

Virtual Meeting Title:	Subcommittee (SC) on Antifungal Susceptibility Tests	Contact:	mhackenbrack@clsi.org
		Secretary	Camille Hamula, PhD, D(ABMM)
Meeting Dates and Times:	Wednesday, 9 June 2021 (12:00 - 3:00 PM Eastern [US] time)		
Meeting Purpose:	The purpose of this meeting is to discuss subcommittee business.		
Requested Attendee(s):	SC members, advisors, and reviewers, CLSI staff, Any interested parties		
Attendee(s):			
Gary W. Procop, MD, MS Chairholder Philippe J. Dufresne, PhD, RMCCM Vice-chairholder Camille Hamula, PhD, D(ABMM) Committee Secretary/Advisor		Cleveland Clinic Institut national de santé publique du Québec Saskatoon Health Region/University of Saskatchewan	
Members:			
Elizabeth Berkow, PhD Kimberly E. Hanson, MD, MHS Sharon K. Cullen, BS, RAC Jeff Fuller, PhD, FCCM, D(ABMM) Nicole M. Holliday, BA Audrey N. Schuetz, MD, MPH, D(ABMM) Paul E. Verweij, MD, FECMM Nathan P. Wiederhold, PharmD Adrian M. Zelazny, PhD, D(ABMM)		Centers for Disease Control and Prevention University of Utah and ARUP Laboratories Beckman Coulter, Inc., Microbiology Business London Health Sciences Centre Thermo Fisher Scientific Mayo Clinic Radboud University Medical Center University of Texas Health Science Center at San Antonio National Institutes of Health	
Advisors Present:			
David Andes, MD Andrew M. Borman, BSc, PhD Mariana Castanheira, PhD Jennifer Chau, PhD Tanis Dingle, PhD, D(ABMM), FCCM Mahmoud A. Ghannoum, PhD, FIDSA, MBA Kerian K. Grande Roche, PhD Scott B. Killian, BS Shawn R. Lockhart, PhD, D(ABMM) Amir Seyedmousavi, VMD, PhD, FECMM Ribhi M. Shawar, PhD, D(ABMM) Sean X. Zhang, MD, PhD, D(ABMM)		University of Wisconsin Madison Medical School Public Health England JMI Laboratories Beckman Coulter, Inc. Alberta Precision Laboratories - Public Health Laboratory Case Western Reserve University FDA Center for Drug Evaluation and Research Thermo Fisher Scientific Centers for Disease Control and Prevention National Institutes of Health FDA Center for Devices and Radiological Health Johns Hopkins University	
Reviewers and Guests Present: See attached list			
Staff:			
Glen Fine, MS, MBA, CAE Emily Gomez, MS, MLS(ASCP)MB Marcy L. Hackenbrack, MCM, M(ASCP) Christine Lam, MT(ASCP)		CLSI CLSI CLSI CLSI	

NOTE: The information contained in these minutes represents a summary of the discussions from a CLSI committee meeting, and do not represent approved current or future CLSI document content. These summary minutes and their content are considered property of and proprietary to CLSI, and as such, are not to be quoted, reproduced, or referenced without the expressed permission of CLSI. Thank you for your cooperation. NOTE: Meeting discussion records may be paraphrased.

Passing Vote Record					Voting Results	Page
Motion made and seconded						
To approve the provisional susceptible-only breakpoints and ECVs for rezafungin with the <i>Candida</i> spp. listed and corrections discussed and a footnote regarding a susceptible-only breakpoint.					9-0-0-0	4
Species	Anidulafungin BPs		Proposed Rezafungin Preliminary BPs (Susceptible)	Rezafungin Preliminary ECVs (97.5%)	8-0-0-1	5
	Susceptible	Resistant				
<i>C. albicans</i>	≤ 0.25	≥ 1	≤ 0.25	0.06		
<i>C. glabrata</i>	≤ 0.12	≥ 0.5	≤ 0.5	0.12		
<i>C. tropicalis</i>	≤ 0.25	≥ 1	≤ 0.25	0.12		
<i>C. krusei</i>	≤ 0.25	≥ 1	≤ 0.25	0.12		
<i>C. parapsilosis</i>	≤ 2	≥ 8	≤ 2	4		
<i>C. auris</i>	NA	≥ 4	≤ 0.5	0.5		
<i>C. dubliniensis</i>			≤0.12	0.12		
To approve the QC strains and MIC ranges (<i>C. albicans</i> ATCC 90028 [0.002-0.016 µg/mL] and <i>C. parapsilosis</i> ATCC 90018 [0.001-0.008 µg/mL] or <i>C. parapsilosis</i> ATCC 22019 [0.008 - 0.06 µg/mL]) recommended for susceptibility testing of VT-1161 (Oteseconazole) with a comment that either <i>C. parapsilosis</i> strain can be used for QC was made and seconded.					9-0-0-0	6
To designate <i>Rhodotorula</i> as intrinsically resistant to fluconazole was made and seconded.					9-0-0-0	6
To designate <i>L. prolificans</i> as intrinsically resistant to fluconazole was made and seconded.					9-0-0-0	6

