



**Centers for Disease Control and Prevention  
Model Performance Evaluation Program**

***Mycobacterium tuberculosis*  
and  
Nontuberculous Mycobacteria Drug  
Susceptibility Testing Program**

**Report of Results  
for the Performance Evaluation Survey  
Conducted During November 2011**

**UNITED STATES DEPARTMENT OF HEALTH AND HUMAN  
SERVICES**

**Use of trade names and commercial sources is for identification only and  
does not imply endorsement by the  
Centers for Disease Control and Prevention, or  
U.S. Department of Health and Human Services.**

## MTB NTM DST Report for November 2011 Samples Survey

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**Purpose** The purpose of this report is to present the results of the Centers for Disease Control and Prevention (CDC) Model Performance Evaluation Program for *Mycobacterium tuberculosis* and Nontuberculous Mycobacteria Drug Susceptibility Testing (MPEP MTB NTM DST) survey sent to participants in November 2011.

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## **Introduction: Analyses of the November 2011 *M. tuberculosis* and Nontuberculous Mycobacteria Drug Susceptibility Test Results Reported by Participating Laboratories**

This report analyzes the laboratory demographic information and drug susceptibility testing results reported to the Centers for Disease Control and Prevention (CDC) by participating laboratories for the panel of five *Mycobacterium tuberculosis* Complex<sup>1</sup> isolates shipped in November 2011. Panels were sent to 98 laboratories and all laboratories participated in evaluation of the panels.

Laboratories performed testing by using Agar Proportion 7H10 (AP 7H10); Agar Proportion 7H11 (AP 7H11) collectively called Agar Proportion methods (AP) when not mentioned individually; BACTEC<sup>TM</sup> 460 TB (BACTEC<sup>TM</sup>); BACTEC<sup>TM</sup> MGIT<sup>TM</sup> 960 (MGIT<sup>TM</sup>); VersaTREK<sup>®</sup> and molecular methods consist of Genotype MTBDRsl; Genotype MTBDRplus; Xpert MTB/RIF; and Laboratory Developed Tests.

This aggregate report is prepared in a format that will allow laboratories to compare their results with those obtained by other participants for the same strains using the same method, drug, and drug concentrations. We encourage circulation of this report to personnel who are involved with drug susceptibility testing, reporting, or interpreting for *M. tuberculosis* isolates.

CDC is neither recommending nor endorsing testing practices reported by participants. For approved standards, participants should refer to consensus documents published by the Clinical and Laboratory Standards Institute (CLSI), "Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes; Approved Standard-Second Edition," M24-A2 (ISBN 1-56238-746-4).[1]

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<sup>1</sup> Historically, the intent of the exercise was to assess performance using organism that were of *Mycobacterium tuberculosis* Complex and were non-tuberculous mycobacteria. Overtime, non-tuberculous mycobacteria have been dropped. Although it is possible that any of the eight species of *Mycobacterium tuberculosis* Complex could be present in the isolates selected, identification is not part of the panel selection nor the exercise and it is presumed *M. tuberculosis* is the dominant species represented. For these reasons and simplicity, we refer to *M. tuberculosis* throughout the report.

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## Susceptibility Testing Results for the *M. tuberculosis* Isolates Panel Shipped November 7, 2011

The table below provides the intended results of the panel shipment that was sent to participants in November 2011. Although CDC recommends broth-based methods for routine *M. tuberculosis* complex drug susceptibility testing, this table provides the results obtained by the reference agar proportion method, except in the case of pyrazinamide, where BACTEC™ was the testing method.

<b>Isolate</b>	<b>Susceptibility Testing Results</b>
<b>F</b>	Resistant to Rifampin (RIF)
<b>G</b>	Resistant to Isoniazid (INH) Resistant to Streptomycin (SM)
<b>H</b>	Resistant to Streptomycin (SM) Resistant to Pyrazinamide (PZA)
<b>I</b>	Susceptible to first-and second-line drugs
<b>J</b>	Resistant to Isoniazid (INH) Resistant to Ethambutol (EMB) Resistant to Kanamycin (KM) Resistant to Capreomycin (CAP) Resistant to Amikacin (AMK)

## Descriptive Information about Participant Laboratories

### Primary Classification

This report contains the drug susceptibility testing results submitted to CDC by 98 laboratories in 41 states and Puerto Rico.

The participants were asked to indicate the **primary classification** of their laboratory.

