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Meeting Title:	**Subcommittee on Antimicrobial Susceptibility Testing (AST)**	**Contact:**	mhackenbrack@clsi.org
Meeting Date:	Sunday – Tuesday, 16 – 18 June 2019		
Start Time:	Sunday, 16 June – 7:30 AM Monday, 17 June – 7:30 AM Tuesday, 18 June – 8:00 AM	**End Time:**	5:00 PM 5:30 PM 11:00 AM
Meeting Purpose:	The purpose of this meeting is to to review and discuss AST WG and SC business in preparation for publication of the next edition of M100 (30th ed). Revision progress on M23 and M39 will also be discussed.		
Requested Attendee(s):	SC Chairholder, Vice-chairholder, Members, Advisors, and Reviewers; Expert Panel on Microbiology Chairholder and Vice-chairholder; Interested Parties; CLSI Staff (see SC roster)		

Attendee(s):	
Melvin P. Weinstein, MD **Chairholder**	**Rutgers Robert Wood Johnson Medical School**
James S. Lewis, PharmD, FIDSA **Vice-chairholder**	**Oregon Health and Science University**
Members Present:	
Sharon K. Cullen, BS, RAC	Beckman Coulter, Inc. Microbiology Business
Marcelo F. Galas	Pan American Health Organization
Howard Gold, MD, FIDSA	Beth Israel Deaconess Medical Center
Romney M. Humphries, PhD, D(ABMM)	Accelerate Diagnostics, Inc.
Thomas J. Kirn, MD, PhD	Rutgers Robert Wood Johnson Medical School
Brandi Limbago, PhD	Centers for Disease Control and Prevention
Amy J. Mathers, MD, D(ABMM)	University of Virginia Medical Center
Tony Mazzulli, MD, FACP, FRCP(C)	Mount Sinai Hospital
Michael Satlin, MD, MS	New York Presbyterian Hospital
Audrey N. Schuetz, MD, MPH, 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.
Janet A. Hindler, MCLS, MT(ASCP)	Los Angeles County Department of Health
Elizabethm Hirsch, PharmD	University of Minnesota College of Medicine
Stephen G. Jenkins, PhD, D(ABMM), F(AAM)	Weill Cornell Medicine
Linda A. Miller, PhD	CMID Pharma Consulting
Greg Moeck, PhD	VenatoRx Pharmaceuticals
Sumathi Nambiar, MD	FDA Center for Drug Evaluatin and Research (CDER)
Navaneeth Narayanan, PharmD	Ernest Mario School of Pharmacy, Rutgers University
Kiyofumi Ohkusu, PhD	Tokyo Medical University
Robin Patel, MD	Mayo Clinic
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

Barbara L. Zimmer, PhD	Beckman Coulter, Inc.
Reviewers Present	
April Abbott, PhD	Deaconess Hospital Laboratory
Kevin Alby, PhD, D(ABMM)	UNC Health
Jane E. Ambler, PhD	Wockhardt, Morton Grove Pharmaceuticals
Victoria Emma Anikst, BA, CMS, M(ASCP)cm	UCLA Health
Robert Bowden, BS	Tufts University Sackler School of Graduate Biomedical Sciences
Kendall Bryant, PhD, D(ABMM)	Kaiser Permanente
Shelley Campeau, PhD, D(ABMM)	Accelerate Diagnostics, Inc.
Darcie E. Carpenter, PhD	IHMA
Patricia S. Conville, MS, MT(ASCP)	FDA Center for Devices and Radiological Health
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
Sharon M. Erdman, PharmD	Purdue University College of Pharmacy/Ezkenazi Health Pharmacist
German Esparza, BSc	Proasecal SAS Colombia
Andrea L. Ferrell, MLS^{CM}(ASCP)	Becton Dickinson
Robert K. Flamm, PhD	JMI Laboratories
Dulini Gamage	Accerlate Diagnostics, Inc.
Avery Goodwin, MS, PhD	FDA Center for Devices and Radiological Health
Dwight J. Hardy, PhD	University of Rochester Medical Center
Andre Hsiung, MS(ASCP)	Hardy Diagnostics
Michael D. Huband, BS	JMI Laboratories
Holly Huse, PhD, D(ABMM), M(ASCP)^{cm}, PHM	Huntington Hospital
Kristie Johnson, PhD, D(ABMM)	University of Maryland
Ronald N. Jones, MD	USCAST
James H. Jorgensen, PhD	University of Texas Health Science Center
Scott B. Killian, BS	Thermo Fisher Scientific
Susan M. Kircher, MS, MT(ASCP)	BD Diagnostic Systems
Laura M. Koeth, MT(ASCP)	Laboratory Specialists, Inc.
Peggy Kohner, BS, MT(ASCP)	Mayo Clinic
Sarah Blaine Leppanen, MT(ASCP)	Blaine Healthcare Associates, Inc.
Nike Litchfield, BS, MS	BD Diagnosticsa
Zabrina Lockett	Beckman Coulter
David Lonsway, MMSc	Centers for Disease Control and Prevention
Dyan Luper, BS, MT(ASCP)SM, MB	BD Diagnostics
Sandra McCurdy, MS	Melinta Therapeutics, Inc.
Rod Mendes, PhD	JMI Laboratories
Stephanie L. Mitchell, PhD, D(ABMM)	University of Pittsburgh and Children's Hospital of Pittsburgh of UPMC
Ian Morrissey, PhD	IHMA Europe Sàrl
Susan O'Rourke, BS	BD Diagnostics
Elizabeth Palavecino, MD	Wake Forest Baptist Medical Center
Jean B. Patel, PhD, D(ABMM)	Beckman Coulter, Inc.
Chris Pillar, PhD	Micromyx, LLC

Mark A. Redell, PharmD	Melinta Therapeutics
Morgan A. Pence, PhD, D(ABMM)	Cook Children's Medical Center
Amity L. Roberts, PhD, D(ABMM)	LabCorp
Helio S. Sader, MD	JMI Laboratories
Nicole Scangarella-Oman, MS, BS	GlaxoSmithKline
Dale A. Schwab, PhD, D(ABMM)^{cm}	Quest Diagnostics Infectious Disease
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.
Simone M. Shurland	FDA Center for Devices and Radiological Health
Dawn M. Sievert, PhD	Centers for Disease Control and Prevention
Paula M. Snippes Vagnone, MT(ASCP)	Minnesota Department of Health
Laura Stewart, MS, RAC	BD Diagnostics
Gregory G. Stone, PhD	Pfizer, Inc.
Susan Thomson	MAST Group
Lauri D. Thrupp, MD	University of California Irvine Medical Center
Maria M. Traczewski, BS, MT(ASCP)	The Clinical Microbiology Institute
Tam Van, PhD, D(ABMM)	Harbor-UCLA Medical Center
Hui Wang, MD	Peking University People's Hospital
Nancy E. Watz, MS, MT(ASCP), CLS	Stanford Health Care
Eric Wenzler, PharmD, BCPS, AAHIVP	University of Illinois at Chicago
Matthew A. Wikler, MD, FIDSA, MBA	IDTD Consulting
Guests (Non-SC-roster attendees)	
Sarah Becket	Johns Hopkins Hosptial - Pathology
Timothy Bensman, PharmD, PhD	FDA Center for Drug Evaluatin and Research (CDER)
Melissa Boddicker	Merck
MaryAnn Brandt	Norman Regional Health System
Jeffrey Brocious	FDA Center for Devices and Radiological Health
Cecilia Carvalhaes	JMI Laboratories
Veronica Mas Casullo	Allergan
Susan Cusick	VenatorRx Pharmaceuticals
Dmitri Debubov	Allergan
David Fam	Shionogi
John Farley	FDA
Kelly Flentie	Selny Diagnostics
Andrew Fuhrmeister	JMI Laboratories
Momoko Fujisaki	Eiken Chemical Co., LTD.
Corey Fyfe	Tetraphase
Barbara Gancarz	bioMérieux USA
Axel Gianetti	bioMérieux
Alice Gray	bioMérieux USA
Andrew Henderson	Princess Alexandra Hospital, Brisbane Australis
Ann Howell	Shionogi
Antonieta Jimiénez	Inciensa-Costa Rica/ PanAmerican Health Organization
Brian Johnson, CEO	IHMA, Inc.
Cherece Jones	bioMérieux
Rianna Malherbe	Hardy Diagnostics
Lisa Mayens	bioMérieux

Roberto Melano	Public Health Ontario/PanAmerican Health Organization
Alita Miller	Entasis Therapeutics
Ruel Mirasol	UCLA
Alice Ngo	Beckman-Coulter, Sacramento
Sean Nguyen	Shionogi, Inc.
Chie Ohno	Eiken Chemical Co., LTD.
Susanne Paukner	Nabriva Therapeutics
Janet Raddatz	MRL
Jean-Yves Ressot	bioMerieux
Todd Riccobene	Allergan
Nilia M. Robles Hernandez	bioMérieux
Jacquelyn Rosenberger	FDA
Barbara Schenk	BD
Linda Schuermeyer	bioMerieux, Inc.
Alisa Serio	Paratek
Kimiyo Shono	Shionogi
Eric Stern	Selux Diagnostics
Miki Takemura	Shionogi
Andy Townsend	Pfizer
Allison Tsan	UCLA Health
Wolfgang Wicha	Nabriva Therapeutics
Yoshinori Yamano	Shionogi
Steven Yan	FDA-CVM
Lynn Yaolin	Allergan PLC.
Jewell Yap	UCLA
Mari Ari Yasu	Shionogi, Co., Ltd.
Staff:	
Katie Barnett	**CLSI**
Kathy Castagna,MS, MT(ASCP)CT, MB	**CLSI**
Glen Fine, MS, MBA, CAE	CLSI
Emily J. Gomez, MS, MLS(ASCP)MB	CLSI
Marcy L. Hackenbrack, MCM, M(ASCP)	CLSI
Christine Lam, MT(ASCP)	CLSI

OPENING PLENARY AGENDA Monday, 17 June 2019 Dallas 1 & 2								
Item #	**Item Title**	**Start**	**End**	**Length (Min)**	**Category**	**Presenter**	**Folder**	**Page(s)**
1	Welcome and Opening Remarks	10:30 AM	10:35 AM	5	N/A	Dr. Weinstein	N/A	7
2	Agenda and January 2019 Meeting Summary	10:35 AM	10:40 AM	5	VOTE	Dr. Weinstein	2	7
3	Updates to Disclosures	10:40 AM	10:45 AM	5	Update	Dr. Weinstein	3	7
4	CLSI Update	10:45 AM	10:50 AM	5	Update	Mr. Fine	N/A	7
5	Table 1 Placement AHWG Presentation	10:50 AM	11:50 AM	60	Presentation Vote	T. Simner G. Eliopoulos	5	7-12
6	Quality Control WG Report	11:50 AM	12:20 PM	40	Report	S. Cullen M. Traczewski	9	12-17
	Luncheon	**12:30 PM**	**1:30 PM**	**60**				
7	Breakpoint WG Report	1:30 PM	3:30 PM	120	Report Votes	J. Lewis M. Satlin G. Eliopoulos	5	17-25
	Break	**3:30 PM**	**3:45 PM**	**15**				
8	Methods Application & Interpretation WG	3:45 PM	4:45 PM	60	Report Votes	B. Limbago T. Kirn	6	25-31
9	Text and Tables WG Report	4:45 PM	5:15 PM	30	Report	A. Bobenchik S. Campeau	10	31-33
10	M39 WG Report	5:15 PM	5:30 PM	10	Update	J. Hindler T. Simner	N/A	33-35
	Adjournment	5:30 PM						

CLOSING PLENARY AGENDA Tuesday, 18 June 2019 Dallas 1 & 2								
Item #	**Item Title**	**Start**	**End**	**Length (Min)**	**Category**	**Presenter**	**Folder**	**Page(s)**
1	Opening Remarks	8:00 AM	8:05 AM	5	Remarks	M. Weinstein	N/A	
2	Methods Development & Standardization WG Report	8:05 AM	10:00 AM	115	Report Vote(s)	B. Zimmer D. Hardy	7	36-44
	Break	**10:00 AM**	**10:15 AM**	**15**				
3	Outreach WG Report	10:15 AM	10:30 AM	15	Report	J. Hindler A. Schuetz	8	44-45
4	M23 WG Report	10:30 AM	11:00 AM	30	Report	M. Wikler A. Goodwin	11	45-46
	Closing Remarks and Adjournment	11:00 AM		N/A	Remarks	M. Weinstein		

Upcoming Meetings of the Subcommittee on Antimicrobial Susceptibility Testing:

26 – 28 January 2020 in Tempe, Arizona, USA (Agenda material submission due date – Wednesday, 11 December 2019)
14 – 16 June 2020 in Baltimore, Maryland, USA (Agenda material submission due date – Friday, 8 May 2020)
24 – 26 January 2021 in Arlington, Texas, USA (Agenda material submission due date – Friday, 11 December 2020)

