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Meeting Title:	**Subcommittee on Antimicrobial Susceptibility Testing (AST)**	**Contact:**	mhackenbrack@clsi.org
Meeting Date:	Sunday – Tuesday, 26 – 28 January 2020		
Start Time:	26 January – 7:30 AM 27 January – 7:30 AM 28 January – 7:30 AM	**End Time:**	5:00 PM 6:00 PM 12:00 PM
Meeting Purpose:	The purpose of this meeting is to review and discuss AST WG and SC business in preparation for publication of the next edition of M100 (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):	
Melvin P. Weinstein, MD Chairholder	**Rutgers Robert Wood Johnson Medical School**
James S. Lewis, PharmD, FIDSA Vice-chairholder	**Oregon Health and Science University**
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)	Accelerate Diagnostics, Inc.
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
Tony Mazzulli, MD, FACP, FRCP(C)	Mount Sinai Hospital
Michael Satlin, MD, MS	New York Presbyterian Hospital
Audrey N. Schuetz, MD, MPH	Mayo Clinic
Patricia J. Simner, PhD, D(ABMM)	Johns Hopkins University School of Medicine, Department of Pathology
Pranita D. Tamma, MD, MHS	Johns Hopkins University School of Medicine, Department of Pediatrics
Advisors Present	
April M. Bobenchik, PhD, D(ABMM)	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
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
Navaneeth Narayanan, PharmD, MPH	Ernest Mario School of Pharmacy, Rutgers University
Kiyofumi Ohkusu, PhD	Tokyo Medical University
Samir Patel, PhD, FCCM, D(ABMM)	Public Health Ontario

Virginia M. Pierce, MD	Massachusetts General Hospital
Sandra S. Richter, MD, D(ABMM), FCAP, FIDSA	bioMérieux
Ribhi M. Shawar, PhD, D(ABMM)	FDA Center for Devices and Radiological Health
John D. Turnidge, MD, BS, FRACP, FASM, FRCPA	University of Adelaide
Barbara L. Zimmer, PhD	Beckman Coulter, Inc
Reviewers Present	
April Abbott, PhD, D(ABMM)	Deaconess Hospital Laboratory
Kevin Alby, PhD, D(ABMM)	UNC School of Medicine
Stella Antonara, PhD, D(ABMM)	OhioHealth
Robert Bowden, BS	Tufts University Sackler School of Graduate Biomedical Sciences - Student
Patricia Bradford, PhD	Antimicrobial Development Specialists, LLC
Kendall Bryant, PhD, D(ABMM)	Kaiser Permanente
Alexandra Lynn Bryson, PhD, D(ABMM)	Virginia Commonwealth University Health
Karen Bush, PhD	Indiana University
Susan Butler-Wu, PhD, D(ABMM), SM(ASCP)	LACUSC Medical Center
Shelley Campeau, PhD, D(ABMM)	Accelerate Diagnostics
Darcie E. Carpenter, PhD	IHMA
Sukantha Chandrasekaran, PhD	University of California
Patricia S. Conville, MS, MT(ASCP)	FDA Center for Devices and Radiological Health
Ian A. Critchley, PhD	Spero Therapeutics
Jennifer Dien Bard, PhD, D(ABMM), F(CCM)	Children's Hospital Los Angeles; University of Southern California
Tanis Dingle, PhD, D(ABMM), FCCM	University of Alberta Hospital
Michael J. Dowzicky	Pfizer Inc
Dana C. Dressel, BS, MT(ASCP)	International Health Management Associates, Inc.
Paul Edelstein, MD	Hospital of the University of Pennsylvania
Andrea L. Ferrell, MLScm(ASCP)	Becton Dickinson
Mark A. Fisher, PhD, D(ABMM)	University of Utah School of Medicine
Graeme Forrest, MBBS	Oregon Health Sciences University
Lawrence V. Friedrich, PharmD	Paratek Pharmaceutical
Beth P. Goldstein, PhD	Beth Goldstein Consultant
Avery Goodwin, MS, PhD	FDA Center for Drug Evaluation and Research
Meredith Hackel, PhD	International Health Management Associates, Inc.
Dwight J. Hardy, PhD	University of Rochester Medical Center
Stephen Hawser, PhD	IHMA Europe Sàrl
Catherine Hogan, MD, MSc, FRCP, D(ABMM), DTM&H	Stanford
Michael D. Huband, BS	JMI Laboratories
Holly Huse, PhD, D(ABMM), M(ASCP)cm, PHM	Huntington Hospital
Kristie Johnson, PhD, D(ABMM)	University of Maryland, Baltimore
Melissa Jones, MT(ASCP),CLS	UNC Healthcare
Ronald N. Jones, MD	JMI Laboratories
Gunnar Kahlmeter, MD, PhD	ESCMID
Asa Karlsson	bioMérieux
Ellen N. Kersh, PhD	Centers for Disease Control and Prevention
Scott B. Killian, BS	Thermo Fisher Scientific
Susan M. Kircher, MS, MT (ASCP)	BD Diagnostic Systems
Cynthia C. Knapp, BS, MS, MT(ASCP)	Thermo Fisher Scientific
Laura M. Koeth, MT(ASCP)	Laboratory Specialists, Inc.
Mark J. Lee, PhD, D(ABMM), M(ASCP)	Duke University Health System
Sarah Blaine Leppanen, MT(ASCP)	Blaine Healthcare Associates, Inc.
Ron Master, SM(AAM)	Quest Diagnostics

Erika Matuschek, PhD	ESCMID
Sarah McLeod	Entasis Therapeutics
Stephanie L. Mitchell, PhD, D(ABMM)	University of Pittsburgh and Children's Hospital of Pittsburgh of UPMC
Ian Morrissey, PhD	IHMA Europe Sárl
Mary R. Motyl, PhD, D(ABMM)	Merck & Co, Inc.
Samia N. Naccache, PhD, M(ASCP)cm, D(ABMM)	LabCorp Seattle
Susan O'Rourke, BS	BD Diagnostic Systems
Elizabeth Palavecino, MD	Wake Forest Baptist Medical Center
Katherine Perez, PharmD	Houston Methodist Hospital
Cau Dinh Pham	Centers for Disease Control and Prevention
Chris Pillar, PhD	Micromyx, LLC
Mark Redell, PharmD	Melinta Therapeutics
L, Barth Reller, MD	Duke University Medical Center
Felicia Rice, MT(ASCP)	Mayo Clinic
Flavia Rossi, MD, PhD	University of Sao Paulo
Helio S. Sader, MD	JMI Laboratories
Katherine Sei, BS	Beckman Coulter, Inc.
Susan Sharp, PhD, D(ABMM)	Copan Diagnostics, Inc.
Rosemary She, MD	University of Southern California
Dee Shortridge, PhD	JMI Laboratories
Carole Shubert, MT	bioMérieux, Inc.
Simone M. Shurland	FDA Center for Drug Evaluation and Research
Dawn M. Sievert, PhD	Centers for Disease Control and Prevention
Pragya Singh, PhD	Specific Diagnostics
Paula M. Snippes Vagnone, MT(ASCP)	Minnesota Department of Health
Laura Stewart, MS, RAC	BD Diagnostics
Gregory G. Stone, PhD	Pfizer, Inc.
Richard B. Thomson, PhD, D(ABMM), FAAM	Evanston Hospital, NorthShore University HealthSystem
Susan Thomson	MAST Group
Lauri D. Thrupp, MD	University of California Irvine Medical Center
Maria M. Traczewski, BS, MT(ASCP)	The Clinical Microbiology Institute
Tam T. Van, PhD, D(ABMM)	Harbor-UCLA Medical Center
Nancy E. Watz, MS, MT(ASCP), CLS	Stanford Health Care
Eric Wenzler, PharmD, BCPS, AAHIVP	University of Illinois at Chicago
Lars F. Westblade, PhD, D(ABMM)	New York Presbyterian Hospital - Weill Cornell Campus
Matthew A. Wikler, MD, FIDSA, MBA	IDTD Consulting
Mandy Wootton, PhD	University Hospital of Wales
Katherine Young, MS	Merck & Co, Inc.
Guests (Non-SC-roster attendees)	
Francis Arhin	Pfizer
Alani Barajas	Hardy Diagnostics
Amelia Bhatnagar	Centers for Disease Control and Prevention
Elise Blackmore	Accelerate Diagnostics, Inc.
Malcom Boswell	Accelerate Diagnostics, Inc.
Maryann Brandt	Norman Regional Hospital
Robin Chamberland	St. Louis University-Laboratory
Jennifer Chau	Beckman Coulter
Carisa De Anda	Merck & Co, Inc.
Andrew DeRyke	Merck & Co, Inc.

Elaine Duncan	Beckman Coulter
Hari Dwivedi	bioMérieux, Inc.
Ed Feng	Merck & Co, Inc
Kelly Flentie	Selux Diagnostics
Willem (Bill) Folkerts	BD
Cynthia Fowler	bioMérieux
Simone Franklin	bioMérieux, Inc.
Cindy Friedman	Centers for Disease Control and Prevention
Andrew Fuhrmeister	JMI Laboratories
Momoko Fujisaki	Eiken Chemical Company, Ltd.
Barb Gancarz	bioMérieux, Inc.
Alice Gray	bioMerieux, Inc.
Natasha Griffen	FDA Center for Devices and Radiologic Health
Kelly Harris	Merck & Co, Inc.
Antonieta Jimenez	Inciensa Costa Rica-PAHO
Brian Johnson	IHMA
Joan T. Johnson	MDC Associates
Matt Johnson	Merck & Co, Inc.
Cherece Jones	bioMerieux, Inc.
Jennifer Kalamatas	IHMA
Ayesha Khan	Center for Antimicrobial Resistance and Microbial Genomics, UT Health
Kenneth Klinker	Merck & Co, Inc
Karen Kryston	Beckman Coulter
Katherine Langford	bioMérieux, Inc.
Xian-Zhi Li	Health Canada
Rachael Liesman	University of Kansas
Luiz Lisboa	Alberta Precision Laboratories
Zabrina Lockett	Beckman Coulter
Rianna Malherbe	Hardy Diagnostics
Katie Marcum	BD
Bob Margadonna	Merck & Co, Inc.
Rebecca M. Marrero Rolon	Mayo Clinic
Lisa Meyers	bioMérieux, Inc.
Alita Miller	Entasis Therapeutics Inc.
Sharon Min	GlaxoSmithKline
Alice Ngo	Beckman Coulter
Susan Novak-Weekley	Quella
Daniel Ortiz	Beaumont Health, Royal Oak
Amanda Paschke	Merck & Co, Inc.
Munjal Patel	Merck & Co, Inc.
Susanne Paukner	Nabriva Therapeutics
Audie Perniciaro	bioMérieux, Inc.
Isobelle Perriaud	bioMérieux
Caelin Potts	Centers for Disease Control and Prevention
Mimi R. Precit	Children's Hospital Los Angeles
Eric Ransom	Washington University
Zachary Ratzlaff	Norman Regional Health System
Jean-Yves Ressot	bioMérieux
Nilia Robles-Hernandez	bioMérieux, Inc.
Daniel Sahm	IHMA Europe
Linda Schuermeyer	bioMérieux
Alisa Serio	Paratek Pharmaceuticals, Inc.

Samantha Shannon	Mayo Clinic
Matthew Simon	Weill Cornell Medicine
Jennifer Smart	Basilea Pharmaceutica International Ltd.
Roger Stephens, PharmD	Nabriva Therapeutics
Eric Stern	SeluxDx
Jolyn Tenllado	bioMérieux, Inc.
Andy Townsend	Pfizer Limited
Priyanka Uprety	Rutgers University
Chairut Vareechon	RWJ Barnabas Health
Leland Vought	Accelerate Diagnostics, Inc.
Xin Wang	Centers for Disease Control and Prevention
Jean Whichard	Centers for Disease Control and Prevention
Tiffany Keepers White	Paratek Pharmaceuticals
Wolfgang Wicha	Nabriva Therapeutics GmbH
Michael Wong	Merck & Co, Inc.
Grace Woods	Centers for Disease Control and Prevention
S. Steve Yan	FDA-CVM
Katsunori Yanagihara	Nagasaki University
Rebecca Yee	Children's Hospital Los Angeles
Staff:	
Kathy Castagna,MS, MT(ASCP)CT, MB	CLSI
Glen Fine, MS, MBA, CAE	CLSI
Marcy L. Hackenbrack, MCM, M(ASCP)	CLSI
Christine Lam, MT(ASCP)	CLSI

OPENING PLENARY AGENDA Monday, 27 January 2020							
Breakfast available: 7:00 AM (Break Stations)							
Item #	**Item Title**	**Start**	**End**	**Length (Min)**	**Category**	**Presenter**	**Page**
1.	Welcome and Opening Remarks	10:00 AM	10:05 AM	5	N/A	Dr. Weinstein	8
2.	Agenda and June 2019 Meeting Summary	10:05 AM	10:10 AM	5	VOTE	Dr. Weinstein	8
3.	Updates to disclosures	10:10 AM	10:15 AM	5	Update	Dr. Weinstein	8
4.	CLSI Update	10:15 AM	10:25 AM	10	Update	Mr. Fine Mr. Mottram	8
5.	Expert Panel Report	10:25 AM	10:35 AM	10	Update	Dr. Thompson	9
6.	Methods Application and Implementation WG Report	10:35 AM	11:30 AM	50	Report/Votes	Dr. Limbago Dr. Kirn	9-14
7.	Outreach WG Report	11:30 AM	11:45 AM	15	Report	Ms. Hindler Dr. Schuetz	14-15
8.	ECV WG Report	11:45 AM	12:00 PM	15	Report	Dr. Schuetz Dr. Eliopoulos	15
	Luncheon (Cloisters/Courtyard)	12:00 PM	1:00 PM	60			
9.	Methods Development and Standardization WG	1:00 PM	2:30 PM	90	Report/Votes	Dr. Hardy Dr. Zimmer	15-20
10.	Implications for commercial AST systems when CLSI and FDA BPs don't agree	2:30 PM	2:50 PM	10	Presentation	Dr. Zimmer	19-20
11.	Streamlined approach to implement BP changes on commercial AST devices	2:40 PM	3:00 PM	20	Presentation	Dr. Shawar	20
	Break (Break Stations)	3:00 PM	3:15 PM	15			
12.	EUCAST Update	3:15 PM	3:35 PM	20	Update	Dr. Giske	21-22
13.	VAST Update	3:35 PM	4:00 PM	20	Update	Mr. Bowden	22-23
14.	QCWG Report	4:00 PM	4:45 PM	45	Report	Ms. Cullen Ms. Traczewski	23-29
15.	Table 1 WG Report	4:45 PM	5:05 PM	20	Report	Dr. Simner Dr. Eliopoulos	29-40
16.	M39 WG Report	5:05 PM	5:35 PM	30	Report	Ms. Hindler Dr. Simner	40-42
17.	M23 WG Report	5:35 PM	5:55 PM	20	Report	Dr. Wikler Dr. Goodwin	42-43
18.	Adjournment	5:55 PM				Dr. Weinstein	43

CLOSING PLENARY AGENDA Tuesday, 28 January 2020							
Breakfast available: 7:00 AM (Break Stations)							
Item #	**Item Title**	**Start**	**End**	**Length (Min)**	**Category**	**Presenter**	**Page**
1.	Meeting opens	7:30 AM			N/A	Dr. Weinstein	44
2.	Cefiderocol Update	7:30 AM	7:40 AM	10	Update	Dr. Lewis	44
3.	Breakpoint WG Report	7:40 AM	9:15 AM	95	Report/Votes	Dr. Lewis	44-54
	Break (Break stations)	**9:15 AM**	**9:30 AM**	**15**			
4.	Breakpoint WG Report (continued)	9:30 AM	11:00 AM	90	Report/Votes	Dr. Lewis	44-54
5.	Joint CLSI/EUCAST Report	11:00 AM	11:20 AM	20	Report	Ms. Hindler Dr. Matuschek	54-55
6.	Text and Tables Report	11:20 AM	11:40 AM	20	Report	Dr. Campeau Dr. Bobenchik	55-58
7.	Other business	11:40 AM	12:00 PM	5	N/A	Dr. Weinstein	58
8.	Adjournment	12:00 PM			Remarks	Dr. Weinstein	58
NOTE:	**The Break stations will be available for those wishing to grab a bite before heading to the airport.**						

Upcoming Meetings of the Subcommittee on Antimicrobial Susceptibility Testing:

14 – 16 June 2020: Hyatt Regency Baltimore Inner Harbor, Baltimore, MD, USA (Agenda material submission due date – **8 May 2020**)
24 – 26 January 2021: Live! by Loews, Arlington, TX, USA (Agenda material submission due date – **9 December 2020**)
27 – 29 June 2021: Westin, San Diego, CA, USA (Agenda material submission due date – **19 May 2021**)

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SUMMARY MINUTES	
Item #	**Description**
Monday, 27 January 2020 (NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2020 January AST Plenary Presentations)	
1.	**Welcome and Opening Remarks: Dr. Weinstein** • Dr. Weinstein opened the meeting at 11:00 AM Mountain (US) time with a tribute to Dr. Mary Jane Ferraro followed by a moment of silence. Those wishing to donate in Dr. Ferraro's memory can send donations to the following address: Department of Pathology, Microbiology Laboratory, Massachusetts General Hospital, Boston, MA 02114. • Dr. Weinstein expressed his gratitude to the Subcommittee (SC) and Workging Group (WG) leadership and members for their hard work and participation. He also thanked the CLSI staff for their support and contributions. • He noted that there was no change in the SC voting membership. New advisors to the SC include: German Esparza, Joseph Kuti, Joseph Lutgring, and Samir Patel. Dr. Stephen Jenkins has retired and has rotated to reviewer.
2.	**Agenda and 2019 Meeting Summary: Vote** • There were no additional edits to the agenda or June 2019 summary minutes. **Motions to accept the agenda and June 2019 meeting summary minutes were made and seconded. VOTES: 12 for; 0 against (Pass).** • The approved summary minutes have been posted on the CLSI website using the following link to the June 2019 AST Meeting Files.
3.	**Disclosures of Interest (DOI) Summary Update** • Dr. Schuetz noted that company for which she is on the scientific advisory board has changed names from Klaris Diagnostics to Pattern Diagnostics. This change will be noted on the DOI summary for June 2020. • There were no other updates to the DOI summary.
4.	**CLSI Update: Mr. Fine** **Mr. Fine provided a CLSI update.** • He provided additional comments and tributes to Dr. Ferraro. • He expressed gratitude to all SC participants for their continued hard work and dedication to CLSI. • It was noted that there has been a record attendance to the January 2020 Committees Week. • Dr. Barbara Zimmer, Beckman-Coulter, has been elected to the Board of Directors • Dr. Jean Patel has been honored with CLSI's highest award, the Eilers Award, and Dr. Linda Miller has been awarded with the Excellence in Standards Development award. Both will be officially recognized at the June 2020 meeting in Baltimore. • To date, M100 free has had over 2,000,000 page hits.

