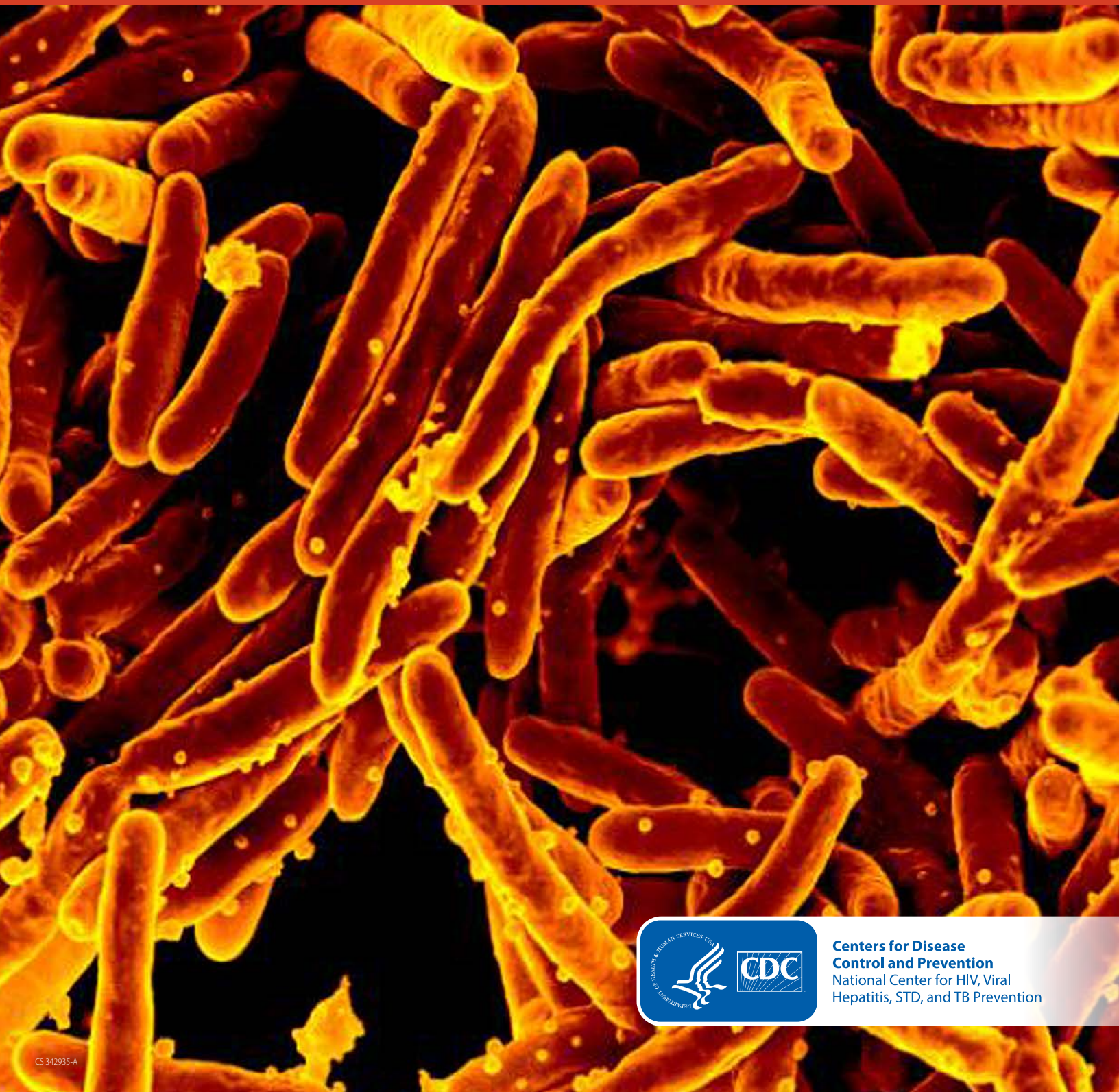
For accessible version: https://www.cdc.gov/tb/topic/laboratory/mpep/2023/march-mpepReport.htm.

# *Mycobacterium tuberculosis* Complex Drug Susceptibility Testing Program

## Model Performance Evaluation Program Report of Results
## March 2023



**Centers for Disease Control and Prevention**
National Center for HIV, Viral Hepatitis, STD, and TB Prevention

CS 342935-A

# Contents

# *Mycobacterium tuberculosis* Complex Drug Susceptibility Testing Report for March 2023 Survey

## 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 survey sent to participants in March 2023.

## Report Content

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## 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™ 960—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, *Nocardiae* spp., and Other Aerobic Actinomycetes" and "M24S: Performance Standards for Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes" [1-3]. Additionally, the World Health Organization (WHO) published two technical reports investigating critical concentrations, by method, for anti-tuberculosis drugs [4, 5].

# Expected Drug Susceptibility Testing Results

Anticipated growth-based and molecular results for the panel of MTBC isolates sent to participants in March 2023 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 [6].

### Table 1. Expected Growth-based Results for March 2023 Survey

Note—S=susceptible, R=resistant

| Isolate | RIF | INH | EMB | PZA | Second-line Drug Resistances: |
|---|---|---|---|---|---|
| 2023A | S | R (high-level*) | R | S | STR†, ETA† |
| 2023B | R | S | S | S | |
| 2023C | R | S | S | S | |
| 2023D | R | S | S | S | |
| 2023E | S | S | S | S | AMK, KAN, CAP |

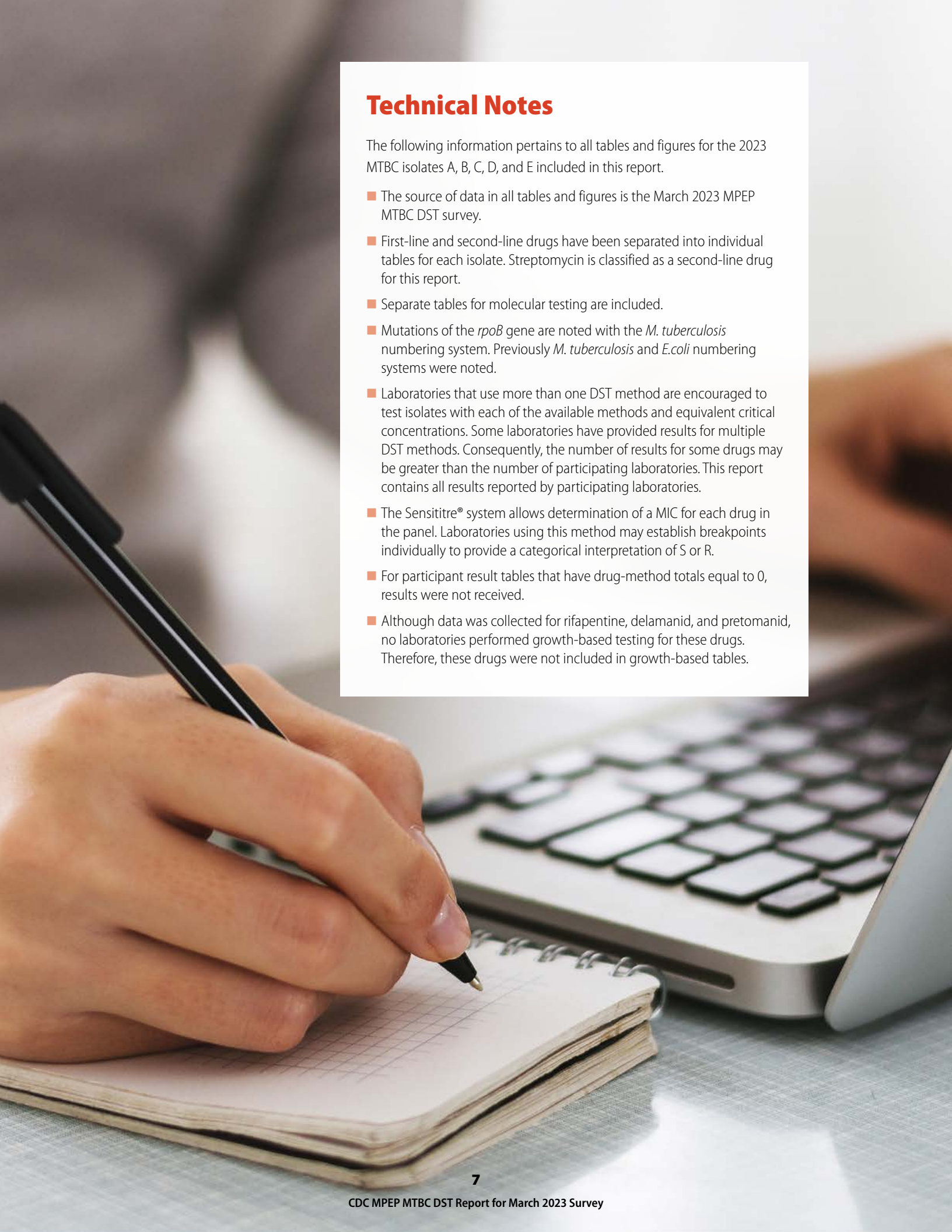
*Resistant at 0.2 µg/ml and 1.0 µg/ml by agar proportion. See Equivalent Critical Concentration table on page 8 for more information.
†Resistance to STR and ETA was not included on Expected Results report.

