td>Drug: Ceftobiprole (5 µg)</td><td>Abbreviation: BPR</td><td>Previous ID: NA</td></tr>
<tr><td>Solvent: No change (DMSO plus glacial acetic acid)</td><td>Diluent: No change (Water, vortex vigorously)</td><td>Preparation: No change</td></tr>
<tr><td>Route of administration: No change</td><td>Class: Cephems (parental)</td><td>Subclass: Cephalosporins with ant-MRSA activity</td></tr>
<tr><td>Study Report by: IHMA</td><td>Pharma Co: Basilea</td><td>Control Drug: Cefotaxime (for E. coli) and Cefoxitin (for S. aureus)</td></tr>
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<tr><th>QC Strain</th><th>Ceftobiprole (5 µg) Proposed Ranges
(WG approved 13 for; 0 against; 0 absent; 1 abstain)</th></tr>
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***E. coli* ATCC 25922**	25-31
***S. aureus* ATCC 25923**	20-27

– **Aztreonam-nacubactam (1:1) MIC QC Ranges**

Drug: Aztreonam/nacubactam (1:1)	**Abbreviation:** to be determined	**Previous ID:** ?
Solvent: Saturated solution of sodium bicarbonate/Water	**Diluent:** Water/Water	**Preparation:** Combine at ratio of 1:1
Route of administration: IV	**Class:** ß-lactam combination agents	**Subclass:** NA
Study Report by: IHMA	**Pharma Co:** Pharma Co: Meiji Seika Pharma Co, Ltd	**Control Drug:** Meropenem/ Nacubactam 1:1

Discussion	Current M100 Glossary I doesn't provide subclass for ß-lactam combination agents or distinguish between agents in this class (Aztreonam/nacubactam consists of a Monobactam/Diazabicyclooctane) Description and example for Tables 6A and 6C can be the same as Meropenem -nacubactam • Prepare 10x starting concentration as 1:1 ratio and dilute as needed. • For a starting concentration of 128/128 in the panel, prepare a 20x stock concentration of 2560 µg/ml for meropenem and 2560 µg/ml for nacubactam. Combine equal amounts of each to the first dilution tube, which will then contain 1280/1280 µg/ml of the combination. Prepare 2-fold serial dilutions and dilute each 1:10 with broth to achieve the final concentration in the microdilution wells.

QC Strain	**Proposed Aztreonam-nacubactam (1:1) MIC QC Ranges** WG Vote: 11/2/0/1 (For, Against, Absent, Abstain) Routine QC testing WG Vote: 13/0/0/1 (either *K. pneumoniae*)
***E. coli* ATCC 25922**	0.06/0.06-0.25/0.25
***P. aeruginosa* ATCC 27853**	2/2-8/8
***K. pneumoniae* ATCC 700603 Routine QC strain**	0.5/0.5-2/2
***K. pneumoniae* ATCC BAA-2814 Routine QC strain**	0.5/0.5-2/2

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Aztreonam MIC Integrity Check (include orange highlighting)

QC Strain	**Proposed Aztreonam MIC Integrity Check Range** **WG vote: 12/1/0/1** **(For, Against, Absent, Abstain)**
***K. pneumoniae* ATCC BAA-2814**	>128

– **Cefepime-nacubactam (1:1) MIC QC Ranges**

Drug: Cefepime/nacubactam (1:1)	**Abbreviation:** ?	**Previous ID:** ?
Solvent: PBS pH 6 0.1 mol/L/ Water	**Diluent:** PBS pH 6 mol/L /Water	**Preparation:** Combine at ratio of 1:1
Route of administration: IV	**Class**: ß-lactam combination agents	**Subclass:** NA
Study Report by: IHMA	**Pharma Co:** Meiji Seika Pharma Co, Ltd	**Control Drug**: Cefepime

Discussion	Current M100 Glossary I doesn't provide subclass for ß-lactam combination agents or distinguish between agents in this class (Cefepime/nacubactam consists of a Cephalosporin IV/Diazabicyclooctane) Description and example for Tables 6A and 6C can be the same as Meropenem-nacubactam • Prepare 10x starting concentration as 1:1 ratio and dilute as needed. • For a starting concentration of 128/128 in the panel, prepare a 20x stock concentration of 2560 µg/ml for meropenem and 2560 µg/ml for nacubactam. Combine equal amounts of each to the first dilution tube, which will then contain 1280/1280 µg/ml of the combination. Prepare 2-fold serial dilutions and dilute each 1:10 with broth to achieve the final concentration in the microdilution wells.

QC Strain	**Proposed Cefepime-nacubactam (1:1) MIC QC Ranges** WG votes: 13/0/0/1 (For, Against, Absent, Abstain) for QC 13/0/0/1 for routine QC with *K. pneumoniae* 2814 only
***E. coli* ATCC 25922**	0.016/0.016-0.12/0.12
***P. aeruginosa* ATCC 27853**	0.5/0.5-2/2
***K. pneumoniae* ATCC 700603**	0.12/0.12-0.5/0.5
***K. pneumoniae* ATCC BAA-2814** **Routine QC strain**	0.5/0.5-2/2

SUMMARY MINUTES

Item #	Description

– **Cefepime Integrity Check**

QC Strain	Proposed Cefepime Integrity Check Range WG vote: 13/0/0/1 (For, Against, Absent, Abstain)
***K. pneumoniae* ATCC BAA-2814**	>32

– **Tier 2 QC Range Voting**

A motion to accept the proposed QC ranges for ceftobiprole, aztreonam-nacubactam, aztreonam integrity check, cefepime-nacubactam, cefepime integrity check as presented was made and seconded. Vote: 11 for; 0 against; 1 absent (Pass).

- **Tier 3 QC**
  - **MIC Active Requests for Feedback or Data**
    - Daptomycin with *E. faecalis* ATCC® 29212:
      - The issue was addressed in M100 troubleshooting guide
      - The request to expand from 1-4 to 1-8 retracted
    - Others

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern
C. difficile ATCC 700057	Fidaxomicin	0.06–0.25	Request feedback for January meeting	Agar dilution, results out reporting MIC out on the low side, observing MIC at 0.03 (Anaerobe WG).
E. coli ATCC 25922	Imipenem	0.06–0.25*	Monitor/request feedback	One source reported 50% of results at low end of range at 0.12.
E. coli NCTC ATCC 13486 or AR Bank 349	Colistin	NA	Additional data needed to meet M23 Tier 2	*E. coli* NCTC 13486: target 4, with only occasional result of 2 or 8. EUCAST based on limited data AR Bank 349: target 2, range 1–4 approved June 2019 with limited disk & media data.

– **MIC QC to monitor for 3 years: Request feedback or data (Forward to the QCWG)**

QC Strain (ATCC)	Antimicrobic	Current Range (µg/mL)	Action Recommended	Concern
S. aureus ATCC 29213	Rifampin	0.004 to 0.016	Monitor/ request feedback	One report of *S. aureus* out low
E. coli ATCC 25922	Imipenem/ relebactam	0.06/4-0.25/4	Monitor/ request feedback	Report from one lab with results out high

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K. pneumoniae ATCC 700603	Imipenem/ relebactam	0.03/4-0.25/4	Monitor/ request feedback	Some out high reported with 2 labs
K. pneumoniae ATCC BAA-1705	Imipenem/ relebactam	0.03/4-0.25/4	Monitor/ request feedback	Results at high end with one lab.
K. pneumoniae ATCC 700603	Ampicillin/ Sulbactam	8/4 – 32/16	Request feedback	Report from one lab with results at 64/32
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. pneumoniae ATCC 49619	Levofloxacin	0.5-2	Monitor/request feedback	Modal 0.5 µg/mL among 1,520 values for 88.5% of results. Consider revising to 0.25-1. (Table 3-27). Refer to USCAST Quinolone report V1.2.
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.