MPEP participants self-classified as

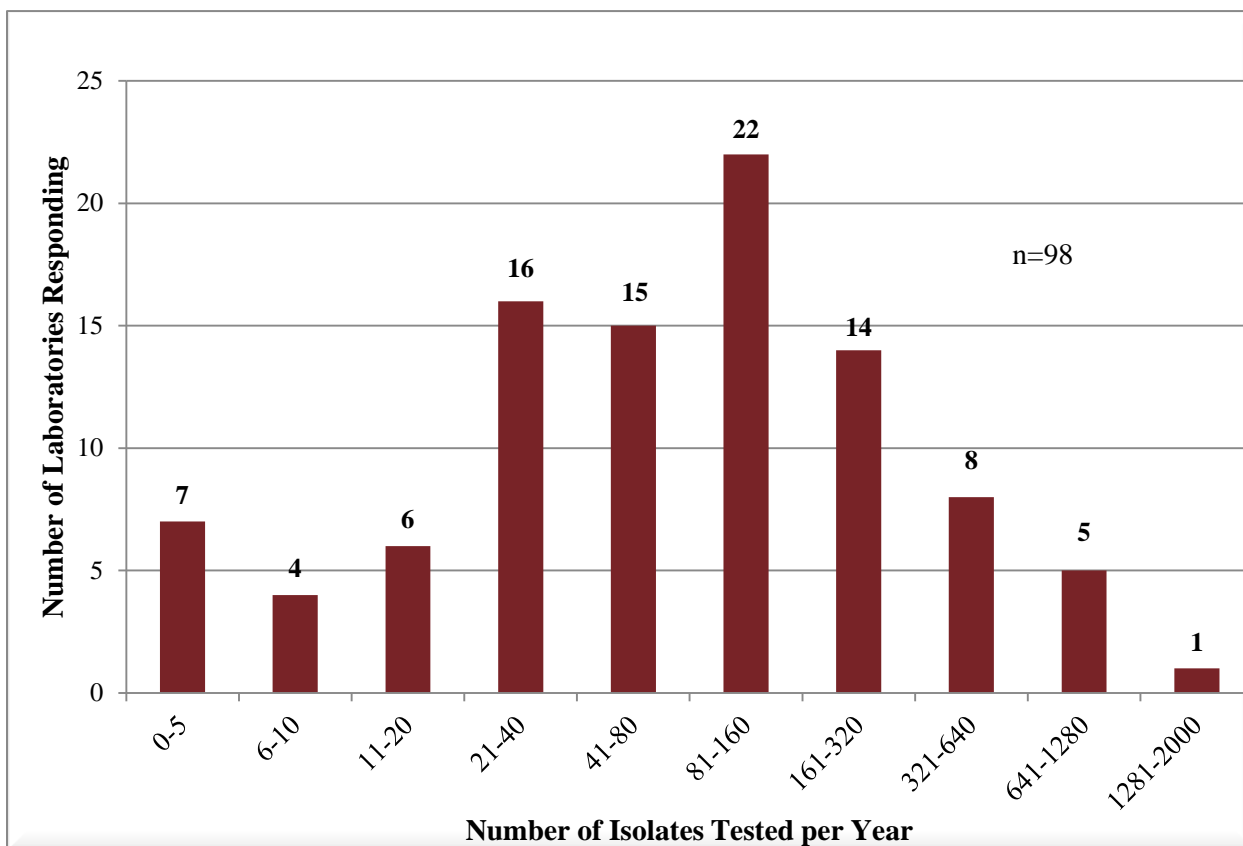
- 62 (63.3%): Health Department (city, county, state, regional, district, or national reference laboratory);
- 25 (25.5%): Hospital [city, county, district, community, state, regional, military, Veterans Administration, Federal government (other than military), privately-owned, university, HMO/PPO\*-owned and operated, or religious-associated];
- 9 (9.2%): Independent [e.g., commercial, commercial manufacturer of reagents, HMO satellite clinic, reference laboratory (non-government affiliated)]; and
- 2 (2.0%): Other [Federal government research (nonmilitary)];

\* HMO: health maintenance organization; PPO: preferred provider organization

## Annual Number of *M. tuberculosis* Drug Susceptibility Tests Performed by Participants

Figure 1 shows the number of drug susceptibility tests performed on *M. tuberculosis* isolates by the 98 participants in one **calendar year**, January 1–December 31, 2010, excluding quality control isolates. The counts range from four to 1,500. Seventeen (17) laboratories reported performing less than 21 drug susceptibility tests per year. To ensure testing proficiency, laboratories with low volumes are encouraged to consider referral of *M. tuberculosis* drug susceptibility testing.

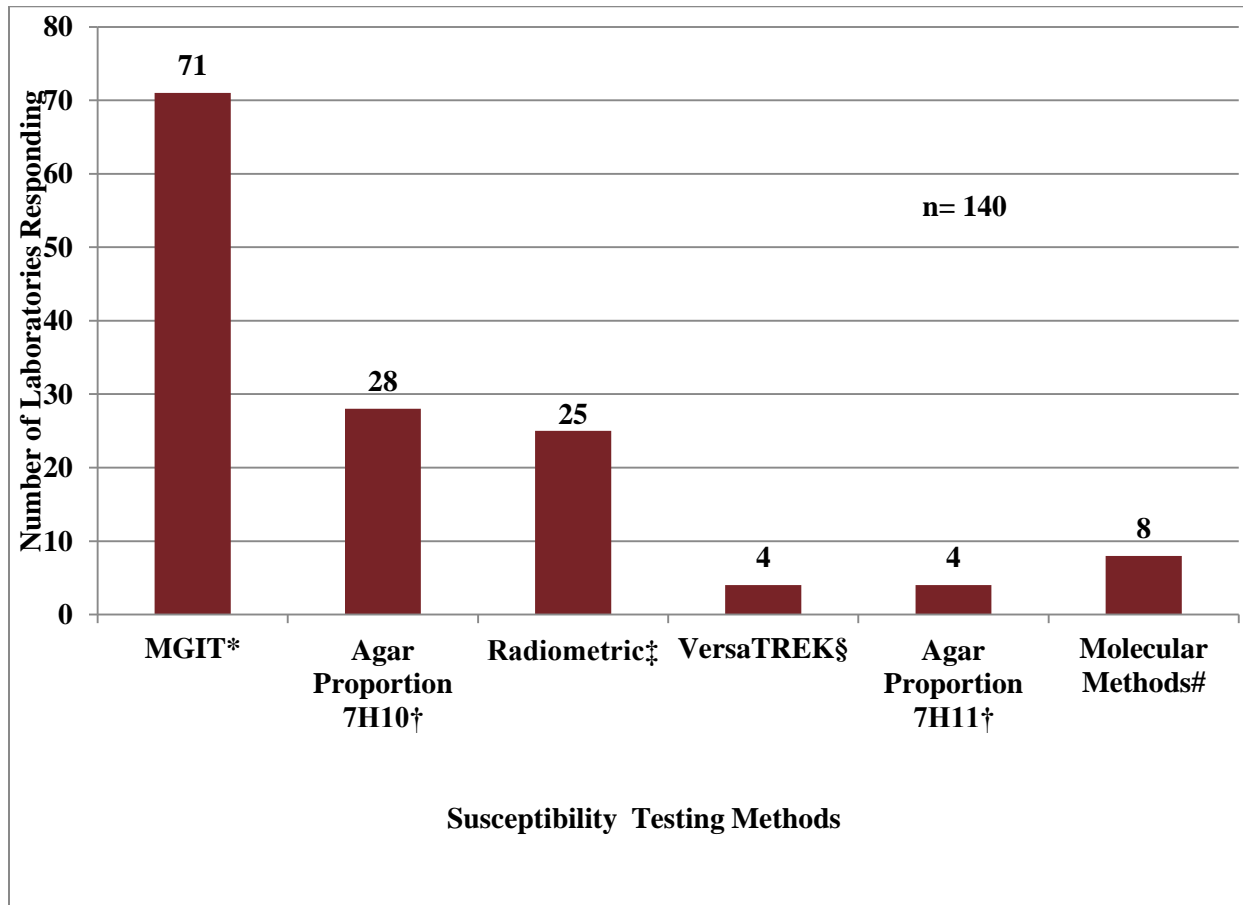
**Figure 1: Distribution of the Annual Volume of *M. tuberculosis* Isolates Tested for Drug Susceptibility by Participants in the 2011 Calendar Year**



## Laboratory Susceptibility Testing Procedures Used by Participants

Participants were asked to report all *M. tuberculosis* susceptibility testing methods that were used to test these isolates. Sixty-two laboratories used only one method for testing, whereas 31 laboratories used two methods, four laboratories used three methods, and one laboratory used four methods. Figure 2 shows the reported susceptibility methods.

