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Meeting Title:	**Subcommittee on Antifungal Susceptibility Tests**	**Contact:**	mhackenbrack@clsi.org
Meeting Date:	Saturday, 27 January 2018	**Secretary**	Camille Hamula, PhD camille.hamula@mountsinai.org
Start Time:	8:00 AM Central (US) time	**End Time:**	2:45 PM
Location:	Westin Galleria 13340 Dallas Parkway Dallas, Texas, USA		
Meeting Purpose:	The purpose of this meeting is to review and discuss subcommittee business.		
Requested Attendee(s):	SC members, advisors, reviewers, and CLSI staff.		

Attendee(s):	
Gary W. Procop, MD, MS Chairholder	Cleveland Clinic
Barbara D. Alexander, MD, MHS Vice-chairholder	Duke University Medical Center
Camille Hamula, PhD Committee Secretary/Advisor	Mount Sinai Health Systems
Members Present:	
Philippe Dufresne, PhD	Institut National de Santé Publique du Québec
Jeff Fuller, PhD, FCCM, D(ABMM)	London Health Sciences Centre
Mahmoud A. Ghannoum, PhD, FIDSA, MBA	Case Western Reserve University
Kimberly E. Hanson, MD, MHS	ARUP at University Hospital
Denise Holliday, MT(ASCP)	BD Diagnostic Systems
Nicole M. Holliday, BA	Thermo Fisher Scientific
Audrey N. Schuetz, MD, MPH, D(ABMM)	Mayo Clinic
Nathan P. Wiederhold, PharmD	University of Texas Health Science Center at San Antonio
Adrian M. Zelazny, PhD	National Institutes of Health
Members Excused:	
Luis Ostrosky-Zeichner, MD, FACP, FIDSA, FSHEA	University of Texas Medical School at Houston
Advisors Present:	
Elizabeth Berkow, PhD	Centers for Disease Control and Prevention
Mariana Castanheira, PhD	JMI Laboratories
Sharon K. Cullen, BS, RAC	Beckman Coulter, Inc. Microbiology Business
Scott B. Killian, BS	Thermo Fisher Scientific
Laura Kovanda, BA, PhD	Astellas Pharma Global Development, Inc.
Shawn R. Lockhart, PhD, D(ABMM)	Centers for Disease Control and Prevention
Jacques F. Meis, MD, PhD, FIDSA	Canisius Wilhelmina Hospital
Nicholas M. Moore, MS	Rush University Medical Center
Mary Motyl, PhD	Merck & Company, Inc.
Anil A. Panackal, MD, SM, FACP	Merck & Co., Inc.
David S. Perlin, MD	New Jersey Medical School-UMDNJ
Ribhi M. Shawar, PhD, D(ABMM)	FDA Center for Devices/Radiological Health
Dee Shortridge, PhD	JMI Laboratories
Sean X. Zhang, MD, PhD	Johns Hopkins University
Reviewers Present:	
Kevin Alby, PhD, D(ABMM)	University of Pennsylvania Health System
Tanaya Bhowmick, MD	Rutgers Robert Wood Johnson Medical School
Tanis Dingle, PhD, D(ABMM)	Provincial Laboratory for Public Health
Beth P. Goldstein, PhD	Consultant

Stephen Hawser, PhD	IHMA Europe Särl
Patricia Hogan, MT(ASCP)	Pfizer Inc.
Cynthia C. Knapp, BS, MS, MT(ASCP)	Thermo Fisher Scientific
Ping Ren, PhD	The University of Texas Medical Branch
Maria M. Traczewski, BS, MT(ASCP)c	The Clinical Microbiology Institute
John D. Turnidge, MD, BS, FRACP, FASM, FRCPA	University of Adelaide
Paul E. Verweij, MD	Radboud University Medical Center
Guests (non-SC-Roster Attendees):	
Stella Antonara, PhD	Nationwide Children's Hospital
Joan-Miguel Balada-Llast	OSU Wexner Medical Center
Paul Bien	Amplex Pharmaceuticals
Mary Ann Brandt	Norman Regional Health System
Alexandra Bryson, MD	Mayo Clinic
Dubraska Diaz-Campos	The Ohio State University
Han Drivedi	bioMeriéux, Inc.
Gina L. Ewald-Saldana	Beckman Coulter, Inc.
Momoko Fujisaki	Eiken Chemical Co. LTD.
Rita Hoffard	Becton Dickinson
Sarah Jury	Mayo Clinic
Asa Karlsson	bioMérieux, SA
Brenda Ling	Astellas Pharm Global Development
Jeffery Locke	Cidara Therapeutics
Roland Martelin	bioMérieux
Stephanie Mitchell, PhD, D(ABMM)	University of Pittsburgh/UPMC
Michael D. Nowak, MD	Emory University Hospital
Jennifer O'Connor	Beckman Coulter
David Paisey	Thermo Fisher UK
Chris Pillar	Micromyx
Jaclyn Priest, PharmD	Texas Health Arlington Memorial
Zachary Ratzleff, MLS(ASCP)	Norman Regional Health System
Nilia M. Robles Hernandez	bioMérieux
Dale Schwab, PhD	Quest Diagnostics Infectious Disease
Katherine Sei	Beckman Coulter
Sharon J. Shinn	Beckman Coulter
Jennifer Smart	Basilea Pharmaceutica
Paula M. Snippes Vagnone	Minnesota Department of Health
Vera Tesic MD, D(ABMM)	University of Chicago
Hui Wang	Peking University People's Hospital
Teresa S. Wong	Beckman Coulter, Inc.
Staff Present:	
Mark Chmielewski, MLS(ASCP)^{CM}	CLSI
Glen Fine, MS, MBA, CAE	CLSI
Marcy L. Hackenbrack, MCM, M(ASCP)	CLSI

