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Summary Minutes
Subcommittee on Antimicrobial Susceptibility Testing
Grand Hyatt Tampa Bay
Tampa, Florida
13-15 January 2013

A meeting of the CLSI Subcommittee on Antimicrobial Susceptibility Testing was held on 13-15 January 2013, at the Grand Hyatt Tampa Bay, Tampa, Florida. The following were in attendance:

Jean B. Patel, PhD, D(ABMM) **Chairholder**	**Centers for Disease Control and Prevention**
Franklin R. Cockerill, III, MD **Vice-Chairholder**	**Mayo Clinic**
Richard B. Thomson, Jr., PhD **Consensus Committee on Microbiology** **Chairholder**	**Evanston Hospital, NorthShore University HealthSystem**
John H. Rex **Consensus Committee on Microbiology** **Vice-Chairholder**	**AstraZeneca**

Members Present

Jeff Alder, PhD	Bayer HealthCare
Patricia A. Bradford, PhD	AstraZeneca Pharmaceuticals
George M. Eliopoulos, MD	Beth Israel Deaconess Medical Center
Dwight J. Hardy, PhD	University of Rochester Medical Center
Janet A. Hindler, MCLS, MT(ASCP)	UCLA Medical Center
Stephen G. Jenkins, PhD, D(ABMM),F(AAM)	New York Presbyterian Hospital
James S. Lewis, II, PharmD	University of Texas Health Science Center
Linda A. Miller, PhD	GlaxoSmithKline
Mair Powell, MD, FRCP, FRCPath	MHRA
John Turnidge	SA Pathology
Melvin P. Weinstein, MD	Robert Wood Johnson Medical School
Barbara L. Zimmer, PhD	Siemens Healthcare Diagnostics Inc.

Advisors Present

Steven D. Brown, PhD, ABMM	The Clinical Microbiology Institute
Karen Bush, PhD	Indiana University
William A. Craig, MD	University of Wisconsin School of Medicine

Michael N. Dudley, PharmD, FIDSA	Rempex Pharmaceuticals, Inc.
Cynthia L. Fowler, MD	MFHSC
Howard Gold	Beth Israel Deaconess Medical Center
Romney M. Humphries, Ph.D., D(ABMM)	UCLA David Geffen School of Medicine
Gunnar Kahlmeter, MD, PhD	ESCMID
Brandi Limbago, PhD	Centers for Disease Control and Prevention
Melissa B. Miller, Ph.D., D(ABMM)	UNC School of Medicine
Sumathi Nambiar, MD, MPH	FDA/CDER
David P. Nicolau, PharmD, FCCP, FIDSA	Hartford Hospital
Robin Patel, MD	Mayo Clinic
Sandra S. Richter, MD, D(ABMM)	Cleveland Clinic
Flavia Rossi, MD	University of Sao Paulo
Jeff Schapiro	Kaiser Permanente
Audrey N. Schuetz, MD, MPH, D(ABMM)*	Weill Cornell Medical College/ NewYork-Presbyterian Hospital
Susan Sharp, PhD, D(ABMM)	ASM Representative from Kaiser Permanente-NW
Ribhi M. Shawar, PhD, D(ABMM)	FDA Ctr. for Devices/Rad. Health (CDRH)
Kerry Snow, MS, MT(ASCP)	FDA/CDER
Jana M. Swenson, MMSc	
Joseph G. Toerner, MD, MPH*	FDA CDER

Reviewers Present

Francis Ahern	The Medicines Company
Paul G. Ambrose, PharmD, FIDSA	ICPD/Ordway Research
Robert E. Badal	International Health Management Assoc Inc.
Bret Benton, PhD	Theravance Inc.
Sujata M. Bhavnani, PharmD	Ordway Research Institute
Donald Biek, PhD	Cerexa, Inc.
Lynn Boyer	Siemens Healthcare Diagnostics
Mary Ann Brandt	OU Medical Center
William B. Brasso	BD Diagnostic Systems
Linda C. Bruno, MA, MT(ASCP)	Saints Mary and Elizabeth Medical Center
Carey-Ann Burnham, PhD, D(ABMM)	Washington University School of Medicine
Kathy Burtner	Siemens Healthcare Diagnostics
Rafael Canton	EUCAST
Mariana Castanheira, PhD	JMI Laboratories
Laurent Chesnel	Cubist Pharmaceuticals, Inc.
Diane M. Citron, M(ASCP)	R.M. Alden Research Laboratory
Christian Coogan	bioMérieux
Ian A. Critchley, PhD	Cerexa, Inc.
Sharon K. Cullen, BS, RAC	Siemens Healthcare Diagnostics Inc.
Michael J. Dowzicky	Pfizer, Inc.
Evelyn Ellis-Grosse, PhD	E2g Consulting
German Esparza, BSc	Hospital Santa Clara
Michelle Evans	Siemens Healthcare Diagnostics

Gina L. Ewald-Saldana, CLS(CA), MT(ASCP)	Siemens Healthcare Diagnostics Inc.
Sheila Farnham	bio Mérieux
Robert K. Flamm, PhD	JMI Laboratories
Thomas R. Fritsche, MD, PhD	Marshfield Clinic
Marcelo Galas	Reference Centres of Latinoamerican Countries
Beth P. Goldstein, PhD	Beth Goldstein Consultant
Meredith Hackel	International Health Management Assoc, Inc.
Henry S. Heine, PhD	Institute of Therapeutic Innovation
Patricia Hogan, MT(ASCP), MBA	Pfizer Inc
Nilda V. Jacobus	Tufts Medical Center
Jack L. Johnson	International Health Management Assoc, Inc.
Judith Johnston, MS	Siemens Healthcare Diagnostics Inc.
Ronald N. Jones, MD	JMI Laboratories
James H Jorgenson, PhD*	University of Texas Health Science Center
Maria Karlsson	CDC
Scott B. Killian	Thermo Fisher Scientific
Cynthia C. Knapp, MS	Thermo Fisher Scientific
Roberta Knefel	bio Mérieux
Laura M. Koeth, MT(ASCP)	Laboratory Specialists, Inc.
Colleen S. Kraft, MD	Emory University School of Medicine
Brigitte Lefebvre	Laboratoire de santé publique du Québec
Xian-Zhi Li	Heath Canada Veterinary Drugs Directorate
Jim Lindsay	Mast International
Jennifer Lorbach	Thermo Fisher Scientific
Dyan Luper, BS, MT(ASCP)SM	BD Diagnostic Systems
Linda M. Mann, PhD, D(ABMM)	Siemens Healthcare Diagnostics Inc.
Maureen Mansfield	Thermo Fisher Scientific
Amy J. Mathers, MD	Univ. of Virginia School of Medicine
Maria Matuschek, PhD	ESCMID
Sandra McCurdy	Cubist
Hiroshige Mikamo, MD, PhD	Aichi Medical Univ Graduate School of Medicine
Greg Moeck	The Medicine Company
Lori T. Moon, MT(ASCP)	MSU Diag Ctr for Population & Animal Health
Ian Morrissey, MBA, PhD, FRSM	IHMA Europe Sàr
Ross Mulder	bio Mérieux
Susan D. Munro, MT(ASCP)	
Susan O'Rourke	BD Diagnostic Systems
Dyan Luper, BS, MT(ASCP)SM	BD Diagnostic Systems
Linda M. Mann, PhD, D(ABMM)	Siemens Healthcare Diagnostics Inc.
Maureen Mansfield	Thermo Fisher Scientific
Amy J. Mathers, MD	Univ. of Virginia School of Medicine
Jennifer O’Connor	Siemens Healthcare Diagnostics Inc.
Elizabeth Palavecino, MD	Wake Forest Univ Baptist Medical Center
Pritty Patel	Covance
Chris Pillar	Micromyx

Shannon Popson	Siemens Healthcare Diagnostics Inc.
Gregory Porter	bio Mérieux
Denise Robinson	OU Medical Center
Nilia Robles-Hernandez	bio Mérieux
Darcie E. Roe-Carpenter, PhD, CIC, CEM	Siemens Healthcare Diagnostics Inc.
James Ross	JMI Laboratories
Helio S. Sader, MD, PhD	JMI Laboratories
Nicole Scangarella-Oman	GlaxoSmithKline
Jonathan Schmitz	Vanderbilt University
Paul C. Schreckenberger,PhD,D(ABMM),F(AAM)	Loyola University Medical Center
Dale A. Schwab, PhD, D(ABMM)	Quest Diagnostics, Nichols Institute
Katherine Sei	Siemens Healthcare Diagnostics
Sharon Shinn	Siemens Healthcare Diagnostics Inc.
Robert Skov, MD	Statens Serum Institut
Phillip B. Sonke	Merck & Company, Inc.
Judith N. Steenbergen, PhD	Cubist Pharmaceuticals, Inc.
William Stubbings	Basilea Pharmaceutical Inc. Ltd.
Gregory G. Stone	AstraZeneca Pharmaceuticals
Debora A. Sweeney	Micromyx, LLC
Kim Sweeney	Rempex Pharmaceuticals
Michael T. Sweeney	Pfizer Animal Health
Kazuhiro Tateda, MD, PhD	Toho University School of Medicine
Fred C. Tenover, PhD, D(ABMM)	Cepheid
Susan Thomson	Mast International
Maria M. Traczewski, BS, MT(ASCP)	The Clinical Microbiology Institute
Kenneth Van Horn, PhD, D(ABMM)	Focus Diagnostics
Dr. Peter Warn	Euprotec Ltd
Nancy Watz	Stanford Hospital and Clinics
Frank O. Wegerhoff, PhD	Covance Central Laboratory Svcs., Inc.
Collette Wehr	Siemens Healthcare Diagnostics Inc.
Matthew A. Wikler, MD, MBA, FIDSA	The Medicines Company
Gregory Williams, PhD	Cerexa, Inc.
Robert L. Williams	Siemens Healthcare Diagnostics Inc.
Teresa Wong	Siemens Healthcare Diagnostics Inc.
Cheung Yee, PhD	Forest Laboratories
Mary K. York, PhD, ABMM	MKY Microbiology Consulting

* Participated by Conference Call

CLSI Staff

Tracy A. Dooley, BS, MLT (ASCP)
Erica Berlanger
Glen Fine, MS, MBA, CAE
Marcy L. Hackenbrack, MCM, M(ASCP)
Luann Ochs, MS

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I. MEETING/OPENING REMARKS

Dr. Jean Patel called the meeting to order at 8:00 a.m. on Monday, 14 January 2013. She reviewed the purpose of the subcommittee's mission statement that is provided in electronic file folder 4 - References for Use on the meeting CD, noting that the ultimate purpose of the subcommittee's mission is to provide useful information to enable laboratories to assist the clinician in the selection of appropriate antimicrobial therapy for patient care.

