CDC Model Performance Evaluation Program (MPEP) for *Mycobacterium tuberculosis* Drug Susceptibility Testing

Attachment 13

Final Report

Mycobacterium tuberculosis Complex

Drug Susceptibility Testing Program

MARCH 2024

U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

Model Performance Evaluation Program

Report of Results, March 2024

Purpose

To present results of the U.S. Centers for Disease Control and Prevention (CDC) Model Performance Evaluation Program (MPEP) for *Mycobacterium tuberculosis* complex (MTBC) drug susceptibility testing panel sent to participants in March 2024.

Report Content

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Model Performace Evaluation Program (MPEP) | Tuberculosis (TB) | CDC

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

Note on Accessibility: Find descriptions and explanations of figures in Appendix 1: Accessible Explanation of Figures on page 39.

Contents

Technical Notes

The following information pertains to all tables and figures for the 2024 MTBC isolates A, B, C, D, and E included in this report.

- The source of data in all tables and figures is the March 2024 MPEP MTBC DST panel.
- First-line and second-line drugs have been separated into individual tables for each isolate. Streptomycin is classified as a second-line drug for this report.
- Separate tables for molecular testing are included.
- Mutations of the *rpoB* gene are noted with the *M. tuberculosis* numbering system.
- Laboratories that use more than one DST method are encouraged to test isolates with each of the available methods and equivalent critical concentrations. Some laboratories have provided results for multiple DST methods. Consequently, the number of results for some drugs may be greater than the number of participating laboratories. This report contains all results reported by participating laboratories.
- The Sensititre® system allows determination of an MIC for each drug in the panel. Laboratories using this method may establish breakpoints individually, for some drugs, to provide a categorical interpretation of S or R.
- For participant result tables that have drug-method totals equal to 0, results were not received.
- Although data was collected for rifapentine, delamanid, and pretomanid, no laboratories reported growth-based testing for these drugs. Therefore, these drugs were not included in growth-based tables of participants' results.

Abbreviations and Acronyms

Acronym	Definition
AMK	Amikacin
AP	Agar proportion — performed on Middlebrook 7H10 or 7H11
CAP	Capreomycin
CDC	U.S. Centers for Disease Control and Prevention
CIP	Ciprofloxacin
CLSI	Clinical and Laboratory Standards Institute
CYS	Cycloserine
DNA	Deoxyribonucleic acid
DST	Drug susceptibility testing
EMB	Ethambutol
ETA	Ethionamide
FQ	Fluoroquinolone
INH	Isoniazid
KAN	Kanamycin
LVX	Levofloxacin
MDR	Multidrug-resistant
MGIT™	BACTEC™ MGIT™ – Mycobacteria Growth Indicator Tube
MIC	Minimum inhibitory concentration
MOX	Moxifloxacin
MPEP	Model Performance Evaluation Program
MTBC	***Mycobacterium tuberculosis*** complex
PAS	***P***-aminosalicylic acid
PZA	Pyrazinamide
OFL	Ofloxacin
R	Resistant
RBT	Rifabutin
RIF	Rifampin
RNA	Ribonucleic acid
S	Susceptible
Sensititre®	Thermo Scientific Sensititre® MYCOTB AST or customized plate
STR	Streptomycin
TB	Tuberculosis
VersaTREK™	Thermo Scientific VersaTREK™ Myco susceptibility
XDR	Extensively drug-resistant

Introduction: Overview of MPEP Final Report

The Model Performance Evaluation Program (MPEP) is an educational, self-assessment tool in which five isolates of *M. tuberculosis* complex (MTBC) are sent to participating laboratories biannually for staff to monitor their ability to determine drug resistance among the isolates. It is not a formal, graded proficiency testing program. The associated report includes results for a subset of laboratories performing drug susceptibility testing (DST) for MTBC in the United States. MPEP is a voluntary program, and this report reflects data received from participating laboratories. This aggregate report is prepared in a format that will allow comparison of DST results with those obtained by other participants using the same methods and drugs, for each isolate. We encourage circulation of this report to personnel who are either involved with DST or reporting and interpreting results for MTBC.

CDC is neither recommending nor endorsing testing practices reported by participants. For standards, participants should refer to consensus documents published by the Clinical and Laboratory Standards Institute (CLSI), "M24: Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes" and "M24S: Performance Standards for Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes" [1, 2]. Additionally, the World Health Organization (WHO) published two technical reports investigating critical concentrations, by method, for anti-tuberculosis drugs [3, 4].

Expected Drug Susceptibility Testing Results

Anticipated growth-based and molecular results for the panel of MTBC isolates sent to participants in March 2024 are shown in the tables below. Although CDC recommends broth-based methods for routine first-line DST of MTBC isolates, the results obtained by the reference agar proportion method (except for pyrazinamide, in which MGIT™ was performed) are shown in Table 1. Molecular results obtained by whole genome sequencing are listed in Table 2.

Table 1. Expected Growth-based Results for March 2024 Panel

Isolate	RIF	INH	EMB	PZA	FQ	Second-line Drug Resistances:
2024A	S	R (low-level*)	S	S	S	ETA‡
2024B	S	S	S	S	R‡	
2024C	S	R (high-level†)	S	S	S	
2024D	R	S	S	S	S	RBT
2024E	S	S	S	R	S	

Note: RIF=rifampin, INH=isoniazid, EMB=ethambutol, PZA=pyrazinamide, FQ=fluoroquinolones, ETA=ethionamide, RBT=rifabutin, S=susceptible, R=resistant.

*Resistant at 0.2 µg/ml by agar proportion. See Equivalent Critical Concentration table on page 8 for more information.

†Resistant at 0.2 and 1.0 µg/ml by agar proportion. See Equivalent Critical Concentration table on page 8 for more information.

‡80% consensus for a single categorical result across all methods reported for this drug of susceptible or resistant was not achieved for these isolates among participating laboratories.

Table 2. Expected Molecular Results (Mutations Detected in Loci Associated with Resistance) for March 2024 Panel

Isolate	*rpoB**	*inhA*	*katG*	*gyrA*	*pncA*
2024A		C-15T			
2024B				Ala90Val	
2024C			Ser315Thr		
2024D	Ser450Leu				
2024E					His57Asp

Note: Empty cell=No mutation detected. High confidence mutations were not detected in these loci: *fabG1, embB, ethA, eis, rrs, and tlyA*.

**M. tuberculosis* numbering system used [5, 6]

Equivalent Critical Concentrations

(Concentrations listed as µg/ml)

Agar Proportion

First-line Drugs	7H10 agar	7H11 agar
Isoniazid	0.2 and 1.0*	0.2 and 1.0*
Rifampin	0.5†	1.0
Ethambutol	5.0	7.5
Pyrazinamide	Not recommended	Not recommended

NOTE—Critical concentrations as indicated in CLSI M24 document, unless otherwise stated [1].

*The higher concentration of INH should be tested as second-line drug after resistance at the critical concentration is detected [1].

†WHO recommended critical concentration of 0.5 µg/ml differs from CLSI critical concentration of 1.0 µg/ml for RIF [1, 4].

Second-line Drugs	7H10 agar	7H11 agar
Streptomycin	2.0	2.0
Levofloxacin	1.0	Not determined
Moxifloxacin	0.5	0.5
Amikacin	4.0†	Not determined
Capreomycin	10.0†	10.0¥
Kanamycin	5.0†	6.0¥
Ethionamide	5.0	10.0
Rifabutin	0.5	0.5
p-Aminosalicylic acid	2.0¥	8.0¥
Rifapentine	Not determined*	Not determined*
Bedaquiline	Not determined*	0.25‡
Linezolid	1.0‡	1.0‡
Clofazimine	Not determined*	Not determined*
Delamanid	Not determined*	0.016‡
Pretomanid	Not determined*	Not determined*

NOTE—Critical concentrations as indicated in CLSI M24 document [1].

*Breakpoints for establishing susceptibility have not been determined.

†CLSI critical concentrations differ from revised WHO recommendations published in 2018 [1, 3].

- For AMK, the WHO recommended critical concentration for 7H10 agar is 2.0 µg/ml.
- For CAP, the WHO recommended critical concentration for 7H10 agar is 4.0 µg/ml and 'Not determined' for 7H11 agar.
- For KAN, the WHO recommended critical concentration for 7H10 agar is 4.0 µg/ml.

¥WHO has withdrawn the recommended critical concentrations for CAP and KAN for 7H11 agar and PAS for 7H10 and 7H11 [3].

‡Critical concentrations as indicated in WHO 2018 Technical Report on critical concentrations [3].

Broth Based Media

First-line Drugs	MGIT™	VersaTREK™
Isoniazid	0.1 (and 0.4*)	0.1 (and 0.4*)
Rifampin	0.5†	1.0
Ethambutol	5.0	5.0 (and 8.0*)
Pyrazinamide	100.0	300.0

NOTE—Critical concentrations as indicated in applicable manufacturer package inserts, unless otherwise stated.

*The higher concentration of INH and EMB should be tested after resistance at the critical concentration is detected [1].

†WHO recommended critical concentration of 0.5 µg/ml differs from CLSI critical concentration of 1.0 µg/ml for RIF [4].

Second-line Drugs	MGIT™
Streptomycin	1.0 (and 4.0*)
Levofloxacin	1.0†
Moxifloxacin	0.25
Amikacin	1.0
Capreomycin	2.5
Kanamycin	2.5
Ethionamide	5.0
Cycloserine	16.0¥
p-Aminosalicylic acid	Not recommended†
Rifapentine	Not determined
Bedaquiline	1.0
Linezolid	1.0
Clofazimine	1.0
Delamanid	0.06
Pretomanid	0.5 and 2.0‡

NOTE—Critical concentrations as indicated in WHO 2018 Technical Report on critical concentrations unless noted otherwise [3]. Data for second-line critical concentrations not available for VersaTREK™.

