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Meeting Title:	**Subcommittee on Antimicrobial Susceptibility Testing (AST)**	**Contact:**	mhackenbrack@clsi.org
Meeting Date:	Sunday – Tuesday, 27 – 29 January 2019		
Start Time:	27 January – 7:30 AM 28 January – 7:30 AM 29 January – 7:30 AM	**End Time:**	5:00 PM 5:00 PM 11:00 AM
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 (30th). 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, D(ABMM)	Mayo Clinic
Patricia J. Simner, PhD, D(ABMM)	Johns Hopkins Hospital - Pathology
Pranita D. Tamma, MD, MHS	Johns Hopkins University School of Medicine
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
Sheila Farnham, MT(ASCP)	bioMérieux, Inc.
Christian G. Giske, MD, PhD	Karolinska University Hospital, Solna
Vanessa G. Allen Gray, MD	Public Health Ontario
Janet A. Hindler, MCLS, MT(ASCP)	Los Angeles County Department of Health
Stephen G. Jenkins, PhD, D(ABMM), F(AAM)	Weill Cornell Medicine
Maria Karlsson, PhD	Centers for Disease Control and Prevention
Linda A. Miller, PhD	CMID Pharma Consulting
Greg Moeck, PhD	VenatoRx Pharmaceuticals
Kiyofumi Ohkusu, PhD	Tokyo Medical University
Virginia M. Pierce, MD	Massachusetts General Hospital
Sandra S. Richter, MD, D(ABMM), FCAP, FIDSA	Cleveland Clinic
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	Deaconess Hospital Laboratory
Jane E. Ambler, PhD	Wockhardt, Morton Grove Pharmaceuticals
Stella Antonara, PhD, D(ABMM)	OhioHealth
Adam Belley, PhD	Allecra Therapeutics SAS
Patricia Bradford, PhD	Antimicrobial Development Specialists, LLC
William B. Brasso, BS	BD Diagnostic Systems
Kendall Bryant, PhD, D(ABMM)	Kaiser Permanente
Karen Bush, PhD	Indiana University
Susan Butler-Wu, PhD, D(ABMM), SM(ASCP)	LACUSC Medical Center
Shelley Campeau, PhD, D(ABMM)	Accelerate Diagnostics, Inc.
Rafael Canton	Hospital Universitario Ramon Y Cajal
Darcie E. Carpenter, PhD	IHMA
Ian A. Critchley, PhD	Spero Therapeutics
Sanchita Das, MD	NorthShore University HealthSystem
Jennifer Dien Bard, PhD, D(ABMM), F(CCM)	Children's Hospital Los Angeles; University of Southern California
Tanis Dingle, PhD, D(ABMM), FCCM	Provincial Laboratory for Public Health
Michael J. Dowzicky	Pfizer, Inc.
Dana C. Dressel, MT(ASCP)	International Health Management Associates, Inc.
Paul Edelstein, MD	Hospital of the University of Pennsylvania
German Esparza, BSc	Proasecal SAS Colombia
Mary Jane Ferraro, PhD, MPH	Massachusetts General Hospital and Harvard Medical School
Andrea L. Ferrell, MLS^{CM}(ASCP)	Becton Dickinson
Mark A. Fisher, PhD, D(ABMM)	University of Utah School of Medicine
Robert K. Flamm, PhD	JMI Laboratories
Graeme Forrest, MBBS	Oregon Health Sciences University
Lawrence V. Friedrich, PharmD	Cubist Pharmaceuticals, Inc.
Thomas R. Fritsche, PhD, FACP, FIDSA	Marshfield Clinic
Beth P. Goldstein, PhD	Beth Goldstein Consultant
Meredith Hackel, PhD	International Health Management Associates, Inc.
Dwight J. Hardy, PhD	University of Rochester Medical Center
Stephen Hawser, PhD	IHMA Europe Sàrl
Andre Hsiung, MS(ASCP)	Hardy Diagnostics
Michael D. Huband, BS	JMI Laboratories
Kristie Johnson, PhD, D(ABMM)	University of Maryland
Melissa Jones, MT(ASCP), CLS	UNC Healthcare
Ronald N. Jones, MD	JMI Laboratories
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.
Joseph Kuti, PharmD	Hartford Hospital
Sarah Blaine Leppanen, MT(ASCP)	Blaine Healthcare Associates, Inc.
Dyan Luper, BS, MT(ASCP)SM, MB	BD Diagnostics
Sandra McCurdy, MS	Melinta Therapeutics, Inc.
Stephanie L. Mitchell, PhD, D(ABMM)	University of Pittsburgh and Children's Hospital of Pittsburgh of UPMC
Ian Morrissey, PhD	IHMA Europe Sàrl

Margaret Ordonez Smith de Danies, PhD	Colegio de Bacteriologia for Microbiology Institue of Colombia
Susan O'Rourke, BS	BD Diagnostics
Elizabeth Palavecino, MD	Wake Forest Baptist Medical Center
David Paisey, Bsc	ThermoFisher Scientific
Jean B. Patel, PhD, D(ABMM)	Centers for Disease Control and Prevention
L. Barth Reller, MD	Duke University School of Medicine
Flavia Rossi, MD, PhD	University of Sao Paulo
Helio S. Sader, MD	JMI Laboratories
Nicole Scangarella-Oman, MS, BS	GlaxoSmithKline
Katherine Sei, BS	Beckman Coulter, Inc.
Susan Sharp, PhD, D(ABMM), F(AAM)	Copan Diagnostics, Inc.
Dee Shortridge, PhD	JMI Laboratories
Carole Shubert, MT	bioMérieux, Inc.
Dawn M. Sievert, PhD	Centers for Disease Control and Prevention
Paula M. Snippes Vagnone, MT(ASCP)	Minnesota Department of Health
Janine Spafford, MT(ASCP), MHA	BD Diagnostics
Susan Thomson	MAST Group
Lauri D. Thrupp, MD	University of California Irvine Medical Center
Maria M. Traczewski, BS, MT(ASCP)	The Clinical Microbiology Institute
Yun F. (Wayne) Wang, MD, PhD	Emory University Hospital/Emory University School of Medicine
Nancy E. Watz, MS, MT(ASCP), CLS	Stanford Health Care
Lars F. Westblade, PhD, D(ABMM)	New York Presbyterian Hospital – Weill Cornell Campus
Matthew A. Wikler, MD, FIDSA, MBA	IDTD Consulting
Katherine Young, AB	Merck & Company, Inc.
Guests (Non-SC-roster attendees)	
Jenny Åhman	EUCAST Development Laboratory
Kevin Alby, PhD, D(ABMM)	University of Pennsylvania
Diane Anastasiore	Paratek
Mari Ariyasu	Shionogi
Eliana Armstrong	Paratek
Amelia Bhathagar	Centers for Disease Control and Prevention
Fabio Brocco	Liofilchem
Ashanti Brown	BD
Alexandra Bryson	Virginia Commonwealth University
Davina Campbell	Centers for Disease Control and Prevention
Cecilia Carvalhaes	JMI Laboratories
Sukantha Chandrasekaran	UCLA
Marie Pierre Chateauninois	bioMerieux
Nicole Cotroneo	Spero Therapeutics, Inc.
Esther Deak	Avails Medical
Dmitri Debubov	Allergan
Boudewjn de Jonge	Pfizer
Federica Demetrio	Liofilchem
Jason Demuth	Tetraphase
Elaine Duncan	Beckman-Coulter
Hari Dwivedi	bioMerieux-
Roger Echols	Shionogi
David Fam	Shionogi
Kelly Flentie	Selny Diagnostics

Bill Folkerts	BD Diagnostics
Andrew Fuhrmeister	JMI Laboratories
Momoko Fujisaki	Eiken Chemical Co., LTD.
Corey Fyfe	Tetraphase
Dulini Gamage	Accerlate Diagnostics, Inc.
Barbara Gancarz	bioMerieux USA
Alice Gray	bioMerieux USA
Camille Hamula	Saskatchewan Health Authority/University of Saskatchewan
Rita Hoffard	Becton Dickenson
Catherine Hogan	Stanford
Nicole Holliday	ThermoFisher Scientific
Nicole Hunter	ThermoFisher Scientific
Holly Huse	Huntington Hospital
Brian Johnson	IHMA, Inc.
Mark Kadlec	bioMerieux USA
Jennifer Kalamatas	IHMA
Gunnar Kahlmeter	EUCAST/ESCMID
Anthony Knoll	Beckman-Coulter Diagnostics
Angharad Laetsch	Accerlate Diagnostics, Inc.
Jamie Lemon	Opgen, Inc.
Xian-Zhi Li	Health Canada
Rianna Malherbe	Hardy Diagnostics
Ron Master	Quest Diagnostics
Sarah McLeod	Entasis Therapeutics
Lisa Meyers	bioMerieux USA
Alita Miller	Entasis Therapeutics
Clifford Mintz	BioInsights, Inc.
Sarah Moore	bioMerieux
Samia Naccache	LabCorp, Seattle
Evelyn Nash	Centers for Disease Control and Prevention
Chie Ohno	Eiken Chemical Co., LTD.
Melanie Olesky	Tetraphase
John Otero	Shionogi
Pritty Patel	Covance Central Labs
Cau Pham	Centers for Disease Control and Prevention
Christopher R. Polage	Duke University
Stefano Pomponio	Liofilchem
Eric Ransom	Centers for Disease Control and Prevention
Zachary Ratzleff	Norman Regional Health System
Mark A. Redell	Melinta Therapeutics
Jean-Yves Ressot	bioMerieux
Felicia Rice	Mayo Clinic, Phoenix, Arizona
Amity Roberts	Labcorp – Southeast Division
Nilia M. Robles Hernandez	bioMerieux
Barbara Schenk	BD
Linda Schuermeyer	bioMerieux, Inc.
Alisa Serio	Paratek
Kimiyo Shono	Shionogi
Pragya Singh	Specific Diagnostics
Eric Stern	Selux Diagnostics
Greg Stone	Pfizer
Jolyn Tenllado	bioMerieux

Mark Thornton	Shionogi & Co., LTD.
Masakatsu Tsuji	Shionogi & Co., LTD.
Priyanka Uprehy	University of Pennsylvania
Michael Urban	Beckman-Coulter Diagnostics
Tam Van	Harbor-UCLA Medical Center
Mandy Wooton	BSAC/EUCAST
Lynn Yaolin	Allergan PLC.
Katsunori Yamagihara	Nagasaki University
Ilonka Zfolt	Ferrer Laboratories (Spain)
Staff:	
Glen Fine, MS, MBA, CAE	CLSI
Marcy L. Hackenbrack, MCM, M(ASCP)	CLSI
Lori T. Moon, MS, MT(ASCP)	CLSI

OPENING PLENARY AGENDA Monday, 28 January 2019 Augustine D Breakfast available: 7:00 – 8:00 AM (Legends 2)							
Item #	**Item Title**	**Start**	**End**	**Length (Min)**	**Category**	**Presenter**	**Page**
1.	Opening Remarks	11:00 am	11:10 am	10	N/A	Dr. Weinstein	8
2.	Agenda and June 2018 Meeting Summary Minutes	11:10 am	11:15 am	5	VOTE	Dr. Weinstein	8
3.	Updates to Disclosure of Interest Summary	11:15 am	11:20 am	5	Update	Dr. Weinstein	8
4.	CLSI Update	11:20 am	11:25 am	5	Update	Mr. Fine	8
5.	Method Development and Standardization WG	11:25 am	12:35 pm	60	Report	Dr. Hardy Dr. Zimmer	9
	Luncheon: 12:35 – 1:30 pm (Legends 2)						
6.	Breakpoint WG (Part 1)	1:30 pm	3:00 pm	90	Report/Votes	Dr. Lewis Dr. Eliopoulos Dr. Satlin	12
7.	Text and Tables WG	3:00 pm	3:30 pm	30	Report	Dr. Bobenchik Dr. Campeau	19
	Break: 3:30-3:45 pm (Foyer)						
8.	Breakpoint WG (Part 2)	3:45 pm	4:45 pm	60	Report/Votes	Dr. Lewis Dr. Eliopoulos Dr. Satlin	21
9.	GC WG	4:45 pm	5:15 am	30	Report	Dr. Ferraro Dr. Allen Gray	24
9.	VAST Update	5:15 pm	5:25 pm	10	Report	Dr. Fritsche	24
	Adjournment	5:25 pm				Dr. Weinstein	25