Dr. Patel discussed the recent changes to the subcommittee including the addition of 3 new voting members: Steve Jenkins from New York Presbyterian Hospital, Jim Lewis from University of Texas Health Science Center, and Linda Miller from GlaxoSmithKline. New advisors include:

– Howard Gold from Beth Israel Deaconess Medical Center
– Romney M. Humphries from UCLA David Geffen School of Medicine
– Melissa B. Miller from UNC School of Medicine
– David P. Nicolau from Hartford Hospital
– Jeff Schapiro from Kaiser Permanente
– Audrey N. Schuetz from Weill Cornell Medical College/ New York Presbyterian Hospital
– Susan Sharp from Kaiser Permanente-NW and representing ASM
– Ribhi M. Shawar from FDA Ctr. for Devices/Rad. Health (CDRH)
– Kerry Snow from FDA Ctr. For Drug Evaluation and Research(CDER)
– Sumati Nambiar from FDA Ctr. For Drug Evaluation and Research (CDER)

Other rotations/changes:

– Freddie Mae Poole and Fred Marsik both advisors from FDA have retired.
– Frank Cockerill who has served as Subcommittee Chairholder for 6 years has rotated to Vice Chairholder.
– Members who rotated to advisors:

- Mike Dudley who has been on the Subcommittee since 1998 has contributed greatly over the years and still continues to do so.
- David Hecht who has been on the Subcommittee since 1997. David was not able to be here at this meeting and unfortunately due to other obligations will be stepping down as an advisor although he will be serving as a member on the CLSI Board of Directors.
- Tom Thomson rotated from Member to Reviewer because of his new role as Chairholder of the Microbiology Consensus Committee

– Advisors who rotated to reviewers:

- Paul Ambrose who has presented excellent PK/PD data over the years and is willing to continue providing his expertise to the subcommittee discussions.

- Ron Jones who has participated on the subcommittee since 1988 and continues to provide data and his expertise.
- Dale Schwab who has been a valuable contributor to the Text and Tables Working Group and continues to do so.

Dr. Patel then introduced Dr. Mary Lou Gantzer, new President of CLSI. Dr. Gantzer welcomed everyone and acknowledged that this was her first opportunity to attend an AST Subcommittee meeting and was looking forward to observing the process and hearing the discussions. She noted that CLSI Leadership is aware of the importance of the work done by the AST Subcommittee. On a recent trip to Japan and China on behalf of CLSI she saw the importance and wide use of the translated susceptibility testing documents. Also with Drs. David Hecht and Matt Wikler now serving as Board members, they have made the Board aware of susceptibility testing and some of the issues this committee faces. There are many positive changes throughout CLSI that are coming up as the Board reviews the CLSI Mission and Vision and strategic planning for the next 5 years that we will keep this committee informed of. She then thanked everyone on behalf of the Board of Directors for their dedication to the work of this subcommittee and all it has done to improve healthcare worldwide.

II. CLSI UPDATE

Ms. Luann Ochs, Senior Vice President of Operations with CLSI welcomed everyone to the meeting and gave an overview of some of the change happening at CLSI. In surveys that were conducted, volunteers told CLSI that we needed to streamline our processes which this subcommittee has been working on over the past year and you will hear more about the progress from the Process Improvement Working Group. Some of the changes CLSI has made recently to modernize its look include:

- A new updated website
- Newly designed brochures
- New document covers that have easier to use color coding within
- New membership options with 3 categories of membership as well as individual memberships
- New electronic eM100 – this product was recently beta-tested by users at Ms. Hindler's and Dr. Thomson's facilities as well as by Ms. Traczewski. Their valuable input will assist us in finalizing the product which will be available in the next few weeks. eM100 will allow users to quickly access M100-S23 information; dynamically filter by tables, organisms, and agents; view only the information the user wants to see; and customize it for the institution’s formulary. Anyone that would like to see how it works can view a demonstration at the registration desk.

Ms. Ochs then introduced CLSI staff present at the meeting as follows:

- Mr. Glen Fine, Executive Vice President;
- Tracy Dooley – Senior Project Manager and Staff Liaison to the Consensus Committee on Microbiology and Consensus Committee on Molecular Methods;
- Marcy Hackenbrack - Project Manager for various projects under Microbiology and Molecular Methods;
- Jenny Sarkisian – Project Manager for various projects under Microbiology as well as Quality Systems and Laboratory Practices and Hematology; and
- Erica Berlanger – Meeting Manager who coordinates all the logistics for these meetings.

III. UPDATES TO THE CURRENT AST DISCLOSURE SUMMARY

Dr. Patel asked the members and advisors for any updates to the current disclosure summary provided on the CD of meeting materials. Below is the update provided:

Dr. Cockerill: Scientific advisor to SVBio

IV. PROCESS IMPROVEMENT WORKING GROUP (Electronic Tab A in the Meeting Agenda)

Chairholder – Jeff Alder

Working Group Members - Susie Sharp, Ron Jones, Fred Marsik, George Eliopoulos, Barb Zimmer, John Turnidge

Dr. Alder's Working Group (WG) along with input from the subcommittee have been discussing and putting into place ways to make this committee work more efficiently. Dr. Alder outlined some of the process improvements already in place such as the tactical aspect on how to review breakpoints (eg, appointing a Rapporteur, off-line meetings of a small ad-hoc working group, submission of a data package with review and input of the subcommittee prior to a meeting) which worked well with the ceftaroline breakpoint presentation. In determining how to move forward with the strategic aspect of how to determine which drugs and drug classes to review, various proposals were reviewed and the subcommittee supported the creation of a standing Breakpoint WG and Methods WG; retain QC and Text & Tables; all other groups are Ad Hoc WGs. The goals this reorganization was: 1) to proactively identify subcommittee work; 2) to prioritize subcommittee work; and 3) to improve subcommittee work efficiency.

Dr. Patel outlined how this new structure will work (refer to Attachment 1 to see structure). There will be four standing WGs – Methods, Breakpoint, QC, and Text &Tables. These four standing WGs will coordinate the work of smaller Ad Hoc WGs that address specific issues. Each Ad Hoc WG would operate as follows:

- Their scope of work and timeline will be determined by the appropriate standing WG
- They would work independently to prepare a proposal for the subcommittee
- The ad hoc WG size should be approximately 3-5 people
- The ad hoc WG will report progress to the appropriate standing WG
- The ad hoc WG will consult with the appropriate standing WG regarding the proposal prior to reporting to the subcommittee
- The ad hoc WG, in consultation with the standing WG chair, can request agenda time at the face-to-face meeting to report progress and/or consult with the full subcommittee before a complete proposal is ready if this will facilitate decision making or WG progress.
- The ad hoc WG develops a rationale document for SC approved proposals.
- The ad hoc WG would be disbanded if appropriate once the assigned task is completed.

In forming the new Methods and Breakpoint WGs, as well as smaller ad hoc WGs, membership will be open to all, with a good representation of advisors and voting members on all standing WGs. CLSI will

send out a Call for Volunteers to the full Subcommittee outlining the WG charter and expertise needed to solicit interested candidates for the new Standing WGs and Ad Hoc WGs as they develop.

The implementation timeline for these changes are as follows:

1. Identify leadership for Methods and Breakpoint WG – January
2. Identify WG membership – February
3. Standing WGs begin communicating/meeting via teleconferences – March to June
   - Subcommittee voting members, advisors, and reviewers submit issues for WG consideration to the methods or breakpoint WG chairs
4. Existing or new ad hoc WGs conduct work toward a proposal – January to June
5. Ad hoc WGs present work to the appropriate standing WG – Sunday of the June Meeting
6. Methods and Breakpoint WGs report recommendations for prioritized work to the subcommittee – Monday of the June Meeting
7. Ad hoc WGs (with complete proposals) present proposals to the subcommittee for consideration - Monday or Tuesday of the June Meeting

V. REPORT OF THE INTRINSIC RESISTANCE WORKING GROUP
***Minutes Submitted by Barb Zimmer and Dyan Luper* (Electronic Tab B in the Meeting Agenda)**

Chairholder – Barb Zimmer

Recording Secretary – Dyan Luper

Working Group Members present – Jeff Alder, Rafael Canton, German Esparza, Sandy Richter, Tom Thomson

Working Group Members absent – Carole Schubert, Kate Murfitt, Paul Schreckenberger, Susan Sharp

1. Tigecycline – inclusion with tetracycline in tables?

   - Vote from June 2012 to include a drug if it was in the QC tables or elsewhere in the document.
   - It may be important to differentiate tetracycline, doxycycline, minocycline and tigecycline in the intrinsic resistance (IR) tables. We examined 4 references for tigecycline, for inclusion of tigecycline in the intrinsic resistance tables:

     1. Li et al. AAC, 1994: *Pseudomonas aeruginosa* – active efflux against tetracyclines
     2. Noskin, CID, 2005 – Tigecycline "Resistance by *P. a*eruginosa and reduced susceptibility among *Proteus* species (including *Morganell*a and *Providencia*) have been noted."
     3. Stein and Craig, CID, 2006 – conclusion same as Noskin reference.
     4. In addition, Peleg et al., CMR 2008 specifically discusses *Acinetobacter* – does not appear to be IR.

Motion made: to add Tigecycline to Tetracycline in heading for *Enterobacteriaceae* appendix B1 for *Proteus, Providencia, Morganella* - **Approved by Subcommittee 11-0; 1 absent**

- Action item: R. Canton is looking for clinical references for *Serratia marcescens*.