^aVoting Key: W-X-Y-Z (for-against-abstain-absent)

SUMMARY MINUTES	
#	Description
1.	OPENING REMARKS (G. Procop) - Dr. Procop opened the meeting at 12:05 PM Eastern US time by thanking the participants for their time and attention. - He noted that there were no additions or comments on the agenda. - He requested that volunteers provide any updates on conflicts during discussions.
2.	CLSI UPDATE (G. Fine) - The organization has managed well during the pandemic. - CLSI staff has been working remotely for the last 15 months and is expected to remain remote until Summer 2022. - The office building was sold in 2020 and no new space has been leased. Mr. Fine noted that the virtual office is working well and, by working virtually, CLSI been able to save money that can be applied to member benefits and to CLSI's mission and activities. Staffing has been very stable. - The plan is to return to in-person meetings in January 2022 (22 January 2022 in Ft. Lauderdale). The meeting is expected to have a hybrid component. CLSI is working on the logistics and mechanics of conducting the hybrid meetings. - The sales of standards have been fluctuating but are normalizing overall. - Mr. Fine expressed his gratitude to all the volunteers who have continued to dedicate their time and expertise to CLSI during a difficult time.
3.	CLSI DOCUMENT UPDATE (M. Hackenbrack) - M27 and M38 last published in 2017 and will be ready for the 5-year review in 2022. - M44 last published in 2018 and will be ready for the 5-year review in 2023 - M51 and M57 were last published in 2010 and 2016, respectively and are due for review to determine if revision, reaffirmation, or archiving is needed. M51 has already been reaffirmed once and, if not revised, will be archived.