**Figure 2: Susceptibility Testing Methods Reported by Participant Laboratories**



\* MGIT™ Mycobacteria Growth Indicator Tube

† Agar Proportion using Middlebrook mediums 7H10 or 7H11

‡ Radiometric is BACTEC™ 460 TB

§ VersaTREK® Myco Susceptibility Kit

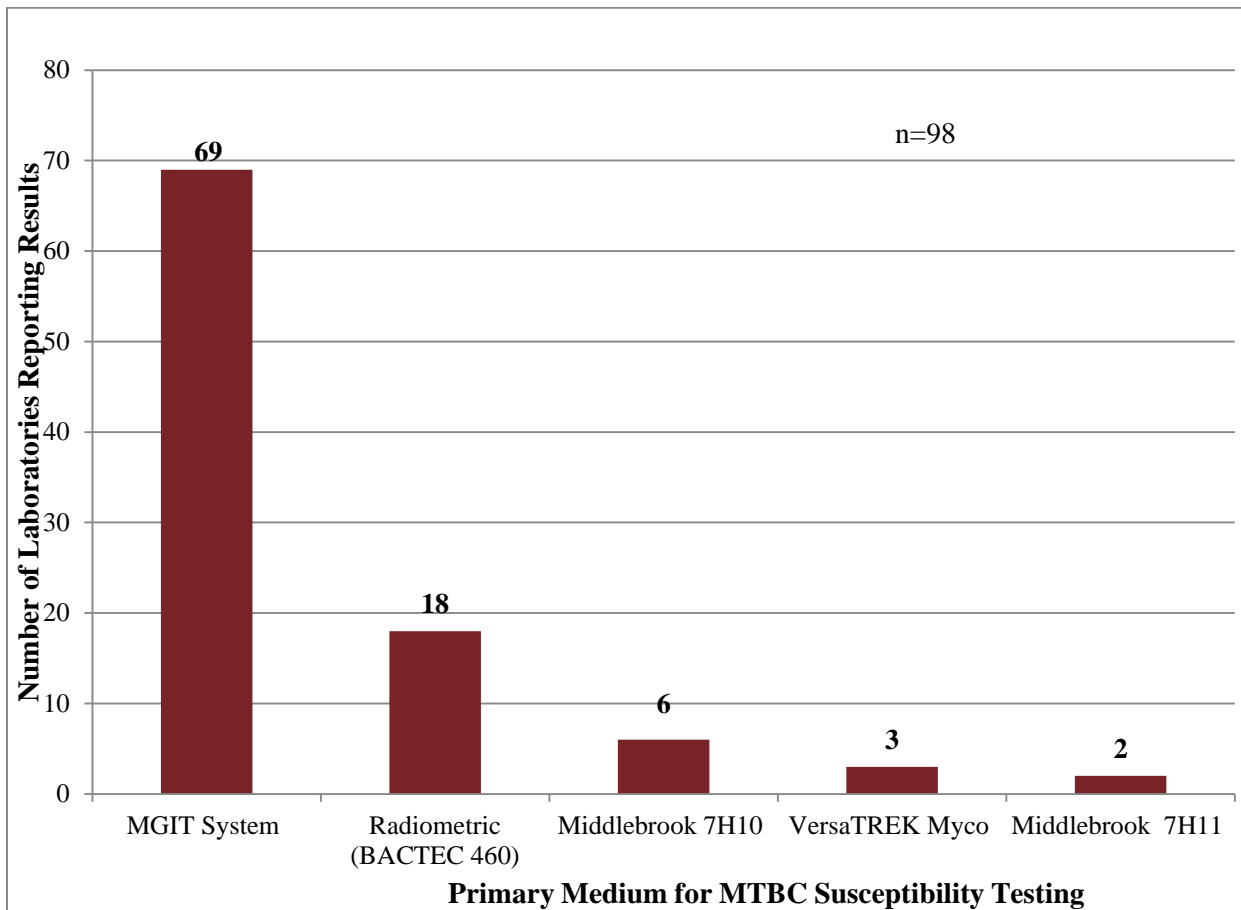
# Molecular methods include: Laboratory Developed Tests (4), Genotype MTBDR*sl* (1), Genotype MTBDR*plus* (1), Xpert MTB/RIF (2) methods



## The Primary *M. tuberculosis* Susceptibility Testing Media Used by Participants

Participants were asked to indicate the **primary** *M. tuberculosis* susceptibility test medium used by their laboratory for the isolates in the November 2011 shipment. Instructions were to select only one method as their primary method. Figure 3 shows the responses submitted by the 98 participants.

**Figure 3: Primary *M. tuberculosis* Susceptibility Test Medium Used by Participants**



Of the 71 laboratories that reported using MGIT™ as one of their methods for testing the MTB NTM DST isolates,

- 69 indicated that the MGIT™ method was their primary method for susceptibility testing; and
- 2 laboratories indicated Agar proportion (AP) was their primary method using AP 7H10.

Of the 28 laboratories who reported using AP 7H10 as a method for testing the isolates,

- 6 used this as their primary method; however, two laboratories did not report AP 7H10 as one of their testing methods in this challenge;
- 19 used MGIT™ as their primary method; and
- 5 used BACTEC™ as their primary method.

Of the 25 laboratories who reported using BACTEC™ 460TB as one of their methods for testing the isolates,

- 18 used this as their primary method;
- 4 used MGIT™ as their primary method;
- 2 laboratory indicated AP was their primary method using AP 7H11; and
- 1 laboratory indicated AP was their primary method using AP 7H10.