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SUMMARY MINUTES	
Item #	**Description**
Monday, 17 June 2019 (NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2019 June AST Plenary Presentations)	
1.	**Opening Remarks: Dr. Mel Weinstein** Dr. Weinstein opened the meeting at 10:30 AM Eastern (US) time by welcoming the attendees and thanking them for their participation. • He thanked Dr. Wikler and Dr. Miller for their training session on M23 and to those involved in the educational session for the excellent presentations and discussion. • He reported that the rationale document pipeline is active and thanked Dr. Humphries and Ms. Castagna for their efforts. – The azithromycin and *N. gonorrheoae* rationale document has published and is available on the CLSI Website – In progress are the carbapenem/*Acinetobacter* and daptomycin/*Enterococcus* documents. • He expressed gratitude to Dr. Schuetz, Ms. Hindler, and the Outreach WG for the excellent, recently published AST Newsletter. • He announced that Dr. Stephen Jenkins is retiring and congratulated him on his retirement.
2.	**January 2019 Meeting Summary Review and Vote** • The summary minutes from the January 2019 AST meeting were reviewed. There were no changes requested.
	A motion to accept the summary minutes from the January 2019 subcommittee meeting was made and seconded. VOTE: 12 for 0 against (Pass).
	• The approved summary minutes have been posted on the CLSI website and can be accessed using the following link to the January 2019 AST Meeting Files.
3.	**Updates to Disclosures** Dr. Weinstein requested any updates to the Disclosure of Interest summary. There were no updates requested.
4.	**CLSI Update: Mr. Glen Fine** Mr. Fine provided a brief CLSI update and expressed his gratitude to all the volunteers for their time and commitment. • New staff members were introduced. – Ms. Christine Lam and Ms. Emily Gomez (Project Managers) will be supporting the Microbiology Expert Panel and the Susceptibility Testing Subcommittees – Ms. Katie Barnett (Director of Membership) was also in attendance filling in for Ms. Megan Hickey. • Mr. Fine reported that M23 is now on the Website, free to view and/or download (M23 Free)
5.	**Table 1 Working Group Report: Dr. Trish Simner (Folder 5, Items 4A-4C)**

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	WG Roster: Trish Simner, George Eliopoulos (Co-Chairholders); Tanaya Bhowmick (absent), April Bobenchik, Carey-Ann Burnham, Virginia Pierce, Barth Reller (absent), Sandra Richter, Lauri Thrupp (Members) • **Background for the reformation of the Table 1 WG was provided.** – During the January 2019 meeting, presentations by the sponsors of minocycline and cefiderocol advocated placing both antimicrobial agents into Table 1 Group A ("primary test and report"). – The requests led to debate regarding the characteristics that qualify an antimicrobial agent for placement into Group A for a given organism or organism group. – The discussion focused on requests for placement of newer agents in Group A while older drugs with no sponsor advocate remain in Group B. – The discussions led to the formation of a reconstituted Table 1 WG to review the issues. • **Historical Background on Table 1 was provided.** – In his presentation, Dr. Thrupp noted that the original intent of the different groups was to present the concept of "cascade reporting". In an attempt to promote antimicrobial stewardship, the idea being to guide laboratories to test and report more narrow spectrum agents before reporting higher-level, broad-spectrum agents. – The table placement's intended use seems to have been lost over time. • **The WG's tasks were reviewed and discussed.** – Determine if Groups A and B should remain separate or be merged. o The AHWG agreed that it is important to retain the hierarchy to provide guidance to smaller laboratories regarding cascade reporting. – Determine if CLSI should revert to the FDA-approved terminology from FDA indications for clinical use. o The original intent of Table 1 was for agents to be included in Table 1 if they were FDA approved, without a need to be specifically cleared or have a clinical indication for use with a specific microorganism-antimicrobial agent combination. o The AHWG unanimously voted to confirm the use of FDA-approved agent terminology. This will be brought forward to the Text and Tables WG. – Origin of the term "Optional" in the Group B header and how to clarify its meaning if retained. o The AHWG agreed to delete the abbreviated definitions to the test/report groups headers. o Full definitions will be added to the top of the tables o SC Discussion ▪ Dr. Carpenter noted that "optional" was added because laboratories were being cited by inspectors for not testing Group B drugs. ▪ Dr. Miller agreed that the longer definitions should be up front but believed the language is clear. She noted that the term "optional" is not needed because the language already in use is explanatory (eg, suggested, may be tested, etc.).

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	▪ Dr. Simner reminded the participants that the ultimate decision on what drugs should be tested and reported is institution dependent. ▪ Ms. Cullen agreed that the suggest changes provide better guidance and that the language should be clarified and communicated to CAP and CMS so that laboratories are not cited when they do not test the "optional" antimicrobial agents. ▪ Dr. Kirn suggested that hyperlinks be added to the comments in the electronic versions of the document. **NOTE:** Links are already available in the Eclipse version of M100. – Determine how the tables should be formatted. The AHWG suggested: o The instructions for use will be moved closer to the beginning of Table 1. The intent is to remind users that the groupings are "suggested" and not mandatory. o The short definitions will be removed from the side headers and full definitions will be placed directly in the table. – Determine how the groups should be assigned. o Current recommendations for placement include considerations for: ▪ Clinical efficacy ▪ Resistance prevalence and minimizing resistance emergence ▪ Cost ▪ FDA indications for use ▪ Current recommendations for primary and alternative use ▪ Use for infection control purposes o The criteria for group placement were presented in a simpler way (see draft tables below). ▪ **Group A**: First-line drug choices for clinical use (drugs that should be tested and reported every time) ▪ **Group B**: Drugs that are not necessarily first-line but for which results may need to be available on the same day as the Group A drug results ▪ **Group C**: Drugs for which it would be rare that clinicians would need to have the result on the first day but might be requested on a subsequent day (phrased this as "typically by clinician request only") o SC Discussion ▪ Dr. Miller suggested that this information should be added to the new edition of M23. ▪ Dr. Kirn suggested that clinical efficacy be noted for organisms in Group in A. ▪ Dr. Edelstein noted that recommending to always test and report may not be correct. Some of these drugs may not be reported based on infection site; therefore, caveats based on infection site need to be included. He suggested that the language be softened and refer to the footnotes. ▪ Dr. Satlin suggested that now that the framework is available, the next step is to determine where to place all drugs. He suggested that a caveat is needed for Group C to help laboratories that need to always report Group C drugs due to known local resistance. ▪ Dr. Mathers noted that the Table 1 WG needs to collaborate with the M23 WG to ensure that the recommendations for table placement are added to M23.

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	▪ Dr. Palavecino noted that in some cases, there are discrepancies with Tables 2 (eg, Group A streptococci should always be tested for penicillin but a comment in Table 2 states to not test). • Suggestions for reworked definitions and tables were presented.

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

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Group	Inclusion Requirements	When to Report
Group C – includes alternative or supplemental antimicrobial agents that may require testing in those institutions that harbor endemic or epidemic strains resistant to several of the primary drugs; for treatment of patients allergic to primary drugs: for treatment of unusual organisms; or for reporting to infection control as an epidemiological aid.		
Group C – Supplemental Report Selectively	FDA- Approved Agent Acceptable *in vitro* test performance Known local resistant strains By clinician request Resistance to Group A and Group B agents	Endemic/epidemic strains that are resistant to multiple group A agents Allergies Unusual organisms Infection control purposes

A motion to accept the WG proposed definitions and to move them into the categories on table with additional text review as presented was made and seconded. VOTE: 12 for, 0 against (Pass). NOTE: It was decided that other changes will be made in the 31st edition of M100.

- The WG agreed that the current group placements are too restrictive and discussed how to re-evaluate the placements using the new criteria.
  - Assign different team members to tackle different organisms
  - Determine which to start with (eg, Group A assignment for penicillin and staphylococci - WG unanimously voted to approve the move to Group C)
  - Determine if the Enterobacterales should be described further due to intrinsic resistance patterns.
  - SC Discussion
    - Dr. Humphries noted that penicillin is still used internationally to treat staphylococci and further discussion is needed.
    - Dr. Mathers agreed that primary testing is done for some *Staphylococcus* spp. that still are treated with penicillins.
    - Ms. Hindler suggested that the *Staphylococcus* spp. should be separated out depending on their resistance to penicillin.
    - Dr. Limbago suggested that penicillin is better in Group B to cover those that are still using and testing it; however, the WG thought it would not fit the criteria for Group B.
    - Dr. Kirn agreed with the move to Group C. Many laboratories don't report penicillin for staphylococci and may not understand the need to do supplemental testing.
    - Dr. Schuetz commented that the definitions need to be further defined and drugs need to be shifted based on the new definitions. She proposed that the revisions wait until the 31st ed. of M100.
    - Dr. Eliopoulos suggested the definitions may need to be refined and that drugs are going to need to be reassigned.
    - Dr. Mathers stated that she supports the change in language and suggested the WG work on reorganizing the table and present it to the SC at a later date.

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	Before the SC discussion, a motion to move penicillin to Group C for *Staphylococcus* spp. based on new criteria was made and seconded. Following SC discussion, the motion was withdrawn. • With support of discussed plan and direction, the WG will continue refining the changes to the tables and suggestions for reassignment and will present a more defined table for presentation at the January 2020 meeting with the goal to include revised Table 1 in the 31st edition of M100 (2021).
6.	**Quality Control Working Group Report: Ms. Sharon Cullen (Folder 9)** **WG Roster**: Sharon Cullen, Maria Traczewski (Co-Chairholders); Michael Huband (WG Secretary); Alexandra Bryson (New), Patricia Conville, Dana Dressel, Janet Hindler, David Lonsway (New), Erika Matuschek (absent), Stephanie Mitchell (New), David Paisey (absent), Elizabeth Palavecino, Chris Pillar, Susan Thomson (Members) **The QCWG meeting agenda was reviewed.** • New WG members were welcomed (Alexandra Bryson, David Lonsway, Stephanie Mitchell, Susan Thomson). The WG is requesting the addition of a new pharmaceutical member. • There were no Tier 2 submissions for review. • The current M23 QC processes were reviewed in preparation for the M23 revision. • The colistin QC proposal was reviewed. • The progress of the Streamlined QC WG was reviewed. • Discussed items related to Tier 3 studies. **The current M23 QC procedures and requirements were reviewed.** • Ms. Cullen noted that although not perfect, Tier 2 studies are reasonably sized and robust; thus, the need for a review process as done periodically with Tier 3 studies. Sufficient data produced from a Tier 3 study is needed when considering a change in ranges. • Data is combined from Tier 2 and Tier 3 data when assessing QC ranges.

Category	Tier 1	Tier 2	Tier 3
Objective	Initial method assessment to determine if labile, inoculum, pH, supplements, etc. Select potential QC strains	Establish QC range, update glossaries. Sponsor notifies CLSI to publish after agent is named	Monitor performance with existing QC ranges. Reassess/revise QC ranges. Compare/consolidate with Tier 2 if available.
Laboratories	1+	7	3

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Media lots	1-2	3	2
Replicates	20-30	10 per lab, individual inoculum, max 4 per Day	10 per lab 50 per media
Disk lots	1	2 (from different mfg)	2
Total results	20-30+	210 (7×3×10 MIC) 420 (7×3×10×2 Disk)	500 disk, 250 MIC Similar totals and criteria as Tier 2, but more flexible & focus on sources of variability

The criteria for QC ranges were reviewed (see the QCWG presentation).

- The following are suggested for addition to M23:
- Example of the report format

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

- Disk and MIC example data summaries
- A note stating that QC ranges for drugs are not added to M100 until they have been named. Sponsors are expected to submit all associated information (eg, abbreviations, solvents, diluents, class, subclass, etc.) to CLSI once that drugs are named.
- The plan for the proposed M23 QC revisions will be discussed by conference call and comments will be requested. Ms. Cullen requested that volunteers contact her (skcullen@beckman.com) if they wish to participate.

Tier 3 MIC report and requests for data

- The WG voted (approved) to delete the QC range for *E. faecalis* ATCC 29212 and plazomicin due to various issues.
- The WG decided to reassess the QC ranges for *E. faecalis* ATCC 29212 for the aminoglyosides due to multiple out-of-range reports and are requesting data for submission.