– **Disk Diffusion Active Requests for Feedback or Data**

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern
P. aeruginosa ATCC 27853	Ceftriaxone	17-23	Request data, reassess range or troubleshooting information. No information on colonies within zones. **No change. Move to archive.**	Seeing colonies within zone of inhibition causing out of specification results
P. aeruginosa ATCC 27853	Amikacin	18-26	June 2019: Proposed 20-26 mm (781 results, 6 labs, 3 disk manufacturers, 4 media manufacturers including MH ref lot). Similar changes made for gentamicin and tobramycin in 2012 (new ranges higher & 7 mm in size). Aug 2020: Added data from UCLA. (99% 22-26 mm). **Summer 2020: Voted to change to 20-26 mm (also discussed option for 20-27 mm).**	• Out high for many labs. • A request was made to change the QC range to 20-26 (99.8% within range) or 20-27 (99.9% within range) mm. This change would be in line with the changes made for *P. aeruginosa* ATCC 27853 other aminoglycosides. • WG Vote was 13/0/0/1 (For, Against, Absent, Abstain)

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	E. coli ATCC 25922	Eravacycline	~~16-23~~ 17-24	Jan 2020: Approved change to 17-24 mm. Recommended review of statistics for next meeting. Summer 2020: Voted to change to 18-24	Results out high with multiple media & labs. Shift toward upper end of range; 4% out high with Tier 3 data. • Additional data requested at the January 2020 meeting. • Data added, 678 results in addition to the original Tier 2 data. • EUCAST has published a range of 18-24 mm. • Approved 17-24 mm. Recommended to review statistics for next meeting. • August 2020: Gavan statistics of Tier 3 data suggests 18-24 mm. 100% Tier 3 data in proposed range (same as EUCAST range). Vote: 13/0/0/1 (For, Against, Absent, Abstain).
	E. coli ATCC 25922	Minocycline	19-25	Request data.	Results at high end of range or out high (2 labs reported).

A motion to approve the revised QC ranges for amikacin with *P. aeruginosa* ATCC® 27853 (20-26 mm) and for eravacycline with *E. coli* ATCC® 25922 (18-24 mm) was made and seconded. Vote: 11 for; 0 against; 1 absent (Pass).

- **Azithromycin QC for *Salmonella* and *Shigella***
  - Azithromycin approved for testing gram-negative organisms (eg, *Salmonella* and *Shigella*).
  - There are currently no expected ranges with gram-negative QC strains.
  - The WG proposed that a comment be added to the QC box in Table 2A: "*Staphylococcus aureus* ATCC® 25923 (disk diffusion) or *Staphylococcus aureus* ATCC 29213 (MIC) (when testing azithromycin against *Salmonella* or *Shigella*)"

- **Future Topics**
  - Complete M23 QC subchapter
  - Revisit streamlined QC

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6.	**Text and Tables WG (TTWG) Report: Dr. Bobenchik/Dr. Campeau (Folders I, J)** **WG Roster**: April Bobenchik, Shelley Campeau (Co-Chairholders); Carey-Ann Burnham (Secretary); Suki Chandrasekharan, 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 Liaison Advisors) **M02 and M07 Revision Update** • M02 and M07 were reviewed by the TTWG and it was determined that a number of revisions are needed. • A proposal has been drafted and, once finalized, will be submitted for approval in the revision process. • Co-chairholders need to be identified as well as WG members to work on revising the documents. **CLSI Breakpoints Additions/Revisions Since 2010 Table** • Ms. Ferrell and Ms. Hindler have worked on revising the CLSI Breakpoints Additions/Revision Since 2010 Table. • The table has been revised to indicate if the breakpoints have been revised or are newly approved. • Because some users have noted that they were unaware of the table, it has been decided to relocate the table to be placed immediately after the Overview of Changes. • The CLSI Archived Resources table will also be relocated to the Overview of Changes. • The CLSI Epidemiological Cutoff Value Additions/Revisions table will be relocated to Appendix G for ECVs. **Table 1 Footnote Reformatting** • The CLSI editorial staff is updating footnotes throughout M100 to better adhere to CLSI style. – Footnote designations are transitioning from symbols to all letters ordered as the footnote appears in the text or table. – The Table 1 footnotes are a mix of symbols and letters and are in no particular order other than to be listed by organism group. – The footnotes will be streamlined and listed in order rather than splitting them up into organism groups. **Non-*Staphylococcus aureus* revisions** • It has been noted that the definitions of the non-*S. aureus* species are confusing to users. • New language from the coagulase-negative *Staphylococcus* (CoNS) WG will be added to highlight *mecA* and PBP2a as most definitive methods. A reference to a publication (submitted) will be added. • How to report resistance if more than one method is used will be clarified. • Current comments (6) (previously 5) and (12)(previously 11) will be revised for clarity. The footnote in the table in comment (6) will also be revised for clarity (see bold and yellow highlighted text). (6) Most methicillin (oxacillin) resistance is mediated by mecA, encoding PBP2a (also called PBP2'). **Testing for *mecA* and PBP2a are the most definitive tests for detection of methicillin (oxacillin) resistance for *Staphylococcus* spp.** Isolates that test positive for mecA or PBP2a should be reported as methicillin (oxacillin) resistant (see Appendix H).

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	Footnote a. For isolates of "other Staphylococcus spp." from serious infections for which the oxacillin MICs are 1–2 µg/mL, **testing for mecA or PBP2a should be considered as these are the most definitive tests for detection of methicillin (oxacillin) resistance** (see comment [18]). **Cefoxitin disk diffusion is not the preferred method for "Other *Staphylococcus* spp. (not listed above) but can be used if this is the only method available**." • It was determined that no formal vote by the SC members was needed. **Splitting Table 3F (New 3G)** • As an action item from the January 2020 meeting, Table 3F (now 3G) (Test for Detecting Methicillin [Oxacillin] in Staphylococcus spp.) has been split into two separate tables (3G-1 and 3G-2) – Table 3G-1 is now *S. aureus*/*S. lugdunensis* – Table 3G-2 is now All other staphylococci • Additional testing and reporting comments have also been streamlined. • The TTWG presented Option 1 to the SC and was accepted. **Glossary II: Update to Antimicrobial Abbreviations** • Glossary II was revised to update the abbreviations and remove abbreviations that are no longer used. • A CLSI recommended (most commonly used) column was added to indicate abbreviations preferred by the Susceptibility Test Manufacturers Association (STMA) and ASM. The abbreviations have been harmonized. It was noted that AST device manufacturer abbreviations may differ from the recommended abbreviations. **Table 2A: Direct Blood Culture for Enterobacterales** • The TTWG agreed with the recommendations presented by the MDSWG. • The procedure will be added to M100 as Table 3F. **Cephem (oral) Breakpoints (BPs)** • Customers have noted category mismatches between cefuroxime AST results and cefazolin AST results to predict cefuroxime activity to treat urinary tract infections. This comment refers to urine BPs only. • Cefuroxime can test as resistant but cefazolin tests as susceptible. • Cefuroxime BPs are based on serum levels and cefazolin BPs are based on urine levels. • It was proposed to add a new comment that addresses the confusion: **"These breakpoints predict activity for infections other than UTI (i.e., the breakpoints are based upon serum concentrations of the drug). Isolates that test resistant to cefuroxime using these breakpoints may test susceptible to cefazolin using the UTI breakpoint (U). Activity of cefuroxime for UTI may best be predicted using cefazolin susceptibility testing."** • The WG questioned whether comments would be needed for the other cephems as well. • The TTWG will plan to work on this issue for the January 2021 meeting and the 32nd edition of M100.

