CLINICAL AND LABORATORY STANDARDS INSTITUTE®

4th Edition

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.

M57S-Ed4
August 2022
Replaces M59-Ed3

Epidemiological Cutoff Values for Antifungal Susceptibility Testing

Gary W. Procop, MD, MS
Philippe J. Dufresne, PhD, RMCCM
Elizabeth Berkow, PhD
Sharon K. Cullen, BS, RAC
Jeff Fuller, PhD, FCCM, D(ABMM)
Kimberly E. Hanson, MD, MHS
Nicole M. Holliday, BA
Shawn R. Lockhart, PhD, D(ABMM), F(AAM)
Audrey N. Schuetz, MD, MPH, D(ABMM)
Paul E. Verweij, MD, FECMM
Nathan P. Wiederhold, PharmD
Adrian M. Zelazny, PhD, D(ABMM)

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 M57[1] and when minimal inhibitory concentrations or minimal effective concentrations are generated according to the reference broth dilution methods described in CLSI documents M27[2] 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.

Clinical and Laboratory Standards Institute (CLSI). *Epidemiological Cutoff Values for Antifungal Susceptibility Testing*. 4th ed. CLSI supplement M57S (ISBN 978-1-68440-158-1 [Print]; ISBN 978-1-68440-159-8 [Electronic]). Clinical and Laboratory Standards Institute, USA, 2022.

CLINICAL AND LABORATORY STANDARDS INSTITUTE®

Suggested Citation

CLSI. *Epidemiological Cutoff Values for Antifungal Susceptibility Testing*. 4th ed. CLSI supplement M57S. Clinical and Laboratory Standards Institute; 2022.

Previous Editions:

M59: April 2016, January 2018, June 2020

M57-Ed1-S-Ed4
ISBN 978-1-68440-158-1 (Print)
ISBN 978-1-68440-159-8 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2914 (Electronic)

Volume 42, Number 18

Contents

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 M57[1]). 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 M27[2]) or the broth microdilution procedure for filamentous fungi (see CLSI document M38[3]).

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 M27[2] 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, µg/mL[b,c,d]
Amphotericin B	*C. albicans*	2
	C. dubliniensis	0.5
	C. glabrata[e]	2
	C. guilliermondii[e]	2
	C. kefyr[e]	2
	C. krusei[e]	2
	C. lusitaniae[e,f]	2
	C. metapsilosis	1
	C. orthopsilosis	2
	C. parapsilosis	1
	C. pelliculosa[e]	**1**
	C. tropicalis	2
	Saccharomyces cerevisiae	**2**
Anidulafungin	***C. auris***	**1**
	C. dubliniensis	0.12
	C. duobushaemulonii	1
	C. haemulonii	**0.5**
	C. kefyr[e]	0.25
	C. lusitaniae[e]	1
	C. metapsilosis	0.5
	C. orthopsilosis	2
	S. cerevisiae	**1**
Caspofungin	***C. auris***	**0.5**
	C. duobushaemulonii	0.25
	C. lusitaniae[e]	1
	C. metapsilosis	0.25
	C. orthopsilosis	1
	S. cerevisiae	**2**
Fluconazole	*C. dubliniensis*	0.5
	C. duobushaemulonii	32
	C. guilliermondii[e]	8
	C. haemulonii	**128**[g]
	C. kefyr[e]	1
	C. lusitaniae[e]	1
	C. metapsilosis	4
	C. orthopsilosis	2
	C. pararugosa[e]	**16**
	C. pelliculosa[e]	**8**
	C. rugosa[e]	**8**
	S. cerevisiae	**32**[h]
Isavuconazole	*C. duobushaemulonii*	0.25

Table 1. (Continued)