SUMMARY MINUTES	
#	Description
	M59, M60, and M61 have been recoded as M57S, M27M44S, and M38M51S, respectively. All three supplements are currently being revised and expected to publish in late 2021.
4.	<u>BREAKPOINT WG (BPWG) REPORT: REZAFUNGIN BREAKPOINTS (D. Andes)</u> WG Roster: David Andes, Andy Borman (Co-Chairholders); Nathan Wiederhold (Secretary); Mariana Castanheira, Kim Hanson (Members); Philippe Dufresne, Gary Procop (Advisors). Background - Rezafungin is in the echinocandin drug class which has a long history of breakpoint success. - Rezafungin is structurally similar to anidulafungin but is modified to have longer half-life. - WG looked at 4 sets of data: - JMI surveillance/ECV data with CDC <i>C. auris</i> data, - Mouse pre-clinical PK/PD data for multiple <i>Candida</i> spp. and rezafungin behaves like other echinocandins. - Population PK Monte Carlo simulations, - Phase 2 clinical data relative to MIC - MIC distribution for rezafungin aligns well with other echinocandins especially anidulafungin BPWG Data Review for <i>C. albicans</i> - Rezafungin has comparable <i>in vitro</i> activity vs <i>Candida</i> and <i>Aspergillus</i> spp. to approved echinocandins (ie, anidulafungin). - Rezafungin ECVs for <i>C. albicans</i> were calculated to be in the range of 0.06-0.12 µg/mL. - It was noted that ECVs are generally a single ECV and not a range. As per Ecoffinder, the ECV appeared to be 0.06 µg/mL. For some of the species, there were out of range values and those were deleted. The final proposal was presented on the summary slide. - The murine PK/PD target studies showed success at all MICs with the highest tested at 0.06 µg/mL. The PK/PD target was similar to all other echinocandins. - Monte Carlo simulations showed <i>C. albicans</i> probability of target attainment (PTA) to be high at MIC of 0.5-1 µg/mL. - Clinical trial outcomes by pathogen and MIC showed that the clinical experience and success with <i>C. albicans</i> with MICs up to 0.12 µg/mL. - For <i>C. albicans</i>, the WG proposed an ECV of 0.06 µg/mL and a susceptible BP of ≤0.25 µg/mL. BPWG Data Review for <i>C. glabrata</i> - Rezafungin ECV for <i>C. glabrata</i> was calculated to be 0.12 µg/mL. - The murine PK/PD target studies showed a significant shift at >0.5 µg/mL. - Monte Carlo simulations showed <i>C. glabrata</i> with a PTA at an MIC of >1 µg/mL. - Clinical trial outcomes by pathogen and MIC showed that the clinical experience and success with <i>C. glabrata</i> was up to 0.25 µg/mL. - For <i>C. glabrata</i>, the WG proposed an ECV of 0.12 µg/mL and a susceptible BP of ≤0.5 µg/mL. BPWG Data Review for <i>C. tropicalis</i> - Rezafungin ECV for <i>C. tropicalis</i> was calculated to be 0.12 µg/mL. - The murine PK/PD target studies showed success at all MICs with the highest tested at 0.06 µg/mL. - Clinical trial outcomes by pathogen and MIC showed that the clinical experience and success with <i>C. tropicalis</i> was up to 0.25 µg/mL. - For <i>C. tropicalis</i>, the WG proposed an ECV of 0.12 µg/mL and a susceptible breakpoint of ≤0.25 µg/mL. BPWG Data Review for <i>C. parapsilosis</i> - Rezafungin ECV for <i>C. parapsilosis</i> was calculated to be at 4 µg/mL. - The murine PK/PD target studies showed success at all MICs with the highest tested at 1.0 µg/mL. - There was no formal Monte Carlo simulation but had a PK/PD target similar to <i>C. albicans</i> and good PTA at 1-2 µg/mL. - Clinical trial outcomes by pathogen and MIC showed that the clinical experience and success with <i>C. parapsilosis</i> was up to 2.0 µg/mL. - For <i>C. parapsilosis</i>, the WG proposed an ECV of 4 µg/mL and a susceptible BP of ≤2 µg/mL. BPWG Data Review for <i>C. dubliniensis</i> - Rezafungin ECV for <i>C. dubliniensis</i> was calculated to be at 0.12 µg/mL.