*Critical concentration as indicated in applicable manufacturer package insert. The higher concentration of STR should be tested after resistance at the critical concentration is detected.

†WHO critical concentrations differ from CLSI M24S recommendations published in 2023 [2, 3].

- For LVX, the CLSI recommended critical concentration for MGIT™ is 1.5 µg/ml.
- For PAS, the CLSI recommended critical concentration for MGIT™ is 4.0 µg/ml.

¥Critical concentration as indicated in WHO 2024 Module 3: Diagnosis—Rapid diagnostics for tuberculosis detection (Third Edition) [7].

‡Per WHO 2024 Module 3: Diagnosis—Rapid diagnostics for tuberculosis detection (Third Edition), no growth at 0.5 µg/ml is susceptible; growth at 0.5 µg/ml and no growth at 2.0 µg/ml is susceptible, but with a comment on uncertainty; growth at 2.0 µg/ml is resistant [7].

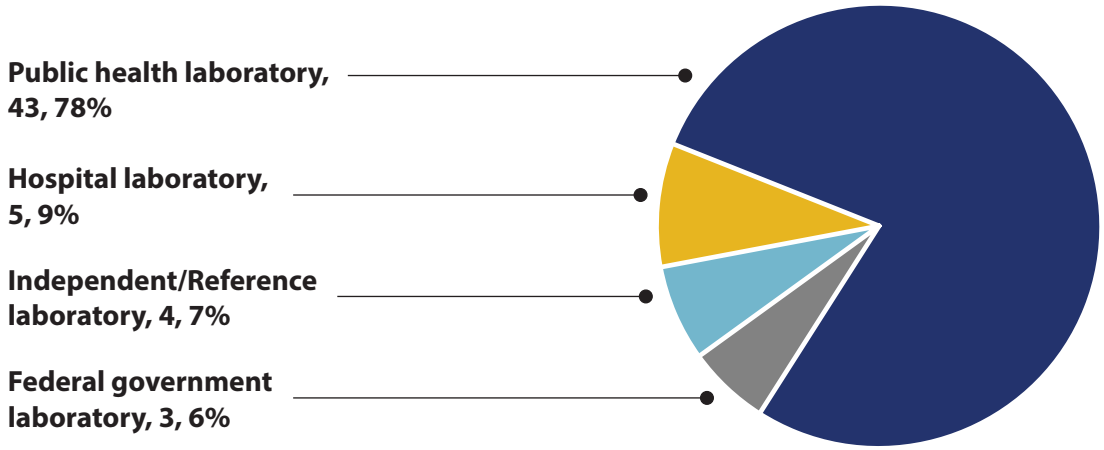
Descriptive Information about Participant Laboratories

Primary Classification

This report contains DST results submitted to CDC by panel participants at 55 laboratories in 31 states, all of whom have participated in previous MPEP panels.

Participants were asked to indicate the primary classification of their laboratory (Figure 1).

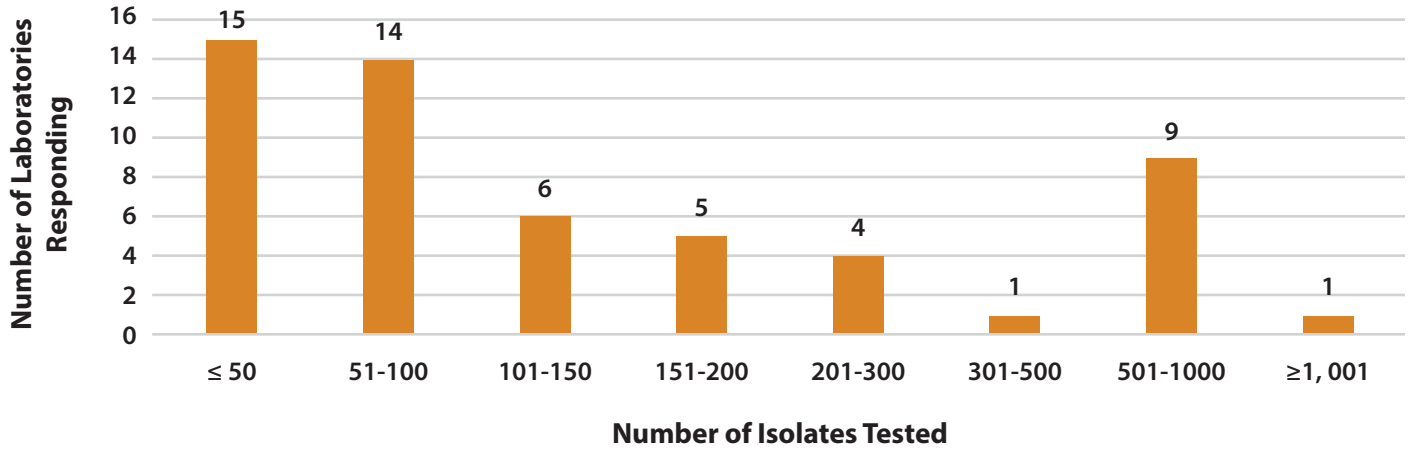
Figure 1. Primary Classification of Participating Laboratories, March 2024



Annual Number of MTBC Drug Susceptibility Tests Performed

The number of MTBC isolates tested for drug susceptibility by the 55 participants in 2023 (excluding isolates used for quality control) is shown in Figure 2. In 2023, the counts ranged from 6 to 1,055 tests. Participants at 15 (27%) laboratories reported testing 50 or fewer DST isolates per year. Laboratories with low MTBC DST volumes are encouraged to consider referral of testing because of concerns about maintaining proficiency [8].

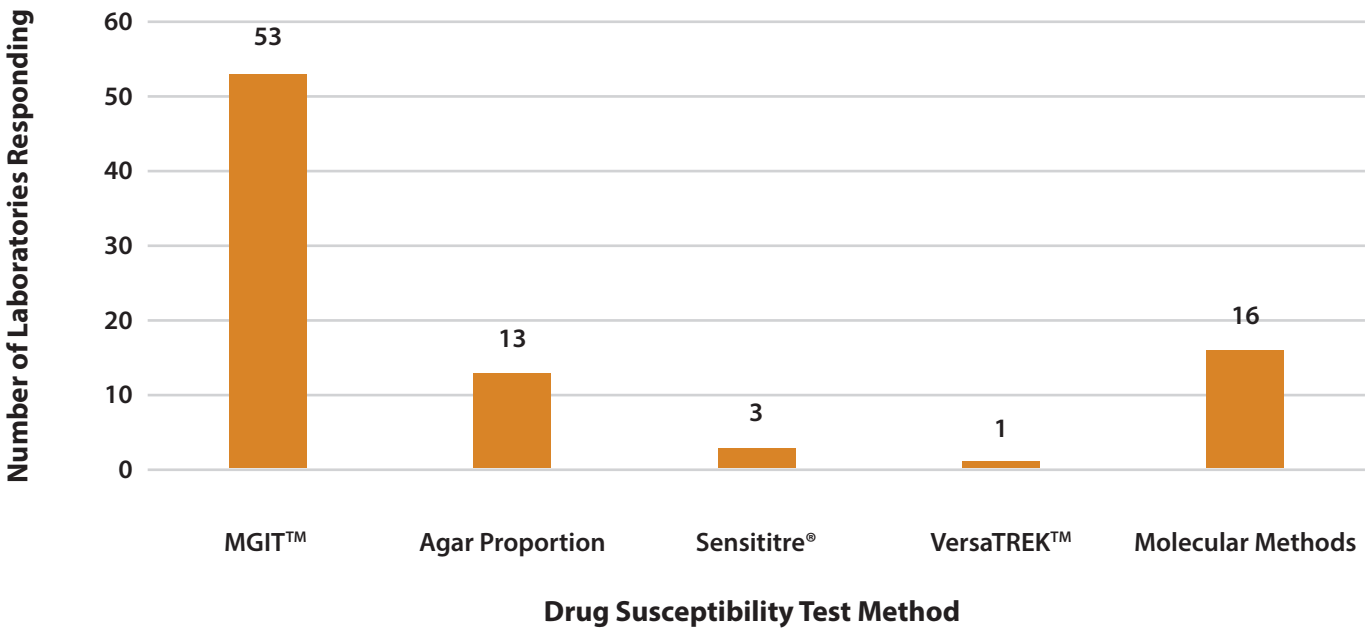
Figure 2. Distribution of the Annual Volume of MTBC Isolates Tested for Drug Susceptibility by Participants in Previous Calendar Year (n=55)



MTBC Drug Susceptibility Test Methods Performed by Participants

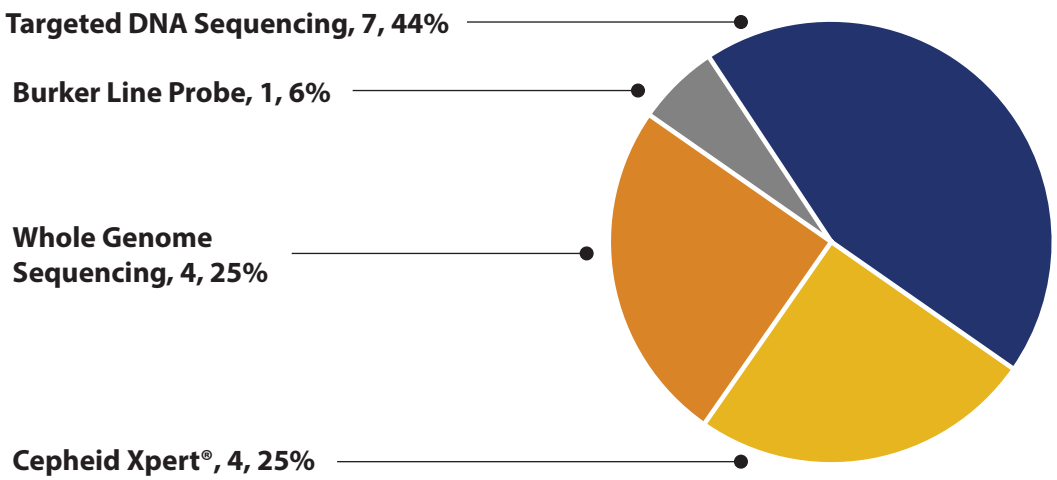
The DST methods that were performed by participating laboratories for this panel of MTBC isolates are displayed in Figure 3. Of participating laboratories, 31 (56%) reported results for only one method, 18 (33%) reported two methods, and 6 (11%) reported three susceptibility methods. Fifty-three (96%) participating laboratories indicated use of MGIT™.

