CLINICAL AND LABORATORY STANDARDS INSTITUTE®

1st Edition

M60

Performance Standards for Antifungal Susceptibility Testing of Yeasts

This document includes updated minimal inhibitory concentration, zone diameter, and quality control tables for the Clinical and Laboratory Standards Institute antifungal susceptibility testing documents M27 and M44.

A CLSI supplement for global application.

Clinical and Laboratory Standards Institute

Setting the standard for quality in medical laboratory testing around the world.

The Clinical and Laboratory Standards Institute (CLSI) is a not-for-profit membership organization that brings together the varied perspectives and expertise of the worldwide laboratory community for the advancement of a common cause: to foster excellence in laboratory medicine by developing and implementing medical laboratory standards and guidelines that help laboratories fulfill their responsibilities with efficiency, effectiveness, and global applicability.

Consensus Process

Consensus—the substantial agreement by materially affected, competent, and interested parties—is core to the development of all CLSI documents. It does not always connote unanimous agreement but does mean that the participants in the development of a consensus document have considered and resolved all relevant objections and accept the resulting agreement.

Commenting on Documents

CLSI documents undergo periodic evaluation and modification to keep pace with advances in technologies, procedures, methods, and protocols affecting the laboratory or health care.

CLSI's consensus process depends on experts who volunteer to serve as contributing authors and/or as participants in the reviewing and commenting process. At the end of each comment period, the committee that developed the document is obligated to review all comments, respond in writing to all substantive comments, and revise the draft document as appropriate.

Comments on published CLSI documents are equally essential and may be submitted by anyone, at any time, on any document. All comments are managed according to the consensus process by a committee of experts.

Appeal Process

When it is believed that an objection has not been adequately considered and responded to, the process for appeal, documented in the CLSI *Standards Development Policies and Processes,* is followed.

All comments and responses submitted on draft and published documents are retained on file at CLSI and are available upon request.

Get Involved—Volunteer!

Do you use CLSI documents in your workplace? Do you see room for improvement? Would you like to get involved in the revision process? Or maybe you see a need to develop a new document for an emerging technology? CLSI wants to hear from you. We are always looking for volunteers. By donating your time and talents to improve the standards that affect your own work, you will play an active role in improving public health across the globe.

For additional information on committee participation or to submit comments, contact CLSI.

Clinical and Laboratory Standards Institute
950 West Valley Road, Suite 2500
Wayne, PA 19087 USA
P: +1.610.688.0100
F: +1.610.688.0700
www.clsi.org
standard@clsi.org

M60, 1st ed.
November 2017
Replaces M27-S4 and M44-S3

Performance Standards for Antifungal Susceptibility Testing of Yeasts

Barbara D. Alexander, MD, MHS
Gary W. Procop, MD, MS
Philippe Dufresne, PhD (RMCCM)
Jeff Fuller, PhD, FCCM, D(ABMM)
Annette W. Fothergill, MA, MBA, MT(ASCP)
Mahmoud A. Ghannoum, PhD, EMBA, FIDSA
Kimberly E. Hanson, MD, MHS
Denise Holliday, MT(ASCP)
Nicole M. Holliday, BA
Luis Ostrosky-Zeichner, MD, FACP, FIDSA, FSHEA
Audrey N. Schuetz, MD, MPH, D(ABMM)
Dee Shortridge, PhD
Nathan P. Wiederhold, PharmD
Adrian M. Zelazny, PhD, D(ABMM)

Abstract

Clinical and Laboratory Standards Institute document M60—*Performance Standards for Antifungal Susceptibility Testing of Yeasts* includes the minimal inhibitory concentration, zone diameter, and QC tables developed following the standards described in CLSI documents M27[1] and M44.[2] The tabular information in this document is valid only when the methodology is followed as described in the current editions of CLSI documents M27[1] and M44.[2] Any previously published tables should be replaced with these new tables. Changes since the last edition appear in boldface type.

Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antifungal Susceptibility Testing of Yeasts.* 1st ed. CLSI supplement M60 (ISBN 1-56238-828-2 [Print]; ISBN 1-56238-829-0 [Electronic]). Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2017.

Suggested Citation

CLSI. *Performance Standards for Antifungal Susceptibility Testing of Yeasts.* 1st ed. CLSI supplement M60. Wayne, PA: Clinical and Laboratory Standards Institute; 2017.

Previous Editions:
M27-S4: May 2004, April 2005, April 2008, December 2012
M44-S3: January 2006, August 2007, August 2009

ISBN 1-56238-828-2 (Print)
ISBN 1-56238-829-0 (Electronic)
ISSN 1558-6502 (Print)
ISSN 2162-2914 (Electronic) Volume 37, Number 14

Committee Membership

Subcommittee on Antifungal Susceptibility Tests

Acknowledgment

CLSI and the Subcommittee on Antifungal Susceptibility Tests gratefully acknowledge the following volunteers for their important contributions to the development of this document:

Barbara D. Alexander, MD, MHS
Duke Univeristy Medical Center
USA

Annette W. Fothergill, MA, MBA, MT(ASCP)
USA

Dee Shortridge, PhD
JMI Laboratories
USA

Acknowledgment

CLSI and the Subcommittee on Antifungal Susceptibility Tests gratefully acknowledge the following former subcommittee members for their review of this document during development:

