MAYO CLINIC LABORATORIES

Test Definition: TBPZA

Susceptibility, Mycobacterium tuberculosis Complex, Pyrazinamide, Varies

Overview

Useful For

Susceptibility testing of *Mycobacterium tuberculosis* complex isolates growing in pure culture against pyrazinamide

This test is **not useful for** *Mycobacterium bovis* and *Myocobacterium bovis* bacille Calmette-Guerin (BCG) isolates as they are intrinsically resistant to pyrazinamide.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
MTBVP	Mtb PZA Confirmation, pncA Sequence	No, (Bill Only)	No

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
STVP	Susceptibility, Mtb Complex, PZA	No, (Bill Only)	Yes

Testing Algorithm

If resistance to pyrazinamide is detected, the reflex sequencing test or confirmation of resistance will be performed at an additional charge.

If the broth microdilution test is unable to be performed (eg, due to reagent shortages, failure of the isolate to grow in the test medium), the reflex sequencing test will be performed at an additional charge.

Special Instructions

- Infectious Specimen Shipping Guidelines

Method Name

Broth Dilution at Critical Drug Concentrations

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

To test for first-line agents, isoniazid, rifampin and ethambutol, order TB1LN / Antimicrobial Susceptibility, *Mycobacterium tuberculosis* Complex, First Line, Varies.

Isolates identified as *Mycobacterium bovis* and *Myocobacterium bovis* bacille Calmette-Guerin (BCG) will not be accepted as they are intrinsically resistant to pyrazinamide.

Additional Testing Requirements

If organism identification is not provided, CTB / Mycobacteria and *Nocardia* Culture, Varies or CTBID / Culture Referred for Identification, *Mycobacterium* and *Nocardia*, Varies **must also** be ordered and will be charged separately.

Shipping Instructions

1. See Infectious Specimen Shipping Guidelines
2. Place specimen in a large infectious container (T146) and label as an etiologic agent/infectious substance.

Necessary Information

Specimen source and suspected organism identification are required.

Specimen Required

Specimen Type: Organism
Supplies: Infectious Container, Large (T146)
Container/Tube: Middlebrook 7H10 agar slant
Specimen Volume: Isolate
Collection Instructions: Organism must be in pure culture, actively growing.

Forms

If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Reject Due To

Agar plate	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

Initial treatment regimens for *Mycobacterium tuberculosis* complex often include isoniazid, rifampin, ethambutol, and pyrazinamide (PZA). Susceptibility testing of *M tuberculosis* complex isolates against these antimycobacterial agents is a key component of patient management.

The Clinical and Laboratory Standards Institute provides consensus protocols for the methods, antimycobacterial agents, and critical concentrations of each agent to be tested to permit standardized interpretation of *M tuberculosis* complex susceptibility test results.

This test uses a US Food and Drug Administration cleared commercial system for rapid broth susceptibility testing of *M tuberculosis* complex against PZA. The literature indicates that broth testing of PZA can, at times, produce falsely resistant results, so resistance to PZA by the broth method is automatically confirmed by *pncA* DNA sequencing. Variants in the *pncA* gene and upstream promoter region have been reported to account for the majority (70%-97%) of PZA-resistant isolates. However, 3% to 30% of PZA-resistant isolates do not have a corresponding *pncA* variant and other genes (eg, *rpsA*) may also play a role.

A separate test is available for testing of the other primary agents (isoniazid, rifampin and ethambutol). If desired, this must be ordered separately; TB1LN / Antimicrobial Susceptibility, *Mycobacterium tuberculosis* Complex, First Line, Varies.

Reference Values

Results are reported as susceptible or resistant.

Interpretation

Mycobacterium tuberculosis complex isolates are reported as susceptible or resistant to pyrazinamide at the critical concentration.

Cautions

For isolates determined to be resistant by the broth method, confirmatory testing using *pncA* DNA sequencing is automatically performed and the presence or absence of *pncA* variations associated with pyrazinamide resistance is reported. Some variants associated with pyrazinamide resistance may occur outside of the *pncA* promoter and gene region and may therefore not be confirmed by DNA sequencing of this target. Presence of a *pncA* mutation associated with resistance confirms the broth susceptibility testing results. Absence of a *pncA* mutation does not rule out possible resistance.

Susceptibility testing should be performed on pure culture isolates of *Mycobacterium tuberculosis* complex.