Figure 3. MTBC Drug Susceptibility Test Methods Performed (n=86 responses)



Molecular methods reported by participants are shown in Figure 4. The method performed most frequently (44%) was targeted DNA sequencing.

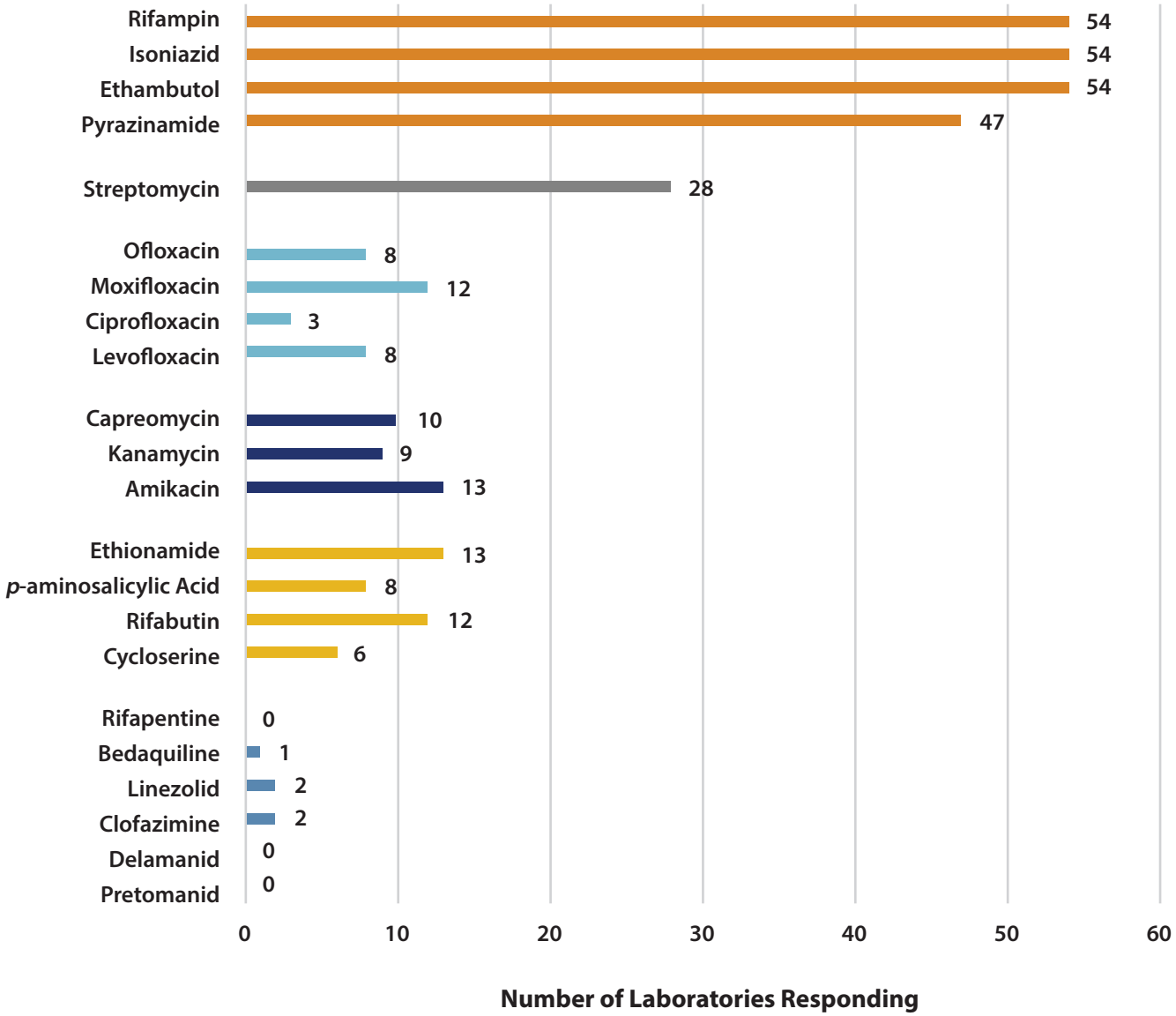
Figure 4. Molecular Method Reported (n=16 responses)



Antituberculosis Drugs Tested by Participants

The number of participating laboratories that reported testing each antituberculosis drug in the March 2024 panel is presented in Figure 5. CLSI recommends testing a full panel of first-line drugs (rifampin [RIF], isoniazid [INH], ethambutol [EMB], and pyrazinamide [PZA])[1] because it represents a combination of tests that provides the clinician with comprehensive information related to the 6- or 9-month four-drug RIPE TB treatment regimen used for many patients. Laboratories should consider the addition of fluoroquinolones (FQ) to their testing panel as CDC recommends susceptibility testing for FQ (e.g., moxifloxacin) with use of the alternate 4-month rifapentine-moxifloxacin treatment regimen; RIF may be used as a proxy for rifapentine [9].

Figure 5. Antituberculosis Drugs Tested by Growth-based Method by Participants



Isolate 2024A

Expected Results:

Drug	Growth-based*	Molecular*
RIF	S	***rpoB*** wild-type
INH	R (low-level†)	***inhA*** C-15T; ***katG*** & ***fabG1*** wild-type
EMB	S	***embB*** wild-type
PZA	S	***pncA*** wild-type
FQ	S	***gyrA*** & ***gyrB*** wild-type
ETA	R‡	***inhA*** C-15T; ***ethA*** wild-type

Note: RIF=rifampin, INH=isoniazid, EMB=ethambutol, PZA=pyrazinamide, FQ=fluoroquinolones, ETA=ethionamide, S=susceptible, R=resistant

*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT™. Molecular expected results performed by whole genome sequencing.

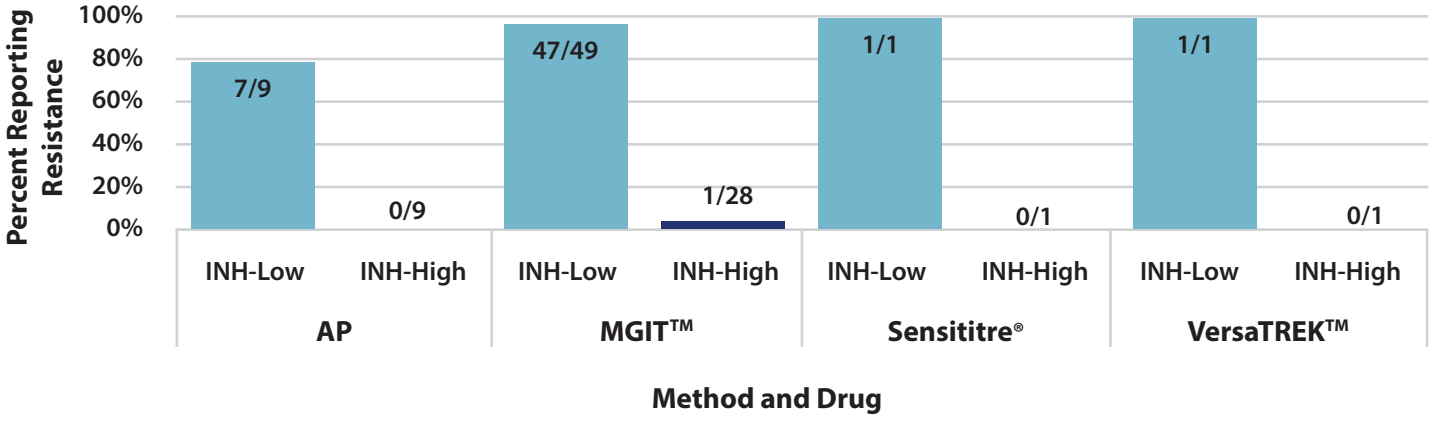
†Resistant at 0.2 µg/ml by agar proportion. See Equivalent Critical Concentration table on page 8 for more information.

‡80% consensus for a single categorical result across all methods reported for this drug of susceptible or resistant was not achieved for these isolates among participating laboratories.

Isoniazid

DNA sequence analysis of *inhA*, *katG*, and *fabG1* of Isolate 2024A revealed a C>T point mutation at nucleotide position -15 of the *inhA* promoter region; *katG* and *fabG1* were wild-type (i.e., no mutations were detected). The *inhA* C-15T mutation is known to cause low-level INH resistance.