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AGENDA					
#	**Start**	**Time**	**Presenter**	**Item**	**Background**
Breakfast available: 7:00 – 8:00 AM					
1.	8:00 AM	10 min	Dr. Procop	Opening Remarks/Introductions	Agenda
2.	8:10 AM	10 min	Mr. Fine	CLSI Update	N/A
3.	8:20 AM	20 min	Dr. Procop	**Annual SC Update** • **Vote:** January 2017 meeting summary • **Rotations:** 2018 Committee roster • **Update:** Antifungal Document status • **Review**: Outstanding action items	Presentation Roster DOI Summary January 2017 Meeting Minutes See action items below
4.	8:40 AM	35 min	Dr. Ghannoum	*Aspergillus* QC for APX001A	Presentation
5.	9:15 AM	35 min	Dr. Ghannoum	*Candida* QC for APX001A	Presentation
	9:50 AM	**15 min**	**Break**		
6.	10:05 AM	20 min	Dr. Pillar	Cidara Tier 2 MIC QC	Briefing document
7.	10:25 AM	35 min	Dr. Dufresne Dr. Lockhart	Discussion on publication of MIC distributions	Proposal
8.	11:00 AM	45 min	Dr. Kovanda	Isavuconazole ECVs	Presentation
9.	11:45 AM	15 min	Dr. Schuetz Dr. Tesic	Consideration for reporting restrictions for certain body sites	Presentation References
	12:00 PM	**60 min**	**Luncheon**		
10.	1:00 PM	30 min	Dr. Schuetz Dr. Tesic	Intrinsic resistance reporting for various fungi	Presentation
11.	1:30 PM	45 min	Dr. Berkow	"Old and New drug testing against a global collection of *Candida auris*"	Presentation (pending)
12.	2:15 PM	25 min	Dr. Procop	Review outstanding and new action items	See table below
13.	2:45 PM	5 min	Dr. Procop	**Plans for next meeting**: Web conference (May or June) or Face-to-face (2 June 2018 – San Diego, California) **January 2019 meeting**: Saturday, 26 January; St. Augustine, Florida	
14.	2:45 PM		Dr. Procop	Adjourn	

Note: All meeting presentations have been posted on the CLSI Website: 2018 January AFSC Presentations

SUMMARY MINUTES	
#	**Description**
1.	Dr. Procop opened the meeting at 8:00 AM by welcoming the attendees and thanking the subcommittee participants for their continued work.
2.	**Mr. Fine provided a brief CLSI organizational update.** • Like M100, a free version of M60 (*Performance Standards for Antifungal Susceptibility Testing of Yeasts*) is now available on the CLSI Website (M100 and M60 Free). – Dr. Alexander noted that M27-S3, not the newer edition, S4, is posted on the FDA website. – It was noted that the FDA is reviewing M60 for placement on the website. • New members of the CLSI Board of Directors have been elected including two with microbiology expertise: Dr. Mary Jane Ferraro and Dr. Susan Sharp.
3.	**Dr. Procop reviewed general subcommittee information.** • The subcommittee membership categories and any appointed role changes for 2018 were reported. – Dr. Procop has rotated to the chairholder role and Dr. Barbara Alexander has rotated to the vice-chairholder role. – The voting members list remains the same for 2018. – Dr. Camille Hamula has been appointed as an advisor and will continue as committee secretary. – Dr. John Rex, Ms. Maria Traczewski, and Dr. Peter Williamson have completed their 4-year appointments as advisor and will continue the subcommittee as reviewers. • The agenda for the 2018 meeting was reviewed. There were no changes to the agenda. **A motion to accept the agenda as presented was made and seconded. VOTE: 9 – 0; 1 absent (Pass)** • The summary minutes from the January 2017 subcommittee meeting were reviewed. There were no changes to the summary. **A motion to accept the January 2017 summary minutes was made and seconded; VOTE: 9 – 0; 1 absent (Pass)** • CLSI committee processes were reviewed. – Voting member and advisors disclosures of interest (DOI) have been provided with the agenda material. No updates to the DOI summary were reported. – Dr. Procop requested that those commenting from the floor provide an introduction and list any potential conflicts of interest. • The subcommittee voting rules were reviewed. – 9 of the 10 voting members were present (Dr. Ostrosky-Zeichner was excused). Pass votes for the meeting included: 10 – 0, 9 – 1, 8 – 2, and 7 – 3 (excluding abstentions). – The email voting procedure was also reviewed. • The document categories and general rules for document review and revision were provided. Updates on the status of all documents in the Antifungal library were provided. – M27 (4th ed.), M38 (3rd ed.), M60 (1st ed.), and M61 (1st ed.) all published in November 2017. M27 and M38 are scheduled for review by November 2020. M60 and M61 can be revised annually or as needed. – M44 is in the process of being revised to the 3rd ed. The draft is currently being edited for proposed draft review and vote. – M51 was reaffirmed in September 2016 and must be reviewed by the end of 2020 for revision, archival, or withdrawal. – M57 (1st ed.) was last published in April 2016 and must be reviewed for action by April 2021. The M59 supplement published at the 2nd ed. in January 2018.
4.	**Dr. Mahmoud Ghannoum presented data analyses for a QC study with *Aspergillus* spp. and APX001A compound.** • He noted that Tanis Dingle from the University of Alberta Hospital Laboratory was omitted from the list of participants in the study. • The objective of the study was to identify candidate QC strains for susceptibility testing on APX001A against filamentous fungi using M38 (broth microdilution) standard methods.