Of the 4 laboratories who reported using VersaTREK® indicated as a method for testing the isolates.

- 3 laboratory indicated this as their primary method; and
- 1 laboratory indicated AP was their primary method using AP 7H10.

Of the 4 laboratories who reported using AP 7H11 as a method for testing the isolates,

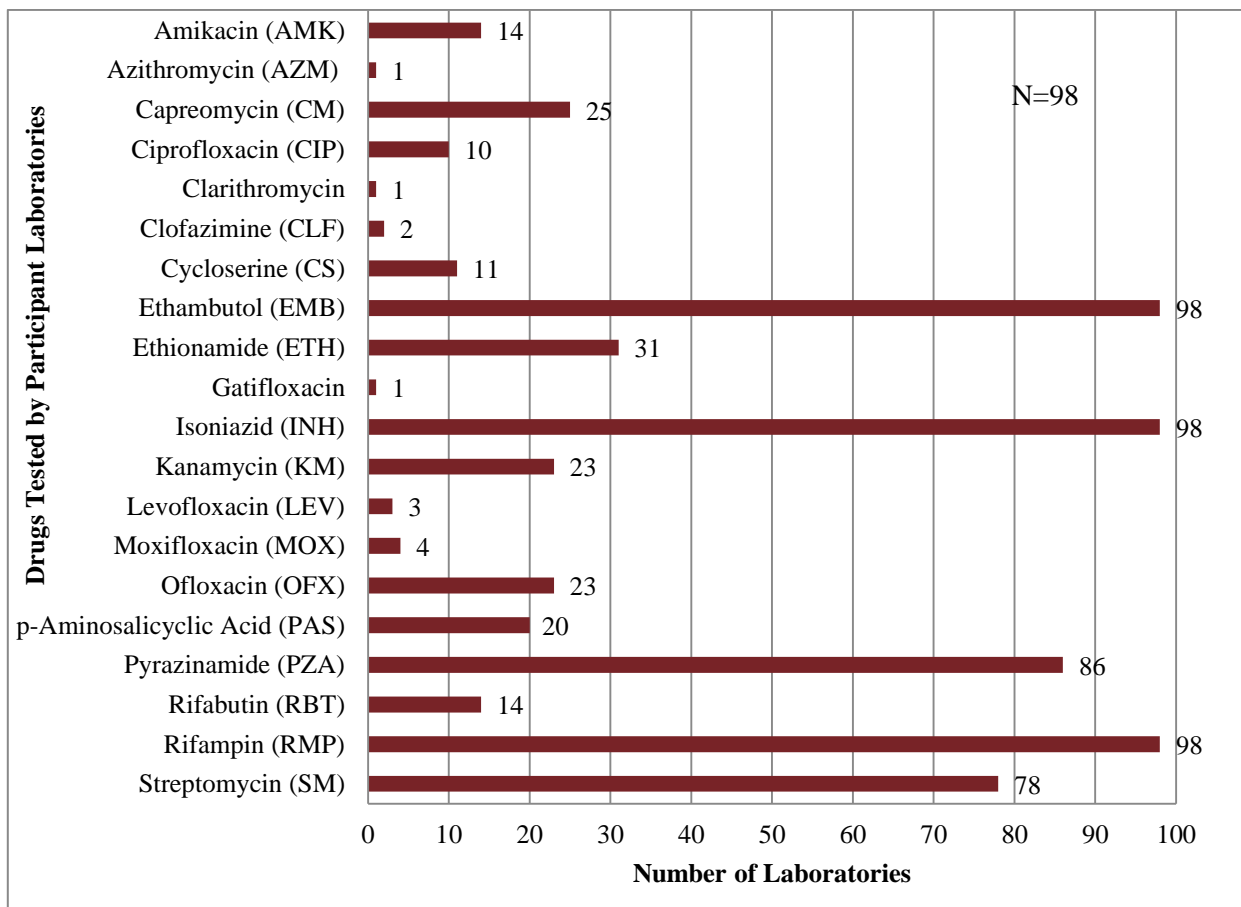
- 2 used this as their primary method;
- 1 used MGIT™ as their primary method; and
- 1 used BACTEC™ as their primary method.

## **Antituberculous Drugs Used by Participants**

CLSI recommends a full panel of first-line (primary) drugs (isoniazid [INH], rifampin [RMP], ethambutol [EMB], and pyrazinamide [PZA])[1], because it represents a combination of tests that provides the clinician with comprehensive information related to the four-drug therapy currently recommended for treatment of most patients in the United States with tuberculosis. All participants reported results for three of the first-line drugs—INH, RMP, and EMB; 86 (87.8%) of the participants also reported results for PZA.

Figure 4 shows the number of laboratories testing each drug. The number at the right of each bar represents the number of laboratories that tested the drug.

**Figure 4: Antituberculous Drugs Used by Participants**



**Note:** Providing test results for all drugs that are reported to CDC by participants should not be construed as a recommendation or endorsement for testing particular drugs or drug concentrations with *M. tuberculosis* isolated from patients. It is assumed that some of the drugs are being tested for research purposes or potential use in the few referral institutions that may treat patients with *M. tuberculosis* isolates resistant to almost all standard drugs. According to CLSI, “Second-line drugs may be tested simultaneously if mutations associated with INH and RMP resistance have been detected by molecular assays, or if epidemiological situations support the practice and resources are available. Second-line drugs, both traditional and newer agents, should be tested for isolates resistant to RMP or any two of the primary drugs. Isolates with mono-resistance to the critical concentration of INH also should be tested for susceptibility to second-line agents if the clinician is planning to include a fluoroquinolone in the treatment regimen. Laboratories should not add drugs to their testing panel without consulting physicians with expertise in treating multidrug-resistant tuberculosis. Laboratories may contact their local tuberculosis control program for referrals to physician experts in the treatment and care of tuberculosis”.

## Tabulated data

This section provides the complete set of data in tabulated format for the *M. tuberculosis* isolates F, G, H, I, and J sent in the November 2011 shipment. The following information/explanation pertains to all the tables.