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	Appendix E: Dosage Regimens • It was noted that Appendix E does not currently include any dosage regimens for anaerobic breakpoints (BPs). • Imipenem-relebactam BPs were recently added and include a specific dosage regimen. • Dr. Carpenter noted that it would be difficult to retrospectively add dosage regimens for agents already in the anaerobe BP table. Therefore, going forward, dosage regimens for anaerobes will be added to Appendix E and the anaerobe BP table. **Appendix I: Cefiderocol Revision** • Revisions for the cefiderocol procedure have been submitted by Dr. Lonsway and the sponsor Shionogi. • Instructions to measure iron levels at multiple steps and ensure all reagents have low levels of iron will be added. • The concentration of HCL for adjusting pH and the calculation for Zn++ addition will also be revised.
7.	**Adjournment** • Dr. Weinstein thanked the Chairholders of the MDS, QC, and TT WGs for their presentations as well as the WGs as a whole. • The meeting was adjourned at 4:15 PM Eastern (US) time.

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#	**Description**
Tuesday, 29 September 2020	
1.	Dr. Weinstein opened the meeting at 12:00 PM Eastern (US) time.
2.	**<u>FDA Update</u>:** (Dr. Nambiar/Dr. Farley) **Dr. Nambiar and Dr. Farley provided an FDA update.** • The FDA is currently working through the documents submitted to the docket. – The submission for azithromycin for *N. gonorrheoae* is currently under review. – The review of the colistin/polymyxin B rationale document is on hold due to the COVID pandemic. • The FDA Susceptibility Test Interpretive Criteria (STIC) website was recently updated on August 25, 2020. – The daptomycin rationale for *E. faecium* was reviewed; however, the CLSI BPs were not recognized as per agency policy because the higher dosage regimen is not on the label. It was noted that the BPs previously were for *Enterococcus* spp. and not individual species. – The agency is trying to be flexible in regard to dosage regimens as long as safety data is available. They did not have access to sufficient data for daptomycin and *E. faecium* to approve the BPs. – Dr. Young stated that Merck would be able to bring any additional data for daptomycin to the SC for review. • Cefiderocol BPs have been approved and post to the STIC website. • SC Discussion (**Note:** Comments or questions may be paraphrased). – Dr. Lewis questioned the decisions made in regard to discrepancies with cefiderocol BPs. – Dr. Nambiar stated that the cefiderocol report should be posted in the near future. She noted that the information available could not support the CLSI-approved cefiderocol BPs. – It was expected that the issues regarding cefiderocol will be discussed during the January 2021 meeting. These issues have been ongoing with the sponsor and it is hoped that additional clinical data and PK/PD will be available for review.
3.	**<u>New Item: M45 Revision</u>** (Dr. Humphries/Dr. Simner) An overview of plans for the revision of M45 (3rd edition published in August 2016) was provided. • The current edition was reviewed by the previous WG co-chairholders, Dr. Richter and Ms. Hindler. • Based on their review and recommendations, a number of updates were suggested. – Update current organism tables including references and guidelines based on current literature. – Request unpublished data for review. – Review BP tables in M100 that may be more appropriate in M45. – Review methods for any potential updates. – Evaluate any new resistance mechanisms and reports on treatment failures. – Add any new organisms not currently in M45 – Simplify the QC tables • The revision has been endorsed by the SC members. – Dr. Humphries and Dr. Simner will serve as Co-chairholders of the WG that will be formed to revise the document.

#	Description

- Suggestions on unmet needs, challenges with current BPs, methods, and QC were requested.
- Anyone with unpublished data and/or expertise should contact Dr. Humphries or Dr. Simner.

- Next steps
  - A revision project proposal has been drafted and is in review.
  - Once finalized, the proposal will be submitted to the Expert Panel on Microbiology for review, possible revision, and endorsement.
  - The endorsed proposal will be submitted to Consensus council for final approval.
  - If approved, a call for volunteers within the SC (and outside, if needed) will be distributed and a WG formed.
  - The final roster will be submitted for approval by the SC Chairholder.
  - Once the roster is approved, the revision will begin.
  - It is expected that the revision will formally begin by June 2021.

4. **Breakpoint WG (BPWG) Report**: Dr. Lewis/Dr. Satlin (Folders E, F, K)

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

Lefamulin BPs (Dr. Lewis)(Folder F – Items 1-8)

Dr. Lewis presented an overview of lefamulin and data to support BPs requested by the sponsor for approval. The proposed BPs have been approved by the FDA.

- General information, approved indications, and dosage schedule were presented.
  - Chemical Structure: Pleuromutilin with targeted anti-bacterial spectrum
  - Low resistance rate
  - Indications: Adults with community-acquired bacterial pneumonia (CABP)
  - Dosage: IV, 150 mg every 12 hours IV infusion over 60 minutes for 5 to 7 days; Oral, 600 mg orally every 12 hours for 5 days
  - Activity against a variety of organisms (eg, gram-positive and fastidious gram-negative organisms). Not active against Enterobacterales and *P. aeruginosa*.
  - FDA has approved interpretive criteria posted on the FDA STIC website. Additional organisms will be reviewed at a future meeting.

Pathogen	MIC (µg/mL)			Disk Diffusion (mm)		
	S	I	R	S	I	R
S. aureus (methicillin [oxacillin]-susceptible)(MSSA)	≤0.25	-	-	≥23	-	-
S. pneumoniae	≤0.5	-	-	≥17	-	-
H. influenzae	≤2	-	-	≥17	-	-

- The sponsor requested for CLSI to approve the current FDA breakpoints and include methicillin (oxacillin)-resistant *S. aureus* (MRSA).
- Lefamulin study data was reviewed.
  - Pharmacokinetic (PK) and pharmacodynamic (PD) target attainment analysis
    - Lung infection studies in neutropenic mice and PK studies in healthy volunteers and patients.
    - Data showed target attainments are above 90% for all the proposed organisms.
  - Clinical efficacy studies: LEAP 1 (IV to oral) and LEAP 2 (Oral)
    - Short course IV and or oral monotherapy with spectrum of activity against CABP pathogens

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- Two Phase 3 trials (IV, IV-oral, oral only) in patients with CABP met the primary endpoint of noninferiority criteria per the EMA and FDA guidance
- Investigator assessment of clinical response (IACR)response rates at test of cure were >85% for lefamulin and exhibited similar success rates to the standard-of-care moxifloxacin across baseline pathogens consistent with CABP
- Overall, lefamulin was generally safe and well tolerated.

- The following BPs were proposed by the sponsor. Note: These are the same as the FDA-approved breakpoints except for *S. aureus*.