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#	**Description**
	• Six candidate strains included *Aspergillus fumigatus* MYA 3627 and *Aspergillus flavus* ATCC® 204304. Four additional non-candidate strains (*A. terreus* MYA 3633, *A. fumigatus* MYA 3626, *A. flavus* MYA 3631, *P. variottii* MYA 3630) were also tested. • Endpoints were read at 24 and 48 hrs. at the minimum effective concentration (MEC) and at 50 and 100%. • *Candida parapsilosis* ATCC® 22019 and *C. albicans* ATCC® 90028 were included as voriconazole internal controls on each run and results were acceptable. • Data was analyzed using RangeFinder for 24 and 48 hour reads. • Recommendations – Minimum Effective Concentration (MEC) following 24 hrs. incubation – *A. fumigatus* MYA 3627 - QC range = 0.016–0.06 µg/ml – *A. flavus* ATCC® 204304 – QC range = 0.008–0.06 µg/ml • Discussion – Dr. Alexander questioned why a 3-dilution range was proposed for *A. fumigatus* but RangeFinder shows a 4-dilution range and if 0.008 is a more appropriate choice for testing. – Ms. Cullen noted that ±1 dilution provided >95% due to interlaboratory variability with no media variability and that ≥ 60% is suggested. She suggested that results continue to be monitored. – Dr. Castanheira suggested 48h reading time for filamentous fungi is needed more than 24h, due to increased workflow variability at 48h. *Aspergillus* is read at 24h for echinocandins. 24 and 48 hr. readings will be retained for *C. parapsilosis* and *C. krusei* for QC of moulds. – Ms. Cullen noted that the 48h and 24h ranges for MEC are the same for *A. fumigatus*, and since *A. flavus* has no range at 48h, laboratories would be confused if only one at read at 48h is recommended. – Dr. Lockhart suggested that a 4-dilution range be used and to clarify the definition for MEC. The range could be extended while additional data is generated. – It was suggested that *A. fumigatus* MYA 3627 be designated as the recommended QC organism and that *A. flavus* ATCC® 204304be designated as a supplemental QC organism to be used for validation studies, troubleshooting, and additional QC. – Ms. Cullen recommended setting a 3-dilution range and continue to collect information on media and laboratory variability. When breakpoints become available, the QC ranges can be re-evaluated. – It was proposed that the other strains be published with *A. fumigatus* MYA 3627 as the recommended QC strain and continue to collect additional data. – The range may need to be extended to 0.04 up to 1 to capture all readings. The *Candida* data will be reviewed and this suggestion will be discussed after the review. • Final proposal and vote.
	A motion to accept a 24-hr. range of 0.008-0.06 µg/ml for *A. fumigatus* MYA 3627 as the recommended QC organism for APX001A was made and seconded – VOTE: 9 – 0; 1 absent (Pass)
	A motion to accept a 48-hr. range of 0.016 – 0.12 µg/ml for *A. fumigatus* MYA 3627 as the recommended QC organism for APX001A was made and seconded – VOTE: 8 – 1; 1 absent (Pass)
	• Dr. Schuetz's dissenting vote was based on her concern that the endpoint was not included in the RangeFinder analysis and the concerns about variability.
5.	**Dr. Ghannoum presented data analyses for a QC study with *Candida* spp. and APX001A compound.** • He noted that Tanis Dingle from the University of Alberta Hospital Laboratory was omitted from the list of participants in the study. • The objective of the study was to identify candidate QC strains for susceptibility testing on APX001A against yeasts using M27 (broth dilution) standard methods. • Candidate QC strains included *Candida parapsilosis* ATCC® 22019 and *Candida albicans* ATCC® 90028. Four additional non-candidate strains were also tested. • Endpoints were read at 24 and 48 hrs. at 50% and 100 % inhibition. • *C. parapsilosis* ATCC® 22019 and *C. albicans* ATCC® 90028 were included as voriconazole internal controls on each run and results were acceptable. • Data was analyzed using RangeFinder for 24 and 48 hour reads. • Recommendations