5.	**Expert Panel Report: Dr. Thomson** **Dr. Tom Thomson provided an update on the activities of the Expert Panel on Microbiology.** • The Expert Panel leadership includes Dr. Jean Patel as Chairholder and Dr. Tom Thomson as Vice-Chairholder. Members are chosen for their expertise and are appointed for one-year terms for up to four years. Advisors are selected to serve in preparation to rotate to member or are previous members who assist new members. • The Consensus Council (CC) liaison to the Microbiology Expert Panel is Dr. Mary Lou Gantzer. • An overview of the Expert Panel's roles and responsibilities was provided. The Expert Panel: – Reports to CC but may take directives from the Board of Directors – Identifies and proposes potential projects to CC – Reviews proposals from working SCs such as AST, Fungal AST, Vet AST and advises the CC – Reviews all microbiology documents every five years (excludes AST-, Antifungal-, and Vet SC-managed documents) – Reviews, comments, and votes on Microbiology documents • The new projects for 2020 that have been approved include: – M63, *Principles and Procedures for the Gram Stain* (Leadership: Tom Thomson and Jane Hata) – M64, *Guideline for Implementation of Taxonomy Nomenclature Changes* (Leadership: Erik Munson and Shawn Lockhart) – Both projects are expected to begin development by June 2020.
6.	**Methods Application and Implementation Working Group (MAIWG) Report: Dr. Kirn (Folder 6)** **WG Roster**: Tom Kirn, Brandi Limbago (Co-Chairholders); Kristie Johnson (Secretary-new); Darcie Carpenter, Steve Jenkins (absent), Joseph Kuti, Samir Patel, Virginia Pierce, Sandra Richter, Susan Sharp, Trish Simner (Members) **Reporting Cefepime Susceptible/Susceptible Dose-Dependent Results for Carbapenemase-Producing *Enterobacteriaceae*:** Dr. Simner and Dr. Burnham • Multiple institutions have reported that carbapenemase producers (mostly KPCs) have cefepime minimal inhibitory concentrations (MICs) that fall into the susceptible (S) or susceptible-dose dependent (SDD) interpretive categories. Guidance is needed on how to handle these scenarios to prevent inappropriate cefepime use when treating carbapenemase-producing *Enterobacteriaceae* [Enterobacterales]. • Differences in AST interpretation using current and historical breakpoints (BPs) for *Enterobacteriaceae* possessing bla_{KPC} were presented. • Three options for reporting were proposed: – Suppress cefepime S or SDD results and do not report – Force cefepime S or SDD results as R – Report cefepime as tested • It was noted that there are limited clinical data as current consensus guidelines do not recommend cefepime. • Dr. David Nicolau was contacted for input. His input included: – His group is seeing the same issues with broth microdilution (BMD). – He was hesitant to review the lower BP as the drug works if given in sufficient doses (Foong KS…Burnham CD, Open Forum Infect Dis, 2019). – He was hesitant to use cefepime for carbapenemase-CRE at any dose due to high probability of microbiological/clinical failure especially since MICs of carbapenemase-producing isolates seem to hover at the upper end of the SDD BMD/zone diameter • It was questioned on what type of guidance should be given. It was suggested that a reference to the molecular tables be provided; however, there is no specific guidance provided in Appendix H, Table H3.

- Dr. Simner proposed adding a row to Table H3 table with recommendations on how to resolve and report discrepancies when a carbapenemase target is detected or there is phenotypic evidence of a carbapenemase (see below). The proposal was approved by the MAIWG.

Indication	Target(s)	Method	Specimen Type	Results		Suggestions for Resolution	Report as:
				Molecular Target Results	Observed Phenotype (if tested)		
Detection of carbapenem resistance in Enterobacterales	KPC, OXA-48-like, VIM, NDM, or IMP OR Phenotypic evidence of a Carbapenemase (such as mCIM or CarbaNP positive)	NAAT, microarray	Colony, blood culture	Detection of any tested carbapenemase target or phenotypic detection of carbapenemase production	Susceptibility (S/SDD) to 3rd and/or 4th generation cephalosporins but intermediate or resistant results to at least one carbapenem tested	Repeat molecular and phenotypic tests.	If the discrepancy is not resolved, repeat AST should be performed using a reference method and the conflicting genotypic and phenotypic testing results should both be reported along with a comment advising caution; current clinical and laboratory evidence is insufficient to conclude whether cephalosporin therapy of carbapenemase-carrying strains with an MIC in the S/SDD range will be effective~~., or whether the molecular assays are completely accurate.~~

- It was proposed that Comment (1) be revised to read, "Multiple β-lactamases may be carried by individual bacterial isolates. Most carbapenemase-producing bacteria are resistant to 3rd- and 4th- generation cephalosporins, although bacteria producing some ~~certain~~ carbapenemase enzymes (eg, OXA-48 and SME), may not be unless they co-produce an ESBL or AmpC enzyme."

- SC Discussion
  - Dr. Humphries: SMEs routinely test susceptible to cephalosporins and this is a common phenotype. For susceptible MICs, carbapenem resistance needs to be demonstrated by showing resistance to meropenem. She suggested adding a footnote that includes this common scenario.
  - Dr. Butler-Wu: The last sentence be revised with a generic statement regarding molecular assays not being completely accurate. The last phrase was deleted (see strikethrough).
  - Dr. Karlsson: Agreed to delete the phrase about molecular testing. She agreed that the statement needs to include exceptions (eg, OXA-48, SME, IMI).
  - Dr. Miller: Requested confirmation that the MIC does not predict resistance or susceptibility.
  - Mr. Esparza: Suggested that a comment could be included in the appropriate Tables 3.
  - Dr. Satlin: Believed that OXA-48 does not need to be called out.
  - Dr. Limbago: The statement on the accuracy of molecular methods could be revised as needed since molecular methods only detect the presence or absence of a gene but can't detect whether the gene is active.
- A motion to adopt the language and revised comment about effectiveness and add a footnote about SME, point mutations, etc. causing discrepancies was made and seconded. Dr. Tamma disagreed that a footnote about SME etc. is needed.

- Dr. Schuetz suggested that the motions be revised and split into separate motions.

A motion to adopt the suggested language in the table without the phrase about molecular accuracy was made and seconded. VOTE: 11 for; 1 against (Pass).

- Dr. Satlin: Opposed the motion because he believed that OXA-48 comment in the footnote should be deleted.
- Dr. Hardy: Requested advice on communicating the molecular results because physicians look for "S" and/or "R" and generally don't read the text.
- Dr. Young: Suggested that it is reasonable to include OXA-48 because there is evidence regarding mutations.
- Dr. Pierce: Suggested that the text in the resolution column about which phenotypic test is being performed (eg, repeat discrepant tests) be very clear.

A motion to add a footnote about situations that could cause discrepancies was made and seconded. VOTE: 11 for; 1 against (Pass). A small group was tasked with revising the footnote for presentation later in the meeting (see below).

- SC Discussion of revision.
  - It was suggested that the text be changed to "some ~~certain~~ carbapenemases"

A motion to accept the revisions to Footnote 1 in Appendix H, Table H3 was made and seconded (see red text above). VOTE: 11 for; 1 against (Pass).

- Dr. Tamma: Opposed the motion as this is an evolving field and may not be comprehensive enough.

WG on AST of Non-fermentative Gram-Negative Bacilli (GNB) (Table 2B-5)

WG Roster: Dwight Hardy (Chairholder); Kevin Alby, April Bobenchik, German Esparza, Kristie Johnson, Joe Kuti, Stephanie Mitchell, Samia Naccache, Helio Sader, Tam Van (Members)

- Questions investigated by the WG included:
  - What are the current BPs for non-fermentative GNB as published in M100, Table 2B-5?
  - How do the BPs published in M100, Table 2B-5 compare to BPs for other organisms published in Tables 2A, 2B-1, 2B-2, 2B-3, and 2B-4?
  - Should revisions be made to Table 2B-5 or moved out of M100?
- Current BPs for non-fermentative GNB with several drugs as currently listed in M100 were reviewed and compared to Enterobacterales, *P. aeruginosa*, and *Acinetobacter*.
  - For a large majority of drugs, BPs are the same. A smaller number of drugs have different BPs.
  - Different BPs were due to revisions to the BPs for some groups but not others.
- For other drugs, there were a variety of differences in BPs for the non-*Enterobacteriaceae*.
- The WG also collected data from their laboratories on which non-*Enterobacteriaceae* were most frequently isolated to determine if these organisms could be separated out into their own tables. *Achromobacter* spp. and a variety of non-*P. aeruginosa Pseudomonas* spp. were the most frequently isolated.
- Based on frequency of isolation, it was decided by the WG that the MIC distributions for the following organisms would be focused on first:
  - *Achromobacter xylosoxidans*
  - *Achromobacter denitrificans*
  - *Pseudomonas putida*

- *Pseudomonas fluorescens*
- *Pseudomonas stutzeri*

- Data for *A. xylosoxidans*, *P. fluorescens*/*putida*, *P. aeruginosa*, and *P.* non-*aeruginosa* were reviewed.
  - Many seem to have poor *in vitro* activity. Clinical data are lacking for these groups.
  - Based on the data, it is not clear which organisms belong in Table 2B-5.
- Options for non-*P. aeruginosa* spp. were presented.
  - Accept BPs currently published in Table 2B-5 or recommend revised breakpoints
  - Recommend ECVs for organisms in Table 2B-5
  - Move organisms to M45 where BP criteria are less stringent
  - Move non-*Pseudomonas* spp. from Table 2B-5 into Table 2B-1 with *P. aeruginosa* (All *Pseudomonas*)
  - Create a new Table for non-*P. aeruginosa* spp.
- Options for *Achromobacter* spp. were presented.
  - Accept BPs currently published in Table 2B-5 or revise the BPs
  - Recommend ECVs for organisms in Table 2B-5
  - Move these organisms in M45 where BP criteria are less stringent
  - Create new Table for *Achromobacter* spp. (**NOTE:** Some MICs of some drugs in Table 2B-5 are intrinsically "high" for this organism – search literature to determine if intrinsic mechanisms of resistance are known in this organism)
- The MAIWG suggested:
  - Collecting more data
  - Determining what the revised tables would look like
  - Determining if the organisms be moved to M45
- SC Discussion
  - Dr. Humphries: Agree that the organisms belong in M45 as there are problems with the data for all *Pseudomonas* spp. being in *P. aeruginosa* table.
  - Dr. Simner: Agree that it makes more sense to move them to M45.
  - Dr. Abbott: Expressed concern that some laboratories don't have access to M45 (**NOTE:** M45 is not available on the Web free of charge and the FDA does not reference M45 on their Website).
  - Dr. Kirn: Suggested moving the whole group to M45 and then revise individual organisms over time.
  - Ms. Hackenbrack: M45 could be recategorized as a supplement and could be revised more frequently (but not on same schedule as M100).
  - Ms. Hindler: Start with a list of organisms that should probably not be in M100. The list could be published in a newsletter first as will take time to complete the transfer.
  - Dr. Bobenchik: More guidance could be provided in M45.
  - Dr. Thrupp: Since a lot of laboratories don't have access to M45, it is preferred to keep the most frequently isolated GNB such as *Achromobacter* in M100.
  - Dr. Limbago: The organisms belong in M45 and they could be removed/retired until can be moved to M45.
  - Dr. Richter: Moving the organisms to M45 would be consistent with what is already included in M45.
  - Dr. Schuetz: M100 is considered a "standard" and should be followed but M45 includes more recommendations that can be considered.

- Ms. Cullen: Commercial systems won't be able to report organisms listed in M45 and suggested that it be considered what can be done to help from a practical perspective.

- **Next steps (Action Items):**
  - Look for supporting data for molecular mechanisms for intrinsic resistance.
  - Proceed by mocking up drafts of separate tables (eg, *Pseudomonas* spp., *Achromobacter* spp. etc, where clinical data are lacking).
  - Develop a timeline for moving the group to M45.

***Burkholderia cepacia* WG Report**

WG Roster: Holly Huse, Susie Sharp (Co-Chairholders); Kendall Bryant, Eileen Burd, Mark Lee, Joe Kuti, Mandy Wooten (Members).

- A study to evaluate reference AST methods (disk diffusion [DD] and BMD) reproducibility and agreement with *Burkholderia cepacia* was reviewed.
  - 100 unique *Burkholderia* isolates were tested by BMD and DD in triplicate
  - DD results were difficult to read due to light growth at 24 hrs.
  - BMD results were read at 24 hrs. and had light growth, but MICs were easier to read than zone sizes.
  - Data analysis showed that there was categorical agreement between BMD and DD. Two analysis methods were used (Method comparison and Error-rate bounded method).
  - Isolates were also tested on Microscan following manufacturer instructions. Some isolates showed poor growth and needed to be confirmed manually.
- Future directions were presented.
  - The plan is to test 100 non-cystic fibrosis (CF) isolates using the same methods.
  - Seven drugs will be tested in 100 CF and 100 non-CF isolates.
- WG Discussion
  - The overall consensus is that there are problems with growth.
  - It was suggested that 20 CF and 20 non-CF isolates with MICs around BPs be selected.
  - It was suggested that BMD, DD, and gradient diffusion be performed on media for fastidious organisms and try longer incubation times (36 and 48 hrs.).
- SC Discussion: The SC agreed to the proposed next steps and there was no further discussion.
- The effect of *Burkholderia* spp. MIC variability on PD and probability of target attainment (PTA) was presented by Dr. Kuti.
  - Monte Carlo simulations were performed for meropenem, ceftazidime, and levofloxacin.
  - Conclusions for meropenem:
    - MIC variability by BMD resulted in < 5% difference in PTA at a given MIC compared with the traditional modal MIC method (exception – pediatrics).
    - Based on the MIC distribution of this isolate collection, the simulated dosages of meropenem provide a low cumulative fraction of response ranging from 3% to 27% that was most dependent on PK used during simulation and dosing regimen.
    - Differences by incorporation of MIC variability were negligible.
  - Conclusions for ceftazidime:
    - Ceftazidime MIC variability by BMD resulted in <10% difference in PTA at a given MIC compared with the traditional modal MIC method (exception - CF simulations).

	○ Based on the MIC distribution of this isolate collection, these simulated dosages of ceftazidime provide an overall low cumulative fraction of response. ○ Differences from incorporating MIC variability were negligible. – Conclusions for levofloxacin: ○ MIC variability by BMD resulted in <6% difference in PTA at a given MIC compared with the traditional modal MIC method. ○ Based on the MIC distribution of this isolate collection, IV levofloxacin 750mg q24h provides an overall low cumulative fraction of response with no difference introduced by MIC variability. **Anaerobe WG Report** **WG Roster**: Darcie Carpenter (Chairholder); Kitty Anderson, Joanne Dzink-Fox, Meredith Hackel, Steve Jenkins (absent), Cindy Knapp, Laura Koeth, Audrey Schuetz (Members) • Requested BP changes for metronidazole were discussed (not approved by the BPWG). • Piperacillin/tazobactam BPs are higher than piperacillin only BPs; therefore, the BPWG voted to drop piperacillin. • CDC and Mayo Clinic have reported QC failures with *C. difficile* and fidaxomicin with QC organisms. The QCWG is reviewing the data. • The anaerobe antibiogram manuscript is in draft form. • An updated antibiogram for M100 is needed but there are only two laboratories left that still report susceptibilities using agar dilution. – A literature search into agar dilution vs gradient diffusion is in progress. A call for data may be made. – It was questioned if a reference method must be used for an antibiogram. It was noted that guidelines do not say that a reference method has to be performed. – It was questioned if the antibiogram have both agar dilution and gradient diffusion combined and if a possible transition could be made from agar dilution to gradient diffusion methods. • Disk diffusion methods are being investigated and the WG will reach out to EUCAST. • The WG requested that gradient diffusion data be submitted to Darcie Carpenter (dcarpenter@ihma.com). **Rifampin Surrogate** • The MAIWG is looking at testing rifampin as a surrogate for rifabutin and rifapentine for staphylococci. • Volunteers are needed!
7.	**Outreach WG Report: Ms. Hindler (Folder 8)** **WG Roster**: Janet Hindler, Audrey Schuetz (Co-Chairholders); Stella Antonara (Secretary); April Abbott, April Bobenchik, Angella Charnot-Katsikas (resigned), Romney Humphries, Graeme Forrest, Nicole Scangarella-Oman, Paula Snippes-Vagnone, Lars Westblade (Members); Shawn Lockhart (Antifungal Liaison/Advisor) **Ms. Hindler provided an update on the activities of the Outreach WG.** • The newest edition of the CLSI AST Newsletter published in January 2020. – Translations in to Spanish and Chinese are in progress. – The Hot Topic written by Dr. Bobenchik discusses the nomenclature changes within the Enterobacterales. • Upcoming newsletter items include:

	– Featured Article: Understanding S, I, I^, SDD, R, WT, NWT. – Case Study: Case where I^ would be useful. – Practical tips: What's wrong with this picture? (ASTs that need attention) series – Hot topic: Requirements for Verification of AST tests • 2020 AST SC Meeting Workshops include: – January: "Beyond SIR: Enhancing Laboratory Reports with Comments to Improve Understanding of the Report's Intent." – June: "Solutions to AST Nuances and Impact on Clinical Outcomes" o *E. coli* – piperacillin-tazobactam o *Staphylococcus aureus* (MRSA) – vancomycin o *Candida auris* – caspofungin and other echinocandins • 2020 Webinars and Presentations include: – AST Annual Update Webinar – February 26 and 27 (Romney Humphries and Audrey Schuetz) – CLSI-SIDP ACCP Annual Webinar – June 2019 (Archived/On-Demand): Merging Microbiology and Stewardship: Making the most of 2019 CLSI Updates on AST for gram-positive and gram-negative bacteria in your stewardship activities. – ASM Microbe 2020 Symposium (22 June 2020): "Importance of Reliable Generation and Appropriate Interpretation of AST Results in 2020" o "Meaningful reporting of AST results" (April Bobenchik) o "The science and the art of setting and revising breakpoints" (Jim Lewis) o "What does MIC, SDD, S, I and R mean to the clinician?" (Amy Mathers) • There were 35 new volunteers at the 2020 orientation. – The WG continues to provide lists of needs for each of the WG (last posted on August 14, 2019). The WG is looking for input on whether this has been helpful. – It is planned to revise the orientation slides and provide Chairholder contact information on the website. • New Outreach WG projects include: – Interactive program for M100 – Slides as companion to News Update – Website Index for News Update articles – Video for navigating website
8.	**Epidemiological Cut off Value (ECV) WG: Dr. Schuetz/Dr. Wikler (Folder 5)** **WG Roster:** Audrey Schuetz, Matthew Wikler (Co-Chairholders); April Bobenchik, Paul Edelstein, George Eliopoulos, Janet Hindler, Susan Kircher, Jim Lewis, Jean Patel (Members) • The report from the ECV WG at the plenary session was cancelled. Rather, the ECV WG presented items for discussion at the Breakpoint Working Group.meeting.
9.	**Methods Development and Standardization WG: Dr. Zimmer (Folder 7)** **WG Roster:** Dwight Hardy, Barbara Zimmer (Co-Chairholders); Katherine Sei (Secretary); Kevin Alby, Jennifer Dien Bard, Susan Butler-Wu, Tanis Dingle, German Esparza, Laura Koeth, Ribhi Shawar (Members)

High Inoculum Cefazolin WG Report

WG Roster: Susan Butler-Wu, Tanis Dingle (Co-Chairholders); Carey-Ann Burnham (Recording secretary); April Abbott, Cesar Arias, Jennifer Dien Bard, Dee Gamage, Stephanie Fritz, William Miller, Jinnethe Reyes, Lars Westblade, Barb Zimmer

- There appear to be problems with the preferred agents (anti-staphylococcal penicillin or cefazolin) for treating bacteremia and infective endocarditis caused by methicillin (oxacillin)-sensitive *S. aureus* (MSSA).
- Clinical failures have been reported with cefazolin due to penicillinase-producing staphylococci that can hydrolyze the drug.
- Clinical failures with cefazolin have been reported for MSSA infections, specifically infective endocarditis.
- Clinical MSSA isolates failing 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 mechanism appears to involve *Blaz* ß-lactamase in a majority of clinical isolates.
- An accurate and reproducible rapid CIE assay is needed to make testing feasible for clinical laboratories
- WG Objectives:
  - Assess the CIE phenotype prevalence in MSSA isolates (US strains)
  - Determine which assay to use to detect CIE in MSSA isolates
  - Validate the assay in a multi-center study
- The Phase 1 study plan and protocol were reviewed. Results will be published by the WG.
- Phase 2 Plan and protocol were reviewed.
  - 100 isolates from Phase 1 will be evaluated at multiple sites for performance on a more rapid and simplified CIE assay (Rapid Disk method)
  - Upon completion, the possibility and feasibility of a Phase 3 plan to look at clinical outcomes will be assessed.
- SC Discussion: The SC agreed with the plan for developing a simplified CIE assay.

Proposed study for AST testing of *H. influenzae* with Mueller-Hinton Fastidious (MH-F) Media

- This will be a joint study (Beckman Coulter, CDC, Instituo Nacional de Salud (Colombia), JMI Laboratories, Pan American Health Organization) with the CDC performing the majority of testing.
- MH-F has already been approved for testing *Streptococcus pneumoniae* (published in M100, 30th ed.).
- The testing is being performed to ensure results are equivalent with EUCAST (different protocols).
- A pilot study with three methods (CLSI BMD, gradient diffusion, EUCAST BMD) was previously presented.
  - The EUCAST and CLSI BMD methods exhibited poor categorical agreement.
  - Gradient diffusion was more consistent with the EUCAST method compared to the CLSI method.
  - This study suggested that ß-lactam susceptibility interpretations for *H. influenzae* could differ based on which method was performed and that additional guidance may improve consistency of MIC identification across laboratories.
- A modified Tier 2 study with 100 isolates tested in three laboratories was proposed. The objectives of the study were;
  - Compare the performance of *Haemophilus* Test Media and MH-F using CLSI BMD and DD for assessing *H. influenzae* susceptibility.
  - Assess the possible need for changes in the approved CLSI QC ranges for the designated QC organisms on MH-F agar and MH-F broth.
  - Assess the need for guidance regarding a "substantially inhibited growth phenotype" when interpreting ß-lactam MICs on *H. influenzae* BMD panels.

- The protocols for the DD and BMD studies were presented. It is expected that the study data will help inform guidelines for *H. influenzae* susceptibility testing.
- SC Discussion: The SC agreed with the plan for the study.

***Stenotrophomonas maltophilia* AST MIC/disk correlate study: Dr. Humphries and Dr. Khan**

- Background
  - *S. maltophilia* is an emerging pathogen in immunocompromised patients and infections results in high morbidity and mortality.
  - It is intrinsically resistant to many antimicrobial agent classes.
  - Trimethoprim-sulfamethoxazole, the primary agent for treatment, has shown a decrease in susceptibility over time.
  - There are also major AST performance issues.
- Proposed Action Items
  - Create an ad-hoc WG to re-evaluate existing contemporary data, outcomes studies, and support study design that fills gaps
    - **MDSWG decisions**: Previous *Stenotrophomonas* and other non-fermenters WG have investigated and will take this on.
  - Develop a rationale document on high-priority agents supported by contemporary data for FDA docket to push recognition of CLSI BPs.
  - Perform a systematic review of disk-to-MIC correlates
    - **WG decisions:** The original presentation also included commercial methods, and this may be done for other purposes.
  - Evaluate ciprofloxacin BPs
- SC Discussion
  - Dr. Lewis: Suggested that the WG also needs to look at moxifloxacin (this will be added to the action item list).

Inherent Variability in Frozen Reference BMD and Impacts to Evaluating M23 Studies: Ms. Sei, Dr. Ullery, Dr. Turnidge

- The M23 WG discussed having a reproducibility standard of >95% essential agreement (EA) to a mode for new antimicrobial agents testing in a frozen reference panel. It was agreed that this is a guideline, not a specification for new drugs.
- It was suggested that the text in M23 might be too rigid for some drug/organism combinations.
- It is generally expected that testing will produce a nice distribution.
  - >95% of MIC results within 3-dilution range, and a nice Gaussian distribution.
  - Mode consists of ≈70% of the results
  - Distributions like this can meet a requirement of >95% EA to a mode.
- Distributions are not always as expected. They may appear lopsided or flat and may not meet the reproducibility requirement of >95% EA to a mode.
- The current statements regarding ±1 doubling dilutions was questioned by the presenters.
- A proposal to test 20 isolates for reproducibility was made.
  - Expect ≥95% EA to mode. EA to mode is dependent on how many variable isolates are in the mix.
  - Failing the ≥95% criterion may not mean that there is something wrong with the frozen reference panel but could be just the inherent variability.
- SC Discussion: The WG requested input on how to proceed.
  - Dr. Shawar: There are several reasons for variability (eg, media, organisms etc). Manufacturers understand the drug best and could provide stability information. Organisms are getting more finicky and sponsors need to take that into consideration.

- Dr. Moeck: The M23 WG is looking at variability in both DD and BMD. Revisions have been proposed to show how to recognize variability and ways to detect it earlier. A study design and options for evaluating variability is being developed (new appendixes in M23). There is not a single MIC for every isolate and guidance on assessing variability will be included in M23.
- Dr. Turnidge: He suggested that CLSI provide guidance on what to do to consider variability. Variability occurs with DD and BMD. A single MIC is not the final answer to treating a patient.
- Ms. Cullen: Basing disk correlates on a single MIC is dangerous unless the testing is very reproducible. Guidance on how to use the study information is needed.
- Mr. Esparza: Suggested that the Outreach WG create a webinar to educate users about variability.
- Dr. Zimmer: A publication by Ms. Sei, Mr. Brasso, Dr. Turnidge, and Dr. Ullery is in the works.

Staphylococcus argenteus and _Staphylococcus schweitzeri_ data (For vote)

- Both species are members of the *S. aureus* complex.
  - Both test coagulase positive and are often incorrectly identified and reported as *S. aureus*. They are often misidentified as *S. aureus*.
  - *S. argenteus* is associated with clinically significant human infections.
- Questions being considered:
  - How should these species be reported (species name only or as *S. aureus* complex)?
  - What BPs should be applied (eg, do *S. aureus* oxacillin and cefoxitin BPs apply to these species)?
- A study protocol for *S. argenteus* was presented. The following test methods were performed on 29 isolates identified as *S. argenteus*.
  - Agar dilution
  - Developed *nucA* real-time PCR for *S. aureus*/*S. argenteus*/*S. schweitzeri*
  - Real-time *mecA* PCR
  - Whole genome sequencing performed on 19 isolates (including type strain)
- AST results showed 3 *mecA*-positive; 27 *mecA*-negative
- Identification methods are not reliable, and the colonies are not easily differentiated from *S. aureus*.
- Conclusions:
  - Better identification tools are needed to reliably differentiate the members of the *S. aureus* complex.
  - It may be necessary to expand *S. aureus* to read "*S. aureus* complex" in pertinent areas of M100.
  - May want to follow recommendations of a recent ESMID paper:
    - If these novel species are explicitly reported, add a specific comment (eg, member of *S. aureus* complex) "to prevent confusion with less or non-pathogenic staphylococci"
    - "Methicillin (oxacillin)-resistant isolates should be handled as recommended for methicillin (oxacillin) *S. aureus* (MRSA)"
- SC Discussion
  - Dr. Schuetz: Cannot always be differentiated on commercial instruments when run on direct specimens.
  - It was proposed to report *S. argenteus* as *S. aureus* complex (unless identified by MALDI-TOF or gene sequencing).
  - If *S. argenteus* is identified and reported, it was proposed that *S. aureus* oxacillin MIC and cefoxitin DD BPs and interpretive categories be applied.

A motion to accept the recommendations to report *S. argenteus* as *S. aureus* complex (when not identified by MALDI-TOF MS or sequencing) or *S. aureus* complex (*S. argenteus*)(when identified MALDI-TOF MS or sequencing). If identified as such, report using *S. aureus* BPs and interpretive categories was made and seconded. VOTE: 11 for; 0 against; 1 abstention (Dr. Schuetz) (Pass).

- **A definition of *S. aureus* complex will be added to M100 (Text and Tables will address).**

Direct Blood Culture AST WG Report/Antibacterial Resistance Leadership Group (ARLG)

- Background
  - A multicenter study assessing DD direct from positive blood culture (BC) bottles for GNB with different reading times was performed.
  - It was hypothesized that direct-from-blood culture DD test read at 16-18 hrs. performs at or above CLSI standards as compared to both standard DD and to reference BMD.
- Testing Protocol
  - BC positive for GNB on Gram stain.
  - Four drops of blood tested on each of two Mueller-Hinton agar plates within 8 hours of flagging positive.
  - 12 antimicrobial agents were tested.
  - Reading notations were made for each drug at 8-10 hr., 16-18 hr., and standard DD time points.
  - QC ranges and workflow followed CLSI instructions. QC ranges for ciprofloxacin read high and for meropenem read low.
- Results
  - Of the original 500 isolates, results from 53 were excluded. Sites were excluded based on workflow and/or patient population. Of the remaining 447 isolates, isolates were excluded:
    - When QC was out of range on two consecutive days
    - When the isolates were intrinsically resistant to the antimicrobial agent tested
    - When either direct reads or standard DD were read outside of time range
  - The overall conclusions of the data review were as follows:
    - It was difficult to draw conclusions for *A. baumannii* and *S. maltophilia* direct read performance due to low isolate numbers
    - More isolates are needed for:
      - *A. baumannii*
      - *P. aeruginosa*: Especially those not susceptible to cefepime, ceftazidime, piperacillin-tazobactam, and meropenem
      - Enterobacterales: Especially those not susceptible to ertapenem, meropenem, and piperacillin-tazobactam
- Future steps
  - Continue to review data for 16-18 hr direct reads and potential issues related to set-up time, comparators, major and minor errors, and QC issues with some agents.
  - Time to review data for Direct BC and MSDWG before next meeting, and all data in June agenda material.
  - Next steps: Seeding studies and review 8-10 hr reads and QC.
- SC Discussion
  - Dr. Miller: Very impressive work. Going forward, inherent variability needs to be considered. Isolates with MICs close to the BP should be included.
  - Dr. Simner: Shorter reads may need to be re-evaluated (Dr. Schuetz agreed).

10.	**Implications for Commercial AST Systems When CLSI and FDA Breakpoints Don't Agree: Dr. Zimmer (Folder 7)** • Dr. Zimmer reported on the consequences of changing BPs for antimicrobial agents without FDA-recognized BPs on commercial AST devices. – The 21st Century Cures act, implemented in 2017, allows the FDA-Center for Drug Evaluation and Research (FDA-CDER) to recognize some CLSI BPs (posted on the FDA website). – Organism groups not listed in the package insert do not have or are not been recognized by FDA-CDER. If the antimicrobial agent is used, CLSI usually has a BP. – Implementing new or revised BPs on legacy systems for one organism group in the US may come with a cost to AST manufacturers for reporting MIC results for other organism groups. – It would be helpful to be able to report the MIC without a BP if FDA does not recognize the BP. – Assistance from CLSI (eg, rationale document) would be helpful. • SC Discussion – Dr. Simner: Are laboratories still able to validate CLSI BPs for drugs that device manufactures can't change. – Dr. Zimmer: It is still possible to do the work off-label or as research-use-only but only the MIC would be reported manually. – Dr. Humphries: A lot of work on rationale documents have been done. However, despite that perhaps we need to look at other issues than just categorial agreement. – Ms. Cullen: At the last meeting, a number of situations where BPs are not recognized were discussed. Perhaps information to guide decisions can be provided to help clinicians make their decisions. – Dr. Shawar: Further discussions are needed between CDER, CDHR, and device manufacturers to resolve the issues. Just providing the MIC may not be the answer.
11.	**Streamlined Approach to Implementing BP Changes on Commercial AST Devices: Dr. Natasha Griffin (CDRH) (Folder 7)** • Dr. Griffen presented the current recommendations to device manufacturers for streamlined implementation of new or revised BPs. • Background and historical perspective – Before 12/2017, the process for FDA to approve devices with a new or revised drug BP took several years to update FDA BPs. The process was linear with multiple 510(k) submissions and many bottlenecks. – With the approval of the 21st Century Cures Act, the FDA-CDER has the authority to directly recognize BPs from recognized standard development organizations (SDOs)(eg, CLSI). The process is designed for approval to take only one year with posting on the Antimicrobial Susceptibility Test Interpretive Criteria (STIC) website. • In the current path, the FDA recommends that AST device manufacturers include a prospective BP change protocol in the original 510(k) submissions. – This may provide a mechanism for updating the device with new BPs without a new 510(k). – The following BP change protocol criteria must be met to move forward without a new 510(k) submission: o There are no modifications to the device's design. o The most recent 510(k) data are availability. o A sufficient number of resistant isolates were tested in the most recent clearance. o Acceptable data performance is shown when evaluated with the new BPs. – Approaches for updating BPs for previously cleared (legacy) AST devices is under discussion and consideration. • New and/or Undefined BPs – FDA-CDRH cannot clear/approve devices with drug/organisms combinations for which there are no FDA-recognized or established BPs.

	– The sponsor or CRO may petition FDA for new/previously undefined BPs via FDA-CDER through the established process or in the new process. • SC Discussion – Dr. Richter: CLSI cefazolin parenteral BPs are different from FDA. The urine BP is not recognized by FDA. – Dr. Goodwin: The BP is usually different when FDA and CLSI dosages are different. – Dr. Humphries: Two rationale documents for cefazolin (urine and systemic) are in progress and will be submitted to the FDA docket.
12.	**EUCAST Update: Dr. Giske (presentation has been posted on the CLSI Website)** **Dr. Giske provided an update on EUCAST activities.** • Committee updates – Dr. Johan W. Mouton was memorialized. Dr. Mouton was an active member of EUCAST and an expert in PK/PD. – Current and new members of the committee were recognized. • Countries where EUCAST BPs and methods are being used and that have national AST committees were identified. • The following BPs consultations were finalized in 2019 or are pending in 2020. – Finalized o Aminoglycoside BPs o Moving wild type (WT) of some species (mainly *P. aeruginosa*) into the Intermediate group o Update of expert rules o *B. pseudomallei* BPs o Temocillin o Mecillinam – expansion of species with BPs for urinary tract infections – Pending o Fosfomycin o Piperacillin-tazobactam and Enterobacterales o Oral aminopenicillin BPs for Enterobacterales o Endocarditis and meningitis BPs • The EUCAST Development Laboratory is working on the following projects: – Developing EUCAST BP table v10.0 (January 2020) – Developing DD criteria for novel agents – AST for *B. pseudomallei* (completed), *Nocardia* spp. and *Vibrio* spp. – Rapid AST directly from BC bottles – DD methodology for rapidly growing anaerobes – AST for fosfomycin, temocillin, ß-lactams vs *H. influenzae* – Colistin gradient tests with addition of Ca^{2+} – *S. pneumoniae* and benzylpenicillin gradient diffusion tests • Recent BP changes include: – Aminoglycosides – Definition of intermediate

TABLE 1 Definitions of the I group

Interpretive category (abbreviation)	Status	Definition
Intermediate (I)	EUCAST previous definition (in common with CLSI)	A microorganism is defined as intermediate by a level of antimicrobial agent activity associated with uncertain therapeutic effect. It implies that an infection due to the isolate may be appropriately treated in body sites where the drugs are physically concentrated or when a high dosage of the drug can be used; it also indicates a buffer zone that should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations.
Susceptible, increased exposure[a] (I)	EUCAST new definition (not shared with CLSI)	A microorganism is categorized as "susceptible, increased exposure" when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.