Pathogen	MIC Breakpoint (Susceptible Only)	DD Breakpoints (Susceptible Only)	Comments
S. pneumoniae	≤ 0.5	≥ 17	• Based on the ECV (99.0%) of 0.5 µg/mL • Non-clinical PK/PD cutoff of ≤ 1 µg /mL (median) • Clinical cutoff of 0.5 µg/mL • High clinical efficacy results for *S. pneumoniae* • No VME or ME at proposed breakpoint
S. aureus (MSSA and MRSA)	≤ 0.25	≥ 22	• ECV (99.0%) of 0.25 µg/mL • Non-clinical PK/PD cutoff of ≤ 0.5 µg/mL (median) • Clinical cutoff of ≤ 0.25µg/mL • For both MRSA and MSSA (proposed breakpoint adjusted from FDA-approved breakpoint to include MRSA) • No VME or ME at proposed breakpoint
H. influenzae	≤ 2	≥ 17	• Based on ECV value (99.0%) of 2 µg/mL and clinical cutoff of ≤ 2 µg/mL • No validated non-clinical mouse model available • *H. influenzae* diagnosed Phase 3 clinical trials) using quantitative real-time PCR. • High success rate for patients positive for *H. influenzae* by PCR only • Assumed that MICs of *H. influenzae* identified by PCR would be below the ECV and therefore the good clinical success for *H. influenzae* in these patients supports a susceptible breakpoint for the wild-type population set at the ECV • No VME or ME at the proposed breakpoint

- Ad Hoc (AHWG) WG Summary
  - PD analyses are not well-defined for Pleuromutilins.
  - The data provided are consistent with the guidance provided in M23.
  - MRSA MIC distribution shifted slightly to the right in some data sets, but this was dependent on the source of the data. The majority of MIC distribution data was from JMI, but other data sets indicated similar results.
  - Clinical response data included a discussion about lower success rates in PSSP (more severe infections) and low numbers of MRSA in clinical trials (but much MIC data).
  - Although CLSI prefers to set BPs with an intermediate category, a very steep PK/PD drop-off and limited information about lefamulin-resistant isolates persuaded AHWG to agree to S only BPs.
  - The AHWG agreed with the FDA and sponsor proposed BPs (4-0).

#	Description

- BPWG Discussion
  - **Question on testing result reproducibility**: Sponsor - There have been no problems observed for both MIC and disk testing variabilities. Reproducibility data are available in the briefing book.
  - **Was there any information about MIC testing variability that might suggest that an Intermediate category was justified**?: Sponsor - There were so few isolates that might fit into the "I" category that it would be difficult to set valid limits.
  - **Question on media used for susceptibility testing studies:** Sponsor - Various media were compared for EUCAST and FDA/CLSI. No significant differences were observed.
  - **Why there was no "I" for *S. pneumoniae* or *H. influenzae***: Sponsor – Non-susceptible BPs were set for isolates that didn't fall within "S" category. If there are very few, or no resistant isolates, it is difficult to know where to draw the line between "I" and "R". Concern regarding "If there is no interpretation provided, clinicians may be prone to make errors in judgement.
  - **Does the "R" category mean the isolate is clinically resistant, particularly with *S. pneumoniae* and *H. influenzae***?: Sponsor - Very few isolates are "R", but needs to be monitored in the future. Data should be available by January, but request that the breakpoints to be published in the January M100 (31st ed).
  - **Note:** The AHWG was comfortable with having MRSA included in the BP proposal.
  - Placement in Appendix A (Confirming AST test results) and Appendix B (intrinsic resistance) also needs to be considered.

- Final Sponsor request with inclusion of MRSA for *S. aureus* with a lower disk zone for *S. aureus* than the FDA to include both MSSA and MRSA (Approved 9 for; 0 against; 3 absent by BPWG).

Pathogen	Minimum inhibitory Concentration (µg/mL)			Disk Diffusion (mm)		
	S	I	NS	S	I	NS
S. pneumoniae	≤0.5	-	≥1	≥17	-	≤16
S. aureus	≤0.25	-	≥0.5	≥22	-	≤21
H. influenzae	≤2	-	≥4	≥17	-	≤16

- Subcommittee Discussion (**Note:** Comments and questions may have been paraphrased)
  - **Dr. Kuti**: Questioned the BPWG about the percent target attainment being lower in epithelial lining fluid (ELF) than in plasma and which thresholds were being used.
    - **Dr. Lewis**: There was concern from the AHWG and it was discussed extensively.
    - **Dr. Scheetz**: Noted that the sponsor used a variety of targets and don't know for certain what the target is. There could be a range of targets that could be appropriate. There might be a lowering of one doubling dilution in the ELF. The AHWG didn't think there was enough variability to discount the BPs set by the FDA. He noted that the he believed the ELF thresholds were being used.
    - **Dr. Wicha** (sponsor representative): Both thresholds were used in the analysis. The differences were considered when the BPs were proposed and are likely due to the differences between the mouse model and man.
  - **Dr. Simner**: In the *S. aureus* BP proposal, initially the more susceptible population data was reviewed and then the more resistant data was reviewed. The WG then decided to switch from ≥23 (FDA) to ≥22 for the susceptible BP. She noted that with the resistant isolates, the BP is getting

#	Description
	close to the cutoff and questioned if the WG still wants to pursue the lower BP. She also asked if the gradient diffusion test had been compared to BMD. She questioned if it was worth switching to the lower BP and subsequently be different than the FDA BPs. o **Dr. Schuetz**: The point is good but there was little discussion on the issue. o **Dr. Pierce**: The sponsor brought additional data regarding incorporating more resistant isolates; however, resistant isolates are very rare. o **Ms. Cullen**: Cautioned that the correlation between gradient diffusion and BMD needs to be known. o **Dr. Paukner**: Noted that a correlation study is in progress and additional data will be available at the January meeting. Overall, the gradient diffusion strips are approved by the FDA and showed good comparability with broth microdilution. The sponsor requested the smaller zone size because they wanted to include MRSA in the BPs. o **Dr. Shawar**: The FDA decision summary showed that the gradient diffusion strips compared well with the broth microdilution test. *S aureus* tended to agree or be within one doubling dilution lower. o **Dr. Satlin**: Agreed with Dr. Simner the BP for *S. aureus* should not be lowered (from FDA-approved BP) based on one isolate.
	A motion (Dr. Satlin) to accept the *S. aureus* (MSSA and MRSA) MIC susceptible-only BP (≤0.25) and the FDA-approved disk diffusion susceptible-only BP (≥23) was made (Dr. Satlin) and seconded (Dr. Simner). Vote: 11 for; 0 against; 0 abstentions; 1 absent (Dr. Mazzulli). (Pass)
	– **Dr. Humphries**: Noted that her approval vote was contingent on getting data from broth microdilution for the challenge isolates that were tested using gradient diffusion. o Dr. Lewis: Noted that the sponsor plans to bring the BMD data to the meeting in January. o Dr. Paukner: Susceptible isolates will also be included in the BMD study. – **Dr. Satlin:** Expressed concern regarding the absence of resistant isolates in the disk correlate studies for *S. pneumoniae*. It is difficult to set disk correlates when VMEs can't be calculated. o **Dr. Lewis**: The AHWG and BPWG discussed this issue at length. o **Dr. Paukner**: Non-susceptible isolates were not available when the studies were performed. For the disk correlate studies, resistant isolates will be included and should be available in January.
	A motion to approve the proposed FDA-approved susceptible-only MIC BPs for lefamulin *S. pneumoniae* (≤0.5) and *H. influenzae* (≤2) and disk diffusion BPs for *S. pneumoniae* (≥17) and *H. influenzae* (≥17) provided more data is presented in January on where resistant isolates would lie was made (Dr. Satlin) and seconded (Dr. Schuetz). Vote: 11 for; 0 against; 0 abstentions; 1 absent (Dr. Mazzulli).(Pass)
	– **Dr. Lewis**: Questioned if a vote in needed for the motion to add a comment similar to that used for drugs that should not be reported for CSF isolates or for patients with meningitis or for urine isolates with Text and Tables will be assigned the task of providing consistent wording for drugs with similar limitations.
	A motion to add a comment with the BPs that is similar to that used for drugs that should not be reported for CSF isolates, for patients with meningitis, or for urinary tract isolates with Text and Tables WG being assigned to provide consistent wording for drugs with similar limitations was made (Dr. Satlin) and seconded (Dr. Mathers). Vote: 11 for; 0 against; 0 abstentions; 1 absent (Dr. Mazzulli). (Pass)
	– **Dr. Weinstein**: Noted that there currently is a warning box regarding this issue in M100 and lefamulin should be added to the list of drugs that should not be tested or reported on CSF isolates.

