M27-S3
Vol. 28 No. 15

Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Third Informational Supplement

This document provides updated tables for the CLSI antimicrobial susceptibility testing standard M27-A3.

An informational supplement for global application developed through the Clinical and Laboratory Standards Institute consensus process.

CLINICAL AND LABORATORY STANDARDS INSTITUTE®
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Clinical and Laboratory Standards Institute

Advancing Quality in Health Care Testing

Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) is an international, interdisciplinary, nonprofit, standards-developing, and educational organization that promotes the development and use of voluntary consensus standards and guidelines within the health care community. It is recognized worldwide for the application of its unique consensus process in the development of standards and guidelines for patient testing and related health care issues. Our process is based on the principle that consensus is an effective and cost-effective way to improve patient testing and health care services.

In addition to developing and promoting the use of voluntary consensus standards and guidelines, we provide an open and unbiased forum to address critical issues affecting the quality of patient testing and health care.

PUBLICATIONS

A document is published as a standard, guideline, or committee report.

Standard A document developed through the consensus process that clearly identifies specific, essential requirements for materials, methods, or practices for use in an unmodified form. A standard may, in addition, contain discretionary elements, which are clearly identified.

Guideline A document developed through the consensus process describing criteria for a general operating practice, procedure, or material for voluntary use. A guideline may be used as written or modified by the user to fit specific needs.

Report A document that has not been subjected to consensus review and is released by the Board of Directors.

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The CLSI voluntary consensus process is a protocol establishing formal criteria for:

- the authorization of a project
- the development and open review of documents
- the revision of documents in response to comments by users
- the acceptance of a document as a consensus standard or guideline.

Most documents are subject to two levels of consensus—"proposed" and "approved." Depending on the need for field evaluation or data collection, documents may also be made available for review at an intermediate consensus level.

Proposed A consensus document undergoes the first stage of review by the health care community as a proposed standard or guideline. The document should receive a wide and thorough technical review, including an overall review of its scope, approach, and utility, and a line-by-line review of its technical and editorial content.

Approved An approved standard or guideline has achieved consensus within the health care community. It should be reviewed to assess the utility of the final document, to ensure attainment of consensus (ie, that comments on earlier versions have been satisfactorily addressed), and to identify the need for additional consensus documents.

Our standards and guidelines represent a consensus opinion on good practices and reflect the substantial agreement by materially affected, competent, and interested parties obtained by following CLSI's established consensus procedures. Provisions in CLSI standards and guidelines may be more or less stringent than applicable regulations. Consequently, conformance to this voluntary consensus document does not relieve the user of responsibility for compliance with applicable regulations.

COMMENTS

The comments of users are essential to the consensus process. Anyone may submit a comment, and all comments are addressed, according to the consensus process, by the committee that wrote the document. All comments, including those that result in a change to the document when published at the next consensus level and those that do not result in a change, are responded to by the committee in an appendix to the document. Readers are strongly encouraged to comment in any form and at any time on any document. Address comments to Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, PA 19087, USA.

VOLUNTEER PARTICIPATION

Health care professionals in all specialties are urged to volunteer for participation in CLSI projects. Please contact us at customerservice@clsi.org or +610.688.0100 for additional information on committee participation.

Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Third Informational Supplement

Abstract

The supplemental information presented in this document is intended for use with the testing procedures published in the CLSI approved standard M27-A3—*Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard—Third Edition.*

The tabular information in this document presents the most current information for drug selection, interpretation, and quality control.

(Clinical and Laboratory Standards Institute. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Third Informational Supplement.* CLSI document M27-S3 (ISBN 1-56238-667-0). Clinical and Laboratory Standards Institute, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA, 2008.)

The data in the interpretive tables in this supplement are valid only if the methodology is followed in CLSI document M27-A3—*Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard—Third Edition.*

M27-S3
ISBN 1-56238-667-0
Volume 28 Number 15
ISSN 0273-3099

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Suggested Citation

(CLSI. *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Third Informational Supplement.* CLSI document M27-S3. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.)