Figure 6. Isolate 2024A: Percent of laboratories reporting INH-Low and INH-High resistance, by growth-based method

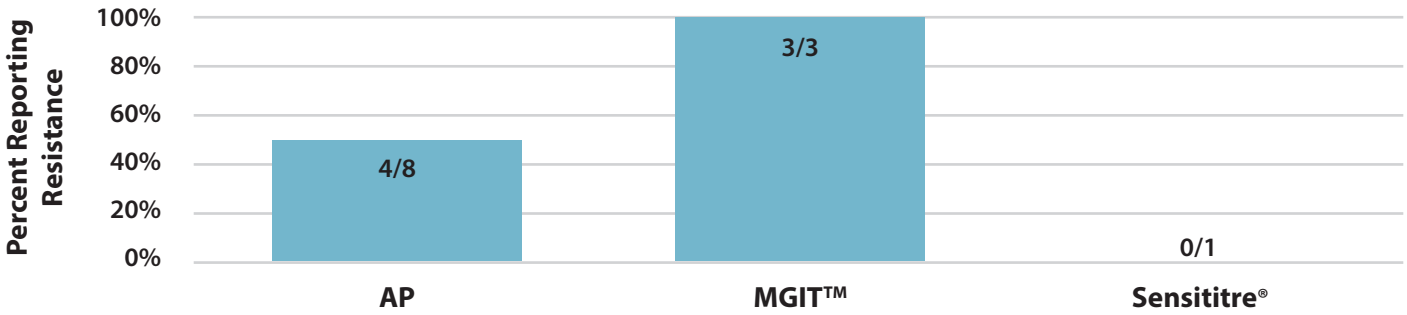


Note—Two laboratories performing Sensititre® reported INH MIC value as 0.25 µg/ml (n=2).

Ethionamide

Resistance to ETA is commonly due to mutations in the *ethA* gene or mutations in *fabG1* or *inhA* resulting in cross-resistance with INH. DNA sequencing analysis revealed the *inhA* C-15T mutation; *ethA* was wild-type (i.e., no mutations were detected).

Figure 7. Isolate 2024A: Percent of laboratories reporting ETA resistance, by growth-based method



Note—Two of the laboratories performing Sensititre® reported an ETA MIC value as 5 µg/ml (n=2), although one laboratory reported 'No Interpretation'.

Complete first-line DST, second-line DST, and molecular results submitted by all participants for Isolate 2023F are listed in Tables 3–10.

Table 3. Isolate 2024A: Participant Results for First-Line DST by AP

Drug	Susceptible	Resistant	Total
Rifampin	10	0	10
Isoniazid—Low	2	7	9
Isoniazid—High	9	0	9
Ethambutol	9	0	9

Table 4. Isolate 2024A: Participant Results for First-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Rifampin	49	0	49*
Isoniazid—Low	2	47	49*
Isoniazid—High	27	1	28
Ethambutol	49	0	49*
Pyrazinamide	43	1	44*†

*One additional laboratory reported 'Contaminated/No Growth' for RIF, INH-Low, EMB, and PZA by MGIT™.

†One additional laboratory reported 'No Interpretation' for PZA by MGIT™.

Table 5. Isolate 2024A: Participant Results for First-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Rifampin	2	0	2
Isoniazid—Low	0	1	1
Isoniazid—High	1	0	1*
Ethambutol	2	0	2

*One additional laboratory reported 'Intermediate' for INH-High by Sensititre®.

Table 6. Isolate 2024A: Participant Results for First-Line DST by VersaTREK™

Drug	Susceptible	Resistant	Total
Rifampin	1	0	1
Isoniazid—Low	0	1	1
Isoniazid—High	1	0	1
Ethambutol	1	0	1
Pyrazinamide	1	0	1

Table 7. Isolate 2024A: Participant Results for Second-Line DST by AP

Drug	Susceptible	Resistant	Total
Streptomycin	9	0	9
Ofloxacin	5	0	5
Ciprofloxacin	3	0	3
Moxifloxacin	3	0	3
Levofloxacin	3	0	3
Amikacin	7	0	7
Kanamycin	5	0	5
Capreomycin	6	0	6
Ethionamide	4	4	8
Rifabutin	5	0	5
Cycloserine	4	0	4
p-Aminosalicylic acid	5	0	5
Bedaquiline	0	0	0
Linezolid	0	0	0
Clofazimine	0	0	0

Table 8. Isolate 2024A: Participant Results for Second-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Streptomycin	17	0	17
Ofloxacin	1	0	1
Ciprofloxacin	0	0	0
Moxifloxacin	7	0	7
Levofloxacin	4	0	4
Amikacin	2	0	2
Kanamycin	1	0	1
Capreomycin	2	0	2
Ethionamide	0	3	3
Rifabutin	3	0	3
Cycloserine	0	0	0
p-Aminosalicylic acid	0	0	0
Bedaquiline	1	0	1
Linezolid	1	0	1
Clofazimine	2	0	2

Table 9. Isolate 2024A: Participant Results for Second-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Streptomycin	2	0	2*
Ofloxacin	1	0	1*
Ciprofloxacin	0	0	0
Moxifloxacin	1	0	1*†
Levofloxacin	0	0	0*
Amikacin	2	0	2*
Kanamycin	1	0	1*
Capreomycin	1	0	1
Ethionamide	1	0	1*
Rifabutin	2	0	2*
Cycloserine	1	0	1*
p-Aminosalicylic acid	2	0	2*
Bedaquiline	0	0	0
Linezolid	1	0	1
Clofazimine	0	0	0

*One additional laboratory reported 'No Interpretation' for STR, OFL, MOX, LVX, AMK, KAN, ETA, RBT, CYC, and PAS by Sensititre®.

†One additional laboratory reported 'No Interpretation' for MOX by Sensititre®.

Table 10. Isolate 2024A: Participant Results for Molecular Testing

Drug	Mutation Not Detected	Mutation Detected	Total
Rifamycins (Rifampin, Rifabutin, Rifapentine)	13	0	13
Isoniazid	0	10[*]	10
Ethambutol	6	1[†]	7
Pyrazinamide	6	0	6
Streptomycin	5	0	5
Fluoroquinolones (Ofloxacin, Ciprofloxacin, Moxifloxacin, Levofloxacin)	8	1[¥]	9
Amikacin	9	0	9
Kanamycin	9	0	9
Capreomycin	8	0	8
Ethionamide	2	4[§]	6
Cycloserine	1	0	1
p-Aminosalicylic acid	1	0	1
Bedaquiline	5	0	5
Linezolid	5	1[€]	6
Clofazimine	5	0	5
Delamanid	1	0	1
Pretomanid	0	0	0

[*]Nine laboratories specifically noted the detection of *inhA* C-15T mutation.

[†]One laboratory noted the detection of *embB* mutation not associated with resistance.

[¥]One laboratory noted the detection of *gyrA* mutation not associated with resistance.

[§]Four laboratories noted the detection of *inhA* C-15T mutation also associated with ETA resistance.

[€]One laboratory noted the detection of *rrl* mutation with uncertain significance.

Isolate 2024B

Expected Results:

Drug	Growth-based*	Molecular*
RIF	S	***rpoB*** wild-type
INH	S	***katG***, ***inhA***, & ***fabG1*** wild-type
EMB	S	***embB*** wild-type
PZA	S	***pncA*** wild-type
FQ	R‡	***gyrA*** Ala90Val; ***gyrB*** wild-type

Note: RIF=rifampin, INH=isoniazid, EMB=ethambutol, PZA=pyrazinamide, FQ=fluoroquinolones, S=susceptible, R=resistant

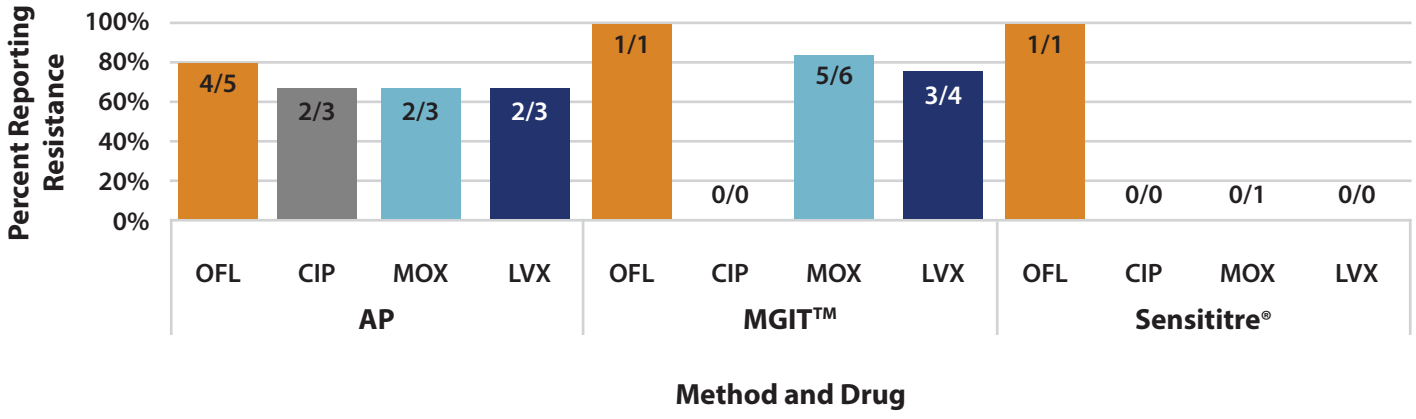
*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT™. Molecular expected results performed by whole genome sequencing.

‡80% consensus for a single categorical result across all methods reported for this drug of susceptible or resistant was not achieved for these isolates among participating laboratories.

Ofloxacin and Ciprofloxacin

DNA sequencing of *gyrA* in Isolate 2024B detected a C>T point mutation in *gyrA* resulting in wild-type alanine being replaced with valine at codon 90 (Ala90Val). The Ala90Val mutation has been associated with low-level FQ resistance, and the MIC for isolates with this mutation could be close to the critical concentration tested thereby impacting reproducibility [3, 10, 11]. Sequencing of the *gyrB* locus for this isolate revealed no mutations (i.e., wild-type sequence).