SUMMARY MINUTES

#	Description																																										
	– The murine PK/PD target studies showed success at all MICs, with the highest tested at 0.06 µg/mL. – Clinical trial outcomes by pathogen and MIC showed that the clinical experience and success with <i>C. dubliniensis</i> was up to 0.06 µg/mL. – For <i>C. dubliniensis</i>, the WG proposed an ECV of 0.12 µg/mL and a susceptible BP of ≤0.12 µg/mL. • BPWG Data Review for <i>C. auris</i> – There was no formal ECV for <i>C. auris</i> but proposed an ECV of 0.5 µg/mL based on a publication (Berkow E., Lockhart S., DMID 2018;90:196-7). – The murine PK/PD target studies included FKS mutants and didn't do well with MICs ≥2 µg/mL. – There was no formal Monte Carlo simulation but had a PK/PD target similar to <i>C. albicans</i> and good PTA at 1-2 µg/mL. – For <i>C. auris</i>, the WG proposed a potential ECV of 0.5 µg/mL and a susceptible breakpoint of ≤0.5-1 µg/mL. It was noted that the CDC ECV for anidulafungin is 1 and closely aligned with rezafungin. • BPWG Data Review for <i>C. krusei</i> – Rezafungin ECV for <i>C. krusei</i> was calculated to be at 0.12 µg/mL. – There was no PK/PD pre-clinical data and no Monte Carlo simulation data. – Clinical trial outcomes by pathogen and MIC showed that the clinical experience and success with <i>C. dubliniensis</i> was up to 0.12 µg/mL. – For <i>C. krusei</i> the WG proposed a potential ECV of 0.12 µg/mL and a susceptible breakpoint of ≤0.25 µg/mL (corrected during meeting from 0.5). • Proposed Rezafungin Provisional Breakpoints and ECVs (see corrections from the original presentation in red) <table><tr><th rowspan="2">Species</th><th colspan="2">Anidulafungin BPs</th><th rowspan="2">Proposed Rezafungin Preliminary BPs (Susceptible)</th><th rowspan="2">Rezafungin Preliminary ECVs (97.5% or 99%)</th></tr><tr><th>Susceptible</th><th>Resistant</th></tr><tr><td><i>C. albicans</i></td><td>≤ 0.25</td><td>≥ 1</td><td>≤ 0.25</td><td>0.06 or 0.12</td></tr><tr><td><i>C. glabrata</i></td><td>≤ 0.12</td><td>≥ 0.5</td><td>≤ 0.5</td><td>0.12 or 0.25</td></tr><tr><td><i>C. tropicalis</i></td><td>≤ 0.25</td><td>≥ 1</td><td>≤ 0.25</td><td>0.12</td></tr><tr><td><i>C. krusei</i></td><td>≤ 0.25</td><td>≥ 1</td><td>≤ 0.25</td><td>0.12</td></tr><tr><td><i>C. parapsilosis</i></td><td>≤ 2</td><td>≥ 8</td><td>≤ 2</td><td>4</td></tr><tr><td><i>C. auris</i> (per CDC)</td><td>NA</td><td>≥ 4</td><td>≤ 0.5 or 4</td><td>0.5</td></tr><tr><td><i>C. dubliniensis</i></td><td></td><td></td><td>≤0.12</td><td>0.12</td></tr></table> • SC Discussion – The ECV WG will look for additional data for the <i>C. auris</i> ECV. <i>C. glabrata</i> BP is higher to split the difference between the clinical data and the Monte Carlo simulation that suggested MIC of >1. Potentially could be revisited in future. ○ It was noted that rezafungin was tested with <i>C. auris fks</i> mutants and had MICs of 2.0. ○ The tentative CDC BP for anidulafungin and <i>C. auris</i> was 4 for resistant, MIC of 2 was no <i>fks</i> mutation (for anidulafungin). ○ The BP of 0.5 is likely too conservative and proposed 1 for S, 2 for I and 4 for R. – It was noted that only the susceptible BPs are listed for Rezafungin but S and R are listed for anidulafungin. It was questioned as to what the proposed R breakpoint is for these organisms. Only the susceptible BP was discussed and no resistant BP was set. It was noted that this has been done before with the echinocandins. As more data is collected, I and R BPs will be added. A comment regarding this situation will be included in the document. – It was questioned why "per CDC" is listed with the <i>C. auris</i> BP and if this will be stated in the document. The data for <i>C. auris</i> was primarily derived from the CDC. A motion to approve the provisional susceptible-only breakpoints and ECVs for rezafungin with the <i>Candida</i> spp. listed and corrections discussed and a footnote regarding a susceptible-only breakpoint was made and seconded. Vote: 9 for; 0 against; 0 abstain; 0 absent (Pass).	Species	Anidulafungin BPs		Proposed Rezafungin Preliminary BPs (Susceptible)	Rezafungin Preliminary ECVs (97.5% or 99%)	Susceptible	Resistant	<i>C. albicans</i>	≤ 0.25	≥ 1	≤ 0.25	0.06 or 0.12	<i>C. glabrata</i>	≤ 0.12	≥ 0.5	≤ 0.5	0.12 or 0.25	<i>C. tropicalis</i>	≤ 0.25	≥ 1	≤ 0.25	0.12	<i>C. krusei</i>	≤ 0.25	≥ 1	≤ 0.25	0.12	<i>C. parapsilosis</i>	≤ 2	≥ 8	≤ 2	4	<i>C. auris</i> (per CDC)	NA	≥ 4	≤ 0.5 or 4	0.5	<i>C. dubliniensis</i>			≤0.12	0.12
Species	Anidulafungin BPs		Proposed Rezafungin Preliminary BPs (Susceptible)	Rezafungin Preliminary ECVs (97.5% or 99%)																																							
	Susceptible	Resistant																																									
<i>C. albicans</i>	≤ 0.25	≥ 1	≤ 0.25	0.06 or 0.12																																							
<i>C. glabrata</i>	≤ 0.12	≥ 0.5	≤ 0.5	0.12 or 0.25																																							
<i>C. tropicalis</i>	≤ 0.25	≥ 1	≤ 0.25	0.12																																							
<i>C. krusei</i>	≤ 0.25	≥ 1	≤ 0.25	0.12																																							
<i>C. parapsilosis</i>	≤ 2	≥ 8	≤ 2	4																																							
<i>C. auris</i> (per CDC)	NA	≥ 4	≤ 0.5 or 4	0.5																																							
<i>C. dubliniensis</i>			≤0.12	0.12																																							