First Informational Supplement
May 2004

Second Informational Supplement
April 2005

Third Informational Supplement
April 2008

ISBN 1-56238-667-0
ISSN 0273-3099

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Contents

Table 1. Interpretive Guidelines for *In Vitro* Susceptibility Testing of *Candida* spp.

Antifungal Agent	Susceptible (S)	Susceptible-dose dependent (S-DD)[a]	Intermediate (I)[b]	Resistant (R)	Nonsusceptible (NS)
Anidulafungin[c]	**≤2**	-	-	-	**>2**
Caspofungin[c]	**≤2**	-	-	-	**>2**
Fluconazole[d]	≤8	16-32	-	≥64	-
Flucytosine[e]	≤4	-	8-16	≥32	-
Itraconazole[f]	≤0.125	0.25-0.5	-	≥1	-
Micafungin[c]	**≤2**	-	-	-	**>2**
Voriconazole[c]	≤1	2	-	≥4	-

NOTE 1: Shown are the breakpoints (µg/mL) for *Candida* spp. against the indicated agents. If minimal inhibitory concentrations (MICs) are measured using a scale that yields results falling between categories, the next higher category is implied. Thus, an isolate with a fluconazole MIC of 12.5 µg/mL would be placed in the S-DD category.

NOTE 2: The MIC breakpoints in boldface type were adopted at a meeting of the subcommittee held on 9 June 2007 in Boston, MA. These breakpoints are considered tentative for one year and are open for comments. There is no Resistant category assigned for the echinocandin agents; isolates with higher MICs may be described as nonsusceptible.

Footnotes

a. Susceptibility is dependent on achieving the maximal possible blood level. For fluconazole, doses of 400 mg/day or more may be required in adults with normal renal function and body habitus. For itraconazole, measures to assure adequate drug absorption and plasma itraconazole concentrations of >0.5 µg/mL may be required for optimal response.

b. The susceptibility of these isolates is not certain, and the available data do not permit them to be clearly categorized as either "susceptible" or "resistant."

c. For these drugs, the data are based substantially on experience with non-neutropenic patients with candidemia, and their clinical relevance in other settings is uncertain.

d. For fluconazole, these guidelines are based on extensive experience with mucosal and invasive infections due to *Candida* spp. It is also pertinent that the 8-µg/mL upper boundary for the susceptible range of fluconazole is not known with certainty—the data would permit selection of either 4 or 8 µg/mL for this cutoff. When an isolate is identified as *Candida glabrata* and the MIC is ≤ 32, patients should receive a maximum dosage regimen of fluconazole. Expert consultation on selection of a maximum dosage regimen may be useful. Finally, isolates of *Candida krusei* are assumed to be intrinsically resistant to fluconazole, and their MICs should not be interpreted using this scale.

e. Flucytosine MIC breakpoints are based largely on historical data and partially on the drug's pharmacokinetics.

f. For itraconazole, the data are based entirely on experience with mucosal infections, and data supporting breakpoints for invasive infections due to *Candida* spp. are not available.

Table 1. (Continued)

References:

1. Rex JH, Pfaller MA, Galgiani JN, et al. Development of interpretive breakpoints for antifungal susceptibility testing: conceptual framework and analysis of in vitro-in vivo correlation data for fluconazole, itraconazole, and candida infections. Subcommittee on Antifungal Susceptibility Testing of the National Committee for Clinical Laboratory Standards. *Clin Infect Dis.* 1997;24(2):235-247.

2. Pfaller MA, Diekema DJ, Rex JH, et al. Correlation of MIC with outcome for Candida species tested against voriconazole: analysis and proposal for interpretive breakpoints. *J Clin Microbiol.* 2006;44(3):819-826.

3. Pfaller MA, Diekema DJ, Sheehan DJ. Interpretive breakpoints for fluconazole and *Candida* revisited: a blueprint for the future of antifungal susceptibility testing. *Clin Microbiol Rev.* 2006;19:435-447.

4. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. *Clin Microbiol Rev.* 2007;20(1):133-163.