CLOSING PLENARY AGENDA Tuesday, 29 January 2019 Augustine D Breakfast available: 7:00 – 8:00 AM (Legends 2)							
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1.	Opening Remarks	7:30 am	7:35 am	5	Remarks	Dr. Weinstein	26
2.	EUCAST Update (added after agenda distributed)	7:35 am	7:45 am	10	Update	Dr. Giske	26
3.	Quality Control WG	7:45 am	8:45 am	60	Report/ Votes	Ms. Cullen Ms. Traczewski	26
4.	Methods Application and Interpretation	8:45 am	10:15 am	90	Report	Dr. Kirn Dr. Limbago	33
	Break (Foyer): 10:15 – 10:30 am						
5.	M39 WG	10:30 am	10:50 am	20	Report	Ms. Hindler Dr. Simner	37
6.	Joint CLSI-EUCAST WG	10:50 am	11:00 am	10	Report	Ms. Hindler Dr. Matuschek	39
7.	Outreach WG	11:00 am	11:15 am	15	Report	Ms. Hindler Dr. Schuetz	40
8.	Rationale Document Update	11:15 am	11:25 am	10	Update	Dr. Humphries	42
9.	M23 Update	11:25 am	11:45 am	20	Update	Dr. Wikler	42
	Adjournment	11:45 am				Dr. Weinstein	43

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SUMMARY MINUTES Monday, 28 January 2019	
Item #	**Description**
Monday, 28 January 2019 (NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2019 January AST Plenary Presentations)	
1.	**Opening Remarks** **Dr. Weinstein opened the meeting at 11:00 AM Eastern (US) time by thanking the participants for their attendance and continued work with the Subcommittee (SC) and its working groups. He provided an update on transitions on the SC roster and expressed his gratitude to those that have served and are rotating to a new position.** • Dr. Jim Lewis has been appointed as the new Vice-chairholder. • Dr. Jean Patel has rotated off as Vice-chairholder and will be participating on the SC as a reviewer and is also the Vice-chairholder of the Expert Panel on Microbiology and will continue to be active on the Subcommittee. • Dr. Trish Simner has been appointed as a new voting member to replace Dr. Lewis. • New appointed advisors include Dr. Carey-Ann Burnham, Dr. Maria Karlsson, Dr. Kiyofumi Ohkusu, and Dr. Sandy Richter. • Advisors completing their appointments and rotation to reviewer include Dr. Patricia Bradford, Dr. Graeme Forrest, Dr. Jean Patel, and Dr. Kazuhiro Tateda. • Dr. Weinstein thanked all the rotating participants for their past and future contributions.
2.	**June 2018 Meeting Summary Minutes Vote:** Previous Meeting Summary Minutes **A motion to accept the summary minutes from the June 2018 subcommittee meeting was made and seconded. VOTE: 12 for; 0 against (PASS).** The approved summary minutes have been posted on the CLSI website using the following link to the Year Month AST Meeting Files.
3.	**Updates to Disclosure of Interest Summary** • **Updates to the disclosure of interest summary included:** – Dr. Linda Miller: Consultant for F2G – Dr. Audrey Schuetz: Scientific advisory board for Klaris diagnostics – Dr. Tony Mazzulli: Consultant for Verative Pharmaceuticals – Dr. Mike Satlin: Consultant Shionogi
4.	**CLSI Update** • **Mr. Glen Fine provided a brief update from CLSI**

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	– Gratitude was expressed on behalf of the Board of Directors and the CLSI staff to the participants for their attendance and ongoing work. – The next meetings will be in Dallas, Texas in June 2019, – This is the 3rd year for free M100 portal. The number of unique users doubled every year. This past year showed 50, 000 unique users and just under a million page hits. • **Mr. Fine provided brief biographies for the award winners. The President of the CLSI Board of Directors, Mr. Carl Mottram, assisted him in presenting the awards.** – John Bergin Award: Dr. Tom Fritsche – Excellence in Consensus Management Award: Dr. George Eliopoulos – Excellence in Standards Development: Dr. Stephen Jenkins
5.	**Methods Development and Standardization (MDS) Working Group (WG) Report (Folder 7)** **WG Roster**: Barbara Zimmer, Dwight Hardy (Co-chairholders), Katherine Sei (Secretary), Bill Brasso, Susan Butler-Wu, Jennifer Dien Bard, Tanis Dingle, Romney Humphries, Laura Koeth, Ribhi Shawar (Members) **Dr. Zimmer presented five topics for discussion**. • The WG requested the formation of an Ad Hoc (AHWG) charged with updating M07, *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically* (Subchapter 3.7.1) and M100, *Performance Standards for Antimicrobial Susceptibility Testing* to: – This revision will be to accommodate newer dispensing systems and to clarify if serial 2-fold dilutions are required. o New options are available with newer systems. o These systems accurately make the two-fold dilutions by direct pipetting, not by volumetric serial dilutions. o If dispensed in the nanoliter to picoliter range of antimicrobial agent, it may be possible to simply dispense less than a microliter of antimicrobial agent in dilute solute or water, freeze the panel, and then rehydrate with 100 µL of appropriate broth. o They will assess if small amounts of surfactant (eg, 0.002% Polysorbate-80) is acceptable for all drugs, unless there is a known issue (eg, colistin). – It will be determined if the sequence in which the broth and drug are mixed has an impact on the dilution if the right concentration is in the final well. – The WG proposed that an AHWG be formed and seek volunteers to participate. Ms. Katherine Sei will lead the group. – The SC agreed that an AHWG should be formed. • Direct Blood Culture Disk Diffusion AHWG Update – A five-site study on 500 patients led by Dr. Schuetz is still in progress. – Issues noted include: o Instructions for reading the panel o QC for *E. coli* ATCC® 25922 with ciprofloxacin and *P. aeruginosa* ATCC 27853 with meropenem.

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	– *Enterobacteriaceae* results will be analyzed first and *Pseudomonas* and *Acinetobacter* spp. will be considered depending on the data. – The AHWG has a conference call scheduled and a report on the study is expected to be ready for the June 2019 meeting. • Antimicrobial susceptibility testing (AST) of Non-*Enterobacteriaceae* (Table 2B-5) – Dr. Hardy presented issues related to Comments 1 (list of organisms included in Table 2B-5) and 2 (recommendation against testing with disk diffusion method). – It is unclear as to what species are included in Table 2B-5 as only exclusions are listed. – Newer methods (eg, MALDI-TOF) provide more accurate identifications; therefore, it was questioned as to why these organisms are grouped together regarding testing methods and breakpoints (BPs). o Are all glucose non-fermenting gram-negative bacilli the same with respect to AST? o It is possible that disk diffusion might be an appropriate method for some organisms within the group. – It was proposed that an AHWG be formed to study testing methods. o M45's approach to adaptive methods will be investigated. Dr. Humphries noted that some of these organisms could be moved to M45. o The AHWG will prioritize the organisms and perform a literature search and report at the June 2019 meeting. – The SC endorsed the formation of the AHWG. Dr. Hardy will lead the group and volunteers willing to participate should contact Dr. Hardy. • Cefazolin high inoculum effect (CIE) in *S. aureus* – An overview was presented to the MDSWG by Cesar A. Arias, MD, PhD and William R. Miller, MD. o CIE has been shown to be associated with clinical failures with deep-seated methicillin susceptible *S. aureus* (MSSA) infections due to the ability of penicillinase-producing staphylococci to hydrolyze the drug. o Clinical MSSA isolates failing therapy were found to have cefazolin MICs that increased in proportion with the bacterial number in the inoculum (Ie, the inoculum effect). It has been shown that CIE is associated with isolates that produce an extracellular staphylococcal ß-lactamase (BlaZ). o Inoculum effect is determined by a significant rise in the MIC at 10^7 CFU/mL compared to the standard 10^5 CFU/mL. o Currently, there is no readily available methodology to detect CIE in the routine clinical microbiology laboratory. o Retrospective studies on nafcillin vs cefazolin showed that patients receiving cefazolin had a 37% reduction in 30-day mortality and a 23% reduction in 90-day mortality compared with patients receiving nafcillin or oxacillin, after controlling for other factors. o A recent prospective study showed that patients infected with isolates that exhibited the CIE and treated with cefazolin were more likely to experience treatment failure and death at one month, as compared to patients with CIE-negative isolates. o There are potential benefits of identifying CIE isolates (eg, source control, defining populations, identify those at risk for failure, generation of surveillance data) o A potential rapid colorimetric test for CIE involving the induction BlaZ was presented. – The MDSWG recommended that an AHWG be formed to study the issue. o A request for strains to study was also made.

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	○ Dr. Butler-Wu and Dr. Dingle will lead the AHWG. Dr. Dien Bard and Dr. Abbott will also participate. – SC Discussion ○ It was questioned as to whether the zone edge test works. This issue will be considered in this study. ○ It was noted that the proposed test is more rapid than the zone edge test. ○ It was questioned if there is correlation with other ß-lactams. It was agreed that the test would need to be done with a higher inoculum to determine if strain has the effect. ○ Dr. Bush suggested looking for inducible ß-lactamase; however, it is not specific for cefazolin, so the test wouldn't be called the cefazolin test. ○ Mr. Esparza suggested that an expert rule is needed for this situation. ○ It was noted that not all ß-lactamases are inducible. ○ Dr. Jenkins suggested that the WG should look at 10^5 vs 10^7. ○ The study will be refined to cover all issues. – The SC endorsed the formation of an AHWG to study the high inoculum issues. • Coordinated Development AHWG Report – Dr. Humphries presented an update to the MDSWG – Progress to date includes: ○ Awareness has been raised on the issue through publications and commentaries. ○ The FDA has published a coordinated development guidance document. ○ An FDA/CDC Antimicrobial Resistance (AR) isolate bank has been created. ○ 21st Century Cures Act was passed (removed list 1 vs list 2 considerations and recognized Standards development organization [CLSI] breakpoints. – These changes provide for faster time to market for manual devices and increased progress for automated AST systems with faster process for submitting for device clearance. – Dr. Patel gave an update on AR laboratories. ○ There is an ongoing study on drugs for treating serious CRE Infections (ie, colistin, ceftazidime-avibactam, meropenem-vaborbactam, imipenem-relebactam, plazomicin, aztreonam-avibactam, cefiderocol). ○ Isolates being studied include *Enterobacteriaceae* resistant to ceftazidime-avibactam or meropenem-vaborbactam, or *Enterobacteriaceae* that are positive for NDM, VIM or IMP by a molecular test. – Ongoing work: ○ Ongoing, open issues to be resolved by FDA CDRH and Susceptibility Testing Manufacturers Association (STMA). ○ Working on improved time to testing on automated devices. ○ Working on improved transparency related to development costs, commercialization, and timelines.

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	○ Decisions need to be made on what to do when USCAST / CLSI / EUCAST / FDA breakpoints differ. • STMA Update – STMA is working with FDA on: ○ Evaluating secondary inoculation methods ○ Breakpoint updates (streamlined processes needed) ○ Isolate needs ○ Changes to required performance: removal of Table 8 with an emphasis on 'on-scale' ○ Challenges with reference method and discrepancy analysis ○ Changes to the disk diffusion process – Upcoming work on the following questions: ○ Is overlap of work (eg, new ß-lactam combination products) possible? ○ Could multiple disks be cleared in one large single-center study? ○ Can new methodologies for disk concentration selection be developed? (EUCAST/CLSI joint working group) ○ Are there potential funding opportunities? ○ Can QC for new drugs be streamlined? ○ Is there availability of breakpoint "challenge" isolates?
6.	**BPWG (Part 1): J. Lewis (Folder 5)** **BPWG Roster**: George Eliopoulos, Jim Lewis, Mike Satlin (Co-Chairholders); Karen Bush (recording secretary); Marcelo Galas, Amy Mathers, Lauri Thrupp, Barbara Zimmer (members present); David Nicolau, Robin Patel, Kerry Snow, Simone Shurland, Hui Wang (members absent); Matthew Wikler (advisor) • **Fosfomycin AHWG Report (Folder 5, 9a-9k)** **NOTE:** Agar dilution is the recommended method for testing fosfomycin **Fosfomycin AHWG Roster**: Robert Flamm, Amy Mathers (Co-chairholders); Kitty Anderson, Betsy Hirsch, Laura Koeth, Kiofumi Ohkusu, Virginia Pierce, Lauri Thrupp, Eric Wenzler, Mandy Wootton. – The AHWG focus was to evaluate fosfomycin (FOS) susceptibility testing for *E. coli* in urine with and without glucose-6-phosphate (G6P). G6P apparently makes the MICs more reproducible and increases drug activity. – Background ○ IV FOS is currently under review by the FDA. Oral FOS is FDA-approved for treating uncomplicated cystitis and used almost exclusively for UTI. ○ Glucose and phosphate concentrations may be variable for *in vitro* testing. ○ G6P lowers MICs, but G6P is not present in the urine. This may affect MICs in urine, but FOS urine levels are highly variable.