### Table 2. Expected Molecular Results (Mutations Detected in Loci Associated with Resistance) for March 2023 Survey

Note—Empty cell=No mutation detected

| Isolate | *rpoB** | *katG* | *embB* | *pncA* | *rrs* | *ethA* |
|---|---|---|---|---|---|---|
| 2023A | | Ser315Thr<br>Arg463Leu† | Met306Val | Ser65Ser† | | Partial deletion |
| 2023B | His445Tyr | | | | | |
| 2023C | Ser450Leu | | | | | |
| 2023D | Val170Phe | | | Thr135Ala◊ | | |
| 2023E | | | | | A1401G | |

* M. tuberculosis numbering system used [7, 8]
† Mutation not associated with resistance [9]
◊ Effect of mutation is unknown.



# Technical Notes

The following information pertains to all tables and figures for the 2023 MTBC isolates A, B, C, D, and E included in this report.

- The source of data in all tables and figures is the March 2023 MPEP MTBC DST survey.
- 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. Previously *M. tuberculosis* and *E.coli* numbering systems were noted.
- 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 a MIC for each drug in the panel. Laboratories using this method may establish breakpoints individually 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 performed growth-based testing for these drugs. Therefore, these drugs were not included in growth-based tables.

# 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 | 1.0† | 1.0 |
| Ethambutol | 5.0 | 7.5 |
| Pyrazinamide | Not recommended | Not recommended |

NOTE—Critical concentrations as indicated in CLSI M24-A2 document [1]

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

† CLSI critical concentrations for RIF differ from revised WHO recommendation of 0.5 µg/ml published in 2021 [1, 10].

| 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-A2 document [1]

*Breakpoints for establishing susceptibility have not been determined.

† CLSI critical concentrations differ from revised WHO recommendations published in 2018 [1, 4].

- 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 [4].

‡ Critical concentrations as indicated in WHO 2018 Technical Report on critical concentrations [4].

## Broth Based Media

| First-line Drugs | MGIT™ | VersaTREK™ |
|---|---|---|
| Isoniazid | 0.1 (and 0.4*) | 0.1 (and 0.4*) |
| Rifampin | 1.0† | 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

*The higher concentration of INH and EMB should be tested after resistance at the critical concentration is detected [2].

† CLSI critical concentrations for RIF differ from revised WHO recommendation of 0.5 µg/ml published in 2021 [10].

| Second-line Drug | 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 |
| *p*-Aminosalicylic acid | Not recommended† |
| Rifapentine | Not determined |
| Bedaquiline | 1.0 |
| Linezolid | 1.0 |
| Clofazimine | 1.0 |
| Delamanid | 0.06 |
| Pretomanid | Not determined |

NOTE—Critical concentrations as indicated in WHO 2018 Technical Report on critical concentrations unless noted otherwise [4]. 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 M62 recommendations published in 2018 [3, 4].

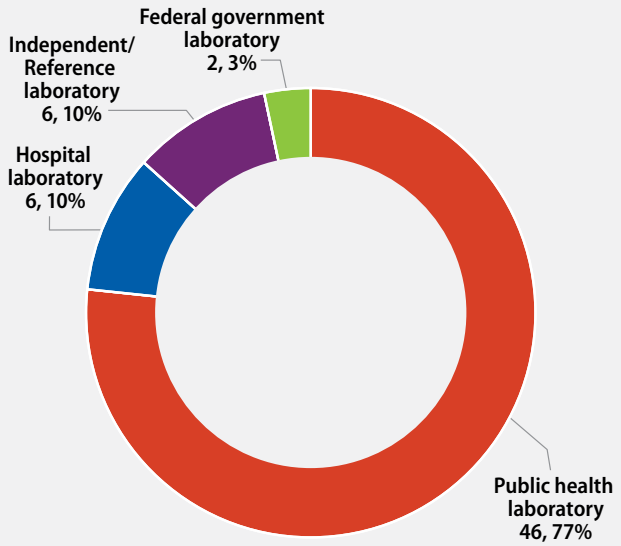
- For LVX, the CLSI recommended critical concentration for MGIT™ is 1.5 µg/ml.
- For PAS, the CLSI recommended critical concentration for MGIT™ is 4.0 µg/ml

# Descriptive Information about Participant Laboratories

## Primary Classification

This report contains DST results submitted to CDC by survey participants at 60 laboratories in 32 states, all of whom have participated in previous MPEP panels. Participants were asked to indicate the primary classification of their laboratory (Figure 1).

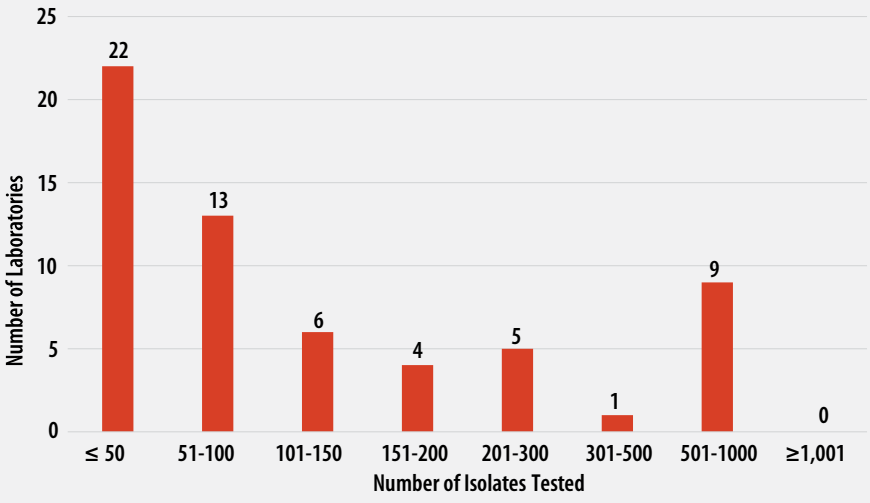
### Figure 1. Primary Classification of Participating Laboratories, March 2023




## Annual Number of MTBC Drug Susceptibility Tests Performed

The number of MTBC isolates tested for drug susceptibility by the 60 participants in 2022 (excluding isolates used for quality control) is shown in Figure 2. In 2022, the counts ranged from 0 to 922 tests. Participants at 22 (37%) 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 [11].