Table 2. Solvents and Diluents for Preparation of Stock Solutions of Antifungal Agents

Antifungal Agent	Solvent (Full Strength and Intermediate Solutions)	Diluent (Final Concentrations)
Amphotericin B	DMSO*	Medium
Anidulafungin	DMSO	Medium
Caspofungin	Water	Medium
Flucytosine	Water	Medium
Fluconazole	Water	Medium
Itraconazole	DMSO	Medium
Ketoconazole	DMSO	Medium
Micafungin	Water	Medium
Posaconazole	DMSO	Medium
Ravuconazole	DMSO	Medium
Voriconazole	DMSO	Medium

* DMSO = dimethyl sulfoxide is potentially toxic.

Table 3. Scheme for Preparing Dilutions of Water-Soluble Antifungal Agents to Be Used in Broth Dilution Susceptibility Tests

Antimicrobial Solution							
Step	Concentration (µg/mL)	Source	Volume + (mL)	Medium = (mL)	Intermediate = Concentration (µg/mL)	Final Concentration at 1:10 (µg/mL)	Log_2
1	5120	Stock	1 mL	7	640 µg/mL	64	6
2	640	Step 1	1.0	1.0	320	32	5
3	640	Step 1	1.0	3.0	160	16	4
4	160	Step 3	1.0	1.0	80	8	3
5	160	Step 3	0.5	1.5	40	4	2
6	160	Step 3	0.5	3.5	20	2	1
7	20	Step 6	1.0	1.0	10	1	0
8	20	Step 6	0.5	1.5	5	0.5	-1
9	20	Step 6	0.5	3.5	2.5	0.25	-2
10	2.5	Step 9	1.0	1.0	1.25	0.125	-3
11	2.5	Step 9	0.5	1.5	0.625	0.0625	-4
12	2.5	Step 9	0.5	3.5	0.3125	0.03125	-5

Table 4. Scheme for Preparing Dilution Series of Water-Insoluble Antifungal Agents to Be Used in Broth Dilution Susceptibility Tests

Antimicrobial Solution							
Step		Source	Volume + (mL)	Solvent = (mL) (eg, DMSO)*	Intermediate = Concentration (µg/mL)	Final Concentration at 1:100 (µg/mL)	Log_2
1	1600	Stock			1600 µg/mL	16	4
2	1600	Stock	0.5	0.5	800	8.0	3
3	1600	Stock	0.5	1.5	400	4.0	2
4	1600	Stock	0.5	3.5	200	2.0	1
5	200	Step 4	0.5	0.5	100	1.0	0
6	200	Step 4	0.5	1.5	50	0.5	-1
7	200	Step 4	0.5	3.5	25	0.25	-2
8	25	Step 7	0.5	0.5	12.5	0.125	-3
9	25	Step 7	0.5	1.5	6.25	0.0625	-4
10	25	Step 7	0.5	3.5	3.13	0.0313	-5

*Dimethyl sulfoxide

Table 5. Recommended 48-Hour MIC Limits for Two Quality Control and Four Reference Strains for Broth Macrodilution Procedures. (From Pfaller MA, Bale M, Buschelman B, et al. Quality control guidelines for National Committee for Clinical Laboratory Standards recommended broth macrodilution testing of amphotericin B, fluconazole, and flucytosine. *J Clin Microbiol.* 1995;33:1104-1107; and Rex JH, Pfaller MA, Lancaster M, Odds FC, Bolstrom A, Rinaldi MG. Quality control guidelines for National Committee for Clinical Laboratory Standards-recommended broth macrodilution testing of ketoconazole and itraconazole. *J Clin Microbiol.* 1996;34:816-817. Reprinted with permission from the American Society for Microbiology and the authors.)

