CLINICAL AND LABORATORY STANDARDS INSTITUTE®

2nd Edition

M60

Performance Standards for Antifungal Susceptibility Testing of Yeasts

This document provides 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.

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Performance Standards for Antifungal Susceptibility Testing of Yeasts

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Abstract

Clinical and Laboratory Standards Institute document M60—*Performance Standards for Antifungal Susceptibility Testing of Yeasts* includes minimal inhibitory concentration, zone diameter, and quality control tables developed following the guidance in CLSI documents M27[1] and M44.[2] The data in the tables are valid only when the methodologies in CLSI documents M27[1] and M44[2] are followed. Users should replace previously published tables with these new tables. Changes in the tables since the previous edition appear in boldface type.

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Contents

Foreword

The breakpoints and interpretive categories provided in this document are generated using the reference methods for antifungal susceptibility testing of yeasts described in CLSI documents M27[1] and M44.[2] These reference methods may be used for:

- Routine antifungal testing of patient isolates to guide therapy
- Evaluation of commercial devices that will be used in medical laboratories
- Testing of 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 commercial device 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 differ from breakpoints 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 that breakpoints may change, as well as 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 the changes 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 device manufacturer decides to implement a breakpoint change. Some regulatory and accreditation requirements permit laboratories using cleared or approved testing devices to use existing regulatory organization breakpoints. Either the regulatory approved breakpoints or CLSI breakpoints may be acceptable to laboratory accreditation organizations. Other regulatory and accreditation requirements vary. Each laboratory should consult its 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.

Following discussions with appropriate stakeholders (eg, infectious diseases practitioners and pharmacy practitioners, the hospital's pharmacy and therapeutics and infection prevention committees), laboratories may implement newly approved or revised CLSI breakpoints as soon as they are published. Some devices might specify antimicrobial test concentrations that are sufficient to interpret susceptibility and resistance to an agent using the CLSI breakpoints. In such cases, after appropriate validation as outlined in CLSI document M52,[4] a laboratory could 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 with both past procedures and associated documents such as CLSI document M27.[1]

Overview of Changes

This document replaces the previous edition of the approved document, M60-Ed1, published in 2017. Several changes were made in this edition, including:

- **Table 1. Minimal Inhibitory Concentration Breakpoints for *In Vitro* Broth Dilution Susceptibility Testing of *Candida* spp. and Select Antifungal Agents After 24-Hour Incubation:**
  - Added footnote and references regarding recommendations for interpreting *Candida parapsilosis* breakpoints
  - Revised footnote regarding intrinsic resistance of *Candida krusei* to fluconazole

- **Table 2. Solvents and Diluents for Preparing Stock Antifungal Agent Solutions for Broth Dilution Testing:**
  - Added solvent and diluent information for:
    - Ibrexafungerp
    - Manogepix
    - Rezafungin

- **Table 3. (formerly Table 4) Recommended 24-Hour Minimal Inhibitory Concentration Limits for Quality Control Strains for Broth Microdilution Procedures:**

  NOTE 1: In the previous edition of M60, Table 3 contained 48-hour QC ranges, and Table 4 contained 24-hour QC ranges. In this edition, the tables have been transposed.

  NOTE 2: The minimal inhibitory concentration (MIC) QC ranges for ibrexafungerp were adopted by the Subcommittee on Antifungal Susceptibility Tests during the annual meetings in January 2019 and January 2020. These QC ranges are tentative and are open for comment for one year from the publication of M60.

  - Added MIC QC ranges for:
    - Ibrexafungerp
      - *C. krusei* ATCC® 6258
      - *C. parapsilosis* ATCC® 22019
    - Manogepix
      - *Candida albicans* ATCC® 90028
      - *C. parapsilosis* ATCC® 22019
    - Rezafungin
      - *C. krusei* ATCC® 6258
      - *C. parapsilosis* ATCC® 22019
  - Revised NOTE regarding MICs
  - ***Deleted*** NOTE regarding tentative 24-hour MIC QC ranges

- **Table 5. Zone Diameter and Equivalent Minimal Inhibitory Concentration Breakpoints for Select Antifungal Agents Against *Candida* spp. After 24-Hour Incubation:**
  - Revised footnote regarding intrinsic resistance of *C. krusei* to fluconazole
  - ***Deleted*** footnotes regarding tentative zone diameter interpretive categories

- **Table 6. Recommended Quality Control Zone Diameter (mm) Ranges After 24-Hour Incubation:**

  NOTE: The QC zone diameter ranges were adopted by the Subcommittee on Antifungal Susceptibility Tests during the annual meetings in January 2019 and January 2020. These zone diameter QC ranges are tentative and are open for comment for one year from the publication of M60.

  - Added disk diffusion QC ranges for:
    - Manogepix
      - *C. albicans* ATCC® 90028
      - *C. parapsilosis* ATCC® 22019
      - *Candida tropicalis* ATCC® 750
    - Rezafungin
      - *C. albicans* ATCC® 90028
      - *C. krusei* ATCC® 6258
      - *C. parapsilosis* ATCC® 22019
      - *C. tropicalis* ATCC® 750
  - ***Deleted*** footnote regarding tentative zone diameter QC ranges

NOTE: The content of this document is supported by the CLSI consensus process and does not necessarily reflect the views of any single individual or organization.

Key Words

Antifungal agent, azole, breakpoint, broth dilution, disk diffusion, echinocandin, interpretive category, minimal inhibitory concentration, quality control, susceptibility testing, yeasts, zone diameter

Abbreviations and Acronyms

ATCC®[a]	American Type Culture Collection
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
ECV	epidemiological cutoff value
I	intermediate
MIC	minimal inhibitory concentration
QC	quality control
R	resistant
S	susceptible
SDD	susceptible-dose dependent

[a] ATCC® is a registered trademark of the American Type Culture Collection.