[a]Exposure is a function of how the mode of administration, dose, dosing interval, and infusion time as well as the distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.

  - New *B. pseudomallei* BPs
  - Temocillin BPs
  - New agents: delafloxacin, ceftolozane-tazobactam, imipenem-relebactam, cefiderocol, lefamulin, bedaquiline (in discussion)
  - Fosfomycin
- Endocarditis and meningitis
  - For endocarditis: Discussions to amend the European guidelines and state that clinical BPs from EUCAST can be used.
  - For meningitis: Removal of some I-groups, general review of all BPs
- SC Questions/Discussion
  - Mr. Esparza: Questioned issues with piperacillin-tazobactam and Enterobacterales and daptomycin for enterococcal endocarditis.
  - Dr. Giske: It is difficult to get a high enough drug exposure to cover endocarditis and subsequently are having issues with adding it to the table. There is a rationale document available and a number of references for guidance. Piperacillin-tazobactam tied to the Merino trial and PK/PD study results. EUCAST is not convinced to go as high as 16.
  - Dr. Moeck: Questioned if the rationale documents have kept up with the many discussed changes.
  - Dr. Giske: It is difficult to keep up but are trying to work towards completion. Rationale can also be found in the consultation documents on the web site.

13. **Veterinary AST (VAST) Update: Mr. Bowden**

An update on Subcommittee on Veterinary Antimicrobial Susceptibility Testing (VAST) activities of the was provided.

- VAST currently has nine active WGs. Current activities by each WG were reviewed.
  - Aquaculture AST Methods: Revising and consolidating current VET03 (DD methodology) and VET04 (BMD methodology) both into a unified document (new VET03). This is projected for projected for publication in May 2020.
  - Aquatic Animals (VET04)
  - Editorial/VAST BP Tables (VET08): Working on the Vet-equivalent of M100 including expansion of group designations and revisions to group definitions. Projected publication date for next edition is August 2020.
  - Education: Educational initiatives include:
    - Presentations on VET09 at national veterinary conferences by WG members
    - Efforts to obtain funding for copies of VET09 to be made available at veterinary schools
    - Future direction: develop topic sessions and webinars (ie. companion animal-focused)
    - Increase international promotion

- "Veterinary Antimicrobial Susceptibility Testing Standards: Recommendations for Researchers and Reviewers Working with Animal-Origin Bacteria" (publication to be submitted to JAC or Veterinary Microbiology)
- Development of an annual VAST newsletter

– Fastidious Organisms (VET06): Investigating possible alternatives to use of Veterinary Fastidious media.
– Generic Drugs: Investigations included:
  - Ceftazidime breakpoints for Enterobacterales and *P. aeruginosa* (dogs)
  - Ampicillin dosage re-evaluation for horses
  - Levofloxacin breakpoints for Enterobacterales and *P. aeruginosa* (dogs)
  - Enrofloxacin breakpoints for *Bordetella bronchiseptica* (swine)
  - Marbofloxacin breakpoints for *P. aeruginosa* (dogs)
  - Meropenem breakpoints for Enterobacterales and *P. aeruginosa* (dogs)
– Bovine Mastitis Interpretive Criteria (BMIC): Proposal for cefoperazone BP coming for a vote.
– Veterinary Breakpoint Rationale
– Veterinary AST Methods Standard (VET01)

- The current status of the VAST document library was reviewed.

Document Code	Year Published	Document Name
VET01	2018 (Re-released in 2019)	*Performance Standards for Disk and Dilution Antimicrobial Susceptibility Testing For Bacteria Isolated From Animals*. 5th ed. CLSI standard VET01.
VET02	2008	*Development of In Vitro Susceptibility Testing Criteria and Quality Control Parameters for Veterinary Antimicrobial Agents*. 1st ed. CLSI guideline VET02.
VET03	2006 (Reaffirmed in 2016)	*Methods for Antimicrobial Disk Susceptibility Testing of Bacteria Isolated From Aquatic Animals*. 1st ed. CLSI guideline VET03.
VET04	2014	*Methods for Broth Dilution Susceptibility Testing of Bacteria Isolated From Aquatic Animals*. 2nd ed. CLSI guideline VET04.
VET03/04S	2014	*Performance Standards for Antimicrobial Susceptibility Testing of Bacteria Isolated From Aquatic Animals*. 2nd ed. CLSI supplement VET03/04.
VET05	2018 (Reaffirmed in 2016)	*Generation, Presentation, and Application of Antimicrobial Susceptibility Test Data for Bacteria of Animal Origin*. 1st ed. CLSI report VET05.
VET06S	2017	*Methods for Antimicrobial Susceptibility Testing of Infrequently Isolated for Fastidious Bacteria Isolated From Animals*. 1st ed. CLSI supplement VET06.
VET08S	2018 (Re-released in 2019)	*Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals*. 4th ed. CLSI supplement VET08.
VET09	2019	*Understanding Susceptibility Data as a Component of Antimicrobial Stewardship in Veterinary Settings*. 1st ed. CLSI report VET09.

14. **Quality Control (QC) WG Report: Ms. Cullen (Folder 9)**

WG Roster: Sharon Cullen, Maria Traczewski (Co-Chairholders); Michael Huband (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)

- **Tier 2 QC studies**: There were no Tier 2 studies for review. It is expected Tier 2 studies will be available for review/vote at the June meeting.

- **Rifampin QC**
  - Dr. Robin Patel requested establishment of QC ranges for non-rifampin rifamycins (eg, rifabutin and rifapentine)
    - A reference method needs to be established before Tier 2 QC studies can be performed.
    - Dr. Patel will explore options with the Methods Development or Breakpoint WG for establishing a reference method and/or using rifampin as a surrogate.
  - Recent rifampin QC tests have shown out-of-range results with *S. aureus* ATCC® 29213.
    - Rifampin and *S. aureus* ATCC® 29213 will be added to the Tier 3 concerns list and the QCWG requested any data be submitted.

- **Colistin QC Issues**
  - Improvements or data are needed. The current QC for BMD doesn't include new QC strains (*mcr1*). *Mcr1* clinical strains often have MICs at the BP and can be variable.
  - Dr. Humphries will be performing a proper colistin QC study to present at the June meeting.
    - The QC strain for broth disk elution (CBDE) and the colistin agar test (CAT)(*E. coli* AR Bank #0349) was approved with limited disk and media data and is not approved for BMD.
    - Strains other than *E. coli* AR Bank #0349 (*mcr-1* positive) may be used for BMD (EUCAST recommends *E. coli* NCTC 13846 [mcr-1 positive]).
    - Additional data requested for both the CLSI and EUCAST QC strains to meet M23 Tier 2 requirements.
  - Next steps
    - Determine if studies are planned to collect additional disk and media data for CBDE and CAT for *E. coli* AR Bank #0349
    - Assess options to compile data from multiple sources for either or both new QC strains (CBDE, CAT, and BMD?)
    - Update routine QC recommendations based on additional data (*E. coli* AR Bank #0349 and/or *E. coli* NCTC 13846).

- **Tier 3 MIC Data was reviewed.**
  - There was no feedback for the following antimicrobial agent/QC strain combinations, so they have been archived.

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern	Date Reported
~~*E. faecalis* ATCC 29212~~	~~Gentamicin~~	~~4-16~~	~~Monitor/ request feedback~~	~~Some out low. Cations, pH in range~~ ~~Report from CDC, out low when testing gram neg panels, other strains in range.~~	Jan-15
~~*E. faecalis* ATCC 29212~~	~~Tobramycin~~	~~8-32~~	~~Monitor/ request feedback~~	~~Some out low. Cations, pH in range~~ ~~Report from CDC, out low when testing gram-neg. panels, other strains in range.~~	Jan-15
~~*P. aeruginosa* ATCC 27853~~	~~Ertapenem~~	~~2-8~~	~~Monitor/ request feedback~~	~~Out low with some labs~~	NA
~~*E. faecalis* ATCC 29212~~	~~Minocycline~~	~~1-4~~	~~Monitor/ request feedback~~	~~Mode at low end at 16 hrs., bimodal at 18 hrs., at middle of range at 20 hrs.~~	NA

~~*S. aureus* ATCC 29213~~	~~Minocycline~~	~~0.06-0.5~~	~~Monitor/ request feedback~~	~~Mode at low end of current range regardless of read time 16-20 hr~~	Jun-13
~~*B. fragilis* ATCC 25285~~	~~Piperacillin-tazobactam~~	~~0.12-1~~	~~Monitor/ request feedback~~	~~Out low (control M23 study Jan 2010)~~	Jun-13
~~*S. pneumoniae* ATCC 49619~~	~~Cefuroxime~~	~~0.25-1~~	~~Monitor/ request feedback~~	~~Mode at 0.25~~	Jun-13
~~*E. faecalis* ATCC 51299~~	~~Gentamicin HLAR~~	~~Resistant~~	~~Request data/ feedback~~	~~Out of range results (susceptible). Organism stability.~~	Jun-17

– Feedback or data are being requested for the following Tier 3 MIC antimicrobial agent/QC strain combinations. These will be monitored for three years (new additions in red text).

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern	Date Reported
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.	Jan-18
E. faecalis ATCC 29212	Amikacin	64-256	Monitor/request feedback	CDC reported out low when testing gram-neg. panels, other strains in range.	Jan-18
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.	Jan-18
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.	Jan-18

QC Strain (ATCC)	Antimicrobic	Current Range (µg/mL)	Action Recommended	Concern	Date Reported
C. difficile ATCC® 700057	Fidaxomicin	0.06-0.25	Request feedback	Agar dilution, results out reporting MIC out on the low side, observing MIC at 0.03 (Anaerobe WG).	Jan-20
S. aureus ATCC® 29213	Rifampin	0.04-0.016	Monitor/ request feedback	One report of S. aureus out low	Dec-19
E. coli ATCC® 25922	Imipenem/ relebactam	0.06/4-0.25/4	Monitor/ request feedback	Report from one lab with results out high	Dec-19
K. pneumoniae ATCC® *700603*	Imipenem/ relebactam	0.03/4-0.25/4	Monitor/ request feedback	Some out high reported with 2 labs	Jan-18
K. pneumoniae ATCC® *BAA-1705*	Imipenem/ relebactam	0.03/4-0.25/4	Monitor/ request feedback	Results at high end with one lab.	Jan-19
K. pneumoniae ATCC® *700603*	Ampicillin/ Sulbactam	8/4 – 32/16	Request feedback	Report from one lab with results at 64/32	Jun-19
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.	Jan-17 Jun-19

– There was no feedback for the following DD antimicrobial agent/QC strain combinations and have been archived.

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recmd	Concern	Date Reported
~~*K. pneumoniae* 700603~~	~~Blactam/ Blactamase inhibitors~~	~~No range~~	~~Collect data for single and combination agent e.g., amoxicillin, ampicillin, ampicillin-sulbactam (2:1), cefepime, ceftaroline~~	~~Alternative for E. coli 35218~~	~~NA~~
~~*P. aeruginosa* 27853~~	~~Imipenem~~	~~20-28~~	~~June 2019: Erika M proposed 20-26 mm (98% in range) or 20-27 mm (99% in range) with 1600 data points. EUCAST data support 20-26, US & recent M23 study data supports 20-28 with some labs >5% out of range. Decision to monitor/don't change. Insufficient signal to take action. 11/0/1/0~~	~~Zones in the lower part or below range reported~~	~~Dec-15~~
~~*E. coli* 25922~~	~~Pefloxacin~~	~~25-33~~	~~EUCAST range 26-32 (97% in range). CLSI 25-33 (100% in range). Evaluated Salmonella strains but are not proposing for use. Recommend including clearer instructions on how to read zone diameter (inner or outer zone diameters, pictures) and/or address in troubleshooting guide.~~	~~Is there a better way to QC this agent? Varies by manufacturer.~~	~~Jan-17~~

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recmd	Concern	Date Reported
~~*S. aureus* 25923~~	~~Tedizolid~~	~~NA~~	~~Request Tier 2 study to establish QC ranges. (Methods Working Group).~~	~~Change in disk mass from 20 to 2 µg being considered. Need new Tier 2 study for QC range change in disk mass from 20 to 2 µg being considered. Need new Tier 2 study for QC range~~	~~Jan-17~~
~~S. aureus 25923~~	~~Linezolid~~	~~NA~~	~~Request Tier 2 study to establish QC ranges. (Methods Working Group).~~	~~Change in disk mass from 30 to 10 µg being considered. Need new Tier 2 study for QC range~~	~~Jan-17~~
~~P. aerug 27853~~	~~Meropenem~~	~~28-33~~	~~Get original M23, Consider range adjustment. June 2019: Considered range adjustment to 28-34 but insufficient data for Tier 3 and not strong enough signal for action. Proposed troubleshooting comment to address results out of range low due to (incorrectly) reading the inner zone with fuzzy edges or discreet colonies within the zone. 11/0/1/0~~	~~Some out out high. Some out of range low due to reading inner zone.~~	~~Jun-15~~

– Feedback or data are being requested for the following Tier 3 DD antimicrobial agent/QC strain combinations. These will be monitored for three years.

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recmd	Concern	Date Reported
P. aeruginosa ATCC® 27853	Ceftriaxone	17-23	Request data, reassess range or troubleshooting information.	Seeing colonies within zone of inhibition causing out of specification results	Jun-17
P. aeruginosa ATCC® 27853	Amikacin	18-26	June 2019: Erika M proposed 20-26 mm (pg 5). 781 data points, 6 labs, disks from 3 manufacturers, media from 4 manufacturers (including the MH ref lot). Similar to changes made for gentamicin and tobramycin 2012	Out high for many labs.	Jan-18

			(new ranges are higher and both are 7 mm). Monitor. Insufficient signal to take action.		
E. coli ATCC® 25922	Eravacycline	16-23	Proposed change to 18-24 not approved. Approved alternative proposal 17-24 (vote 10/2/2). See next discussion for details.	Results with multiple media and labs out high at 18.	2019?

- **Tier 3 DD QC: *E. coli* ATCC® 25922 and Eravacycline (20 µg)**
  - Current QC range based on original Tier 2 Data: 16–23 mm.
  - Different zones are being seen with three media manufacturers: 20, 18, 21 mm (for median, mean & mode)
  - Data from four laboratories show ranges in the upper end of the range (18-24 mm) and EUCAST recently published this range.
  - Proposals to the QCWG
    - Proposal 1: change the range to 18-24 mm
    - Proposal 2: change the range to 17-24 (Approved 10/2/2). (The original Tier 2 data were reviewed, and the data supported the original range and the proposed range of 17-24 mm. Statistics will be reviewed to determine if 16-24 should be the range.)

A motion to accept the revised QC range of 17-24 mm for eravacycline with *E. coli* ATCC® 25922 was made and seconded. Vote: 11 for; 0 against; 1 absent (Pass).

- **QC boxes at the top of Tables 2**
  - When to include a reference to Tables 4A-2 and 5A-2 was discussed.
  - All Tables 2 include this reference except Tables 2G and 2H-2.
  - The WG agreed that most Table 2 QC boxes seem clear and appropriate based on the agents included but that fastidious organisms are not as clear and would be good to review/reassess.
  - **Action Item**: Review QC recommendations for ß-lactam combinations for fastidious organisms on Tables 2E, 2G, 2H-2, 4 and 5 (Ms. Traczewski and Dr. Palavecino)

- **Troubleshooting Guide Additions**
  - Reading Meropenem disk zones
    - Troubleshooting guide does not address double-zone or fuzzy edges as stated in Table 4A-2.
    - **Action Item:** Propose clarifications as appropriate at June 2020 meeting (Ms. Hindler and Dr. Conville).
  - MIC QC failures with *S. pneumoniae* ATCC® 43619
    - MICs too low or zone sizes too large
    - The WG proposed adding recommendations for MIC troubleshooting guide: WG Approved 14/0/0 (approved in red); SC agreed with the addition (no vote was needed).

Antimicrobial Agent	QC Strain	Observation	Probable Cause	Comments/Suggested Actions
ALL AGENTS				
Various	*S. pneumoniae* ATCC® 49619	Zones too large Lawn of growth scanty	Inoculum source plate too old and contains too many nonviable cells. Plate used to prepare inoculum should be 18–20 hours.	Subculture QC strain and repeat QC test, or retrieve new QC strain from stock.
Various	*S. pneumoniae* ATCC® 49619	MICs too low Light growth	Inoculum source plate too old and contains too many nonviable cells. Plate used to prepare inoculum should be 18–20 hours.	Subculture QC strain and repeat QC test, or retrieve new QC strain from stock.

- **Future Agenda Topics**
  - Streamlined QC for single agents (Dr. Humphries Ad Hoc WG)
  - Further develop recommendations for routine vs supplemental QC

- **M23 Improvements Review**: Revisions to be added to the next edition of M23 (also see the QC presentation on the CLSI Website)
  - M23 QC procedures

Category	Tier 1	Tier 2	Tier 3
Objective	Initial method assessment to determine if labile, inoculum, pH, supplements, etc. Select potential QC strains	Establish QC range, update glossaries. Sponsor notifies CLSI to publish after agent is named	Monitor performance with existing QC ranges. Reassess/revise QC ranges. Compare/consolidate with Tier 2 if available.
Laboratories	1+	7	3
Media lots	1-2	3	2
Replicates	20-30	10 per lab, individual inoculum, max 4 per Day	10 per lab 50 per media
Disk lots	1	2 (from dif mfg)	2
Total results	20-30+	210 (7x3x10 MIC) 420 (7x3x10x2 Disk)	500 disk, 250 MIC Similar totals and criteria as Tier 2, but more flexible & focus on sources of variability

- **Overview of Criteria for QC Ranges**
  - Calculate with traditional methods and Rangefinder method
    - Disk: Gavan statistic based on median; MIC: Mode ± 1 dilution,
    - Expand or adjust range if:
      - Initial range includes less than 95% of results.
      - Other considerations: General guidance but not absolute. Balance robustness of range & ability to detect problems.
        - Shoulder (second most frequent result) is >60% of the mode for MICs
        - Large variability in media, laboratories, etc.