Organism	Purpose	Antifungal Agent	MIC Range (µg/mL)	% of MICs Within Range
Candida parapsilosis ATCC® 22019	QC	Amphotericin B Fluconazole Itraconazole Ketoconazole Flucytosine (5-FC)	0.25-1.0 2.0-8.0 0.06-0.25 0.06-0.25 0.12-0.5	99.1 99.1 99.0 99.0 98.6
*Candida krusei** ATCC® 6258	QC	Amphotericin B Fluconazole Itraconazole Ketoconazole Flucytosine (5-FC)	0.25-2.0 16-64 0.12-0.5 0.12-0.5 4.0-16	99.5 99.1 94.0 100.0 96.8
Candida albicans ATCC® 90028	Reference	Amphotericin B Fluconazole Flucytosine (5-FC)	0.5-2.0 0.25-1.0 0.5-2.0	91.9 97.3 95.0
Candida albicans ATCC® 24433	Reference	Amphotericin B Fluconazole Flucytosine (5-FC)	0.25-1.0 0.25-1.0 1.0-4.0	99.5 95.9 91.9
Candida parapsilosis ATCC® 90018	Reference	Amphotericin B Fluconazole Flucytosine (5-FC)	0.5-2.0 0.25-1.0 ≤0.12-0.25	96.4 98.2 99.5
Candida tropicalis ATCC® 750	Reference	Amphotericin B Fluconazole Flucytosine (5-FC)	0.5-2.0 1.0-4.0 ≤0.12-0.25	93.7 95.5 99.5

NOTE: ATCC® is a registered trademark of the American Type Culture Collection.

* As *Issatchenkia orientalis* is now known to be the sexual form (the teleomorph) of *C. krusei*, it would be technically correct to use *I. orientalis* as the name for this fungus. However, this change would confuse most users and the far more widely used name *C. krusei* is retained.

Table 6. Recommended 24- and 48-Hour MIC Limits for Two Quality Control Strains for Broth Microdilution. (From Barry AL, Pfaller MA, Brown SD, et al. Quality control limits for broth microdilution susceptibility tests of ten antifungal agents. *J Clin Microbiol.* 2000;38:3457-3459; and Krisher K, Brown SD, Traczewski MM. Quality control parameters for broth microdilution tests of anidulafungin. *J Clin Microbiol.* 2004;42:490. Reprinted with permission from the American Society for Microbiology and the authors.)

MIC (µg/mL) Ranges for Microdilution Tests							
		24-Hour		% Within	48-Hour		% Within
Organism	**Antifungal Agent**	**Range**	**Mode**	**Range**	**Range**	**Mode**	**Range**
Candida parapsilosis ATCC® 22019	Amphotericin B	0.25-2.0	0.5	97.1	0.5-4.0	2.0	91.7
	Anidulafungin	0.25-2.0	1.0	95.0	0.5-2.0	1.0	95.0
	Caspofungin	0.25-1.0	0.5	96.7	0.5-4.0	1.0	92.9
	Flucytosine (5-FC)	0.06-0.25	0.12	99.2	0.12-0.5	0.25	97.9
	Fluconazole	0.5-4.0	2.0	98.2	1.0-4.0	2.0	98.1
	Itraconazole	0.12-0.5	0.25	95.8	0.12-0.5	0.25	97.5
	Ketoconazole	0.03-0.25	0.06/0.12	97.5	0.06-0.5	0.12	98.3
	Micafungin	**0.5-2**	**1**	**100.0**	**0.5-4**	**1**	**100.0**
	Posaconazole	0.06-0.25	0.12	96.7	0.06-0.25	0.12	98.8
	Ravuconazole	0.016-0.12	0.06	95.8	0.03-0.25	0.06	98.3
	Voriconazole	0.016-0.12	0.06	100.0	0.03-0.25	0.06	100.0
Candida krusei ATCC® 6258	Amphotericin B	0.5-2.0	1.0	100.0	1.0-4.0	2.0	100.0
	Anidulafungin	0.03-0.12	0.06	97.9	0.03-0.12	0.06	97.5
	Caspofungin	0.12-1.0	0.5	98.8	0.25-1.0	0.5	97.5
	Flucytosine (5-FC)	4.0-16	8.0	97.5	8.0-32	16	99.6
	Fluconazole	8.0-64	16	100.0	16-128	32	100.0
	Itraconazole	0.12-1.0	0.5	95.8	0.25-1.0	0.5	100.0
	Ketoconazole	0.12-1.0	0.5	95.4	0.25-1.0	0.5	99.6
	Micafungin	**0.12-0.5**	**0.25**	**99.6**	**0.12-0.5**	**0.25**	**99.0**
	Posaconazole	0.06-0.5	0.25	100.0	0.12-1.0	0.5	99.6
	Ravuconazole	0.06-0.5	0.25	93.3	0.25-1.0	0.5	100.0
	Voriconazole	0.06-0.5	0.25	98.3	0.12-1.0	0.5	100.0

NOTE 1: The MIC QC ranges in boldface type were adopted at a meeting of the subcommittee held on 20 January 2007 in Tampa, FL. These breakpoints are considered tentative for one year and are open for comments.