SUMMARY MINUTES

#	Description																																																														
5.	OTESECONAZOLE (VT-1161) QC RANGES (M. Ghannoum) • Background – The objective of the study was to identify candidate QC strains for the susceptibility testing of VT-1161 against yeasts using the CLSI M27-A4 standard. – Seven laboratories participated in the QC study. – Six ATCC <i>Candida</i> spp. strains were tested using CLSI methodology. ○ <i>C. parapsilosis</i> ATCC 22019 ○ <i>C. krusei</i> ATCC 6258 ○ <i>C. albicans</i> ATCC 90028 ○ <i>C. albicans</i> ATCC 24433 ○ <i>C. parapsilosis</i> ATCC 90018 ○ <i>C. tropicalis</i> ATCC 750 – The agent was tested in a range of 0.0005-0.25 µg/mL and were read at 24 and 48 hrs. incubation at 50% and 100% inhibition. – Voriconazole was included as an internal control. • Analysis data for candidate strains were reviewed (see presentation). – No QC ranges were proposed for <i>C. krusei</i> ATCC 6258 or <i>C. tropicalis</i> ATCC 750 with oteseconazole. – Based on the analyzed data the following recommendations were made: ○ Reading at 50% inhibition following 24 hrs. incubation ○ <i>C. albicans</i> ATCC 90028 - range 0.002-0.016 µg/ml ○ <i>C. parapsilosis</i> ATCC 90018 - range 0.001-0.008 µg/ml – The QC ranges for the internal control (voriconazole) with <i>C. krusei</i> ATCC 6258 and <i>C. parapsilosis</i> ATCC 22019 were acceptable. • QC Summary <table><tr><td>Drug: Oteseconazole</td><td>Abbreviation (Glossary): xx</td><td>Previous ID: VT-1161)</td></tr><tr><td>Solvent (Table xx): DMSO</td><td>Diluent (Table xx): RPMI-1640</td><td>Preparation: NA</td></tr><tr><td>Route of administration (Glossary II): Oral</td><td>Class (Glossary xx): Azole</td><td>Subclass (Glossary xx): Triazole</td></tr><tr><td>Study Report by: Dr. Mahmoud Ghannoum</td><td>Pharma Co: Mycovia</td><td>Control Drug: Voriconazole</td></tr></table> <table><tr><td>Additional Information (M23 requirements)</td><td>• Tier 1 Impact Assessment (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): None or list those applicable</td></tr><tr><td>Footnotes:</td><td>• Recommendations for Troubleshooting Guide: N/A</td></tr><tr><td>Notes</td><td>The proposed dosing regimen for the prevention of recurrent vulvovaginal candidiasis is 600 mg Oteseconazole (4x150 mg capsules) on Day 1, 450 mg Oteseconazole (3x150 mg capsules) on Day 2, and on Day 14 being 150 mg Oteseconazole once weekly for 11 weeks.</td></tr></table> <table><tr><th>QC Strain (incubation time/inhibition)</th><th>Range</th><th>% In</th><th>Mode</th><th>Dil</th><th>Shoulder</th><th>Media Mode</th><th>Lab Mode</th><th>M23 Range</th><th>Range Finder</th><th>Comments</th></tr><tr><td><i>C. albicans</i> ATCC 90028 (24 hr, 50%)</td><td>0.002-0.016</td><td>95.3</td><td>0.004</td><td>4</td><td>82% @ 0.008</td><td>2@ 0.004 1@0.008</td><td>3@0.004 4@0.008 1@0.0164</td><td>0.002-0.016</td><td>NA</td><td>Some outliers 5@0.06 and 6@0.12. Recommended strain</td></tr><tr><td><i>C. parapsilosis</i> ATCC 90018 (24 hr, 50%)</td><td>0.001-0.008</td><td>99.2</td><td>0.004</td><td>4</td><td>90% @ 0.002</td><td>2@0.004 1@0.002</td><td>3@0.002, 4@0.004, 1@0.008</td><td>0.001-0.008</td><td>NA</td><td>Recommended strain</td></tr><tr><td><i>C. parapsilosis</i> ATCC 90018 (24 hr, 100%)</td><td>0.004-0.03</td><td>99.6</td><td>0.008</td><td>4</td><td>80% @ 0.016</td><td>2@0.008, 1@0.016</td><td>5@0.008, 2@0.016, 1@0.03</td><td>0.004-0.03</td><td>NA</td><td></td></tr></table>	Drug: Oteseconazole	Abbreviation (Glossary): xx	Previous ID: VT-1161)	Solvent (Table xx): DMSO	Diluent (Table xx): RPMI-1640	Preparation: NA	Route of administration (Glossary II): Oral	Class (Glossary xx): Azole	Subclass (Glossary xx): Triazole	Study Report by: Dr. Mahmoud Ghannoum	Pharma Co: Mycovia	Control Drug: Voriconazole	Additional Information (M23 requirements)	• Tier 1 Impact Assessment (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): None or list those applicable	Footnotes:	• Recommendations for Troubleshooting Guide: N/A	Notes	The proposed dosing regimen for the prevention of recurrent vulvovaginal candidiasis is 600 mg Oteseconazole (4x150 mg capsules) on Day 1, 450 mg Oteseconazole (3x150 mg capsules) on Day 2, and on Day 14 being 150 mg Oteseconazole once weekly for 11 weeks.	QC Strain (incubation time/inhibition)	Range	% In	Mode	Dil	Shoulder	Media Mode	Lab Mode	M23 Range	Range Finder	Comments	<i>C. albicans</i> ATCC 90028 (24 hr, 50%)	0.002-0.016	95.3	0.004	4	82% @ 0.008	2@ 0.004 1@0.008	3@0.004 4@0.008 1@0.0164	0.002-0.016	NA	Some outliers 5@0.06 and 6@0.12 . Recommended strain	<i>C. parapsilosis</i> ATCC 90018 (24 hr, 50%)	0.001-0.008	99.2	0.004	4	90% @ 0.002	2@0.004 1@0.002	3@0.002 , 4@0.004 , 1@0.008	0.001-0.008	NA	Recommended strain	<i>C. parapsilosis</i> ATCC 90018 (24 hr, 100%)	0.004-0.03	99.6	0.008	4	80% @ 0.016	2@0.008 , 1@0.016	5@0.008 , 2@0.016 , 1@0.03	0.004-0.03	NA	
Drug: Oteseconazole	Abbreviation (Glossary): xx	Previous ID: VT-1161)																																																													
Solvent (Table xx): DMSO	Diluent (Table xx): RPMI-1640	Preparation: NA																																																													
Route of administration (Glossary II): Oral	Class (Glossary xx): Azole	Subclass (Glossary xx): Triazole																																																													
Study Report by: Dr. Mahmoud Ghannoum	Pharma Co: Mycovia	Control Drug: Voriconazole																																																													
Additional Information (M23 requirements)	• Tier 1 Impact Assessment (stability, inoculum, reading, incubation time, cations, zinc, surfactants, etc): None or list those applicable																																																														
Footnotes:	• Recommendations for Troubleshooting Guide: N/A																																																														
Notes	The proposed dosing regimen for the prevention of recurrent vulvovaginal candidiasis is 600 mg Oteseconazole (4x150 mg capsules) on Day 1, 450 mg Oteseconazole (3x150 mg capsules) on Day 2, and on Day 14 being 150 mg Oteseconazole once weekly for 11 weeks.																																																														
QC Strain (incubation time/inhibition)	Range	% In	Mode	Dil	Shoulder	Media Mode	Lab Mode	M23 Range	Range Finder	Comments																																																					
<i>C. albicans</i> ATCC 90028 (24 hr, 50%)	0.002-0.016	95.3	0.004	4	82% @ 0.008	2@ 0.004 1@0.008	3@0.004 4@0.008 1@0.0164	0.002-0.016	NA	Some outliers 5@0.06 and 6@0.12 . Recommended strain																																																					
<i>C. parapsilosis</i> ATCC 90018 (24 hr, 50%)	0.001-0.008	99.2	0.004	4	90% @ 0.002	2@0.004 1@0.002	3@0.002 , 4@0.004 , 1@0.008	0.001-0.008	NA	Recommended strain																																																					
<i>C. parapsilosis</i> ATCC 90018 (24 hr, 100%)	0.004-0.03	99.6	0.008	4	80% @ 0.016	2@0.008 , 1@0.016	5@0.008 , 2@0.016 , 1@0.03	0.004-0.03	NA																																																						