– Laboratory data can be excluded if there are statistical outliers for 2-3 parameters using Rangefinder (mean, median, mode). Don't exclude if outlier for only one parameter.
– Media (both MIC and DD) and disk lots: Investigate if significant differences

- A sample data summary will be included in M23.

Drug: xx	**Abbreviation: xx**	**Previous ID: xx**
Solvent: xx	Diluent: xx	Preparation: xx (for disks indicate content/mass)
Route of administration: xx	Class: xx	Subclass: xx
Study Report by: xx	Pharma Co: xx	Control Drug: xx

Footnotes:	• **xx**
Discussion	• Include discussion points/feedback requested. Update with key discussions and decisions from meeting.

– Class and Subclass are suggested by sponsor and determined by the Subcommittee (not the QCWG)
– Solvent, diluent, preparation needed for M100 (provided by sponsor)
– Abbreviation: Determined after compound is named. Consult STMA who maintains list of use/available abbreviations.
– Pharma to notify CLSI after agent is named so it can be published.
– Best practice: Sponsors create a summary slide using this template

15. **Table 1 WG Report: Dr. Simner (Folder 5)**

WG Roster: George Eliopoulos, Trish Simner (Co-Chairholders); Virginia Pierce (Recording secretary); Tanaya Bhowmick, April Bobenchik, Carey-Ann Burnham, Linda Miller, Barth Reller, Sandra Richter, Lauri Thrupp, Matt Wikler (Members)

Dr. Simner reported on the WG's progress. A vote is planned for the June meeting.

- **Refresher on the definitions of what qualifies an agent to be placed in different groups**
  – The intent of the suggested groupings is to assist small laboratories that lack a microbiology director to assist with decisions.
  – Laboratories need to work with stakeholders (eg, pharmacy, infectious diseases etc.) to make decisions for each hospital laboratory
  – The WG discussed the intent of each group (A, B, and C)

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 (first-line choices for clinical use - drugs you'd want to test and report every time)	• 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 (those additional drugs for which you need to have the results available right away [on the same day as the Group A drug results] as necessary	• 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 (those additional drugs for which it would be rare that clinicians would need to have the result on the first day but that they might request secondarily on a subsequent day [phrased this as "typically by clinician request only"]	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 (ie, 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 (ie, ceftazidime for *A. baumannii* vs cefotaxime/ceftriaxone)

  - Smaller groups will be working on individual assignments.

- Division of the Enterobacterales was discussed.
  - It was suggested to separate Enterobacterales into two groups.
    - New category for *Salmonella* and *Shigella*
    - All other Enterobacterales
  - Suggested revisions were presented for discussion (changes in yellow; votes/comments in pink)
  - The goal is to encourage cascade reporting (moves combo agents to C).

- Enterobacterales

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.		
	Enterobacterales (Changes)* Add footnote about IR and refer to Appendix B	*Salmonella/Shigella* (new category)
Ampicillin[c]		Ampicillin
Cefazolin[d]		Ciprofloxacin Levofloxacin
Gentamicin		Trimethoprim-sulfamethoxazole
Cefotaxime[c,d] or ceftriaxone[c,d]	Move to A; Vote: 8-0	
Piperacillin-tazobactam	Move to A; Vote: 6-2	
Gentamicin[c] ~~Tobramycin[c]~~	Move tobramycin to B; No official vote recorded	

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.		
Amikacin[c]		Azithromycin
Tobramycin	Moved from A to B. No official vote recorded.	Ceftriaxone
Amoxicillin-clavulanate Ampicillin-sulbactam		
~~Ceftazidime-avibactam~~	Move to C; Vote:6-0-1	
~~Ceftolozane-tazobactam~~	Move to C; Vote:6-0-1	
~~Meropenem-vaborbactam~~	Move to C; Vote:6-0-1	
~~Piperacillin-tazobactam~~	Move to A; Vote: 6-2	
Cefuroxime		
Cefepime	There was a vote to move cefepime to A but it did not pass: 5-3	
Cefotetan Cefoxitin		
~~Cefotaxime[c,d] or ceftriaxone[c,d]~~	Move to A; Vote: 6-2	
Ciprofloxacin[c] Levofloxacin[c]		
~~Doripenem~~ Ertapenem, Imipenem Meropenem	Remove doripenem.	
Tetracycline, minocycline, doxycycline*	Moved tetracycline from C to B and added mino/doxy. No official vote recorded.	
Trimethoprim-sulfamethoxazole[c]		

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 prevention as an epidemiological aid.		
	Enterobacterales	*Salmonella*/*Shigella* (new category)
Aztreonam Ceftazidime		Chloramphenicol
Ceftaroline		
Ceftazidime-avibactam	Move to C from B; Vote:6-0-1	
Ceftolozane-tazobactam	Move to C from B; Vote:6-0-1	
Meropenem-vaborbactam	Move to C from B; Vote:6-0-1	
Cefiderocol	Voted to add since FDA breakpoints are now available.	
Chloramphenicol[b,c]		
Tetracycline[a]	Moved to B	
Group U: Includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating UTIs.		
Cefazolin (surrogate test for uncomplicated UTI)[‡]		
Fosfomycin[e]		
Nitrofurantoin		
Sulfisoxazole		
Trimethoprim		

- ***Pseudomonas aeruginosa***

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Ceftazidime	
Cefepime	Move from B to A; No official vote recorded.
Gentamicin Tobramycin	Voted to leave tobramycin in A: 5 to 2
Piperacillin-tazobactam	
Ciprofloxacin Levofloxacin	Moved from B to A: 5 to 2

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.	
Amikacin	
Aztreonam	
~~Cefepime~~	Moved to A
~~Ceftazidime-avibactam~~	Moved to C
~~Ceftolozane-tazobactam~~	Moved to C
~~Ciprofloxacin, Levofloxacin~~	Moved to A
~~Doripenem~~ Imipenem	Remove doripenem completely

Meropenem	

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 prevention as an epidemiological aid.	
Ceftazidime-avibactam	Move to C from B; Vote:6-0-1
Ceftolozane-tazobactam	Move to C from B; Vote:6-0-1
Cefiderocol	Voted to add since FDA breakpoints are now available.

- ***Staphylococcus* spp.**

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Azithromycin[b] or clarithromycin[b] or erythromycin[b]	A and C: Should these be 'B'? I could see why you would retain erythro for MLSb concerns, but with regards to clinical outcomes for the use of macrolides, that's somewhat limited for staph. Decided to leave in A but no vote.
Clindamycin[b]	Add footnote about D-test.
Oxacillin[i,k,*,†,§] **Cefoxitin[i,k,†] (surrogate test for oxacillin)**	
~~**Penicillin[i]**~~	Move to C. Unanimously (6,0,0) voted to move penicillin into Group C for *Staphylococcus* spp at June meeting.
Doxycycline **Minocycline[b]** **Tetracycline[a]**	Moved from B to A. Voted 4 to 2.
Trimethoprim-sulfamethoxazole	
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.	
Ceftaroline[h]	
Daptomycin[j,*]	
Linezolid **Tedizolid[h]**	
~~**Doxycycline**~~ ~~**Minocycline[b]**~~ ~~**Tetracycline[a]**~~	Tetracycline: Could this be 'A'? it meets the proven clinical efficacy/expert opinion criteria, it's in the IDSA skin/soft tissue guidelines as a recommended option, similar to TMP/SMZ which is 'A'
Vancomycin[*]	Question about possible Group A placement as often used as empiric therapy. Voted to leave in B: 5 to 2.
Rifampin[g]	

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 prevention as an epidemiological aid.	
Penicillin	Moved from A to C. Make sure Group C criteria cover the penicillin scenario.
Chloramphenicol[b]	
Ciprofloxacin or levofloxacin	
Moxifloxacin	
Gentamicin[l]	
Dalbavancin[h,*]	
Oritavancin[h,*]	
Telavancin[h,*]	
Group U: Includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating UTIs.	
Nitrofurantoin	
Sulfisoxazole	
Trimethoprim	

- ***Enterococcus*** spp.

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Ampicillin[n] **Penicillin[o]**	
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 A.	
Daptomycin[j,*]	
Linezolid **Tedizolid[p]**	
Vancomycin	Discussions about moving to A but voted to stay in B. Vote: 2-5
Gentamicin (high-level resistance testing only)	Moved from C to B. No official vote recorded.
Streptomycin (high-level resistance testing only)	Moved from C to B. No official vote recorded.

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 prevention as an epidemiological aid.	
~~Gentamicin (high-level resistance testing only)~~	Moved to B. No official vote recorded. Discussion around Amp and CTX.
~~Streptomycin (high-level resistance testing only)~~	Moved to B. No official vote recorded. Discussion around Amp and CTX

Dalbavancin[r,*]	
Oritavancin[r,*]	
Telavancin[r,*]	
~~Quinupristin-dalfopristin~~	O agent now. FDA VRE indication revoked.
Group U: Includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating UTIs.	
Ciprofloxacin Levofloxacin	
Fosfomycin[q]	
Nitrofurantoin	
Tetracycline[a]	This might warrant another footnote, tetracycline is fine for UTIs, but doxy and mino don't go through the kidneys and their experience in treating UTIs is minimal, this footnote would suggest that the surrogate susceptibilities may serve as therapeutic alternatives.

- ***Acinetobacter* spp.**

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Ampicillin-sulbactam	
Ceftazidime	
Cefepime	Moved from B to A.
Ciprofloxacin Levofloxacin	
Doripenem Imipenem Meropenem	
Gentamicin Tobramycin	Amikacin looks like the recommended AMG. If gent/tobra R, report amikacin.
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.	
Amikacin	
Piperacillin-tazobactam	
~~Cefepime~~	Move to A.
~~Cefotaxime~~ ~~Ceftriaxone~~	Move to C.
~~Doxycycline~~	Move to C.
Minocycline	Leave in B
Trimethoprim-sulfamethoxazole	
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 prevention as an epidemiological aid.	
Cefotaxime Ceftriaxone	Move to C based on *A. baumannii* data. Discussions that A. non-baumannii species have higher S%. Most non-baumannii species are also S to ceftazidime. Look at surveillance data.

Colistin **Polymycin B**	Added as part of treatment guidelines for MDR *A. baumannii*.
Doxycycline	Moved to C from B.
Group U: Includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating UTIs.	
Tetracycline[a]	

- ***Burkholderia cepacia* complex**

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Levofloxacin[*]	No mention of levo in treatment guidelines?
Meropenem	
Ceftazidime	Move to A but follow up with BCC WG. Vote: 5 to 1.
Minocycline	Move to A but follow up with BCC WG. Vote: 5 to 1.
Trimethoprim-sulfamethoxazole	
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.	
~~Ceftazidime~~	Move to A but follow up with BCC WG.
~~Minocycline~~	Move to A but follow up with BCC WG.
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 prevention as an epidemiological aid.	
Chloramphenicol[b,*]	

- ***Stenotrophomonas maltophilia* (The *Stenotrophomonas* WG reviewed this and voted in June 2019.**

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Levofloxacin **Minocycline** **Trimethoprim-sulfamethoxazole**	
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.	
Ceftazidime[*]	
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 prevention as an epidemiological aid.	
Chloramphenicol[b,*]	
Group U: Includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating UTIs.	

- **Other Non-Enterobacterales**: The WG questioned if this can be divided further.

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Ceftazidime	

Gentamicin **Tobramycin**	Intrinsically high MICs among *Achromobacter*
Piperacillin-tazobactam	Move from B to A. Vote: 8-0.
Trimethoprim-sulfamethoxazole	Intrinsically high MICs among non-*aeruginosa Pseudomonas*. Vote: 8-0.
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.	
Amikacin	
Aztreonam	
Cefepime	
Ciprofloxacin **Levofloxacin**	
Imipenem **Meropenem**	
~~**Piperacillin-tazobactam**~~	
~~**Trimethoprim-sulfamethoxazole**~~	
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 prevention as an epidemiological aid.	
Cefotaxime **Ceftriaxone**	
Chloramphenicol[b]	
Group U: Includes certain antimicrobial agents (eg, nitrofurantoin and certain quinolones) that are used only or primarily for treating UTIs.	
Sulfisoxazole	
Tetracycline[a]	

- ***Haemophilus influenzae*** and ***parainfluenzae***

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Ampicillin[d,f]	
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.	
Ampicillin-sulbactam	
Cefotaxime[d] **or** **ceftazidime**[d] **or** **ceftriaxone**[d]	
Ciprofloxacin or **levofloxacin or** **moxifloxacin**	
Meropenem[d]	
Trimethoprim-sulfamethoxazole	Moved from C to B.

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 prevention as an epidemiological aid.	
Azithromycin[e] **Clarithromycin[e]**	
Aztreonam	
Amoxicillin-clavulanate[e]	
Cefaclor[e] **Cefprozil[e]**	
Cefdinir[e] or **cefixime[e] or** **cefpodoxime[e]**	
Ceftaroline[g]	
Cefuroxime[e]	
Chloramphenicol[c]	
Ertapenem or **imipenem**	
Rifampin[h]	
Tetracycline[b]	
~~Trimethoprim-sulfamethoxazole~~	**Moved from C to B.**

- ***Neisseria gonorrhoeae***: No suggested changes.

- ***Streptococcus pneumoniae:*** No changes to Group C

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Erythromycin[a,c]	
Penicillin[k] **(oxacillin disk)**	Remove oxacillin parenthetical comment in the spirit of consistency
Trimethoprim- **sulfamethoxazole**	
Cefotaxime[k,*] **Ceftriaxone[k,*]**	Moved from B to A. Vote: 6-0.
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.	
Cefepime[*] **~~Cefotaxime[k,*]~~** **~~Ceftriaxone[k,*]~~**	Keep cefepime in B. O agent for meningitis vs B for non-meningitis.
Clindamycin[c]	
Tetracycline[b] **Doxycycline**	Added Tetracycline and doxycycline in the same box.

Levofloxacin[j] Moxifloxacin[j]	
Meropenem[k,*]	
~~Tetracycline~~[b]	Move in same box with Doxycycline
Vancomycin[k]	

- ***Streptococcus* spp. ß-Hemolytic Group:** No changes suggested

- ***Streptococcus* spp. Viridans Group**

Group A: Antimicrobial agents considered to be appropriate for inclusion in a routine, primary testing panel, as well as for routine reporting of results for the specific organism group.	
Ampicillin[m,*] Penicillin[m,*]	
Cefotaxime Ceftriaxone	Move from B to A. Vote 8-0.
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.	
Cefepime ~~Cefotaxime~~ ~~Ceftriaxone~~	Move Cefotaxime and ceftriaxone to A. Vote: 8-0.
Vancomycin	

- **Anaerobes:** No changes suggested

- SC Discussion
  - Dr. Moeck: He congratulated the WG on their good work. He suggested, that for group C agents, there should be wording regarding resistance to primary drugs (Group A or Group A and B). The term primary drug needs to be defined. He also suggested that delaying testing with novel combination agents for 24 hrs. will likely lead to poor patient outcomes. For drugs in Group C, the WG may be overlooking the clinical data regarding time to result.
  - There was discussion regarding *in vitro* activity of oritavancin for *E. faecium* and vancomycin-resistant *E. faecalis*; however, no vote was taken. Dr. Moeck pointed to this differentiation vs other agents in this Group C.
  - Dr. Simner: The definition of primary drugs can be clarified. We are still trying to determine the best use of combination agents.
  - Mr. Esparza: South America has seen a significant number of *Salmonella* spp. that produce ESBLs. He suggested that ceftriaxone should be tested and reported early. He will provide data to review in June.
  - Dr. Simner: Some agents were excluded because the Table's title refers to US laboratories and that non-US laboratories may have to select drugs differently. She commented that the WG may need to consider re-evaluating the definition to include laboratories outside of the US.
  - Dr. Weinstein: The title has been retained from the days when CLSI was more US-centric.
  - Mr. Lee: Those in laboratories should know their own hospital's microbial ecology and they can adjust their testing rules as needed. He suggested that Group C drugs will be ignored by smaller laboratories as too expensive and where users may not understand their use or even have them available. Improved education and examples for hospitals is needed for laboratories to understand that they need to consider group C drugs.