Motion made: Add Tigecycline to Tetracycline in heading in non-fermenter appendix B2 for *Pseudomonas aeruginosa* and amend comment for *S. maltophilia* to state: "*Stenotrophomonas maltophilia* is intrinsically resistant to tetracycline but not to doxycycline, minocycline, or tigecycline." – **Approved by Subcommittee 11-0; 1 absent**

Future: work on how to display the drugs (separate columns, all in one column)

2. Aminoglycoside rules for *Enterobacteriaceae (*appendix B1) – specifically *Providencia* spp. and *Serratia marcescens*

- The Working Group examined references for aminoglycoside intrinsic resistance:

1. Armstrong: "*P. stuartii* should be listed as resistant to GEN, NET, TOB" but "*P. rettgeri* should not be listed as IR to these agents."
2. Rather: Chromosomal aac(2")-Ia gene in *P. stuartii*…confers resistance to…gentamicin, tobramycin, netilmicin."
3. Livermore: (cites *Providencia* spp., Natural Resistance to gentamicin, netilmicin, tobramycin)
4. EUCAST: includes note. Rafael commented that aminoglycosides are complicated – that's why EUCAST used footnotes!

Motion made: Add aminoglycosides to *Enterobacteriaceae* appendix B1 – handle with footnotes* for *Providencia stuartii* indicating **P. stuartii* should be considered resistant to gentamicin, netilmicin, and tobramycin but not intrinsically resistant to amikacin. – **Approved by Subcommittee 12-0**

- Action item: R. Canton is looking for clinical references for *Serratia marcescens* – they produce AAC6 and may test as susceptible but resistant mutants emerge during treatment. See footnote in EUCAST IR tables.

3. Items for further discussion from last meeting and continuing:

- *Acinetobacter* vs. cefotaxime, ceftriaxone, and ceftazidime – Working Group examined 2 references, Peleg et al. CMR 2008 and Steinbakk et al. Acta Path. Microbiol. Imm. Scand. 1987.
- Difference between activity of (cefotaxime and ceftriaxone) and ceftazidime
- Looking for clinical data for June (reference also Poirel AAC 2010)

VI. REPORT OF *ENTEROBACTERICEAE/PSEUDOMONAS AERUGINOSA* WORKING GROUP - *Minutes Submitted by Steve Jenkins* (Electronic Tab C in the Meeting Agenda)

Chairholder – Steve Jenkins

Recording Secretary *Enterobacteriaceae* – Patricia Bradford

Recording Secretary *Pseudomonas*/Non-Fermenters - Dwight Hardy

Working Group Members present – **-** Paul Ambrose, Bill Craig, Mike Dudley, Ron Jones, Jim Lewis, Paul Schreckenberger, John Turnidge, Mel Weinstein, Barb Zimmer

Working Group Members absent - Audrey Schuetz, Lauri Thrupp

I. Meeting objectives

A. Consider the information and tentative recommendations of the ad hoc working group chaired by Dr. Paul Schreckenberger on potential revised breakpoints and interpretive categories for cefepime when testing the Enterobacteriaceae.

B. Review the progress made to date by the ad hoc working group chaired by Dr. James Lewis on assessment of breakpoints for *Acinetobacter* spp. for the carbapenems (other than doripenem).

C. Review the steps taken thus far by the ad hoc working group chaired by Dr. Audrey Schuetz on interpretive criteria for first generation cephalosporins as they relate to urinary tract isolates of Enterobacteriaceae, particularly in light of the perceived increase in resistance rates among strains of *E. coli* since recent changes in breakpoints for cefazolin were adopted.

D. Assess the accuracy and need for the following comment in the draft version M100-S23 that states: "For isolates with positive MHTs, perform MIC tests before reporting any carbapenem results, since carbapenem MIC interpretations are based solely on the MIC and should not be changed regardless of the MHT result."

E. To review data provided by the Centers for Disease Control and Prevention on disk diffusion antimicrobial susceptibility testing of *Salmonella* spp., and to decide whether development of MIC and disk diffusion breakpoints for azithromycin when testing *Salmonella* spp. is warranted.

II. Items for Discussion/Vote

A. Informational presentation from the cefepime ad hoc working group - P. Schreckenberger

Cefepime Ad Hoc Working Group - Paul Schreckenberger, Chair; Members - Mike Dudley, Howard Gold, Brandi Limbago, David Nicolau.

1. Background

   a) January 2011, AST subcommittee approved request by *Enterobacteriaceae* Working Group to review cefepime breakpoints.

   b) Between January and June Mike Dudley stepped down as Chair of *Enterobacteriaceae* Working Group and Steve Jenkins was appointed as the new Chair of the Working Group in June 2011.

   c) October 2011 Ad Hoc Working Group appointed to carry out request to review cefepime breakpoints.

2. Current breakpoints

Cefepime v. Enterobacteriaceae

Cefepime	S	I	R	Dosage
Current CLSI/FDA	≤8	16	≥32	1 g every 8 h or 2 g every 12 h
EUCAST	≤1	2-4	≥8	1 g x 3 or 2 g x 3

3. Data for consideration

   a) Microbiologic - Some carbapenemase and ESBL producing strains test with cefepime MICs of 4 or 8 µg/mL. Data was provided for *E. coli, K. pneumoniae, K. oxytoca* and *P. mirabilis*.

   b) There was some discussion regarding the hydrolysis of cefepime by CTX-M-type enzymes and KPC. Cefepime is not hydrolyzed to the same extent by these enzymes as is ceftazidime of ceftriaxone.

Action item: A request was made to provide histograms for *Citrobacter* spp. and *Enterobacter* spp.

4. Pharmacologic- Mike Dudley and David Nicolau

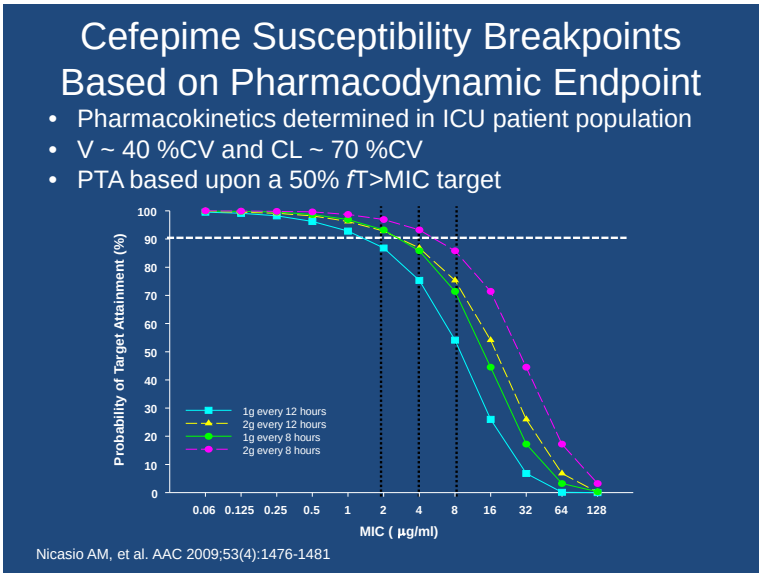
a) Cephalosporin breakpoints were analyzed as part of review of class in early 2000's for the dosage regimens that covered the wide range provided in prescribing labels.

CEFEPIME

	Every	8	Hrs		Every	12	Hrs
% T>MIC	40	50	60	70	40	50	60	70
hrs >MIC	3.2	4	4.8	5.6	4.8	6	7.2	8.4
1 g								
MIC:								
0.25	100	100	100	100	100	100	100	100
0.5	100	100	100	100	100	100	100	99.8
1	100	100	100	100	100	100	99.8	97.5
2	100	100	100	99.8	100	99.7	96.1	82.6
4	100	100	99.4	95.8	99.4	91.3	66.5	34.6
8	99.6	94.8	77.1	47.9	77.1	35.9	9.8	1.8
16	59	23.2	5.8	1.1	5.8	0.6	0	0
32	0	0	0	0	0	0	0	0
2 g								
MIC:								
1	100	100	100	100	100	100	100	100
2	100	100	100	100	100	100	100	91.4
4	100	100	100	100	100	99.5	95.9	81.6
8	100	100	99.4	95.3	99.4	90.6	65.6	33.8
16	100	94.4	76.6	20.1	76.6	35.5	9.7	2.1
32	58	23.1	6.4	1.6	6.4	0.7	0.1	0

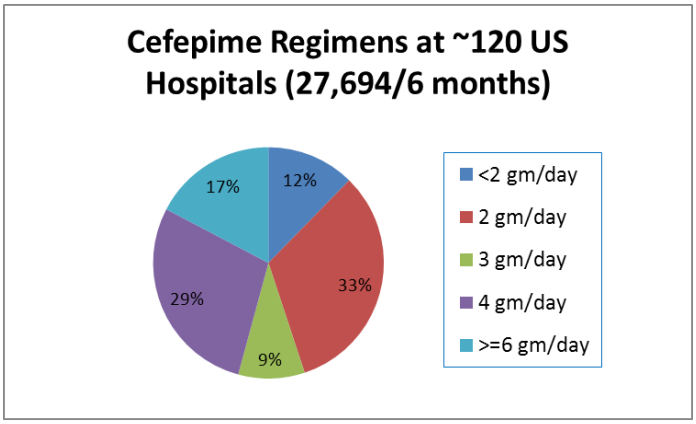
A question was raised regarding the appropriateness of using 50%>MIC. Cefepime has a better penetration rate and faster killing rate than other expanded-spectrum cephalosporins.

b) PK/PD suggests that the commonly used dose of 1g q12hr does not support a breakpoint of 8 µg/mL. A high dose of 2g q8hr would be required to obtain 50% T>MIC of 8 µg/mL.



5. Clinical data- Howard Gold

a) Cefepime is generally dosed at greater than 1g q12hr



CAVEAT: does not account for dose reduction due to renal function

Data c/o Vikas Gupta, Pharm.D., BCPS, Director, CareFusion MedMined™ services

b) A review of the clinical literature showed reduced efficacy in patients infected with organisms for which the cefepime MICs exceeded 8 µg/mL or that produced ESBLs. Some of the authors suggested that the susceptible breakpoint of 8 µg/mL may not be appropriate. One caveat to note is that many of the infections in the group with cefepime MICs ≥8 µg/mL were caused by *P. aeruginosa*.