Figure 8. Isolate 2024B: Percent of laboratories reporting OFL, CIP, MOX, and LVX resistance, by growth-based method



Note—Three of the laboratories performing Sensititre® reported FQ MIC values for OFL as 8 µg/ml (n=2), MOX as 2 µg/ml (n=3), and LVX as 4 µg/ml (n=1).

Complete first-line DST, second-line DST, and molecular results submitted by all participants for Isolate 2024B are listed in Tables 11–18.

Table 11. Isolate 2024B: Participant Results for First-Line DST by AP

Drug	Susceptible	Resistant	Total
Rifampin	10	0	10
Isoniazid—Low	9	0	9
Isoniazid—High	9	0	9
Ethambutol	9	0	9

Table 12. Isolate 2024B: Participant Results for First-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Rifampin	49	0	49*
Isoniazid—Low	49	0	49*
Isoniazid—High	19	0	19
Ethambutol	49	0	49*
Pyrazinamide	45	0	45*

*One additional laboratory reported 'Contaminated/No Growth' for RIF, INH-Low, EMB, and PZA by MGIT™.

Table 13. Isolate 2024B: Participant Results for First-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Rifampin	2	0	2
Isoniazid—Low	1	0	1
Isoniazid—High	2	0	2
Ethambutol	2	0	2

Table 14. Isolate 2024B: Participant Results for First-Line DST by VersaTREK™

Drug	Susceptible	Resistant	Total
Rifampin	1	0	1
Isoniazid—Low	1	0	1
Isoniazid—High	1	0	1
Ethambutol	1	0	1
Pyrazinamide	1	0	1

Table 15. Isolate 2024B: Participant Results for Second-Line DST by AP

Drug	Susceptible	Resistant	Total
Streptomycin	9	0	9
Ofloxacin	1	4	5
Ciprofloxacin	1	2	3
Moxifloxacin	1	2	3
Levofloxacin	1	2	3
Amikacin	7	0	7
Kanamycin	6	0	6
Capreomycin	6	0	6
Ethionamide	8	0	8
Rifabutin	5	0	5
Cycloserine	4	0	4
p-Aminosalicylic acid	5	0	5
Bedaquiline	0	0	0
Linezolid	0	0	0
Clofazimine	0	0	0

Table 16. Isolate 2024B: Participant Results for Second-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Streptomycin	16	0	16
Ofloxacin	0	1	1
Ciprofloxacin	0	0	0
Moxifloxacin	1	5	6
Levofloxacin	1	3	4
Amikacin	2	0	2
Kanamycin	1	0	1
Capreomycin	2	0	2
Ethionamide	3	0	3
Rifabutin	3	0	3
Cycloserine	0	0	0
p-Aminosalicylic acid	0	0	0
Bedaquiline	1	0	1
Linezolid	1	0	1
Clofazimine	2	0	2

Table 17.	Isolate 2024B: Participant Results for Second-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Streptomycin	2	0	2*
Ofloxacin	0	1	1*
Ciprofloxacin	0	0	0
Moxifloxacin	1	0	1*
Levofloxacin	0	0	0*
Amikacin	2	0	2*
Kanamycin	1	0	1*
Capreomycin	1	0	1
Ethionamide	1	0	1*
Rifabutin	2	0	2*
Cycloserine	0	0	0*
p-Aminosalicylic acid	2	0	2*
Bedaquiline	0	0	0
Linezolid	1	0	1
Clofazimine	0	0	0

*One additional laboratory reported 'No Interpretation' for STR, OFL, MOX, LVX, AMK, KAN, ETA, RBT, CYS, and PAS by Sensititre®.

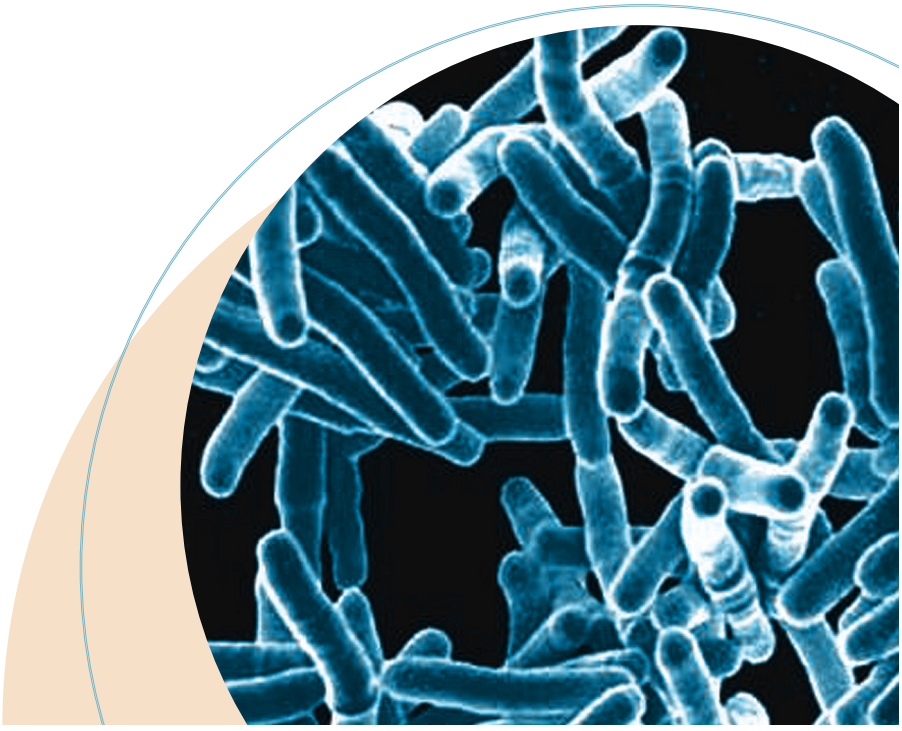


Table 18. Isolate 2024B: Participant Results for Molecular Testing

Drug	Mutation Not Detected	Mutation Detected	Total
Rifamycins (Rifampin, Rifabutin, Rifapentine)	13	0	13
Isoniazid	9	1*	10
Ethambutol	7	0	7
Pyrazinamide	6	0	6
Streptomycin	5	0	5
Fluoroquinolones (Ofloxacin, Ciprofloxacin, Moxifloxacin, Levofloxacin)	0	9†	9
Amikacin	9	0	9
Kanamycin	9	0	9
Capreomycin	8	0	8
Ethionamide	6	0	6
Cycloserine	1	0	1
p-Aminosalicylic acid	1	0	1
Bedaquiline	5	0	5
Linezolid	6	0	6
Clofazimine	5	0	5
Delamanid	1	0	1
Pretomanid	0	0	0

*This laboratory noted the detection of a silent *katG* mutation.

†Seven laboratories noted the detection of *gyrA* Ala90Val mutation.

Isolate 2024C

Expected Results:

Drug	Growth-based*	Molecular*
RIF	S	***rpoB*** wild-type
INH	R (high-level†)	***katG*** Ser315Leu; ***inhA*** & ***fabG1*** wild-type
EMB	S	***embB*** wild-type
PZA	S	***pncA*** wild-type
FQ	S	***gyrA*** & ***gyrB*** wild-type

Note: RIF=rifampin, INH=isoniazid, EMB=ethambutol, PZA=pyrazinamide, FQ=fluoroquinolones, S=susceptible, R=resistant

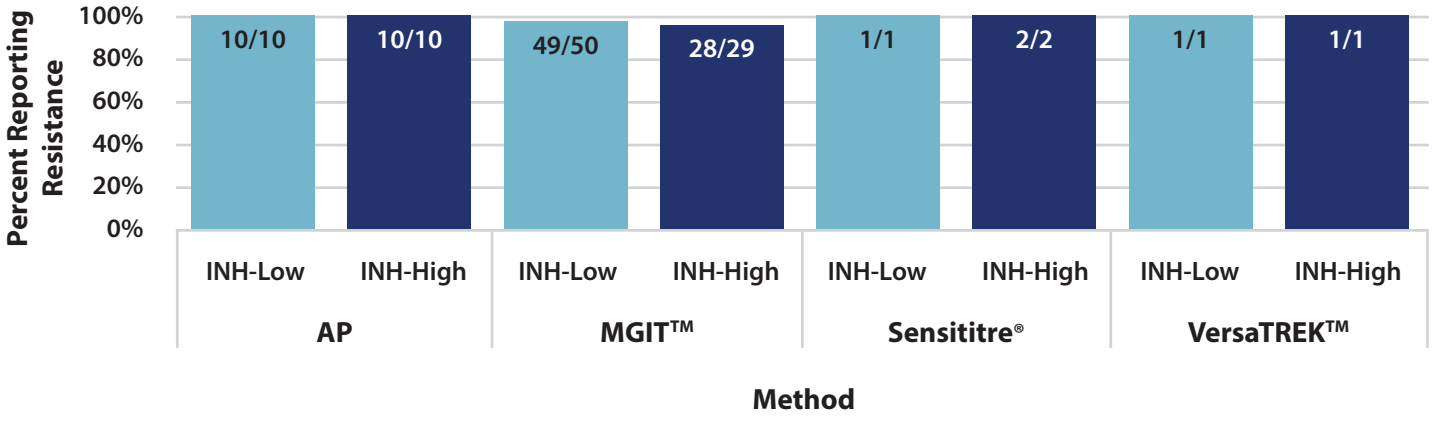
*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT™. Molecular expected results performed by whole genome sequencing.

