Subcommittee on Antifungal Susceptibility Tests
Grand Hyatt Tampa Bay, Tampa, Florida
12 January 2013

Summary Minutes

A meeting of the Clinical and Laboratory Standards Institute Subcommittee (SC) on Antifungal Susceptibility Tests was held on Saturday, 12 January 2013 in Tampa, Florida. Those in attendance are listed below.

Mahmoud A. Ghannoum, MSc, PhD, EMBA **Chairholder**	**Case Western Reserve University**
Barbara D. Alexander, MD, MHS **Vice Chairholder**	**Duke University Medical Center**

Members Present

William B. Brasso	BD Diagnostic Systems
Sharon K. Cullen, BS, RAC	Siemens Healthcare Diagnostics Inc.
Ana Espinel-Ingroff, PhD	VCU Medical Center
Annette W. Fothergill, MA, MBA, MT(ASCP)	University of Texas Health Science Center
Shawn R. Lockhart, PhD, D(ABMM)	Centers for Disease Control and Prevention
Jacques F. Meis, MD, PhD	Canisius Wilhelmina Hospital
David S. Perlin, PhD	New Jersey Medical School-UMDNJ
Neil S. Ryder, PhD	Consultant
Nancy L. Wengenack, PhD, D(ABMM), FIDSA	Mayo Clinic
Peter R. Williamson, MD, PhD	National Institutes of Health

Members Absent (with notice)

Michael A. Pfaller, MD	University of Iowa College of Medicine

Advisors

Maiken Cavling Arendrup, MD, PhD	Statens Serum Institut
Lynette Y. Berkely, PhD	FDA CDER
Steven D. Brown, PhD, ABMM	The Clinical Microbiology Institute
Mariana Castanheira, PhD	JMI Laboratories
Kimberly E. Hanson, MD	University of Utah and ARUP Laboratories
Cynthia C. Knapp, MS	Thermo Fisher Scientific
Michael LaFleur, PhD	Arietis
Cynthia L. Fowler, MD	MFHSC
Mary R. Motyl, PhD, D(ABMM)	Merck Sharp & Dohme Corp.
Gary W. Procop, MD	Cleveland Clinic
John H. Rex, MD, FACP	AstraZeneca Pharmaceuticals
Ribhi M. Shawar, PhD, D(ABMM)	FDA Ctr. Devices/Rad. Health
Kenneth Van Horn, PhD, D(ABMM)	Focus Diagnostics

Thomas J. Walsh, MD	Weill Cornell Medical Center of Cornell University

Reviewers

Vishnu Chaturvedi, PhD	New York State Department of Health
Philippe Dufresne, PhD	Institut National de Santé Publique
Jeff Fuller, PHD, FCCM, ABMM	Alberta Health Services
Beth P. Goldstein, PhD	Beth Goldstein Consultant
Patricia Hogan, MT(ASCP), MBA	Pfizer Inc.
Scott B. Killian	Thermo Fisher Scientific
Laura Kovanda	Astellas Pharma
Linda M. Mann, PhD, D(ABMM)	Siemens Healthcare Diagnostics Inc.
Maureen Mansfield	Thermo Fisher Scientific
Stephen A. Moser, PhD	University of Alabama, Birmingham
Maria M. Traczewski, BS, MT(ASCP)	The Clinical Microbiology Institute
John Turnidge	SA Pathology

Guests

Carey-Ann Burnham	Washington University School of Medicine
Kathy Burtner	Siemens Healthcare Diagnostics
Jenifer Dawson Driscoll	Siemens Healthcare Diagnostics
Gina Ewald-Saldana	Siemens Healthcare Diagnostics
Sheila Farnham	bioMérieux, Inc.
Elaine Goldwater	Merck
Nilia M. Robels Hernandez	bioMérieux, Inc.
Romney M. Humphries, PhD, D(ABMM)	UCLA David Geffen School of Medicine
Åsa Karlsson	bioMérieux SA
Roberta Knefel	bioMérieux, Inc.
Jennifer Lorber	Thermo Fisher Scientific
Ian Morrissey	IHMA Europe Sárl
Sumathi Nambiae	FDA
Elizabeth Palavechino, MD	Wake Forest Baptist Medical Center
Jonathan Schmitz	Vanderbilt Universit Medical Center
Katherine Sei	Siemens Healthcare Diagnostics
Sharon Shinn	Siemens Healthcare Diagnostics
Jennifer Smart	Astellas Pharma
Kerry Snow	FDA
Phillip B. Sonke	Merck, Sharp & Dohme Inc.
Will Stubbings	Basilea Pharmaceutica
Debora Sweeney	Micromyx
Michael Sweeney	Pfizer Animal Health
Peter Warn	Euprotek
Collette Wehr	Siemens Healthcare Diagnostics
Nathan Wiederhold	UT Health Science Center
Rob Williams	Siemens Healthcare Diagnostics
Teresa Wong	Siemens Healthcare Diagnostics