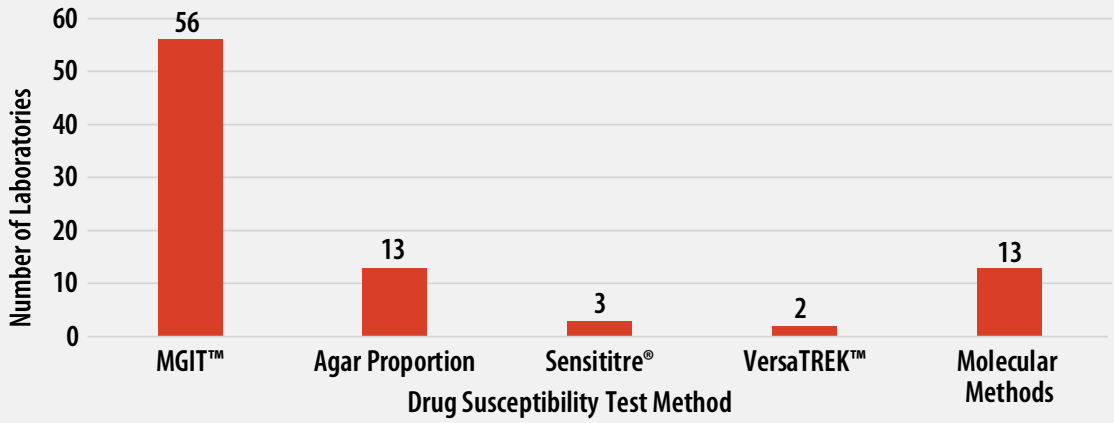
### Figure 2. Distribution of the Annual Volume of MTBC Isolates Tested for Drug Susceptibility by Participants in Previous Calendar Year (n=60)



## MTBC Drug Susceptibility Test Methods Performed by Participants

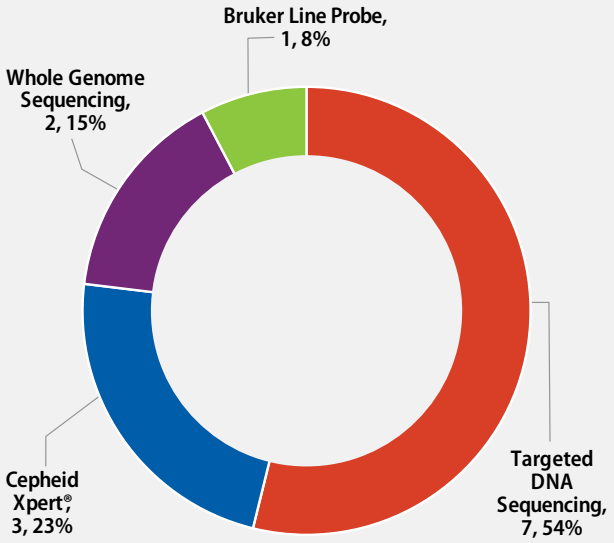
The DST methods that were performed by participating laboratories for this panel of MTBC isolates are displayed in Figure 3. Of participating laboratories, 37 (62%) reported results for only one method, 19 (32%) reported two methods, and 4 (7%) noted three susceptibility methods. Fifty-six (93%) participating laboratories indicated use of MGIT.

### Figure 3. MTBC Drug Susceptibility Test Methods Performed (n=87 responses)




Molecular methods reported by participants are shown in Figure 4. The method performed most frequently (54%) was targeted DNA sequencing.

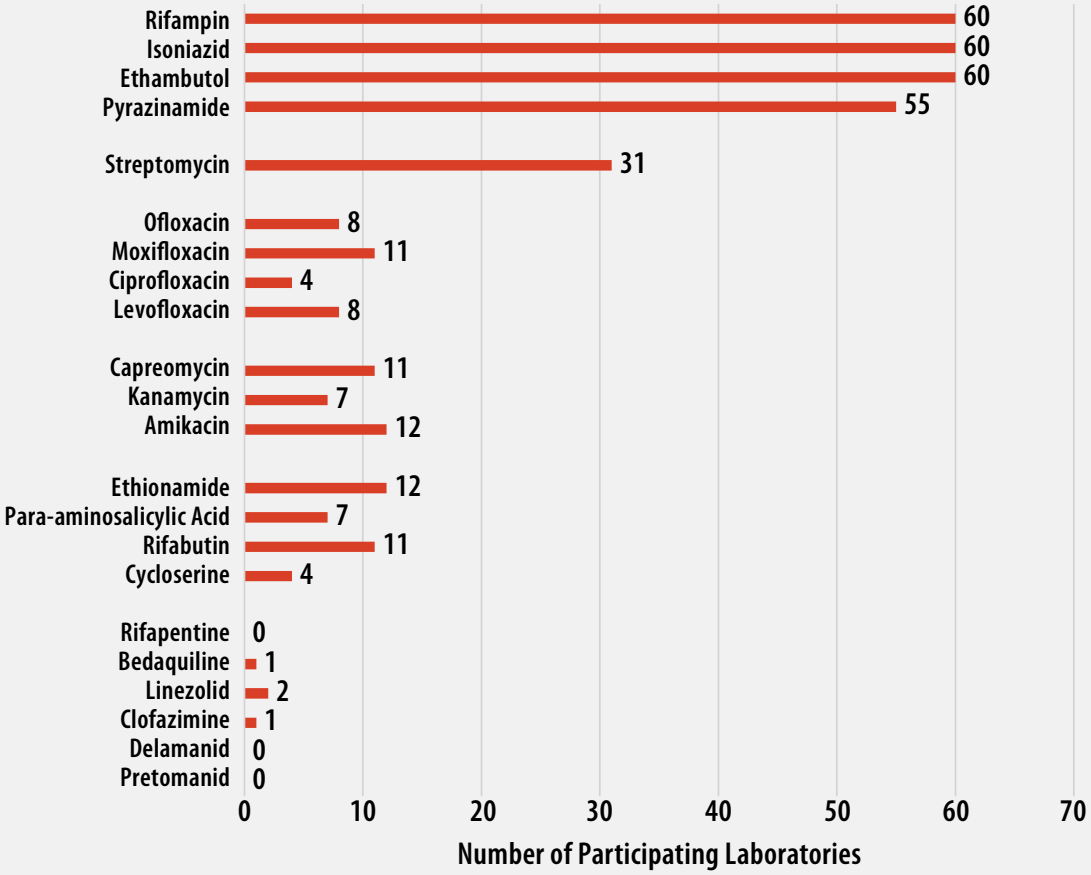
### Figure 4. Molecular Method Reported (n=13 responses)



## Antituberculosis Drugs Tested by Participants

The number of participating laboratories that reported testing each antituberculosis drug in the March 2023 survey is presented in Figure 5. CLSI recommends testing a full panel of first-line drugs (rifampin [RIF], isoniazid [INH], *etha*mbutol [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 to their testing panel as CDC recommends susceptibility testing for fluoroquinolones (e.g., moxifloxacin) with use of the alternate 4-month rifapentine-moxifloxacin treatment regimen; RIF may be used as a proxy for rifapentine [12]

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



# Isolate 2023A

## Expected Results:

| Drug | Growth-based* | Molecular* |
|---|---|---|
| RIF | S | *rpoB* wild-type |
| INH | R (high-level†) | *katG* Ser315Thr & Arg463Leu§ |
| EMB | R | *embB* Met306Val |
| PZA | S | *pncA* Ser65Ser§ |
| Fluoroquinolones | S | *gyrA* & *gyrB* wild-type |
| ETA | R | *ethA* partial deletion |
| STR | R | *rrs* or *rpsL* wild-type |

Note—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 and 1.0 µg/ml by agar proportion. See Equivalent Critical Concentration table on page 8 for more information.