Antifungal Agent	Species	ECV, µg/mL[b,c,d]
Itraconazole	*C. dubliniensis*	0.25
	C. duobushaemulonii	1
	C. glabrata[e]	4
	C. guilliermondii[e]	2
	C. kefyr[e]	0.5
	C. krusei[e]	1
	C. lusitaniae[e]	1
	C. metapsilosis	1
	C. orthopsilosis	0.5
	C. parapsilosis	0.5
	C. pelliculosa[e]	**1**
	C. tropicalis	0.5
	S. cerevisiae	**2**
Micafungin	***C. auris***	**0.5**
	C. dubliniensis	0.12
	C. duobushaemulonii	0.5
	C. kefyr[e]	0.12
	C. lusitaniae[e]	0.5
	C. metapsilosis	1
	C. orthopsilosis	1
	C. pelliculosa[e]	**0.12**
	S. cerevisiae	**0.5**
Posaconazole	*C. albicans*	0.06
	C. dubliniensis	0.12
	C. duobushaemulonii	1
	C. glabrata[e]	1
	C. guilliermondii[e]	0.5
	C. haemulonii	**1**
	C. kefyr[e]	0.5
	C. krusei[e]	0.5
	C. lusitaniae[e]	0.06
	C. metapsilosis	0.25
	C. orthopsilosis	0.25
	C. parapsilosis	0.25
	C. pelliculosa[e]	**2**
	C. tropicalis	0.12
	S. cerevisiae	**2**
Voriconazole	*C. duobushaemulonii*	0.5
	C. glabrata[e]	0.25
	C. haemulonii	**2**
	C. metapsilosis	0.06
	C. orthopsilosis	0.12
	C. pelliculosa[e]	**0.25**
	S. cerevisiae	**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											
Candida albicans	ECV	BP/ECV	BP	BP/ECV	-	-	-	BP/ECV	ECV	**BP/ECV**	BP/ECV
Candida auris	**-**	**ECV**	**ECV**	**-**	**TR-L**	**-**	**-**	**ECV**	**-**	**BP/ECV**	**-**
Candida dubliniensis	ECV	ECV	-	ECV	TR-L	-	ECV	ECV	ECV	**BP/ECV**	-
Candida duobushaemulonii	**TR-H**	ECV	ECV	ECV	TR-L	ECV	ECV	ECV	ECV	**-**	ECV
Candida glabrata[b]	ECV	BP/ECV	BP	BP/ECV	-	-	ECV	BP/ECV	ECV	**BP/ECV**	ECV
Candida guilliermondii[b]	ECV	BP/ECV	BP/ECV	ECV	TR-L	-	ECV	BP/ECV	ECV	**-**	-
Candida haemulonii	**-**	**ECV**	**-**	**ECV**	**-**	**-**	**-**	**-**	**ECV**	**-**	**ECV**
Candida kefyr[b]	ECV	ECV	-	ECV	TR-L	-	ECV	ECV	ECV	**-**	-
Candida krusei[b]	ECV	BP/ECV	BP	IR	-	-	ECV	BP/ECV	ECV	**BP/ECV**	BP/ECV
Candida lusitaniae[b]	ECV	ECV	ECV	ECV	TR-L	-	ECV	ECV	ECV	-	-
Candida metapsilosis	ECV	ECV	ECV	ECV	TR-L	-	ECV	ECV	ECV	-	ECV
Candida orthopsilosis	ECV	ECV	ECV	ECV	TR-L	-	ECV	ECV	ECV	-	-
Candida parapsilosis	ECV	BP/ECV	BP/ECV	BP/ECV	TR-L	TR-L	ECV	BP/ECV	ECV	**BP/ECV**	BP
Candida pararugosa[b]	**-**	**-**	**-**	**ECV**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Candida pelliculosa[b]	**ECV**	**-**	**-**	**ECV**	**TR-L**	**-**	**ECV**	**ECV**	**ECV**	**-**	**ECV**
Candida rugosa[b]	**-**	**-**	**-**	**ECV**	**-**	**-**	**-**	**-**	**-**	**-**	**TR-L**
Candida tropicalis	ECV	BP/ECV	BP	BP/ECV	-	-	ECV	BP/ECV	ECV	**BP/ECV**	BP/ECV
Cryptococcus gattii (VGI)	ECV	IR	IR	ECV	ECV	-	ECV	IR	-	**-**	ECV

CLINICAL AND
LABORATORY
STANDARDS
INSTITUTE®

PRINT ISBN 978-1-68440-158-1

ELECTRONIC ISBN 978-1-68440-159-8

M57-Ed1-S-Ed4