CLSI Staff Present

Tracy A. Dooley, BS, MLT(ASCP)
Marcy L. Hackenbrack, MCM, M(ASCP), BA

Meeting Materials Provided Prior to Meeting

- Epidemiologic Cut-off Value (ECV/ECOFF) workshop agenda
- Antifungal Subcommittee Meeting Agenda
- Internet link to copies of presentations, reference articles, draft documents, and other background material needed for review during meeting
- Information on marking up PDFs

Purpose of Webinar

The purpose of the meeting was to review and discuss ECV/ECOFF and QC data, address issues needing discussion by the subcommittee, and to review draft documents for revision.

Opening Remarks

Dr. Ghannoum opened the meeting at 10:00 am US Eastern time by welcoming the participants and expressing his gratitude for their hard work and attendance.

He reviewed the "rules of the road" including the introduction of new subcommittee voting members and advisors. It was noted that all voting members were present at the meeting except one; therefore, the 10 – 0 voting rules would apply for any votes taken during the meeting (pass = 10 – 0, 9 – 1, 8 – 2, and 7 – 3). He also reminded the participants to note any changes in disclosures.

Meeting Discussion

The main topics of discussion are list below (see table). **NOTE:** All presentations and data were distributed electronically prior to the meeting and are available for review on the Antifungal SC page on the CLSI website. Any revised presentations not distributed prior to the meeting are also available on the CLSI website.

Agenda Topic		Committee Discussion Points/Rational for Decisions Made and/or Path Forward
1.	**Agenda Item 1A**: Document Review	• It was agreed that: – M27 and M27S be revised. A working group has already been formed to create epidemiologic cut-off value (ECV) language for the documents (Dr. Pfaller, Dr. Turnidge, Ms. Cullen, Dr. Motyl, Dr. Espinel-Ingroff, Dr. Arendrup) – M38 will be revised and a supplement created – M44 and M44S will be revised – M51-A will require review of the document and new QC data. Ms. Fothergill and Dr. Motyl volunteered to review the document and present recommendations at the next meeting (possible webinar in June). • It was suggested that the supplements for each document could be combined to form two supplements for antifungal susceptibility information with one for yeasts and the other for moulds. The SC agreed to create one supplement for the yeasts (M27S and M44S) and one for moulds (M38S [new] and M51S) and to include all ECVs with explanatory language on how to utilize the information. These revisions will begin after the webinar to tentatively be held in June.
2.	**Agenda Item 1G**: Summary Minutes	• A vote to approve the summary minutes of the Antifungal SC webinar held on 30 July 2013 was held and the minutes were approved (**10 – 0; 1 absent**).
3.	**Agenda Item 2**: An Intralaboratory Study for the Testing of Isavuconozole Against *Aspergillus* and *Candida*	Dr. Ghannoum provided an overview of a study for testing isavuconozole against *Aspergillus* and *Candida.* • A question regarding testing with only one lot of plates (it, same trays with 3 different lots of media) was raised. – Ms. Cullen reminded the participants of the CLSI M23 process for developing QC ranges. She indicated that studies have shown that the comparison from laboratory to laboratory, day-to-day testing, and data from tester to tester is more important than the test panel manufacturer. – It was suggested that more Tier 3 data could be gathered over time and reviewed in the future. – The method for calculating the percent agreement was also reviewed (eg, calculated around the mode of the range selecting a 3 dilution range for those with a strong mode or a 4 dilution range for those with strong mode and shoulder). – Dr. Rex suggested that Dr. Brown prepare a brief slide presentation explaining how MIC ranges are determined. This would be presented at the next meeting for all those volunteers that are new to the committee. • Discussion – The study showed the following: – There was excellent interlaboratory agreement of isavuvonazole MICs against *Aspergillus* with >90% agreement in all strains at 100% inhibition point; therefore, it is recommended reading at 100% inhibition endpoint. – For *Candida*, there was >90% interlab agreement in 8 of 15 strains at 50% inhibition; however, the MIC endpoint was more difficult to read due to trailing growth with both isavuvonazole and voriconazole. Therefore, it was recommended that *Candida* be read at 50% inhibition point. • Vote