Sharon K. Cullen, BS, PMP, RAC
Beckman Coulter, INc.
USA

Shawn R. Lockhart, PhD, D(ABMM)
Centers for Disease Control and Prevention
USA

David S. Perlin, PhD
New Jersey Medical School-UMDNJ
USA

Nancy L. Wengenack, PhD, D(ABMM)
Mayo Clinic
USA

Contents

Foreword

Users of CLSI documents M27[1] and M44[2] and this document should recognize that the standard methods described in CLSI documents are reference methods. These methods may be used for:

- Routine antifungal testing of patient isolates to guide therapy
- Evaluating commercial devices that will be used in medical laboratories
- Testing new agents or systems by drug or device manufacturers

Results generated by reference methods, such as those described in CLSI documents, may be used by regulatory authorities to evaluate commercial susceptibility testing device performance as part of the approval process. Regulatory clearance indicates that the commercial susceptibility testing device provides results that are substantially equivalent to those generated using reference methods for the organisms and antimicrobial agents described in the device manufacturer's approved package insert.

However, CLSI breakpoints may also differ from those approved by various regulatory organizations for many reasons, including:

- Database differences
- Data interpretation
- Dosage amounts used in different parts of the world
- Public health policies

Differences also exist because CLSI proactively evaluates the need for changing breakpoints. The reasons why breakpoints may change, and the manner in which CLSI evaluates data and determines breakpoints, are described in CLSI document M23.[3]

When CLSI decides to change an existing breakpoint, regulatory organizations may also review data to determine how changing breakpoints may affect antimicrobial agent safety and effectiveness for the approved indications. When a regulatory authority changes breakpoints, commercial device manufacturers may have to conduct a clinical trial, submit the data to the regulatory organization, and await review and approval. For these reasons, a delay of one or more years may be needed if a breakpoint change is to be implemented by a device manufacturer. Some regulatory and accreditation requirements allow laboratories using cleared or approved testing devices to use existing regulatory organization breakpoints. Either those or CLSI susceptibility breakpoints may be acceptable to laboratory accreditation organizations. Other regulatory and accreditation requirements may vary. Each laboratory should check with its antimicrobial susceptibility test system manufacturer for additional information on the breakpoints used in its system software. Laboratories should be aware of their specific regulatory and accreditation requirements for using CLSI breakpoints.

Once verified by the CLSI document development process, breakpoints may be implemented as soon as they are published in a supplement. However, medical laboratories should discuss this implementation with appropriate stakeholders, such as infectious disease practitioners and the pharmacy department, as well as the hospital pharmacy and therapeutics and infection control committees, before implementing newly approved or revised breakpoints. When a device includes antimicrobial test concentrations that are sufficient to interpret susceptibility and resistance to an agent using the CLSI breakpoints, a laboratory could, after appropriate validation as outlined in CLSI document M52,[4] choose to interpret and report results from that device using CLSI breakpoints.

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 to both past procedures and associated documents such as CLSI document M27.[1]

Overview of Changes

This document replaces the previous editions of the approved supplements M27-S4, published in 2012, and M44-S3, published in 2009. Several changes were made in this edition, including:

- **General:**
  - Combined information from M27-S4 (antifungal broth dilution susceptibility testing) and M44-S3 (antifungal disk diffusion testing) into one informational supplement, which has been recoded as M60. Revised the title to harmonize with other CLSI susceptibility testing informational supplements
  - Moved tables showing schemes for preparing dilution series of water-soluble and water-insoluble antifungal agents to be used in broth dilution susceptibility testing (originally Tables 4 and 5 in M27-S4) to the broth dilution testing document (CLSI document M27[1])
  - Moved tables showing the formulation for Roswell Park Memorial Institute (RPMI) 1640 culture medium (originally Table 8 in M27-S4) to the broth dilution testing document (CLSI document (M27[1])
  - Deleted modifications for special circumstances of broth dilution testing (originally Table 9 in M27-S4)
  - Deleted the glossary with abbreviations, routes of administration, and drug classes for antifungal agents
- **Foreword:**
  - Added a **NOTE** regarding changing fungal nomenclature and use of traditional fungal names
- **Table 1 – Breakpoints and Interpretive Categories for *In Vitro* Broth Dilution Susceptibility Testing of *Candida* spp. and Select Antifungal Agents:**
  - Revised the footnote regarding interpretation of the intermediate category
  - Changed the voriconazole "susceptible-dose dependent" category to "intermediate"
  - Combined breakpoints for all antifungal agents into a single table
  - Added a footnote regarding variability in results for susceptibility testing with caspofungin
  - Added a footnote regarding the intrinsic resistance of *Candida krusei* to fluconazole
  - Added a **NOTE** explaining the deletion of breakpoints for *Candida* spp. when testing against itraconazole and flucytosine
  - Added seven new references
- **Table 2 – Solvents and Diluents for Preparing Stock Antifungal Agent Solutions for Broth Dilution Testing:**
  - Deleted water as a solvent or diluent for fluconazole and flucytosine
  - Added solvent and diluent information for isavuconazole