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	○ Most PK/PD studies are pre-1980, using bioassays so data are limited. ○ Drug use is primarily off-label for complicated UTI and dosing are inconsistent. – Dr. Wenzler presented a current PK/PD data study to evaluate FOS in urine to determine FOS levels. ○ MICs were determined according to resistance mechanisms. ○ Urine bactericidal titers were much lower in urine tested without G6P. – It was questioned if the methodology needs to be revised as there are problems with both broth and agar dilution. ○ There is no clinical evidence that the current breakpoints are leading to clinical failures. ○ Low resistance rates have been seen, even where FOS has been used more extensively. – The AHWG requested suggestions for the next steps. The BPWG suggested to: ○ Contact European investigators about clinical failures with FOS. ○ Evaluate data about fitness costs of FOS-R strains. ○ Retain G6P when testing for FOS agar dilution assays. ○ EUCAST ECOFF data should be evaluated. EUCAST offered to work with CLSI to evaluate data. – SC Discussion ○ Since methods for evaluating variability and reproducibility have improved, it was suggested that broth microdilution (BMD) may be revisited. It was noted that the data with BMD is in the old agenda books and it could be re-evaluated. ○ JMI has performed a small study with BMD with and without G6P. Generally, with BMD there is a correlation around 80% but does not reach the 90% correlation needed and is species specific. There are continuing issues with variability. • **Minocycline Table 1 Placement (Folder 5; 7a-7j)** – Dr. McCurdy and Dr. Redell presented data for requesting that minocycline be moved to a separate box in Group A for *Stenotrophomonas maltophilia* in Table 1 and Table 2B-4. The only other drug in Group A is trimethoprim-sulfamethoxazole (TMP-SMX). – The rationale for the move included: ○ Clinicians need updates on antimicrobial agents which demonstrate susceptibilities to key problem pathogens of >90% compared to other agents with FDA or CLSI breakpoints. ○ oMinocycline demonstrates >90% *in vitro* susceptibility to *S. maltophilia* similar to trimethoprim-sulfamethoxazole. Compared to levofloxacin and ceftazidime, two Group B agents, minocycline is far more active *in vitro* and should be placed into Group A. Group B agents, ceftazidime and levofloxacin, show *in vitro* susceptibilities of only ≈40% and ≈70%, respectively. ○ *S. maltophilia* is of growing epidemiologic concern and has demonstrated important trends of increasing resistance. ○ A retrospective study of patients receiving minocycline showed that this pathogen constituted a significant percentage of those recovered; susceptibilities were 100% and clinical response was 80% among 30 seriously ill patients with bacteremia or pneumonia. – BPWG Discussion ○ A question was raised as to whether an organism must be listed in the drug's label in order to be in Group A.

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	○ It was noted that by being in Group B, laboratories test for minocycline, but they are not required to report results. ○ A motion was made and seconded to obtain PK/PD data for minocycline with *S. maltophilia* as the basis for a rationale document supporting a possible move for minocycline to Group A in Tables 1 and 2B-4. **Vote:** 6 (Yes)-1 (No)-1 (Abstain). Motion passed. – SC Discussion ○ Table 1 placement needs to be revisited. This was discussed in the Executive session and it was decided to form a new Table 1 AHWG to review the definitions for placing drugs in Table 1 as As or Bs. Dr. Simner and Dr. Eliopoulos will lead the AHWG to study Table 1. ○ Dr. Thrupp provided a short history of selective reporting. He noted that Table 1 drug placement in A or B was intended to provide guidance on selective testing and reporting. If the older drugs were susceptible they would be reported. Many users don't understand the intent or application of selective reporting. ○ Dr. Abbott noted that it is not specifically stated in M100 that a group A drug must be tested and reported. Some of the drugs are not on all panels. Clarification on how to interpret Table 1 is needed. ○ Dr. Hardy stated that Group B drugs are currently listed as optional to test. The word "optional" is confusing. In the past, it was meant to be primary test and selective reporting. He agreed that minocycline should be moved to group A. ○ Dr. Giske noted that there is PK available to review. ○ Additional data may be needed as the organisms have been shown to be susceptible *in vitro* but result in treatment failures. ○ Dr. Simner believed that the Subcommittee needs to better describe when and how drugs are placed and moved. ○ Dr. Tamma agreed that minocycline is a good option and has good activity when there are issues with TMP-SFX. It could be moved as clinicians may not know to consider minocycline since not in Group A. ○ Dr. Schuetz agreed with Dr. Tamma and we are probably not going to get much data. Minocycline is being testing routinely many laboratories. ○ Dr. Humphries stated that in the study mentioned by Dr. Thrupp that 48 laboratories reported TMP-SFX but none reported minocycline showing that placement does matter. ○ Dr. Satlin stated that clarification on the definitions of A and B must be determined before a decision is made. ○ Dr. Reller agreed with Dr. Satlin. He noted that the group has gotten away from the original intent of the table as a guide for most prudent use possible of antimicrobial agents for therapy. Drugs are placed in Group A to recommend first choice of therapy based on efficacy, etc. Nothing precludes any drug in Table 1, Group B from being reported concurrently with Group A. ○ Dr. Jenkins noted that TMP-SMX has no PK/PD data for *S. maltophilia* either and not listed in package insert as treatment for *S. maltophilia* even though it is clinically the drug of choice. ○ Dr. Kirn stated the SC needs to revisit Table 1 and can wait until June to make a decision. ○ Ms. Cullen agreed that it is better to make decision in June; however, it may be difficult to get additional data by June. – Issues ○ Should the SC recommend that that the sponsor generate additional PK/PD data for *S. maltophilia*. ○ Is a motion needed to ask the sponsor for additional data?

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	A motion to request additional PK/PD for minocycline and *S. maltophilia* to be placed in Group A was made and seconded. No Vote taken.
	○ Dr. Ferraro stated that expecting sponsors to provide PKPD data for consideration for placement in Table 1 is not required according to M23. ○ Dr. Galas stated that the SC needs to define the criteria for placing drugs in any Group before a decision can be made about minocycline. ○ Dr. Lewis mentioned that studies with older drugs that for which breakpoints were set with limited data. The difference with TMP-SMX is that it has much clinical efficacy data whereas minocycline does not. It would be helpful to see some type of data to justify the move. ○ Dr. Edelstein noted that asking for PK/PD usually means the breakpoint is being evaluated so that should be done first. ○ Dr. Limbago commented that it looks like an M23 signal is being sought when none is evident and a precedent for asking for additional data just to place a drug in Table 1. ○ Dr. Humphries stated that if the breakpoint is reassessed, it might become an ECV and it is doubtful that the SC wants to go in that direction.
	A revised motion to request that the sponsor obtain additional clinical efficacy evidence to support request to move minocycline from B to A for *S. maltophilia* was made and seconded. VOTE: 4 for; 8 against (FAIL)
	○ The reasons for the votes against were: ▪ Dr. Humphries stated that data would need to be generated and it is difficult to obtain and would create additional confusion. ▪ Dr. Kirn agreed with Dr. Humphries and that the whole table needs to be reviewed before any changes are made. ▪ The other nay voter agreed with Dr. Kirn and that Table 1 needs to be revised and clarified. Additional guidance needs to be provided to laboratories on how to use Table 1. – It was decided to reconvene the Table 1 WG and charge it with redefining Categories A and B before any changes are made on minocycline placement. The WG will also revisit how drugs are placed in the table and how users should interpret the table. • **Cefiderocol Disk Breakpoint Request (Folder 5; 4A)** – The sponsor requested that CLSI evaluate disk diffusion (DD) BPs and Table 1 placement. – Investigational MIC breakpoints have been approved and published in M100-29. – MIC/disk correlation studies were performed, and DD BPs were proposed. ○ Discussion was focused on proper assignment of the intermediate range. Minor error rates were quite high. ○ The sponsor agreed to re-evaluate the data with a tighter intermediate range for disk results. ○ Data were presented from one lot of disks from one manufacturer. ○ After much discussion, the WG asked the sponsor to return with additional analyses to try to lower the number of minor errors.

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- After the sponsor performed additional analysis by dBETS software, the following disk diffusion breakpoints were proposed:

	Interpretation (mm)		
	Susceptible	Intermediate	Resistant
	MIC: ≤4 µg/mL	MIC: 8 µg/mL	MIC: ≥16 µg/mL
***Enterobacteriaceae* disk zone**	≥15	12-14	≤11
***P. aeruginosa* disk zone**	≥16	13-15	≤12
***A. baumannii* disk zone**	≥15	12-14	≤11
***S. maltophilia* disk zone**	≥16	13-15	≤12

- The study design was reviewed.
  - 30 µg cefiderocol disks were used and testing was on Mueller-Hinton agar.
  - 1319 isolates were tested.
  - The isolates were tested with one media lot, 1 manufacturer and tested one time in one laboratory.
  - Analysis was performed by dBETS and using IHMA's original software.
- Final Summary
  - The dBETS summary showed agreement with the BPs listed above.
  - The sponsor requested feedback on a 3 mm vs a 4 mm intermediate zone for *Enterobacteriaceae*. It was ultimately decided that the 3 mm range was preferred.
  - The sponsor is asking for the BPs to be approved.
- SC Discussion
  - Dr. Galas questioned if the organisms were tested with different media to check variability. Dr. Lewis stated that there is no additional data other that what was presented during the BPWG meeting. The data were only re-analyzed using the dBETS software.
  - Dr. Mathers asked if the sponsor is going to request BPs from FDA as well. The sponsor stated that if CLSI approves the dBETS analysis, the sponsor will amend the NDA before it is submitted to the FDA.
- Dr. Simner asked if testing multiple lots of media and disks is required. Ms. Cullen stated that multiple lots of disks and media were tested for the QC ranges. It is intended that additional requirements will be added to M23 for setting disk correlates. The sponsor stated that some variability was encountered in the M23 study for the agar media. There was media variability, but the QC range was approved and set to accommodate the variability. If this variability exists, additional assessment may be needed.
- Dr. Humphries stated that the ranges are very tight, so it is expected they will need to be reassessed after more data is generated from multiple lots of media and disks.
- Dr. Mathers asked what happens with the vote as the minor error rates are high and it is expected that the zones will need to be revisited. What are the implications for waiting? It was noted that M100-30th edition does not publish until January 2020.

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	– The sponsor stated that the FDA has the M23 study and the data shown here. The BP is based on data other than that from dBETS. The sponsor prefers to submit the dBETS data as it is better. They will submit with this data if CLSI approves it. – Dr. Satlin noted that the M23 requirements were met for media and replicates. It seems that the requirement for the disk diffusion "I" range to be at least 50% of QC range. Some of the organisms seem to fit these criteria. – **MOTION**: Dr. Humphries motioned to defer the vote so that everyone can review the data before a vote by email (no second). o Dr. Ferraro stated that it seems that the sponsor has completed the appropriate analysis and that a decision should be made now to assist the sponsor. o Dr. Satlin suggested that the vote be deferred until Day 2 so that data can be reviewed with options for the way data has been presented.
	A motion to accept the *Enterobacteriaceae* breakpoints with an intermediate range of 12-15 mm was made and seconded. VOTE: 10 – 0; 2 abstain (PASS). NOTE: Although the motion passed, it was decided to have the sponsor present the data with wider intermediate zone and defer the vote to until Day 2.
	– Reanalyzed data and scattergrams for cefiderocol were presented (Day 2). o The sponsor reanalyzed the disk correlate data based on the M23 recommendation for the intermediate range to be at least 50% of the QC strain ranges. o After reviewing the reanalyzed data, adjustments were made to the intermediate zone ranges.
	A revised motion to accept the disk diffusion breakpoints for cefiderocol and *Enterobacteriaceae* (S = ≥16; I = 12-15; R = ≤11) was made and seconded. VOTE: 10 for; 0 against; 1 abstain (conflict); 1 absent (PASS). NOTE: Vote to be confirmed after additional reproducibility testing data is reviewed.
	A motion to accept the disk diffusion breakpoints for cefiderocol and *P. aeruginosa* (S = ≥18; I = 13-17; R = ≤12) with a 5 mm intermediate range was made and seconded. VOTE: 10 for; 0 against; 1 abstain (conflict); 1 absent (PASS). NOTE: Vote to be confirmed after additional reproducibility testing data is reviewed.
	– It was questioned as to why a 4 mm range was not used for the intermediate. o Five was chosen because of the M23 recommendation that the intermediate range should be at least 50% of the QC strain range.
	A motion to accept the disk diffusion breakpoints for cefiderocol and *Acinetobacter* spp. (S = ≥15; I = 11-14; R = ≤10) with a 4 mm intermediate range was made and seconded. VOTE: 9 for; 1 against; 1 abstain (conflict); 1 absent (PASS). NOTE: Vote to be confirmed after additional reproducibility testing data is reviewed.
	– Dr. Limbago questioned whether the intermediate ranges meet the M23 criteria. o Dr. Lewis noted that the 5 mm range barely crossed the limit of 40.