NOTE 2: ATCC® is a registered trademark of the American Type Culture Collection.

NOTE 3: The MIC for anidulafungin, caspofungin, and micafungin is the lowest concentration at which a score of 2 (prominent decrease in turbidity; see CLSI document M27-A3, Section 7.6.3) is observed after 24 hours incubation.

Table 7. Composition of RPMI 1640 Medium (with glutamine and phenol red but without bicarbonate)

Constituent	**g/L** Water	**Constituent**	**g/L** Water
L-arginine (free base)	0.200	Biotin	0.0002
L-aspargine (anhydrous)	0.050	D-pantothenic	0.00025
L-aspartic acid	0.020	Choline chloride	0.003
L-cystine • 2HCl	0.0652	Folic acid	0.001
L-glutamic acid	0.020	Myoinositol	0.035
L-glutamine	0.300	Niacinamide	0.001
Glycine	0.010	PABA (para-aminobenzoic acid)	0.001
L-histidine (free base)	0.015	Pyridoxine HCl	0.001
L-hydroxyproline	0.020	Riboflavin	0.0002
L-isoleucine	0.050	Thiamine HCl	0.001
L-leucine	0.050	Vitamin B_{12}	0.000005
L-lysine • HCl	0.040	Calcium nitrate • H_2O	0.100
L-methionine	0.015	Potassium chloride	0.400
L-phenylalanine	0.015	Magnesium sulfate (anhydrous)	0.04884
L-proline	0.020	Sodium chloride	6.000
L-serine	0.030	Sodium phosphate, dibasic (anhydrous)	0.800
L-threonine	0.020	D-glucose	2.000
L-tryptophan	0.005	Glutathione, reduced	0.001
L-tyrosine • 2Na	0.02883	Phenol red, Na	0.0053
L-valine	0.020		

Table 8. Modifications for Special Circumstances

Drug	Organism	Modification	Reference
Amphotericin B	*Candida* spp.	Use of Antibiotic Medium 3 and a 24-hour end point has enhanced detection of resistance in some reports, but this medium is not standardized, substantial lot-to-lot variability is possible, and experience has varied.	See Section 7.7.1 of CLSI document M27-A3. 1, 2
All drugs	*C. neoformans*	Use of Yeast Nitrogen Base may enhance the growth of *C. neoformans* and improve the clinical relevance of antifungal MICs.	3, 4
All drugs	All organisms	Supplementation of the test medium so it contains glucose at a final concentration of 20 g/L may simplify end-point determination.	5

NOTE: These modifications are not a part of the formal CLSI document M27-A3 methodology and the utility of each of these modifications remains to be established. This table is provided solely as a reference for laboratories that are interested in studying adaptations of CLSI document M27-A3 that may enhance its utility under specific circumstances.

References:

1. Lozano-Chiu M, Nelson PW, Lancaster M, Pfaller MA, Rex JH. Lot-to-lot variability of antibiotic medium 3 when used for susceptibility testing of *Candida* isolates to amphotericin B. *J Clin Microbiol.* 1997;35:270-272.
2. Pfaller MA, Buschelman B, Bale MJ, et al. Multicenter comparison of a colorimetric microdilution broth method with the reference macrodilution method for *in vitro* susceptibility testing of yeast isolates. *Diagn Microbiol Infect Dis.* 1994;19:9-13.
3. Pfaller MA, Grant C, Morthland V, et al. Comparative evaluation of alternative methods for broth dilution susceptibility testing of fluconazole against *Candida albicans*. *J Clin Microbiol.* 1994;32:506-509.
4. Ghannoum MA, Ibrahim AS, Fu Y, Shafiq MC, Edwards JE, Criddle RS. Susceptibility testing of *Cryptococcus neoformans*: a microdilution technique. *J Clin Microbiol.* 1992;30:2881-2886.
5. Rodriguez-Tudela JL, Martinez-Suarez JV. Improved medium for fluconazole susceptibility testing of *Candida albicans*. *Antimicrob Agents Chemother.* 1994;38:45-48.