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	A motion to delete the QC range for *E. faecalis* ATCC 29212 and plazomicin was made and seconded. Vote: 12 for, 0 against (Pass). **A motion to reassess the QC ranges for *E. faecalis* ATCC 29212 and the aminoglycosides was made and seconded. Vote: 12 for, 0 against (Pass).**
	Data requested for Tier 3 MIC QC ranges • QC ranges for *E. faecalis* ATCC 51299 for gentamycin HLAR were reviewed. The WG agreed that there was not a strong enough signal for action but are monitoring and request data. • QC ranges for *K. pneumoniae* ATCC 700603 for ampicillin-sulbactam were reviewed. The WG agreed there was not a strong enough signal for action but are monitoring and request data. • The WG proposed potentially establishing a range for *E. coli* NCTC 13486 or *E. coli* AR Bank #0349 for colistin and the colistin broth disk elution (CBDE) and the agar dilution methods. Additional data is needed. EUCAST data will be reviewed for possible harmonization. **Tier 3 Disk diffusion report and requests for data** • QC ranges for *E. coli* ATCC 25922 for ciprofloxacin were reviewed. In 2017, the range was changed from 30–40 (11 mm) to 29–37 (9mm). Tier 3 data from multiple sources show results are in the upper end of the range or out of range. The WG voted and approve a changed in the QC range to 29–38 (10 mm).
	A motion to change the disk diffusion QC range for *E. coli* ATCC 25922 and ciprofloxacin to 29-38 mm. Vote: 12 for, 0 against (Pass)
	• QC ranges for *P. aeruginosa* ATCC 27853 for meropenem were considered for readjustment due to some out-of-range results (high and low). The WG decided that the Tier 3 data provided an insufficient signal for action. The WG voted and approved the addition of a troubleshooting comment to address incorrect low out-of-range results due to (incorrectly) reading the inner zone with fuzzy edges or discreet colonies within the zone. • QC ranges for *P. aeruginosa* ATCC 27853 for imipenem were reviewed for possible revision as proposed by EUCAST. The WG agreed that there are insufficient data to signal a revision. The WG voted and approved the plan to continue monitoring. • QC ranges for *P. aeruginosa* ATCC 27853 for amikacin were reviewed for possible revision as proposed by EUCAST. The WG agreed that there are insufficient data to signal a revision. The WG voted and approved the plan to continue monitoring. • QC ranges for *E. coli* ATCC 25922 for eravacycline were reviewed for possible revision as proposed by EUCAST. The WG agreed that there are insufficient data to make a change and decided to request additional data for review in January 2020. **Colistin QC for colistin broth disk elution (CBDE), colistin agar dilution test (CAT), and broth microdilution (BMD)** • Better QC is needed for the dilutions that are routinely tested. • The current QC range is 4 dilutions for *P. aeruginosa* ATCC 27853 (0.5-4) and *E. coli* ATCC 25922 (0.25-2); however, the dilutions tested for CBDE and CAT are 0.4, 1, 2, and 4. The current strains and ranges don't detect issues during testing sufficiently.

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- Options for developing new QC strains and ranges.
  - CLSI study for alternative methods tested *E. coli* AR Bank #0349 as a potential QC strain since it possesses *mcr1*.
  - EUCAST recommends *E. coli* NCTC 13846 (*mcr-1* positive). Dr. Matuschek will be requested to provide the EUCAST method and data for evaluation at the January 2020 meeting.
  - If method is approved, QC will be needed to perform the test (Tier 2 study data)

- Colistin QC Study Design for BMD, CBDE, and CAT

Requirement	Met in study?	Notes
7 laboratories	Yes	
10 replicates of the QC strain per laboratory	Yes	3 laboratories generated 13-15 results (not included in this study); only the first 10 results were used to analyze to not add bias to the results
3 lots of CAMHB	Yes	50% of results (N=35/70?) for the Oxoid media were out of control for P. aeruginosa 27853; > 95% results for E. coli CDC 349 yielded MICs within the proposed QC range (i.e., 1 – 4 ug/mL)
Individually prepared inoculums	Yes	-
CAMHB qualified for AST	Yes	-
Minimum of 3 days of testing per laboratory	Yes	-
Twofold dilution schedule for on-scale QC results	Yes	Exception is for P. aeruginosa 27853 on Oxoid (out of QC on low end, off-scale)
Control antimicrobial of same/similar class tested in same way	No	No QC ranges are available for E. coli CDC 349 for any antimicrobial; rather, testing P. aeruginosa 27853 for colistin was used to ensure method / panels was acceptable
Colony counts performed	No	Only by 2 laboratories

  - Although the study design does not follow Tier 2 exactly but was deemed "equivalent" except for requirement for 3 media lots as 1 media lot was excluded due to out-of-range results for *P. aeruginosa* ATCC 27853 and 2 disk lots.
  - The QC was not in control with all media.
  - The data for the alternate methods looks better.
  - WG Decisions (WG Voted and approved): *E. coli* AR Bank #0349 QC range of 1–4 ug/mL was proposed for CBDE and CAT (not for BMD) with recommended footnotes:
    - Recommended for routine user QC.

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	○ Investigate if repeated results of 1 or 4 µg/mL are obtained. ○ These QC ranges were established with limited disk and/or media manufacturers and are considered tentative until additional testing is performed to meet M23 guidelines. ○ The alternative was not included in the motion. ○ There were 2 dissenting votes due to not meeting the M23 study design. The rationale for approving the method was the urgent need and, if the method is approved, the QC should be sufficient. – WG Action Items ○ Test additional media to fulfill M23 requirements and potentially remove footnotes for CBDE and CAT and establish a QC range for BMD with *E. coli* AR Bank #0349. ○ Evaluate the EUCAST *E. coli* NCTC 13846 (target value 4 µg/ml) as an additional or potential primary QC – SC Discussion ○ Dr. Galas: Laboratories are already using the disk elution method in other countries but need to know how to get the organism. **NOTE:** The AR bank isolate is being submitted to ATCC and is currently available from the AR bank. ○ The QCWG recommended that AR Bank #0349 be approved for QC (with footnotes) on alternate methods (CBDE and CAT) with caveats (tentative range) and reassess at January 2020 meeting or pull the QC if methods are not approved
	A motion to accept the QC strain and range as provisional for CBDE and CAT with footnotes and assuming the methods are approved was made and seconded. Vote: 12 for, 0 against (Pass).
	Streamlined QC AHWG Progress Report **AHWG Roster**: Romney Humphries and Elizabeth Palavecino (co-chairholders); Angharad Laetsch (recording secretary); Nancy Anderson, Victoria Anikst, Kendall Bryant, Sharon Cullen, Janet Hindler, Susie Sharp, Jewell Yap • **Issue:** With new antimicrobials that require special QC strains, laboratories have an increasing requirement for performing QC. Is there a more effective approach for laboratories? • Options discussed included: – Selecting QC strains and testing based on risk-analysis. – Identifying practices outside QC testing that mitigate risks (eg, training and competence, antibiogram trending, investigating abnormal results, purity plates, expert rules, verification studies, supervisor reviews, turnaround time etc.) – Clarifying manufacturer and laboratory responsibilities for AST QC. Possibly align with M50. – Evaluating current QC strain ranges vs BPs and likely dilutions to test to determine what is being QC'd. – The AHWG will continue work through fall 2019 to identify and highlight laboratory vs manufacturer QC requirements and to develop risk-based approached to QC recommendations. The AHWG appreciates any feedback. • SC Discussion

<table>
<tr><th colspan="2">SUMMARY MINUTES</th></tr>
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<tr><td colspan="2">Monday, 17 June 2019 (NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2019 June AST Plenary Presentations)</td></tr>
<tr><td></td><td>– Dr. Moeck questioned whether the WG has thought of when the recommendations for limiting QC strains are made appropriate for routine QC how they might be identified in the large tables (Tables 4 and 5). The QCWG will discuss how to address the communications.

<u>Future agenda topics</u>
• Need to decide what QC strain to use when testing azithromycin disks with Salmonella typhi isolates
– Not addressed in "Routine QC Recommendations" box on Table 2A for Enterobacterales.
– Used standard QC strains with M45 (eg, S. aureus ATCC 25923 on MHA to QC erythromycin disks when testing Campylobacter isolates)
– Decision: Add footnote where Salmonella typhi BPs are listed or in the routine QC box to refer to S. aureus ATCC 25923 for QC (Passed: 12/0/0/0)</td></tr>
<tr><td></td><td>A motion to add a footnote where S. typhi BPs or in routine QC box to refer to S. aureus ATCC 25923 for QC (text and tables determine where to place the footnote and to wordsmith). Vote: 12 for, 0 against (Pass).</td></tr>
<tr><td>7.</td><td><u>Breakpoint (BP) Working Group (WG)</u>: Dr. James Lewis (Folder 5)
WG Roster: James Lewis, George Eliopoulos, Michael Satlin (Co-Chairholders); Karen Bush (WG Secretary - Absent); Marcelo Galas, Romney Humphries, Amy Mathers, Navaneeth, Narayanan, David Nicolau (Absent), Robin Patel (Absent), Simone Shurland, Lauri Thrupp, Hui Wang (Absent), Barbara Zimmer (Members); Matt Wikler (Technical Advisor - Absent). NOTE: Dr. Satlin acted as the recording secretary for this meeting.

<u>Ceftazidime-avibactam Disk Diffusion Breakpoints (Folder 5, Item 2)</u>
• During the January 2019 meeting, it was questioned if there could be an intermediate (I) category for disks only.
– It was noted that CLSI has a history of setting a BP for disk diffusion only.
– It previously looked like the PK/PD data could support an I category.
– The data to select an I zone (3mm) was reanalyzed by Dr. Sader.
– The analysis results showed that introducing an I zone changes the error rates. Conclusions from the re-analysis included:
– Keep the suggested footnote as is with no revision (When disk diffusion zones are in the range of 19–22 mm, a confirmatory MIC test should be performed).
– Introduce an I range for disk only (2 or 3 mm) resulting in lower very major errors (VME) and major errors (ME).

<table>
<tr><th>Error Rate</th><th>No Intermediate S/R at ≥ 21/≤ 20 mm</th><th>2 mm Intermediate S/R at ≥ 22/≤ 19 mm</th><th>3 mm Intermediate S/R at ≥ 23/≤ 19 mm</th></tr>
<tr><td>VM</td><td>7.5</td><td>3.9</td><td>1.8</td></tr>
<tr><td>Major</td><td>5.5</td><td>1.9</td><td>1.9</td></tr>
<tr><td>Minor</td><td>-</td><td>19.9</td><td>32.2</td></tr>
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	• BPWG Discussion – Since most I ranges are at least 3 mm, it was suggested that care should be taken about choosing a 2 mm range. – The need for laboratories to validate an I disk breakpoint should be considered. – Concern was expressed regarding confusion if an I category is present for disks, but not for MIC. – It was noted that as per M23, disk zones should be half the QC MIC range; however, the WG believed that this would not apply to a footnote. – The BPWG voted an approved a motion to keep Footnote 8 in Table 2A but change 18-20 to 20-22 in footnote ("Confirmatory MIC testing is indicated for isolates with zones of 20–22 mm")(Approved: 7-0, 2 abstentions). • SC Discussion – Dr. Thrupp questioned if the minor errors (32%) are in the direction of patient safety (overcalling resistant) or if it is overcalling Intermediate. and expressed concern for overcalling susceptibility. – Dr. Sader noted that both have been seen and that as it stands now, resistance is being overcalled.
	A motion to accept the revision of Comment 8 in Table 2A (Confirmatory MIC testing is indicated for isolates with zones of 20–22 mm) was made and seconded. Vote: 12 for, 0 against (Pass).
	• The BPWG will continue to review the issue and discuss the possibility of setting an I zone during the January 2020 meeting. **<u>Cefiderocol Disk Correlates (Folder 5, Items 5A-B)</u>** • Disk diffusion BPs were approved at the January 2019 meeting, but it was noted that the vote would be confirmed after additional reproducibility testing data was reviewed. – A study was performed by the sponsor to evaluate cefiderocol 30 µg disks to cover both the EUCAST and CLSI guidelines. – One lot of disks from two manufacturers tested. – Mueller-Hinton (MH) agar from one manufacturer. – Two QC strains (*E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853) and 13 clinical isolates tested (represent one wild-type and at least one isolate with elevated MICs). – Inter-day and inter-lot disk reproducibility studies were performed. • Results – Inter-day reproducibility study – The inhibition zone variation between test days and readers for a single isolate was within expected range for a reproducible test. – There were only minor differences between the two manufacturer disks. – Some isolates showed colonies in the zone; however, results were based on readings without colonies. – Inter-lot reproducibility study

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	– Reproducibility on standard MH agar was confirmed and confirmed the relevance of the BPs approved. • BPWG discussion – It was noted that colonies in the zone of inhibition (zone) were ignored (zone edge read) for the comparative studies. – Dr. Thrupp questioned how often the colonies in the zone were seen. The sponsor responded that: ○ The data were shown (including the colonies in the zone) and looked reasonable and comparable to the reproducibility when the colonies were ignored. ○ The sponsor also clarified that colonies were counted within the zone when collecting data for disk correlates with MIC results. ○ Dr. Lewis, Dr. Humphries, and Dr. Mathers noted that the default is to count the colonies within the zone when doing disk susceptibility testing (unless stated otherwise). – There seemed to be issues with the media from different manufacturers although the results from the different disks matched. – Only one brand of media was analyzed which goes against M23. – No vote taken by the WG as it was believed that the additional data justified the decision made in January 2019. • SC discussion – Dr. Richter suggested that there might be an issue with the iron and questioned if the iron may be causing the issue. – Dr. Simner noted that the results (colonies in the zone) look to be organism specific (ie, *Klebsiella* and *Acinetobacter* only) which does not appear to be a media issue. – Ms. Cullen stated that the QC summary from the January 2017 meeting showed good reproducibility study results but QCWG observed that the medians for the different media for *E. coli* and *Pseudomonas* showed a 2 mm difference and that different media has an impact on results. She noted that she would like to see the data from the different media lots (if available) to see if they are categorically the same with different media lots. – Dr. Galas noted that there were significant differences between the two media. – Dr. Humphries questioned what can be done to correct/clarify the process so that sponsors don't need to keep submitting additional data. – Ms. Cullen stated that issues will be seen when monitoring QC; however, she was not sure if issues will be seen with the BPs. She reiterated that she would like to see disk diffusion results with more than one media brand. She stated that if there are issues with the media, QC issues will be seen as the QC is monitored over time. Categorical calls with clinical isolates may not be seen unless it is specifically monitored. – Dr. Weinstein stated that the disk diffusion correlates will be retained as is and the SC will continue to monitor as laboratories start to test the drug (not yet available) and make corrections, as needed. **Polymyxin Breakpoints** AHWG Roster: Jean Patel, Romney Humphries (co-chairholders); Jim Lewis, Rodger Nation, Mike Satlin, John Turnidge (members).