### Explanation of Tables 1 through 5

- In the following tables, the shaded rows indicate critical concentrations for each test method. For each drug, the critical concentration is defined as the lowest concentration that inhibits 95% of “wild-type” strains of *M. tuberculosis* organisms that have not been exposed to the drug; but that simultaneously does not inhibit strains of the *M. tuberculosis* considered resistant that are isolated from patients who are not responding to therapy.[1]
- The test results (S represents susceptible and R represents resistant) are listed in the appropriate columns along with a corresponding total number of tests (Sum column) to provide a denominator for determining the level of consensus. This report contains all results reported by participating laboratories, including many drug concentrations with only one result.
- Participants should note that the CLSI approved standard “Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes,” M24-A2 (ISBN 1-56238-746-4) CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA, 2011 recommends testing streptomycin as a second line drug and also adds ofloxacin and rifabutin to the list of recommended secondary drugs. For a complete list of drugs to be tested, consult the CLSI document M24-A2.[1]
- Concentrations are listed in micrograms per milliliter ( $\mu\text{g/ml}$ ).
- A concentration of 0.00 is entered for results associated with genetic testing [Hain GenoType<sup>®</sup> MTBDR<sub>plus</sub> Assay or Hain GenoType<sup>®</sup> MTBDR<sub>sl</sub> Kit (HAIN Lifescience, Germany); Xpert MTB/RIF(Cepheid) ; and Laboratory Developed Tests] for which no drug concentration is required.

## Isolate F, *M. tuberculosis*–resistant to Rifampin at 1.0µg/ml by Agar Proportion

Rifampin (RMP) is a first-line drug for treatment of all forms of tuberculosis caused by organisms known or presumed to be susceptible to this drug. It is bactericidal for *M. tuberculosis* at the critical concentration of 1.0µg/ml for AP (on Middlebrook 7H10 and 7H11 agars) and equivalent critical concentrations for BACTEC460™, MGIT960™, and VersaTREK® of 2.0µg/ml, 1.0µg/ml, and 1.0µg/ml, respectively. The mechanism of action of RMP is to inhibit mycobacterial transcription by targeting DNA-dependent RNA polymerase[2]. More than 96% of RMP-resistant isolates contain a mutation in the 81-base pair (bp) central region of the *rpoB* gene that encodes the β-subunit of the bacterial DNA-dependent RNA polymerase[2]. The activity of RMP in RMP-resistant isolates depends on both the mutation position and the type of amino acid change in the *rpoB* gene. Mutations in codons 531, 526, and 516 are among the most frequent mutations in RMP-resistant isolates and serve as predictors of RMP resistance. DNA sequence analysis of *rpoB* of Isolate F revealed a C>T point mutation in the *rpoB* locus resulting in histidine being replaced by tyrosine at codon 526 (His526Tyr).

Ninety-eight laboratories reported RMP results for this isolate at the critical concentration. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 100% (27/27) of the laboratories reporting AP results;
- 100% (18/18) of the laboratories reporting BACTEC™ results;
- 100% (70/70) of the laboratories reporting MGIT™ results;
- 100% (4/4) of the laboratories reporting VersaTREK® results; and
- 100% (5/5) of the laboratories reporting molecular method results

### Rifabutin

Rifabutin (RBT) belongs to same drug class as RMP. It has the same bactericidal mechanism of activity. Less than 20% RMP resistant strains are susceptible to RBT[3].

Six laboratories tested RBT at the critical concentration of 0.5µg/ml by AP and all reported resistance.

### Pyrazinamide

This isolate was susceptible to PZA by BACTEC™, the CLSI- recommended method; **however the isolate** was reported resistant by:

- 100 % (3/3) of the laboratories reporting VersaTREK® results and
- 31.8% (21/66) of the laboratories reporting MGIT™ method.

See Table 1 for the complete results submitted by all participants for Isolate F.

**Table 1: Participant results for *M. tuberculosis*, Isolate F–resistant to Rifmapin at 1.0µg/ml by AP**

Drug	Conc.	Test Method											
		AP Results			BACTEC Results			MGIT Results			Other Results*		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.00											3	3
Isoniazid	0.10				17	2†	19	68	1	69		4	4
Isoniazid	0.20	25		25				1		1			
Isoniazid	0.40				5		5	27		27		4	4
Isoniazid	1.00	24		24	1		1						
Isoniazid	5.00	4		4									
Isoniazid	10.00	1		1									
Rifampin	0.00											5	5
Rifampin	1.00		27	27		4	4		70	70		4	4
Rifampin	2.00					18	18						
Rifampin	5.00		3	3		1	1						
Rifampin	10.00					1	1						
Pyrazinamide	5.00							1		1			
Pyrazinamide	20.00				1		1						
Pyrazinamide	100.00				13		13	45	21	66			
Pyrazinamide	300.00											3	3
Ethambutol	0.00											1	1
Ethambutol	2.50				15	2†	17						
Ethambutol	5.00	22	1	23	2	1†	3	69	1	70		4	4
Ethambutol	7.50	2		2	2		2	1		1			
Ethambutol	8.00											3	3
Ethambutol	10.00	9		9									
Streptomycin	1.00					1	1	50	1	51			
Streptomycin	2.00	25		25	15	3	18						
Streptomycin	4.00	1		1	1		1	7		7			
Streptomycin	6.00				2		2						
Streptomycin	10.00	21		21	1		1						
Ethionamide	1.25					2	2						
Ethionamide	2.50				1	1	2						
Ethionamide	5.00	21	1	22		1	1	2		2			
Ethionamide	10.00	4		4									
Kanamycin	0.00											1	1
Kanamycin	2.50				1		1						
Kanamycin	5.00	11		11	2		2						
Kanamycin	6.00	10		10									
Capreomycin	0.00											1	1
Capreomycin	1.25				1		1						
Capreomycin	2.50				1		1	1		1			
Capreomycin	3.00							1		1			
Capreomycin	5.00				2		2						
Capreomycin	10.00	20		20									
Cycloserine	30.00	10		10									
Cycloserine	60.00	1		1									