Clinical and Laboratory Standards Institute consensus procedures include an appeals process that is described in detail in Section 8 of the Administrative Procedures. For further information, contact CLSI or visit our website at www.clsi.org.

Summary of Delegate Comments and Committee Responses

M27-S3: *Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Third Informational Supplement*

1. M27-S3 clearly communicates results of studies of 24- and 48-hour reference MIC ranges for microdilution testing of both established and newly introduced antifungal agents. This document offers laboratory professionals essential, current information for broth dilution antifungal susceptibility testing of yeasts in a concise, tabular format. I only have one minor suggestion for CLSI's consideration: to include the applicability of individual tables to microdilution or macrodilution (or both) testing.

- **The tables that are specific to micro- or macrodilution are titled as such—the others apply to both. No change has been made to the supplement.**

The Quality Management System Approach

Clinical and Laboratory Standards Institute (CLSI) subscribes to a quality management system approach in the development of standards and guidelines, which facilitates project management; defines a document structure via a template; and provides a process to identify needed documents. The approach is based on the model presented in the most current edition of CLSI/NCCLS document HS1—*A Quality Management System Model for Health Care.* The quality management system approach applies a core set of "quality system essentials" (QSEs), basic to any organization, to all operations in any health care service's path of workflow (ie, operational aspects that define how a particular product or service is provided). The QSEs provide the framework for delivery of any type of product or service, serving as a manager's guide. The QSEs are:

Documents & Records	Equipment	Information Management	Process Improvement
Organization	Purchasing & Inventory	Occurrence Management	Customer Service
Personnel	Process Control	Assessments—External and Internal	Facilities & Safety

M27-S3 addresses the QSEs indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials section on the following page.

Documents & Records	Organization	Personnel	Equipment	Purchasing & Inventory	Process Control	Information Management	Occurrence Management	Assessments —External and Internal	Process Improvement	Customer Service	Facilities & Safety
M7					X M2 M7 M11 M23 M24 M29 M38						M29

Adapted from CLSI/NCCLS document HS1—*A Quality Management System Model for Health Care*.

Path of Workflow

A path of workflow is the description of the necessary steps to deliver the particular product or service that the organization or entity provides. For example, CLSI/NCCLS document GP26—*Application of a Quality Management System Model for Laboratory Services* defines a clinical laboratory path of workflow which consists of three sequential processes: preexamination, examination, and postexamination. All clinical laboratories follow these processes to deliver the laboratory's services, namely quality laboratory information.

M27-S3 addresses the clinical laboratory path of workflow steps indicated by an "X." For a description of the other documents listed in the grid, please refer to the Related CLSI Reference Materials Publications section on the following page.

Preexamination				**Examination**			**Postexamination**	
Examination ordering	Sample collection	Sample transport	Sample receipt/processing	Examination	Results review and follow-up	Interpretation	Results reporting and archiving	Sample management
			M24	X M24 M38	X M2 M7 M11 M24 M38	X M2 M7 M11 M24 M38	X M2 M7 M11 M24 M38	X M24 M38

Adapted from CLSI/NCCLS document HS1—*A Quality Management System Model for Health Care*.

Related CLSI Reference Materials*

M2-A9 **Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard—Ninth Edition (2006).** This document contains the current Clinical and Laboratory Standards Institute-recommended methods for disk susceptibility testing, criteria for quality control testing, and updated tables for interpretive zone diameters.

M7-A7 **Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Seventh Edition (2006).** This document addresses reference methods for the determination of minimal inhibitory concentrations (MICs) of aerobic bacteria by broth macrodilution, broth microdilution, and agar dilution.

M11-A7 **Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard—Seventh Edition (2007).** This standard provides reference methods for the determination of minimal inhibitory concentrations (MICs) of anaerobic bacteria by agar dilution and broth microdilution.