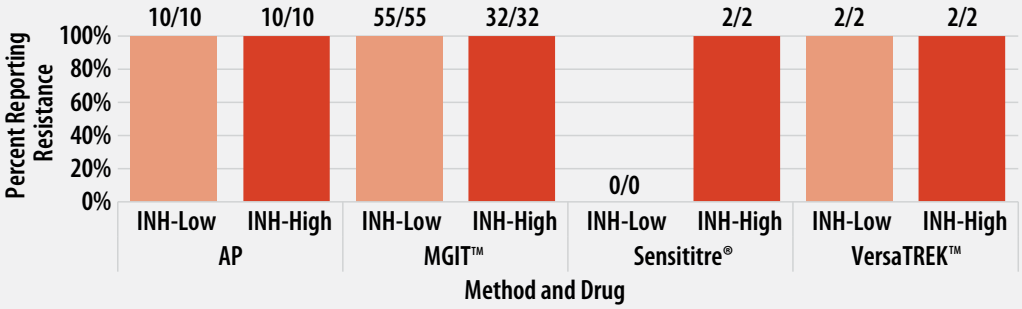
§ Mutation not associated with resistance. [9]

## Isoniazid

DNA sequence analysis of *inhA*, *katG*, *fabG1*, and *ahpC* of Isolate 2023A revealed a G>C point mutation in the *katG* locus resulting in wild-type serine being replaced by threonine at codon 315 (Ser315Thr); *inhA*, *fabG1*, and *ahpC* were wild-type (i.e., no mutations were detected). The Ser315Thr mutation confers resistance to INH at both the low and high concentrations [6, 9, 13].

For internal comparison purposes, this isolate was previously sent as MPEP 2020H where comparable results, by method, were reported as resistant for INH.

### Figure 6. Isolate 2023A: Percent of laboratories reporting INH-Low and INH-High resistance, by growth-based method.



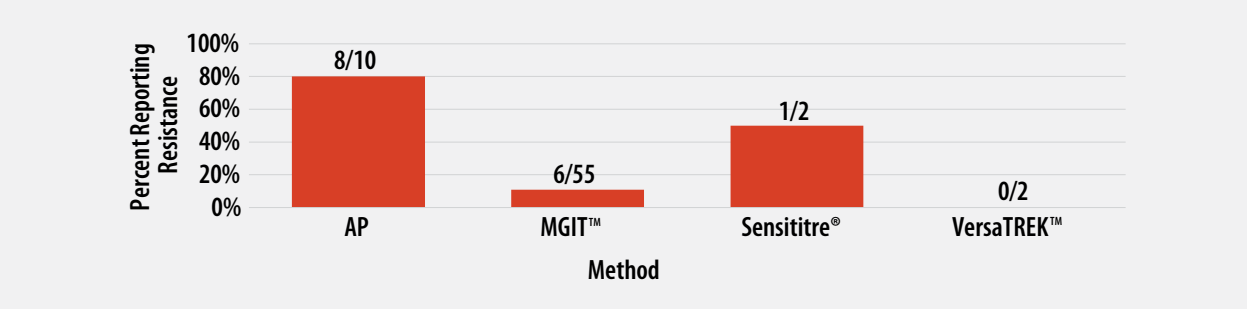

Note—Two laboratories performing Sensititre® reported INH MIC value as 4.0 µg/ml (n=2).

## Ethambutol

DNA sequence analysis of *embB* of Isolate 2023A revealed a A>G point mutation in the *embB* gene resulting in wild-type methionine being replaced by valine at codon 306 (Met306Val). Certain *embB* mutations at the 306 codon, such as Met306Val and Met306Leu, are associated with EMB resistance [6, 9].

For internal comparison purposes, this isolate was previously sent as MPEP 2020H where comparable results, by method, were reported.

**Figure 7. Isolate 2023A: Percent of laboratories reporting EMB resistance, by growth-based method.**



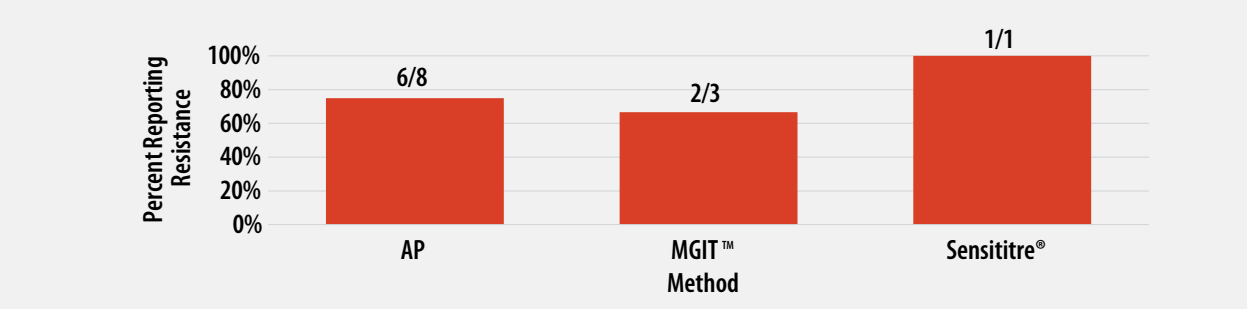

Note—Two of the laboratories performing Sensititre® reported EMB MIC values as 2.5 µg/ml (n=1) and 8 µg/ml (n=1).

## 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 a partial deletion of *ethA*; *inhA* and *fabG1* were wild-type (i.e., no mutations were detected).

For internal comparison purposes, this isolate was previously sent as MPEP 2020H where 64% (9/14) of AP results, 100% (3/3) of MGIT™ results, and 0% (0/1) of Sensititre® results were reported as resistant.

**Figure 8. Isolate 2023A: Percent of laboratories reporting ETA resistance, by growth-based method.**



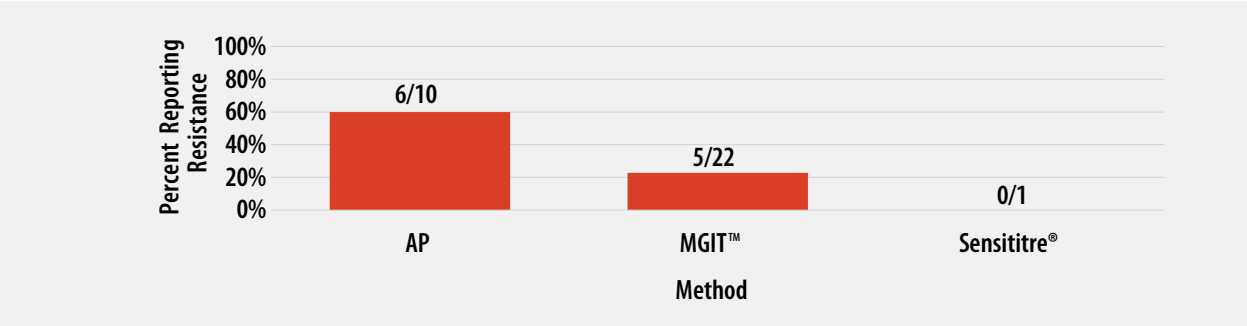

Note—One of the laboratories performing Sensititre® reported an ETA MIC value as 10 µg/ml (n=1).

## Streptomycin

DNA sequencing analysis did not reveal a mutation in *rrs* or *rpsL*; other mechanisms of resistance may be important.

For internal comparison purposes, this isolate was previously sent as MPEP 2020H where 76% (11/14) of AP results, 48% (16/33) of MGIT™ results, and 100% (1/1) of Sensititre® results were reported as resistant.