6. No request for a vote was made at this meeting. The collection of data from the ad-hoc Working Group will continue. A straw poll of the *Enterobacteriaceae* Working Group showed interest in pursuing the subject of reviewing the appropriateness of cefepime breakpoints. It was brought to our attention that at least one of the sponsors for cefepime has their USPI under review at FDA.

B. Report of progress made by the *Acinetobacter*/carbapenem ad-hoc working group - Jim Lewis

A conference call was held to discuss the issue, which included some experts from the US military who have experience with patients infected with these resistant organisms coming back from the Middle East. There is very little data available regarding PK/PD or clinical data for *Acinetobacter* spp. The original breakpoints were set based upon MIC distributions available at the time of the drug approval. Members of the WG include: Jim Lewis – Chair; Members Helio Sader, Dwight Hardy, Clint Murray, Emil Lescho, Joe Kuti.

C. Interpretive criteria for Azithromycin for *Salmonella* - Maria Karlsson

1. Recap from the June 2012 meeting:

   a) Salmonella/azithromycin MIC and disk diffusion distributions and MIC zone diameter scattergrams presented.
   b) Double zone phenomenon associated with disk diffusion test.

   c) Lack of QC strain for azithromycin and *Enterobacteriaceae*

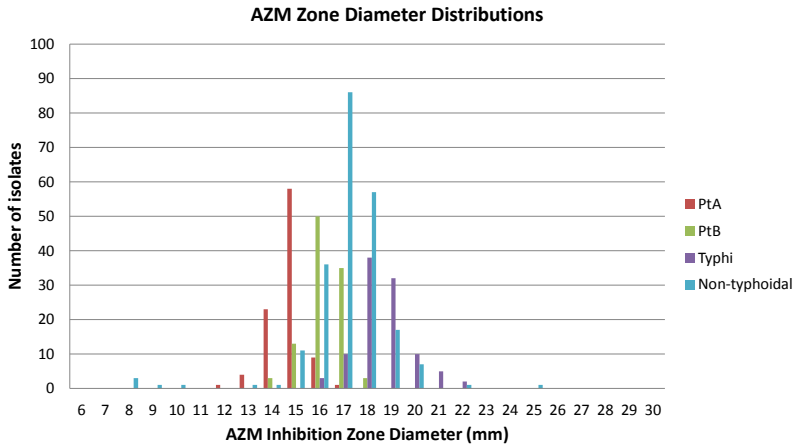
2. New Data

   a) Evaluation of different media and disks showed little variability
      (1) There were slightly better results when tests were read using reflected light
      (2) Some strains showed a double zone; reading was performed on the inner zone.

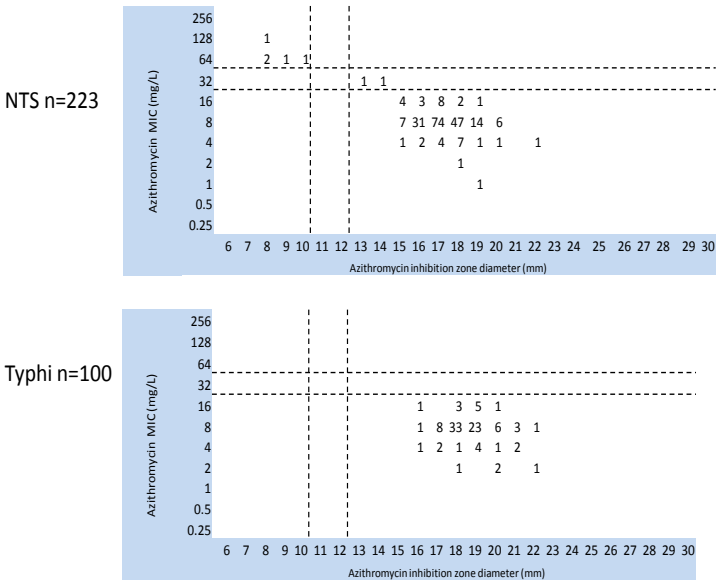
   b) QC with *S. aureus* 25923 correlates well with *Salmonella*

   c) Interlab variation: Less variation seen with transmitted light read at 18 hours

   d) Overall distributions are fairly consistent



   e) Zone diameter results from disk diffusion correlate well with MIC data using CSLI method (18hr, reflected light)



3. Three questions for the Working Group:

a) Is there a need to establish an *Enterobacteriaceae* QC organism for azithromycin or can the already established *S. aureus* ATCC 25923 be used?

(1) A comment was made that although *S. aureus* ATCC 25923 performed well, it might be good to have an alternative gram-negative organism available for QC purposes.
(2) A suggestion was made to propose a QA strain instead of developing a required QC strain for *Salmonella*.
(3) A representative from the QC Working Group suggested proceeding with the already established *S. aureus* QC.

b) Is there enough data to conclude we have a working disk diffusion method for azithromycin and *Salmonella*? Is reading after 18h with transmitted light the best method?

(1) Members of the Working Group were somewhat concerned about the double zones that were seen with some media.

(2) A concern was also raised about recommending a difference in reading recommendations that differs from the standard method.

c) Is there enough data to establish breakpoints?

(1) Clinically, there is sufficient use of azithromycin, especially in pediatric patients, to warrant the establishment of the test.

(2) A request was made for the data to be presented with a very clear delineation of the method that was used and a clear recommendation based upon that data.

(3) A suggestion was made to form a small ad-hoc WG to sort through these issues.

4. Issues with developing interpretive criteria

a) PK data for azithromycin lacking and difficult to interpret
b) Need for clinical correlate data to support possible breakpoint of 16 µg/mL (study from Viet Nam)
c) Sense of *Enterobacteriaceae* Working Group that a clinical need for establishment of these breakpoints exists
d) There was a consensus from the Working Group (but no official vote) to recommend that an ad hoc Working Group be established to move these efforts forward and assist with addressing the multiple questions that exist.

D. Oral Cephalosporin Ad Hoc WG - Ron Jones

Issue: Is there a drug which can be tested as a surrogate that will accurately predict the activity of the oral cephalosporins for treatment of urinary tract infections? Members of the WG include: Audrey Schuetz, Chair; Members – Bill Brasso, Jared Crandon, Dwight Hardy, Ron Jones, Barth Reller.

1. Background information

a) Reexamination of JMI's cephalosporin data originally presented to the SAST in 2009.
b) Ron Jones has supplemented the data with some cross-susceptibility/ resistance analyses which weren't originally presented in 2009.
c) Two laboratories are continuing to collect urinary Enterobacteriaceae isolates for possible future testing.
d) Another conference call will be arranged after the CLSI meeting to discuss the data, decisions, and plans

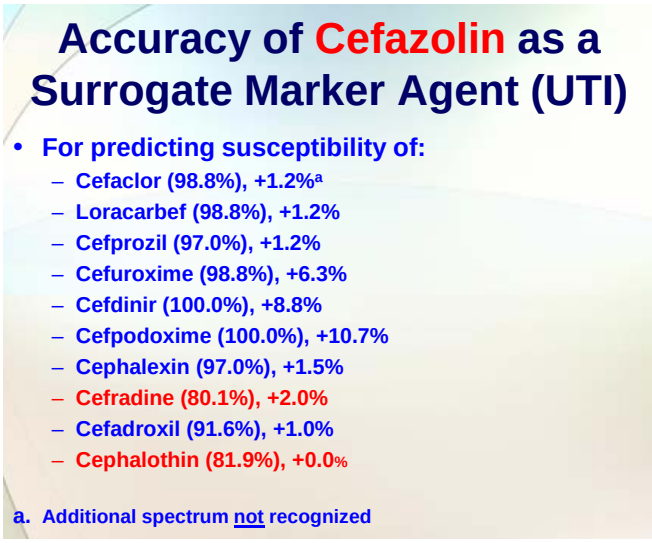
2. Points to consider

a) Are there other drugs which are worth analyzing?
b) Do we want to look at more specific strain choices?
c) This study was performed in 2009; are the isolate resistance patterns sufficiently different now to consider running additional testing and isolates?

3. New information

a) A study was conducted with Enterobacteriaceae performing both MIC and disk tests for ten oral cephalosporins

(1) Intra-drug correlation between MIC and disk was very good.
(2) When using cephalothin to predict: Consistently failed to recognize the additional spectrum of some of these drugs. For example, cephalothin often under- represented susceptibility to cefazolin.
(3) Cefazolin is recommended as a surrogate with a breakpoint of 16 µg/mL for UTI only for most of the oral cephalosporins. This makes the assumption that S +I correlates for UTI correlates with S for systemic infections.



4. Discussion:

a) Do we need more data? We may have enough data, but the data must be reviewed to parse out β-lactamase positive vs. β-lactamase isolates.
b) Several comments were made regarding the approved indications for these drugs and also the IDSA guidelines for UTI.
c) Assessment of urine levels for all drugs must be completed.
d) Does it require the creation of a new table in M100?

E. Modified Hodge Test

There were some letters received regarding the following comment in M100 Table 2A Supplemental Table 2:

"For isolates with positive MHTs, perform MIC tests before reporting any carbapenem results, since carbapenem MIC interpretations are based solely on the MIC and should not be changed regardless of the MHT result."

The question for the WG:

i) Is the comment accurate?

ii) Do we need to change the comment?

Concerns:

1) If laboratories are using new carbapenem breakpoints, there is no need to do the MHT and results should be reported as they test.
2) If laboratories are using old breakpoints, isolates should be reported as resistant if the MHT is positive
3) How long should CLSI refer to old breakpoints in the document? For some of the drugs, the USPI still has the old breakpoints. Therefore, these are the legal breakpoints for manufacturers of AST devices. At the present time, users must manually change the breakpoints in their systems.

