CLINICAL AND LABORATORY STANDARDS INSTITUTE®

3rd Edition

M24

Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes

This standard provides protocols and related quality control parameters for antimicrobial susceptibility testing of mycobacteria, *Nocardia* spp., and other aerobic actinomycetes.

A standard for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes

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Abstract

Clinical and Laboratory Standards Institute standard M24—*Susceptibility Testing of Mycobacteria,* Nocardia *spp., and Other Aerobic Actinomycetes* includes susceptibility testing procedures for *Mycobacterium tuberculosis* complex (MTBC), clinically significant slowly and rapidly growing mycobacterial species, *Nocardia* spp., and other aerobic actinomycetes. Also included in this standard are recommendations for selecting agents for first-line and second-line drug testing, organism group–specific methodologies, reporting recommendations, and organism quality control criteria. Recommendations regarding agent selection for testing mycobacteria are based primarily on published guidelines. For testing MTBC, M24 recognizes agar proportion as the reference methodology on which all other methodologies are based. In addition, this standard includes recommendations for using commercial broth susceptibility methods with shorter incubation times, which are now in widespread use for MTBC susceptibility testing, and information on molecular methods for detecting drug resistance and their integration with culture-based methods.

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Contents

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Foreword

This standard includes recommendations for testing *Mycobacterium tuberculosis* complex (MTBC), certain nontuberculous mycobacteria (NTM), *Nocardia* spp., and other aerobic actinomycetes. Currently, sufficient data exist to support recommendations for antimicrobial susceptibility testing (AST) of MTBC, *Mycobacterium avium* complex (MAC), *M. kansasii, M. marinum,* the rapidly growing mycobacteria (RGM), *Nocardia* spp., and certain other aerobic actinomycetes. Breakpoints for some NTMs, *Nocardia* spp., and other aerobic actinomycetes are based on organism population distributions, clinical data, breakpoints used for other organisms, and the experience of experts in the field. M24 was revised in response to new developments in mycobacterial susceptibility testing and comments from laboratorians who perform routine mycobacterial and/or aerobic actinomycete testing. Additional revisions are anticipated as more relevant data become available.

Overview of Changes

This standard replaces the previous edition of the approved standard, M24-A2, published in 2011. Several changes were made in this edition, including:

- Removed information related to the short-incubation, liquid-radiometric testing system, because this system is no longer available

- Expanded the description of molecular testing for both MTBC and NTM to determine antimicrobial susceptibility or resistance
  - For MTBC, Table 3 (Considerations for Molecular or Repeat Testing After Initial Testing on MTBC Using a Commercial Short-Incubation Broth System) and text are included to describe the integration of molecular and culture-based test results for the best possible prediction of the expected drug efficacy.

  - For NTM, text is included to describe integration of molecular techniques to assist in determining efficacy of macrolides and amikacin in the treatment of infections caused by MAC and various RGM.

- Added a description of recently discovered challenges to MTBC AST accuracy with use of rapid broth systems and/or the agar proportion method, particularly limited sensitivity in detection of low-level resistance to rifampin and ethambutol

- Added information in Appendix A regarding the relationship of pharmacokinetics and pharmacodynamics in determining breakpoints and interpretive criteria

- Updated all breakpoint and quality control tables and moved them to a newly created informational supplement, CLSI document M62[1]

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

Key Words

Aerobic actinomycetes, antimicrobial susceptibility testing, antimycobacterial drugs, antituberculous drugs, *Mycobacterium tuberculosis* complex, *Nocardia* spp., nontuberculous mycobacteria

Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes

Chapter 1: Introduction

This chapter includes:

- Standard's scope and applicable exclusions
- Background information pertinent to the standard's content
- Standard precautions information
- "Note on Terminology" that highlights particular use and/or variation in use of terms and/or definitions
- Terms and definitions used in the standard
- Abbreviations and acronyms used in the standard

1.1 Scope

M24 includes antimicrobial susceptibility testing (AST) protocols for three major categories of mycobacterial species:

- *Mycobacterium tuberculosis* complex (MTBC)
- The slowly growing nontuberculous mycobacteria (SGM)
- The rapidly growing mycobacteria (RGM)

Also provided are:

- AST recommendations for *Nocardia* spp. and other aerobic actinomycetes
- Guidance on selecting first-line and, for some organisms, second-line antimicrobial agents for testing and reporting
- Instructions for performing the standard agar proportion (AP) method for MTBC and broth microdilution for mycobacteria and aerobic actinomycetes
- Molecular methods for detecting mutations associated with MTBC drug resistance
- QC protocols for each organism category

Testing and reporting recommendations and QC procedures apply to both reference methods and commercial shorter-incubation broth systems that have been regulatory organization cleared or approved for testing MTBC. This standard does not cover identification methods, nor does it provide an in-depth discussion of molecular test procedures. This standard is intended for use by hospital, public health, and referral laboratories that perform AST on MTBC, nontuberculous mycobacteria (NTM), *Nocardia* spp., and/or other aerobic actinomycetes.