## Figure 9. Isolate 2023A: Percent of laboratories reporting STR resistance, by growth-based method.




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

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

## Table 3. Isolate 2023A—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 | 2 | 8 | 10 |

## Table 4. Isolate 2023A—Participant Results for First-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Rifampin | 54 | 1 | 55 |
| Isoniazid—Low | 0 | 55 | 55 |
| Isoniazid—High | 0 | 32 | 32 |
| Ethambutol | 49 | 6 | 55 |
| Pyrazinamide | 53 | 2 | 55 |

### Table 5. Isolate 2023A—Participant Results for First-Line DST by Sensititre®

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

### Table 6. Isolate 2023A—Participant Results for First-Line DST by VersaTREK™

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

### Table 7. Isolate 2023A—Participant Results for Second-Line DST by AP

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 4 | 6 | 10 |
| 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 | 7 | 0 | 7 |
| Ethionamide | 2 | 6 | 8 |
| Rifabutin | 5 | 0 | 5 |
| Cycloserine | 2 | 1 | 3 |
| *p*-Aminosalicylic acid | 5 | 0 | 5 |
| Bedaquiline | 0 | 0 | 0 |
| Linezolid | 0 | 0 | 0 |
| Clofazimine | 0 | 0 | 0 |

## Table 8. Isolate 2023A—Participant Results for Second-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 16 | 5 | 21 |
| Ofloxacin | 2 | 0 | 2 |
| Ciprofloxacin | 1 | 0 | 1 |
| Moxifloxacin | 8 | 0 | 8 |
| Levofloxacin | 5 | 0 | 5 |
| Amikacin | 3 | 0 | 3 |
| Kanamycin | 2 | 0 | 2 |
| Capreomycin | 3 | 0 | 3 |
| Ethionamide | 1 | 2 | 3 |
| Rifabutin | 4 | 0 | 4 |
| Cycloserine | 0 | 0 | 0 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 1 | 0 | 1 |
| Linezolid | 1 | 0 | 1 |
| Clofazimine | 1 | 0 | 1 |

## Table 9. Isolate 2023A—Participant Results for Second-Line DST by Sensititre®

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 1 | 0 | 1* |
| Ofloxacin | 1 | 0 | 1 |
| Ciprofloxacin | 0 | 0 | 0 |
| Moxifloxacin | 2 | 0 | 2 |
| Levofloxacin | 1 | 0 | 1 |
| Amikacin | 2 | 0 | 2 |
| Kanamycin | 1 | 0 | 1 |
| Capreomycin | 1 | 0 | 1 |
| Ethionamide | 0 | 1 | 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 'Indeterminate' for STR and 'No Interpretation' for CYC by Sensititre®.

## Table 10. Isolate 2023A—Participant Results for Molecular Testing

| Drug | Mutation Not Detected | Mutation Detected | Total |
|---|---|---|---|
| Rifamycins (Rifampin, Rifabutin, Rifapentine) | 11 | 0 | 11 |
| Isoniazid | 0 | 8* | 8 |
| Ethambutol | 0 | 5[†] | 5 |
| Pyrazinamide | 3 | 2[¥] | 5 |
| Streptomycin | 1 | 2[‡] | 3 |
| Ofloxacin | 6 | 1[ℓ] | 7 |
| Ciprofloxacin | 6 | 1[ℓ] | 7 |
| Moxifloxacin | 6 | 1[ℓ] | 7 |
| Levofloxacin | 6 | 1[ℓ] | 7 |
| Amikacin | 5 | 1[€] | 6 |
| Kanamycin | 4 | 2[€] | 6 |
| Capreomycin | 5 | 0 | 5 |
| Ethionamide | 3 | 1[§] | 4 |
| Cycloserine | 1 | 0 | 1 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 3 | 0 | 3 |
| Linezolid | 3 | 0 | 3 |
| Clofazimine | 3 | 0 | 3 |
| Delamanid | 1 | 0 | 1 |
| Pretomanid | 0 | 0 | 0 |

*Seven laboratories specifically noted the *katG* Ser315Thr mutation.

[†] All 5 laboratories noted the *embB* Met306Val mutation.

[¥] Both laboratories noted the *pncA* Ser65Ser mutation, specifically noting that it was not associated with PZA resistance.

[‡] One laboratory noted a frameshift deletion at 116 in gidB and one laboratory noted a deletion at 115 in gid_c.

[ℓ] This laboratory noted the detection of a gyrA mutation not associated with FQ resistance.

[€] Laboratories noted an eis C(-100)T mutation.

[§] This laboratory noted an *ethA* deletion.

# Isolate 2023B

## Expected Results:

| Drug | Growth-based* | Molecular* |
|---|---|---|
| **RIF** | R | ***rpoB* His445Tyr** |
| **INH** | S | ***katG*, *inhA*, & *fabG1* wild-type** |
| **EMB** | S | ***embB* wild-type** |
| **PZA** | S | ***pncA* wild-type** |
| **Fluoroquinolones** | S | ***gyrA* & *gyrB* wild-type** |

Note—S=susceptible, R=resistant

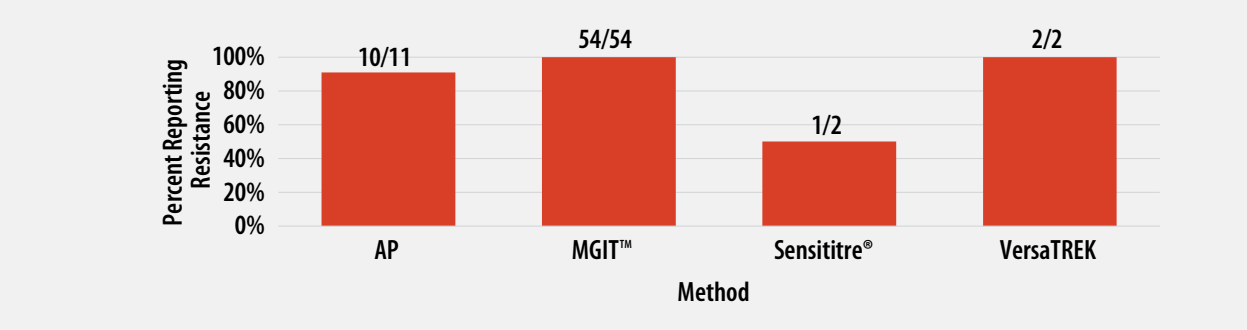
*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT. Molecular expected results performed by whole genome sequencing.

## Rifampin

DNA sequence analysis of *rpoB* in Isolate 2023B revealed a C>T point mutation in codon 445 resulting in wild-type histidine being replaced by tyrosine (His445Tyr). Isolates with His445Tyr mutations consistently test resistant to RIF in growth-based assays [9, 13-15].

For internal comparison purposes, this isolate was previously sent as MPEP 2019H where comparable results, by method, were reported for RIF.

**Figure 10. Isolate 2023B: Percent of laboratories reporting RIF resistance, by growth-based method.**




Note—Two of the laboratories performing Sensititre® reported RIF MIC values as 0.25 µg/ml (n=1) and 16 µg/ml (n=1).

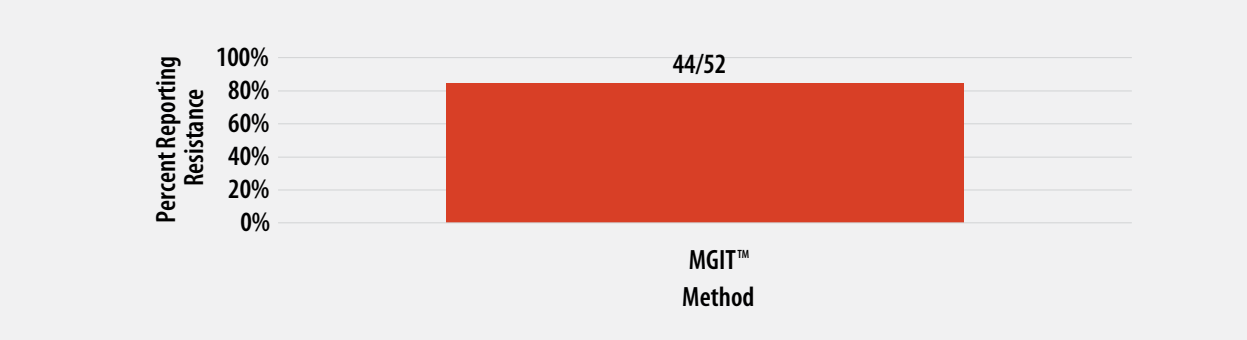
## Pyrazinamide

For Isolate 2023B, DNA sequencing of the *pncA* gene did not reveal a mutation. There may be additional mechanisms of resistance to PZA besides nucleotide changes in the *pncA* gene that are still unknown [16]. Issues with false-resistance to PZA have been reported as well [17] and remain a potential concern.