\* VersaTREK®, Hain GenoType®, or Molecular Methods

† Includes borderline results

**Table 1 continued: Participant results for *M. tuberculosis*, Isolate F– resistant to Rifampin at 1.0µg/ml by AP**

Drug	Conc.	Test Method														
		AP Results			BACTEC Results			MGIT Results			Other Results*					
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum			
p-Aminosalicylic acid	2.00	17		17												
p-Aminosalicylic acid	4.00							1		1						
p-Aminosalicylic acid	8.00	2		2												
p-Aminosalicylic acid	10.00	4		4												
Amikacin	0.00											1		1		
Amikacin	1.00							1		1						
Amikacin	1.50							1		1						
Amikacin	2.00	1		1	1		1									
Amikacin	2.50				1		1									
Amikacin	4.00	3		3												
Amikacin	5.00	1		1												
Amikacin	6.00	6		6												
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												
Ofloxacin	0.00											1		1		
Ofloxacin	0.60	1		1												
Ofloxacin	1.00	2		2	2		2									
Ofloxacin	1.25				1		1									
Ofloxacin	2.00	15		15	5		5									
Ofloxacin	4.00	1		1	1		1									
Ciprofloxacin	0.00											1		1		
Ciprofloxacin	1.00	2		2	2		2		1		1					
Ciprofloxacin	2.00	6		6	1		1									
Ciprofloxacin	4.00				1		1									
Azithromycin	3.00		1	1												
Clarithromycin	3.00		1	1												
Clofazimine	0.06				1		1									
Clofazimine	0.12				1		1									
Clofazimine	0.25				1		1									
Clofazimine	0.50				3		3									
Clofazimine	1.00	1		1												
Gatifloxacin	0.00											1		1		
Levofloxacin	1.50							1		1						
Levofloxacin	2.00				2		2									
Moxifloxacin	0.00											1		1		
Moxifloxacin	0.25							1		1						
Moxifloxacin	1.00	1		1												
Moxifloxacin	5.00	1		1												
Rifabutin	0.50		6	6			3	3								
Rifabutin	1.00		2	2			1	1								
Rifabutin	2.00		8	8												

\* VersaTREK®, Hain GenoType®, XPERT MTB/RIF or Molecular Methods

## Isolate G, *M. tuberculosis*–resistant to Isoniazid at 0.2µg/ml and 1.0µg/ml and Streptomycin at 2.0µg/ml and 10.0µg/ml by Agar Proportion

### Isoniazid

Isoniazid (INH) is the most widely used first-line anti-TB drug. It is the cornerstone of all effective regimens for the treatment of TB disease and latent infection. INH is a prodrug and is activated by the catalase-peroxidase enzyme encoded by the *katG* gene.[4, 5] The target of activated INH is enoyl-acyl-carrier protein reductase (*InhA*) which is required for mycolic acid biosynthesis. There are two described mechanisms that account for the majority of INH resistance[5]. The most common method, mutations in *katG*, is generally associated with high-level resistance to INH. Resistance to INH can also occur by mutations in the promoter region of the *inhA* gene which are generally associated with low-level resistance to INH and are less frequent than *katG* mutations. DNA sequence analysis of *inhA* and *katG* of Isolate G revealed a G>C point mutation in the *katG* locus resulting in serine being replaced by threonine at codon 315 (Ser315Thr); *inhA* was wild-type (i.e., no mutations were detected).

The recommended critical concentration and additional higher concentrations for testing INH using the AP method are 0.2 µg/ml and 1.0 µg/ml respectively. The equivalent concentrations for BACTEC™, MGIT™, and VersaTREK® are 0.1 µg/ml and 0.4 µg/ml. It is recommended that all laboratories perform testing at the critical concentration; if resistant, then testing at the higher recommended concentration should be performed.

Ninety-eight laboratories reported INH results for this isolate at the critical concentration. (Some laboratories submitted results for more than one method.) This isolate was reported resistant by:

- 100% (27/27) of the laboratories reporting AP results;
- 100% (20/20 ) of the laboratories reporting BACTEC™ results;
- 100% (69/69) of the laboratories reporting MGIT™ results;
- 100% (4/4) of the laboratories reporting VersaTREK® results.

Laboratories also reported resistance at recommended higher concentration.

The laboratories using Hain GenoType® MTBDR*plus* and laboratory developed tests reported INH resistance.

### Streptomycin

Streptomycin (SM) belongs to the aminoglycoside class of drugs and its primary mechanism of action is to inhibit the initiation of translations by binding to the 16S rRNA. In *M. tuberculosis*, the genetic basis of resistance to SM is usually due to mutations in *rrs* or *rpsL*[6].

Seventy-seven laboratories reported SM results for this isolate at the critical concentration. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 96.3% (26/27) of the laboratories reporting AP results;



- 100% (18/18) of the laboratories reporting BACTEC™ results; and
- 100% (51/51) of the laboratories reporting MGIT™ results.

Laboratories also reported SM resistance at recommended higher concentration.

See Table 2 for the complete results submitted by all participants for Isolate G.

**Table 2: Participant results for *M. tuberculosis* Isolate G–resistant to INH at 0.2µg and 1.0µg /ml and Streptomycin at 2.0µg/ml and 10.0µg/ml by AP method**

Drug	Conc.	Test Method											
		AP Results			BACTEC Results			MGIT Results			Other Results*		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.00											3	3
Isoniazid	0.10				20	20		69	69		4	4	
Isoniazid	0.20	27	27		1	1		1	1				
Isoniazid	0.40				5	5		35	35		4	4	
Isoniazid	1.00	27	27		2	2							
Isoniazid	2.00				1	1							
Isoniazid	5.00	2	2	4	1		1						
Isoniazid	10.00		1	1									
Rifampin	0.00										5	5	
Rifampin	1.00	26		26	4	4		70	70		4	4	
Rifampin	2.00				18	18							
Rifampin	5.00	3		3									
Pyrazinamide	5.00							1	1				
Pyrazinamide	20.00				1	1							
Pyrazinamide	100.00				14	14		64	2	66			
Pyrazinamide	300.00				1	1					4	4	
Ethambutol	0.00										1	1	
Ethambutol	2.50				17	17							
Ethambutol	5.00	22	1	23	3	3		70	70		4	4	
Ethambutol	7.50	2		2	3	3		1	1				
Ethambutol	8.00										4	4	
Ethambutol	10.00	9		9									
Streptomycin	1.00				1	1		51	51				
Streptomycin	2.00	1	26	27	18	18							
Streptomycin	4.00	1	1	2	1	1		9	9				
Streptomycin	6.00				3	3							
Streptomycin	10.00		23	23	1	1							
Ethionamide	1.25				2	2							
Ethionamide	2.50				2	2							
Ethionamide	5.00	7	16 <sup>†</sup>	23	1	1		2	2				
Ethionamide	10.00	2	2	4									
Kanamycin	0.00										1	1	
Kanamycin	2.50				1	1							
Kanamycin	5.00	11		11	2	2							
Kanamycin	6.00	10		10									
Capreomycin	0.00										1	1	
Capreomycin	1.25				1	1							
Capreomycin	2.50				1	1		1	1				
Capreomycin	3.00							1	1				
Capreomycin	5.00				2	2							
Capreomycin	10.00	20		20									
Cycloserine	30.00	10		10									
Cycloserine	60.00	1		1									