†Resistant at 0.2 and 1.0 µg/ml by agar proportion. See Equivalent Critical Concentration table on page 8 for more information.

Isoniazid

DNA sequence analysis of *inhA*, *katG*, and *fabG1* of Isolate 2024C revealed a G>C point mutation in the *katG* locus resulting in wild-type serine being replaced by leucine at codon 315 (Ser315Leu); *inhA* and *fabG1* were wild-type (i.e., no mutations were detected). The *katG* Ser315Leu mutation is known to cause high-level INH resistance.

Figure 9. Isolate 2024C: Percent of laboratories reporting INH-Low and INH-High resistance, by growth-based method



Note—Two of the laboratories performing Sensititre® reported INH MIC values as 2 µg/ml (n=2).

Complete first-line DST, second-line DST, and molecular results submitted by all participant for Isolate 2024C are listed in Tables 19–26.

Table 19. Isolate 2024C: Participant Results for First-Line DST by AP

Drug	Susceptible	Resistant	Total
Rifampin	11	0	11
Isoniazid—Low	0	10	10
Isoniazid—High	0	10	10
Ethambutol	10	0	10

Table 20. Isolate 2024C: Participant Results for First-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Rifampin	50	0	50
Isoniazid—Low	1	49	50
Isoniazid—High	1	28	29
Ethambutol	50	0	50
Pyrazinamide	39	4	43*

*One additional laboratory reported 'Contaminated/No Growth' and two additional laboratories reported 'No Interpretation' for PZA by MGIT™.

Table 21. Isolate 2024C: Participant Results for First-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Rifampin	2	0	2
Isoniazid—Low	0	1	1
Isoniazid—High	0	2	2
Ethambutol	2	0	2

Table 22. Isolate 2024C: Participant Results for First-Line DST by VersaTREK™

Drug	Susceptible	Resistant	Total
Rifampin	1	0	1
Isoniazid—Low	0	1	1
Isoniazid—High	0	1	1
Ethambutol	1	0	1
Pyrazinamide	1	0	1

Table 23. Isolate 2024C: Participant Results for Second-Line DST by AP

Drug	Susceptible	Resistant	Total
Streptomycin	10	0	10
Ofloxacin	5	0	5
Ciprofloxacin	3	0	3
Moxifloxacin	3	0	3
Levofloxacin	3	0	3
Amikacin	7	0	7
Kanamycin	6	0	6
Capreomycin	6	0	6
Ethionamide	8	0	8
Rifabutin	5	0	5
Cycloserine	4	0	4
p-Aminosalicylic acid	5	0	5
Bedaquiline	0	0	0
Linezolid	0	0	0
Clofazimine	0	0	0

Table 24. Isolate 2024C: Participant Results for Second-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Streptomycin	18	0	18
Ofloxacin	1	0	1
Ciprofloxacin	0	0	0
Moxifloxacin	7	0	7
Levofloxacin	4	0	4
Amikacin	3	0	3
Kanamycin	1	0	1
Capreomycin	3	0	3
Ethionamide	4	0	4
Rifabutin	3	0	3
Cycloserine	0	0	0
p-Aminosalicylic acid	0	0	0
Bedaquiline	1	0	1
Linezolid	1	0	1
Clofazimine	2	0	2

Table 25.	Isolate 2024C: Participant Results for Second-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Streptomycin	2	0	2*
Ofloxacin	1	0	1*
Ciprofloxacin	0	0	0
Moxifloxacin	1	0	1*†
Levofloxacin	1	0	1
Amikacin	2	0	2*
Kanamycin	1	0	1*
Capreomycin	1	0	1*
Ethionamide	1	0	1*
Rifabutin	2	0	2*
Cycloserine	0	0	0*†
p-Aminosalicylic acid	1	0	1*†
Bedaquiline	0	0	0
Linezolid	1	0	1
Clofazimine	0	0	0

*One additional laboratory reported 'No Interpretation' for STR, OFL, MOX, LVX, AMK, KAN, ETA, RBT, CYC, and PAS by Sensititre®.

†One additional laboratory reported 'No Interpretation' for MOX, CYC, and PAS by Sensititre®.

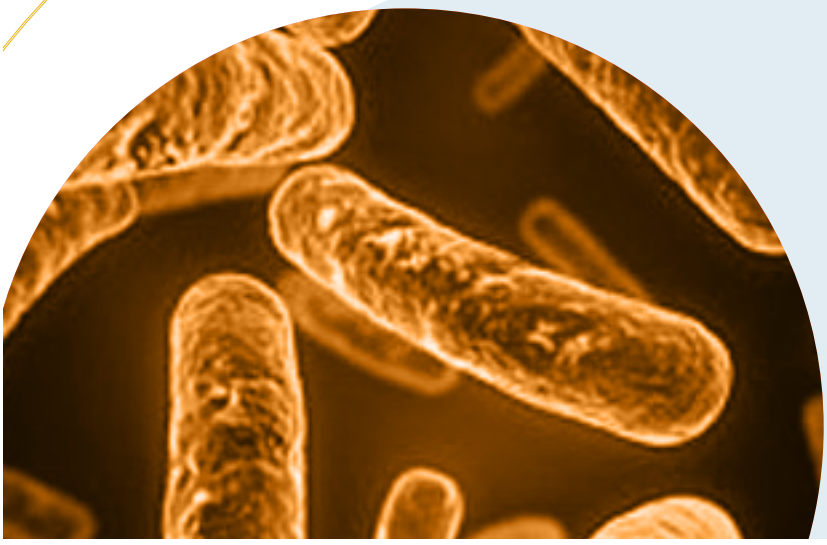


Table 26. Isolate 2024C: Participant Results for Molecular Testing

Drug	Mutation Not Detected	Mutation Detected	Total
Rifamycins (Rifampin, Rifabutin, Rifapentine)	13	0	13
Isoniazid	0	10*	10
Ethambutol	7	0	7
Pyrazinamide	6	0	6
Streptomycin	5	0	5
Fluoroquinolones (Ofloxacin, Ciprofloxacin, Moxifloxacin, Levofloxacin)	8	1†	9
Amikacin	9	0	9
Kanamycin	9	0	9
Capreomycin	8	0	8
Ethionamide	6	0	6
Cycloserine	1	0	1
p-Aminosalicylic acid	1	0	1
Bedaquiline	5	0	5
Linezolid	6	0	6
Clofazimine	5	0	5
Delamanid	1	0	1
Pretomanid	0	0	0

*Eight laboratories noted the detection of *katG* Ser315Leu mutation.

†This laboratory noted the detection of a *gyrA* mutation not associated with FQ resistance.

Isolate 2024D

Expected Results:

Drug	Growth-based*	Molecular*
RIF	R	***rpoB*** **Ser450Leu**
INH	S	***katG***, ***inhA***, & ***fabG1*** **wild-type**
EMB	S	***embB*** **wild-type**
PZA	S	***pncA*** **wild-type**
FQ	S	***gyrA*** & ***gyrB*** **wild-type**

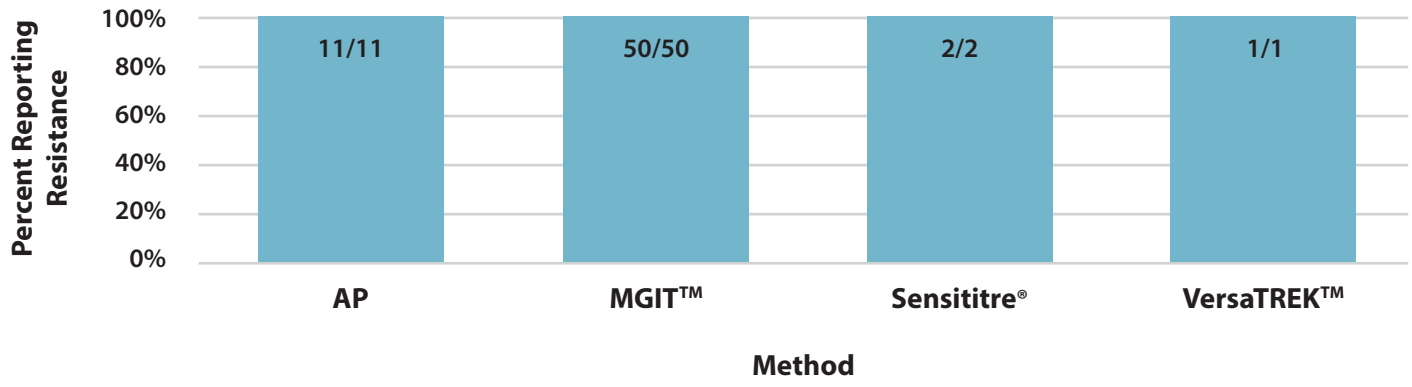
Note: RIF=rifampin, INH=isoniazid, EMB=ethambutol, PZA=pyrazinamide, FQ=fluoroquinolones, S=susceptible, R=resistant

*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT™. Molecular expected results performed by whole genome sequencing.

Rifampin

DNA sequence analysis of *rpoB* in Isolate 2024D revealed a C>T point mutation in codon 450 resulting in wild-type serine being replaced by leucine (Ser450Leu). Isolates with Ser450Leu mutations are associated with RIF resistance and should reliably test as resistant in growth-based assays [12-14].

Figure 10. Isolate 2024D: Percent of laboratories reporting RIF resistance, by growth-based method



Note—Two of the laboratories performing Sensititre® reported RIF MIC values as 16.0 µg/ml (n=1) and >16 µg/ml (n=1).

Complete first-line DST, second-line DST, and molecular results submitted by all participants for Isolate 2024D are listed in Tables 27–34.