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	• The AHWG problems to address were reviewed. – CLSI has no Enterobacterales BP for colistin but does have ECV. – The ECV cannot be used for treatment decisions by hospital laboratories – FDA cannot approve a diagnostic device for reporting an ECV and cannot publish an ECV as a clinical breakpoint. – CLSI has no polymyxin B BP for Enterobacterales – Polymyxin B is the only polymyxin available in some countries (eg, Brazil) and they do not have access to alternative agents – CLSI has (old) polymyxin B BPs for *P. aeruginosa* and *Acinetobacter* spp. It was questioned if these are still appropriate. – It was questioned if an "or" be used between colistin and polymyxin B. • Other issues for considering a BP were presented. – Newer antimicrobial agents are not available in many parts of the world. For these countries, polymyxins are the drugs of last resort for multi-resistant Enterobacterales. – Lack of BPs is not in the best interest of patients in these areas. It was suggested that: – A BP provides an opportunity to add a "black box" warning about the drug's use and why a BP has not been available in the past. – An intermediate only BP send a message that there is no "likely clinical success". • New guidelines published on optimal polymyxin and colistin dosing were reviewed. The guideline stated that: – The AUCs at 24hr for colistin are of ≈50 mghour/L is required to equal steady-state plasma concentration (Css,avg) of ≈2 mg/L for total drug (not free drug) which is the maximum tolerable exposure and it is likely suboptimal for lower respiratory tract infections. – A target plasma colistin Css, avg of 2 mg/L was recommended for systemic administration. – The target was based on the following (see https://accpjournals.onlinelibrary.wiley.com/doi/epdf/10.1002/phar.2209): ○ It accounts for the difference in the extent of protein binding between the plasma of mice and critically ill patients. ○ Protein binding in human plasma is ≈50%. ○ Based on the thigh infection model this exposure would be expected to achieve bactericidal activity against an isolate with an MIC of 2 mg/L (the EUCAST and CLSI BP [ECV]). • A summary of outcome studies was reviewed. The general consensus was that: – The drug is not as effective or as safe compared to other available drugs. – Many publications are available that indicate high mortality and clinical failures when the drug is used for treatment. • Comments suggested to accompany all polymyxin BPs for Enterobacterales included: – Clinical and PK/PD data demonstrate this agent is of limited clinical efficacy, even if a susceptible result is obtained.

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	– If available, alternative non-polymyxin agents are strongly preferred. If these agents are not available, this breakpoint presumes use of colistin in combination with one or more additional, active antimicrobials. – Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses. – Polymyxin B should be given with a loading dose and maximum recommended doses. – When given intravenously, this drug is unlikely to be effective for pneumonia. • A summary was provided. – Outcomes of drug use are bad in general; however, it can be argued that something is better than nothing if there are no other options. – Due to pharmacokinetic/toxicodynamics, the BP cannot be >2 µg/mL. – To avoid cutting into wild type (WT), the BP cannot be <2 µg/mL – The only option is ≤ 2 µg/mL. • BPWG Votes and Discussion – 1st vote ○ **Motion:** Accept the proposal of colistin BPs: S: ≤2; R: ≥4 but make it stronger with a big black box warning. Vote: 8-2, no abstentions. ○ **No votes:** Thought BPs should be ≤ 1µg/mL or ≤ 0.5 µg/mL (could not justify). ○ The WG reviewed definition of susceptible (S) and agreed that S does not fit ○ The definition of intermediate was also reviewed with the idea of setting an intermediate and R and resistant only BPs. ○ A category defined by a breakpoint that includes isolates with MICs or zone diameters within the intermediate range that **approach usually attainable blood and tissue levels and for which response rates may be lower than for susceptible isolates** – 2nd vote ○ **Second motion -** Accept the proposal of colistin BPs: I at ≤2; R at ≥4 and there will not be an Susceptible BP. This will apply for both colistin and poly B and include the warning. Vote: 7-3, no abstentions. ○ Opposed ○ Some were not comfortable with having an I/R designation and questions on how this would be implemented. ○ The FDA would need to be consulted and it is not clear what "I" means. ○ There was concern that MIC of 0.25 µg/mL is really S; however, it is being called it an "I". ○ S-DD has been confusing and this will be even more confusing. – **Final Motion** - Which of the 2 motions is preferred: **S** at ≤2 µg/mL option or **I** at ≤2 µg/mL option. ○ **I** preferred by vote of 7-3 ○ All in agreement that poly B should be handled the same as colistin • BPWG Proposal for Enterobacterales

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LIPOPEPTIDES
(a) The only approved MIC method for testing is broth microdilution. Gradient diffusion methods should not be performed.
(b) Several species are intrinsically resistant to the lipopeptides (colistin and polymyxin B). Refer to Appendix B
(c) Isolates susceptible to colistin are susceptible to polymyxin B and vice versa. (NOTE: This comment In M100, 39th ed. has been revised to read: "Isolates intermediate or resistant to colistin are intermediat or resistant to polymyxin B and vice versa."

	S	I	R	Note
Colistin	-	≤2	≥4	See next slide

- SC Discussion
  - Dr. Galas noted that intermediate is not understood by clinicians and as a result treat the BP as a resistant result. In some countries, there are only a few drugs available for treatment and none have BPs with CLSI. He also noted that colistin is always used in Latin America in combination (eg, meropenem, tigecycline). Additional training for clinicians will be needed.
  - Dr. Humphries commented that colistin can't be used without knowledge of dosing and the damage associated with it; therefore, it may be a good thing that intermediate is misunderstood as R.
  - Dr. Castanheira questioned if the dose has changed and if so, why?
  - Dr. Lewis stated that due to the high creatinine clearance, the drug can't get to the active concentration.
  - Dr. Kirn questioned if there should always be 3 interpretive categories as agreed to in an earlier meeting.
  - Dr. Moeck noted that the 3 categories were indicated for all new antimicrobial agents.
  - Dr. Limbago agreed that a BP needs to be set but had concerns about only having an I category. She suggested that education will be needed.
  - Dr. Miller stated that it would be difficult to call an S category especially since more is known about the drug's dangerous aspects. The criteria for setting an S BP really hasn't been met. She stated that an I BP was preferred but there is concern and hopes reporting an I result will trigger a call to an infectious disease specialist.
  - Dr. Mathers believes the I and R BPs are correct. The SC needs to be very clear and know how important this issue is. She expressed concern that the comments may be lost in translation and believes that clinicians do know what an I category means.
  - Dr. Palavecchio agreed that this is a difficult issue. If nothing else, it shouldn't be used without testing in combination with another drug.
  - Dr. Richter and Dr. Bobenchik preferred a more ambiguous report such as "no interpretation".
  - Dr. Narayanan suggested that if all other drugs are resistant, seeing an I BP may provide hope to the clinician. It is desired for clinicians to use ceftazidime-avibactam in this country despite the higher cost. It is hoped that the I result may cause people to use better drug in US.
  - Dr. Schuetz commented that laboratories are reporting the ECV as an S interpretation and selecting colistin instead of other available drugs because of the lower cost.

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	– Dr. Miller questioned the status of the EUCAST BP. Dr. Humphries indicated that EUCAST also has an ECV and studying the possibility of setting a BP. – Dr. Jenkins remarked that CLSI needs to provide direction beyond an ECV and it is often difficult for laboratories to communicate the comments. • The options for action were reviewed. – Status quo: Don't make any changes. – Accept the compromise of setting I and R BPs with the associated comments. – Try to come up with other options.
	A motion to set the colistin BPs as I at ≤2 µg/mL and R at ≥4 µg/mL for Enterobacterales with associated warnings and comments was made and seconded. Vote: 11 for, 1 against (Pass)
	Comments (to include): – **Clinical and PK/PD data demonstrate this agent is of limited clinical efficacy.** – **If available, alternative non-polymyxin agents are strongly preferred. If these agents are not available, this breakpoint presumes use of colistin in combination with one or more additional, active antimicrobials.** – **Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses.** – **When given ~~IV~~ systemically, this drug is unlikely to be effective for pneumonia** – Dr. Galas' negative vote was due to reasons stated above regarding laboratories interpreting I as resistant. – It was requested that in the comments, the term "IV" be changed systemically (see comment list above). – The Outreach WG will work to develop educational materials and to discuss translating the educational materials into other languages (eg, Spanish, French, Portuguese, Asian languages). • The BPWG also reviewed the old *Pseudomonas* and *Acinetobacter* BPs. – The WG proposed that *Pseudomonas* and *Acinetobacter* should have the same BPs as Enterobacterales (see below) – The same comments as for Enterobacterales will be used for *Pseudomonas* and *Acinetobacter*. • BPWG Proposal for Nonfermenters

	S	I	R	Note
P. aeruginosa	-	≤2	≥4	See below
Acinetobacter spp	-	≤2	≥4	See below

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	• Comments: – Clinical and PK/PD data show this agent is of limited clinical efficacy. – If available, alternative non-polymyxin agents are strongly preferred. If these agents are not available, this breakpoint presumes use of colistin in combination with one or more additional, active antimicrobials. – Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses. – When given ~~intravenously~~ **systemically**, this drug is unlikely to be effective for pneumonia.
	A motion to accept the BPs for *Pseudomonas* and *Acinetobacter* as I at ≤2 µg/mL and R at ≥4 µg/mL with the same comments (see above) as for Enterobacterales was made and accepted. Vote: 11 for, 1 against (Pass)
	– Dr. Galas objected for the same reasons as for Enterobacterales. – It was noted that the current rationale document will need to be revised. **Polymyxin B Breakpoints** • The BPWG presented the same proposal for polymyxin B as for colistin for all three organism groups. • The consensus guideline for dosing was reviewed. – Similar targets for polymyxin B as those listed for colistin are recommended. – (AUCss,24 hr) of ≈50 mghour/L is required to equal steady-state plasma concentration (Css,avg) of ≈2 mg/L for total drug. – Data are lacking for AUCss,24 hr targets for polymyxin B. – It appears that there may be a different toxicodynamic profile for polymyxin B than colistin. AUCss,24 hr target of 50–100 mghour/L, corresponding to a Css,avg of 2–4 mg/L, MAY be acceptable from a toxicity standpoint. • Summary – Outcomes with polymyxin B are generally bad; however, it can be argued that something is better than nothing if there are no other options. – Based on pharmacokinetic/toxicodynamic data, the BP cannot be >2 µg/mL. – To avoid cutting into wild type, the BP cannot be <2 µg/mL. • BPWG Final Polymyxin B Proposal
	LIPOPEPTIDES **(a) The only approved MIC method for testing is broth microdilution. Gradient diffusion methods should not be performed.** **(b) Several species are intrinsically resistant to the lipopeptides (colistin and polymyxin B). Refer to Appendix B** **(c) Isolates susceptible to colistin are susceptible to polymyxin B and vice versa (NOTE: This comment In M100, 39th ed. has been revised to read: "Isolates intermediate or resistant to colistin are intermediat or resistant to polymyxin B and vice versa."**

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	S	I	R	Note
Enterobacterales	-	≤2	≥4	Same as for colistin (see above)
P. aeruginosa	-	≤2	≥4	Same as for colistin (see above)
Acinetobacter spp.	-	≤2	≥4	Same as for colistin (see above)

A motion to accept the proposed BPs, I at ≤2 µg/mL and R at ≥4 µg/mL with same warning and comments was made and seconded. Vote: 11 for, 1 against (Pass).

- Dr. Galas expressed the same concerns as with colistin.