\* VersaTREK®, Hain GenoType®, XPERT MTB/RIF or Molecular Methods

† Includes borderline results

**Table 2 Continued: Participant results for *M. tuberculosis* Isolate G–resistant to INH at 0.2µg and 1.0µg/ml and Streptomycin at 2.0µg/ml and 10.0µg/ml by AP method**

Drug	Conc.	Test Method												
		AP Results			BACTEC Results			MGIT Results			Other Results*			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
p-Aminosalicylic acid	2.00	18		18										
p-Aminosalicylic acid	4.00							1		1				
p-Aminosalicylic acid	8.00	2		2										
p-Aminosalicylic acid	10.00	4		4										
Amikacin	0.00										1		1	
Amikacin	1.00							1		1				
Amikacin	1.50							1		1				
Amikacin	2.00	1		1	1		1							
Amikacin	2.50				1		1							
Amikacin	4.00	3		3										
Amikacin	5.00	1		1										
Amikacin	6.00	6		6										
Amikacin	8.00				1		1							
Amikacin	12.00	2		2										
Ofloxacin	0.00										1		1	
Ofloxacin	0.60	1		1										
Ofloxacin	1.00	2		2	2		2							
Ofloxacin	1.25				1		1							
Ofloxacin	2.00	15		15	5		5							
Ofloxacin	4.00	1		1	1		1							
Ciprofloxacin	0.00										1		1	
Ciprofloxacin	1.00	2		2	2		2	1		1				
Ciprofloxacin	2.00	6		6	1		1							
Ciprofloxacin	4.00				1		1							
Clofazimine	0.06						1	1						
Clofazimine	0.12				1		1							
Clofazimine	0.25				1		1							
Clofazimine	0.50				3		3							
Clofazimine	1.00	1		1										
Gatifloxacin	0.00										1		1	
Gatifloxacin	0.00										1		1	
Levofloxacin	1.50							1		1				
Levofloxacin	2.00				2		2							
Moxifloxacin	0.00										1		1	
Moxifloxacin	0.25							1		1				
Moxifloxacin	1.00	1		1										
Moxifloxacin	5.00	1		1										
Moxifloxacin	5.00	1		1										
Rifabutin	0.50	6		6	2		2							
Rifabutin	1.00	2		2	1		1							
Rifabutin	2.00	8		8										

\* VersaTREK®, Hain GenoType®, XPERT MTB/RIF or Molecular Methods

## **Isolate H, *M. tuberculosis*–resistant to Streptomycin at 2.0µg/ml by AP method and Pyrazinamide at 100.0µg/ml by MGIT method.**

### **Streptomycin**

As previously stated, streptomycin (SM) belongs to the aminoglycoside class of drugs and its primary mechanism of action is to inhibit the initiation of translations by binding to the 16S rRNA. In *M. tuberculosis*, the genetic basis of resistance to SM is usually due to mutations in *rrs* or *rpsL*[6].

Seventy-five laboratories reported SM results for this isolate at the critical concentration. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 92.0% (23/25) of the laboratories reporting AP results;
- 100% (18/18) of the laboratories reporting BACTEC™ results; and
- 100% (51/51) of the laboratories reporting MGIT™ results.

Laboratories also reported SM resistance at recommended higher concentration.

### **Pyrazinamide**

Pyrazinamide (PZA) is an important first-line drug used with INH and RMP for treatment of tuberculosis. The role of PZA is to shorten TB treatment to 6 months because it kills a population of persistent and semi-dormant bacilli in the acidic pH environment in the lesions that are not killed by other drugs. Pyrazinamide is a prodrug that requires conversion to its active form, pyrazinoic acid, by the pyrazinamidase (PZase) encoded by the *pncA* gene of *M. tuberculosis*. Resistance to PZA is usually caused by diverse nucleotide changes scattered throughout the *pncA* gene, and PZA-resistant *M. tuberculosis* strains lose PZase activity. .

Eighty-four laboratories reported PZA results for this isolate at the critical concentration. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 7.0% (1/14) of the laboratories reporting BACTEC™ results;
- 75.8% (50/66) of the laboratories reporting MGIT™ results; and
- 50.0% (2/4) of the laboratories reporting VersaTREK® results.

One laboratory reported susceptible using Laboratory Developed Tests.

Only one out of 14 laboratories reported Isolate H as PZA resistant using BACTEC, the CLSI-recommended method for PZA testing.

Standard culture-based PZA susceptibility tests are difficult to perform as a result of poor buffering of test media, the use of acidic medium pH that inhibits growth, and excessively large inoculum that reduce the activity of PZA [7]. Among culture based DST methods, the BACTEC™ radiometric method is probably the most reliable and is currently the reference method for choice for PZA DST [1]. MGIT had widely replaced the BACTEC™

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radiometric method. However, MGIT™ may over report PZA resistance [7, 8]. Tests for PZase activity and for the detection of mutations in *pncA* may be used as alternative methods for the detection of PZA resistance in *M. tuberculosis* [7, 8].

Isolate H did not have a mutation detected in *pncA*. Both MGIT tubes used in the PZA DST test (growth control and PZA-containing tube) were positive for PZase activity. In addition, only one out of 14 laboratories reported Isolate H as PZA resistant using BACTEC, the CLSI-recommended method for PZA testing. All of these results lead us to suspect that the MGIT™ DST results were falsely resistant. Further study is needed to ascertain the exact cause of this problem.