A motion was made that this comment should be deleted. Working Group vote- *for/against/abstain* 9/0/0. **Approved by Subcommittee 12-0.**

VII. REPORT OF THE DATA ANALYSIS WORKING GROUP

***Minutes Submitted by John Turnidge* (Electronic Tab D in the Meeting Agenda)**

Chairholder – John Turnidge

Working Group Members: Steve Brown, Bob Rennie, Ian Morrisey, Bob Badal

The Data Analysis Working Group had a presentation from Bruce Craig and Glen DePalma from the Statistics department at Purdue University on their software program (dBETS) under development designed to calculate zone diameter correlates given and MIC distribution and its associated breakpoints. The program is written in an open source program widely used by the academic statistics community called "R". The authors are currently working with a third party, R Studio, on a freely-accessible internet version. The current version offers three approaches to determining the correlates: the M23-prescribed error rate bounded method, a logistic method and a nonparametric spline method. Preliminary testing on a range of data sets suggests that the spline method yields the least biased estimates of zone diameter correlates. Once the program is available on the web, slated for end of January, potential users will be notified. By the June meeting it is hoped that many users will have tried the software out, and looked for areas of improvement if they are needed. It is hoped that this software will become the default method for estimating zone diameter correlates, and that testing over the next 5 months will resolve which of the three methods included gives the best results.

VIII. REPORT OF THE QUALITY CONTROL WORKING GROUP

***Minutes Submitted by Steve Brown* (Electronic Tab E in the Meeting Agenda)**

Co-Chairholder - Steven Brown

Co-Chairholder - Sharon Cullen

Working Group Members present- Bill Brasso, Janet Hindler, Ross Mulder, Susan Munro, Bob Rennie, Frank Wegerhoff, Mary York

Working Group Members absent – Stephen Hawser, Michael Huband, Ron Jones, Ann Macone

Quality Control Ranges Approved by the QC Working Group:

CLSI January 2013 Tampa,						
Report of the QC Working						
Name	Ceftazidime/ avibactam (NXL104) disk diffusion 30/20 µg disk	Previous ID		Abbrev		Votes - (For/Opposed/Abstained/ Not present) WG: Total 9 , 8 for, 1 abstained
Solvent	NA	Diluent	NA	Rev History		
Route of Administration		Class	CEPHEM	Subclass	CEPHALOSPORIN III	
QC Strain (ATCC)	Acceptable	# mm or dil	% In range	Median	Shoulder	Variability/Comments
Streptococcus pneumoniae 49619		23-31 (9 mm)	96.5%	27	NA	22-33 mm (12 mm)proposed by the Rangefinder Method, 99.5% Included Media lot C had larger zone sizes, Lab 2 larger zones but not statistical outlier.

Name	Aztreonam/ avibactam (NXL104)	Previous ID		Abbrev		Votes (For/Opposed/Abstained/Not present) WG - Total 9 , 8 for, 1 abstained
Solvent	Saturated solution sodium bicarbonate	Diluent	WATER	Rev History		35218 provides no additional value avibactam not affected by TEM1, 700603 is preferred QC. Address routine & supplemental recommendations at a later time
Route of Administration		Class	MONOBACTAM	Subclass		
QC Strain (ATCC)	Acceptable	# mm or dil	% In range	MODE	Shoulder	Variability/Comments
E. coli ATCC 35218		0.015-0.06 (3)	99.2%	0.03		
E. coli ATCC 25922		0.03-0.12 (3)	98.8%	0.03		
K. pneumoniae ATCC 700603		0.06-0.5 (4)	100.0%	BIMODAL (0.25-0.12)	98.3	SHOULDER @ 0.12 µG/ML
P. aeruginosa ATCC 27853		2-8 (3)	100.0%	4		

Name	**Aztreonam**	**Previous ID**		**Abbrev**		**Votes (For/Opposed/Abstained/Not present) WG - Total 9 , 8 for, 1 abstained**
Solvent	**Saturated solution sodium bicarbonate**	**Diluent**	**WATER**	**Rev History**		
Route of Administration		**Class**	**MONOBACTAM**	**Subclass**		
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**MODE**	**Shoulder**	**Variability/Comments**
***E. coli* ATCC 35218**		**0.03-0.12 (3)**	**99.6%**	**0.06**		
***K. pneumoniae* ATCC 700603**		**8-64 (4)**	**100.0%**	**32**	**65.5**	**BIMODAL, SHOULDER @ 16 µg/mL To be listed as a footnote like other drugs for now. Consider routine vs. supplemental for future.**

Name	**Colistin with 0.002% Polysorbate 80**	**Previous ID**		**Abbrev**		**Votes (For/Opposed/Abstained/Not present) WG - Total 9 , 6 for, 2 abstained (includes Poly and Colistin) Includes recommendation for QC ranges as proposed with P80 in test (which QC WG recommends inclusion) in order for the test to be reproducible. Add footnote j from Table 4A For 8, 0 against and 0 abstained.**
Solvent	**WATER**	**Diluent**	**WATER**			
Route of Administration		**Class**	**LIPOPEPTIDE**	**Subclass**	**POLYMYXIN**	
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**MODE**	**Shoulder**	**Variability/Comments**
***E. coli* ATCC 25922**		**0.03-0.25**	**99.2%**	**0.06**	**62%**	**BIMODAL**
***P. aeruginosa* ATCC 27853**		**0.12-0.5**	**97.5%**	**0.25**		

Name	**Colistin without Polysorbate 80**	**Previous ID**		**Abbrev**		**Votes For/Opposed/Abstained/Not present) WG - No vote taken.**
Solvent	**WATER**	**Diluent**	**WATER**	**Rev History**		
Route of Administration		**Class**	**LIPOPEPTIDE**	**Subclass**	**POLYMYXIN**	
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**MODE**	**Shoulder**	**Variability/Comments**
***E. coli* ATCC 25922**		**0.25-2 (4)**	**99.2%**	**0.5**	**41%**	**97.1% OF VALUES COULD BE INCLUDED WITHIN A 34 DILUTION RANGE FROM 0.25-1, BUT NO CHANGE PROPOSED FROM CURRENT CLSI 4 DILUTION QC RANGE**
***P. aeruginosa* ATCC 27853**		**0.5-4 (4)**	**95.9%**	**1**	**72%**	**NO CHANGE PROPOSED FROM CURRENT CLSI QC RANGE**

Name	**Polymyxin B with 0.002% Polysorbate 80**	**Previous ID**		**Abbrev**		**Votes (For/Opposed/Abstained/Not present) WG- Total 9 , 6 for, 2 abstained (includes Poly and Colistin) Includes recommendation for QC ranges as proposed with P80 in test (which QCWG recommends inclusion) in order for the test to be reproducible. Add footnote j from Table 4A For 8, 0 against and 0 abstained.**
Solvent	**WATER**	**Diluent**	**WATER**	**Rev History**		
Route of Administration		**Class**	**LIPOPEPTIDE**	**Subclass**	**POLYMYXIN**	**POLYMYXIN**
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**Median**	**Shoulder**	**Variability/Comments**
***E. coli* ATCC 25922**		**0.03-0.25 (4)**	**97.1%**	**0.06**	**95%**	**BIMODAL**
***P. aeruginosa* ATCC 27853**		**0.06-0.5 (4)**	**97.2%**	**0.25**		**4 DILUTION RANGE BASED UPON THE RANGEFINDER METHOD. LAB #4 PRODUCED UNUSUAL RESULTS, BUT WAS NOT A STATISTICAL OUTLIER FOR ANY MEASURE OF CENTRA TENDENCY.**

Name	Polymyxin B without Polysorbate 80	Previous ID		Abbrev		Votes (For/Opposed/Abstained/Not present)
Solvent	WATER	Diluent	WATER	Rev History		
Route of Administration		Class	LIPOPEPTIDE	Subclass	POLYMYXIN	*P. aeruginosa* current range is 1-4 should be changed to 0.5-2 as proposed as an alternative range in case P80 recommendation is not approved, 8 for, 0 against, 0 abstain. Note: no change to E. coli 25922 range.
QC Strain (ATCC)	Acceptable	# mm or dil	% In range	MODE	Shoulder	Variability/Comments
E. coli ATCC 25922		0.25-2 (4)	99.6%	0.5	70%	BIMODAL
P. aeruginosa ATCC 27853		0.5-2 (3)	95.9%	1		CURRENT CLSI RANGE OF 1-4 INCLUDED ONLY 80.5% OF VALUES.

Name	**Biapenem**	**Previous ID**		**Abbrev**		**Votes (For/Opposed/Abstained/Not present)** **Sponsor requested including 4 or 8 as the denominator for RPX7009 in tables to allow for inclusion of both in investigational studies and would decide which to use later for routine use (before breakpoints are established). Note: QC ranges are the 6 for, 2 opposed, 0 abstain – see tables that follow**
Solvent	**0.85% Saline**	**Diluent**	**0.85% Saline**	**Rev History**		
Route of Administration		**Class**	**penem**	**Subclass**	**Carbapenem/ carbapenemase inhibitor**	
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**MODE**	**Shoulder**	**Variability/Comments**
***S. aureus* ATCC 29213**		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***E. coli* 25922**		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***E. coli* ATCC 35218**		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***K. pneumoniae* ATCC 700603**		**0.03-0.12 (3) (0.03-0.25) (4)**	**95% (99.6%)**	**0.06**		**8-0-0 for 3 dilution range (0.03-0.12) – this was a separate vote take by the WG since there were 2 ranges presented.**
***K. pneumoniae* ATCC BAA-1705**		**>1**	**100.0%**	**>1**		
***P. aeruginosa* ATCC 27853**		**0.5-2 (3)**	**100.0%**	**1**		

Name	**Biapenem/ RPX7009 fixed 4µg/mL**	**Previous ID**	**New name carbavance**	**Abbrev**		**Votes (For/Opposed/Abstained/Not present) Sponsor requested including 4 or 8 as the denominator for RPX7009 in tables to allow for inclusion of both in investigational studies and would decide which to use later for routine use (before breakpoints are established). Note:**
Solvent	**0.85% Saline**	**Diluent**	**0.85% Saline**	**Rev History**		
Route of Administration		**Class**	**penem**	**Subclass**	**Carbapenem/ carbapenemase inhibitor**	**RPX7009 is fairly stable (has been stressed with high temperatures and no degradation**
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**MODE**	**Shoulder**	**Variability/Comments**
***S. aureus* ATCC 29213**		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***E. coli* 25922**		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***E. coli* ATCC 35218**		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***K. pneumoniae* ATCC 700603**		**0.03-0.12 (3)**	**97.5%**	**0.06**		
***K. pneumoniae* ATCC BAA-1705**		**0.015-0.12 (4)**	**97.5%**	**0.06**	**68.2%**	**Should be tested routinely since this is the only strain that shows the activity of both the carbapenem and inhibitor. Note: need to include description of resistance that this strain has for**
***P. aeruginosa* ATCC 27853**		**0.5-2 (3)**	**100.0%**	**1**		