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	○ There are no *Acinetobacter* QC ranges, so it was decided that this was acceptable and that going to a 5 mm range would increase the minor error rate to >40%. ○ Ms. Cullen remarked that she is not sure that the M23 recommendation has been followed. She questioned if there was reproducibility data on the disks replicates on multiple media lots. ○ The sponsor stated that no disk reproducibility studies are available. ○ Ms. Cullen stated that she would support the 4 mm range based on the difference in error rates. ○ Dr. Limbago noted that M23 also states that if there are discrepancies greater than 2-fold above or below the MIC, they should be repeated. She questioned if that had been performed. ○ The SC requested that the sponsor perform reproducibility testing for all four organisms particularly for resistant isolates. These would be duplicate studies with additional media.
	A motion to accept the disk diffusion breakpoints for cefiderocol and *S. maltophilia* (S = ≥17; I = 13-16; R = ≤12) with a 4 mm intermediate range was made and seconded. VOTE: 9 for; 1 against; 1 abstain (conflict); 1 absent (PASS). NOTE: Vote to be confirmed after additional reproducibility testing data is reviewed.
	– It was decided to defer the Table 1 placement discussion until the June meeting pending the decisions made on by the Table 1 AHWG. • **Daptomycin *Enterococcus faecium* Breakpoints Revisited (Folder 5; 5a-5f)** – Dr. Patel presented data showing that for the daptomycin breakpoints approved in June 2018 (S / S-DD / R = ≤1 / 2-4 / ≥ 8 mg/ml), the S breakpoint is lower than the ECV and splits the WT population between S and SDD, with high variation in replicate testing of isolates with MICs of 1 and 2 mg/ml (ECV = 4 mg/mL). – It was questioned how to differentiate between *E. faecalis* and other *Enterococcus* spp. – One option was to add language to M23 that PK/PD may recommend BPs that are lower than ECV, but problems arise when BPs are less than the ECV. – WG proposed and approved: SDD only = ≤ 4; R = ≥8 with approved dosage (8-12 mg/kg/day) in adults – Discussion ○ It was questioned whether device manufacturers could implement an SDD category. It was noted that the BP is already being used with a new name. ○ It was noted that FDA doesn't currently recognize SDD, but the category could be changed in the user's LIS. A comment could be added to the LIS if S can't be changed to SDD for affected organisms. ○ In the past, *E. faecium* didn't have an FDA BP and it couldn't be put on devices before. Setting this BP helps since *E. faecium* is now included. ○ Dr. Kuti stated that most human data come from *E. faecium* so there is not much data for *E. faecalis*; however, studies in the mouse thigh model showed that while killing is difficult, stasis is achieved.

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	○ It was noted that the rationale document (in progress) will explain the reasons for making these BP changes. ○ Dr. Humphries suggested that a notification should be sent to users to refrain from validating the M100-29th breakpoints as changes will be coming in the 30th ed. in 2020.
	A motion to accept the proposed breakpoints for daptomycin against *E. faecium* as SDD = ≤ 4 µg/mL; R = ≥8 µg/ml) with the comment, "The SDD category is based on a dosage regimen of 8-12 mg/kg/day in adults and is intended for serious infections due to *Enterococcus faecium*. Consultation with an infectious diseases specialist is recommended" was made and seconded. VOTE: 12 for; 0 against (PASS).
	○ Ms. Cullen requested isolates with MICs around the BP for variability studies. – Non-*E. faecium* spp. *(Enterococcus* spp. including *E. faecalis*) ○ The WG proposed breakpoints for *Enterococcus* spp. other than *E. faecium* were S = ≤ 2; I = 4; R = ≥ 8 with a dosage of 6mg/kg/mL in adults. ○ Discussion ▪ Daptomycin used rarely for isolates other than *E. faecium* (PKPD data built with *E. faecium*). Only stasis (not killing) occurs with *E. faecalis*. ▪ Dr. Patel requested a BP of ≤4 for S which is the same as with FDA and devices. ▪ It was suggested that another SDD be set at 4 as 2 is very close to WT distribution. ▪ Dr. Miller reminded the SC that the daptomycin WG worked several years to develop these BPs and have had many similar discussions.
	A motion to approve the BPs for *Enterococcus* spp. other than *E. faecium* with comment about dose [S = ≤ 2; I = 4; R = ≥8] with a comment that the breakpoint is based on a dosage regimen of 6mg/kg/mL in adults was made and seconded. VOTE: 12 for; 0 against (PASS).
7.	**Text and Tables WG Report (Folder 10)** **WG Roster:** Shelley Campeau and April Bobenchik (Co-chairholders); Carey-Ann Burnham (recording secretary); Suki Chandrasekaran, Mary-Jane Ferraro, Andrea Ferrell, Janet Hindler, Melissa Jones, Dyan Luper, Jean Patel, Barth Reller, Felicia Rice, Flavia Rossi, Nancy Watz (members present); Victoria Anikst, Peggy Kohner, Dale Schwab, Maria Traczewski (members absent). **Dr. Bobenchik reported on four topics.** • **Clarifying language for inducible clindamycin resistance (ICR).** – In June 2018, revision of the ICR comment in Tables 2C, 2G, and 2H-1 was approved. The current comment was revised to read (new in red): "For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for inducible clindamycin resistance is required before reporting clindamycin…"

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	– In June 2018, there was also a discussion regarding uncertainty as to whether erythromycin had been tested. The TTWG proposed a clarification to the comment in Table 3G: Report isolates with inducible clindamycin resistance as "clindamycin resistant." The following comment may be included with the report when the isolate is ICR positive: **"This isolate is presumed to be resistant based on detection of inducible clindamycin resistance, as determined by testing in combination with erythromycin."** – Clarification for the ICR for group B streptococcus specific comments was also addressed. o Comment "o" in Table 1B and comment (12) in Table 2H-1 will be revised as follows: **"o. Rx: Recommendations for intrapartum prophylaxis for group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin. Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin, but may be resistant to erythromycin and clindamycin. When group B *Streptococcus* is isolated from a pregnant woman with severe penicillin allergy (high risk for anaphylaxis), erythromycin and clindamycin (including inducible clindamycin resistance) should be tested, and only clindamycin should be reported. Erythromycin, even when tested for determination of ICR, should not be reported. See Table 3G."** o Table 3G comment, footnote a will be split into footnotes a (general testing) and b GBS-related) **a. Antimicrobial susceptibility testing (AST) of β-hemolytic streptococci does not need to be performed routinely (see general comment [4] in Table 2H-1). When susceptibility testing is clinically indicated, ~~it~~ testing should include tests for ~~testing for~~ inducible clindamycin resistance in strains that are erythromycin resistant and clindamycin susceptible or intermediate.** **b. In accordance with 2010 guidance from the Centers for Disease Control and Prevention, colonizing isolates of group B streptococci from penicillin-allergic pregnant women should be tested for clindamycin (including inducible clindamycin resistance) (see comment [12] in Table 2H-1).[1] ~~The following comment may be included with the report.~~ For isolates that test susceptible or intermediate to clindamycin (with erythromycin induction), consider adding the following comment to the patient's report: "This Group B Streptococcus does not demonstrate inducible clindamycin resistance as determined by testing in combination with erythromycin.".** • **Standardizing *Staphylococcus*-related terminology and nomenclature in M100 (will include next revision of M02 and M07).** – "CoNS" will be removed throughout M100, 30th ed. and replaced with "Other *Staphylococcus* spp.", "*Staphylococcus* spp. other than…", etc. – "Methicillin (oxacillin)-resistant" will be used for defining MRS or MRSA throughout the document. – Table 3E will be updated with an additional column to include all testing methods around detecting resistance. • **Special media, testing, and investigational drug information placement.**

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	– Concerns were raised regarding excessive detail in the Testing Conditions box at the front of each Table 2. – It was decided to maintain special media/testing requirements in Testing Conditions box, with specific details in comments next to the drug as done for cefiderocol in M100, 29th ed. • **Testing and reporting comment inconsistency.** – There are numerous examples of similar comments being stated in different ways. – The TTWG will review the use of "only" in table comments and determine which ones require that "only" be included (eg, data showed the drug is inappropriate or should not be tested) and which do not.
8.	**BPWG Report (Part 2) (Folder 5)** • **Dr. Paul Edelstein presented data to support the re-evaluation of amoxicillin-clavulanate breakpoints. (Folder 5; 1a-1z)** – AST data from 1983 and 1989 and other publications were reviewed. Based on the data reviewed, he proposed that an UTI only BP for *Enterobacteriaceae* be created or to decrease the BP for non-UTI isolates (if lower, % *E. coli* that are susceptible very low – not applicable for *Enterobacteriaceae* in non-UTI). o 2004 PK/PD study: For 875/125 and 2000/125 mg doses, target attainment was low for amoxicillin MICs >2 mg/mL. o 2016 study: Amoxicillin-clavulanate probability of target attainment (PTA) confirms the 2004 results. o If 90% PTA is assumed with 875/125 mg tid dose, <5% PTA is attained, even with a BP of 0.5 mg/mL. o There is no strong signal for clinical failures and there is a high cure rate if the MIC ≤ 8 mg/mL. o The published clinical data, and available data from clinical trials, are insufficient to determine if 875/125 bid is effective for non-UTI infections caused by Enterobacteriaceae – Discussion o In the 1980s,there were no PK/PD data reviewed but BP were selected based on MIC distributions. o There are no current data available to reassess and no obvious clinical signals for failure. Amoxicillin-clavulanate is used primarily without performing AST. o If the amoxicillin-clavulanate BP is going to change, ampicillin and ampicillin-sulbactam would need to be assessed as well. o Empiric therapy has been used successfully so there may not be a need to reassess the BPs. o It was noted that M23 process uses different criteria other than clinical signals for reassessing BPs and the M23 process should be considered. o Prophylaxis practices differ throughout the world with much heterogeneity. It was noted that it can be difficult to detect a clinical signal from older drugs. o Dr. Schuetz remarked that based on various antibiograms, there is variable susceptibility and that the BP is wrong. o Dr. Zimmer commented that device manufacturers prioritize changes based on clinical signal, so amoxicillin-clavulanate would be low on the priority list.

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	○ Dr. Tamma suggested that this be left to stewardship programs etc. to determine if the recommendations should change as there has not been any clinical signals of failure when used as oral step-down therapy for intra-abdominal infections.. ○ Options include: ▪ Retain the BP for UTI only. ▪ Add comment recommending against using the drug for primary therapy for sites other than the urinary tract. ▪ Reassess ampicillin and ampicillin-sulbactam based on M23 recommendations ○ It was suggested that an AHWG might be formed to reassess amoxicillin-clavulanate, amoxicillin, ampicillin, and ampicillin-sulbactam. • **Correlation between MIC and Disk Diffusion results for ceftazidime-avibactam when testing *Enterobacteriaceae* isolates (Folder 5; 3A-3C)** – Dr. Sader presented information regarding high error rates for CRE isolates with ceftazidime-avibactam. – Historically, the current disk diffusion BPs were established with very few CRE isolates. – A three-laboratory study of 112 *Enterobacteriaceae* isolates tested by BMD and disk diffusion methods was performed. Conclusions from the study were: ○ The current CLSI disk diffusion BPs (≥21/≤20 mm for S/R) provided the lowest discrepancy rates for the ceftazidime-avibactam 30-20-µg disk. ○ Results support the comment added to the 2019 M100-29 document: "when DD results are in the 18 – 20 mm range, a confirmatory MIC test should be performed". ○ There were no major differences in error rates were observed between agar or disk manufacturers. ○ The vast majority of errors occurred with isolates having ceftazidime-avibactam MIC values within ±2 doubling dilutions of the breakpoint. – The BPWG recommended keeping the current disk breakpoints for the ceftazidime-avibactam 30-20 mg disk. The results also support the comment added to the 2019 M100-29 document: "When disk diffusion zones are in the range of 18-20 mm, a confirmatory MIC test should be performed." – The BPWG proposed a change in language of the comment: "When disk diffusion zones are in the range of 19-22 mm, a confirmatory MIC test should be performed (Approved by WG)". – SC Discussion ○ Dr. Satlin noted that the 19-22 range straddles major and very major errors. ○ Dr. Ferraro stated that there are examples of drugs for which there are no "I" for the disk and the comment looks like it is referring to an "I" category. She suggested that it might be better to have an "I" range for both MIC and disk diffusion. ○ Dr. Kahlmeter suggested that the disk content may be the issue. EUCAST uses a different disk mass and doesn't encounter this issue. ○ Dr. Sader stated that both disk masses were tested and the same issue occurred with both. ○ Intermediate is not understood well by users and a comment is more explanatory for these situations.