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	A motion to place lefamulin in Group B in Tables 1 for *S. aureus* and *S. pneumoniae*, and Group C for *H. influenzae* as proposed by the sponsor with the caveat that Table 1 is being reassessed and may alter the placement was made (Dr. Satlin) and seconded (Dr. Kirn). Vote: 11 for; 0 against; 0 abstentions; 1 absent (Dr. Mazzulli). (Pass)
	As motion to accept the Appendix A, Category 1 placement for lefamulin was made (Dr. Simner) and seconded (Dr. Limbago). Vote: 11 for; 0 against; 0 abstentions; 1 absent (Dr. Mazzulli).(Pass)

- The intrinsic resistance WG will review the data for inclusion of lefamulin in Appendix B.

Linezolid Susceptibility as a Surrogate to Predict Tedizolid Susceptibility Against Indicated Species (Dr. Lewis)(Folder E – Item 2)

- Background
  - Tedizolid is approved (FDA and EMA) for treating acute bacterial skin and soft tissue infections.
  - The FDA recognizes the susceptibility interpretive criteria published in CLSI M100.
  - EUCAST includes a note with the MIC breakpoints for *Staphylococcus* spp. and *Streptococcus* groups A, B, C and G that states: "Isolates susceptible to linezolid can be reported as susceptible to tedizolid".
  - Objectives were to:
    - To evaluate if the susceptible MIC results obtained for linezolid correlate to susceptible results for tedizolid when tested against FDA-approved species
    - To propose footnotes at the appropriate CLSI M100 Tables indicating that linezolid susceptible MIC results can be used to report as susceptible results to tedizolid

CLSI				EUCAST		
Tables (Species)	Breakpoint[a]			Tables (Species)	Breakpoint[a]	
	S	I	R		S	R
Staphylococcus spp. (*S. aureus*)	≤0.5	1	≥2	*Staphylococcus* spp.	≤0.5	>0.5
Enterococcus spp. (*E. faecalis*)	≤0.5	—	—	*Enterococcus* spp.	IE	IE
ß-hemolytic streptococci (*S. pyogenes* and *S. agalactiae*)	≤0.5	—	—	*Streptococcus* groups A, B, C and G	≤0.5	>0.5
Viridans group streptococci (*S. anginosus* group)[b]	≤0.25	—	—	Viridans group streptococci (*S. anginosus* group)[b]	≤0.25	>0.25

[a] S, susceptible; I, intermediate; R, resistant; "—", breakpoint not available; IE, insufficient evidence
[b] Includes *Streptococcus anginosus*, *S. intermedius* and *S. constellatus*

- A study was performed to determine if susceptible results obtained for linezolid correlate to the susceptible results for tedizolid when tested against FDA-approved species.
  - Method: Reference BMD
  - Surveillance isolates from the STAR program were tested
  - Surrogacy analysis performed by scattergram graphs plotting tedizolid against linezolid MIC results obtained against each indicated species and respective current CLSI susceptibility criteria were applied.

- Conclusions: Data presented support using a susceptible linezolid MIC result to predict a susceptible result to tedizolid.
  - *S. aureus*, *S. pyogenes*, *S. agalactiae*, and *S. anginosus* group that showed susceptible MIC results to linezolid were susceptible to tedizolid.
  - *E. faecalis* that showed susceptible MIC results to linezolid were susceptible to tedizolid.
  - MIC results categorized as susceptible to linezolid and resistant to tedizolid were not observed ("false susceptible").

- **Proposal: Add footnotes (*Isolates susceptible to linezolid can be reported susceptible to tedizolid*) to Tables 2C, 2D, 2H-1 and 2H-2 in CLSI M100 tables indicating that linezolid susceptible MIC results can be used to report susceptible results for tedizolid. The vote passed in the BPWG.**

- Subcommittee Discussion (**Note:** Comments and questions may have been paraphrased.)
  - **Dr. Humphries**: For consistency within M100, Text and Tables should revise the comment to clarify that resistance to linezolid doesn't necessarily indicate that tedizolid is also resistant and the isolate should be tested against tedizolid.
  - **Señor Esparza**: Will this apply to both MIC and disk diffusion testing results? Dr. Mendes noted that there currently is no disk data.
  - **Dr. Satlin**: Should *E. faecium* be included in the comment.
    - Dr. Humphries noted that there currently is no BP for *E. faecium* and tedizolid, so it is questionable to report as tedizolid susceptible of linezolid is susceptible.
    - Dr. Mathers: Agreed with omitting *E. faecium*.
  - **Mr. Bowden**: Is the intent to test linezolid and, if susceptible, report out tedizolid as susceptible to report linezolid as susceptible and add a comment that tedizolid be considered susceptible?
    - **Dr. Weinstein**: There is precedent for reporting a result when a surrogate is tested.
    - **Dr. Humphries**: Stated that the decision on how to report should be decided within the individual laboratories.
    - It was agreed that since this testing only goes in the direction of susceptibility but not resistance, the drugs are not equivalent.

A motion to add footnotes to Tables 2C, 2D, 2H-1 and 2H-2 in CLSI M100 tables stating that, "Organisms that test susceptible to linezolid by MIC are also considered susceptible to tedizolid (ie, *S. aureus*, *S. pyogenes*, *S. agalactiae*, *S. anginosus* group and *E. faecalis*)" and data do not currently exist for disk diffusion was made (Dr. Mathers) and seconded (Dr. Humphries).. Vote: 11 for, 0 against, 0 abstentions, 1 absent (Dr. Mazzulli). (Pass)

SUMMARY MINUTES	
#	Description

Azithromycin/*Shigella* Breakpoints (Dr. Satlin)(Folder E – Items 1a – 1h)

- Background
  - BPs proposed by the CDC National Center for Emerging and Zoonotic Infectious Diseases
  - As of 2015, there are epidemiological cut off values (ECVs) for azithromycin with *Shigella* spp. published in M100, Appendix G (wild type [WT] = ≤ 16; non-wild type [NWT] = ≥32 for *S. sonnei* and WT = ≤8, NWT ≥16 for *S. flexneri*).
  - Rationale for setting BPs included:
    - Azithromycin is a recommended treatment for shigellosis.
    - Azithromycin NWT has dramatically increased (as per the National Antimicrobial Resistance Monitoring System [NARMS]). Resistance to all other agents routinely reported by clinical laboratories is common.
    - Clinical laboratories are not performing azithromycin susceptibility testing because there are no BPs and patients with NWT infections are treated with azithromycin and have poor outcomes.
    - BPs will facilitate FDA approval of clinical testing devices and setting azithromycin breakpoints will improve patient care.

- Recap from the January 2020 Meeting
  - Data from a prospective clinical outcome a UVA-Bangladesh study (Houpt et al. CID 2020) was presented.
  - CLSI recommendations included:
    - Present a breakdown of outcomes by MIC
    - Present disk diffusion correlates by species

- Data presented included:
  - *Shigella*/azithromycin outcomes by MIC from the UVA-Bangladesh study (MICs using dry BMD panels).
  - *Shigella*/azithromycin outcomes by MIC using frozen BMD panels.
  - Results from a cohort of patients infected with azithromycin-NWT *Shigella* from California Dept of Public Health.
  - MIC and disk diffusion data for *S. flexneri* and *S. sonnei*.

- Conclusions
  - There were challenges reading MIC (endpoint issues) and disk diffusion results (differences due to medium used) with *S. sonnei*.
  - There were few VMEs and MEs but some mEs.