	– Dr. Simner: Intense education is needed so that laboratories really understand the purpose of Tables 1. – Dr. Schuetz: She supported expanding the definition of the tables beyond FDA indications. The Subcommittee needs to understand the impact on susceptibility testing device manufacturers. She questioned why some drugs are listed in Table 2 but not in Table 1 and believes this is confusing for laboratories. She also commented that the term "primary drug" is confusing and a new term might be needed. – Dr. Galas: Table 1 is helpful for educating laboratories on cascade testing. Tetracycline is a good drug for *Salmonella* and *Shigella* and proposed it be placed in Group A for both. – Dr. Alby: This is a best practice document in terms of placement. Education on new agents and how to use them in community hospitals is needed. This seems to force laboratories to use expanded panels and report all new drugs. – Dr. Palavecino: CLSI might consider consulting with public health laboratories on what the problems are being seen in hospitals and get suggestions for where to place certain drugs. – Ms. Cullen: A table for laboratories outside the US might be needed but might require significant work. She suggested that examples could be provided for other countries. She noted that from a device perspective, these suggestions are helpful and should help laboratories with inspections. – Ms. Hindler: M100 definitions (eg, selectively, etc.) need to be consistent with M39. She stated that it needs to be demonstrated in M100 that the new drugs are available for problem organisms and laboratories need to be able to test them. – Dr. Limbago: Another issue for laboratories outside the US are discontinued drugs that are not available in US. Institutions need to involve stakeholders in making testing decisions before determining what to test. This point needs to be emphasized and guidance should be placed closer to Table 1 rather than in the Instructions for use. Perhaps a tool for determining what to test could be developed. – Dr. Bush: She expressed concern about the ß-lactam combination agents because some of the most effective drugs would be moved Group C and their use would probably be discouraged. – Dr. Simner: She suggested that the definition for Group C may need to be clarified. – Dr. Tamma: She emphasized that hospitals need to have a stewardship program. Smaller hospitals need to be encouraged to form a stewardship team to work with laboratories. Education is really important for laboratories to understand how to use the tables. – Dr. Shawar: It may not be necessary to have the newer drugs on the panel. Some could be tested using disk diffusion. – Dr. Wikler: He agreed that results for all drugs are needed as soon as possible. The drugs can be tested but reported selectively (have the result ready but don't report unless needed). – Dr. Zimmer: Encouraged the SC to consider including a global view on testing. • Additional feedback on drug placement should be forwarded to Dr. Simner before the June meeting.
16.	**M39 WG Report: Dr. Simner (Folder 12)** **WG Roster:** Janet Hindler, Trish Simner (Co-Chairholders); April Abbott (Secretary); Faiza Benahmed, Tanaya Bhowmick, Sanchita Das, Sharon Erdman, Andrea Ferrell, Kristie Johnson, Brian Lubbers, Ron Master, Jimish Mehta, Ian Morrissey, Melinda Neuhauser, Mark Redell, Helio Sader, Dawn Sievert, Paul Snippes-Vagnone, John Stelling (Members) **Dr. Simner provided and update on the status of the M39 revision.** • The WG has been split into three teams working on specific chapters in the document – Review current M39 and expand specific ways to use local antibiogram for antimicrobial stewardship programs (ASP) and include guidance for long-term care facilities (LTCF). – Antimicrobial resistance surveillance program design and multi-facility antibiogram and publication – Information technology: Data extraction and presentation

- New content has been added to the document and now has eight parts separated into chapters.
  - Part 1: Introductory Information
    - Chapter 1: Introduction – Lots of new terminology
    - Chapter 2: Information System Design – Many changes (AST instrument, LIS, EHR)
  - Part 2: Routine Cumulative Antibiogram
    - Chapter 3: Data Analysis for Construction of the Antibiogram– Validation of the antibiogram/ result suppression and selective and cascade reporting
    - Chapter 4: Data Presentation – Final checks of the antibiogram
    - Chapter 5: "Unique Considerations for Data Analysis and Presentation" NEW
  - Part 3: Other Types of Antibiograms
    - Chapter 6: The Enhanced Antibiogram - Combining AMR with the antibiogram
    - Chapter 7: The Long Term Care Facility (LTCF) Antibiogram - NEW
    - Chapter 8: The Veterinary Antibiogram – NEW
  - Part 4: Using the Routine Antibiogram – NEW content added
    - Chapter 9: Intended Use of the Antibiogram Report – Added %S Threshold
    - Chapter 10: Distribution and Communication – Web-based, smart phone apps, etc.
    - Chapter 11: Antimicrobial Stewardship Programs and Use of the Cumulative Antibiogram – NEW
  - Part 5: Multi-Facility Antibiograms (NEW) – Will cover aggregating cumulative AST data outside of a single institution.
  - Part 6: Use of Statistics with Cumulative AST Data (NEW content added) – percentiles, interquartile range, MIC_{50}/MIC_{90}
  - Part 7: Considerations for Publishing Cumulative AST Data (NEW) - Publication of cumulative AST data reports in peer-reviewed literature.
  - Part 8: Conclusions & Supplemental Information (NEW)
    - Examples of Gram-positive, yeast, combined Gram-positive & Gram-negative & multi-facility antibiograms
    - Step-wise instructions to prepare a multi-facility combined antibiogram
    - Review of antibiogram content prior to release of the report
    - FAQ section
- The revised guideline will include considerations of all isolates to detect emerging resistance including:
  - Capturing rarely encountered resistance on the routine antibiogram
  - Identifying emerging resistance
  - Analyzing susceptibility profiles of select organisms
  - Presenting percent susceptible data graphically to illustrate emerging resistance trends
  - Basic M39 recommendations will include the first isolate per patient during analysis period. The purpose of the report is to guide empiric therapy of initial infections.
- It was questioned as to what %S is considered acceptable for choosing empiric therapy: SC Discussion
  - Dr. Tamma and Dr. Galas both questioned 80-90% cutoff. It was noted that this is addressed in stewardship subchapter.
  - Dr. Mathers stated that 80% is common for drafting institutional guidelines regarding empiric therapy and agreed with 80%. She noted that there is much literature on the subject.
  - Ms. Hindler noted that the document cites literature that provides 80% significance cutoff acceptable for empiric therapy.
  - Dr. Galas commented that sometimes ECVs are the only method to evaluate.

	• Next steps – Clean up the draft (eg, review references, appendixes, tables, graphs, formatting etc.) – WG members will critically review the draft and provide feedback. – It is planned to submit the entire M39 document in the materials for the June meeting. – A 2021 publication is expected.
17.	**M23 WG Report: Dr. Wikler (Folder 11)** **WG Roster:** Avery Goodwin, Matthew Wikler (Co-Chairholders); Romney Humphries (Recording secretary); Timothy Bensman, Mariana Castanhiera, Patricia Conville, Sharon Cullen, Linda Miller, Stephanie Mitchell, Greg Moeck, Margaret Ordoñez Smith de Danies, Michael Satlin, Simone Shurland, Zhixia (Grace) Yan (Members) Dr. Wikler provided an update on the revision of M23. • The timeline for the project was reviewed. The original timeline has been modified – February 2020-May 2020: Additional teleconferences with various subchapter groups to deal with remaining Issues – May 2020: Submit near final document to agenda book – June 2020: WG meeting, and finalization of work from other WGs required for M23 document – July 2020-October 2020: Final revisions to M23 – October 2020-November 2020: Dr. Humphries and Dr. Mitchell review and revise the draft to assure clarity and consistency – December 2020: Submit proposed draft to the agenda book for the January 2021 AST meeting – January 2021: Present the final proposed draft for vote by AST SC for approval – Standard CLSI review and comment periods, leading up to publication o Formal editing for proposed draft review and vote o 60-day formal proposed draft review and voting period (AST SC, M23 WG, Microbiology Expert Panel, CLSI member delegates, public review) o Comment resolution o Editing for final draft vote (Consensus council) o Editing for publication o Publication expected late 2021 • Dr. Wikler presented a question for SC discussion: Subchapter 4.4 – Periodic Breakpoint Reviews – Subchapter 4.4 includes language regarding periodic breakpoint reviews. He believed that no reviews have been done since the language was added to the document. He suggested that the language be deleted or that a process for performing a review be developed. – Dr. Weinstein: The SC has been performing reviews to some extent (eg, aminopenicillins etc.). Because PK/PD is lacking for older drugs, it is difficult to do some reviews. – Dr. Shawar: A more formalized schedule for review be developed. – Dr. Humphries: Old BPs should be reviewed to determine if they are still relevant. – Dr. Kuti: An AHWG under BPWG pull together a list to review and commit to the task of reviewing the and bringing it to the full WG for consideration. – Dr. Wikler: BPs could be reaffirmed if no new information was available. – Dr. Romney: The review is part of the rationale document development process.

	– Ms. Cullen: The process is like a QC Tier 3 review and requires significant work. The process is to look for signals that there is a change and if there is none, no change is needed. The review could be done by drug class. An assessment would be done to determine if there is a big problem and look at more closely if there is a signal. – Dr. Humphries: If a signal is found, a call for "evidence" on a particular drug class or drug could be made. – Dr. Mathers: Put a schedule together but keep the dates flexible. The schedule could be kept in M23. – Dr. Edelstein: A systematic approach to evaluate BPs is needed. Create a list of criteria to review (eg, PKPD, reports of clinical failure, etc). – Robert Bowden: don't do it as a table-based review; signals for common and not for uncommon • It was decided to keep the language in the document and have the BPWG work on a procedure.
18.	**Adjournment** The meeting was adjourned at 5:50 PM.

SUMMARY MINUTES	
Item #	**Description**
Tuesday, 28 January 2020	
1.	Dr. Weinstein opened the meeting at 7:30 AM Eastern (US) time.
2.	**Cefiderocol Update: Dr. Lewis** Dr. Lewis provided an update on the approved BPs for cefiderocol. • The FDA-approved BPs are lower than the investigational CLSI BPs for Enterobacterales and P. aeruginosa and no BPs for *Stenotrophomonas* or *Acinetobacter*. – The FDA expressed concerns with mortality signal in CREDIBLE-CR. – The number of *P. aeruginosa* isolates tested were limited except for urine isolates. – The AST leadership is having ongoing discussions with FDA and the sponsor. The FDA is waiting for submission of the nosocomial pneumonia study. – Awaiting the nosocomial pneumonia study • It is expected that a presentation on clinical data will be submitted for the June meeting. • It was questioned if the BP differences should be communicated to clinical laboratories. • SC Discussion – Dr. Kuti: This is not first time there has been a discrepancy with FDA. The CLSI BP is based only on PK/PD so we probably should look at the clinical data. – Dr. Humphries: Test that are available are disks and laboratories generally use M100 and not the FDA website so they will likely interpret using CLSI BPs. – Dr. Mathers: A plan for education is needed. We need to do everything we can to review the BPs for June. The clinical data need to be reviewed and perhaps change the BPs to align with the FDA. – It was suggested that for disk diffusion, users should be directed to the package insert. – Dr. Weinstein: Do we need to do something now before June (eg, memo)? Do we need to address this in M100, 31st ed. – Dr. Giske: EUCAST expects to have a preliminary BP proposal from EUCAST in the near future. – Dr. Lewis: Agreed that something needs to be done to communicate the differences to the laboratories.
3.	**Breakpoint (BP) WG Report: Dr. Lewis/Dr. Satlin (Folder 5)** **WG Roster**: George Eliopoulos, James Lewis, Michael Satlin (Co-Chairholders); Karen Bush (Recording Secretary); Marcelo Galas, Romney Humphries, Amy Mathers, Navaneeth Narayanan, Robin Patel, Simone Shurland, Lauri Thrupp, Barbara Zimmer (Members); Matthew Wikler (Advisor) **Imipenem-relebactam Breakpoints (Folder 5, 09A-09B)** • Dr. Katherine Young, Dr. Munjal Patel, and Dr. Amanda Paschke presented microbiological, PK/PD, and clinical trial data, respectively, to the BPWG for imipenem-relebactam (Imi-Rel). – The FDA has already approved the requested BPs. – Unless otherwise noted, key Enterobacterales include *C. freundii*, *E. cloacae*, *E. coli*, *K. aerogenes*, *K. oxytoca* and *K. pneumoniae*. – The BPs are not applicable to the *Morganellaceae* as nonsusceptibility to imipenem in *Morganellaceae* is due to differences in target penicillin-binding proteins (PBPs), not to ß-lactamases. – The sponsor requested validation of the FDA BPs with publication in M100 and placed in Table 1A, Group B. • Background – Imipenem: Broad-spectrum (gram-negative, gram-positive, anaerobes), bacteriocidal, and active against ESBLs

Item #	Description

- Relebactam: ß-lactamase inhibitor with no intrinsic antibacterial activity that enhances imipenem activity against aerobes and retains activity against anaerobes but doesn't increase susceptibility.

- The data from studies were reviewed.
  - ECV analysis
    - ECVs determined using ECOFFinder_XL_2010_v2.0 are less than or equal to the proposed susceptibility BPs.
    - ECVs by visual inspection are equal to (Enterobacterales, anaerobes) or greater than (*P. aeruginosa*) the proposed susceptibility BPs.
  - Disk correlate studies: Zones reproducibility data met CLSI criteria.
  - PKPD analyses
    - Using the hollow fiber infection model, the PK/PD index correlated with efficacy.
    - In the murine thigh infection model, the log-kill target values were consistent and target attainment performed well.
  - Clinical studies
    - In Phase 2 studies, both trials met primary endpoint for non-inferiority.
    - In Phase 3 studies, Imi/Rel was effective in the treatment of Imi-nonsusceptible infections.
  - Outcomes by MIC for USPI-indicated pathogens showed:
    - Favorable clinical response and microbiological response rates in participants who received Imi/Rel (250 mg) were generally high across the different baseline Imi/Rel MICs.
    - No trend in microbiological or clinical response by imipenem/REL MIC by indication or across all indications combined was observed.
- Summary: Proposed clinically relevant BMD BPs for Imi/Rel (500 mg/250 mg every 6 hours via IV infusion) by different BP methods

	Pathogen	Breakpoints by Different Methods (µg/mL)			
		ECV[a]	Non-Clinical PK/PD Cutoff	CER Cutoff[b]	Clinical Cutoff[c]
Proposed Clinically Relevant Breakpoints[d]	Enterobacterales	< 0.25/1	≤ 2	NA	NA
	P. aeruginosa	< 1/8	≤ 2	NA	NA
	Anaerobes	< 2/4	NA	NA	NA

NA=Not Available
[a] Based on ECOFF 95% /Visual Inspection
[b] Based on exploratory exposure-response analysis, there was no trend observed between exposures and efficacy (Refer to Section 5.6)
[c] Clinical outcomes data did not show a correlation between outcomes and MIC and therefore did not provide meaningful evidence to either support or reject the nonclinical PKPD and CER cutoffs (Refer to Section 8.4)
[d] Relebactam included at fixed 4 µg/mL

- Breakpoint request with placement in Table 1A, Group B.

	MIC (µg/mL)			Disk Diffusion (zone diameter in mm)		
Pathogen	**S**	**I**	**R**	**S**	**I**	**R**
Enterobacterales[a]	≤1/4	2/4	≥4/4	≥25	21-24	≤20
P. aeruginosa	≤2/4	4/4	≥8/4	≥23	20-22	≤19
Anaerobes[b,c]	≤4/4	8/4	≥16/4	NA	NA	NA

Item #	Description

S = Susceptible; I = Intermediate; R = Resistant
For disk diffusion, use paper disks impregnated with imipenem/relebactam at a concentration of 10/25 µg/mL.
[a] Clinical efficacy was shown for *Klebsiella aerogenes*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii*, *Klebsiella oxytoca*.
[b] Clinical efficacy was shown for *Bacteroides caccae*, *Bacteroides fragilis*, *Bacteroides ovatus*, *Bacteroides stercoris*, *Bacteroides thetaiotaomicron*, *Fusobacterium nucleatum*, *Parabacteroides distasonis*.
[c] Agar dilution method.

Dosage regimen: 500 mg/250 mg every 6 hours via IV infusion
Disk concentration: 10/25 µg/mL

- BPWG Discussion
  - AHWG issues noted:
    - There were slight differences with EUCAST BPs (1 dilution for Enterobacterales).
    - There was a trend toward higher MICs at lower pH (IMI instability?).
    - The PK/PD suggested using higher doses for higher MICs.
    - There was an occurrence of colonies within zones of inhibition.
    - All questions were addressed by the sponsor in a revised presentation
    - The AHWG voted to approve the request (6-0).
  - The BPWG questioned if a laboratory can infer susceptibility to Imi-Rel from Imi susceptibility BP and suggested that a comment might be included. The sponsor provided references and additional data were provided in the agenda material.
    - Because the same IMI dose is being used as for IMI alone, the BPWG thought that it makes sense to have the same BPs as for IMI.
    - It was noted that the BPs were proposed to cover the worst-case scenario (for *P. aeruginosa*.)
    - It was noted that IMI-REL provides increased coverage of *S. marcescens* compared to IMI. The sponsor agreed to consider current surveillance data.
  - BPWG vote: Accept the FDA BPs 9-0 with 2 abstentions with the same table placement as similar compounds.
- SC Discussion
  - Dr. Humphries: Cutting through the MIC distribution may cause testing problems.
  - Dr. Kuti: Questioned if there was PK/PD data for KPCs? The sponsor noted that little REL is needed to restore Imi susceptibility for KPCs as shown in a small resistance trial.
  - Dr. Moeck: The BP bisects population of *Pseudomonas* and variability of PD targets has a large range of PD effect. The sponsor noted that prolonged infusion doesn't have impact. In a trial with 5 KPCs, 4 of 5 had a positive clinical impact.

A motion to accept the proposed (FDA-approved) breakpoints for DD and BMD for Enterobacterales and *P. aeruginosa* with a comment that the BPs don't apply to the *Proteaceae*, and a comment that if an isolate is S to IMI, it does not need to be tested for IMI-REL was made and seconded. VOTE:12 for; 0 against (Pass).

A motion to accept the proposed (FDA-approved) breakpoints for anaerobes with a comment to be drafted that states if isolate is S to Imi, it does not need to be tested for Imi-Rel. VOTE: 12-0; Pass

A motion was made to address *Proteaceae*, *Providencia*, *Morganella*, and *Serratia* at the June meeting to improve comment etc. was made and seconded. VOTE: 11 for; 0 against; 1 abstention

- Table 1 placement was deferred to the June meeting as Tables 1 revision is in progress.

Ceftolozane-tazobactam *H. influenzae* BPs (Folder 5, 08A-08B)

- The sponsor made a request for ceftolozane-tazobactam (TOL-TAZ) BPs vs *H. influenzae* for pneumonia (hospital-acquired [HABP] and ventilator-acquired [VABP] pneumonia).
  - These are the same as the current FDA-MIC BPs and would be ratified and added to M100, 31st ed.
  - CLSI currently has BPs for TOL-TAZ for complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI) 1.5 g (1g/0.5g) administered every 8 hrs.
- The current FDA BPs are at S = ≤ 0.5/4 µg/mL based on a dose of 1.5g every 8 hrs. EUCAST has BPs similar to FDA
- Data review
  - The MIC frequency distributions of clinical trial isolates were similar to large scale surveillance isolates.
  - The PK/PD data support the FDA and EUCAST BPs. Probable target attainment was at >90% at the proposed BP.
  - There was appropriate correlation of efficacy outcomes to MIC values and high rates of clinical and microbiological responses.
- Sponsor Proposal: S = ≤ 0.5/4 ug/mL

Ceftolozane/Tazobactam
Proposal to CLSI for *H. influenzae* Breakpoints

- The totality of the data that have been presented support the approved FDA *H. influenzae* breakpoints for HABP/VABP, based on the dose of 3 g q8h by IV infusion over 1 hour
- Merck requests CLSI to ratify the FDA *H. influenzae* breakpoint for ceftolozane/tazobactam, and propose to include it in Table 2E of the M100

	Minimum Inhibitory Concentration (mcg/mL)		
Pathogen	S	I	R
Haemophilus influenzae	≤0.5/4	-	-
S = Susceptible; I = Intermediate; R = Resistant			

- For *H. influenzae*, we propose that ceftolozane/tazobactam is placed in Group C in Table 1B of the M100

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- WG Discussion
  - There was no data that showed the TAZ added to the efficacy of the combined drug.
  - It was questioned if the drug is needed for *H. influenzae* but agreed that it is useful for mixed infections.
  - It was noted that there are possible resistance mechanisms (eg, PBP3 mutations in *H. influenzae*).
  - A WG motion to ratify the FDA BPs and to place the drug in Table 1B, Group C was made and seconded: VOTE: 8-0; 1 abstention (due to an FDA conflict).