Isolate 2023B was expected to be susceptible to PZA; however, of those testing PZA, resistance was reported.

For internal comparison purposes, this isolate was previously sent as MPEP 2019H where 60% (39/65) of MGIT™ results and 0% (0/1) of VersaTREK™ results were reported as resistant.

### Figure 11. Isolate 2023B: 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 2023B are listed in Tables 11–18.*

*Two laboratories noted contaminated/no growth for Isolate 2023B and did not report results for at least one antituberculosis drug tested.*

### Table 11. Isolate 2023B—Participant Results for First-Line DST by AP

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

### Table 12. Isolate 2023B—Participant Results for First-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Rifampin | 0 | 54 | 54 |
| Isoniazid—Low | 54 | 0 | 54 |
| Isoniazid—High | 21 | 0 | 21 |
| Ethambutol | 54 | 0 | 54 |
| Pyrazinamide | 8 | 44 | 52 |

## Table 13. Isolate 2023B—Participant Results for First-Line DST by Sensititre®

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

## Table 14. Isolate 2023B—Participant Results for First-Line DST by VersaTREK™

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

## Table 15. Isolate 2023B—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 | 4 | 1 | 5 |
| Capreomycin | 7 | 0 | 7 |
| Ethionamide | 8 | 0 | 8 |
| Rifabutin | 0 | 5 | 5 |
| Cycloserine | 2 | 1 | 3 |
| *p*-Aminosalicylic acid | 5 | 0 | 5 |
| Bedaquiline | 0 | 0 | 0 |
| Linezolid | 0 | 0 | 0 |
| Clofazimine | 0 | 0 | 0 |

## Table 16. Isolate 2023B—Participant Results for Second-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 22 | 0 | 22 |
| Ofloxacin | 2 | 0 | 2 |
| Ciprofloxacin | 1 | 0 | 1 |
| Moxifloxacin | 8 | 0 | 8 |
| Levofloxacin | 5 | 0 | 5 |
| Amikacin | 4 | 0 | 4 |
| Kanamycin | 1 | 1 | 2 |
| Capreomycin | 4 | 0 | 4 |
| Ethionamide | 4 | 0 | 4 |
| Rifabutin | 1 | 4 | 5 |
| Cycloserine | 0 | 0 | 0 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 1 | 0 | 1 |
| Linezolid | 1 | 0 | 1 |
| Clofazimine | 1 | 0 | 1 |

## Table 17. Isolate 2023B—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 | 0 | 0 | 0* |
| 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 CAP and CYS by Sensititre®.

## Table 18. Isolate 2023B—Participant Results for Molecular Testing

| Drug | Mutation Not Detected | Mutation Detected | Total |
|---|---|---|---|
| Rifamycins (Rifampin, Rifabutin, Rifapentine) | 0 | 12* | 12 |
| Isoniazid | 8 | 0 | 8 |
| Ethambutol | 5 | 0 | 5 |
| Pyrazinamide | 5 | 0 | 5 |
| Streptomycin | 3 | 0 | 3 |
| Ofloxacin | 6 | 1† | 7 |
| Ciprofloxacin | 6 | 1† | 7 |
| Moxifloxacin | 6 | 1† | 7 |
| Levofloxacin | 6 | 1† | 7 |
| Amikacin | 6 | 0 | 6 |
| Kanamycin | 6 | 0 | 6 |
| Capreomycin | 5 | 0 | 5 |
| Ethionamide | 4 | 0 | 4 |
| Cycloserine | 1 | 0 | 1 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 3 | 0 | 3 |
| Linezolid | 3 | 0 | 3 |
| Clofazimine | 3 | 0 | 3 |
| Delamanid | 1 | 0 | 1 |
| Pretomanid | 0 | 0 | 0 |

*Seven laboratories noted the detection of *rpoB* His445Tyr mutation. Additionally, two laboratories performing Xpert® MTB/RIF assay noted Probe D did not bind.
† This laboratory noted the detection of a *gyrA* mutation not associated with FQ resistance.

# Isolate 2023C

## 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 |
| Fluoroquinolones | S | *gyrA* & *gyrB* wild-type |

Note—S=susceptible, R=resistant

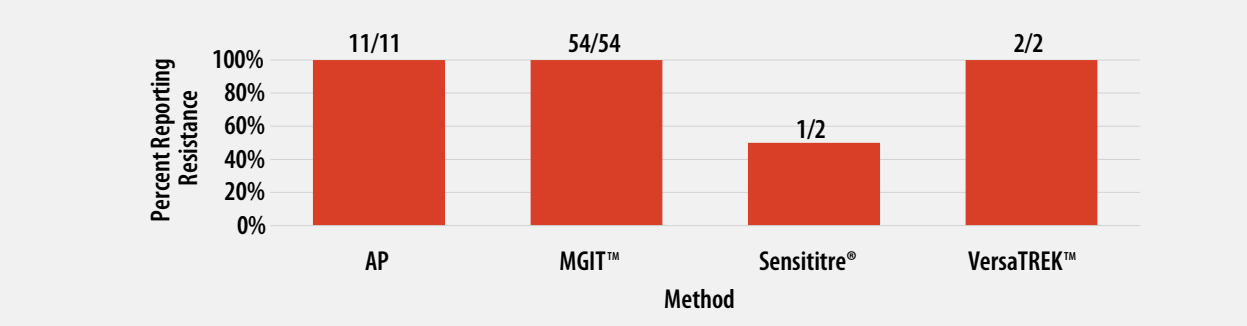
*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT. Molecular expected results performed by whole genome sequencing.

## Rifampin

DNA sequence analysis of *rpoB* in Isolate 2023C revealed a C>T point mutation in codon 450 in wild-type serine being replaced by leucine (Ser450Leu). Isolates with Ser450Leu mutations consistently test resistant to RIF in growth-based assays [9, 13-15].

For internal comparison purposes, this isolate was previously sent as MPEP 2020J where 88% (15/17) of AP results, 98% (58/59) of MGIT™ results, 100% (3/3) of Sensititre® results, and 100% (2/2) of VersaTREK™ results were reported as resistant.

### Figure 12. Isolate 2023C: Percent of laboratories reporting RIF resistance, by growth-based method.




Note—Two of the laboratories performing Sensititre® reported RIF MIC values as 0.5 µg/ml (n=1) and 16 µg/ml (n=1).

*Complete first-line DST, second-line DST, and molecular results submitted by all participant for Isolate 2023C are listed in Tables 19–26.*

### Table 19. Isolate 2023C—Participant Results for First-Line DST by AP

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

## Table 20. Isolate 2023C—Participant Results for First-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Rifampin | 0 | 54 | 54 |
| Isoniazid—Low | 54 | 0 | 54 |
| Isoniazid—High | 21 | 0 | 21 |
| Ethambutol | 54 | 0 | 54 |
| Pyrazinamide | 54 | 0 | 54 |

## Table 21. Isolate 2023C—Participant Results for First-Line DST by Sensititre®

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

## Table 22. Isolate 2023C—Participant Results for First-Line DST by VersaTREK™

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

## Table 23. Isolate 2023C—Participant Results for Second-Line DST by AP

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 10 | 0 | 10 |
| Ofloxacin | 5 | 0 | 5 |
| Ciprofloxacin | 2 | 1 | 3 |
| Moxifloxacin | 3 | 0 | 3 |
| Levofloxacin | 3 | 0 | 3 |
| Amikacin | 7 | 0 | 7 |
| Kanamycin | 5 | 0 | 5 |
| Capreomycin | 7 | 0 | 7 |
| Ethionamide | 8 | 0 | 8 |
| Rifabutin | 1 | 4 | 5 |
| Cycloserine | 3 | 0 | 3 |
| *p*-Aminosalicylic acid | 5 | 0 | 5 |
| Bedaquiline | 0 | 0 | 0 |
| Linezolid | 0 | 0 | 0 |
| Clofazimine | 0 | 0 | 0 |