- Final CDC Proposal for a unified BP

Pathogen	MIC (µg/mL)			Disk Diffusion (mm)		
	S	I	R	S	I	R
Shigella spp.	≤ 8	16	≥ 32	≥ 16	12-15	≤ 11

  - Best fit for clinical and microbiological data
  - Tough to find a good, single set of disk BPs for *S. flexneri* and *S. sonnei*
  - Disk might overcall resistance for sonnei in some cases (hazy, swarmy growers)
  - Alternative: Recommend MIC testing?

#	Description

- BPWG Discussion
  - There were concerns that many laboratories cannot distinguish the species so a unified BPs would be optimal.
  - It was agreed that the UVA-Bangladesh clinical data was useful, but the other data was of less value.
  - QC information from the studies is needed.
  - Appears to be a similar situation as seen with disk diffusion AST for *Campylobacter* and macrolides: Isolates with no zones are resistant but an MIC is needed for any tests with a zone of inhibition.
  - BPWG Motions/votes:
    - Motion #1: Set *Shigella* breakpoints for the entire genus as suggested by CDC.
      - S: ≤8; I: 16; R: ≥32 (µg/mL)
      - Passed: Yes (10), No (0), Abstain (1), Absent (2)
    - Motion #2: Isolates with no zone of inhibition would be considered resistant. If there is a zone of inhibition, MIC testing is recommended - Did not pass: Yes (1), No (9), Abstain (1), Absent (2).
    - Motion #3: Set disk diffusion breakpoints with a comment that if the diffusion result is Intermediate, an MIC test is recommended.
      - S: ≥16 mm; I: 11-15 mm; R: ≤10 mm
      - Passed: Yes (10), No (0), Abstain (1), Absent (2)
  - Proposed text updates for M100, 31st edition, Table 2A included:
    - Add comment for *Shigella* testing:
      - "Azithromycin disk diffusion zones and MIC endpoints can be hazy and difficult to measure for *Shigella* spp., especially *sonnei*. If an isolate has a zone of inhibition that is difficult to measure, an MIC may help to distinguish S, I or R. Media source may impact the clarity of the endpoints for disk diffusion tests."
    - Delete second sentence of comment 43 (that references *Shigella* ECVs)
      - "(43) *S. enterica* ser. Typhi only: breakpoints are based on MIC distribution data and limited clinical data. ~~For S. flexneri and S. sonnei, see Appendix G, Table G1.~~"
    - Regarding Routine QC Recommendations:
      - Add "*S. aureus* ATCC® 29213 (for MIC testing of azithromycin)"
      - Adjust parenthetical for *S. aureus* ATCC® 25923 to read "for *S. enterica* ser. Typhi **and *Shigella*** azithromycin disk diffusion testing only; see Table 4A-1"

- Subcommittee Discussion (**Note:** Comments or questions may be paraphrased.)
  - **Dr. Schuetz**: Questioned if there were different BPs when CDC brought additional data (No).
  - **Dr. Shawar**: Questioned if there were multiple lots of disks, multiple brands of disks or media, etc.
    - **Dr. Galas:** Noted that the values came from one laboratory in Canada and there was one brand of media.
    - **Dr. Humphries**: Noted that it has been shown that certain brands of Mueller-Hinton had a propensity for hazy growth and without naming brands this could be brought to user attention.
    - **Ms. Cullen:** There are a number of mEs for disk testing which are concerning. She suggested that a statement regarding additional testing by MIC when testing intermediate may be needed.
    - **Dr. Whichard**: *S. sonnei* can be a challenge to read to hazy swarming. *S. sonnei* seems to be the cause of the mEs being elevated.
  - It was suggested the motions could be broken into one of MIC and one for disk diffusion or one for *S. flexneri* and one for *S. sonnei*.
    - **Dr. Lewis:** The WG tried to avoid splitting the motions because so many laboratories only perform disk diffusion and also may not be able to identify the organisms to the species.

#	Description
	○ **Dr. Mathers**: Noted that this was discussed at length in the BPWG meeting and it is recognized that these BPs are greatly needed. The data show that there are significant increases in NWT and not having a disk diffusion breakpoint available would create significant problems for testing laboratories. ○ **Dr. Humphries**: There are issues with the disk diffusion results most likely issues with swarming. Work may be needed to make the disk diffusion easier to perform. ○ **Dr. Shawar**: For problematic species, perhaps the laboratories could be directed to do further species identification. ○ **Dr. Whichard**: The dBets analysis shows a much smaller range for intermediate. ○ **Dr. Humphries**: the CLSI process doesn't allow a small intermediate range. ○ **Ms. Hindler**: EUCAST did a study with *S. sonnei*, and saw issues with one media brand. She suggested that a QC organism could be identified that manufacturers could use to test their media.
	A motion to accept the *Shigella* MIC azithromycin BPs for the entire species as proposed by the CDC (S=≤ 8; I =16; R= ≥ 32 µg/mL) was made (Dr. Humphries) and seconded (Dr. Mathers). Vote: 9 for; 0 against; 0 abstentions; 3 absent (Dr. Mazzulli, Dr. Limbago, Dr. Kirn) (Pass).
	A motion to accept the *Shigella* disk diffusion azithromycin breakpoints for the entire species as proposed by the CDC (S = ≥ 16; I = 11-15; R = ≤ 10) with a comment stating that if the results is intermediate, that an MIC test is recommended (see below) was made (Dr. Satlin) and seconded (Dr. Humphries). Vote: 7 for; 2 against; 0 abstentions; 3 absent (Dr. Mazzulli, Dr. Limbago, Dr. Kirn) (Pass).
	Comment: "Azithromycin disk diffusion zones and MIC endpoints can be hazy and difficult to measure for *Shigella* spp., especially *sonnei*. If an isolate has a zone of inhibition that is difficult to measure, an MIC may help to distinguish S, I or R. Media source may impact the clarity of the endpoints for disk diffusion tests." – Dr. Richter and Dr. Schuetz both believed that it would be better to set the disk diffusion breakpoints for the species separately. – Additional suggestions for edits in M100 did not require a vote.
5.	**Table 1 Revision Discussion: T. Simner (Folder K)** **NOTE: This item was discussed during a separate virtual meeting held on 20 October 2020.** **Table 1 WG roster:** George Eliopoulos, Trish Simner (Co-Chairholders); Virginia Pierce (Secretary); Tanaya Bhowmick, April Bobenchik, Carey-Ann Burnham, Barth Reller, Sandy Richter, Lauri Thrupp, Matt Wikler **Dr. Simner provided a recap of the WG's activity since the January 2020 meeting.** • The definitions that qualified antimicrobial agents to Groups A through C were refined.