Item #	Description

- SC Discussion
  - Dr. Kuti: The data showed an extrapolated (from *P. aeruginosa*) PD threshold. Although he was not comfortable with extrapolating from other organisms, it doesn't appear to be a problem based on other data.
  - Dr. Thrupp: Questioned if the infections treated were monomicrobic (yes).
  - Dr. Kahlmeter: TAZ doesn't seem to add much to the efficacy. There are PBP mutations in some strains, but it is not obvious that they are significant in the clinical outcomes and don't seem to affect the BP.
  - Dr. Schuetz: The FDA has a S-only breakpoint while EUCAST has both S and R BPs. She questioned if CLSI could consider setting BPs for both S and R. She questioned if there are any additional data that could be reviewed.
  - Dr. Kahlmeter: There are no clinical data for a R BP but it could be added as data comes forward.
  - Dr. Motyl (sponsor): Agreed that an R BP could be set.

A motion to accept the proposal for susceptible-only BP of ≤ 0.5/4 µg/mL for *H. influenzae* was made and seconded. VOTE: 12 for; 0 against (PASS)

  - It was decided to discuss Table 1 placement until the tables are revised.

Coagulase-negative Staphylococcus WG Report (Folder 5, 05A-05B)

WG Roster: Jennifer Dien Bard and Lars Westblade (Co-chairholders); Carey-Ann Burnham, Shelley Campeau, Tanis Dingle, Paul Edelstein, Romney Humphries (Members)

- Oxacillin breakpoints and disk diffusion testing for coagulase-negative *Staphylococcus* spp.
  - Background
    - The group agreed that testing for the presence of *mecA* is the gold-standard method for determining if a coagulase-negative *Staphylococcus* spp. is methicillin (oxacillin) resistant.
    - It suggested that it be determined which of the following methods is best and if Table 2C can be simplified.
  - The design for studies performed were reviewed.
    - BMD and DD for oxacillin and cefoxitin tests were performed
    - PBP2a (RUO for non-*S. aureus*) and *mecA* and *mecC* PCR were performed.
    - Three different *S. aureus* QC strains were used.
  - MICs for the following species were presented.
    - *S. capitis*
    - *S. haemolyticus*
    - *S. warneri*
    - *S. hominis*
  - The PBP2a results were as expected.
  - Aggregate Results (including *S. epidermidis*)

	S. capitis		*S. haemolyticus*		*S. hominis*		*S. warneri*		*S. epidermidis*	
Test/Breakpoint	VME	ME	VME	ME	VME	ME	VME	ME	VME	ME
OX MIC / CoNS	0%	0%	3.8%	1.4%	0%	6.7%	0%	19.0%	0%	2%

Item #	Description

OX MIC / SAU	0%	0%	18.2%	0%	0%	0%	0%	0%	17%	2%
OX disk / CoNS	0%	0%	4.6%	0%	5.3%	0%	0%	79.8%	0%	0%
FX MIC / SAU	0%	0%	7.7%	0%	8.0%	6.7%	3.4%	0%	3.6%	3.9%
FX disk / CoNS	0%	0%	3.8%	0%	0%	12%	0%	0%	0%	0%
FX disk / SAU	0%	0%	5.1%	0%	4%	0%	1.7%	0%	4.9%	0%

- The oxacillin and cefoxitin MIC and DD test performance (with and without *S. epidermidis*) were reviewed.
- Based on the data, the following proposals were made.

Staphylococcus spp., Oxacillin Testing		**Disk breakpoint (mm)**		**MIC breakpoint (µg/mL)**	
	Disk content	S	R	S	R
S. aureus and *S. lugdunensis* (Oxacillin)	-	Do not test		≤2	≥4
S. aureus and *S. lugdunensis* (Cefoxitin, surrogate agent for oxacillin)	Cefoxitin 30 ug	≥22	≤21	≤4	≥8
Staphylococcus other than *S. aureus*, *S. lugdunensis*, *S. pseudintermedius* and *S. schleiferi* (Oxacillin)	-	Do not test		**≤0.5**	**≥1**
Staphylococcus other than *S. aureus*, *S. lugdunensis*, *S. pseudintermedius* and *S. schleiferi* (Cefoxitin, surrogate agent for oxacillin)	Cefoxitin 30 ug	≥25	≤24	Do not test	
S. pseudintermedius and *S. schleiferi*	Oxacillin 1 ug	≥18	≤17	**≤0.5**	**≥1**
S. pseudintermedius and *S. schleiferi*	Cefoxitin	Do not test		Do not test	

  - Increase oxacillin susceptible breakpoint from ≤0.25 µg/mL to ≤0.5 µg/mL for all staphylococci except *S. aureus* and *S. lugdunensis*.
  - Remove oxacillin disk breakpoint for *S. epidermidis* (to simplify Table 2C).
  - Potentially revise the current comment (For Staphylococcus spp. other than S. aureus, S. lugdunensis, S. epidermidis, S. pseudintermedius, and S. schleiferi, oxacillin MIC breakpoints may overall resistance. Isolates for which the oxacillin MICs are 0.5-2 µg/mL have been shown to be mecA positive and mecA negative. Isolates from serious infections with MICs in this range may be tested for mecA or PBP2a.)

- BPWG Discussion
  - It was questioned if the comment about possible *mecA* or PBP2a should be retained if the oxacillin MIC BP is revised.
  - There was concern about removing the oxacillin disk BP for *S. epidermidis*.
  - There was discussion on whether this proposal is simpler and what the impact on manufacturers would be.
  - BPWG Votes
    - Increase S BP for all staphylococci other than *S. aureus* and *S. lugdunensis* from S: ≤0.25 µg/mL to S: ≤0.5 µg/mL and keep a revised comment about considering PBP2a/*mecA* test for organisms with MICs of 0.5-2 µg/mL. Vote: Yes (8), No (2), Abstain (1)(Pass). The negative voters believed that the comment makes it difficult to know what to do with PBP2a and *mecA* tests.
    - Remove oxacillin disk BP for S. epidermidis. Vote: Yes (9), No (1), Abstain (1) (Pass). The negative voter believed that the test is good and shouldn't be removed.

Item #	Description

- **SC Discussion**
  - **Proposal 1**: Increase S BP from ≤0.25 to ≤0.5; R from ≥0.5 to ≥1 and keep the comment with revisions.

	Susceptible (µg/mL)	Resistant (µg/mL)
Proposed Breakpoints	≤0.5	>1

    - It was noted that the comment in M100, 30th edition is not same as what displayed.
    - Dr. Humphries: We need to differentiate reference methods from commercial methods.
    - Dr. Zimmer: This will make a big impact on commercial manufacturers, so we need to ensure that the change is worth it.
    - Dr. Mathers: PBP2a testing is better than the surrogates and believed the tables can be used in current form.
    - Dr. Kirn: Appendix H discussed PBP2a testing.
    - Dr. Humphries: Old data were reviewed and error rates high. The old BPs were based on inadequate data.

A motion to revise the oxacillin BPs as shown for *Staphylococcus* spp. other than *S. aureus* and *S. lugdunensis* was made and seconded. VOTE:12 for; 0 against (PASS).

A motion to include a comment saying *mecA* and PBP2a are the most definitive tests for methicillin(oxacillin) resistance for the whole group was made and seconded. VOTE: 12 for; 0 against (Pass).

- Ms. Cullen: The BP changes need to be communicated quickly to assist laboratories with the transition. An explanation for changes should be included and so laboratories can develop an interim plan.
- Dr. Palavecino: There are currently no FDA approved PBP2a tests available for Coagulase-negative *Staphylococcus* spp.
- Dr. Mathers: It needs to be emphasized that PBP2a is the best test.
- Dr. Eliopoulos: The proposal makes it more difficult to determine susceptibility. The comment should read any BP ≥0.25 needs to be tested.
- Dr. Shawar: From a stewardship perspective, the PBP2a test and rapid and more accurate.

- **Proposal 2: Remove the oxacillin disk diffusion BPs for *S. epidermidis* and include it with other *Staphylococcus* spp. (**simplify the table)
  - The oxacillin disk only works for *S. epidermidis*.
  - Dr. Limbago: Suggested keeping the BP and add a comment for laboratories that don't speciate coagulase-negative *Staphylococcus* spp.
  - Dr. Simner: Disliked removing something from the document just for simplification.
  - M. Hindler: Suggested it would be better to use the smaller table at the beginning of 2C (comment [5]).

A motion was made to remove oxacillin DD for S. epidermidis was made and seconded. VOTE: 7 for; 5 against (FAIL).

- Those opposed believed that something that is not wrong should not be remove.

A motion to retain the table as is and note that if the isolate isn't speciated, testing with the cefoxitin disk is preferred to oxacillin disk. VOTE: 12 for; 0 against (Pass).

Item #	Description

Determining the Susceptible BP Equivalence for Azithromycin Disk Diffusion in *N. gonorrhoeae* (GC) (Dr. Cau Pham)(Folder 5, 07)

- Background
  - Azithromycin has been FDA-approved since 1980s for gonococcal urethritis. The current treatment recommendation is ceftriaxone plus azithromycin.
  - An azithromycin/GC ECV was established in 2016. The agar dilution susceptible BP for azithromycin was approved by CLSI and published in M100; however, most laboratories can't do agar dilution. Therefore, a disk diffusion test is needed.
  - The CDC conducted a study to establish disk correlates to the agar dilution MICs.
- The DD/azithromycin study protocol and results were reviewed.
  - 112 GC isolates were tested using 1 disk and 1 media lot using CLSI disk diffusion and BMD methods. *N. gonorrheoae* ATCC 49226 was used for QC.
  - The optimal BPs were S at ≥ 30 m with VME at 1% and ME at 2%. This showed good correlation with DD.
  - Proposal:

	Disk Diffusion		MIC	
	S	R	S	R
Current Breakpoints	-	-	≤1	-
Proposed Breakpoints	≥30 mm	-	≤1	-

    - **Current comment:** These breakpoints presume that azithromycin (1 g single dose) is used in an approved regimen that includes an additional antimicrobial agent (ie, ceftriaxone 250 mg IM single dose).

- BPWG Discussion: Voted to approve
  - There were challenges in reading zone of inhibition sizes.
  - There were concerns about how the disk test would perform in laboratories that are not as experienced as at CDC.
  - Dr. Jones commented that similar findings were seen 25-30 years ago (wild-type population with MICs ≤1 µg/mL and disk zones of ≥30 mm).
  - The BPWG voted to approve the proposal (9-0; 1 abstention – Pass)

- SC Discussion
  - It was questioned how to communicate to laboratories if the CDC changes its recommendations.
  - Since most cases are treated empirically, testing would only occur in suspected treatment failures.
  - Dr. Palavecino: Resistance to azithromycin needs to be monitored and testing is the only way to monitor for resistance.
  - Dr. Galas: Agree with the S BP but questioned if a R BP can be established. Dr. Bush concurred.

A motion to accept a S-only DD BP and keep the current comment as proposed was made and seconded. VOTE: 11 for; 0 against; 1 abstention (PASS).

- Dr. Schuetz abstained due to a potential conflict of interest.
- Dr. Shawar: Suggested including a footnote regarding contacting the public health department as GC is reportable.
- Dr. Turnidge: The data were consistent with M23 guidance.

Item #	Description

Azithromycin/*Shigella* Breakpoints (information only)(Folder 5, 04A-04B)

- Azithromycin is one of the most commonly used treatments for *Shigella* infection, particularly with rising fluroquinolone resistance.
- ECVs have been set but BP could not be set due to lack of clinical and PK/PD data.
- Results of a prospective study of isolates from Bangladesh was reviewed. Clinical outcomes data showed the following:

Clinical Outcomes

	Susceptible	Non-wild-type*	P value
Diarrhea persistent at day 5	10 (12%)	20 (31%)	0.004
Diarrhea resolved at day 5	75 (88%)	44 (69%)	
Shigella culture positive at day 5 or 6	4 (5%)	16 (35%)	0.0005
Shigella culture negative at day 5 or 6	77 (95%)	46 (65%)	
Hospitalization required	33 (39%)	37 (58%)	0.03
Not required	52 (61%)	27 (42%)	
Duration at ICDDRB** hospital (hours)	17.7 +/- 15.3 (n=84)	22.7 +/- 29.5 (n=63)	0.17
IV fluids provided	6 (7%)	3 (5%)	NS
Days until resolution of diarrhea	3.6 +/- 1.8 (n=85)	4.6 +/- 2.3 (n=64)	0.002
Days until resolution of bloody diarrhea	2.2 +/- 1.0 (n=59)	3.4 +/- 2.2 (n=38)	0.0006
Days until resolution of fever	1.6 +/- 0.8 (n=36)	1.9 +/- 0.9 (n=24)	0.2

*Non-wild-type defined as MIC above ECV ≤ 8 µg/ml (*S. flexneri*) or ≤ 16 µg/ml (*S. sonnei*, others)
** International Centre for Diarrhoeal Disease Research in Dhaka, Bangladesh

- Clinical data from an outbreak in the US were also shown.
  - 24 patients with culture-confirmed infections with all having the same resistance profile with azithromycin (MICs >32 µg/mL) and all isolates having the *mphA* and *ermB* genes.
  - 4 patients were treated with azithromycin for 3-5 days. All continued to have diarrhea despite treatment and 2 of the 4 2/4 had subsequent positive cultures
- BPWG Discussion
  - The clinical data should assist in setting a BP (potential for June meeting)
  - The BPWG will discuss whether there should be separate breakpoints (currently separate ECVs) or a unified breakpoint.
  - Additional data were requested.
    - Breakdown of outcomes by MIC instead of just wild-type or non-wild-type
    - DD to BMD comparison by species
- The SC had no additional suggestions.

Ampicillin/Aminopenicillin (A4) WG Report: Dr. Edelstein (Folder 5, 01A-01ZO)

- The A4 WG reported that there is discordance between CLSI and EUCAST BPs.
- There is no PK/PD support for the current CLSI BPs. There are clinical data for the drugs that may work effectively for at least some infections.
- In review of previous CLSI meeting minutes, there is no rationale for ampicillin BPs except for *N. meningitidis*.

Item #	Description

- There is significant work to review the aminopenicillin BPs and there will be more to come in June.

Aminoglycoside Issues: Dr. Castanheira (Folder 5; 02A-02B)

	Susceptibility Breakpoint (mg/mL)	
	CLSI	EUCAST
Amikacin	≤16	≤8
Gentamicin	≤4	≤2
Tobramycin	≤4	≤2

- It was reported that USCAST BPs which are the lowest of all (not shown above) are based on a stasis endpoint, not a 1 log kill.
  - These drugs are used most commonly in combination and rarely used as monotherapy.
  - It was reported that the BPs were originally assigned for *Enterobacteriaceae*. It was questioned how CLSI will address the nomenclature change to Enterobacterales.
  - Clinical data suggest that some infections may not respond well and there are safety issues.
  - It was proposed that the BPs need to be re-evaluated.
- It is expected that plazomicin will be discussed in June. This should lead to a review of the aminoglycosides with possible revision.

Anaerobe WG Report: Dr. Carpenter (Folder 5, 03A-03F)

- Metronidazole BPs for Anaerobes
  - The WG proposed that the metronidazole BPs be revised to be consistent with EUCAST (S/≤4 µg/mL; I/ 8 µg/mL; R/≥16 µg/mL).
  - BPWG Discussion
    - The BPWG agreed that there has been no clinical signal for a change in BPs.
    - There have been a few reports of metronidazole-resistant *B. fragilis* isolates.
    - Overall, the consensus was that the current CLSI BPs are adequate.
    - An update on the possibility of moving the anaerobes to M45 will be provided in June.
    - A motion was made and seconded that the current BPs be retained for metronidazole. Vote: 9-1; 1 abstention
  - SC Discussion
    - Dr. Weinstein: There is a lack of the appropriate data.
    - Dr. Schuetz: Historically, the required data for the BP have not been available. She suggested that the anaerobes could be moved to M45.
    - Dr. Giske: Agreed with collaboration with EUCAST on anaerobes. There is emerging resistance in some parts of the world with *B. fragilis*.

- Piperacillin for Anaerobes
  - It was proposed that piperacillin be removed from M100 for anaerobes. It is no longer available in the US (as a single agent) and is usually used in combination with tazobactam.
  - The BPWG voted to remove piperacillin (single agent) from Table 2J (Anaerobes) in M100.

A motion to remove piperacillin (single agent) from Table 2J (Anaerobes) in M100 was made and seconded. VOTE: 11 for; 0 against; 1 absent (Pass).