SUMMARY MINUTES	
#	**Description**
	– Read results at 50% inhibition following 24 hr. incubation – *C. parapsilosis* ATCC® 22019 – QC range = 0.016–0.12 µg/ml (recommended QC organism) – *C. albicans* ATCC® 90028 – QC range = 0.016–0.06 µg/ml (supplemental QC organism) • Discussion – It was suggested that a percentage be identified. It was agreed that 50% will be used. 48 hr. readings will be excluded. – Dr. Castanheira noted that reading the 50% endpoints appears to be more consistent. – It was noted that the percentage for *C. parapsilosis* at 50% after 24 hrs. should read 99.6% (not 96.6%). – It was noted that when the ranges are eventually added to M60 and M61, only 24 hr. reads will be added to M60 and 24 and 48 hr. reads will be added to M61. – There was concern that there is only one strain for QC . It was suggested that one QC strain be selected and include a second strain as a supplemental QC strain. • Final proposals **A motion to accept a QC range of 0.016 – 0.12 µg/ml at 24 hrs. at 50% inhibition for *C. parapsilosis* ATCC® 22019 as the recommended QC strain and *C. albicans* at 0.016 – 0.06 µg/ml as a supplemental QC strain for APX001A in M60 was made and seconded. VOTE: 9 – 0; 1 absent (Pass)** **A motion to accept a QC range of 0.016 – 0.12 µg/ml at 48 hrs. at 50% inhibition for *C. parapsilosis* ATCC® 22019 as the recommended QC strain and *C. albicans* at 0.016 – 0.06 µg/ml as a supplemental QC strain for APX001A in M61 was made and seconded. VOTE: 9 – 0; 1 absent (Pass)** – It was noted that currently, there are no QC ranges for voriconazole in M60. Since the QC with voriconazole tested during the APX001A studies met the M23 criteria, it was proposed that the voriconazole ranges be added to M60. **A motion to accept a QC range of 0.016 – 0.06 µg/ml at 24.1hrs. at 50% inhibition for *C. albicans* ATCC® 90028 and voriconazole in M60 was made and seconded. VOTE: 9 – 0; 1 absent (Pass)**
6.	**Dr. Chris Pillar presented a Tier 2 QC broth dilution QC study for CD101 (Rezafungin).** • Rezafungin is a novel echinocandin with potent activity against *Candida* spp. • Isolates tested as potential QC organisms included *C. parapsilosis* ATCC® 22019 and *C. krusei* ATCC® 6258. • The study followed CLSI M23 guidelines and included micafungin as a control. • Data was analyzed using RangeFinder and the following ranges were proposed. – *C. parapsilosis* ATCC® 22019 o 24 hrs.: 0.25 – 1 µg/ml o 48 hrs.: 0.25 – 2 µg/ml – *C. krusei* ATCC® 6258 o 24 hrs.: 0.015 – 0.12 µg/ml o 48 hrs.: 0.015 – 0.12 µg/ml **A motion to accept the proposed QC ranges for *C. parapsilosis* and *C. krusei* as presented above with 24 hr. ranges in M60 and 24 and 48hr. ranges in M61 was made and seconded. VOTE: 9 – 0; 1 absent (Pass).** • The proposed range for testing was discussed. – Dr. Pillar stated that for the QC study the testing range was 0.008 – 8 µg/ml. – Ms. Cullen stated that the range for QC studies is broader than for patient testing to ensure that there is at least one on-scale QC. Patient testing is usually performed at least 1 dilution above and 1 dilution below. – It was suggested that when breakpoints are presented that a recommended testing range be included in the presentation so that there is no truncated data. – It was noted that a range of 0.002-4 µg/mL was tested with mutant strains testing up to 16; eight could be used as upper range. To prevent truncation, a proposed range of 0.008-8 was suggested. A different range for this drug may be needed for moulds and yeast.