Clinical Reference

1. Nahid P, Mase SR, Migliori GB, et al. Treatment of Drug-Resistant Tuberculosis. An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline [published correction appears in Am J Respir Crit Care Med. 2020 Feb 15;201(4):500-501
2. Dormandy J, Somoskovi A, Kreiswirth BN, Driscoll JR, Ashkin D, Salfinger M. Discrepant results between pyrazinamide susceptibility testing by the reference BACTEC 460TB method and pncA DNA sequencing in patients infected with multidrug-resistant W-Beijing Mycobacterium tuberculosis strains. Chest. 2007;131(2):497-501. doi:10.1378/chest.06-1899
3. Chedore P, Bertucci L, Wolfe J. Potential for erroneous results indicating resistance when using the BACTEC MGIT 960 system for testing susceptibility of mycobacterium tuberculosis to Pyrazinamide. J Clin Microbiol 2010;48(1):300-301

4. Campbell PJ, Morlock GP, Sikes RD, et al. Molecular resistance of mutations associated with first- and second-line drug resistance compared with conventional drug susceptibility testing of Mycobacterium tuberculosis. Antimicrob Agents Chemother. 2011;55(5):2032-2041
5. Shi W, Zhang X, Jiang X, et al. Pyrazinamide inhibits trans-translation in Mycobacterium tuberculosis. Science. 2011;333(6049):1630-1632
6. Clinical and Laboratory Standards Institute (CLSI). Susceptibility Testing of Mycobacteria, Nocardia spp., and Other Aerobic Actinomycetes. 3rd ed. CLSI standard M24. CLSI; 2018
7. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Susceptibility Testing of Mycobacteria, Nocardia spp., and Other Aerobic Actinomycetes. 2nd ed. CLSI supplement M24S. CLSI; 2023
8. Espasa M, Salvado M, Vicente E, et al. Evaluation of the versaTREK system compared to the Bactec MGIT 960 system for first-line drug susceptibility testing of Mycobacterium tuberculosis. J Clin Microbiol. 2012;50:488-491
9. Somoskovi A, Dormandy J, Parson LM, et al. Sequencing of the pncA gene in members of the Mycobacterium tuberculosis complex has important diagnostic applications: Identification of a species-specific pncA mutation in "Mycobacterium canettii" and the reliable and rapid predictor of pyrazinamide resistance. Confirmation of pyrazinamide resistance is done using Sanger dideoxy sequencing of approximately 700bp of the *pncA* gene and promoter region. J Clin Microbiol. 2007;45(2):595-599
10. Jureen P, Werngren J, Toro JC, Hoffner S: Pyrazinamide resistance and pncA gene mutations in Mycobacterium tuberculosis. Antimicrob Agents Chemother 2008;52(5):1852-1854

Performance

Method Description

This test is based on presence or absence of growth of an *Mycobacterium tuberculosis* complex isolate in broth cultures in the presence of critical concentrations of the antimycobacterial drug pyrazinamide. One of two FDA-cleared platforms (BD MGIT 960 or the VersaTREK) will be used. (Brown-Elliott, BA, Cirillo DM, Musser KA, Rowlinson M-C. Susceptibility Test Methods: Mycobacteria, Nocardia, and Other Actinomycetes. In: Carroll KC, Pfaller MA, eds. Manual of Clinical Microbiology, 13th Edition. ASM Press, 2023)

The BACTEC MGIT 960 platform measures fluorescence in a Mycobacterial Growth Indicator Tube (MGIT) containing an *M tuberculosis* complex isolate in the presence of a critical concentrations of pyrazinamide (Package insert: BACTEC MGIT 960 SIRE Kit, BD Diagnostics, 9/2019)

The VersaTrek platform inside bottles containing *M tuberculosis* complex isolates in the presence of a critical concentration of the antimycobacterial PZA. (Package insert: VersaTREK Mycobacteria Detection and Susceptibility Testing system, TREK Diagnostics, 04/2014)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

10 to 21 days

Specimen Retention Time

1 year

Performing Laboratory Location

Rochester

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

87188-Susceptibility, *Mycobacterium tuberculosis* Complex, Pyrazinamide
87153-Mtb PZA Confirmation, pncA Sequencing (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TBPZA	Susceptibility, Mtb Complex, PZA	56026-8

Result ID	Test Result Name	Result LOINC® Value
TBPZA	Susceptibility, Mtb Complex, PZA	56026-8