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	A motion to accept the BPWG's proposed comment ("When disk diffusion zones are in the range of 19-22 mm, a confirmatory MIC test should be performed") was made and seconded. VOTE: 7 for; 4 against; 1 absent (FAIL).

	– Discussion
	  o Dr. Simner believed that this could be tabled until June since it wouldn't take effect until January 2020.
	  o Dr. Galas commented that the number of strains needing confirmation is relatively high and the laboratory may not have the ability to do MICs.
	  o Dr. Schuetz suggested she would like to discuss the possibility of an intermediate range.
	– Path forward
	  o BPWG will explore the possibility of creating an intermediate zone.
	  o Dr. Sader will reanalyze the data for MIC and disk diffusion and present the results for an intermediate range in June.
	  o Dr. Kuti noted that there is adequate PKPD data to justify an intermediate zone for MIC and disk diffusion.
	
	• **Merino Trial Results: Meropenem vs Piperacillin-tazobactam (Pip-Tazo) (Folder 5; 6A-6F)**
	– The BPWG discussed the outcomes of a clinical trial for meropenem vs pip-tazo for blood infections with ESBLs.
	  o Improved survival with meropenem compared to Pip-Tazo.
	  o All outcomes (primary and secondary) favor meropenem.
	  o There was no correlation between pip-tazo MIC and clinical cure.
	
	  o There were questions about clinical microbiology testing, using ceftriaxone-NS as an indicator for Pip-Tazo resistance and/or ESBL production.
	–
	– Data from Dr. Turnidge shows very poor correlation between MICs determined by BMD and gradient diffusion. Additional work is ongoing.
	– It was questioned if the SC should make any recommendations on the matter.
	– BPWG agreed that the data are too premature to make a comment at this time. It was suggested that the issue might be discussed at a future time when more data are available.
	• **Cefazolin over Nafcillin/Oxacillin for Methicillin Susceptible *S. aureus* (MSSA) treatment (Folder 5; 8A-8K)**
	– Mr. Esparza provided a presentation outlining the recent controversy regarding the use of cefazolin over nafcillin/oxacillin for treating MSSA strains that exhibit the inoculum effect.
	  o Inoculum issues have been reported for cefazolin and have an influence on clinical outcomes.
	  o It was proposed that CLSI address this by proposing a phenotypic test or a cautionary statement.
	– The BPWG agreed that the data are controversial, but it is too premature to make a recommendation.

9.	**GCWG Report (Folder 11)**

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	GCWG roster: Mary Jane Ferraro, Vanessa Allen Gray (Co-chairholders); Marcelo Galas, Ron Jones, Ellen Kesh, Jean Patel, Nicole Scangarella-Oman (members) Dr. Gray provided a report from the GCWG. She outlined the WG's three goals. • **Re-evaluate the possibility of setting resistant breakpoints for ceftriaxone and cefixime.** – The WG reviewed data from the late 80s on ceftriaxone and there are little clinical data which is primarily restricted to pharyngeal infections with variable MICs. o Currently there are not enough data to set a resistance breakpoint. o The susceptible breakpoint is currently for urogenital infections only. o The ECVs for ceftriaxone are compatible o It was also questioned if the current dose should be retained and added to M100. Revisions in recommendation for dosage regimen are being revised so it was decided to table the issue. – Cefixime o Treat failures have been seen with MICs for infections from all sites. o Currently there are not enough data to change the breakpoint. o Dosage recommendations will be discussed at a later date. o Other oral cephalosporins will be explored in collaboration with CDC. • **Establishing disk diffusion BPs for azithromycin** – A susceptible only MIC BP is currently listed in M100-29 with the caveat to treat in conjunction with ceftriaxone. – Studies have been performed to establish disk diffusion breakpoints (CDC). – Additional data are needed for multiple media lots. • **Next steps for gentamicin as an alternate treatment for gonorrhea**. – CDC is performing studies for establishing disk diffusion breakpoints for gentamicin. – Additional clinical data are needed. – No decisions were made by the WG. • There are two new promising drugs in pipeline and these will be discussed as they develop.
10.	**SC on Veterinary Antimicrobial Susceptibility Testing (VAST) Report** **Dr. Fritsche provided a report on the VAST SC activities. He stated that the SC and its associated document development committees and WG have been very active and have made much progress.** • VET01, *Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals* and VET08, *Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated From Animals* (M100 equivalent) published in 2018

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	– Both documents were significantly revised and harmonized with the human AST documents. – The WG is currently working on the next revision of VET08 for publication on a 2-year schedule. – A Webinar on updates to both documents was presented in September 2018 by Mr. Mike Sweeney, Dr. Dubraska Diaz-Campos, and Dr. Claire Burbick. • VET06, *Methods for Antimicrobial Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria Isolated From Animals* (M45 equivalent). – First published in 2016 – Revision expected in 2021. • VET02, *Development of In Vitro Susceptibility Testing Criteria and Quality Control Parameters for Veterinary Antimicrobial Agents* (M23 equivalent) – Published in 2008 – Revised edition is projected for publication later in 2019. • WG on Aquaculture – Charged with updating and consolidating the VET03 (disk diffusion) with VET04 (broth dilution) into a new VET03 guideline that combines both disk diffusion and broth dilution methods. – Scheduled to be published later in spring of 2020 in conjunction with a new VET04 that will serve as the breakpoint supplement. • VET09, *Understanding Susceptibility Test Data as a Component of Antimicrobial Stewardship in Veterinary Settings* – Currently in progress and expected to publish in 2019. – Document acts as a "bridge' from laboratory data to assist practitioners with a better understanding of such data, how it is generated, interpreted and reported. – Document will be useful for practitioners, educators, students, residents and laboratorians among others and may serve as a model for the AST Subcommittee for developing a similar product. • Additional projects – Developing specialized media for fastidious pathogens – Setting generic drug breakpoints – Continuing education projects
11.	The opening plenary meeting was adjourned at 5:30 PM Eastern (US) time.

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Tuesday, 29 January 2019	
1.	Dr. Weinstein opened the meeting at 7:30 AM Eastern (US) time.
2.	**EUCAST Update: Christian Giske** **EUCAST 2019 SC**: Christian G. Giske (Chairholder), John Turnidge (scientific secretary), Rafael Canton, Gunnar Kahlmeter, Sören Gatermann, Christoffer Lindemann, Johan Mouton, Alasdair MacGowan, Gerard Lina, Efi Petinaki, Cidália Pina Vaz Dr. Giske provided an update on EUCAST's activities. • The number of laboratories using EUCAST breakpoints in Europe and parts of Asia was over 50% in 2018. • Currently EUCAST has three standing Subcommittees (Antifungal, Veterinary, Antimycobacterials) and six Ad Hoc Subcommittees (Intrinsic Resistance/Expert Rules, MIC distributions/ECOFFs, CLSI/EUCAST Disk mass/QC development, whole genome sequencing and phenotypic AST, Anaerobic AST) • Breakpoint consultations completed in 2018-2019. – Oral aminopenicillin breakpoints (*H. influenzae* and *S. pneumoniae*) – Definition of the I-category – Carbapenem breakpoints – Piperacillin-tazobactam breakpoints in *H. influenzae* – Tigecycline – Adapting the breakpoint table to the "I" category changes • Upcoming consultations: Aminoglycoside, Temocillin, and Fosfomycin Breakpoints • Activities of the EUCAST Development Laboratory – Developing EUCAST breakpoint table v 9.0 (published January 2019) – Colistin susceptibility testing: Evaluating commercially available methods for broth microdilution, agar dilution, gradient testing, disk diffusion. – Rapid AST directly from blood culture bottles – Disk diffusion methodology for rapidly growing anaerobes – Surveying the quality of antibiotic disks from nine manufacturers. • Redefining the Intermediate Category as Susceptible Increased Exposure – Plan to redefine "I" to prevent clinicians from refraining from using antimicrobial agents if the result is "I". – Rebranded the I-group to emphasize that the strains should still be regarded susceptible if a higher exposure is achieved.
3.	**QCWG Report: Sharon Cullen and Maria Traczewski (Folder 9)** **QCWG Roster**: Sharon Cullen and Maria Traczewski (co-chairholders); Michael Huband (recording secretary); Dana Dressel, Elizabeth Palavecino, Dave Paisey (members present); Patricia Conville, Chris Pillar, Erika Matuschek, Denise Holliday, Janet Hindler (members absent); Susan Munro, Mary York (retired). • Ms. Cullen and Ms. Traczewski stated that new volunteers are needed to join the WG. Interested volunteers should contact them (skcullen@beckman.com; mtrac@clinmicroinst.com). A call for volunteers will be distributed.

Item #	Description

- **Reports on M23 Tier 2 Studies**
  - **Cefepime-enmetatazobactam disk diffusion (DD) ranges**

Drug Name: Cefepime-enmetazobactam (30/20-µg disks)	**WG Votes:** 5/0/5/1 (7 mm ranges approved for all organisms)	
Drug: cefepime-enmetazobactam	**Abbreviation:** FPE	**Previous ID:** cefepime-AAI101
Solvent: Phosphate buffer pH 6.0, 0.1 mol/L / Water	**Diluent:** Phosphate buffer pH 6.0, 0.1 mol/L / Water	**Preparation:** 30/20 µg
Route of administration: IV	**Class**: ß-lactam combination agent	**Subclass:** ß-lactam combination agent
Study Report by: JMI	**Pharma Co:** Allecra Therapeutics	**Control Drug**: piperacillin-tazobactam

QC Strain	Range	% In	Median	Mm	Comments
***E. coli* ATCC 25922**	**32-38**	**97.1%**	**35**	**7**	
***E. coli* ATCC 35218**	32-38	100%	35	7	
***E. coli* NCTC 13353**	~~28-32~~ 27-33	~~95.6%~~ 100%	30	~~5~~ 7	**Recommended routine QC strain (CTX=M-15)** Expanded to 7mm due to distribution & large # @ 28 and 32.
***K. pneumoniae* ATCC 700603**	26-32	98.3%	29	7	
***P. aeruginosa* ATCC 27853**	26-32	99.4%	29	7	

Footnotes:	Add footnote "QC ranges for cefepime-enmetazobactam was established using data from only one disk manufacturer. Disks from other manufacturers were not available at the time of testing."

A motion to accept the disk diffusion QC ranges as listed above for cefepime-enmetazobactam as approved by the QCWG was made and seconded. VOTE: 11 for; 0 against; 1 absent (PASS).

  - **Cefepime DD ranges**

Drug Name: Cefepime (30 µg disks)	Votes: 5/0/5/1 (6 mm range approved) few results at bottom Of range, only 2 values out.

Item #	Description

QC Strain	Range	% In	Median	mm	Comments
***E. coli* ATCC 35218**	**31-37**	**100%**	**34**	**7**	None

A motion to accept the disk diffusion QC ranges for cefepime as approved by the QCWG was made and seconded. VOTE: 11 for; 0 against; 1 absent (PASS).

- **Ozenoxacin MIC QC ranges**

Drug name: Oxenoxacin	Votes: 6/0/5/0 Approved the 3 Gram-positives and NOT the *E. coli* (media variation and out of control QC for ciprofloxacin)

Drug: Ozenoxacin	**Abbreviation:** TBD	**Previous ID:** ??
Solvent: ??	**Diluent:** ??	**Preparation:** ??
Route of administration: ??	**Class:** fluoroquinolone	**Subclass:** des-fluoroquinolone
Study Report by: Dr. Rafael Cantón, Hospital Universitario Ramón y Cajal	**Pharma Co:** Ferrer, S.A	**Control Drug:** (ciprofloxacin and levofloxacin

QC Strain	Range	% In	Mode	Dil	Comments
S. aureus ATCC 29213	0.001-0.004	99.8%	0.002	3	
E. faecalis ATCC 29212	0.015-0.06	99.2%	0.03	3	
E. coli ATCC 25922	0.008-0.06	94%	0.015	4	Control ciprofloxacin 85% (15% out high at 0.03), levofloxacin 100% (top of range). Media variabiliy. 3% out at 0.12 with Lot D and 0.004 with Lots A&B. Request for ranges withdrawn.
S. pneumoniae ATCC 49619	0.008-0.06	99.3%	0.03	4	

A motion to accept the MIC QC ranges for ozenoxacin and *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, and *S. pneumoniae* ATCC 49619 was made and accepted. VOTE: 12 for, 0 against (PASS).