Table 27. Isolate 2024D: Participant Results for First-Line DST by AP

Drug	Susceptible	Resistant	Total
Rifampin	0	11	11
Isoniazid—Low	9	1	10
Isoniazid—High	10	0	10
Ethambutol	10	0	10

Table 28. Isolate 2024D: Participant Results for First-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Rifampin	0	50	50
Isoniazid—Low	50	0	50
Isoniazid—High	20	0	20
Ethambutol	50	0	50
Pyrazinamide	44	2	46

Table 29. Isolate 2024D: Participant Results for First-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Rifampin	0	2	2
Isoniazid—Low	1	0	1
Isoniazid—High	2	0	2
Ethambutol	2	0	2

Table 30. Isolate 2024D: Participant Results for First-Line DST by VersaTREK™

Drug	Susceptible	Resistant	Total
Rifampin	0	1	1
Isoniazid—Low	1	0	1
Isoniazid—High	1	0	1
Ethambutol	1	0	1
Pyrazinamide	1	0	1

Table 31. Isolate 2024D: Participant Results for Second-Line DST by AP

Drug	Susceptible	Resistant	Total
Streptomycin	10	0	10
Ofloxacin	5	0	5
Ciprofloxacin	3	0	3
Moxifloxacin	3	0	3
Levofloxacin	3	0	3
Amikacin	7	0	7
Kanamycin	6	0	6
Capreomycin	6	0	6
Ethionamide	8	0	8
Rifabutin	0	5	5
Cycloserine	4	0	4
p-Aminosalicylic acid	5	0	5
Bedaquiline	0	0	0
Linezolid	0	0	0
Clofazimine	0	0	0

Table 32. Isolate 2024D: Participant Results for Second-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Streptomycin	17	0	17
Ofloxacin	1	0	1
Ciprofloxacin	0	0	0
Moxifloxacin	7	0	7
Levofloxacin	4	0	4
Amikacin	3	0	3
Kanamycin	1	0	1
Capreomycin	3	0	3
Ethionamide	4	0	4
Rifabutin	4	0	4
Cycloserine	0	0	0
p-Aminosalicylic acid	0	0	0
Bedaquiline	1	0	1
Linezolid	1	0	1
Clofazimine	2	0	2

Table 33. Isolate 2024D: Participant Results for Second-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Streptomycin	2	0	2*
Ofloxacin	1	0	1*
Ciprofloxacin	0	0	0
Moxifloxacin	1	0	1*†
Levofloxacin	1	0	1
Amikacin	2	0	2*
Kanamycin	1	0	1*
Capreomycin	1	0	1
Ethionamide	1	0	1*
Rifabutin	0	2	2*
Cycloserine	0	0	0*†
p-Aminosalicylic acid	2	0	2*
Bedaquiline	0	0	0
Linezolid	1	0	1
Clofazimine	0	0	0

*One additional laboratory reported 'No Interpretation' for STR, OFL, MOX, LVX, AMK, KAN, ETA, RBT, CYC, and PAS by Sensititre®.

†One additional laboratory reported 'No Interpretation' for MOX and CYC by Sensititre®.

Table 34. Isolate 2024D: Participant Results for Molecular Testing

Drug	Mutation Not Detected	Mutation Detected	Total
Rifamycins (Rifampin, Rifabutin, Rifapentine)	0	14*	14
Isoniazid	9	1†	10
Ethambutol	7	0	7
Pyrazinamide	6	0	6
Streptomycin	5	0	5
Fluoroquinolones (Ofloxacin, Ciprofloxacin, Moxifloxacin, Levofloxacin)	8	1¥	9
Amikacin	9	0	9
Kanamycin	9	0	9
Capreomycin	8	0	8
Ethionamide	6	0	6
Cycloserine	1	0	1
p-Aminosalicylic acid	1	0	1
Bedaquiline	5	0	5
Linezolid	6	0	6
Clofazimine	5	0	5
Delamanid	1	0	1
Pretomanid	0	0	0

*Eight laboratories noted the detection of *rpoB* Ser450Thr mutation. Additionally, three laboratories performing Xpert® MTB/RIF assay noted Probe E.

†This laboratory noted the detection of a silent *katG* mutation.

¥This laboratory noted the detection of *gyrA* mutation not associated with FQ resistance.

Isolate 2024E

Expected Results:

Drug	Growth-based*	Molecular*
RIF	S	***rpoB*** wild-type
INH	S	***katG, inhA*** & ***fabG1*** wild-type
EMB	S	***embB*** wild-type
PZA	R	***pncA*** His57Asp
FQ	S	***gyrA*** & ***gyrB*** wild-type

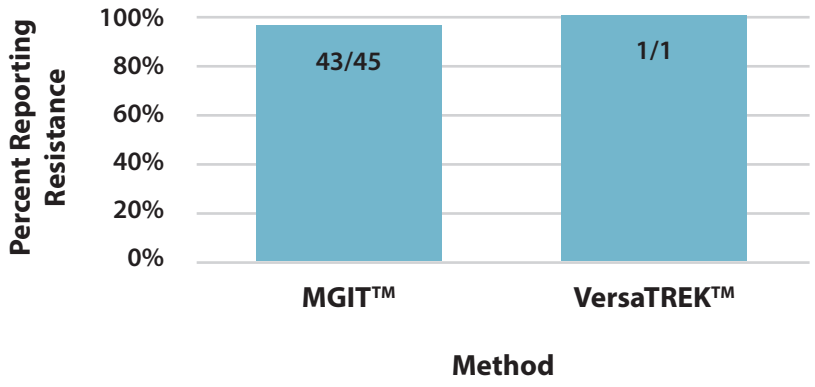
Note: RIF=rifampin, INH=isoniazid, EMB=ethambutol, PZA=pyrazinamide, FQ=fluoroquinolones, S=susceptible, R=resistant

*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT™. Molecular expected results performed by whole genome sequencing.

Pyrazinamide

DNA sequence analysis of *pncA* in Isolate 2024E revealed a single point mutation of C>G at nucleotide position 169 of the *pncA* gene resulting in aspartic acid replacing histidine at codon 57 (His57Asp). *M. bovis* has inherent resistance to PZA caused by this characteristic His57Asp mutation. This substitution causes defective pyrazinamidase activity and confers natural PZA resistance in *M. bovis* strains, including BCG substrains [15, 16].

Figure 11. Isolate 2024E: Percent of laboratories reporting PZA resistance, by growth-based method



Complete first-line DST, second-line DST, and molecular results submitted by all participants for Isolate 2024E are listed in Tables 35–42.

Table 35. Isolate 2024E: Participant Results for First-Line DST by AP

Drug	Susceptible	Resistant	Total
Rifampin	10	0	10
Isoniazid—Low	9	0	9
Isoniazid—High	9	0	9
Ethambutol	9	0	9

Table 36. Isolate 2024E: Participant Results for First-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Rifampin	50	0	50
Isoniazid—Low	48	2	50
Isoniazid—High	19	0	19
Ethambutol	50	0	50
Pyrazinamide	2	43	45

Table 37. Isolate 2024E: Participant Results for First-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Rifampin	2	0	2
Isoniazid—Low	1	0	1
Isoniazid—High	2	0	2
Ethambutol	2	0	2

Table 38. Isolate 2024E: Participant Results for First-Line DST by VersaTREK™

Drug	Susceptible	Resistant	Total
Rifampin	1	0	1
Isoniazid—Low	1	0	1
Isoniazid—High	1	0	1
Ethambutol	1	0	1
Pyrazinamide	0	1	1

Table 39. Isolate 2024E: Participant Results for Second-Line DST by AP

Drug	Susceptible	Resistant	Total
Streptomycin	9	0	9
Ofloxacin	5	0	5
Ciprofloxacin	3	0	3
Moxifloxacin	3	0	3
Levofloxacin	3	0	3
Amikacin	7	0	7
Kanamycin	6	0	6
Capreomycin	6	0	6
Ethionamide	8	0	8
Rifabutin	5	0	5
Cycloserine	4	0	4
p-Aminosalicylic acid	5	0	5
Bedaquiline	0	0	0
Linezolid	0	0	0
Clofazimine	0	0	0

Table 40. Isolate 2024E: Participant Results for Second-Line DST by MGIT™

Drug	Susceptible	Resistant	Total
Streptomycin	16	0	16
Ofloxacin	1	0	1
Ciprofloxacin	0	0	0
Moxifloxacin	7	0	7
Levofloxacin	4	0	4
Amikacin	2	0	2
Kanamycin	1	0	1
Capreomycin	2	0	2
Ethionamide	2	1	3
Rifabutin	3	0	3
Cycloserine	0	0	0
p-Aminosalicylic acid	0	0	0
Bedaquiline	1	0	1
Linezolid	1	0	1
Clofazimine	2	0	2

Table 41. Isolate 2024E: Participant Results for Second-Line DST by Sensititre®

Drug	Susceptible	Resistant	Total
Streptomycin	2	0	2*
Ofloxacin	1	0	1*
Ciprofloxacin	0	0	0
Moxifloxacin	1	0	1*†
Levofloxacin	1	0	1
Amikacin	2	0	2*
Kanamycin	1	0	1*
Capreomycin	1	0	1
Ethionamide	1	0	1*
Rifabutin	2	0	2*
Cycloserine	0	0	0*†
p-Aminosalicylic acid	1	0	1*†
Bedaquiline	0	0	0
Linezolid	1	0	1
Clofazimine	0	0	0

*One additional laboratory reported 'No Interpretation' for OFL, MOX, AMK, KAN, ETA, RBT, CYC, and PAS by Sensititre®.

