



CLINICAL AND
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M57S

Epidemiological Cutoff Values for Antifungal Susceptibility Testing

This document includes epidemiological cutoff values developed according to the criteria in the Clinical and Laboratory Standards Institute (CLSI) guideline M57 and generated according to the reference broth dilution methods described in the CLSI standards M27 and M38.

A CLSI supplement for global application.

Epidemiological Cutoff Values for Antifungal Susceptibility Testing

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Abstract

Clinical and Laboratory Standards Institute document *M57S—Epidemiological Cutoff Values for Antifungal Susceptibility Testing* includes epidemiological cutoff values (ECVs) and quality control tables developed following the guidance in CLSI document M57.¹ These ECVs are valid only when they are developed in accordance with CLSI document M57¹ and when minimal inhibitory concentrations or minimal effective concentrations are generated according to the reference broth dilution methods described in CLSI documents M27² and M38.³ Users should replace previously published tables with these new tables. Changes in the tables since the previous edition was published appear in boldface type.

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Foreword

With the development of standard methodologies for testing the susceptibility of fungal species to several antifungal agents, minimal inhibitory concentration (MIC) and minimal effective concentration (MEC) distributions are available to determine epidemiological cutoff values (ECVs) for ascomycete yeasts (*Candida* spp. and *Saccharomyces* spp.), basidiomycete yeasts (*Cryptococcus* spp., *Rhodotorula* spp., *Trichosporon* spp.), and *Aspergillus* spp. of clinical importance. The ECVs provided in this document were established using the guidance in CLSI document M57.¹ **The ECV, which is the MIC or MEC that separates fungal populations into those with and without acquired and/or mutational resistance based on their phenotypes (wild-type [WT] or non-wild-type [NWT]),** is useful for distinguishing between WT isolates without acquired resistance mechanisms and NWT isolates harboring acquired resistance mechanisms. Unlike breakpoints, ECVs do not classify isolates as treatable (susceptible) or untreatable (resistant). In lieu of breakpoints, clinicians can use ECVs alone when deciding whether to treat a patient with a certain agent (see CLSI document M57¹). However, ECVs do not predict therapeutic response. For ECVs to be clinically useful, the MIC or MEC should be determined using the broth microdilution procedure for yeasts (see CLSI document M27²) or the broth microdilution procedure for filamentous fungi (see CLSI document M38³).

NOTE: Current fungal taxonomy is under revision. Many genera have both a teleomorph (sexual state) and an anamorph (asexual state) name. In this document, the traditional *Candida* anamorph names are used to provide continuity with both past procedures and associated documents such as CLSI document M27² and others.⁴⁻⁶

NOTE: When serial twofold dilution MICs are being prepared and tested, the actual dilution scheme is, eg, 128, 64, 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.125, 0.0625, 0.03125 µg/mL, etc. For convenience only, and not because these are the actual concentrations tested, it was decided to use the following values in M57S: 128, 64, 32, 16, 8, 4, 2, 1, 0.5, 0.25, 0.12, 0.06, 0.03 µg/mL, etc. The values that appear in the tables are equivalent to the actual values tested, eg, 0.12 µg/mL = 0.125 µg/mL, and laboratories should report an ECV of ≤ 0.125 µg/mL as ≤ 0.12 µg/mL.

Table 1. Epidemiological Cutoff Values for *In Vitro* Susceptibility Testing of *Candida* spp. and Other Ascomycete Yeasts With No Breakpoints^{1-6,a}

Antifungal Agent	Species	ECV, $\mu\text{g/mL}$ ^{b,c,d}
Amphotericin B	<i>C. albicans</i>	2
	<i>C. dubliniensis</i>	0.5
	<i>C. glabrata</i> ^e	2
	<i>C. guilliermondii</i> ^e	2
	<i>C. kefyr</i> ^e	2
	<i>C. krusei</i> ^e	2
	<i>C. lusitaniae</i> ^{e,f}	2
	<i>C. metapsilosis</i>	1
	<i>C. orthopsilosis</i>	2
	<i>C. parapsilosis</i>	1
	<i>C. pelliculosa</i>^e	1
	<i>C. tropicalis</i>	2
	<i>Saccharomyces cerevisiae</i>	2
	Anidulafungin	<i>C. auris</i>
<i>C. dubliniensis</i>		0.12
<i>C. duobushaemulonii</i>		1
<i>C. haemulonii</i>		0.5
<i>C. kefyr</i> ^e		0.25
<i>C. lusitaniae</i> ^e		1
<i>C. metapsilosis</i>		0.5
<i>C. orthopsilosis</i>		2
<i>S. cerevisiae</i>		1
Caspofungin		<i>C. auris</i>
	<i>C. duobushaemulonii</i>	0.25
	<i>C. lusitaniae</i> ^e	1
	<i>C. metapsilosis</i>	0.25
	<i>C. orthopsilosis</i>	1
	<i>S. cerevisiae</i>	2
Fluconazole	<i>C. dubliniensis</i>	0.5
	<i>C. duobushaemulonii</i>	32
	<i>C. guilliermondii</i> ^e	8
	<i>C. haemulonii</i>	128^g
	<i>C. kefyr</i> ^e	1
	<i>C. lusitaniae</i> ^e	1
	<i>C. metapsilosis</i>	4
	<i>C. orthopsilosis</i>	2
	<i>C. pararugosa</i>^e	16
	<i>C. pelliculosa</i>^e	8
	<i>C. rugosa</i>^e	8
<i>S. cerevisiae</i>	32^h	
Isavuconazole	<i>C. duobushaemulonii</i>	0.25