Item #	Description

– **Sulopenem DD QC Ranges**

Drug Name: Sulopenem	**Vote:** 6/0/5/0 add comment for 1 manufacturer of disk

Drug: Sulopenem	Abbreviation: SLP, SULO in current glossary.	Previous ID: CP70429
Solvent: no change	Diluent: no change	Preparation: 2µg disk
Route of administration: Oral and IV	Class: penem	Subclass: penem
Study Report by: Laboratory Specialists, Inc.	Pharma Co: IterumTherapeutics (licensed from Pfizer)	Control Drug: Meropenm

Footnotes:	• **Add footnote:** "QC ranges for Sulopenem was established using data from only one disk manufacturer. Disks from other manufacturers were not available at the time of testing."
Discussion:	• 2, 5 and 10 µg disks evaluated. 2 µg disks 6-11 mm with MICs >2 vs 6-14 with 5 µg disks. • Reproducibility with 3 ESBL, 1 meropenem borderline susceptible and 1 meropenem resistant strains. • Sponsor is suggesting different abbreviations & needs to follow up with STMA

QC Strain	Range	% In	Median	mm	Comments
E. coli ATCC 25922	24-30	99.0%	27	7	2 disks from 1 manufacturer, Add footnote until 2nd manufacturer data available and reviewed

A motion to accept the disk diffusion QC ranges for sulopenem with 2 lots from 1 manufacturer as approved by the QCWG was made and seconded. VOTE: 12 for; 0 against; (PASS).

– **Tedizolid DD QC Ranges**

Drug Name: Tedizolid	Votes: 6/0/5/0 for *S. aureus* Transmitted light 6/0/5/0 for *E. faecalis* – supplemented QC only, troubleshooting guide with pictures 5/1/5/0 for *S. pneumoniae* (opposed wants 18-24)

Item #	Description

Drug: Tedizolid	**Abbreviation:** no change	**Previous ID:** no change
Solvent: no change	**Diluent:** no change	**Preparation:** 2 µg disk
Route of administration: no change	**Class:** oxazolidinone	**Subclass:** no change
Study Report by: Laboratory Specialists, Inc.	**Pharma Co:** Merck & Company, Inc.	**Control Drug**: Linezolid 10 and 30 µg disks

Footnotes:	• Supplemental QC with *E. faecalis* ATCC 29212 to assist with reading proficiency. Acceptable range is 14-21mm.
Discussion	• Initially, the tedizolid 20 µg disk was recommended for testing. • January 2017: Data were presented to CLSI showing scatterplots for *Staphylococcus* spp. with false susceptible disk results using the tedizolid 20 µg disk. Scatterplots of 2 and 5 µg disk (Mfr: Liofilchem) data were presented with the recommendation that the development of a tedizolid 2 µg disk should proceed to a Tier 2 QC study. • Approved but don't publish until disk correlates are established for 20 µg disk. Add 2µg disk when removing 20 µg disk information to avoid confusion. • M02, Subchapter 3.7, Reading Plates and Interpreting Results: If linezolid and tedizolid are tested against *Staphylococcus* spp., the zone diameters need to be read with transmitted light. No change recommended. Propose to add pictures and add to troubleshooting guide (See Below).

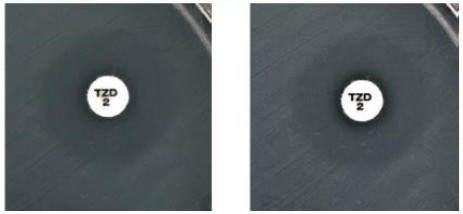
QC Strain	Range	% In	Median	mm	Comments
***S. aureus* ATCC 25923 Transmitted read**	18-24	98.9%	20	7	Lab 2: 13% @ 24. Proposed tighter range, only 2 at 17.
***S. aureus* ATCC 25923 Reflected read**	NA	NA	NA		
***E. faecalis* ATCC 29212**	14-21	97.3%	17	8	Supplemental QC (assist with reading). Lab variability. Lab 1 at bottom (not an outlier). Lab 6 at top.
***S. pneumoniae* ATCC 49619**	18-25	99.8%	22	8	

A motion to accept the DD QC ranges for tedizolid and *S. aureus* ATCC 25923, *E. faecalis* ATCC 29212, and *S. pneumoniae* ATCC 49619 and to add photographs to the troubleshooting guide was made and accepted. VOTE: 12 for, 0 against (PASS).

Item #	Description

Troubleshooting Guide

Antimicrobial agent	QC Strain	Observation	Probable Cause	Comments/Suggested Acton
Tedizolid	E. faecalis ATCC 29212	Zones with *Enterococcus* species are difficult to read	Light growth on MHA	*E. faecalis* ATCC 29212 is provided as supplemental QC to assist in personnel training and assessment of proper reading. Refer to XXX for example picture.



- **Tier 3 QC Process Improvements and MIC Recommendations**
  - **Imipenem-relebactam**
    - The WG proposed that the MIC QC range for imipenem-relebactam and *K. pneumoniae* ATCC BAA-2814 should be changed from 0.06-0.25 to 0.06-0.5.

A motion to change the imipenem-relebactam MIC QC range for *K. pneumoniae* ATCC BAA-2814 to 0.06-0.5 was made and seconded. VOTE: 12 for, 0 against (PASS).

    - The WG agreed that no change in QC ranges was needed for imipenem-relebactam and *K. pneumoniae* ATCC 1705.

  - Eravacycline
    - The WG discussed changing the MIC QC ranges for eravacycline and E. coli ATCC 25922.
    - A range of 0.016-0.12 was proposed; however, the QCWG came to no conclusion.
    - It was suggested that the vote either be tabled to June or voted on at this meeting.

A motion to change the eravacycline MIC QC range for *E. coli* ATCC 25922 to 0.016-0.12 was made and seconded. VOTE: 12 for; 0 against. (PASS).

  - Data for MIC Tier 3 QC was requested.

Item #	Description

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern	Date Reported
S. pneumoniae ATCC 49619	Levofloxacin	0.5-2	Request data/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	Request data/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
H. influenzae ATCC 49247	Moxifloxacin	0.008-0.03	Request data/feedback	80.0% at upper extreme (0.03 µg/mL) of MIC range (results from only one study, Table 3-29) Refer to USCAST Quinolone report V1.2.	Jan-18
E. faecalis 51299	Gentamicin HLAR	Resistant	Request data/feedback	Out of range results (susceptible). Organism stability.	Jun-2017

- Recommendations for follow-up in June 2019

QC Strain (ATCC)	Antimicrobic	Current Range	Action Recommended	Concern	Report Date
P. aeruginosa 27853	Imipenem	20-28	Consider 20-26 (98% in range) or 20-27 mm (99% in range). Issue when analyzing data vs target values. European data support 20-26, US 2001 support 20-27 mm	Zones in the lower part or below range reported (1600 results, including 480 from 2001 M23)	Dec-15
P. aeruginosa 27853	Ceftriaxone	17-23	Request data, reassess range or troubleshooting information.	Colonies within zone causing, out of range	Jun-17
P. aeruginosa 27853	Amikacin	18-26	Consider 20-26 mm. 100% in range, Similar to gentamicin and tobramycin changes in 2012 (new ranges higher, 7 mm).	Out high for many labs, 781 results. No results at 18-19	Jan-18
E. coli 25922	Eravacycline	16-23	Request data to reassess range. Analyze by media.	374 results multiple media lots. Shift to upper end of range with 4% out high	Jan-19
E. coli 25922	Ciprofloxacin	29-37	Request data/feedback.	One source with results are upper end of range.	june-18

- Proposed revision to the M23 QC subchapter
  - Include summary information and report templates as examples

Item #	Description

– Include recent QC process improvements
– Potentially harmonize with the EUCAST study design (revise to harmonize or define supplemental data)
– Strengthen guidance on the of the ISO standard to qualify media and for Tier 1 study conclusions on potential AST impact (eg, pH, inoculum, stability, cations) to be reported and considered in Tier 2 reviews
– It was requested that any additional revisions should be provided to Ms. Cullen.

- A proposal regarding streamlined user QC was made.
  – The QC WG proposed that an AHWG be formed to develop recommendations for streamlining QC for AST.
  – Dr. Humphries will lead the group and requests volunteers to join the WG.
  – The streamlined QC recommendations will be added to M100 and subsequently to M02 and M07 when revised.
  – Concepts presented in M50 and IQCP would be used.

- Table 4A2 and 5A2 for combination agent revisions.
  – Need feedback on changes
  – Discontinued drugs will be moved to an archive table for QC on the Web site.

4.

Methods Application and Interpretation WG (MAIWG) (Folder 6)

MAIWG Roster: Brandi Limbago, Tom Kirn (Co-Chairholders); Trish Simner (Recording Secretary); J. Kristie Johnson, Joseph Kuti, Susan Sharp, Samir Patel, Virginia Pierce, Stephen Jenkins (Members); Darcie Roe-Carpenter, Sandra Richter (Text & Tables liaisons).

Dr. Kirn presented one topic for vote and several informational topics.

- **M100, Appendix A Revisions**
  – The table was renamed as "Suggestions for Confirming Antimicrobial Susceptibility Test Results and Organism Identification for Agents approved by the US Food and Drug Administration for Clinical Use" with the attached footnotes.
    - When testing agents before FDA approval follow Category 1 recommendations when organisms test not susceptible.
    - Excludes those organisms with intrinsic resistance to listed agents as described in Appendix B.
  – The definitions for Categories I, II, and III were updated.

Occurrence and Significance of Resistance and Actions to Take Following Confirmation of Results[a]		
Category I	**Category II**	**Category III**
Not reported or only rarely reported to date	Uncommon in most institutions	May be common, but is generally considered of epidemiological concern
Action Steps:		
• Confirm ID and susceptibility.[a] • Report to infection prevention.	• Confirm ID and susceptibility if uncommon in the institution.[a]	• Confirm ID and susceptibility if uncommon in the institution.[a]

Item #	Description

• Check with public health department to determine appropriate reporting and isolate referral procedures . • Save isolate. **NOTE:** It may be appropriate to notify infection prevention of preliminary findings before confirmation of results.	• Check with infection prevention in the facility to determine if special reporting procedures or additional actions are needed. • Check with public health department to determine appropriate reporting and isolate referral procedures	• Check with infection prevention in the facility to determine if special reporting procedures or additional action are needed.

- The way the drugs are listed in the table has been changed to be sorted by class and subclass. The order is consistent with the listings in Tables 2.
- New agents with FDA approval have been added (eg, ceftazidime-avibactam, ceftolozane-tazobactam, meropenem-vaborbactam, plazomicin) as well as new ECVs (*Shigella* and azithromycin non-wild type).
- Categorical changes were made for some organisms.