- Housekeeping Items
  - The BPs will apply to all Enterobacterales and not just those that had an ECV (language not to be added to M100).
  - The ECV will be deleted from M100 (vote not needed).
  - A reference to the treatment guideline will be added to Tables 2A, 2B-1, and 2B-2 and to Appendix E.
  - It was suggested that colistin and/or polymyxin B be added to Table 1 in Group C and an "or" be added between colistin and polymyxin B in Table 1.
  - Dr. Schuetz questioned the decision to place the drugs in Table 1, Group C.
  - Dr. Humphries stated that it was believed users would be confused if the drugs weren't in Table 1 but had BPs.
  - Ms. Hindler noted that the group is noted in all Tables 2.
  - It was agreed that the drugs will not be added to Table 1 until it is decided how the table will be revised. Both will be retained as "O" in Tables 2.

- It was questioned if polymyxin B susceptibility can predict colistin susceptibility.
  - Based on data from the January 2018 agenda material, it was shown that colistin and predict polymyxin B and vice versa.
  - Dr. Shawar commented that it is premature to say that results of one drug can predict the other based on the error rates.

A motion to include the comment that polymyxin B can predict colistin results (and vice versa) was made and seconded. Vote: 11 for, 1 against (Pass).

- Dr. Schuetz opposed the motion due to the low number of resistant *Pseudomonas* in the data set.

8.	**Method Application and Interpretation Working Group Report: Dr. Tom Kirn (Folder 6)**

SUMMARY MINUTES	
Item #	**Description**
Monday, 17 June 2019 (NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2019 June AST Plenary Presentations)	
	WG Roster: Brandi Limbago, Tom Kirn (Co-Chairholders); Trish Simner (WG Secretary); Darcie Carpenter, Steve Jenkins, Kristie Johnson, Joseph Kuti (absent), Samir Patel (absent), Virginia Pierce, Sandra Richter, Susan Sharp (Members) ***Stenotrophomonas maltophilia* AHWG Report** **AHWG Roster:** Dwight Hardy (Chairholder); Stephanie Mitchell (recording secretary); Kevin Alby, April Bobenchik, Carey-Ann Burnham, German Esparza, Kristie Johnson, Joe Kuti, Samia Naccache, Helio Sader, Tam Van, Melanie Yarborough (Members). • Data were presented in regard to Table 1 placement (*in vitro* data, PK/PD data, clinical data). – Based on the presented data, the following conclusions and recommendations were made: ○ Although limited (and from retrospective reviews only), there is clinical data to support use of trimethoprim-sulfamethoxazole (TMP-SMX), minocycline, and levofloxacin against *S. maltophilia*. There is limited data for use of ceftazidime and no BP for ciprofloxacin. ○ The AHWG recommended that: ▪ TMP-SMX, levofloxacin, and minocycline be placed in same "Box" in Table 1A with ceftazidime placed in one "Box" lower (MAIWG approved 9-0-0). ▪ Chloramphenicol be removed from Table 1A and 2B-4 (plan to research data for setting the original BP). ▪ Ticarcillin-clavulanate be removed from Table 2B-4 (unavailable in some areas). ▪ BPs for levofloxacin be considered for revision since BPs for *Pseudomonas* were revised and lowered. ▪ BPs for ciprofloxacin be considered and adoption of BPs discussed. – SC discussion ○ Dr Lewis questioned if there was any discussion of moxifloxacin. IT does look most active; however, moxifloxacin and other drugs were not reviewed. ○ Dr. Sader stated that an analysis of quinolones and there were limited cases for moxifloxacin. ○ Dr. Satlin commented that the study compared quinolones with TMP-SMX and they were comparable; however, he questioned whether this is the right time to make changes for *S. maltophilia* with Table 1 being revised. ○ Dr. Simner suggested that the changes be made for the M100, 30th ed. ○ Dr. Castanheira noted that there is potential for induced resistance. ○ Dr. Jenkins supported the changes because clinicians do ask for reports.
	A motion to accept the proposal to move levofloxacin and minocycline to Group A in same box with TMP-SMX above ceftazidime in Table 1, Group A and to list the drugs alphabetically. Vote: 11 for, 0 against; 1 absent (Pass).
	– Other conclusions and recommendations ○ It was noted that there is no PK/PD available for quinolones and *Stenotrophomonas*.

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	○ Dr. Hardy requested BPs be set for ciprofloxacin (no dose) and *Stenotrophomonas* and suggested that there be a discussion either way and justification be provided for the decision. ○ Dr. Weinstein questioned if an AHWG is needed to study. Dr. Hardy stated that there is limited clinical data available. This may be investigated for a future discussion. ○ Dr. Sader reported that ciprofloxacin is 1 dilution less active than levofloxacin but they are the same clinically. The same BP applied to ciprofloxacin as levofloxacin, the results would primarily be resistant. There are very limited PK/PD data for ciprofloxacin. ○ Dr. Schuetz noted that there are still requests for ticarcillin-clavulanate results on *Stenotrophomonas* although it is listed as no longer available. ○ Dr. Kirn reported that chloramphenicol is still listed in Sanford guide for *Stenotrophomonas,* but it is rarely used. ○ Dr. Satlin questioned if the BPs of the whole class needs to be reassessed for *Stenotrophomonas* and that data is limited. ○ It was agreed that it would be beneficial to address ciprofloxacin for *Stenotrophomonas* even though it shouldn't work. The BPWG will perform a review for the January 2020 meeting. ○ DR. Hardy noted that the levofloxacin BP changed for all but *Acinetobacter* and *Stenotrophomonas* – lower as for *Pseudomonas (*looking at that) • Next steps (for BPWG?) – Review archived minutes and data from the meetings when BPs were set for *S. maltophilia* (if available) to better understand: ○ Why chloramphenicol BPs were set ○ How other BPs were set (especially levofloxacin) ○ Why no ciprofloxacin BPs were established **Appendix A Revision** • Appendix A revisions were approved by the SC in January 2019. • The Text and Tables WG (TTWG) added some edits in response to the TTWG review and comment period. • The project has been completed. **Research Use Only (RUO) AST in Clinical Laboratories** **AHWG Roster:** Romney Humphries, Stephanie Mitchell (Co-chairholders); April Bobenchik (Recording Secretary); Elizabeth Hirsch, Catherine Hogan, Sandra McCurdy, Elizabeth Palavecino, Virginia Pierce, Tam Van, Paula Snippes-Vagnone (Members). • The AHWG investigated the possibility of providing guidance to laboratories that are using RUO labeled AST devices for patient testing. – Many use RUO because no IVD product is available. – Tests are RUO because: ○ There are no FDA recognized breakpoints (eg, colistin) for some organisms

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	○ There are no FDA breakpoints for organism desired to be tested (eg, meropenem and *A. baumannii* after 2009) ○ FDA and CLSI breakpoints differ (eg, cefazolin) ○ Manufacturer does not seek claims for unusual organisms (eg, nonfermenters, fastidious organisms, etc) ○ NDA approved before AST device IVD (eg, all new drugs) – CLSI has breakpoints that are not FDA approved (ie, endorsing off-label use but do not provide guidance on how to accomplish this) • **Original goal:** Provide guidance in M52 (*Verification of Commercial Microbial Identification and Antimicrobial Susceptibility Testing Systems*). Topics to cover would include: – Regulatory category definitions for AST (RUO vs IVD vs LDT) – Reasons why AST is RUO – Discussion of the pro/cons for using RUO ASTs – General guidance on how to validate performance – Guidance on reporting considerations • A project proposal was prepared and submitted to the Expert Panel on Microbiology for review and endorsement. – The project proposal was not endorsed due to objections by the FDA representative and others on the panel. – The AHWG discussed other possible mechanisms for providing guidance ○ Collaborate with ASM ○ Develop educational material ○ Develop a point/counterpoint publication with expert opinions • SC Discussion – Dr. Zimmer warned that the SC needs to be careful due to differences in BPs between CLSI and FDA. She noted that the guidance in M52 is already satisfactory. – Dr. Shawar stated that the practice of using RUO products should not be endorsed. – Dr. Patel agreed that when a commercial organization releases an RUO, CLSI shouldn't get in between the manufacturer and the FDA. – Dr. Schuetz noted that other avenues may be available for providing guidance. It might be possible to get expert opinions without using the organization's name. – Dr. Edelstein questioned the meaning of RUO such as using gradient diffusion with CLSI BPs that are not in the package insert. – There is confusion about different between off-label use and RUO (eg, reporting MIC without an interpretation for drugs not having BPs). – Dr. Shawar noted that there is an FDA guidance document for RUOs (labelled as RUO) and a clear distinction from off-label use. Off-label use of an FDA-cleared test can be verified in a particular laboratory (eg, different specimen type). – The SC agreed that education regarding the differences between RUO and off-label use is needed.

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Monday, 17 June 2019 (NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2019 June AST Plenary Presentations)	
	***Burkholderia cepacia* complex (BCC) AHWG Report** **AHWG Roster**: Susan Sharp, Holly Huse (Co-chairholders); Rosemary She (Recording Secretary); Kendall Bryant, Eileen Burd, Joe Kuti, Mandy Wootton (Members) • *B. cepacia* complex – There are 18 species that cause a wide variety of infections in immunocompromised patients – It is a well-known pulmonary pathogen in cystic fibrosis (CF) patients • **Clinical problem**: Clinicians use AST to guide therapy and eligibility for lung transplants in CF patients – There are discrepancies on recommendations from CLSI and EUCAST ○ EUCAST does not recommend AST on the complex organisms ○ CLSI provides MIC and disk diffusion BPs – There are problems with current AST methods and no evidence relating MIC and outcomes. – ECVs cannot be established. – There is a wide MIC distribution, so it is difficult to set an ECV. • EUCAST Study – The best method was researched (disk diffusion vs BMD; gradient diffusion vs BMD) – BMD was reproducible for minocycline, ciprofloxacin, and chloramphenicol – Poor reproducibility for meropenem, TMP/SMX, and ceftazidime. – Very poor reproducibility for amikacin and piperacillin-tazobactam – Agar dilution (AD) had poor correlation with BMD and AD's reproducibility was slightly better than BMD. – Gradient diffusion had poor correlation with BMD and AD – The EUCAST disk diffusion was not able to separate wild type and non-wild type using CLSI BPs. • Two other studies were reviewed and neither provided reproducibility data. • The AHWG proposed a study to evaluate reproducibility and agreement of reference AST methods for CF and non-CF, BCC isolates – 100 unique CF isolates (50 *B. cenocepacia* and 50 *B. multivorans*) – Perform BMD and disk diffusion in triplicate over three days. – Use the same McFarland for both BMD and disk diffusion – Compare data to 100 non-CF isolates – Results will be presented at the January 2020 meeting.

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	Anaerobe AHWG **AHWG Roster**: Darcie Roe-Carpenter (Chairholder); Karen (Kitty) Anderson, Diane Citron, Joanne Dzink-Fox, Meredith Hackel, Steve Jenkins, Cindy Knapp, Laura Koeth, Audrey Schuetz. • Continue to investigate metronidazole BPs. • Working on an antibiogram manuscript. • Investigating the possibility of adding *Parabacteroides* to the intrinsic resistance table. • Discussing updates to the antibiogram in M100. **Intrinsic Resistance (IR) AHWG Report** **AHWG Roster**: Barbara Zimmer (Chairholder); Dyan Luper (Recording Secretary); Susan Butler-Wu, Rafael Canton, German Esparza, Mark Fisher, Sandy Richter, Susan Sharp, Rosemary She, Carole Shubert (Members); Jeff Alder and Tom Thomson (Retired) • The IR of *Hafnia alvei* to colistin is under review. – Two studies that were reviewed showed that *H. alvei* may have IR to colistin. – EUCAST describes *H. alvei* as IR to colistin and the WG discussed harmonizing with EUCAST. – Dr. Pierce will be using the agar screen method for colistin resistance organism in GI colonization and test these isolates using BMD. Data will be provided to the AHWG for review. **Reporting Cefepime S and SDD Results for Carbapenemase-Producing Enterobacterales** (Submitted by Trish Simner and Carey-Ann Burnham) • The issues being studied included: – Multiple institutions have noted that carbapenemase producers (mostly KPC producers) have cefepime MICs that fall into the susceptible (S) or susceptible-dose dependent (SDD) interpretive categories. – Guidance from CLSI is being proposed on how to handle these scenarios to prevent the inappropriate use of cefepime for treating carbapenemase-producing Enterobacterales. • Five options were presented for SC discussion. – Suppress cefepime S or SDD results and not report for carbapenem-resistant organisms – Force cefepime S or SDD results as R – Report cefepime as tested – Revise cefepime BP – None of the above