†One additional laboratory reported 'No Interpretation' for MOX, CYC, and PAS by Sensititre®.

Table 42. Isolate 2024E: Participant Results for Molecular Testing

Drug	Mutation Not Detected	Mutation Detected	Total
Rifamycins (Rifampin, Rifabutin, Rifapentine)	13	0	13
Isoniazid	9	1*	10
Ethambutol	6	1†	7
Pyrazinamide	0	8¥	8
Streptomycin	5	0	5
Fluoroquinolones (Ofloxacin, Ciprofloxacin, Moxifloxacin, Levofloxacin)	7	2§€	9
Amikacin	9	0	9
Kanamycin	9	0	9
Capreomycin	8	0	8
Ethionamide	6	0	6
Cycloserine	1	0	1
p-Aminosalicylic acid	1	0	1
Bedaquiline	5	0	5
Linezolid	6	0	6
Clofazimine	5	0	5
Delamanid	1	0	1
Pretomanid	0	0	0

*This laboratory noted the detection of silent *katG* mutation.

†This laboratory noted the detection of silent *embB* mutation not associated with resistance.

¥Five laboratories noted the detection of *pncA* His57Asp mutation.

§One laboratory noted the detection of *gyrA* mutation not associated with resistance.

€One laboratory noted the detection of *gyrB* mutation with uncertain significance.

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Appendix 1: Accessible Explanations of Figures

Figure 1. The primary classification of the 55 laboratories participating in the March 2024 MPEP panel is shown in this pie chart. The largest slice represents 44 laboratories, or 78% of 55 that have self-classified as a health department laboratory. The next major slice signifies 5 laboratories, or 9% of 55 that self-classified as hospital laboratories. The remaining two slices of the pie chart represent 4, or 7% of 55 that self-classified as independent laboratories; and 3, or 6% of 55 that self-classified as federal government laboratories.

Figure 2. The annual volume of MTBC isolates tested for drug susceptibility by participating laboratories (N=55) in 2023 is displayed in this vertical bar graph. The vertical y–axis is the number of laboratories responding and ranges from 0 to 16 using increments of 2. Along the horizontal x-axis are eight vertical bars representing the number of isolates tested per year. From left to right, 15 laboratories tested less than or equal to 50 isolates per year; 14 laboratories tested between 51 to 100 isolates per year; 6 laboratories tested between 101 to 150 isolates per year; 5 laboratories tested between 151 to 200 isolates per year; 4 laboratories tested between 201 to 300 isolates per year; 1 laboratory tested between 301 to 500 isolates per year; 9 laboratories tested between 501 to 1000 isolates per year; and 1 laboratory tested greater than or equal to 1,001 isolates per year.

Figure 3. The drug susceptibility testing methods performed by MPEP participants (N=86) are displayed in this vertical bar graph. The vertical y-axis is the number of laboratories reporting with ranges from 0 to 60, by increments of 10, and the horizontal x- axis lists the susceptibility testing methods. Each bar represents the number of reporting laboratories performing a particular drug susceptibility test method. From left to right: 53 performed MGIT™, 13 performed agar proportion, 3 performed Sensititre®, 1 performed VersaTREK™, and 16 performed molecular methods.

Figure 4. The molecular methods performed by MPEP participants (N=16) are displayed in this pie chart. The largest slice represents the 7 laboratories that performed targeted DNA sequencing. The next three slices represent 4 laboratories that performed the Cepheid Xpert® MTB/RIF assay, 4 laboratories that performed whole genome sequencing, and 1 laboratory that performed the Bruker line probe assay.

Figure 5. The antituberculosis drugs tested by growth-based method by MPEP participants are displayed in a horizontal bar graph. The vertical y -axis contains a list of each drug tested and the horizontal x-axis contains the number of laboratories with ranges from 0 to 60, by increments of 10. There are 22 horizontal bars with each bar representing the number of laboratories reporting a result for a particular drug for susceptibility testing. 54 laboratories tested rifampin; 54 laboratories tested isoniazid; 54 laboratories tested ethambutol; 47 laboratories tested pyrazinamide; 28 laboratories tested streptomycin; 8 laboratories tested ofloxacin; 12 laboratories tested moxifloxacin; 3 laboratories tested ciprofloxacin; 8 laboratories tested levofloxacin; 10 laboratories tested capreomycin; 9 laboratories tested kanamycin; 13 laboratories tested amikacin; 13 laboratories tested ethionamide; 8 laboratories tested PAS; 12 laboratories tested rifabutin; 6 laboratories tested cycloserine; 0 laboratories tested rifapentine; 1 laboratory tested bedaquiline; 2 laboratories tested linezolid; 2 laboratories tested clofazimine; 0 laboratories tested delamanid; and 0 laboratories tested pretomanid.

Figure 6. The percent of laboratories reporting resistance to isoniazid (low and high concentrations), by growth-based method, for isolate 2024A is displayed in this vertical bar graph. The vertical y-axis is the percent of laboratories reporting resistance with ranges from 0% to 100%, by increments of 20, and the horizontal x-axis lists the method and drugs. Each bar represents the percent of laboratories reporting resistance. From left to right: laboratories performing agar proportion for INH-Low is 7 of 9 (78%) reporting resistance and INH-High is 0 of 9 (0%) reporting resistance; laboratories performing MGIT™ for INH-Low is 47 of 49 (96%) reporting resistance and INH-High is 1 of 28 (4%) reporting resistance; laboratories performing Sensititre® for INH-Low is 1 of 1 (100%) reporting resistance and INH-High is 0 of 1 (0%) reporting resistance; and laboratories performing VersaTREK™ for INH-Low is 1 of 1 (100%) reporting resistance and INH-High is 0 of 1 (0%) reporting resistance.

Figure 7. The percent of laboratories reporting resistance to ethionamide, by growth-based method, for isolate 2024A is displayed in this vertical bar graph. The vertical y-axis is the percent of laboratories reporting resistance with ranges from 0% to 100%, by increments of 20, and the horizontal x-axis lists the method. Each bar represents the percent of laboratories reporting resistance. From left to right: laboratories performing agar proportion for ethionamide is 4 of 8 (50%) reporting resistance; laboratories performing MGIT™ for ethionamide is 3 of 3 (100%) reporting resistance; and laboratories performing Sensititre® for ethionamide is 0 of 1 (0%) reporting resistance.

Figure 8. The percent of laboratories reporting resistance to ofloxacin, ciprofloxacin, moxifloxacin, and levofloxacin, by growth-based method, for isolate 2024B is displayed in this vertical bar graph. The vertical y-axis is the percent of laboratories reporting resistance with ranges from 0% to 100%, by increments of 20, and the horizontal x-axis lists the method and drugs. Each bar represents the percent of laboratories reporting resistance. From left to right: laboratories performing agar proportion for OFL is 4 of 5 (80%) reporting resistance, CIP is 2 of 3 (67%) reporting resistance, MOX is 2 of 3 (67%) reporting resistance, LVX is 2 of 3 (67%) reporting resistance; laboratories performing MGIT™ for OFL is 1 of 1 (100%) reporting resistance, CIP is 0 of 0 (0%) reporting resistance, MOX is 5 of 6 (83%) reporting resistance, LVX is 3 of 4 (75%) reporting resistance; and laboratories performing Sensititre® for OFL is 1 of 1 (100%) reporting resistance, CIP is 0 of 0 (0%) reporting resistance, MOX is 0 of 1 (0%) reporting resistance, LVX is 0 of 0 (0%) reporting resistance.

Figure 9. The percent of laboratories reporting resistance to isoniazid (low and high concentrations), by growth-based method, for isolate 2024C is displayed in this vertical bar graph. The vertical y-axis is the percent of laboratories reporting resistance with ranges from 0% to 100%, by increments of 20, and the horizontal x-axis lists the method and drugs. Each bar represents the percent of laboratories reporting resistance. From left to right: laboratories performing agar proportion for INH-Low is 10 of 10 (100%) reporting resistance and INH-High is 10 of 10 (100%) reporting resistance; laboratories performing MGIT™ for INH-Low is 49 of 50 (98%) reporting resistance and INH-High is 28 of 29 (97%) reporting resistance; laboratories performing Sensititre® for INH-Low is 1 of 1 (100%) reporting resistance and INH-High is 2 of 2 (100%) reporting resistance; and laboratories performing VersaTREK™ for INH-Low is 1 of 1 (100%) reporting resistance and INH-High is 1 of 1 (100%) reporting resistance.

Figure 10. The percent of laboratories reporting resistance to rifampin, by growth-based method, for 2024D is displayed in this vertical bar graph. The vertical y-axis is the percent of laboratories reporting resistance with ranges from 0% to 100%, by increments of 20, and the horizontal x-axis lists the method. Each bar represents the percent of laboratories reporting resistance. From left to right: laboratories performing agar proportion for rifampin is 11 of 11 (100%) reporting resistance; laboratories performing MGIT™ for rifampin is 50 of 50 (100%) reporting resistance; laboratories performing Sensititre® for rifampin is 2 of 2 (100%) reporting resistance; and laboratories performing VersaTREK™ for rifampin is 1 of 1 (100%) reporting resistance.

Figure 11. The percent of laboratories reporting resistance to pyrazinamide, by growth-based method, for isolate 2024E is displayed in this vertical bar graph. The vertical y-axis is the percent of laboratories reporting resistance with ranges from 0% to 100%, by increments of 20, and the horizontal x-axis lists the method. Each bar represents the percent of laboratories reporting resistance. From left to right: laboratories performing MGIT™ for pyrazinamide is 43 of 45 (96%) reporting resistance; and laboratories performing VersaTREK™ for pyrazinamide is 1 of 1 (100%) reporting resistance.