## Table 24. Isolate 2023C—Participant Results for Second-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 22 | 0 | 22 |
| Ofloxacin | 2 | 0 | 2 |
| Ciprofloxacin | 1 | 0 | 1 |
| Moxifloxacin | 8 | 0 | 8 |
| Levofloxacin | 5 | 0 | 5 |
| Amikacin | 4 | 0 | 4 |
| Kanamycin | 2 | 0 | 2 |
| Capreomycin | 4 | 0 | 4 |
| Ethionamide | 4 | 0 | 4 |
| Rifabutin | 1 | 4 | 5 |
| Cycloserine | 0 | 0 | 0 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 1 | 0 | 1 |
| Linezolid | 1 | 0 | 1 |
| Clofazimine | 1 | 0 | 1 |

## Table 25. Isolate 2023C—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 MOX and CYC by Sensititre®.

## Table 26. Isolate 2023C—Participant Results for Molecular Testing

| Drug | Mutation Not Detected | Mutation Detected | Total |
|---|---|---|---|
| Rifamycins (Rifampin, Rifabutin, Rifapentine) | 0 | 12* | 12 |
| Isoniazid | 8 | 0 | 8 |
| Ethambutol | 5 | 0 | 5 |
| Pyrazinamide | 5 | 0 | 5 |
| Streptomycin | 3 | 0 | 3 |
| Ofloxacin | 6 | 1† | 7 |
| Ciprofloxacin | 6 | 1† | 7 |
| Moxifloxacin | 6 | 1† | 7 |
| Levofloxacin | 6 | 1† | 7 |
| Amikacin | 6 | 0 | 6 |
| Kanamycin | 6 | 0 | 6 |
| Capreomycin | 5 | 0 | 5 |
| Ethionamide | 4 | 0 | 4 |
| Cycloserine | 1 | 0 | 1 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 3 | 0 | 3 |
| Linezolid | 3 | 0 | 3 |
| Clofazimine | 3 | 0 | 3 |
| Delamanid | 1 | 0 | 1 |
| Pretomanid | 0 | 0 | 0 |

*Seven laboratories noted the detection of *rpoB* Ser450Leu mutation. Additionally, two laboratories performing Xpert® MTB/RIF assay noted Probe E did not bind.
† This laboratory noted the detection of a *gyrA* mutation not associated with FQ resistance.

# Isolate 2023D

## Expected Results:

| Drug | Growth-based* | Molecular* |
|---|---|---|
| RIF | R | *rpoB* Val170Phe |
| INH | S | *katG*, *inhA*, & *fabG1* wild-type |
| EMB | S | *embB* wild-type |
| PZA | S | *pncA* Thr135Ala¥ |
| Fluoroquinolones | S | *gyrA* & *gyrB* wild-type |

Note—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.

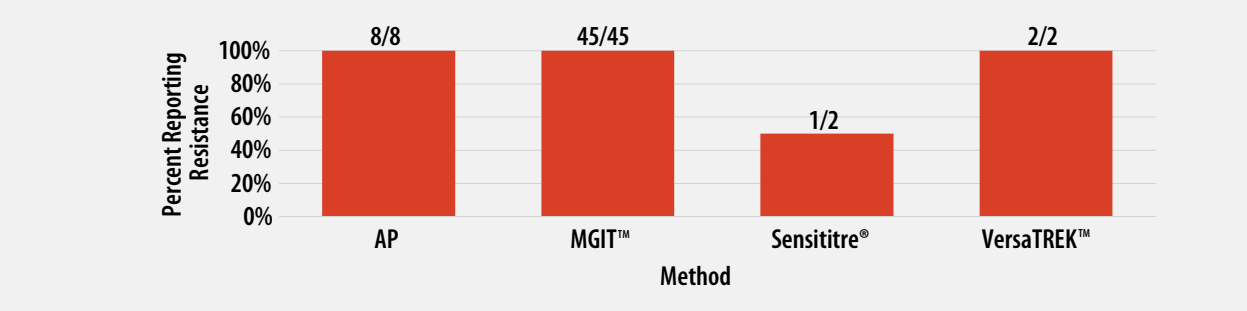
¥ Effect of mutation is unknown.

## Rifampin

DNA sequence analysis of *rpoB* in Isolate 2023D revealed a G>T point mutation in codon 170 of *rpoB* resulting in wild-type valine being replaced by phenylalanine (Val170Phe). Isolates with Val170Phe mutation have been shown to confer resistance [9, 18]. The Val170Phe mutation is outside the rifampin resistance determining region tested by Cepheid® Xpert® MTB/RIF assay.

For internal comparison purposes, this isolate was previously sent as MPEP 2020D where 94% (16/17) of AP results, 90% (38/42) of MGIT™ results, 100% (4/4) of Sensititre® results, and 100% (2/2) of VersaTREK™ results were reported as resistant.

**Figure 13. Isolate 2023D: Percent of laboratories reporting RIF resistance, by growth-based method.**




Note—Two of the laboratories performing Sensititre® reported RIF MIC values as 0.5 µg/ml (n=1) and 16 µg/ml (n=1).

## Pyrazinamide

DNA sequence analysis of *pncA* in Isolate 2023D revealed a A>G point mutation in codon 135 resulting in wild-type threonine being replaced by alanine (Thr135Ala). The effect of the *pncA* Thr135Ala mutation for this isolate is unknown and 49/50 (98%) of laboratories performing MGIT reported PZA susceptible.

For internal comparison purposes, this isolate was previously sent as MPEP 2020D where comparable results were reported.

*Complete first-line DST, second-line DST, and molecular results submitted by all participants for Isolate 2023D are listed in Tables 27–34.*

*Nine laboratories noted contaminated/no growth for Isolate 2023D and did not report results for at least one antituberculosis drug tested.*

## Table 27. Isolate 2023D—Participant Results for First-Line DST by AP

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Rifampin | 0 | 8 | 8 |
| Isoniazid—Low | 8 | 0 | 8 |
| Isoniazid—High | 7 | 0 | 7 |
| Ethambutol | 8 | 0 | 8 |

## Table 28. Isolate 2023D—Participant Results for First-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Rifampin | 0 | 45 | 45* |
| Isoniazid—Low | 44 | 0 | 44*† |
| Isoniazid—High | 18 | 0 | 18*† |
| Ethambutol | 45 | 0 | 45* |
| Pyrazinamide | 49 | 1 | 50*¥ |

*Four additional laboratories reported No Interpretation for RIF, INH—Low, INH—High, and EMB by MGIT™.
† One additional laboratory reported No Interpretation for INH—Low and INH—High by MGIT™.
¥ One additional laboratory reported No Interpretation for PZA by MGIT™.

## Table 29. Isolate 2023D—Participant Results for First-Line DST by Sensititre®

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

## Table 30. Isolate 2023D—Participant Results for First-Line DST by VersaTREK™

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

## Table 31. Isolate 2023D—Participant Results for Second-Line DST by AP

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

*One additional laboratory reported No Interpretation for OFL by AP.

## Table 32. Isolate 2023D—Participant Results for Second-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 15 | 2 | 17* |
| Ofloxacin | 2 | 0 | 2 |
| Ciprofloxacin | 1 | 0 | 1 |
| Moxifloxacin | 6 | 0 | 6 |
| Levofloxacin | 5 | 0 | 5 |
| Amikacin | 4 | 0 | 4 |
| Kanamycin | 2 | 0 | 2 |
| Capreomycin | 3 | 0 | 3† |
| Ethionamide | 4 | 0 | 4 |
| Rifabutin | 2 | 3 | 5 |
| Cycloserine | 0 | 0 | 0 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 0 | 0 | 0 |
| Linezolid | 0 | 0 | 0 |
| Clofazimine | 0 | 0 | 0 |

*Two additional laboratories reported No Interpretation for STR by MGIT™.