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	• SC Discussion – Dr. Miller suggested looking at the MIC, and if it is low, call it as S even if resistance mechanism present. She noted that the EUCAST BP is low to catch ESBL producers. – Mr. Esparza noted that data on treatment with cefepime monotherapy. – Dr. Moeck commented that this is more a KPC issue than a carbapenemase-producing organisms issue. – Dr. Satlin noted that there is data showing that KPC hydrolyzes cefepime and cautioned against using them for treatment. – Dr. Mathers agreed that clinicians should be alerted against using cefepime for treating carbapenemase. – Dr. Kirn noted that this issue is partially addressed in molecular tables published in M100. • The options for a path forward were discussed. – Dr. Limbago suggested narrowing the options that were presented. – Dr. Weinstein commented that there seems to be insufficient data to make a decision. – Dr. Gold stated that more information is needed to make any changes. He suggested that the result should be reported as tested. – Dr. Galas agreed that more clinical data is needed. – Dr. Tamma stated that more clinical data are needed, and the data should be reviewed with the idea of reviewing the data for changing the BP. – Dr. Mathers commented that if the KPC marker is known, cefepime wouldn't be used. She suggested to report cefepime as tested. – Dr. Limbago and Dr. Satlin agreed to report the result as tested. – Dr. Simner and Dr. Mazzulli suggested forcing the report to R if the isolate is KPC+ and follow the molecular table recommendations. – Dr. Schuetz suggested conferring with Dr. David Nicolau since he has extensively studied cefepime. – Dr. Kirn suggested reporting the isolate as tested (Option 3) and obtain more data, especially from Dr. Nicolau.
N/A	**FDA update (Dr. Nambiar)** • The submitted rationale documents on the docket are being reviewed by the FDA. • The FDA Web group is refining the process for updating the website when the reviews are completed.
9.	**Text and Tables Working Group (TTWG) Report: Dr. Shelley Campeau (Folder 10)** **WG Roster:** Shelley Campeau, April Bobenchik (Co-Chairholders); Carey-Ann Burnham (WG Secretary); Victoria Anikst, Alexandra Bryson, Suki Chandrasekaran (absent), Mary Jane Ferraro (absent), Andrea Ferrell, Janet Hindler, Melissa Jones (absent), Peggy Kohner, Dyan Luper, Jean Patel (absent), Barth Reller (absent), Felicia Rice (absent), Flavia Rossi (absent), Dale Schwab, Maria Traczewski, Nancy Watz (Members); Darcie Carpenter, Sandra Richter, Barbara Zimmer (WG Liaisons) **Organization of M100.** • The revision and review processes are being improved. • A document to provide structure and guidance to volunteers is being developed. The guidance will include:

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Monday, 17 June 2019 (NOTE: All presentations from the plenary sessions are now available on the CLSI Website (2019 June AST Plenary Presentations)	
	– A general timeline for meetings, staff revisions, TTWG/SC review periods, etc. – Roles of TTWG vs CLSI Staff – Areas to focus on during review – How to complete the CLSI Comment Table provided for TTWG/SC reviews (eg, editorial vs technical vs general comments) – Include a review checklist • Groups will be assigned to review specific sections of the document. **<u>*Staphylococcus* spp. Revisions Review</u>** • Revisions to Table 3E were reviewed. – The WG agreed to update the results interpretation to be consistent with Table 2C. – An issue was raised regarding laboratories that test by methods where highest dilution is 4 µg/mL. It was questioned whether there would be confusion that ≥8 µg/mL is the same as >4 µg/mL. – The TTWG will consider including additional language in front of document to clarify the issue. • Other *Staphylococcus* spp. with oxacillin MICs of 0.5 – 2 µg/mL – 28th edition: The recommendation for using cefoxitin test was removed from Comment (17) until the CoNS Ad Hoc WG completed testing of additional non-*S. epidermidis* staphylococci (underway). This created confusion around cefoxitin recommendations in the methods table at the beginning of Table 2C vs what is in Comment (17). Clarification will be added to the 2C introductory table as a footnote: **"For other *Staphylococcus* spp., cefoxitin disk diffusion is not currently recommended for isolates from serious infections for which the oxacillin MICs are 0.5-2 µg/mL. See comment (17) for recommendations on testing for *mecA* or for PBP2a."** – In addition, Comment (17) in Table 2C will be revised to read: **"Oxacillin MIC breakpoints may overcall resistance. Some isolates for which the that have oxacillin MICs are of 0.5-2 µg/mL have been shown to be *mecA* positive and are *mecA* negative. Isolates from serious infections with MICs in this range may be tested for *mecA* or for PBP2a. Isolates that test either *mecA* or PBP2a negative should be reported as oxacillin susceptible." (NOTE: The comment in M100, 30th ed. has been revised to read: "Oxacillin MIC breakpoints may overcall resistance. Some isolates for which the oxacillin MICs are 0.5-2 µg/mL have been shown to be *mecA* positive and are *mecA* negative. Isolates from serious infections with MICs in this range may be tested for *mecA* or for PBP2a. Isolates that test either *mecA* or PBP2a negative should be reported as methicillin (oxacillin) susceptible.")** • Discussion of whether guidance for other *Staphylococcus* spp. is needed in the molecular tables in Appendix H. – Currently, there is only guidance for *S. aureus*. – It was suggested that guidance for non-*S. aureus* needs to be added Appendix H. – It was agreed that the Methods Application and Interpretation will work on revising Appendix H. **<u>Duplication of dosage information in Tables 2 and Appendix E.</u>** • Since all dosage information is listed in Appendix E, it was suggested in a review comment to delete the information from Tables 2 and refer to Appendix E. The WG agreed to the change but requested input from the SC.

<table>
<tr><th colspan="2">SUMMARY MINUTES</th></tr>
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<tr><td></td><td>
• Dr. Mathers liked the idea if links to the Appendix could be added.
• Dr. Schuetz, Dr. Satlin, and Dr. Limbago all agreed that the information should be listed in both Tables 2 and Appendix E.
• Dr. Patel noted that the Appendix is a good reference for the pharmacy. She agreed that it should be retained as is and that it is acceptable to have the information in both places.
• The SC decided to retain the information in both Tables 2 and Appendix E.

<u>Comment consistency for drugs in multiple tables</u>
• The WG is addressing comment consistency for drugs in multiple tables (eg, interference of doxycycline and/or minocycline from tetracycline results, etc)
• Also, being reviewed are comments that include the word “only” (eg, reporting comments).
• The TTWG will performing a full review of all comments.

<u>Removal of Norfloxacin from the QC tables</u>.
• It was questioned why norfloxacin was removed from document. It was stated that the drug was removed because it was believed to be no longer available.
• It was proposed that the drug and ranges need to be re-inserted into the QC tables, Table 2A for <u>urine only,</u> and all glossaries.

A motion to reinstate norfloxacin in the QC tables, Table 2A for urine only, and in all glossaries was made and seconded. Vote: 11 for, 0 against;1 absent (Pass)
</td></tr>
<tr><td>10.</td><td>
<u>M39 Working Group Report</u>: Dr. Trish Simner
WG Roster: Janet Hindler; Trish Simner (Co-Chairholders); April Abbott (WG Secretary); Faiza Benahmed, Tanaya Bhownick, Sanchita Das, Sharon Erdman, Andrea Ferrell, Kristie Johnson, Ron Master, Jimish Mehta, Ian Morrissey, Melinda Neuhauser, Michael Nowak, Mark Redell, Helio Sader, Dawn Sievert, Paula Snippes-Vagnone, John Stelling

• The team and its tasks were reviewed.
<table>
<tr><th>Team #1</th><th>Team #2</th><th>Team #3</th></tr>
<tr><td>Review current M39
Expand specific ways to use local antibiogram for ASP and include guidance for LTCF</td><td>Antimicrobial Resistance Surveillance Program Design → Multi-Facility Antibiogram & Publication</td><td>IT – Data extraction & presentation</td></tr>
<tr><td>Erdman, Sharon - LEAD</td><td>Redell, Mark - LEAD</td><td>Das, Sanchita - LEAD</td></tr>
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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	

- The draft has been reorganized based on a chapter cross-walk.
  - **Part 1: Introductory Information**
    - Chapter 1: Introduction (Much new terminology)
    - Chapter 2: Information System Design (Many changes [AST instrument, LIS, EHR])
  - **Part 2: Routine Cumulative Antibiogram**
    - Chapter 3: Data Analysis (Validating the antibiogram)
    - Chapter 4: Data Presentation (Final checks of the antibiogram)
  - **Part 3: Other Types of Antibiograms**
    - Chapter 5: The Enhanced Antibiogram (Combining AMR with the antibiogram)
    - Chapter 6: The Long Term Care Facility (LTCF) Antibiogram (NEW)
    - Chapter 7: The Veterinary Antibiogram (NEW)
  - Part 4: Using the Routine Antibiogram (NEW content added)
    - Chapter 8: Intended Use of the Antibiogram Report (Added %S Threshold)
    - Chapter 9: Distribution and Communication (Web-based, smart phone apps, etc.)
    - Chapter 10: Antimicrobial Stewardship Programs and Use of the Cumulative Antibiogram (NEW)
  - **Part 5: Multi-Facility Antibiograms – NEW**
  - **Part 6: Use of Statistics with Cumulative AST Data (NEW content added – percentiles, interquartile range, MIC50/MIC90)**
  - **Part 7: Considerations for Publishing Cumulative AST Data (NEW)**
  - **Part 8: Conclusions & Supplemental Information**

- New information to be added includes:
  - Examples of gram-positive, yeast, combined gram-positive and gram-negative & multi-facility antibiograms.
  - Step-wise instructions to prepare a multi-facility combined antibiogram
  - Review of antibiogram content before the report is released

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	– Frequently asked questions section • Path Forward and Next Steps – A merged working draft is available. – The WG will review presentation of the content in the Crosswalk. – WG members will review the document critically and provide feedback. – The references, bibliography, appendixes, tables, graphs, and formatting will be reviewed. – Each group will work on companion manuscripts. – The WG will clean-up the draft between now and November. – It is expected that the draft will be submitted for the January 2020 meeting. – Publication is expected sometime in 2021.
11.	**Adjournment** Dr. Weinstein adjourned the meeting at 5:50 PM Central (US) time. He stated that the meeting on Tuesday, 18 June 2019 would begin at 7:30 AM.

SUMMARY MINUTES	
#	**Description**
Tuesday, 18 June 2019	
1.	Dr. Weinstein opened the meeting at 7:30 AM Eastern (US) time.
2.	**Methods Development and Standardization Working Group Report: Dr. Dwight Hardy (Folder 7)** **WG Roster:** Dwight Hardy/Barbara Zimmer (Co-Chairholders); Katherine Sei (WG Secretary); Jennifer Dien Bard, Bill Brasso, Susan Butler-Wu, Laura Koeth, Tanis Dingle, Ribhi Shawar (Members). **NOTE:** The WG is looking to add new members. Any interested volunteers can contact Marcy Hackenbrack (mhackenbrack@clsi.org). **Joint CLSI-EUCAST Disk Content Selection and QC WG (Folder 7, Items 3A-3D)** AHWG Roster: See table

CLSI	EUCAST
Janet Hindler (Co-chair)	Erika Matuschek (Co-chair)
Mariana Castanheira	Christian Giske
Sharon Cullen	Gunnar Kahlmeter
Laura Koeth	Mandy Wootton (Recording Secretary)
Maria Traczewski	John Turnidge (Statistical advisor)

- The CLSI and EUCAST disk diffusion test methods are the same. The WG was formed to potentially harmonize disk content (potency) criteria and QC, and to establish QC ranges.
  - Draft standard operating procedures (SOPs) have been circulated to the SC members, advisors, and reviewers for comment.
  - Comments should be submitted to Janet Hindler.

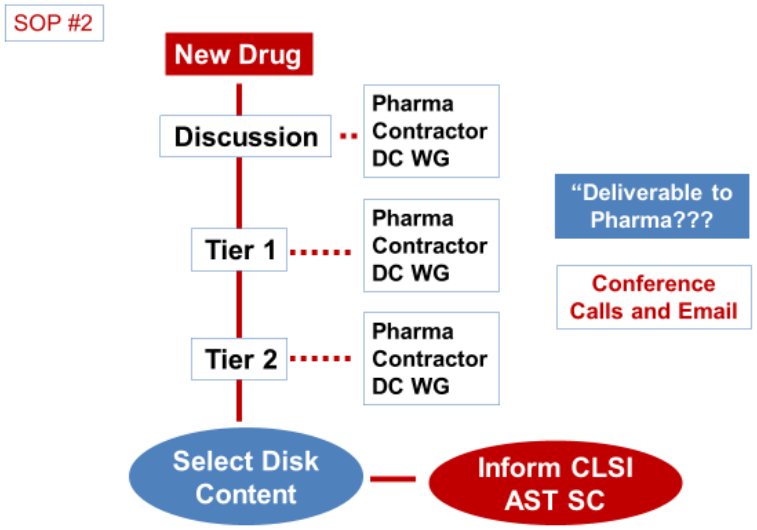
- Disk Content Selection
  - Currently, CLSI is not involved in determining disk content. Pharmaceutical sponsors select the disk content based on M23 requirements.
  - EUCAST is usually contacted after the content for the US market has already been decided which has led to the differences.
  - It is hoped that CLSI and EUCAST collaboration early in the process will help standardize disk testing globally.
  - The goal is to develop processes for how CLSI can be involved.