Table 1. (Continued)

Antifungal Agent	Species	ECV, µg/mL ^{b,c,d}
Itraconazole	<i>C. dubliniensis</i>	0.25
	<i>C. duobushaemulonii</i>	1
	<i>C. glabrata</i> ^e	4
	<i>C. guilliermondii</i> ^e	2
	<i>C. kefyri</i> ^e	0.5
	<i>C. krusei</i> ^e	1
	<i>C. lusitaniae</i> ^e	1
	<i>C. metapsilosis</i>	1
	<i>C. orthopsilosis</i>	0.5
	<i>C. parapsilosis</i>	0.5
	<i>C. pelliculosa</i>^e	1
	<i>C. tropicalis</i>	0.5
	<i>S. cerevisiae</i>	2
	Micafungin	<i>C. auris</i>
<i>C. dubliniensis</i>		0.12
<i>C. duobushaemulonii</i>		0.5
<i>C. kefyri</i> ^e		0.12
<i>C. lusitaniae</i> ^e		0.5
<i>C. metapsilosis</i>		1
<i>C. orthopsilosis</i>		1
<i>C. pelliculosa</i>^e		0.12
<i>S. cerevisiae</i>		0.5
Posaconazole		<i>C. albicans</i>
	<i>C. dubliniensis</i>	0.12
	<i>C. duobushaemulonii</i>	1
	<i>C. glabrata</i> ^e	1
	<i>C. guilliermondii</i> ^e	0.5
	<i>C. haemulonii</i>	1
	<i>C. kefyri</i> ^e	0.5
	<i>C. krusei</i> ^e	0.5
	<i>C. lusitaniae</i> ^e	0.06
	<i>C. metapsilosis</i>	0.25
	<i>C. orthopsilosis</i>	0.25
	<i>C. parapsilosis</i>	0.25
	<i>C. pelliculosa</i>^e	2
	<i>C. tropicalis</i>	0.12
	<i>S. cerevisiae</i>	2
Voriconazole	<i>C. duobushaemulonii</i>	0.5
	<i>C. glabrata</i> ^e	0.25
	<i>C. haemulonii</i>	2
	<i>C. metapsilosis</i>	0.06
	<i>C. orthopsilosis</i>	0.12
	<i>C. pelliculosa</i>^e	0.25
<i>S. cerevisiae</i>	0.5	

Abbreviation: ECV, epidemiological cutoff value.

Table 6. Summary of Available Epidemiological Cutoff Values and/or Breakpoints by Fungal Species

Species	Antifungal Agent										
	Amphotericin B	Anidulafungin	Caspofungin	Fluconazole	Flucytosine	Isavuconazole	Itraconazole	Micafungin	Posaconazole	Rezafungin ^a	Voriconazole
YEASTS											
<i>Candida albicans</i>	ECV	BP/ECV	BP	BP/ECV	-	-	-	BP/ECV	ECV	BP/ECV	BP/ECV
<i>Candida auris</i>	-	ECV	ECV	-	TR-L	-	-	ECV	-	BP/ECV	-
<i>Candida dubliniensis</i>	ECV	ECV	-	ECV	TR-L	-	ECV	ECV	ECV	BP/ECV	-
<i>Candida duobushaemulonii</i>	TR-H	ECV	ECV	ECV	TR-L	ECV	ECV	ECV	ECV	-	ECV
<i>Candida glabrata</i> ^b	ECV	BP/ECV	BP	BP/ECV	-	-	ECV	BP/ECV	ECV	BP/ECV	ECV
<i>Candida guilliermondii</i> ^b	ECV	BP/ECV	BP/ECV	ECV	TR-L	-	ECV	BP/ECV	ECV	-	-
<i>Candida haemulonii</i>	-	ECV	-	ECV	-	-	-	-	ECV	-	ECV
<i>Candida kefyr</i> ^b	ECV	ECV	-	ECV	TR-L	-	ECV	ECV	ECV	-	-
<i>Candida krusei</i> ^b	ECV	BP/ECV	BP	IR	-	-	ECV	BP/ECV	ECV	BP/ECV	BP/ECV
<i>Candida lusitanae</i> ^b	ECV	ECV	ECV	ECV	TR-L	-	ECV	ECV	ECV	-	-
<i>Candida metapsilosis</i>	ECV	ECV	ECV	ECV	TR-L	-	ECV	ECV	ECV	-	ECV
<i>Candida orthopsilosis</i>	ECV	ECV	ECV	ECV	TR-L	-	ECV	ECV	ECV	-	-
<i>Candida parapsilosis</i>	ECV	BP/ECV	BP/ECV	BP/ECV	TR-L	TR-L	ECV	BP/ECV	ECV	BP/ECV	BP
<i>Candida pararugosa</i> ^b	-	-	-	ECV	-	-	-	-	-	-	-
<i>Candida pelliculosa</i> ^b	ECV	-	-	ECV	TR-L	-	ECV	ECV	ECV	-	ECV
<i>Candida rugosa</i> ^b	-	-	-	ECV	-	-	-	-	-	-	TR-L
<i>Candida tropicalis</i>	ECV	BP/ECV	BP	BP/ECV	-	-	ECV	BP/ECV	ECV	BP/ECV	BP/ECV
<i>Cryptococcus gattii</i> (VGI)	ECV	IR	IR	ECV	ECV	-	ECV	IR	-	-	ECV

Sample



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