SUMMARY MINUTES											
#	Description										
	<i>C. parapsilosis</i> ATCC 90018 (48 hr, 50%)	0.002-0.16	97.9	0.008	4	86% @ 0.004	1@0.004 , 2@0.008	3@0.004 , 3@0.008 , 2@0.016	0.002-0.16		
	<i>C. parapsilosis</i> ATCC 90018 (48 hr, 100%)	0.008-0.06	100	0.03	4	95% @ 0.016	1@0.008 , 2@0.03	1@0.008 , 4@0.03 , 3@0.16	0.008-0.06	NA	
	SC Discussion 50% reads were easier to interpret than the 100% reads. Inter lab agreement was better at 24 hrs. than at 48 hrs. - It was questioned why <i>C. parapsilosis</i> ATCC 90018 instead of 22019 as recommended QC isolate. ATCC 90018 showed better agreement than 22019. It was noted that if both QC strains are reasonable, both could be published and note that either could be used as routine QC. - It was questioned if clinical isolates are supposed to be read at 50% inhibition. All clinical isolates and QC isolates should be read at 50% inhibition at 24 hrs.										
	A motion to approve the QC strains and MIC ranges (<i>C. albicans</i> ATCC 90028 [0.002-0.016 µg/mL] and <i>C. parapsilosis</i> ATCC 90018 [0.001-0.008 µg/mL] or <i>C. parapsilosis</i> ATCC 22019 [0.008 - 0.06 µg/mL]) recommended for susceptibility testing of VT-1161 (Oteseconazole) with a comment that either <i>C. parapsilosis</i> strain can be used for QC was made and seconded. Vote: 8 for; 0 against; 0 abstain; 1 absent (Pass).										
6.	ANTIFUNGAL REPORTING WG REPORT FOR INTRINSIC RESISTANCE (IR) SUBGROUP (A. Schuetz) WG Roster: Audrey Schuetz, Vera Tesic (Co-Chairholders); Tanis Dingle (Secretary); Kim Hanson, Stephanie Mitchell, Natasha Pettit, Priyanka Uprety, Tom Walsh, Nathan Wiederhold, Matt Wikler, Nancy Zhao (Members). Intrinsic Resistance Definition: Inherent or innate (not acquired) antimicrobial resistance, which is reflected in wild-type antimicrobial patterns of all or almost all representatives of a species. Intrinsic resistance is so common that susceptibility testing is unnecessary... “A small percentage (1-3%) may appear susceptible due to method variation, mutation, or low levels of resistance expression. Data reviewed by WG to make decisions - MIC distributions (CLSI methodology, species-specific [when applicable], ID based on sequencing rather than primarily on morphology) - Clinical data - Expert opinion (eg, professional society guidelines) WG Proposals for IR (for vote) <i>Rhodotorula</i> spp. and fluconazole - Studies show reduced susceptibility of <i>Rhodotorula</i> (<i>R. mucilaginosa</i> most common) to fluconazole using reference broth microdilution and YeastOne Sensititre. - Published studies show little or no <i>in vitro</i> activity for fluconazole against <i>Rhodotorula</i>. Very few isolates have MICs <32 µg/mL. - The draft of the ECMM guideline for rare yeast infections to be published recommends against use of triazoles and echinocandins (Global Guideline for the Diagnosis and Management of Invasive Infections Caused by Emerging, Uncommon Rare Yeasts: An Initiative of the European Confederation of Medical Mycology) A motion to designate <i>Rhodotorula</i> as intrinsically resistant to fluconazole was made and seconded. Vote: 9 for; 0 against; 0 abstain; 0 absent (Pass). <i>Lomentospora prolificans</i> and fluconazole - Fluconazole was separated from the other azoles. - MIC₉₀ ≥16 µg/mL - Some MICs were seen at around 0.5 to 1 µg/mL for isavuconazole and voriconazole. - Wu Y. et al. (ACC 2021 64[11]) identified 3 amino acid residues in the Cyp51 protein may be linked to intrinsic azole resistance in <i>L. prolificans</i>. - Troke et al. AAC 2008;52(5):1743 16/36 (44%) patients with <i>L. prolificans</i> were successfully treated with voriconazole monotherapy. Patients with <i>L. prolificans</i> infection were significantly less likely										