- Determining optimum disk content for disk diffusion susceptibility testing: SOP#1
  - The goal is to provide step-by-step instructions for determining optimal disk content. The SOP is planned to be added to the next M23 edition.
  - The guidance in M23 will be harmonized with EUCAST SOP 9.1.

- Managing the process – Establish a process for working with stakeholders to comply with the recommended “science”: SOP#2
  - EUCAST has already established this process.
  - THE SOP would describe a process for how CLSI would work with pharma and the FDA.

#	Description

– The plan is to determine if data produced during disk content development by either CLSI or EUCAST will be acceptable to stakeholder organizations.
– Flow chart for SOP#2 process



- The WG requested that the AST SC consider the following:
  – Where should the SOPs be published and when? The goal is to publish the appropriate language in the new edition of M23.
  – Where should the data be stored?
  – Will the disk content (DC) WG make final decision? If so:
  – They would give the sponsor a "GO"!
  – They would communicate to AST SC at January and June meetings
  – It was questioned how the stability of the DCWG membership would be maintained.

- The proposed content of SOP#1 (Science) was reviewed (see the Methods Development presentation on the CLSI Website for details). The SOP includes criteria for disks with drug content that:
  – Produce reproducible inhibition zones
  – Reproducibly distinguish between isolates with different MIC values
  – Can be used for all species
  – Results in an increase in zone diameters of 2-3 mm with each $\log_2$ decrease in MIC for non-wild type (NWT) isolates (dose response)
  – Results in inhibition zone diameters between 15 and 35 mm for wild-type (WT) species.
  – Results in optimal separation between WT and NWT (when present).
  – Results in optimal separation between NWT isolate with differing MICs (not dependent on resistance mechanisms)

#	Description

– Tier 1 and Tier 2 testing criteria and analysis methods were reviewed (see the Methods Development presentation on the CLSI Website for details).
– Testing parameters for Tier 1 and Tier 2 studies

Parameter	Tier 1	Tier 2
# Disk Contents	10	2-3
Lots Mueller-Hinton agar	1	2 manufacturers
Isolates	2/relevant species	30/species 60/organism group (targeted for drug) (50% WT/50% NWT, if available)

- Statistics will be calculated using the CLSI error-rate bounded method (M23), and an additional statistical methods (dBETs).

- Issues to consider were reviewed
  – Availability of commercial disks disk content studies: Not all manufacturers make disks according to international standards.
  – QC criteria for experimental disks: These are generally tighter than CLSI M100 QC ranges.
  – Other considerations
  – Definition of target species
  – Isolate source(s)
  – Disk concentration assay
  – Disk stability
  – Number of readers (blinded
  – Criteria for acceptable disk test
  – Statistical formula
  – Allowable disk content (as per regulatory organizations)

- SC Discussion
  – Dr. Castanheira noted that the implementation timeframe depends on M23 publication.
  – Dr. Galas commented that defining the quality of the disk is difficult and looking at the standard deviation should be considered.
  – Dr. Thrupp commented that there could be complications with other parameters. A rapid FDA approved direct rapid disk reading procedure is needed. The stability of the zone at 8 hrs. compared to 16–24 hrs. could be different based on the disk mass.
  – Dr. Shawar stated that the protocol needs to be less prescriptive (eg, best practice points to consider etc.) in order to take differences in drugs and organisms into consideration.
  – Ms. Hindler noted that it needs to be ensured that reviewing of the data by both organizations is acceptable. She also questioned if all data need to be presented to the DCWG. That will need to be decided.
  – Dr. Castanheira noted that it would be easier and less burdensome for disks to be harmonized in both the US and Europe early in the development process. Currently, sponsors must do the studies twice, once for the FDA and again for Europe.

- Dr. Moeck commented that it's a worthwhile goal to harmonize disk content. The suggested protocol is an excellent plan. There are concerns about the multiple touchpoints that need to be managed. It is hoped that the sponsor's timeline doesn't get delayed due to the interaction with the DCWG and sponsors.
- Dr. Galas remarked that it will be beneficial to have harmonized disks that can be applied to both CLSI and EUCAST.
- Dr. Hardy noted that the DCWG should be empowered by the SOP to quickly approve the content not delay the sponsor.
- Ms. Cullen noted that for clarification, the Tier 2 is not the Tier 2 QC study but two phases of studies for determining disk content. The intention is that these studies are performed in research laboratory and are not performed on a large scale. She suggested that the timeline for comments should align with EUCAST's deadline for comments.
- Dr. Castanheira provided a brief overview of how disk content is currently being selected. The sponsor will select a tentative content based on experience. The sponsor will select a research organization (eg, JMI, CMI) to test and analyze the disk. The disk content selected often depends on which organization analyzes the data and can differ from the content selected by the sponsor.
- Several other noted that EUCAST has in their guidance that they are the final arbiter for disk selection in Europe and to get a CE mark on the disk for use in Europe must follow EUCAST guidance.

Colistin Testing Methods AHWG

AHWG Roster: Romney Humphries (Chairholder); Dan Green, Audrey Schuetz, Trish Simner (Members)

- Studies for two methods for colistin AST were presented.
  - Colistin disk broth elution (CBDE)
  - Colistin Agar Test (CAT) using a 1 µL and 10 µL calibrated loop or pipette for inoculum
  - Both methods were compared to broth microdilution (BMD), performed using 3 lots (brands) of cation adjusted Mueller-Hinton broth (CAMHB), at three sites with isolates from stock laboratory collections, and challenge isolates compiled from all sites

- CBDE Method
  - Disks: BD, 10 µg colistin disk
  - CA-MHB: Remel (10 mL or 25 mL)
    - 0 disk = growth control
    - 1 disk to 25 mL = 0.4 µg/mL
    - 1 disk to 10 mL = 1 µg/mL
    - 2 disks to 10 mL = 2 µg/mL
    - 4 disks to 10 mL = 4 µg/mL
  - Incubate the tubes at room temperature for at least 30 min but no more than 60 min.
  - Add 50 µL 0.5 McFarland organism and vortex.
  - Incubate the tubes at 35°C for 18–20 hr.
  - Read MIC based on growth and no growth in each tube.

- CAT Method
  - Used 0, 0.5, 1, 2 and 4 µg/mL colistin MHA plates (3 manufacturers)
  - Inoculated with 1 µL or 10 µL loopful of a 1:10 dilution of a 0.5 McFarland suspension

- Incubated 16-20 hr and read visually for any growth as (+).

- Study Design
  - For each isolate, the same inoculum was used to perform the BMD, CBDE, CAT methods in parallel.
  - QC: "routine" *P. aeruginosa* 27583 and "supplemental" CDC 349 *E. coli* with *mcr-1* (anticipated on-scale results).
  - If QC was out, 1+ result outside categorical agreement (CA) or skipped wells were observed, testing was repeated by all methods 1×.
  - Data analysis (see the Methods Development presentation on the CLSI Website for details).
  - Accuracy: Both challenge and stock isolates were included in the evaluation and essential agreement (EA) and CA were calculated as per M23.
  - Precision: Just the challenge isolate results were analyzed.

- CBDE Results

	N	**%**
EA	592	94.42
CA	615	97.93
Very major errors (VME)	9	3.23
Major errors (ME)	3	0.86

  - 4 VME due to *Acinetobacter* spp. (not in EA)
  - 5 VME due to *E. coli* (4 *mcr-1*) – in 4/5 in EA
  - 2 ME due to *Acinetobacter* spp.
  - 1 ME due to *P. aeruginosa*

- CAT Results: 1µL

	N	%
EA	593	94.88
CA	606	96.96
Very major errors (VME)	19	6.83
Major errors (ME)	0	0.00

- CAT Results: 10µL

	N	%
EA	603	96.17
CA	616	98.25
Very major errors (VME)	11	3.94
Major errors (ME)	0	0.00

SUMMARY MINUTES	
#	Description

- Summary of the testing method results
  - Enterobacterales

Method	CA	VME	ME	Notes	Recommendation
CBDE	98.6%	2.6%	0%	VME but in EA for 4/20 *mcr-1* tests	Approve Method
1 µL CAT	99.4%	1.0%	0%		Don't approve (easier to read 10 µL)
10 µL CAT	99.7%	0.5%	0%	Felt 10 µL loop easier to read	Approve Method

  - *P. aeruginosa*

Method	CA	VME	ME	Notes	Recommendation
CBDE	98.6%	0%	0.7%		Approve Method
1 µL CAT	98.6%	8.3%	0%	1 VME only, no growth on repeat, 10 µL ok	Don't approve (easier to read 10 µL)
10 µL CAT	100%	0%	0%		Approve Method

  - *Acinetobacter* spp.

Method	CA	VME	ME	Recommendation
CBDE	95.4%	5.7%	3.3%	**Do not approve**
1 µL CAT	88.5%	21.4%	0%	**Do not approve**
10 µL CAT	92.3%	14.3%	0%	**Do not approve**

- The WG requested approval for both methods for Enterobacterales and *Pseudomonas* only.

- SC Discussion
  - Dr. Shawar noted that these are basically qualitative tests (only 2 points of data) and has concerns with the VME and ME evaluations.
  - Dr. Moeck expressed concern about the CA errors with the Enterobacterales at 2 µg/mL. There seems to be a lack of visibility for the potential for CA errors. Colistin has been shown to non-specifically bind to glass and plastic and a surfactant can't be used. There is also a problem with the 30 min. incubation period for CBDE and questioned whether that is controllable in the laboratory. He suggested that the type of tube (glass vs plastic) needs to be specified as colistin binds to plastic and the binding is time dependent.
  - Dr. Simner reported that the group tried to look for isolates in the US that were at the cutoff or were resistant; however, they are rare.
  - Dr. Galas stated that CBDE has been validated in Latin America for 1 mL (final volume) and works well. He also noted that 30 min. is sufficient for the drug to elute.

SUMMARY MINUTES	
#	Description
	– Dr. Edelstein asked for clarification that a single manufacturer broth was used (Dr. Simner stated that only broth [multiple lots] from 1 manufacturer was available that is already aliquoted into tubes). He questioned whether the test will be manufacturer specific for media and suggested that proof is needed that the test works with broth from additional manufacturers. – Ms. Cullen stated that, as per M23 for method development, three broth lots from one manufacture are acceptable. If problems are seen with the media, further evaluation may be needed. QC studies were performed with 3 lots of media from multiple manufacturers and that the method should be approved or disapproved based on QC. – Dr. Carpenter reported that problems with the disk elution procedure were found (reproducibility) with anaerobes so the test was dropped. She recommended caution. – Dr. Kitty Anderson asked if a comparison between colistin concentration in broth before (prepared from stock) vs from elution with broth had been considered and suggested that the CDC could do the testing. – Dr. Simner noted that CBDE tends to test 1 dilution different and that most are *mcr* strains. – Dr. Satlin stated that, currently, laboratories now have no way to identify isolates that are truly resistant to colistin or polymyxin B and something is needed to help laboratories test. – Ms. Cullen suggested that comment be included with the procedure stating that only one manufacturer, but multiple disk lots were used in the study. In the meantime, data with additional manufacturers and disk could be performed. – Dr. Galas stated that he will share the validation data for CBDE from Latin America. • Votes
	A motion to approve the colistin agar test (CAT) for 10 µL inoculum with Enterobacterales and *Pseudomonas aeruginosa* as presented in the agenda material was made and seconded. Vote: 11 for, 0 against, 1 absent (Pass).
	A motion to add a comment to the CAT method that the procedure is based on limited data (see below) was made and seconded. Vote: 11 for, 0 against, 1 absent (Pass).
	A motion to approve the colistin broth disk elution test (CBDE) for Enterobacterales and *Pseudomonas* with a comment be added that the procedure is based on limited data was made and seconded. Vote: 10 for, 1 against, 1 absent (Pass).

	– Motion Discussion
	  ○ Dr. Edelstein noted that since only one broth manufacturer and one disk manufacturer that the procedure specifically state that only certain manufacture materials should be used. **NOTE:** As per CLSI policy, specific manufacturers cannot be mentioned in CLSI documents.
	  ○ Dr. Mathers commented that although the data is limited, more data might be collected in time to verify that the data that was presented.
	  ○ Ms. Hackenbrack stated that the final reviewed and SC approved draft must be submitted to the editors to prepare to publish by mid-October.
	– **Voting comment**: Dr. Schuetz did not approve the method because she would like to see more data and believes this procedure is too premature to publish.
	
	• **Ms. Cullen drafted a comment to include with methods:** "These methods were established with limited reagent manufacturers and are considered provisional until additional testing is performed to meet M23 guidelines."