#	Description
	– Testing the higher end of the range to ensure detection of resistant isolates is more important to clinical laboratories. Clinical laboratories do not care about "less than". It was proposed that the range go one dilution below QC range at the high end so that isolates are not missed. – Suggested ranges for testing included: ○ 0.008-4 µg/mL ○ 0.008-8 µg/mL ○ 0.016-8 µg/mL (in line with other echinocandins) – Discussion on testing ranges will continue the next conference call.
7.	**Dr. Dufresne presented a proposal and criteria for publishing antifungal MIC distributions.** • An overview of the current and upcoming epidemiological cut off values (ECVs) and breakpoints (BPs) was provided. • For various reasons, some ECVs are not published (M59). – Insufficient data on rare species (eg, insufficient isolate numbers or number of laboratories) – Truncated data (results are too high or low) or mode is too low – Abnormal distributions (multimodal or cryptic species needed molecular identification) • It was suggested that MIC distributions be published when ECVs or BPs cannot be set. – Clinical use for rare species – Truncated data may indicate intrinsic resistance or *in vitro* susceptibility – To provide transparency by disclosing data • Proposal – Publish MIC distributions produced using M27 or M38 methodology for the following: – Currently approved BPs and ECVs (this was later rejected by the SC) – Rare species where there is insufficient data or laboratories – Truncated distributions that cover the recommended concentration ranges for a given agent – Abnormal multi-modal distributions **would not** be published • Criteria for publication was presented – Proposed criteria for MIC/MEC data to be used to publication of MIC/MEC distributions for which an ECV cannot be generated (in red those that differ for ECV criteria). **NOTE: Table copied from presentation (see below)**

Criteria	ECV (M57)	Publication of MIC distribution with no ECV (Proposa)
Minimal MIC data points (1 clinical strain/patient)	Min. 100	Min. 20
Number of submitting labs	Min. 3 labs (weighed if needed)	Min 3 labs (weighed if needed) No minimum for rare species.
Methodology	CLSI M27 or M38	CLSI M27 or M38 (reading time and inoculum may need to be disclosed)
Species identification method	Molecular confirmed by MALDI-TOF or sequencing (ECV WG may be more specific for some species which are more difficult to ID)	Molecular confirmed by MALDI-TOF or sequencing (ECV WG may be more specific for some species which are more difficult to ID)
QC strains data	Must be provided and within accepted range	Must be provided and within accepted range
Truncated dataset	Not accepted	Accepted if they cover recommened CLSI M27 and M38 concentration ranges for a given antifungal agent
Dataset that are not within 1-2 dilutions of pooled dataset	Reviewed as potential outliers, rejected if it is the case	Reviewed as potential outliers, rejected if it is the case Not applicable in cases where for which the number of labs is too few
Abnormal or multimodal MIC/MEC lognormal distribution	Rejected	Rejected

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#	Description

		But a note would be included to MIC distribution listing

  - A table similar to that published on the EUCAST Website would be created and posted on the CLSI website.
- Questions and details to consider were reviewed.
  - Who should have access (ie, available to anyone or only those with CLSI membership or subscription?)
  - Where to post the information (eg, current antifungal page or a new dedicated page?
  - What is the criteria for generating MICs incorporated into a new edition of M57?
  - If data verified by the ECV WG does not meet the ECV criteria, does it need approval from the subcommittee?
  - How to keep track of all the data?
- Discussion
  - Dr. Alexander questioned how users will be educated to use the information. She stated that the data should be clean and anonymized. She suggested that data should not be published if there are set BPs or ECVs.
  - It was questioned as to how to handle raw data that needs to be weighted.
  - Consideration for whether CLSI has the technological capability to provide a website (not yet available) that may need to be closed (access restricted to a specified group). It was suggested that the SC draft a proposal to present to the CLSI leadership stating what the SC would like to do and see how it can be accomplished.
  - Data should also include an explanation for why an ECV or BP could not be set.
  - The ECV WG will determine which species to target and decide which molecular method to use for each species as a policy change would be needed to accommodate other methods.
  - Only data from the reference method will be used

Action Items:

- **Ms. Hackenbrack will investigate the information technology needed to maintain an MIC data table.**
- **A "wish list" of rare species to target will be compiled by the ECV WG.**

A motion to provide MIC data for organism/drug combinations for which there are no BPs or ECVs (rare species with insufficient data or laboratories or have truncated data) according to the presented criteria and for this information to be managed by the ECV WG and approved by the Antifungal Subcommittee was made and seconded. VOTE: 9 – 0; 1 absent (Pass).