		– A motion was made and seconded that the described method be used for testing *Aspergillus* – **Pass (10 – 0; 1 absent)** – A motion was made and seconded that the described method be used for testing Candida – **Pass (10 – 0; 1 absent)** • A question was raised regarding reading of *Candida* results at 24 and/or 48 hr. – It was noted that some of the sites in the study reported only 24 hr data while others reported both 24 and 48 hr data. – It was noted that the 48 hr data meets the requirements for an M23 study but not the 24hr data. – It was agreed that another study will be performed to produce both 24 and 48 hrs data and a laboratory to laboratory comparison will be generated. – For the new study, a range lower than the one used in this study will be tested and QC will be included in the study to determine if there is plast to plate variation.
4.	**Item 3**: An Interlaboratory Study for the Identification of QC Strains for Testing Isavuconazole against *Aspergillus* and *Candida*.	Dr. Ghannoum provided an overview of a study for the identification of QC strains for testing isavuconazole against *Aspergillus* and *Candida*. • Discussion – The study showed the following: – QC strains for inclusion in the CLSI standards were based on MICs falling within the range recorded for the majority of the clinical strains tested (Item 2) with >90% interlab agreement. – The QC strains recommended for testing of isavuconazole (48 hr reads) against *Aspergillus* are *Paecilomyces variottii* MYA 3630 at a range of 0.06 – 0.5 µg/ml and *Aspergillus flavus* ATCC 204304® at a range of 0.5 – 4 µg/ml. – The QC strains recommended for testing of isavuconazole (48 hr reads) against *Candida* are *Candida parapsilosis* ATCC 22019 at a range of 0.015 – 0.12 µg/ml and *Candida krusei* ATCC 6258 at a range of 0.06 – 0.5 µg/ml. • Vote – A motion was made and seconded to accept *Paecilomyces variottii* MYA 3630 at a range of 0.06 – 0.5 µg/ml and *Aspergillus flavus* ATCC 204304® at a range of 0.5 – 4 µg/ml for testing of isavuconazole (48 hr reads) against *Aspergillus*. **Pass (10 – 0; 1 absent)** – A motion was made and seconded to accept *Candida parapsilosis* ATCC 22019 at a range of 0.015 – 0.12 µg/ml and *Candida krusei* ATCC 6258 at a range of 0.06 – 0.5 µg/ml for testing of isavuconazole (48 hr reads) against *Candida*. It was noted that the same issue regarding reading results at 24 and 48 hrs exists for the QC study (see Item 2). It was agreed that a vote on the QC organisms for testing Candida will be revisited after data for 24 and 48 hrs is available.
5.	Item 5: ECVs of Amphotericin B, Caspofungin, Itraconazole, Posaconazole, and	Dr. Espinel-Ingroff presented data

	Voriconazole for Aspergillus spp., Using the	
6.	**Item 4:** ECVs of CLSI M38 Microdilution Method Isavuconazole for Aspergillus spp., Using the CLSI M38 Microdilution Method	Dr. Espinel-Ingroff presented data for recommendation of proposed ECV/ECOFFs for four species of Aspergillus and isavuconazole. • It was noted that a number of voting members expressed discomfort with approving the ECVs without a review of the raw data used to designate the ECVs. It was suggested that a vote on the ECVs be tabled until the subcommittee can review the raw data used to develop the recommended ECVs. –
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Action Items – By 15 May 2013 (for next meeting/webinar to be determined)

	Specific Action Item Descriptions	Responsible Individual (NOTE: Include Date if different from above)
1.	Review M51-A and new QC data and provide input on need to revise the document.	Ms. Fothergill Dr. Motyl
2.	Prepare a brief slide presentation on how MIC ranges are determined.	Dr. Brown
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Next Meeting Reminder:

The next meeting of the Antifungal Subcommittee

Adjournment

Respectfully submitted,

Marcy L. Hackenbrack, MCM, M(ASCP)
Clinical and Laboratory Standards Institute