SUMMARY MINUTES	
#	Description
	to achieve a successful clinical response compared to those patients with <i>S. apiospermum</i> infection. ○ The new ECMM rare mold infection management guidelines strongly support first-line voriconazole in combination with terbinafine plus or minus other antifungal agents for <i>L. prolificans</i> infections (Hoenigl, M., et al. 2021. Lancet ID https://doi.org/10.1016/S1473-3099(20)30784-2). ○ The WG concluded that <i>L. prolificans</i> is IR to fluconazole. Intrinsic resistance to posaconazole, itraconazole and isavuconazole cannot be determined based on available <i>in vitro</i> susceptibility data (as some isolates test with low MICs to these agents) and based on lack of treatment outcome data). A motion to designate <i>L. prolificans</i> as intrinsically resistant to fluconazole was made and seconded. Vote: 9 for; 0 against; 0 abstain; 0 absent (Pass). – <i>Candida haemulonii</i> for IR to fluconazole ○ A systematic literature review on <i>in vitro</i> antifungal susceptibility using CLSI methods for antifungal susceptibility including use of a variety of AST methods including CLSI, YeastOne Sensititre, and Vitek 2, for <i>C. haemulonii</i> complex to fluconazole. Combining data from all studies, 41/42 (98%) had MIC $\geq$ 64 μg/mL. The other isolate had an MIC = 32 μg/mL. ○ ECV data for <i>C. haemulonii sensu stricto</i> showed an ECV of 128 μg/mL. ○ The IRWG did not vote formally on the proposal but did support IR for fluconazole. • SC Discussion – It was questioned if the data was for <i>C. haemulonii</i> or <i>C. haemulonii</i> complex. Unless ID is done using sequencing or MALDI-TOF MS, then it is difficult to separate out cryptic species. MICs for the separate species do have some differences so the resistance may not be for all species in the complex. It was noted that some are likely to be susceptible. It was also noted that the ECV data was from <i>sensu stricto</i>. – It was suggested that the IRWG should separate out the specific species rather than stating that the complex is IR fluconazole. – <i>C. haemulonii</i> grows slowly at CLSI temperature and some of the testing may be held closer to 48hrs. which may affect the results. – No motion was proposed and no vote was taken. • Suggestions for Table Placement – M59 (M57S): IRWG agreed with M59 authors that only those IR recommendations for those organisms which either have BPs or have ECVs should be included in Table 6 of M59. – M60 (M27M44S) ○ Body site reporting could be listed as Appendix A (recommendation of AHWG) or could be incorporated as Table 1 or Table 7 (before or after BP tables) ○ IR could be listed as Appendix B (to include those yeasts which are not listed in M59 [M57S] Table 6 currently, such as <i>Rhodotorula</i> and <i>Trichosporon</i>). Only yeasts will be listed in the IR table. – M61 (M38M51S): IR table for molds could be listed as Appendix A (to include those molds which are not listed in the current M59 [M57S] Table 6, such as <i>P. lilacinum</i>). Only moulds will be listed the in IR table. • Ongoing and Future Assessments – <i>L. prolificans</i> and echinocandins – <i>Fusarium</i> and echinocandins (IRWG will not pursue <i>Fusarium</i> for IR assessment for amphotericin B since no IR is likely) • Future Steps – Submit a publication outside of CLSI documents and update the supplements as suggested above.
7.	ADJOURNMENT (G. Procop) Dr. Procop thanked the participants for their time and attention. The next meeting will be held on Saturday, 22 January 2022 in Ft. Lauderdale, FL. The meeting was adjourned at 2:15 PM Eastern (US) time.

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

Antifungal Subcommittee Reviewers and Guests

Full Name	Organization/Company Name
Alexander Lepak	University of Wisconsin
Amanda Kuperus	Microbiologics
Beth P Goldstein	Beth Goldstein Consultant
Cecilia Carvalhaes	JMI Laboratories
Chris Pillar	Microbiologics
Jeff Locke	Cidara Therapeutics
Jennifer Chau	Beckman Coulter
Jennifer Slaughter	bioMerieux, Inc.
Nancy Wengenack	Mayo Clinic
Stephanie Mitchell	Cepheid (DanaHER)
Sukantha Chandrasekaran	UCLA
Vera Tesic	University of Chicago
Yanan Zhao	CDI, HMM