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

## Table 33. Isolate 2023D—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 | 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 MOX by Sensititre®.

## Table 34. Isolate 2023D—Participant Results for Molecular Testing

| Drug | Mutation Not Detected | Mutation Detected | Total |
|---|---|---|---|
| Rifamycins (Rifampin, Rifabutin, Rifapentine) | 8 | 4* | 12 |
| Isoniazid | 8 | 0 | 8 |
| Ethambutol | 5 | 0 | 5 |
| Pyrazinamide | 1 | 4† | 5 |
| Streptomycin | 2 | 1¥ | 3 |
| Ofloxacin | 7 | 0 | 7 |
| Ciprofloxacin | 7 | 0 | 7 |
| Moxifloxacin | 7 | 0 | 7 |
| Levofloxacin | 7 | 0 | 7 |
| Amikacin | 6 | 0 | 6 |
| Kanamycin | 6 | 0 | 6 |
| Capreomycin | 5 | 0 | 5 |
| Ethionamide | 4 | 0 | 4 |
| Cycloserine | 1 | 0 | 1 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 3 | 0 | 3 |
| Linezolid | 3 | 0 | 3 |
| Clofazimine | 3 | 0 | 3 |
| Delamanid | 1 | 0 | 1 |
| Pretomanid | 0 | 0 | 0 |

*These 4 laboratories noted the detection of the *rpoB* Val170Phe mutation.

† Three laboratories noted the detection of the *pncA* Thr135Ala mutation.

¥ This laboratory noted a deletion in *gidB*.

# Isolate 2023E

## 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 |
| Fluoroquinolones | S | *gyrA* & *gyrB* wild-type |
| Second-line Injectables | AMK R, KAN R, CAP R | *rrs* A1401G |

Note—S=susceptible, R=resistant

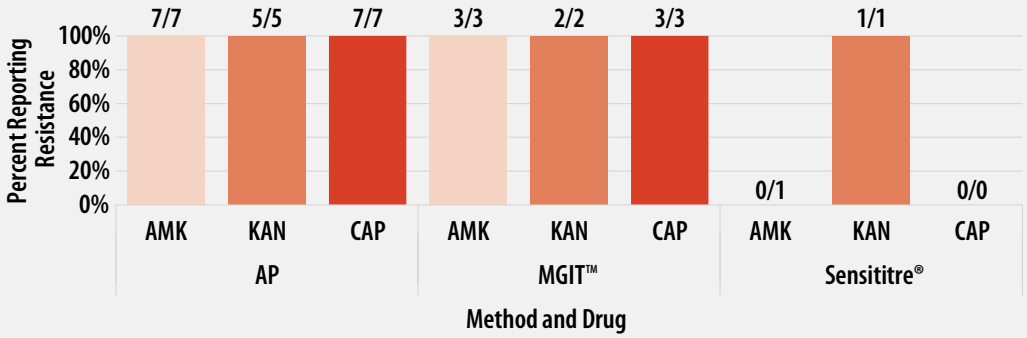
*Growth-based expected results performed by agar proportion, except for PZA which was performed by MGIT. Molecular expected results performed by whole genome sequencing.

## Second-line Injectables

DNA sequence analysis of *rrs* in Isolate 2023E revealed an A>G point mutation in codon 1401 (A1401G); *eis* and *tlyA* were wild-type (i.e., no mutations were detected). Isolates with A1401G mutation have been shown to confer resistance [18, 19].

For internal comparison purposes, this isolate was previously sent as MPEP 2017C where comparable results were reported for AMK, KAN, and CAP.

### Figure 14. Isolate 2023E: Percent of laboratories reporting AMK, KAN, and CAP resistance, by growth-based method.




Note—Two laboratories performing Sensititre reported MIC values for second-line injectable drugs. Reported MIC values were as follows: AMK were 16 µg/ml (n=2), KAN at 40 µg/ml (n=1), and CAP MIC value as 20 µg/ml (n=1).

*Complete first-line DST, second-line DST, and molecular results submitted by all participants for Isolate 2023E are listed in Tables 35–42.*

### Table 35. Isolate 2023E—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 2023E—Participant Results for First-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Rifampin | 55 | 0 | 55 |
| Isoniazid—Low | 55 | 0 | 55 |
| Isoniazid—High | 23 | 0 | 23 |
| Ethambutol | 55 | 0 | 55 |
| Pyrazinamide | 51 | 4 | 55 |

## Table 37. Isolate 2023E—Participant Results for First-Line DST by Sensititre®

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

*One additional laboratory reported Indeterminate for EMB by Sensititre®.

## Table 38. Isolate 2023E—Participant Results for First-Line DST by VersaTREK™

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

## Table 39. Isolate 2023E—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 | 0 | 7 | 7 |
| Kanamycin | 0 | 5 | 5 |
| Capreomycin | 0 | 7 | 7 |
| Ethionamide | 7 | 0 | 7* |
| Rifabutin | 5 | 0 | 5 |
| Cycloserine | 3 | 0 | 3 |
| *p*-Aminosalicylic acid | 5 | 0 | 5 |
| Bedaquiline | 0 | 0 | 0 |
| Linezolid | 0 | 0 | 0 |
| Clofazimine | 0 | 0 | 0 |

*One additional laboratory reported No Interpretation for ETA by AP.

## Table 40. Isolate 2023E—Participant Results for Second-Line DST by MGIT™

| Drug | Susceptible | Resistant | Total |
|---|---|---|---|
| Streptomycin | 22 | 0 | 22 |
| Ofloxacin | 2 | 0 | 2 |
| Ciprofloxacin | 1 | 0 | 1 |
| Moxifloxacin | 7 | 0 | 7 |
| Levofloxacin | 5 | 0 | 5 |
| Amikacin | 0 | 3 | 3 |
| Kanamycin | 0 | 2 | 2 |
| Capreomycin | 0 | 3 | 3 |
| Ethionamide | 3 | 0 | 3 |
| Rifabutin | 4 | 0 | 4 |
| Cycloserine | 0 | 0 | 0 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 1 | 0 | 1 |
| Linezolid | 1 | 0 | 1 |
| Clofazimine | 1 | 0 | 1 |

## Table 41. Isolate 2023E—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 | 1 | 0 | 1* |
| Kanamycin | 0 | 1 | 1 |
| Capreomycin | 0 | 0 | 0* |
| 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 MOX, AMK, CAP, and CYS by Sensititre®.

## Table 42. Isolate 2023E—Participant Results for Molecular Testing

| Drug | Mutation Not Detected | Mutation Detected | Total |
|---|---|---|---|
| Rifamycins (Rifampin, Rifabutin, Rifapentine) | 11 | 0 | 11 |
| Isoniazid | 8 | 0 | 8 |
| Ethambutol | 5 | 0 | 5 |
| Pyrazinamide | 5 | 0 | 5 |
| Streptomycin | 2 | 1 | 3 |
| Ofloxacin | 6 | 1* | 7 |
| Ciprofloxacin | 6 | 1* | 7 |
| Moxifloxacin | 6 | 1* | 7 |
| Levofloxacin | 6 | 1* | 7 |
| Amikacin | 0 | 6† | 6 |
| Kanamycin | 1 | 5† | 6 |
| Capreomycin | 0 | 5† | 5 |
| Ethionamide | 4 | 0 | 4 |
| Cycloserine | 1 | 0 | 1 |
| *p*-Aminosalicylic acid | 1 | 0 | 1 |
| Bedaquiline | 1 | 2¥ | 3 |
| Linezolid | 3 | 0 | 3 |
| Clofazimine | 1 | 2¥ | 3 |
| Delamanid | 1 | 0 | 1 |
| Pretomanid | 0 | 0 | 0 |

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

† Five laboratories noted the detection of the *rrs* A(1401)G mutation.

¥ Both laboratories noted the detection of the rv0678 Asp141 frameshift.

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