Group	Inclusion Requirements	When to Report

Group A- are considered appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism groups		
Group A – Primary Test and Report	FDA- Approved Agent Proven clinical efficacy for the organism group Clinical outcome studies & expert opinion indicating primary use Representative narrow-spectrum agent(s) of the class Acceptable *in vitro* test performance	Routinely test and report.
Group B- includes antimicrobial agents that may warrant primary testing, but they may be reported only selectively, such as when the organism is resistant to agents of the same antimicrobial class, as in group A.		
Group B – Primary Test Report Selectively	FDA- Approved Agent Resistance to Group A agent(s) Acceptable *in vitro* test performance Known local resistant strains	Routinely test and report selectively (unless resistant) Can consider reporting routinely based on: Institution guidelines Due to resistance to agent(s) in Group A (i.e., cascade reporting) Due to allergies or intolerance Epidemiologic aid Polymicrobial infections Infections involving multiple sites with different microorganisms Nosocomial infections Failure to respond to an agent(s) in group A

Group	Inclusion Requirements	When to Report
Group C – includes alternative or supplemental antimicrobial agents that may require testing in those institutions that harbor endemic or epidemic strains resistant to several of the primary drugs; for treatment of patients allergic to primary drugs: for treatment of unusual organisms; or for reporting to infection control as an epidemiological aid.		
Group C – Supplemental Report Selectively	• FDA- Approved Agent • Resistance to Group A and Group B agents • Acceptable *in vitro* test performance • Known local resistant strains	• Test and report by clinician request Can consider testing and/or reporting routinely based on: • Institution guidelines • Due to resistance to agent(s) in Groups A and B (i.e., cascade reporting) • Due to allergies or intolerance • Unusual organisms • Epidemiologic aid • Polymicrobial infections • Infections involving multiple sites with different microorganisms • Nosocomial infections • Failure to respond to an agent(s) in groups A and B • Oral agents for outpatient setting • Long acting agents • Agents with limited to no extended activity over Group A agents (i.e., ceftazidime for *A. baumannii* vs cefotaxime/ceftriaxone)

- WG voted to move new agents (eg, ceftazidime-avibactam, ceftolozane-tazobactam, etc.) to Group C (6-0-1)

SUMMARY MINUTES	
#	Description
	• Agents for the various organism groups were rearranged based on the new definitions and the changes that the WG voted on were reviewed and presented to the plenary at the January 2020 meeting. • Feedback from the plenary was given to the WG; however, no AST SC votes were taken as the tables (not available before the plenary). • Since January, the WG has been working to address the concerns about placement of new agents into Group C. – Published data have shown that delaying initiation of novel ß-lactamase combination agents for treating Enterobacterales resistant to empiric therapies may lead to poor clinical outcomes. Placing the agents in Group C will delay AST results for these agents. – Smaller hospital laboratories may not understand how to use Group C or to define when a resistant agent is endemic. They may disregard any Group C agents and opt not to test them. – Placing the agents in Group C sends an unintended message that the novel agents are not as effective as those listed in Groups A and B. – Placement in Group C may delay testing and, subsequently, treatment. – Group C has been historically included agents of last resort (eg, colistin). • Three options for placement of new agents were presented along with pros and cons of each option. Option 3 was slightly preferred by the WG members. – Place the novel agents into Group B with or without a comment and address the Group B and C definitions. – Place the novel agents in Group C with a comment regarding cascade reporting. Address the Group B and C definitions. – Create a new group: A (current A), B1 (current B), B2 (novel agents), and C (current C). • The WG requested that the SC provide direction on the next steps. – January 2021: Review the definitions and assign agents to various groups and vote. – June 2021: Submit WG proposal for agent placement based on organism group and request an SC vote – It was noted that any major revisions to the table would be included in M100, 32nd edition to publish in 2022. • Subcommittee Discussion (**Note:** Comments or questions may be paraphrased.) – **Dr. Gold:** Made a motion to accept Option 3 (new category for new agents). Seconded by Dr. Kirn. – **Dr. Satlin**: B1 includes agents that may warrant primary testing. Questioned if the agents in B2 may also warrant primary testing. – **Dr. Simner**: B2 also covers those agents that may be used for treatment of resistant organisms that may be present in an individual institution. They could be included on the primary panel for that institution. – **Dr. Narayanan**: Questioned if other agents currently in Group B could also be moved to Group B2 (eg, aminoglycosides). – **Dr. Simner**: The intent of the groups is to encourage cascade reporting based on institutional guidelines. The WG will re-review the current agents to determine if others can be included in Group B2. – **Dr. Limbago**: All the revisions are going to require a major education initiative. She suggested renaming the groups to eliminate the stigma associated with the groups and create a whole new concept (eg, primary report [A], cascade report [B], report only on request [C]). – **Dr. Simner**: Agreed that this would highlight the concept of cascade reporting. – **Dr. Humphries**: Asked for confirmation of her understanding that with Option 3, there would be tiers of reporting and to test and report Group C if needed. She asked if other drugs already in the tables be re-evaluated and regrouped.

#	Description
	– **Dr. Simner**: Agreed with the 3 reporting tiers. She noted that all current placements will be re-evaluated. The placement of Enterobacterales may also be re-evaluated based on resistance factors. – **Dr. Carpenter**: Believes that creating a new category emphasizes that are different and that footnotes tend to get lost. – **Dr. Narayanan**: Expressed concern that having 2-B categories implies that B1 should always be tested and reported and B2 may be tested and reported. – Several participants noted that education is going to be critical for users to understand the changes. – **Dr. Simner**: Suggested that for the upcoming M100 update that the purpose of Tables 1 and indicate that changes are coming. – **Dr. Motyl**: Questioned if the WG had taken IDSA guidance into account when placing agents in groups. She also suggested that laboratories will prefer to use only 1 drug panel. She was also concerned that there may need to add B3, B4, etc. She endorsed the suggestion made by Dr. Limbago. – **Dr. Lewis:** Believed the B2 category does encourage testing in institutions with resistant organisms and does fit well with the IDSA guidelines. – **Dr. Thrupp**: Commented that B2 option is favored and seems to be reasonable. He noted that all the new agents have been grouped in B. He suggested that the message needs to be out to users sooner than later. – **Dr. Limbago**: The reporting piece needs to be emphasized. If the message is clear, laboratories will be able to make their own decisions on what to test.
	A motion to accept Option 3 to add the B2 category was made (Dr. Gold) and seconded (Dr. Kirn). VOTE: 9 for, 2 against, 0 abstain, 1 absent (Dr. Mazzulli).
	– The negative votes were related to concern Dr. Limbago's opposition to the grouping names and Dr. Humphries' concern that the revisions are not ready to move forward and that there is still confusion. – Consideration of Dr. Limbago's suggestion to create a more functional classification will be considered for M100, 32nd edition. – In regard to the implementation of the approved revision, Ms. Hackenbrack explained that the production of M100, 31st edition is on a very short timeline and there is insufficient time to make extensive revisions to Table 1. She noted that the draft must be voted on and submitted to the editors before the January meetings. • Plans for implementing the revisions in Tables 1 were discussed. (**Note:** Comments or questions may be paraphrased.) – **Dr. Satlin**: Agreed that there isn't sufficient time to have the revisions ready for the next edition of M100 (31st). Reorganization of agents needs to be done carefully. – **Dr. Simner**: There is still a lot of work to do and shouldn't be rushed. – **Dr. Weinstein**: Lefamulin and cefiderocol will be added to group B as approved. – **Dr. Mathers**: Agrees with users being notified during the annual M100 webinar that major changes are coming to Tables 1. – **Dr. Humphries**: Suggested to consider that Tables 1 might not belong in M100 but perhaps be an "adjunct" document to M100. Tables 1 refers to FDA-approved agents while M100 is considered to be an international document. It might be a good idea to create a document that would provide more guidance on how the tables should be used. – **Dr. Weinstein**: Agreed that this idea provides food for thought. An issue that has come up is that CLSI should take a more active role in antimicrobial stewardship. To date, IDSA has taken the lead on stewardship and questions how involved CLSI should be. He questioned how useful a separate document might be. – **Dr. Simner**: The WG is planning to discuss the US-centric nature of Tables 1 during the January meeting. Also, the WG will discuss leaving the table in M100 but perhaps creating an additional document with detailed guidance on its use.