M23-A2 **Development of *In Vitro* Susceptibility Testing Criteria and Quality Control Parameters; Approved Guideline—Second Edition (2001).** This document addresses the required and recommended data needed for the selection of appropriate interpretive standards and quality control guidelines for new antimicrobial agents.

M24-A **Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes; Approved Standard (2003).** This standard provides protocols and related quality control parameters and interpretive criteria for the susceptibility testing of mycobacteria, *Nocardia* spp., and other aerobic actinomycetes.

M29-A3 **Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Third Edition (2005).** Based on US regulations, this document provides guidance on the risk of transmission of infectious agents by aerosols, droplets, blood, and body substances in a laboratory setting; specific precautions for preventing the laboratory transmission of microbial infection from laboratory instruments and materials; and recommendations for the management of exposure to infectious agents.

M38-A **Reference Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi; Approved Standard (2002).** This document addresses the selection of antifungal agents; preparation of antifungal stock solutions and dilutions for testing; implementation and interpretation of test procedures; and quality control requirements for susceptibility testing of filamentous fungi (moulds) that cause invasive fungal infections.

* Proposed-level documents are being advanced through the Clinical and Laboratory Standards Institute consensus process; therefore, readers should refer to the most current editions.

NOTES

NOTES

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St. Mary Medical Center (CA)
St. Mary's Health Center (MO)
St Mary's Healthcare (SD)
St. Mary's Medical Center (IN)
St. Michael's Hospital Diagnostic Laboratories & Pathology (Canada)
St. Tammany Parish Hospital (LA)
St. Thomas More Hospital (CO)
Sampson Regional Medical Center (NC)
Samsung Medical Center (Korea)
San Francisco General Hospital-University of California San Francisco (CA)
Sanford USP Medical Center (SD)
SARL Laboratoire Carron (France)
Saudi Aramco Medical (Saudi Arabia)
Scott Air Force Base (IL)
Scott & White Memorial Hospital (TX)
Seoul National University Hospital (Korea)
Seton Medical Center (CA)
Shamokin Area Community Hospital (PA)
Sheik Kalifa Medical City (UAE)
Shore Memorial Hospital (NJ)
Shriners Hospitals for Children (SC)
Singapore General Hospital (Singapore)
SJRMC Plymouth Laboratory (IN)
Sky Lakes Medical Center (OR)
South Bend Medical Foundation (IN)
South County Hospital (RI)
South Dakota State Health Laboratory (SD)
South Miami Hospital (FL)
Southern Health Care Network (Australia)
Southern Maine Medical Center (ME)
Southwest Nova District Health Authority (Canada)
Speare Memorial Hospital (NH)
Spectrum Health - Blodgett Campus (MI)
Stanford Hospital and Clinics (CA)
State of Connecticut Department of Public Health (CT)
State of Hawaii Department of Health (HI)
State of Washington-Public Health Labs (WA)
Steele Memorial Hospital (ID)
Stillwater Medical Center (OK)
Stony Brook University Hospital (NY)
Stormont-Vail Regional Medical Center (KS)
Sudbury Regional Hospital (Canada)
Suncoast Medical Clinic (FL)
Sunnybrook Health Science Center (ON, Canada)
Sunrise Hospital and Medical Center (NV)
Swedish Medical Center (CO)
Sydney South West Pathology Service (Australia)
T.J. Samson Community Hospital (KY)
Taipei Veterans General Hospital (Taiwan)
Taiwan Society of Laboratory Medicine
Tallaght Hospital
Tartu University Clinics (Tartu)
Temple Univ. Hospital - Parkinson Pav. (PA)
Texas Children's Hospital (TX)
Texas Department of State Health Services