SUMMARY MINUTES	
#	**Description**
8.	Dr. Laura Kovanda presented an overview of *in vitro* susceptibility testing data for isavuconazole and *Candida* spp. for developing ECVs. • Isavuconazole ECVs for *Aspergillus* spp. have been published in M59; however, data is needed for publishing ECVs for *Candida* spp. • Available data for *Candida* spp. are truncated at the upper or lower ends or have multiple modes. Dr. Alexander reviewed data presented at a past meeting. • An issue with the QC ranges for *C. parapsilosis* ATCC® 22019 published in M60 has been detected. – The SC approved 24 hr. ranges in September 2013 based on an appropriate study. – M60 is not consistent with the submitted information. – M60 currently lists the Mode as 0.06 and the MICs in range as 90.5%. – Based on the presented data, the mode should be listed as 0.03 and MICs in range as 98.3%. – A correction in M60 may be needed. – Isavuconazole data for ECVs from January 2014 needs to be reviewed and combined with the previous data and re-analyzed. Issues included: o *C. albicans*: 4 laboratories, one with truncated data and large number of isolates. No ECV. o *C. glabrata*: 2 modes more than 2 dilution difference. No ECV. o *C. tropicalis*: Truncated data o *C. parapsilosis*: Truncated data o *C. krusei*: 2 modes. – It was questioned if the recommended testing ranges be lowered and if the 24 hr. QC range for *C. parapsilosis* be a 4 dilution rather than a 3-dilution range so that the mode is not at the higher end of the range. • Discussion – There is so much variability with this drug not seen with other azoles data. The testing laboratories are not likely to have reading errors. – Data from past meetings and decisions were reviewed showed multiple discrepancies. **Action Item: Collect January 2014 isavuconazole and combine with previous data and reanalyze to correct the QC information (Dr. Alexander and Dr. Kovanda).**
9.	**Dr. Audrey Schuetz presented a proposal with Dr. Vera Tesic regarding body site reporting restrictions for antifungal agents.** • A phase II requirement has been added to the CAP checklist regarding which antifungal agents to routinely test and report. The question states that there must be written policies to ensure the only antifungal agents appropriate for the organism and body site are routinely tested and reported. • The Antimicrobial Subcommittee (AST) has included restrictions for reporting for certain drugs and body sites in M100. • The Infectious Disease Society of America Clinical Practice Guidelines also recommend reporting restrictions for echinocandins and azoles. • Proposal: Provide guidance for when to restrict testing and reporting of certain antifungal agents with isolates from specific body sites. – CLSI does not currently provide guidance on restrictive reporting by body site; however, laboratories do discuss testing and reporting options with healthcare providers and antibiotic stewardship team. – CLSI should consider restricting reporting of certain antifungal agents from urinary sources (ie, voriconazole and echinocandins on urinary isolates). • The following was suggested for consideration: – For *Candida* urinary isolates, test and report on request. – If requested to report echinocandin results, consider a reporting comment such as: "Echinocandins are not considered adequate for treatment of urinary candidiasis." • Discussion Suggestions and Comments – PK-PD data doesn't always agree with what is occurring at the infection site and that clinical data needs to be considered. More information on how the drug works is needed. – Laboratories must not over-interpret serum PKs. This information could be provided with the breakpoints but not associate it with a restriction.

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	– A footnote could be included on the report. **Action Item: For the next M60 revision, collect and review clinical data on the echinocandins and add information on restricting reporting. A WG will be formed to address the issues.**
10.	**Dr. Schuetz presented a proposal with Dr. Tesic on reporting intrinsic resistance on various fungi.** • Antimicrobial Stewardship teams encourage appropriately testing and reporting appropriation antimicrobial agents. M100 includes intrinsic resistance tables. • Laboratories have questions regarding the acceptability of reporting an intrinsically resistant agent as resistant even if it has not been tested. • M60 already includes a footnote to Table 1 that states: "Isolates of *C. krusei* are assumed to be intrinsically resistant to fluconazole, so their MICs should not be interpreted using this scale." • Proposal: Recommend that a comment regarding intrinsic resistance for specific organisms be reported. – *Aspergillus terreus* and amphotericin B – *A. fumigatus* and fluconazole – *Candida lusitaniae* and amphotericin B – *Cryptococcus* spp. and echinocandins – *Rhodotorula* and azoles and echinocandins – *Trichosporon* and echinocandins – Mucorales and voriconazole and echinocandins – *Scedosporium apiospermum*/*P. boydii* and echinocandins – Suggested comment: "This antifungal agent is not considered adequate for treatment." • Discussion: Comments and Suggestions – Need to start with a framework for nomenclature for wild type and resistance. – Define the criteria and collect scientific evidence for designating an organism as intrinsically resistant and determine how to handle cryptic species. **Action Item: Form a working group to develop criteria for reporting an isolate as intrinsically resistant to a particular agent or group of agents. Interested volunteers should contact Dr. Schuetz or Dr. Tesic about joining the group.**
11.	**Dr. Elizabeth Berkow provided a presentation on novel antifungal compound test for *Candida auris*.** • *C. auris* is an emerging public health problem that can be misidentified as other *Candida* spp., has the ability to withstand standard infection control practices, and can exhibit *in vitro* resistance to one or more antifungal agents. • Nine antifungal agents were tested on the Centers for Disease Control and Prevention (CDC) collection of global isolates (4 clades) using the broth microdilution method according to CLSI standards. – SCY-078 (Scynexis) – VL-2397 (Vical Inc.) – VT-1598 (Viamet Pharmaceuticals) – VT-1161 (Viamet Pharmaceuticals) – CD101 (Cidara Therapeutics) – CSA131 (N8Medical LLC) – iKIX-1 (Harvard University) – DFCl-1 (Harvard University) – APX001A (Amplyx Pharmaceuticals) • Conclusions – APX001A o Shows activity against all *C. auris* clades tested o Resistance to azoles or echinocandins has no impact o Showed strong activity against isolates with are otherwise pan resistant – Scy-078 o Activity against most *C. auris* isolates tested, including some echinocandin resistant isolates (Exception: South American isolates) o MIC_{50} values like those reported for other *Candida* spp. (eg, *C. albicans* and *C. glabrata*) o In phase 2 clinical trials for invasive candidiasis and aspergillosis.