Name	**Biapenem/ RPX7009 fixed 8µg/mL**	**Previous ID**		**Abbrev**		**Votes (For/Opposed/Abstained/Not present) – Separate vote for 8µg/mL was not taken by WG**
Solvent	**0.85% Saline**	**Diluent**	**0.85% Saline**	**Rev History**		
Route of Administration		**Class**	**penem**	**Subclass**	**Carbapenem/ carbapenemase inhibitor**	**RPX7009 is fairly stable (has been stressed with high temperatures and no degradation**
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**MODE**	**Shoulder**	**Variability/Comments**
***S. aureus* ATCC**		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***E. coli* 25922**		**0.03-0.12 (3)**	**99.6%**	**0.06**		
E. coli ATCC 35218		**0.03-0.12 (3)**	**100.0%**	**0.06**		
***K. pneumoniae* ATCC 700603**		**0.03-0.12 (3)**	**99.2%**	**0.06**		
***K. pneumoniae* ATCC BAA-1705**		**0.015-0.12 (4)**	**99.2%**	**0.06**	**85.8%**	**Should be tested routinely since this is the only strain that shows the activity of both the carbapenem and inhibitor. Note: need to include description of resistance that this strain has for appendix**
***P. aeruginosa* ATCC 27853**		**0.5-2 (3)**	**99.6%**	**1**		

Name	**Eravacycline Disk Diffusion**	**Previous ID**		**Abbrev**		**Votes (For/Opposed/Abstained/Not present)**
Solvent	**WATER**	**Diluent**	**WATER**	**Rev History**		
Route of Administration		**Class**	**TETRACYCLINE**	**Subclass**		**Motion to accept ranges as proposed for *S. aureus, S. pneumo* and *E. coli*. WG Vote 8 for, 0 opposed , abstained 0 Discussion on *P. aeruginosa* concern about potential confusion with very small zone and no range is recommended.**
QC Strain (ATCC)	**Acceptable**	**# mm or dil**	**% In range**	**MODE**	**Shoulder**	**Variability/Comments**
***S. aureus* ATCC 25923**		**19-26 (8 mm)**	**98.7%**			
***S. pneumoniae* ATCC 49619**		**23-30 (8 mm)**	**98.5%**			
***E. coli* 25922**		**16-23 (8 mm)**	**99.4%**			
~~**Pseudomonas aeruginosa 27853**~~		~~**6-11 (6 mm)**~~	~~**99.7%**~~			**Discussion on P. aeruginosa concern about potential confusion with very small zone and no range is recommended.**

All QC reflected in the tables above were approved by the Subcommittee 11-0; 1 abstain.
Future action: Create table summarizing ATCC 35218 and ATCC 700603 ranges available and proposal for routine or supplemental testing.

Notes: Carbavance: need to clarify later (before breakpoints are available, what QC strains to use for routine vs. supplemental QC.

User QC Subgroup

1. Vote to accept proposal from user subgroup to remove *E. coli* ATCC 25922 from routine QC testing box for Table 2B-1 *Pseudomonas aeruginosa* table except for TP-434 (eravacycline) which would have a note similar to that used with 35218 - when testing beta-lactamase inhibitors since QC range doesn't exist for Ps. 27853 (eg, *E. coli* ATCC 25922 would be added back once eravacycline has approved interpretive criteria added to Table 2B-1 with note). WG Vote 6 for, 1 against, 0 abstain. **Approved by the Subcommittee 12-0.**

   Rationale: QC with *Escherichia coli* ATCC® 25922 provides no added benefit to the other two QC strains listed. All antimicrobial agents included in Table 2B-1 have QC ranges established with either *P. aeruginosa* ATCC 27853 or *E. coli* ATCC 35218.

Routine QC Recommendations (See Tables 3A and 4A for acceptable QC ranges.)
~~*Escherichia coli* ATCC® 25922~~
Pseudomonas aeruginosa ATCC® 27853
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

2. Vote to approve adding *P. aeruginosa* ATCC 27853 to Table 2A Enterobacteriaceae for carbapenems only. WG vote - 6 for, 1 opposed, 0 abstain. **Approved by the Subcommittee 12-0.**

Routine QC Recommendations (See Tables 3A and 4A for acceptable QC ranges.)

Escherichia coli ATCC® 25922
Pseudomonas aeruginosa ATCC® 27853 (for carbapenems)
Escherichia coli ATCC® 35218 (for β-lactam/β-lactamase inhibitor combinations)

Rationale: *P. aeruginosa* 27853 is a better indicator of QC problems with carbapenems than *E. coli* 25922 (see troubleshooting tables 3D and 4G). Minimal additional work burden for clinical labs.

Continuing QC Issues (No Votes Taken)

1. 3X5 replicate QC plan: ongoing communications with CMS/CLIA to coordinate this new CLSI recommendation with CMS regulatory requirements.

2. Can QC frequency be reduced from 3x5 replicate plan (e.g. to 5 days?) when a new drug is added to an existing battery?

   a. Chris Doern has volunteered to analyze disk data for frequency of QC errors to support reducing QC.

   b. Use M52 survey (guidance document in development, Verification of Commercial AST Systems).

3. Verification of Disk Diffusion Testing. Verification of disk diffusion testing when the method is first introduced in a laboratory, or a new disk is added to the testing panel. Inserting specific language in M100-S23 about disk diffusion verification was delayed until consensus recommendations for how to verify disk diffusion are determined. Text withheld from Page 22: "(Note: Even though disk diffusion is also a reference method, CLIA requires a clinical lab verify disk diffusion in their laboratory prior to use in the US)"

   a. The M52 group will develop recommendations for the M52 document.

Tier 3 Monitoring

1. **Tier 3 Monitoring: Request for Data from All Participants**
   a. Ampicillin Disk Diffusion vs. *E.coli* 25922
   b. Meropenem Disk Diffusion vs. *P. aeruginosa* 27853
   c. Teicoplanin MIC vs. *E. faecalis* 29212

IX. REPORT OF THE FLUOROQUINOLONE BREAKPOINT WORKING GROUP *Minutes Submitted by Karen Bush* (Electronic Tab F in the Meeting Agenda)

Chairholder – Cynthia Fowler
Recording Secretary – Karen Bush

Working Group Members present - Jeff Alder, Sujata Bhavnani, George Eliopoulos, Robert Flamm, Marcelo Galas, Elizabeth Palavecino, Mair Powell, Barth Reller, Helio Sader, Mel Weinstein

Working Group Members absent – Lauri Thrupp

Salmonella spp. Disk Diffusion Testing

Discussions were focused on screening tests for fluoroquinolones and salmonellae. The goal is to identify a reliable, robust, low cost screen for quinolone sensitivity in *Salmonella* spp. that will be available for publication in CLSI documents in 2014.

Items for Discussion and Input

Although a disk diffusion test for ciprofloxacin was previously approved, the data do not reliably differentiate organisms with resistance mechanisms from wild type (WT) organisms. Because the data were not available for inclusion in the agenda book, an informational presentation was made at the Working Group meeting by Dr. Robert Skov who had generated a set of disk diffusion data for various quinolones tested against 126 isolates: 43 with no identified resistance mechanisms (WT), 37 with *qnr* genes, 45 strains with QRDR mutations and one strain with the *aac(6')-Ib-cr* gene and another undefined resistance mechanism. Other collaborators on the project included Erika Matuschek and Gunnar Kahlmeter from the EUCAST Laboratory for AST, and Maria Karlsson and Rebecca Howie from the CDC. The results showed that ciprofloxacin, levofloxacin, ofloxacin, enoxacin and nalidixic acid disks did not completely separate the WT population from the strains with resistance mechanisms, whereas pefloxacin performed with a sensitivity of 100% and a specificity of 99.6%

The following motions were made at the Working Group:

- The Fluoroquinolone Working Group authorizes Dr. Skov to move forward with appropriate activities to validate pefloxacin as a surrogate fluoroquinolone for disk testing for Salmonellae, including development of QC for pefloxacin.
  - *Working Group Vote: Yes (11) No (0) Abstain (0)*

- The Fluoroquinolone WG requests Dr. Skov and collaborators that they adhere to the CLSI QC guidelines to develop QC criteria for pefloxacin disk diffusion testing. If additional laboratories (up to 7 laboratories) are able to retest current strains, supplemented to reach 100 resistant strains, they are encouraged to do so in an effort to generate data by the June meeting.
  - *Working Group Vote: Yes (11) No (0) Abstain (0)*
- AST Subcommittee discussion:
  - Additional strains should be added to the population, including 10 WT strains and 20 strains with resistance factors, including *aac(6')-Ib-cr*. Data generated should meet or exceed M23 requirements.
  - Further discussion is necessary to determine how the data would be used. One possibility is to develop disk diffusion correlations between pefloxacin and ciprofloxacin, levofloxacin or ofloxacin MICs. Another possibility is to describe the screen as one that can differentiate between organisms that possess or don't possess resistance mechanisms, with MIC testing to be conducted for the fluoroquinolone of choice
- It is anticipated that results will be presented in June 2013.

Rationale document

Dr. Romney Humphries presented a prototype of a rationale document that could be housed separately on the CLSI website to explain changes in interpretive criteria, with links to appropriate supporting documents. Dr. Fowler will circulate the information to the Working Group for further comments before the June meeting.