Organism	Agents	Category
Enterobacteriales	Ceftazidime-avibactam – R Meropenem-vaborbactam – I or R	II
Enterobacteriales	Colistin– NWT (applies only to those orgnisms speciified in Table G1)	Change from I to II
Escherichia coli, *Klebsiella pneumoniae* complex, *K. oxytoca* and *Proteus mirabilis*	Plazomicin – R (except *P. mirabilis*)	I
Salmonella and *Shigella* spp.[c]	Azithromycin - NWT	II
Acinetobacter baumannii complex	Any carbapenem	Change from II to III
Pseudomonas aeruginosa	Ceftolozane-tazobactam	II
Stenotrophomonas maltophilia	Trimethoprim-sulfamethoxazole – I or R	Change from II to III
Neisseria gonorrhoeae	Azithromycin – NS	I
Staphylococcus aureus	Vancomycin – I[e] Vancomycin – R	II Changed from II to I

Item #	Description
	– The MAIWG approved all changes (10 approved, 0 opposed, 0 abstained). – SC Discussion o The SC needs to decide between Enterobacteriales vs Enterobacteriaceae. Dr. Kirn stated that it is probably time to move in that direction. o A footnote will be added to clarify intrinsic resistance to the listed agents. o Plazomicin has FDA breakpoints but, as yet, has no CLSI breakpoints and should be noted on the table. This the same for tigecycline.
	A motion to accept the Appendix A revisions as presented in the agenda book and the newly updated version was made and seconded. VOTE: 11 for; 0 against; 1 absent. (PASS).
	• **Research Use Only (RUO) AST in Clinical Labs** – It was questioned whether laboratories should use RUO-labeled devices for clinical testing. It was agreed that although they shouldn't be used for clinical testing, many laboratories do so because there is no regulatory-cleared product available (eg, no FDA recognized breakpoints for the drug or with a specific organism, BPs differ from CLSI etc). – There is also confusion around the definitions for RUO, modified FDA cleared, and laboratory developed test (LDT). – Challenges associated with RUO use include: o Physicians need AST results for these patients (new drugs, odd organisms). o New devices are limited in the drugs that can be tested and/or approved. o Manufacturers cannot disclose data on the performance of their devices (good or bad) for RUO combinations. o Many laboratories are confused about these challenges and many hospitals prohibit use of "RUO" products but don't understand the challenges. – CLSI should address this issue because CLSI has BPs that are not FDA approved (ie, endorsing off-label use but do not provide guidance on how to accomplish this). – The MAIWG proposed that an AHWG be formed to develop guidance and education materials for laboratories. Key topics will include: o Define RUO vs *In vitro* device vs laboratory developed tests o Guidance on understanding "RUO" test performance o Risks and benefits of RUO-AST use o Guidance on validating modifications and RUO tests o Guidance on reporting RUO and/or LDT AST tests – The SC endorsed and will form an AHWG. Dr. Humphries has agreed to lead the WG. • **AST of *Burkholderia cepacia* complex** – It was questioned whether testing is accurate by current methods. – Data were presented by Dr. Holly Huse and Dr. Mandy Wootton on cystic fibrosis (CF) patients comparing disk diffusion and BMD and gradient diffusion. o Many CF patients are infected and are difficult to treat due to intrinsic resistance. o Clinicians use AST to determine whether infections can be controlled pre- and post-lung transplant. o There are discrepancies in recommendations for AST between CLSI and EUCAST.

Item #	Description
	– Studies using different methods showed that when compared to BMD, disk diffusion and gradient diffusion did not meet all acceptance criteria for any drugs tested and that differences in AST methods should be considered when CF patients are being evaluated for lung transplant. – Due reproducibility issues, EUCAST does not recommend AST on *B. cepacia* complex as MIC BPs have not been established and the methodology is problematic. – EUCAST Conclusions o BMD was reproducible for minocycline, ciprofloxacin, and chloramphenicol. o Reproducibility was poor for meropenem, cotrimazole, and ceftazidime and very poor for amikacin and piperacillin-tazobactam. o Agar dilution had poor correlation with BMD but slightly better reproducibility than BMD. o Gradient diffusion had poor correlation with BMD and agar dilution. o The EUCAST disk diffusion test was not able to separate wild-type and non-wild type. – The WG proposed that an AHWG be formed to evaluate current methods, BPs etc. and provide recommendations to change or not. o Dr. Sharp will chair an AHWG to investigate. o Dr. Jenkins noted that there are isolates available for study. – The SC endorsed the formation of an AHWG to study the issue. • **Ciprofloxacin: Table 6A Solvents and Diluents** – Table 6A currently states that water is the solvent; however, the powder doesn't dissolve in water. – This disagrees with the current safety data sheet. – It was agreed that a comment regarding consultation with the manufacturer about appropriate solvent should be added to the table. • **Anaerobe WG Report** **Anaerobe WG roster**: Darcie Roe-Carpenter (Chairholder), Kitty Anderson, Diane Citron, Joanne Dzink-Fox, Meredith Hackel, Audrey Schuetz, Steve Jenkins, Laura Koeth, Cindy Knapp. – Agents to be discussed with the BPWG include metronidazole, amoxicillin-clavulanate, ß-lactam inhibitors. – Fidaxomicin drug solubility has been shown to be an issue. This issue is being investigated and methods are being compared. – M11, 9th edition published in November 2018. – The WG discussed whether *Parabacteroides* spp. be included in Appendix B6 (IR for Anaerobic Gram-negative Bacilli). The WG voted to retain the table as is pending additional research. – Other items discussed and in progress o Wording on ß-lactamase testing on *Parabacteroides* was reviewed and retained as currently written. o AST using gradient diffusion was discussed. It was noted that the Antifungal SC will be discussing the possibility of addressing gradient diffusion testing for fungi in some fashion. o There is currently no Piperacillin-tazobactam gradient strip available in the US. Since it is commonly used for anaerobe infections, and there is a medical need, the use of gradient diffusion data along with agar dilution is being evaluated. o Possible updates to the Appendix D antibiogram were discussed. • **Intrinsic Resistance (IR) WG Update**

Item #	Description
	– Significant changes to the IR tables were made in the 29th edition of M100. – The WG is continuing to review other sections of the table for possible revisions.
5.	**M39 WG Update (Folder 13)** **M39 WG Roster**: Janet Hindler, Trish Simner (Co-chairholders); April Abbott (Recording secretary)

Team #1	Team #2	Team #3
Review current M39 Expand specific ways to use local antibiogram for ASP and include guidance for LTCF	Antimicrobial Resistance Surveillance Program Design	IT – Data extraction & presentation
Erdman, Sharon - LEAD	Redell, Mark - LEAD	Das, Sanchita - LEAD
Hindler, Janet - Coordinator	Simner, Patricia - Coordinator	Abbott, April - Coordinator
Johnson, Kristie	Benahmed, Faiza	Ferrell, Andrea
Master, Ron	Morrissey, Ian	Mehta, Jimish
Neuhauser, Melinda	Sader, Helio	Nowak, Michael
Bhowmick, Tanaya	Sievert, Dawn	Stelling, John
	Snippes-Vagnone, Paula	

Dr. Simner provided a report on the status of the M39 revision.

- Outline
  - Chapter 1: Introduction
  - Chapter 2: Information System Design – many changes
  - Chapter 3: The Routine Cumulative Antibiogram
  - Chapter 4: The Enhanced Antibiogram
  - Chapter 5: Multicenter Antibiograms – many changes
  - Chapter 6: The Long Term Care Facility (LTCF) Antibiogram - NEW
  - Chapter 7: Antimicrobial Stewardship Programs - NEW
  - Chapter 8: The Veterinary Antibiogram - NEW
  - Chapter 9: Conclusion
  - Chapter 10: Supplemental Information

- **Terminology Updates**
  - Antibiogram: replaces cumulative antimicrobial susceptibility test data
  - Title Change: "Analysis and Presentation of the Antibiogram"

Item #	Description
	– Breakpoint: replaces interpretive criteria – Antimicrobial: replaces antibiotic – Blood: replaces bloodstream isolate/culture – Empiric: replaces empirical – Healthcare facility: replaces hospital, facility, and institution – Electronic Health Record: replaces Electronic Medical Record • **General Updates** – Remove as much redundancy between subchapters and refer to pertinent subchapters – Each group to work on companion manuscripts – Include a "Frequently Asked Question Section" within the document and on the website – Add a troubleshooting guide both within the document and as a companion manuscript and/or a document placed on the website – Add brief definitions of MDR, XDR, PDR • **Chapter 2 (Information Design Changes) revisions: Provide the a**dvantages and disadvantages of pulling data from the AST instrument, LIS or EHR. • **Chapter 5 (Multicenter Antibiograms):** Provide recommendations for aggregating cumulative AST date outside of a single institution. – Discuss when to use local data versus external data for antibiograms – Differences between single facility antibiograms vs multicenter antibiograms – How to aggregate (with step-by-step instructions) and design reports to communicate results of multifacility antibiograms – Use of multifacility antibiograms by various stakeholders • **New Chapters** – Chapter 6: The Long Term Care Facility (LTCF) Antibiogram – Chapter 7: Antimicrobial Stewardship Programs – Chapter 8: The Veterinary Antibiogram • **Plan Forward** – March 2019: Each group should have material submitted to the M39 WG – March-May 2019: Final revisions – May 2019: Submit for the June meeting – Expected publication: 2020 • **SC Discussion** – It was questioned if a subchapter on bias in surveillance will be added. It was agreed that the subject will be addressed.
6.	**Joint CLSI/EUCAST WG Report**

Item #	Description
	CLSI/EUCAST WG Roster: Janet Hindler, Erika Matuschek (Co-Chairholders); Mariana Castanheira, Sharon Cullen, Laura Koeth, Maria Traczewski (CLSI members); Christian Giske, Gunnar Kahlmeter, Mandy Wootton (recording secretary); John Turnidge (Statistical advisor) (EUCAST members **Ms. Hindler provided an overview of the activities of the WG.** • **The goal is to harmonize the disk diffusion test.** – Harmonize disk content (potency) criteria and criteria for an acceptable disk diffusion test – Harmonize QC by establishing QC ranges and the role and usefulness of QC targets – Harmonize statistical methods for all procedures. • **Disk Content (Potency) Selection** – CLSI: Disk content is decided by pharma based on basic requirements in M23 – EUCAST: Contacted after the disk content for the US market is decided – Ideally, CLSI involvement with disk content selection could assist in standardizing global disk content. – Goal is for CLSI/EUCAST collaboration on disk content selection early in the process • **Disk Content (Potency) Selection Process and Management** – Develop process (step-by-step instructions) for determining optimum disk content for disk diffusion susceptibility testing and insert it into M23 and harmonize with EUCAST SOP 9.1. – Develop process for working with stakeholders to comply with the recommended "science" and determine if data produced during disk content development by either CLSI or EUCAST will be acceptable to stakeholder organizations. • **Disk Content Selection Criteria (typically done before BPs are established)** – One disk content for all species – An increase in zone diameters of 2-3 mm with each $\log_2$ decrease in MIC for non-wild type (NWT) isolates. – Inhibition zone diameters between 15 and 35 mm for wild type (WT) isolates of relevant species with an ECV/ECOFF close to 15 mm for the least susceptible species. – Optimal separation between WT and NWT isolates if NWT isolates exist. – Optimal separation between NWT isolates with low MICs and high MICs. • **Disk Content Testing Process** – Tier 1 testing involves initial screening of at least 10 different disk contents to select 2-4 disk contents for Tier 2 studies. – Tier 1 analysis is for identifying 2-4 disk contents with greatest discriminatory power (eg, the part of the curve where the zone diameter increment between MIC values is the greatest, ie, the steepest part of the curve) – Tier 2 testing involves further investigation of the 2 - 4 selected disk contents with 30-60 isolates and relevant species or organism groups. • **Harmonizing Disk Diffusion QC involves:** – Developing a bridging protocol for CLSI to accept/use EUCAST QC data (with QC WG).

Item #	Description
	– Developing procedures for validating disks if only available from one manufacturer in Tier 2 QC study. – Retrospectively examining some recent QC study data to determine if data from 7 labs is statistically more significant than data from 6 or 5 labs. • **Next steps for the WG** – Draft SOP #1 (disk content selection) for agenda book June 2019 – SOP #2 (Pharma-CLSI process) – CLSI DD WG will work with CLSI leadership and Pharma to begin defining the "process" – CLSI & EUCAST continue work on DD QC harmonization • **SC Discussion** – Dr. Miller questioned if the WG will suggest including error rates on the graphs. Ms. Hindler stated breakpoints are not know at this point but knowing how the disk content was selected might help understand if a test is viable. Dr. Kahlmeter stated that a number of different breakpoints could be tried and generate the error rates and show what breakpoints work and which don't. – Dr. Giske: Try different BP and compromise between clinical BP – Mr. Brasso stated that it would have been desirable to include manufacturers on the WG and is hoping for better communications. FDA has changed requirements of FDA submissions and wonder how that will affect submission. Ms. Hindler stated that from her discussions with FDA, the joint work should not be an issue. – Dr. Shawar suggested that a representative of CDER and/or CDRH be added to the WG. – Dr. Kahlmeter reminded everyone that when CLSI and EUCAST use the same disk content (potency), the QC ranges and MICs are the same. By harmonizing the process, the results are the same and both can review the data. – Dr. Castanheira noted that single disk content and harmonization will make it easier for manufacturers and users and for the SC to make decisions. – Dr. Hardy suggested that the isolates to be tested should be international and geographically dispersed. Dr. Kahlmeter suggested that the manufacturer needs to know what the specific targets are when developing the drug. – Dr. Ambler agreed with the idea of one disk content as it helps the sponsor with cost and timelines. She asks if a WG to present this data on disk content and get approval before the manufacturer presents the breakpoint data. – Dr. Moeck questioned if there will be guidance for combination agents. The WG has plans to address this issue. – It was noted that a disk is needed for clinical trials in population of resistant organisms.
7.	**<u>Outreach WG (ORWG) Report (Folder 8)</u>** **ORWG Roster:** Janet Hindler, Audrey Schuetz (Co-Chairholders); Stella Antonara (recording secretary); April Abbot, April Bobenchik, Mariana Castanheira, Graeme Forrest, Angie Charnott-Katsikas, Megan Hickey (CLSI staff), Romney Humphries, Patrick McGinn (CLSI staff), Nicole Scangarella-Oman, Paula Snippes Vagnone, Lars Westblade (Members) **Ms. Hindler provided an update from the Outreach WG.** • A reminder of the goals of the ORWG were provided. – Educate practicing clinical microbiologists and health care professionals about AST practices and recommendations. – Provide resources to facilitate individuals in their understanding and implementation of CLSI AST recommendations.