SUMMARY MINUTES	
#	**Description**

	– CD101
	  ○ Designated a Qualified Infectious Disease Product with fast track status
	  ○ Given orphan drug designation by FDA for invasive candidiasis
	  ○ MIC values indicate good *in vitro* activity and consistent with MIC values observed with other *Candida* spp. for all clades
	  ○ *FKS* mutations plays a role in resistance to one or more echinocandins
	– VT-1161 and VT-1598
	  ○ Showed activity against all *C. auris* test to various degrees
	  ○ MIC_{50} values among fluconazole susceptible isolates like the value for fluconazole-resistant isolates
	  ○ Has orphan drug designation for treating Valley Fever
	  ○ In Phase 2 clinical trials for onychomycosis and RVVC
	– CSA-131
	  ○ Microtiter plate types may impact MIC value due to compound "stickiness"
	  ○ Showed activity against all *C. auris* isolates
	  ○ Values across the 4 clades was comparable
	  ○ Not impacted by echinocandin- or azole-resistance
	– iKIX1/DFCl-1
	  ○ MIC distributions is wider for iKIX1 than for DFCl-1
	  ○ Activity across the clades comparable
	  ○ MIC values like those observed in other *Candida* spp.; clinical interpretation of MICs is unknown
	  ○ Not impacted by echinocandin- or azole-resistance
	– VL-2397
	  ○ MIC_{50} values for VL-2397 relatively high against many *C. auris* isolates
	  ○ Value within one clade are somewhat lower; however, these values are not as low as what has been reported for *C. glabrata* and *Aspergillus* spp.
	  ○ Phase 1 trial completed (March 2017) and Phase 2 trial in invasive aspergillosis being planned
	• Discussion
	– *In vitro* AST for *C. auris* may not predict *in vivo* outcomes.
	– Treatment failures could be due to the organism hiding in different body sites. Echinocandin R isolates often start as urinary tract isolates exposed to low levels of drug due to the poor penetration and the low level exposure causes resistance.

12.	**Dr. Mariana Castanheira provided an update from the AST Outreach WG.** • Items in progress include: – Newsletters are published twice a year which includes news updates related to susceptibility testing, case studies, answers to burning questions, etc. – Developing and presenting periodic webinars covering important topics related to antimicrobial susceptibility testing – Information on AST subcommittee activities • An Outreach WG report will become a standing meeting agenda item.

13.	**Dr. Procop reviewed outstanding action items.**
	• Draft and distribute emails requesting that laboratories if they perform broth microdilution or know of laboratories that do.
	– The email has been distributed.
	– Few responses have been received. 5 – 6 laboratories will be sending in data once it is decided which specific targets are needed.
	– The isolate submission form is posted on the CLSI website (ECV Data Submission Form and Instructions).
	– Suggestions for collecting data
	  ○ Compile a list of laboratories that perform broth microdilution
	  ○ Compile a list of organisms for which data is needed
	  ○ Request that data be submitted periodically
	  ○ Designate a laboratory to act as a "middle man" (eg, CDC, UCLA etc.)

SUMMARY MINUTES	
#	**Description**
	Action Item: The ECV WG will collect isolates from laboratories that perform broth microdilution. This with isolates should notify Ms. Hackenbrack (mhackenbrack@clsi.org) if there are isolates to submit. The ECV WG will indicate what types of isolates are needed.
	• Revisit voriconazole data for *C. glabrata* (in progress). – Dr. Alexander and Dr. Fuller are compiling old data from past meetings. – It is expected a report will be available for the summer Web conference. • Draft a footnote regarding the lack of established ECV due to MIC values falling below the MIC range tested (completed). • Collect additional data for *Aspergillus nidulans* for all antifungal agents (in progress). – The ECV WG is still waiting for isolates to be submitted. – Any submitted isolates will need molecular ID.
	Action item: Request industrial partners to provide small grants to help with data collection and for supplies to perform testing (G. Procop).
	• Reanalyze posaconazole data for *A. fumigatus* with data from Dr. Meis included. – Data from sequence strains are needed. – A representative of Merck stated that they can provide data from their collected isolates and will be able to present their data in the future. • The following action items will be tabled until the ECV WG can re-request data from the laboratories originally performed the testing. – Submit raw *Fusarium* data to ECV Working Group / Data Repository. – Re-analyze *Fusarium* ECV data for amphotericin B, itraconazole, posaconazole, voriconazole for SC review. – Submit raw Mucorales data to ECV Working Group / Data Repository. – Re-analyze Mucorales data for amphotericin B, posaconazole & itraconazole. • Review and re-analyze data for *Candida* spp. and isavuconazole (see Item 8; in progress). • New Items: See Action Item table.
14.	**Next meetings:** • A Web conference will be scheduled for Summer 2018. A poll will be distributed in the near future. • Saturday, 26 January 2019, Renaissance Workd Golf Village, St. Augustine, Florida
15.	Dr. Procop thanked the participants for their time and continuing work. The meeting was adjourned at 2:30 PM.