Thomason Hospital (TX)
Timmins and District Hospital (Canada)
The Toledo Hospital (OH)
Touro Infirmary (LA)
Tri-Cities Laboratory (WA)
Trident Medical Center (SC)
Trinity Medical Center (AL)
Tripler Army Medical Center (HI)
Tufts New England Medical Center Hospital (MA)
Tulane Medical Center Hospital & Clinic (LA)
Turku University Central Hospital
UCI Medical Center (CA)
UCLA Medical Center Clinical Laboratories (CA)
UCSD Medical Center (CA)
UCSF Medical Center China Basin (CA)
UMass Memorial Medical Center (MA)
UMC of Southern Nevada (NV)
UNC Hospitals (NC)
Union Clinical Laboratory (Taiwan)
United Christian Hospital (Hong Kong)
United Clinical Laboratories (IA)
Unity HealthCare (IA)
Universita Campus Bio-Medico (Italy)
Universitair Ziekenhuis Antwerpen (Belgium)
University College Hospital (Ireland)
University Medical Center at Princeton (NJ)
University of Alabama-Birmingham Hospital (AL)
University of Arkansas for Medical Sci. (AR)
University of Chicago Hospitals (IL)
University of Colorado Health Sciences Center (CO)
University of Colorado Hospital
University of Iowa Hospitals and Clinics (IA)
University of Kentucky Med. Ctr. (KY)
University of Maryland Medical System (MD)
University of Medicine & Dentistry, NJ University Hosp. (NJ)
University of Miami (FL)
University of Missouri Hospital (MO)
University of MN Medical Center - Fairview
University of MS Medical Center (MS)
University of So. Alabama Children's and Women's Hospital (AL)
University of Texas Health Center (TX)
The University of Texas Medical Branch (TX)
University of the Ryukyus (Japan)
University of Virginia Medical Center
University of Washington
UPMC Bedford Memorial (PA)
U.S.A. Meddac (Pathology Division) (MO)
UW Hospital (WI)
UZ-KUL Medical Center (Belgium)
VA (Asheville) Medical Center (NC)
VA (Bay Pines) Medical Center (FL)
VA (Chillicothe) Medical Center (OH)
VA (Cincinnati) Medical Center (OH)
VA (Dallas) Medical Center (TX)
VA (Dayton) Medical Center (OH)
VA (Decatur) Medical Center (GA)
VA (Hines) Medical Center (IL)
VA (Indianapolis) Medical Center (IN)
VA (Iowa City) Medical Center (IA)
VA (Long Beach) Medical Center (CA)
VA (Miami) Medical Center (FL)
VA New Jersey Health Care System (NJ)
VA Outpatient Clinic (OH)
VA (Phoenix) Medical Center (AZ)
VA (San Diego) Medical Center (CA)
VA (Seattle) Medical Center (WA)
VA (Sheridan) Medical Center (WY)
VA (Tucson) Medical Center (AZ)
Valley Health (VA)
Vancouver Hospital and Health Sciences Center (BC, Canada)
Vancouver Island Health Authority (Canada)
Vanderbilt University Medical Center (TN)
Via Christi Regional Medical Center (KS)
Virga Jessezieukenhuis (Belgium)
ViroMed Laboratories (LabCorp) (MN)
Virtua - West Jersey Hospital (NJ)
WakeMed (NC)
Walter Reed Army Medical Center (DC)
Warren Hospital (NJ)
Washington Hospital Center (DC)
Waterbury Hospital (CT)
Waterford Regional Hospital (Ireland)
Wayne Memorial Hospital (NC)
Weirton Medical Center (WV)
Wellstar Douglas Hospital Laboratory (GA)
Wellstar Paulding Hospital (GA)
Wellstar Windy Hill Hospital Laboratory (GA)
West China Second University Hospital, Sichuan University (P.R. China)
West Valley Medical Center Laboratory (ID)
Westchester Medical Center (NY)
Western Baptist Hospital (KY)
Western Healthcare Corporation (Canada)
Wheaton Franciscan & Midwest Clinical Laboratories (WI)
Wheeling Hospital (WV)
Whitehorse General Hospital (Canada)
William Beaumont Army Medical Center (TX)
William Beaumont Hospital (MI)
William Osler Health Centre (Canada)
Winchester Hospital (MA)
Winn Army Community Hospital (GA)
Wisconsin State Laboratory of Hygiene (WI)
Wishard Health Sciences (IN)
Womack Army Medical Center (NC)
Woodlawn Hospital (IN)
York Hospital (PA)

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