SUMMARY MINUTES	
#	Description
	A motion to approve the comment to be added to the CAT and CDE methods as written was made and seconded. Vote:11 for, 0 against, 1 absent (Pass).
	Cefiderocol Method • The MIC methodology for cefiderocol using iron-depleted CAMHB (ID-CAMHB) and QC criteria was approved at January 2016 CLSI meeting. However, the exception is not shown in the list of exceptions in the current edition of M07 (11th). • A photograph was provided to help with reading the endpoint. • The sponsor requested that M07 be modified to include the information. **NOTE:** M07 was last published in January 2018 and, is not scheduled to begin revision until at least 2021. • It was questioned where to place the instructions until M07 is revised. Options included: – Add a new table in M100 for instructions for preparing media. A reference would be added where the drug is cited in Tables 2. – Add as an appendix **NOTE:** After a discussion with CLSI management, it has been decided that the methodology instructions should be located in M100 until M07 is revised. The photographs and procedure are located on the CLSI shared drive. The Methods Development and Text and Tables WGs will work together to place the procedure in M100. ***Haemophilus influenzae* AST Method Comparison** • CDC is investigating higher resistance in *H. influenzae* strains. • Three methods were performed and compared to confirm the observed reduced susceptibility. – CLSI BMD – Gradient diffusion – EUCAST BMD • Summary – CLSI and EUCAST BMDs have poor CA and EA (particularly for β-lactams) – CA with E-test is better for EUCAST BMD than CLSI BMD – Reduced susceptibility interpretations for BMD assays are often caused by "substantially inhibited growth" phenotypes – BMD was reassessed using different criteria for the MIC – CLSI BMD assay was more affected by change in interpretation criteria. – CLSI: CA of two interpretations (<45% for 10 antibiotics). – EUCAST: CA of two interpretations (>73% for 11 antibiotics) – Exclusion of "substantially inhibited growth" improved categorical agreement of both BMD assays with E-test – A multi-laboratory study to compare media (HTM and MH fastidious) that is being used for AST was proposed. **AHWG Updates** • Due to lack of time, reports from the following WGs were postponed. Please see the MDSWG presentation posted on the CLSI Website for more information. – Direct BC AST AHWG – BMD Reference Method Revision AHWG

SUMMARY MINUTES	
#	Description
	– Coordinated Development AHWG – Coagulase-Negative *Staphyloncus* AHWG – Cefazolin High-Inoculum AHWG
3.	**Outreach Working Group Report: Dr. Audrey Schuetz/Ms. Janet Hindler (Folder 8)** **WG Roster:** Janet Hinder, Audrey Schuetz (Co-Chairholders); Stella Antonara (WG Secretary); April Abbott, April Bobenchik, Angella Charnot-Katsikas, Romney Humphries, Graeme Forrest, Nicole Scangerella-Oman, Paula Snippes-Vagnone, Lars Westblade (Members); Katie Barnett for Megan Hickey (CLSI staff) • The most recent issue of the AST newsletter was published in June and it being translated into Spanish and Chinese. The newsletter included: – An "In Memorium" article for Dr. Sidney Finegold – Featured article: Practical Approach to Evaluating Requests to Test New Antimicrobials – Practical Tips: Where Can We Find the Latest Resources for *C. auris*. – Hot Topic: The Antibiotic Resistance Laboratory Network – Bridging the Gap by Offering Expanded Antimicrobial Susceptibility Testing • Items to be included in the upcoming Fall 2019 newsletter include: – Featured Article: Point-Counterpoint Centralized vs. Decentralized AST Processing in Clinical Laboratories (workflow) – Case Study: *Staphylococcus* spp. not *S. aureus* – Practical tips: Fungal Nomenclature – Hot topic: Enterobacterales • 40 new volunteers have been oriented to the SC process. • The ORWG distributed a "wish list" of needs for each WG. The list will be distributed by July 1st to reflect needs identified during the June meeting. • Recent and upcoming AST SC Meeting Workshops were reviewed. – June 2019: "To MIC or Not to MIC – That is the Question: Molecular Characterization of Antimicrobial Resistance for Healthcare in 2019" – January 2020:"Beyond SIR: Enhancing Laboratory Reports with Comments to Improve Understanding of the Report's Intent." • Recent and upcoming Webinars were reviewed. – Recent o THE 2019 annual M100 update (29th ed) was held on February 20th and 21st. o The CLSI/SIDP/ACCP Annual Webinar, "Merging Microbiology and Stewardship: Making the most of 2019 CLSI updates on antimicrobial susceptibility testing for your stewardship activities", was held in May. – Upcoming o The CLSI-APHL Joint Webinar: "Understanding MDROs: the implications for the laboratory and IPs" is scheduled for September 19, 2019 o CAP-CLSI Joint Webinar – TBD o Rationale Documents Updates – TBD o Fall 2019: VET09 - "Understanding Susceptibility Test Data as a Component of Antimicrobial Stewardship in Veterinary Settings" o 2020 ▪ M100 (30th ed.) annual update

<table>
<tr><th colspan="2">SUMMARY MINUTES</th></tr>
<tr><th>#</th><th>Description</th></tr>
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Staphylococci other than S. aureus
Nomenclature updates
M39 Antibiogram (following publication)
Annual webinars with organizational partners

The 2019 ASM Symposium will be held on June 23: “Progress in Detection of Antimicrobial Resistance: CLSI, FDA and Public Health Solutions”

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)

The CLSI Website now has improved search capabilities

Tags and searches within documents
Searches and prompts for frequently asked questions

New projects were outlined

Colistin issues
Bench to bedside series for clinicians and trainees (methods with case example; expect collaboration with ORWG and IDSA)
Additional clinical laboratory technologist materials (collaborate with APHL, ASM etc.)
In process of obtaining new antifungal liaison

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<tr><td>4.</td><td>
<u>M23 Working Group Report</u>: Dr. Matt Wikler/Dr. Avery Goodwin (Folder 11)
WG Roster: Matt Wikler, Avery Goodwin (Co-Chairholders); Timothy Bensman, Mariana Castanheira, Patricia Conville, Sharon Cullen, Romney Humphries, Linda Miller, Stephanie Mitchell, Greg Moeck, David Nicolau, Margaret Ordoñez de Danies, Michael Satlin, Simone Shurland, Hui Wang (Members)

The anticipated timeline for the revision was provided

June 2019: Open WG meeting to present and discuss suggestions and recommendations for each area
June 2019-December 2019: members/groups refine suggestions through teleconferences
December 2019: Specific proposed wording for each section to be submitted for inclusion in the January 2020 AST agenda book
January 2020: Open WG meeting to review the entire document and discuss the remaining items needing discussion
January 2020 – March 2020: Final revisions made by each group
April 2020-May 2020: Dr. Humphries and Dr. Miller perform a one voice edit to assure clarity and consistency
May 2020: Proposed final document submitted for inclusion in the June 2020 agenda book
June 2020: Proposed final revised M23 draft presented for vote by AST Subcommittee for approval (<u>NOTE:</u> this draft will be submitted for formal 60-day proposed draft vote by the SC members and CLSI member delegates and review by the SC advisors and reviewers, and M23 WG.)
Standard CLSI review and comment periods, leading up to publication

Items discussed at the M23 overview session

Currently there is no process in M23 for new breakpoints for a new organism group not originally requested by the sponsor.

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SUMMARY MINUTES	
#	**Description**
	– What to do if the breakpoint isn't in agreement with the sponsor's request and they withdraw the request. – What to do if the sponsor never comes to SC with a request (eg, tigecycline) – Deferral period for the sponsor (Chapter 4) needs to be clarified. – Requests for new information: Ensure the sponsor knows what is needed vs. a moving target – The work plan for breakpoints will be assessed. – Plan for announcing ad hoc workgroups more systematically – Talk about note re: limited data used to establish breakpoint in M100 – Clarify investigational (INV) vs provisional (PROV). M23 says CLSI doesn't publish, but we did for INV; clarify the difference. – How to evaluate MIC variance for non-clinical cut offs – Create a template to help sponsors provide the data CLSI needs.
5.	**Adjournment** • Dr. Weinstein thanked the participants for their attention and the WG and SC members for the continued hard work and commitment. • The next meeting of the AST Subcommittee is scheduled for 26 – 28 January 2020 in Tempe, Arizona. Agenda materials are due for submission by **Wednesday, 11 December 2019.** • The meeting was adjourned at 10:50 AM Central (US) time.

Upcoming Meetings of the Subcommittee on Antimicrobial Susceptibility Testing:

26 – 28 January 2020 in Tempe, Arizona, USA (Agenda material submission due date – Wednesday, 11 December 2019)
14 – 16 June 2020 in Baltimore, Maryland, USA (Agenda material submission due date – Friday, 8 May 2020)
24 – 26 January 2021 in Arlington, Texas, USA (Agenda material submission due date – Friday, 11 December 2020)

	ACTION ITEMS	Responsible
1.	Review and reassign the antimicrobial agents in Table 1 as appropriate. Present the revised table at the January 2020 meeting.	Table 1 WG
2.	Review archived minutes and data from the meetings when BPs were set for *S. maltophilia* (chloramphenicol, levofloxacin).	BPWG
3.	Submit comments on draft SOPs from the Joint CLSI-EUCAST WG to Janet Hindler.	All

Summary of Passing Votes			
#	**Motion Made and Seconded**	**Results***	**Page**
1.	To accept the summary minutes from the January 2019 subcommittee meeting.	12-0-0-0 (Pass)	7
2.	To accept the WG proposed definitions for Groups A, B, and C in Table 1 and to move them into the categories on Table 1. NOTE: It was decided that these changes will be made in the 31st edition of M100.	12-0-0-0 (Pass)	11
3.	To delete the QC range for *E. faecalis* ATCC 29212 and plazomicin.	12-0-0-0 (Pass)	13
4.	To reassess the QC ranges for *E. faecalis* ATCC 29212 and the aminoglycosides.	12-0-0-0 (Pass)	14
5.	To change the disk diffusion QC range for *E. coli* ATCC 25922 and ciprofloxacin to 29-38 mm.	12-0-0-0 (Pass)	14
6.	To accept the QC strain (*E. coli* AR Bank #0349) and range (1 – 4 µg/mL) as provisional for colistin broth disk elution and colistin agar test with footnotes and with the assumption that the methods are approved.	12-0-0-0 (Pass)	16
7.	To add a footnote where *S. typhi* BPs or in routine QC boxes to refer to *S. aureus* ATCC 25923 for QC. Text and tables will determine where to place the footnote and to wordsmith.	12-0-0-0 (Pass)	17
8.	To accept the revision of Footnote 8 in Table 2A ("Confirmatory MIC testing is indicated for isolates with zones of 20–22 mm").	12-0-0-0 (Pass)	18
9.	To set the colistin BPs as intermediate at ≤2 µg/mL and resistant at ≥4 µg/mL for Enterobacterales with associated warnings and comments. • Clinical and PK/PD data demonstrate this agent is of limited clinical efficacy. • If available, alternative non-polymyxin agents are strongly preferred. If these agents are not available, this breakpoint presumes use of colistin in combination with one or more additional, active antimicrobials. • Colistin (methanesulfonate) should be given with a loading dose and maximum renally adjusted doses. • When given systemically, this drug is unlikely to be effective for pneumonia	11-1-0-0 (Pass)	23
10.	To accept the colistin BPs for *Pseudomonas* and *Acinetobacter* as intermediate at ≤2 µg/mL and resistant at ≥4 µg/mL with the same comments (see above) as for Enterobacterales.	11-1-0-0 (Pass)	24
11.	To accept the proposed polymyxin B BPs as intermediate at ≤2 µg/mL and resistant at ≥4 µg/mL with same warning and comments as for Enterobacterales.	11-1-0-0 (Pass)	25
12.	To accept the proposal to move levofloxacin and minocycline to Group A in Table 1 in same box with TMP-SMX above ceftazidime and to list the drugs alphabetically.	11-0-0-1 (Pass)	26
13.	To reinstate norfloxacin in the QC tables, Table 2A for urine only, and in all glossaries was made and seconded.	11-0-0-1 (Pass)	33
14.	To approve the colistin agar test (CAT) for 10 µL inoculum for testing with Enterobacterales and *Pseudomonas aeruginosa* as presented in the agenda material.	11-0-0-1 (Pass)	42
15.	To add a comment to the CAT method that the procedure is based on limited data.	11-0-0-1 (Pass)	42
16.	To approve the colistin broth disk elution test (CBDE) for Enterobacterales and *Pseudomonas* with a comment be added that the procedure is based on limited data.	10-1-0-1 (Pass)	42
17.	To approve the comment to be added to the CAT and CDE methods as written (These methods were established with limited reagent manufacturers and are considered provisional until additional testing is performed to meet M23 guidelines").	11-0-0-1 (Pass)	43

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

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