X. REPORT OF THE TEXT AND TABLES WORKING GROUP
***Minutes Submitted by Jana Swenson* (Electronic Tab G in the Meeting Agenda)**

Co - Chairholder – Jana Swenson

Co - Chairholder – Maria Traczewski

Working Group Members present – Janet Hindler, Judy Johnston, Dyan Luper, Linda Mann, Susan Munro, Flavia Rossi, Jeffrey Schapiro, Dale Schwab, Tom Thomson, and Mary York

1. A letter was received by CLSI requesting that we consider revision of M02 and M100 to allow for placing up to 6 disks on a 100-mm disk diffusion plate. The reason for the request was that even with 6 disks on a small plate the disks can be placed ≥24 mm apart which is what is currently stated in M02, section 9.2 (1). The current general comment in Tables 2A-2D states:

(1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and 5 disks on a 100-mm plate (see M02, Section 9.2)."

- The working group recommended the following revision of that comment:
  (1) For disk diffusion, test a maximum of 12 disks on a 150-mm plate and up to 6 disks on a 100-mm plate; disks should be placed no less than 24 mm apart, center to center (~~see~~ M02, Section 9.2 will be updated during its next scheduled revision to include this recommendation for disk placement on 100-mm plates)**.** Each zone diameter should be able to be clearly measured. "

- Working Group: Approved 11-0
- Subcommittee: **Approved12-0**

2. During the latest review of M100, it was suggested that we consider cleaning up Tables 2 by removing the General Comment explaining agents with 'susceptible' only breakpoints.

   - The working recommended that the comment be removed from all Tables 2 and that an explanation be included in the Instructions for Use of the Tables in M100. The following changes were made to section II. A. 5:
     II A.

     5. Interpretive Criteria

     Interpretive criteria are the MIC or zone diameter values used to indicate susceptible, intermediate, and resistant breakpoints.

Antimicrobial Agent	Disk Content	Zone Diameter Interpretive Criteria nearest whole mm			MIC Interpretive Criteria (µg/mL)		
		S	I	R	S	I	R
X	30 µg	≥20	15–19	≤14	≤4	8–16	≥32
Y	—	—	—	—	≤1	2	≥4
Z	**10 µg**	**≥ 16**	**--**	**--**	**≤ 1**	**--**	**--**

     For example, for antimicrobial agent X with interpretive criteria in the table **above**, the susceptible breakpoint is 4 µg/mL or 20 mm and the resistant breakpoint is 32 µg/mL or 14 mm.

     For some antimicrobial agents **(eg, antimicrobial agent Y),** only MIC criteria may be available. For these agents, the disk diffusion zone diameters do not correlate with MIC values; only MIC methods should be used to test and report agent Y. Technical issues may also preclude the use of the disk diffusion method for some agents.

     For some antimicrobial agents (eg, antimicrobial agent Z), only susceptible criteria exist. For these agents, the absence or rare occurrence of resistant strains precludes

defining any results categories other than "susceptible." For strains yielding results suggestive of a "nonsusceptible" category, organism identification and antimicrobial susceptibility test results should be confirmed. (See Appendix A).

Laboratories should only report results for agents listed in the Table 2 specific to the pathogen being tested; it is not appropriate to apply disk diffusion or MIC interpretive criteria taken from an alternative Table 2. There may be rare cases where an agent may be appropriate for an isolate but for which there are no CLSI interpretive criteria (eg, tigecycline). In these cases the FDA prescribing information document for the agent should be consulted.

- Subcommittee: Approved the removal of the 'susceptible' only general comment in the Table 2's and adding the bolded above in the Instructions for Use section (**Approved 12-0**).

3. Corrections to the Screening Test Table in M100 Instructions for Use section VII were recommended for Further Testing or Confirmation of β-lactamase tests for *S. aureus.*

The current table is:

Organism Group	**Table Location**	**Resistance Phenotype or Mechanism**	**Screening Tests**	**Further Testing or Confirmation Required?**
Staphylococcus aureus	2C Supplemental Table 1	β-lactamase production	Penicillin disk diffusion zone-edge test or other method	Yes, if screen test negative, repeat penicillin MIC and β-lactamase test(s) (eg, penicillin disk diffusion zone-edge test or induced β-lactamase test) on subsequent isolates from same patient (if penicillin MIC ≤0.12 μg/mL or zone ≥29 mm); PCR for *blaZ* may be considered.

Suggested changes (shown bolded):**Organism Group**	**Table Location**	**Resistance Phenotype or Mechanism**	**Screening Tests**	**Further Testing or Confirmation Required?**
Staphylococcus aureus	2C Supplemental Table 1	β-lactamase production	Penicillin disk diffusion zone-edge test	**No**
			Chromogenic cephalosporin	**No, if the test is positive; report the results as positive for β-lactamase (or penicillin resistant).** **Yes, if test is negative in cases where penicillin may be used for therapy (eg, endocarditis), the penicillin zone-edge test should be performed before reporting the isolate as penicillin susceptible.**

- Working Group: Approved 11-0
- Subcommittee: **Approved 12-0**

4. A suggestion to revise how the supplemental Mechanism of Resistance tables are displayed in M100 was submitted to the Working Group by Drs. Tom Thomson and Patricia Bradford. Their recommendation was that the supplemental tables be moved from each Table 2 to an Appendix at the end of M100 and displayed either by organism (as currently displayed) or by resistance mechanism (as shown below).

   Option 2. (Resistance Mechanisms by Mechanism):

   Appendix F-1. Screening and Confirmatory Tests for ESBL's in *Klebsiella pneumonia, Klebsiella oxytoca, Escherichia coli and Proteus mirabilis*

   Appendix F-2. Screening and Confirmatory Tests for Carbapenemase Production in *Enterobacteriaceae*

   Appendix F-3. Detection of Beta-Lactamase Production in *Staphylococcus aureus*

   Appendix F-4.Detection of Methicillin-Resistance (Oxacillin-Resistance) in *Staphylococcus* species

   Appendix F-5. Detection of Vancomycin MIC > 8 ug/mL in *Staphylococcus* species and *Enterococcus* species

   Appendix F-6. Detection of Inducible Clindamycin Resistance in *Staphylococcus* species, *Streptococcus pneumoniae* and *Streptococcus* species Beta-hemolytic Group

   Appendix F-7. Detection of High-Level Mupirocin Resistance in *Staphylococcus aureus*

   Appendix F-8. Detection of High-Level Aminoglycoside Resistance (HLAR) in *Enterococcus* species

   - The Working Group recommended Option 2 (approved 8-3).
   - Subcommittee: **Approved 12-0**

5. The following question was received by CLSI and was to be handled as a Comment with Subcommittee Response (ie, a Q&A):

   "Our Laboratory is using MaldI-TOF (mass spec) for identification of our organisms. My question is do CLSI interpretations apply to the newly described organisms being identified by the MALDI-TOF? Can I group them as *Enterobacteriaceae*, Non-*Enterobacteriaceae, Staphylococcus* spp. etc and use the interpretive criteria for these groups? How do I test and report organisms that I have never heard of?

Some examples are *Herbaspirillum* spp, *Trueperellabernardiae* (Nonfermenters), *Gordonibacter pamelaeae* and *Paenibacillus urinalis* which are anaerobes."

The working group reviewed several responses that were handled by email with the co-chairs of the Working Group and Drs. Patel and Thomson. After lengthy discussion it was decided by the Working Group that we should wait until June to finalize a response for this question and this was presented to the Subcommittee for input and discussion only.

However, because of some confusion during the email interactions, it was assumed that the response was to be published in M100-S23. Consequently the following Q&A was published:

4. I am responsible for building and keeping the database up-to-date for the clinical microbiology laboratory. We are now using MALDI-TOF [matrix-assisted laser desorption/ionization time-of-flight mass spectrometry] for identification of our organisms. My question is: do CLSI interpretations apply to the newly described organisms being identified by mass spectrometry? I try to group them accordingly for in the past I designed the database like CLSI so that all *Enterobacteriaceae, Staphylococcus* spp., etc. would be grouped together and interpretations done accordingly. Now, with all of the organisms I have never heard of, what do we do about susceptibility interpretations? Examples are *Herbaspirillum* spp., *Trueperellabernardiae,* (nonfermenters),and *Gordonibacter pamelaeae* and *Paenibacillus urinalis* which are anaerobes.

- **It is unlikely that isolates from these species were adequately represented in the data packages used to establish CLSI breakpoints in CLSI documents M100, M45, or M11. For this reason, we have no evidence-based guidance for applying interpretive criteria. If antimicrobial susceptibility testing is needed, a few options used by laboratories are below.**

  Perform antimicrobial susceptibility testing using an MIC method and in conjunction with infectious disease and pharmacy specialists consultation:

  – **Report the MICs without an interpretation.**

  – **Apply interpretive criteria from a closely related group of bacteria if there is literature supporting such a practice (the literature should be cited).**

  – **Apply an epidemiological cutoff as the breakpoint (ie, if the MIC is outside the normal distribution the isolate could be reported as nonsusceptible). The epidemiological cutoff could be identified based upon information in the literature.[1]**

  Reference:

[1]Turnidge J, Paterson DL. Setting and revising antibacterial susceptibility breakpoints. *ClinMicrobiol Rev.* 2007;20(3):391-408.

The working group will review this response in June in order to determine if additional explanation or guidance is needed.

XI. RATIONALE DOCUMENTS (Electronic Tab H in the Meeting Agenda)

Ms. Janet Hindler provided an overview on the need for rationale documents in that they provide reliable and retrievable documentation and also can be used to explain changes in recommendations to users. Currently there are 2 rationale documents posted on the CLSI website on the AST Subcommittee Page

- Carbapenem Breakpoints for *Enterobacteriaceae* written by Dr. Jim Lewis
- Doxycycline/Tetracycline Breakpoints for *Streptococcus pneumoniae* written by Dr. Jim Jorgensen

Ms. Hindler worked with Drs. Romney Humphries and Jennifer Dien-Bard to try and develop a standardized format that can be used going forward. The suggested structure includes:

- Introduction
- Old (if available) and new breakpoints (recommendations)
- Microbiologic data summary
- PK/PD summary and standard dosing data
- Clinical outcome summary
- Correlation of MIC and zone diameter summary
- Clinical considerations when adopting
- Laboratory considerations when adopting
- Chronology of discussions – summary from each time point
- References - links to pertinent background data housed on the CLSI website
- References - other (eg, published data)

They drafted for review 2 proposed rationale documents:

- Fluoroquinolone breakpoints for *Salmonella* spp. – this rationale document will be circulated to the Fluoroquinolone Working Group for review and input.