Item #	Description
	– Solicit suggestions from members of other CLSI Working Groups for educational activities; encourage AST SC volunteers to engage in these educational activities • An overview of the latest edition (January 2019) of the CLSI AST New Update was provided. • The Spring 2019 newsletter is in progress and will likely include: – A feature article on Selective Reporting (drug suppression) Clinical AST Reports – A case study on *Pseudomonas putida* – Practical tips for different ECVs and the activity of echinocandins and *C. parapsilosis* – A hot topic on metallo-ß-lactamase producers • A welcome gathering for new AST volunteers was held before the Sunday reception. – There were 35 new AST volunteers at the meeting. The orientation slides were provided to the new attendees. – Information on how to join a WG were provided to the new attendees. – The WG will draft a flier that lists needs such as WGs that need help and organisms and data needed. • SC Meeting Workshops for 2019 include: – January 2019 - "Recent Advances in PK/PD and Its Use in Setting Breakpoints" – June 2019 – "Molecular Characterization of Antimicrobial Resistance for Healthcare in 2019" • Webinars and Presentations for 2019 include: – The annual M100 update will be provided on Wednesday, February 20th from 1:00 – 2:30 PM Eastern (US) time and on Thursday, February 21st from 3:00 – 4:30 Pm Eastern (US) time. Dr. Humphries and Dr. Schuetz will be presenting. – CLSI-SIDP ACCP Annual Webinar: "Merging Microbiology and Stewardship: Making the most of 2019 CLSI updates on antimicrobial susceptibility testing for your stewardship activities. Dr. Lewis will be presenting. – CAP-CLSI Joint Webinar: Considering Taxonomy changes and AST was one of the possible topics. • Archived Webinars include: – CAP-CLSI Webinar: Resources for Implementation of MALDI-TOF MS in the Clinical Microbiology Laboratory (N=127 sites registered): Presented by Carey Ann Burnham and Kaede Oda Sullivan – Preparation, Presentation and Promotion of Cumulative Antibiograms To Support Antimicrobial Stewardship Programs (N=97 sites registered): Presented by Sharon Erdman and Trish Simner • 2019 ASM Microbe Lectures – ASM Award for Research and Leadership in Clinical Microbiology award lecture: "Strategies for addressing the newest CLSI developments for detecting and reporting AR" (Steve Jenkins) – "AST support outside the clinical laboratory: the role of reference and public health laboratories" (Jean Patel) – "FDA 's role in increasing the reliability and availability of essential ASTs" (John Farley) • New ORWG Projects – Help develop a brief You-tube type tutorial on navigating the website. – Bench to bedside series for clinicians and trainees – How to implement testing of new drugs in clinical labs – Additional clinical laboratory technologist materials

SUMMARY MINUTES Tuesday, 29 January 2019	
Item #	**Description**
8.	**Rationale document update** **Dr. Humphries provided an update on the development of rationale documents.** • A medical writer has been hired to assist with drafting the rationale documents. • The documents provide a summary of the data and decisions made for new or revised breakpoints. These are submitted to the FDA docket for review and approval. • The rationale document status was provided. – The colistin document has been published and posted on the FDA website. – The Fluoroquinolone document for *Pseudomonas* and *Acinetobacter* has been submitted for final approval. **NOTE:** The Fluoroquinolone document has now been published and has been submitted to the FDA. – The *Acinetobacter*-carbapenems document is being prepared for editorial review and is scheduled for a February 2019 publication. – The *Neisseria gonorrheoae*-azithromycin document is under project manager review and is expected to publish in late February or early March. – The *S. aureus*-ceftaroline draft was completed and is being reviewed. – The *Enterococcus*-daptomycin draft has been reviewed but was on hold pending the discussion during the January meeting. • The next steps include: – Determining the next set of priorities. – Determine how to handle ECVs.
9.	**M23 Update (Folder 12)** **M23 WG Roster:** Matt Wikler (Chairholder); Romney Humphries (recording secretary), Timothy Bensman, Mariana Castanheira, Patti Conville, Sharon Cullen, Avery Goodwin, Linda, Miller, Stephanie Mitchell, Greg Moeck, David Nicolau, Margaret Ordonez Smith de Danies, Michael Satlin, Simone Shurland, Hui Wang **Dr. Wikler provided an update on the revision of M23.** • A Co-chairholder representing the FDA will be appointed. • A large group was appointed to cover all needed expertise and required perspectives. • The plan for revision was reviewed. – Proposed areas for revision were reviewed. – WG members were assigned to evaluate specific areas and provide suggestions at June 2019 WG meeting. – Between January and June, the members and groups evaluating specific areas will hold conference calls to prepare for the June meeting. – During the June 2019 meeting, suggestions and recommendations will be discussed. – Between June and December 2019, groups will discuss and refine their recommendations for presentation at the January 2020 meeting. – After the January meeting, revisions will be made to the draft and the draft will be included in the materials for the June 2020 meeting. • Items to evaluate for possible revision were discussed. – Possible modification of the acceptable criteria for minor and major discrepancies between disk diffusion and broth dilution methods. – Harmonization of disk content with EUCAST. – Clarifying language regarding the use of M23 by Antifungal and VET Subcommittees. – Including an intermediate breakpoint for disk diffusion when one does not exist for broth dilution.

SUMMARY MINUTES Tuesday, 29 January 2019	
Item #	**Description**
	– Revisions needed to address CLSI being designated as an official standards development organization by the FDA. – Revisions to the QC Chapter as suggested by the QCWG. – Clarifying the requirements for disk diffusion testing media. – Defining the variability of broth microdilution for each drug. – Clarifying the criteria for disk evaluation and performance. – Potential revision of the ECV language. – Clarifying the circumstances for the SDD category and using doses above those indicated by regulatory organizations.
10.	Dr. Weinstein thanked the participants for their attention and continued hard work. The meeting was adjourned at 11:30 PM Eastern (US) time.

Upcoming Meetings of the Subcommittee on Antimicrobial Susceptibility Testing:

16 – 18 June 2019 at the Westin Galleria, Dallas, Texas, USA (Agenda material submission due date – 10 May 2019)
26 – 28 January 2020 at the Tempe Mission Palms Hotel, Tempe, Arizona, USA (Agenda material submission due date – 6 December 2019)
14 – 16 June 2020 at the Hyatt Regency Baltimore Inner Harbor, Baltimore, Maryland, USA (Agenda material submission due date – 8 May 2020)

ACTION ITEMS		Responsible
1.	Form new AHWGs on: • Using RUO AST in Clinical Laboratories (R. Humphries) • Streamlining QC for New Agents (R. Humphries) • Revisions to Reference BMD & New Dispensing Systems (K. Sei) • AST of Non-Enterobacteriaceae (including *Stenotrophomonas*) (D. Hardy) • High Inoculum Cefazolin Testing (CIE) (S. Butler-Wu, T. Dingle) • *Burkholderia cepacia* complex AST (S. Sharp) • Table 1 Placement (T. Simner, G. Eliopoulos) • Aminopenicillin (aPCN) and aPCN/BLI BPs (P. Edelstein)	Staff and proposed chairholders (In progress)
2.	Perform reproducibility testing with cefiderocol disks for all four organisms particularly for resistant isolates.	Sponsor

Summary of Passing Votes			
#	**Motion Made and Seconded**	**Results***	**Page**
1.	To accept the summary minutes from the June 2018 subcommittee meeting.	12-0-0-0; PASS	8
2.	To accept the disk diffusion breakpoints for cefiderocol and *Enterobacteriaceae* (S = ≥16; I = 12-15; R = ≤11). **NOTE:** Vote to be confirmed after additional reproducibility testing data is reviewed.	10-0-1-1; PASS	17
3.	To accept the disk diffusion breakpoints for cefiderocol and *P. aeruginosa* (S = ≥18; I = 13-17; R = ≤12) with a 5 mm intermediate range. **NOTE:** Vote to be confirmed after additional reproducibility testing data is reviewed.	10-0-1-1; PASS	17
4.	To accept the disk diffusion breakpoints for cefiderocol and *Acinetobacter* spp. (S = >15; I = 11-14; R = <10) with a 4 mm intermediate range. **NOTE:** Vote to be confirmed after additional reproducibility testing data is reviewed.	9-1-1-1; PASS	17
5.	To accept the disk diffusion breakpoints for cefiderocol and *S. maltophilia* (S = >17; I = 13-16; R = <12) with a 4 mm intermediate range. **NOTE:** Vote to be confirmed after additional reproducibility testing data is reviewed.	9-1-1-1; PASS	18
6.	To accept the proposed breakpoints for daptomycin against *E. faecium* as SDD = ≤ 4 µg/mL; R = ≥8 µg/ml) with the comment, "The SDD category is based on a dosage regimen of 8–12 mg/kg/day in adults and is intended for serious infections due to *Enterococcus* spp. Consultation with an infectious diseases specialist is recommended"	12-0-0-0; PASS	19
7.	A motion to approve the BPs for *Enterococcus* spp. other than *E. faecium* with comment about dose [S = ≤ 2; I = 4; R = ≥8] with a comment that the breakpoint is based on a dosage regimen of 6mg/kg/mL in adults was made and seconded. VOTE: 12 for; 0 against (PASS).	12-0-0-0; PASS	19
8.	To accept the disk diffusion QC ranges for cefepime-enmetazobactam as approved by the QCWG. **QC Strain** / **Range** *E. coli* ATCC 25922 — 32–38 *E. coli* ATCC 35218 — 32–38 *E. coli* NCTC 13353 — 27-33 *K. pneumoniae* ATCC 700603 — 26-32 *P. aeruginosa* ATCC 27853 — 26-32	11-0-0-1; PASS	28
9.	To accept the disk diffusion QC ranges for cefepime as approved by the QCWG. **QC Strain** / **Range** *E. coli* ATCC 35218 — 31-37	11-0-0-1; PASS	29
10.	To accept the MIC QC ranges for ozenoxacin and *S. aureus* ATCC 29213, *E. faecalis* ATCC 29212, and *S. pneumoniae* ATCC 49619.	12-0-0-0; PASS	29

<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</th></tr>
<tr><td></td><td><table><tr><th>QC Strain</th><th>Range</th></tr><tr><td>S. aureus ATCC 29213</td><td>0.001-0.004</td></tr><tr><td>E. faecalis ATCC 29212</td><td>0.015-0.06</td></tr><tr><td>S. pneumoniae ATCC 49619</td><td>0.008-0.06</td></tr></table></td><td></td><td></td></tr>
<tr><td>11.</td><td>To accept the disk diffusion QC ranges for sulopenem with 2 lots from 1 manufacturer as approved by the QCWG.<table><tr><th>QC Strain</th><th>Range</th></tr><tr><td>E. coli ATCC 25922</td><td>24-30</td></tr></table></td><td>12-0-0-0; PASS</td><td>30</td></tr>
<tr><td>12.</td><td>To accept the DD QC ranges for tedizolid and S. aureus ATCC 25923, E. faecalis ATCC 29212, and S. pneumoniae ATCC 49619 and to add photographs to the troubleshooting guide.<table><tr><th>QC Strain</th><th>Range</th></tr><tr><td>S. aureus ATCC 25923
Transmitted read</td><td>18-24</td></tr><tr><td>E. faecalis ATCC 29212</td><td>14-21</td></tr><tr><td>S. pneumoniae ATCC 49619</td><td>18-25</td></tr></table></td><td>12-0-0-0; PASS</td><td>31</td></tr>
<tr><td>13.</td><td>To change the imipenem-relebactam MIC QC range for K. pneumoniae ATCC BAA-2814 to 0.06-0.5.</td><td>12-0-0-0; PASS</td><td>32</td></tr>
<tr><td>14.</td><td>To change the eravacycline MIC QC range for E. coli ATCC 25922 to 0.016-0.12.</td><td>12-0-0-0; PASS</td><td>32</td></tr>
<tr><td>15.</td><td>To accept the Appendix A revisions as presented in the agenda book and the newly updated version.</td><td>11-0-0-1; PASS</td><td>36</td></tr>
</table>

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

Respectfully submitted,

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