Voting Summary		
#	**Motion Made and Seconded**	**Results**
1.	To accept the agenda as presented.	9 – 0; 1 absent (Pass)
2.	To accept the January 2017 summary minutes as presented.	9 – 0; 1 absent (Pass)
3.	To accept a 24-hr. range of 0.008–0.06 µg/ml for *A. fumigatus* MYA 3627 as the recommended QC organism for APX001A.	9 – 0; 1 absent (Pass)
4.	To accept a 48-hr. range of 0.016 – 0.12 µg/ml for *A. fumigatus* MYA 3627 as the recommended QC organism for APX001A.	8 – 1; 1 absent (Pass)
5.	To accept a QC range of 0.016 – 0.12 µg/ml at 24 hrs at 50% inhibition for *C. parapsilosis* ATCC® 22019 as the recommended QC strain and *C. albicans* at 0.016 – 0.06 µg/ml as a supplemental QC strain for APX001A.	9 – 0; 1 absent (Pass)
6.	To accept a QC range of 0.016 – 0.12 µg/ml at 48 hrs at 50% inhibition for *C. parapsilosis* ATCC® 22019 as the recommended QC strain and *C. albicans* at 0.016 – 0.06 µg/ml as a supplemental QC strain for APX001A in M61.	9 – 0; 1 absent (Pass)
7.	To accept a QC range of 0.016 – 0.06 µg/ml at 24 0.1hrs. at 50% inhibition for *C. albicans* ATCC® 90028 and voriconazole in M60.	9 – 0; 1 absent (Pass)
8.	To accept the proposed QC ranges for *C. parapsilosis* and *C. krusei* as presented above with 24 hr. ranges in M60 and 24 and 48hr. ranges in M61.	9 – 0; 1 absent (Pass)
9.	To provide MIC data for organism/drug combinations for which there are no BPs or ECVs (rare species with insufficient data or laboratories or have truncated data) according to the presented criteria and for this information to be managed by the ECV WG and approved by the Antifungal Subcommittee.	9 – 0; 1 absent (Pass)

ACTION ITEMS			
#	**Description**	**Responsible**	**Status/ Due date**
1.	Collect January 2014 isavuconazole and combine with previous data and reanalyze for correcting the QC information.	B. Alexander L. Kovanda	
2.	Form a working group to develop criteria for reporting an isolate as intrinsically resistant to a particular agent or group of agents. Interested volunteers should contact Dr. Schuetz or Dr. Tesic about joining the group.	A. Schuetz V. Tesic	Completed Nov 2018
3.	Investigate the information technology needed to post and maintain an MIC data table for organism/drug combinations for which there are no BPs or ECVs.	M. Hackenbrack	Completed Marketing can create
4.	Generate a "wish list" of rare species to target will be compiled by the ECV WG.	ECV WG	
5.	Notify CLSI (mhackenbrack@clsi.org) if your laboratory has isolates to submit. The ECV WG will indicate what types of isolates are needed.	All	
6.	Collect and review clinical data on the echinocandins and add information on restricting reporting to M60.	A. Schuetz V. Tesic	
7.	Revisit voriconazole data for *C. glabrata* (in progress).	B. Alexander J. Fuller	
8.	Collect additional data for *Aspergillus nidulans* for all antifungal agents.	P. Dufresne D.Perlin	
9.	Request industrial partners to provide small grants to help with data collection and for supplies to perform testing	G. Procop	
10.	Submit raw *Fusarium* data to ECV Working Group / Data Repository.	Tabled	
11.	Re-analyze *Fusarium* ECV data for amphotericin B, itraconazole, posaconazole, voriconazole for SC review.	Tabled	
12.	Submit raw Mucorales data to ECV Working Group / Data Repository.	Tabled	
13.	Re-analyze Mucorales data for amphotericin B, posaconazole & itraconazole.	Tabled	

Respectfully submitted,
Camille Hamula, PhD
Marcy L. Hackenbrack, MCM, M(ASCP)