SUMMARY MINUTES	
#	**Description**
	• Formal votes on azithromycin and ceftolozane-tazobactam placement. – Azithromycin is designated as INV in Table 2-A for *Salmonella enterica* ser. Typhi with no designated for the newly approved breakpoints for Shigella spp. – Ceftolozane-tazobactam breakpoints for *H. influenzae* were approved but no vote was taken on placing it in Group C as suggested by the sponsor.
	A motion to place azithromycin in Group B for *Salmonella enterica* ser. Typhi and *Shigella* spp. Table 1A for Enterobacterales with a footnote stating that the azithromycin grouping only applies to the specific pathogens listed was made (Dr. Simner) and seconded (Dr. Gold). VOTE: 11 for, 0 against, 0 abstentions, 1 absent (Pass)
	• SC Discussion (**Note:** Comments or questions may be paraphrased.) – **Ms. Cullen**: Table 1 is currently described as for FDA-approved agents. She questioned if azithromycin is FDA approved for the suggested indications. – **Dr. Schuetz**: Noted that her understanding was that if there is not FDA approval of a breakpoint and they are not in Table 1 but are in Table 2 that they should be designated as an "O". – **Ms. Cullen**: The definition in the Instructions for Use in the current edition (30th) states: "includes antimicrobial agents that have a clinical indication for the organism group but are generally not candidates for routine testing and reporting in the United States" – **Dr. Weinstein**: The lack of an FDA indication for azithromycin for treating *Salmonella* and *Shigella* is not an issue.
	A motion to place ceftolozane-tazobactam in Group C in Table 1B for *H. influenzae* was made (Dr. Satlin) and seconded (Dr. Humphries). VOTE: 11 for, 0 against, 0 abstentions, 1 absent (Pass).
6.	**Adjournment (Dr. Weinstein)** **Tuesday, 29 September 2020** • Dr. Weinstein thanked the participants for their time and dedication. The meeting was adjourned at 3:15 PM Eastern (US) time. Dr. Weinstein noted that a 90-minute virtual meeting will be scheduled to discuss the Table 1 revisions. **Tuesday, 20 October 2020 (Table 1 WG report)** • Dr. Weinstein thanked the participants for their time and dedication. The meeting was adjourned at 11:20 AM Eastern (US) time.

Upcoming Meetings of the Subcommittee on Antimicrobial Susceptibility Testing:

January/February 2021: Virtual meetings (dates/times to be determined)

- Tentative meeting schedules
  - Ad Hoc WGs: During the week of 18 January 2021
  - Primary WGs: During the week of 25 January 2021
  - Plenaries: During the week of 1 February 2021
- Agenda requests (only) submission due date – **21 December 2020**
- Agenda materials and presentation, final submission due date – **6 January 2021**

27 – 29 June 2021: San Diego, California, USA (Agenda material submission due date – 19 May 2021)
23 – 25 January 2022: Ft. Lauderdale, Florida, USA (Agenda material submission due date – 8 December 2021)
26 – 28 June 2022: Chicago, Illinois, USA (Agenda material submission due date – 20 May 2022)

ACTION ITEMS		Responsible
1.	Review data needed for inclusion of lefamulin in Appendix A.	Intrinsic resistance WG
2.	Revisit Table 1 definitions and agent placement.	Table 1 WG

Summary of Passing Votes

#	Motion Made and Seconded	Results*	Page
1.	To approve the summary minutes from the January 2020 subcommittee meeting.	11-0-0-1	5
2.	To approve the direct BC susceptibility testing method for aztreonam, ampicillin, ceftazidime, ceftriaxone, tobramycin, and trimethoprim-sulfamethoxazole with Enterobacterales using the breakpoints listed in Table 2A (with implementation process to follow).	11-0-0-1	8
3.	To approve the proposed QC ranges for ceftobiprole, aztreonam-nacubactam, aztreonam integrity check, cefepime-nacubactam, cefepime integrity check as presented.	11-0-0-1	12

QC Strain	Proposed Ceftobiprole QC Ranges
E. coli ATCC® 25922	25–31
S. aureus ATCC® 25923	20–27

QC Strain	Proposed Aztreonam-Nacubactam QC Ranges
E. coli ATCC 25922	0.06/0.06-0.25/0.25
P. aeruginosa ATCC® 27853	2/2-8/8
K. pneumoniae ATCC® 700603 (Routine QC strain)	0.5/0.5-2/2
K. pneumoniae ATCC® BAA-2814 (Routine QC strain)	0.5/0.5-2/2

QC Strain	Proposed Aztreonam Integrity Check
K. pneumoniae ATCC® BAA-2814	>128

QC Strain	Proposed Cefepime-Nacubactam QC Ranges
E. coli ATCC® 25922	0.016/0.016-0.12/0.12
P. aeruginosa ATCC® 27853	0.5/0.5-2/2
K. pneumoniae ATCC® 700603	0.12/0.12-0.5/0.5
K. pneumoniae ATCC® BAA-2814 (Routine QC strain)	0.5/0.5-2/2

QC Strain	Cefepime Integrity Check
K. pneumoniae ATCC® BAA-2814	>32

4.	To approve the lefamulin *S. aureus* (MSSA and MRSA) MIC susceptible-only BP (≤0.25) and the FDA-approved disk diffusion susceptible-only BP (≥23).	11-0-0-1	22
5.	To approve the proposed FDA-approved susceptible-only MIC BPs for *S. pneumoniae* (≤0.5) and *H. influenzae* (≤2) and disk diffusion BPs for *S. pneumoniae* (≥17) and *H. influenzae* (≥17) providing more data is presented in January 2021 on where resistant isolates would lie.	11-0-0-1	22

6.	To add a comment with the lefamulin BP that is similar to that used for drugs that should not be reported for CSF isolates, for patients with meningitis, or for urinary tract isolates with Text and Tables WG being assigned to provide consistent wording for drugs with similar limitations.	11-0-0-1	22
7.	To place lefamulin in Group B in Tables 1 for *S. aureus* and *S. pneumoniae*, and Group C for *H. influenzae* as proposed by the sponsor with the caveat that Table 1 is being reassessed and may alter the placement.	11-0-0-1	23
8.	To approve the Appendix A, Category 1 placement for lefamulin.	11-0-0-1	23
9.	To add footnotes to Tables 2C, 2D, 2H-1 and 2H-2 in CLSI M100 tables stating that, "Organisms that test susceptible to linezolid by MIC are also considered susceptible to tedizolid (ie, *S. aureus*, *S. pyogenes*, *S. agalactiae*, *S. anginosus* group and *E. faecalis*)".	11-0-0-1	24
10.	To approve the *Shigella* MIC azithromycin breakpoints for the entire species as proposed by the CDC (S=≤ 8; I =16; R= ≥ 32 µg/mL).	9-0-0-3	27
11.	To approve the *Shigella* disk diffusion azithromycin breakpoints for the entire species as proposed by the CDC (**S = ≥ 16; I = 11-15; R = ≤ 10**) with a comment stating that if the results are intermediate, that an MIC test is recommended. Comment to add: *Azithromycin disk diffusion zones and MIC endpoints can be hazy and difficult to measure for Shigella spp., especially sonnei. If an isolate has a zone of inhibition that is difficult to measure, an MIC may help to distinguish S, I or R. Media source may impact the clarity of the endpoints for disk diffusion tests.*	7-2-0-3	27
12.	Place azithromycin in Group B for Salmonella enterica ser. Typhi and Shigella spp. in Table 1A for Enterobacterales with a footnote stating that the azithromycin grouping only applies to the specific pathogens listed.11 for, 0 against, 0 abstentions, 1 absent (Pass)	11-0-0-1	31
13.	Place ceftolozane-tazobactam in Group C in Table 1B for *H. influenzae*	11-0-0-1	31
14.	Vote to approve 2020 Summer AST Virtual Meeting Summary: Approved 24 November 2020	10-0-0-2	

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

Respectfully submitted,

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