- Elimination of *Staphylococcus* β-lactam Breakpoints for Agents Other Than Oxacillin/Cefoxitin, Penicillin and Ceftaroline - this rationale document was circulated to the Staphylococcal/Streptococcal Working Group prior to the meeting for review and input. Some of the suggested edits include simplifying the document and make it more concise; only include information used by the subcommittee to make the final decision, as well additional suggestions outlined in more detail below in the minutes of the Working Group.

Ms. Hindler and Drs. Humphries and Dien-Bard will revise the 2 rationale documents they drafted based on Working Group input and then they will be circulated to Subcommittee members and advisors for review and approval prior to being posted to the CLSI website.

CLSI has initiated development of a draft template for rationale documents and will update this for review based on feedback received. Some suggestions include:

- Add a section for chronology of discussions to include a brief summary from each time point as was done in the 2 rationale documents submitted by Ms. Hindler and colleagues.
- Clinical outcomes summary – just have a brief summary of Working Group conclusions noting the appropriate references.
- Require certain elements in certain sections of the template (eg, PK/PD section include what was the target)
- When Ad Hoc Working Groups have a proposal for a breakpoint change they include the draft rationale document as part of the package that is to be voted on.

The key aspect to get these rationale documents done once a template is approved is to assign the task to someone when the Ad Hoc Working group initiates their work.

XII. REPORT OF THE M100 AD HOC WORKING GROUP

Co-Chairholder – Susie Sharp

Co-Chairholder – Mary Jane Ferraro (unable to attend)

Working Group Members present **–** George Eliopoulos, Jeff Schapiro, Steve Brown

- Charge of the Working Group:
  - Initiate the review of M100 and identify:
    - Outdated methods
    - Outdated antimicrobial agents
    - Outdated breakpoints/methods
    - Other areas that need to be 'cleaned up'
  - Make recommendations to the Subcommittee
  - Subcommittee will decide whether to develop additional Ad Hoc WGs to address these issues
- Issues for today:
  - Footnotes/comments
    - Streamline
    - Simplify (user friendly)
    - Check for consistency throughout (fresh eyes are needed to review this)
    - Relevance/accuracy
    - Location (eM100 ease)

- R_x/dosage regimen comments & "Warning" comments
  - Is CLSI making dosage recommendations?
    - If yes, should this be happening?
  - If CLSI continues to make dosage recommendations?
    - Do it consistently and relevantly
    - Should criteria be developed for when this type of information is included in the document?
  - If CLSI shouldn't be making these recommendations -
    - How can we be clear the with the R_X comments that CLSI is not practicing medicine?
  - How can CLSI make these comments actually usable?
    - We heard yesterday that microbiology laboratories are not sending R_X recommendations with susceptibility results.
    - Pharmacy document? (on-going)
  - Relocate dosage information with better explanations and limit "clutter" in breakpoint tables

- Screening tests

  - Review for relevance (Do they still do what we think they do? Are they outdated?)
  - Define when, and perhaps when not, to use the screening rests (review for consistency)
  - Perhaps also include (or separate issues/Ad Hoc WG):
    - When to recommend repeat isolate testing for R-development and unusual phenotypes
    - Clarify when/how to use/expand the IR tables, incorporation into Tables, etc. (We heard yesterday that more instruction is needed on how/when to use these tables.)
    - Clarify surrogate/predictive/"OR" testing and extrapolation comments throughout the document (Heard lots of discussion yesterday regarding cephalothin/cefazolin).

- 'Other Non-Enterobacteriaceae' breakpoints (Table 2B-5)

  - Relevant / Correct?
  - Do they work?
  - References?
  - Can CLSI continue to support this Table? (no M23 study)

- Issues for June 2013
  - Global document: FDA-regulated & non FDA-regulated agents (indicated, reorganization or other approach)

    - Is there is a need to 'reorganize' (or other approach; designate, define, expand) the document into FDA-regulated & non FDA-regulated agents? Will review in June 2013
    - Will ask additional CLSI AST participants to join this discussion
    - Include the Group "O" agents?

- Other issues discussed
  - Archival information - CLSI issue? (We heard yesterday the importance of keeping data on how decisions were historically made and the importance of maintaining information that has been deleted from M100 → Ad Hoc WG?)

The M100 Ad Hoc WG expects to meet in June 2013 and perhaps again in January 2014, then disband.
• New Ad Hoc WGs:

  – It is expected that the newly formed Ad Hoc WGs will come up with other issues as they discuss these topics.
  – These Ad Hoc WGs will meet, review issues, undertake investigations, and make recommendations to the full Subcommittee.

Review:
• 4 Issues today: Development of Ad Hoc WGs for the following areas:
  – Footnotes/comments
  – Therapy/dosage & warning comments
  – Screening tests
  – Other Non-Enterobacteriaceae breakpoints (Table 2B-5)

XIII. REPORT OF THE STAPHYLOCOCCAL AND STREPTOCOCCAL WORKING GROUP - *Minutes Submitted by Brandi Limbago*

Chairholder – Brandi Limbago

Recording Secretary – Sandy Richter

Working Group Members present - Patricia Bradford, George Eliopoulos, Susan Sharp
Jana Swenson, Maria Traczewski, Robert Skov, Tom Thomson, Mel Weinstein

Working Group Members absent - William Craig, Mike Dudley, Dan Sahm

I. Items Proposed for Vote

Vancomycin disk diffusion screen test:

A proposal to classify the vancomycin disk diffusion (DD) for *S. aureus* as a "screen test" with addition of a footnote to Table 1A and test details to Table 2C Supplemental Table 2 was circulated for review and comment before the meeting. The proposal is shown in Tab G (files 3 1 and 3 2) of the agenda materials.

Numerous Working Group members and observers did not think the vancomycin DD screen test was useful because of the need to determine a vancomycin MIC regardless of the result. The vancomycin DD breakpoints were previously removed from Table 2C because of test limitations, but comment 19 was left in the document. No zone of inhibition indicates possible VRSA and a zone indicates VISA or VSSA – further MIC testing is required. Since VRSA strains are rare, the DD screen has the potential for a high false positive rate and performance characteristics are only known for *vanA* - mediated resistance.

The Working Group rejected the proposal and voted to remove the vancomycin DD screen test from M100 by deleting comment 19 (Working Group Vote: 9+/1 abstain/3 absent). The Subcommittee voted to accept the Working Group recommendation (**Approved 9-3**). Descriptions of the vancomycin DD test for staphylococcus in M2 and M7 will be deleted when those documents are revised. The DD vancomycin QC range for *S. aureus* ATCC 25923 will remain in Table 3A to assess disk potency.

II. Items for Discussion and Input

A. Rationale document for recent changes to Table 2C:

A draft document explaining the removal of *Staphylococcus* spp. breakpoints for β-lactams other than oxacillin, cefoxitin, penicillin, and ceftaroline was distributed before the meeting for review and comment (see Tab H, file 1 3). The authors of the draft (Janet Hindler and Jennifer Dien-Bard) presented a proposed outline for rationale documents (Tab H, file 1 1). The need for rationale documents was acknowledged by observers and Working Group members. Reviewer comments that had been submitted for the rationale document were discussed and the following changes were recommended by the Working Group:

1) The document should be more clear and concise with only essential information. Content should reflect discussion that actually occurred during CLSI conference calls and meetings.

2) Introduction, delete 1st paragraph. 2nd paragraph: Remove text suggesting that the establishment of penicillin, oxacillin, and cefoxitin as surrogates for other agents followed the current M23 process.

3) Create repository for old breakpoints.

4) Table 2.2: Delete "actual"; add footnote stating isolates reported as penicillin S must be β-lactamase negative.

5) Remove "Harmonization" section and place relevant comments regarding discrepancies between standard-setting groups in the "Laboratory Considerations" section.

6) The *in vitro* susceptibility (Table 4.2) and clinical outcome data (Section 5) should be removed since this was not part of WG or SC discussions.

7) Section 7: Delete following section "Consider reporting penicillin S results only in cases…."

8) Section 7 and throughout: Replace ceftaroline testing guidance with instructions to test if reported.

B. Future rationale documents related to *Staphylococcus* species:

Brandi Limbago volunteered to write a rationale document for the removal of the vancomycin disk diffusion test.

Robert Skov agreed to draft a document explaining changes to β-lactamase testing published a year ago.

XIV. AGENDA BOOK SUBMISSIONS FOR 23-25 JUNE 2013 MEETING IN BALTIMORE

Materials for the June meeting will be distributed to the subcommittee prior to the meeting. The meeting rooms will be equipped with power strips for those who prefer to view the material on their computer instead of printing the material. Please note there will not be internet access in the meeting rooms.

To meet the schedule to have materials available for review a few weeks prior to the meeting, submission due dates and requirements must be met. In order to present at the 23-25 June 2013 meeting please:

1) Submit agenda materials electronically as a PDF file **on or before Friday, 17 May 2013.**
Please Note: For QC submissions based on M23 Tier 2 Studies please make sure to include information for the solvent and diluent to include in Table 5, antimicrobial class and subclass, antimicrobial agent abbreviation, and route of administration for inclusion in Glossary I and II.

2) E-mail proposed agenda topics to Jean B. Patel, PhD, D(ABMM) (vzp4@cdc.gov), Franklin R. Cockerill, III, MD (cockerill.franklin@mayo.edu) please copy his Administrative Assistant JoAnn Brunette (Brunette.Joann@mayo.edu) and also to Tracy Dooley (tdooley@clsi.org) for review.

Note: The 23-25 June 2013 meeting will be held in Baltimore, Maryland at the Hyatt Baltimore hotel. Additional meeting details will be provided in March when the announcement is circulated.

XV. ADJOURNMENT - The meeting adjourned at 10:10 a.m. on Tuesday, 15 January 2013.

Respectfully submitted,

Tracy A. Dooley, BS, MLT (ASCP),
Senior Project Manager