SUMMARY MINUTES	
Item #	**Description**
	• **<u>Merino Trial – Meropenem: Dr. Mathers (Folder 5, 6A-6F)</u>** – Testing piperacillin/tazobactam is a major problem with false-susceptible results being common. A better test needs to be designed. – A motion to form an AHWG to study piperacillin-tazobactam efficacy in therapeutic studies and its variability in AST was made and seconded by the BPWG. Vote: 11-0 (BPWG approved)
4.	**<u>Joint CLSI/EUCAST WG Report</u>: Ms. Hindler (Folder 14)** **WG Roster:** Janet Hindler (CLSI), Erika Matuschek (EUCAST) (Co-Chairholders); Mandy Wootton (EUCAST) (Recording secretary); Members: Mariana Castanhiera, Sharon Cullen, Laura Koeth, Maria Traczewski (CLSI); Christian Giske, Gunnar Kahlmeter, John Turnidge (EUCAST). • The goal of the WG was to harmonize disk content (potency) criteria for DD testing and develop and harmonize QC recommendations. • The WG has been developing a technical standard operating procedure (SOP) with step-by-step instructions for determining optimal disk content. – The WG is working on process for approving disk content in real time in between meetings. – The current plan is to add the SOP to the revised CLSI document M23. – EUCAST will harmonize it with their SOP 9.1. • The WG has been working with stakeholders to comply with the recommended SOP. – Comments from a stakeholder review were evaluated and addressed. – The SOP has already been established by EUCAST. – For CLSI to implement: o The stakeholder will present data to Joint Disk Content WG for approval o The Joint WG will send their recommendations to CLSI AST SC for final approval using a mechanism similar to that used by the QCWG. o The plan is for disk contents to be approved in real time by electronic communication and vote and not wait for publication in M100. o Currently, there is no requirement for pharmaceutical manufacturers that have disks in development to use any part of this SOP. Once finalized, it will only apply to new disks. o Goal is to enable selection of an optimal disk content for both US and EUCAST quickly and to avoid delays that will negatively impact timelines established by pharmaceutical manufacturers. • Selection criteria for disks with single antimicrobial agent include: – Reproducible inhibition zone diameters – A single disk content (potency) that can be used for all relevant species (target organisms) – A general discriminatory power of 2-3 mm increase in zone diameters with each $\log_2$ decrease in MIC for non-wild type isolates – Inhibition zone diameters between 15 and 35 mm for wild-type isolates of relevant species (target organisms) – Optimal separation between wild-type and non-wild type isolates – Optimal separation between non-wild type isolates with different MICs • A test study using the SOP was performed for ceftibuten/VNRX-5236 (Micromyx) – Based on Tier I testing, VNRX-5236 disk contents of 2.5 and 5 µg are appropriate. – In testing with 2 disk lots and 2 media lots, there was no apparent lot-to-lot variation for the ceftibuten and ceftibuten/VNRX-5236 disks regardless of disk content. – Based on Tier IIA, it appeared that for ceftibuten alone a disk content of 5 µg was more appropriate than the 10 and 30 µg disks. This ceftibuten disk content also appeared to be the most appropriate when testing in combination with VNRX-5236.

SUMMARY MINUTES	
Item #	**Description**
	– Additional testing in Tier IIB with the ceftibuten 5 µg disk alone and in combination with VNRX-5236 at 2.5 and 5 µg showed that both ceftibuten/VNRX-5236 5/5 µg and 5/2.5 µg disks appear suitable for development. – Dr. Pillar noted that following the SOP required a little more work than previously done but came to the same conclusions. • Plan forward – Finalize the SOP and obtain approval from EUCAST and CLSI AST SC. – Obtain approval from the CLSI AST SC for review process. – Insert into CLSI M23 when the draft is ready for publication. – Post the final version of the SOP on EUCAST website. – Begin working on QC harmonization. • SC Discussion – Dr. Miller: The SOP doesn't seem to need a lot of additional work. She was concerned with a possible delay in getting approval and who the final approval comes from. – Ms. Hindler: Completed Tier 1 data would be shared with the disk WG. – Dr. Matuschek: Proposed to have a CLSI and EUCAST member review the submitted data and determine if it looks acceptable or needs to be passed on to additional reviewers. – Dr. Lewis: There is no historical precedent for approving disk content (potency). A defined approval process can be developed to be able to approve the disk contents (potency) quickly. – Dr. Moeck: A decision could be made by the Joint WG data are acceptable/unacceptable as reviewed and approved/disapproved. • Next steps – Finalize the procedure and distribute to the SC for approval. – Determine how to get it posted on the Web site until M23 is published.
5.	**<u>Text and Tables WG</u>: Dr. Bobenchik (Folder 10)** **WG Roster:** April Bobenchik, Shelley Campeau (Co-Chairholders); Carey-Ann Burnham (Secretary); Victoria Anikst, Suki Chandrasekaran, Mary Jane Ferraro, Andrea Ferrell, Janet Hindler, Melissa Jones, Jean Patel, Barth Reller, Felicia Rice, Flavia Rossi, Dale Schwab, Maria Traczewski, Nancy Watz (Members); Darcie Carpenter, Sandra Richter Barbara Zimmer (Advisors/WG Liaisons) • M100 review process – The WG is continuing with section review assignments. – A draft checklist to guide TTWG review was reviewed. – The WG discussed the possibility of using individual checklists for specific WG changes. • Volunteers are needed to perform a review on M02 and M07 – Volunteers will perform a preliminary (high-level) review and identify the scope of revisions needed. – Potential chairholder/co-chairholders will be identified. – A project proposal will be drafted, submitted to the Microbiology expert panel for review and endorsement, and subsequently to the Consensus Council for approval. – Additional pictures/images of DD and BMD are needed to be incorporated into the reading guide.

SUMMARY MINUTES	
Item #	**Description**

- The M100, 30th ed., comments that were deferred to the 31st edition were reviewed, and actions taken.

Location	Item	Proposed Change	Action
Intro sections	Breakpoints Additions/Revisions Table	• Complete table so each addition/revision has a comment and that they are consistent	Informational only Received volunteers
Reporting Results	Additional clarification around lowest MICs not always representing clinical efficacy	• Add mention of lowest MIC ≠ clinical efficacy. • Based on additional discussion, also incorporate mention that interpretation with most updated breakpoints should be used	Informational only Discussed: mock-up and present to our group in June
Tables 2A, 2B-1, and 2B-2	Move all colistin/polymyxin B references to separate table	• TTWG voted **(10-0-0)** to leave in Tables 2 (as was voted on by SC) but possibly ok to move some of the side comments into the comments under the lipopeptide header	Informational only Discussed: mock-up and present to our group and SC in June
Table 2C	Table 2C: Specifying strain-specific indications, inconsistent	• TTWG discussed moving the comment to column but could not agree **(6-4-0)**	**Vote/ input requested**
Staph	Refer to *S. pseudintermedius* as *S. intermedius* Group (*S. intermedius, S. pseudintermedius,* and *S. delphinii)*	• TTWG decided to leave as "*S. pseudintermedius*" only	Informational only Request for CoNS WG to consider *S. intermedius* and *S. delphinii* (testing and/or terminology)
Table 3F	Complicated and confusing, not user-friendly	• TTWG voted (**11-0-0)** to split into 2 tables (3F-1, 3F-2) for *S. aureus*/*S. lugdunensis* and Other *Staphylococcus;* will mock up for June • Hold off on other major changes/modifications until all CoNS work is completed	Informational only, unless SC disagrees
Appendix A	Reorder organisms to match ordering in Tables 2	• TTWG decided to reorder	Informational only

- Table 2C: Calling out MRSA in a number of places (eg, *S. aureus* including MRSA)
  - The TTWG questioned why MRSA is called out and are they in the right locations in the table.
  - Table 2C is the only table including species indications. It was suggested that the indication be moved to the far right comment column.
  - The TTWG requested input from the SC for where to locate the comment. Options included:
    - Keep all indications comments in the indications column
    - Move all indications comments MRSA to the comments column
    - Keep the current format
  - The SC agreed to keep the comments in the indications column. The other tables will be reviewed to determine if this can be done throughout the document.

- Table 3F. Test for Detecting Methicillin (Oxacillin) Resistance in *Staphylococcus* spp.
  - Due the large amount of information, the table is difficult to follow.
  - The TTWG suggested that the table be revised and separated out by species (eg, *S. aureus*, *S. lugdunensis*, and other *Staphylococcus* spp.)
  - Revised tables will be mocked-up and presented at the June meeting.

Item #	Description

- Table 2D and Warning Box Discussion items.

Location	Item	TTWG Decision	Action
Table 2D	Remove quinupristin-dalfopristin as the only indication was for enterococci was removed by FDA and manufacturer in 2010	• TTWG agreed to remove from Table 2D but want to run by SC	**Vote requested** **NOTE: The SC decided that more information was needed and to discuss the issue again in June. It was believed that the drug doesn't work and should be moved to the archive table. The drug may need to be retained for use outside the US. BPWG will investigate for the June meeting.**
Table 2D Comment 7	"Since combination therapy for *E. faecalis* endocarditis is now often treated with dual ß-lactam therapy, and since some use dual ß-lactam therapy for *E. faecium* endocarditis, it is reasonable to mention the use of dual ß-lactam therapy as well. The 2015 AHA guidelines for enterococcal endocarditis include this as a reasonable option instead of a ß-lactam plus aminoglycoside regimen." Proposed language to add (In red)	• TTWG voted against the addition (**11-0-0**) – Nothing in the document about validated susceptibility testing methods that could guide such use – Request of additional information regarding amp-R *E. faecalis* **Suggested Edits: Rx:** Combination therapy with ampicillin, penicillin or vancomycin (for susceptible strains only), plus an aminoglycoside, is usually indicated for serious enterococcal infections, such as endocarditis, unless high level resistance to both gentamicin and streptomycin is documented; such combinations are predicted to result in synergistic killing of enterococci. Ampicillin plus ceftriaxone therapy is an alternative option for ampicillin-susceptible isolates, and for ampicillin-resistant *E. faecalis*. For strains with low-level penicillin or ampicillin resistance when combination therapy with a ß-lactam is being considered, also see additional testing and reporting information in Table 3J."	Requested that Aminopenicillin WG discuss this topic and bring approved comment to TTWG.
Table 2D	• Clarify what is meant by "low-level" resistance • Edit 1st sentence to say "…synergistic killing of **enterococci**" from "…synergistic killing of the *Enterococcus.*"	• Low-level resistance is defined in Table 3J, which is referenced in the comment and TTWG felt it didn't need additional clarification here but defer back to Aminopenicillin WG • TTWG agreed to edit sentence	Informational only Red revised text will be added.
Warning box	Consideration for adding ertapenem, minocycline, and also amoxicillin-clavulanate to the "Warning" box	• Add additional reference to intro text to refer to Glossary for drugs within the classes listed below since minocycline is covered under "Tetracyclines" • Add reference to carbapenems but specify not meropenem • Request that Aminopenicillin WG evaluate addition of amoxicillin-clavulanate IV to Warning box	Request for Aminopenicillin WG to discuss addition of amoxicillin-clavulanate IV addition

SUMMARY MINUTES	
Item #	**Description**
	– Proposed changes to the Warning Box **"Warning": The following antimicrobial agents that are included in this document should not be routinely reported for bacteria isolated from CSF (refer to Glossary I for individual agents within the drug classes listed below). These antimicrobial agents are not the drugs of choice and may not be effective for treating CSF infections caused by these organisms (ie, the bacteria included in Tables 2A through 2J):** • Agents administered by oral route only • 1st- and 2nd-generation cephalosporins and cephamycins • Carbapenems (doripenem, ertapenem, and imipenem only) • Clindamycin • Macrolides • Tetracyclines • Fluoroquinolones
6.	**Other Business** **There was no other business to discuss.**
7.	**Adjournment** Dr. Weinstein thanked the participants for their time, hard work, and attention. The meeting was adjourned at 11:30 AM.

Upcoming Meetings of the Subcommittee on Antimicrobial Susceptibility Testing:

14 – 16 June 2020: Hyatt Regency Baltimore Inner Harbor, Baltimore, MD, USA (Agenda material submission due date – **8 May 2020**)
24 – 26 January 2021: Live! by Loews, Arlington, TX, USA (Agenda material submission due date – **9 December 2020**)
27 – 29 June 2021: Westin, San Diego, CA, USA (Agenda material submission due date – **19 May 2021**)

	ACTION ITEMS	Responsible
1.	For Table 2B-5: • Look for supporting data for molecular mechanisms for intrinsic resistance. • Mock up drafts of separate tables (eg, *Pseudomonas* spp., *Achromobacter* spp. etc, where clinical data are lacking). • Develop a timeline for moving the group to M45.	Non-fermentative GNB WG
2.	Submit gradient diffusion data for the Anaerobe antibiogram.	Darcie Carpenter
3.	Investigate whether or not quinupristin-dalfopristin should be removed from Table 2D.	BPWG
4.	Provide an approved, revised comment for Table 2D, Comment 7.	Aminopenicillin WG
5.	Discuss addition of amoxicillin-clavulanate IV addition to the Warning Box regarding drugs to report for bacteria isolated from CSF.	Aminopenicillin WG
6.	Review QC recommendations for ß-lactam combinations for fastidious organisms on Tables 2E, 2G, 2H-2, 4 and 5 (Ms. Traczewski and Dr. Palavecino)	Maria Traczewski Elizabeth Palavecino
7.	Propose clarifications for guidance on reading meropenem DD zones for the DD troubleshooting guide for presentation at the June 2020 meeting.	Janet Hindler Patti Conville

<table>
<tr><th colspan="4">Summary of Passing Votes</th></tr>
<tr><th>#</th><th>Motion Made and Seconded</th><th>Results*</th><th>Page(s)</th></tr>
<tr><td>1.</td><td>To accept the agenda and June 2019 meeting summary minutes.</td><td>12-0-0-0</td><td>8</td></tr>
<tr><td>2.</td><td>To adopt the suggested language in Appendix H, Table H3 without the phrase about molecular accuracy.
(If the discrepancy is not resolved, repeat AST should be performed using a reference method and the conflicting genotypic and phenotypic testing results should both be reported along with a comment advising caution; current clinical and laboratory evidence is insufficient to conclude whether cephalosporin therapy of carbapenemase-carrying strains with an MIC in the S/SDD range will be effective.)</td><td>11-1-0-0</td><td>10-11</td></tr>
<tr><td>3.</td><td>To add a footnote to Appendix H, Table H3 about situations that could cause discrepancies (see vote #4).</td><td>11-1-0-0</td><td>10-11</td></tr>
<tr><td>4.</td><td>To accept the revisions to Footnote 1 in Appendix H, Table H3.
(Multiple ß-lactamases may be carried by individual bacterial isolates. Most carbapenemase-producing bacteria are resistant to 3rd- and 4th- generation cephalosporins, although bacteria producing some certain carbapenemase enzymes (eg, OXA-48 and SME), may not be unless they co-produce an ESBL or AmpC enzyme.)</td><td>11-1-0-0</td><td>10-11</td></tr>
<tr><td>5.</td><td>To accept the recommendations to report S. argenteus as S. aureus complex (when not identified by MALDI-TOF MS or sequencing) or S. aureus complex (S. argenteus) (when identified MALDI-TOF MS or sequencing). If identified as such, report using S. aureus BPs and interpretive categories.</td><td>11-0-1-0</td><td>19</td></tr>
<tr><td>6.</td><td>To accept the revised QC range of 17-24 mm for eravacycline with E. coli ATCC® 25922.</td><td>11-0-1-0</td><td>27</td></tr>
<tr><td>7.</td><td>To accept the proposed (FDA-approved) breakpoints for DD and BMD for Enterobacterales and Ps. aeruginosa with a comment that the BPs don't apply to the Proteaceae, and a comment that if an isolate is S to IMI, it does not need to be tested for IMI-REL.
<table>
<tr><th></th><th colspan="3">MIC
(µg/mL)</th><th colspan="3">DD
(zone diameter in mm)</th></tr>
<tr><th>Pathogen</th><th>S</th><th>I</th><th>R</th><th>S</th><th>I</th><th>R</th></tr>
<tr><td>Enterobacterales[a]</td><td>≤1/4</td><td>2/4</td><td>≥4/4</td><td>≥25</td><td>21-24</td><td>≤20</td></tr>
<tr><td>P. aeruginosa</td><td>≤2/4</td><td>4/4</td><td>≥8/4</td><td>≥23</td><td>20-22</td><td>≤19</td></tr>
</table></td><td>12-0-0-0</td><td>47-48</td></tr>
<tr><td>8.</td><td>To accept the proposed (FDA-approved) breakpoints for anaerobes with a comment to be drafted that states if isolate is S to Imi, it does not need to be tested for Imi-Rel.
<table>
<tr><th></th><th colspan="3">MIC
(µg/mL)</th><th colspan="3">DD
(zone diameter in mm)</th></tr>
<tr><th>Pathogen</th><th>S</th><th>I</th><th>R</th><th>S</th><th>I</th><th>R</th></tr>
<tr><td>Anaerobes[b,c]</td><td>≤4/4</td><td>8/4</td><td>≥16/4</td><td>NA</td><td>NA</td><td>NA</td></tr>
</table></td><td>12-0-0-0</td><td>47-48</td></tr>
<tr><td>9.</td><td>To address Proteaceae, Providencia, Morganella, and Serratia at the June meeting to improve comment etc..</td><td>11-0-1-0</td><td>47-48</td></tr>
<tr><td>10.</td><td>To accept the proposal for susceptible-only BP for ceftazidime-tazobactam of ≤ 0.5/4 µg/mL for H. influenzae.</td><td>12-0-0-0</td><td>49</td></tr>
<tr><td>11.</td><td>To revise the BPs as shown for Staphylococcus spp. other than S. aureus and S. lugdunensis.
<table>
<tr><th></th><th>Susceptible (µg/mL)</th><th>Resistant (µg/mL)</th></tr>
<tr><td>Proposed Breakpoints</td><td>≤0.5</td><td>>1</td></tr>
</table></td><td>12-0-0-0</td><td>51</td></tr>
<tr><td>12.</td><td>To include a comment stating that mecA and PBP2a are the most definitive tests for methicillin (oxacillin) resistance for the whole group.</td><td>12-0-0-0</td><td>51</td></tr>
<tr><td>13.</td><td>To retain Table 2C as is and note that if the isolate isn't speciated, testing with the cefoxitin disk is preferred to oxacillin disk.</td><td>12-0-0-0</td><td>52</td></tr>
</table>

<table>
<tr><th colspan="4">Summary of Passing Votes</th></tr>
<tr><th>#</th><th>Motion Made and Seconded</th><th>Results*</th><th>Page(s)</th></tr>
<tr><td>14.</td><td>To accept an azithromycin susceptible-only MIC BP for N. gonorrheoae and keep the current comment as proposed.
<table>
<tr><th></th><th colspan="2">Disk Diffusion</th><th colspan="2">MIC</th></tr>
<tr><td></td><td>S</td><td>R</td><td>S</td><td>R</td></tr>
<tr><td>Proposed Breakpoints</td><td>≥30 mm</td><td>≤29 mm</td><td>≤1</td><td>-</td></tr>
</table>
Current comment: These breakpoints presume that azithromycin (1 g single dose) is used in an approved regimen that includes an additional antimicrobial agent (ie, ceftriaxone 250 mg IM single dose).</td><td>11-0-1-0</td><td>53</td></tr>
<tr><td>15.</td><td>To remove piperacillin (single agent) from Table 2J (Anaerobes) in M100.</td><td>11-0-0-1</td><td>54</td></tr>
</table>

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

Respectfully submitted,

Marcy L. Hackenbrack, MCM, M(ASCP)
CLSI