See Table 3 for the complete results submitted by all participants for Isolate H.

**Table 3: Participant results for *M. tuberculosis* Isolate H-resistant to Streptomycin at 2.0µg/ml by AP method and Pyrazinamide at 100.0µg/ml by MGIT method**

Drug	Conc.	Test Method											
		AP Results			BACTEC Results			MGIT Results			Other Results*		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.00										3		3
Isoniazid	0.10				20		20	68		68	4		4
Isoniazid	0.20	23		23				1		1			
Isoniazid	0.40				5		5	26	1	27	4		4
Isoniazid	1.00	22		22	1		1						
Isoniazid	5.00	3		3									
Isoniazid	10.00	1		1									
Rifampin	0.00										5		5
Rifampin	1.00	24		24	4		4	69		69	4		4
Rifampin	2.00				18		18						
Rifampin	5.00	3		3									
Pyrazinamide	0.00										1		1
Pyrazinamide	5.00								1	1			
Pyrazinamide	20.00				1		1						
Pyrazinamide	100.00				13	1	14	16	50 <sup>†</sup>	66			
Pyrazinamide	300.00				1		1				2	2	4
Ethambutol	0.00										1		1
Ethambutol	2.50				17		17						
Ethambutol	5.00	19	2	21	3		3	69		69	3		3
Ethambutol	7.50	2		2	3		3	1		1			
Ethambutol	8.00										4		4
Ethambutol	10.00	8		8									
Streptomycin	1.00					1	1			51	51		
Streptomycin	2.00	2	23	25		18	18						
Streptomycin	4.00	1	1	2		1	1			9	9		
Streptomycin	6.00					3	3						
Streptomycin	10.00					1	1						
Ethionamide	1.25				1		1						
Ethionamide	2.50				2		2						
Ethionamide	5.00	16	4 <sup>†</sup>	20	1		1	2		2			
Ethionamide	10.00	3		3									
Kanamycin	0.00										1		1
Kanamycin	5.00	10		10	1		1						
Kanamycin	6.00	9		9									
Kanamycin	6.00	9		9									
Capreomycin	0.00										1		1
Capreomycin	2.50							1		1			
Capreomycin	3.00							1		1			
Capreomycin	5.00				2		2						
Capreomycin	10.00	17		17									
Cycloserine	30.00	7	1 <sup>†</sup>	8									
Cycloserine	60.00	1		1									

\* VersaTREK®, Hain GenoType®, XPERT MTB/RIF or Molecular Methods

† Includes borderline results

**Table 3 Continued: Participant results for *M. tuberculosis* Isolate H-resistant to Streptomycin at 2.0µg/ml by AP method and Pyrazinamide at 100.0µg/ml by MGIT method**

Drug	Conc.	Test Method														
		AP Results			BACTEC Results			MGIT Results			Other Results*					
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum			
p-Aminosalicylic acid	2.00	15		15												
p-Aminosalicylic acid	4.00								1		1					
p-Aminosalicylic acid	8.00	2		2												
p-Aminosalicylic acid	10.00	4		4												
Amikacin	0.00											1				1
Amikacin	1.00								1		1					
Amikacin	1.50								1		1					
Amikacin	2.00	1		1	1		1									
Amikacin	2.50				1		1									
Amikacin	4.00	2		2												
Amikacin	5.00	1		1												
Amikacin	6.00	5		5												
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												
Ofloxacin	0.00											1				1
Ofloxacin	0.60	1		1												
Ofloxacin	1.00	2		2	2		2									
Ofloxacin	2.00	14		14	4		4									
Ofloxacin	4.00	1		1	1		1									
Ciprofloxacin	0.00											1				1
Ciprofloxacin	1.00	2		2	2		2		1		1					
Ciprofloxacin	2.00	4		4	1		1									
Ciprofloxacin	4.00				1		1									
Clofazimine	0.06						1		1							
Clofazimine	0.12						1		1							
Clofazimine	0.25						1		1							
Clofazimine	0.50				2		2									
Clofazimine	1.00	1		1												
Gatifloxacin	0.00											1				1
Gatifloxacin	0.00											1				1
Levofloxacin	1.50								1		1					
Levofloxacin	2.00				2		2									
Moxifloxacin	0.00											1				1
Moxifloxacin	0.25								1		1					
Moxifloxacin	1.00	1		1												
Rifabutin	0.50	6		6	1		1									
Rifabutin	1.00	2		2	1		1									
Rifabutin	2.00	7		7												

\* VersaTREK®, Hain GenoType®, XPERT MTB/RIF or Molecular Methods

## **Isolate I, *M. tuberculosis*–susceptible to first-line and second-line drugs**

This isolate is susceptible to all first and second line drugs at recommended testing concentrations.

Isolate I was reported resistant by:

Laboratories using AP methods:

5.3% (1/19) reported resistant to Ethambutol  
10.5% (2/19) reported resistant to Ethionamide

Laboratories using BACTEC™ method:

4.8% (1/21) reported resistant to Isoniazid  
5.6% (1/18) reported resistant to Ethambutol  
15.8% (3/19) reported resistant to Streptomycin

Laboratories using MGIT™ method:

7.6% (5/66) reported resistance to Pyrazinamide

Laboratories using VersaTREK® method:

66.7% (2/3) reported resistance to Pyrazinamide

See Table 4 for the complete results submitted by all participants for Isolate I.



**Table 4: Participant results for *M. tuberculosis*, Isolate I– susceptible to first-line and second-line drugs**

Drug	Conc.	Test Method												
		AP Results			BACTEC Results			MGIT Results			Other Results*			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
Isoniazid	0.00											3		3
Isoniazid	0.10				20	1	21	68		68		4		4
Isoniazid	0.20	21		21				1		1				
Isoniazid	0.40				5		5	28		28		3		3
Isoniazid	1.00	21		21	1		1							
Isoniazid	5.00	3		3										
Isoniazid	10.00	1		1										
Rifampin	0.00											5		5
Rifampin	1.00	23		23	4		4	69		69		4		4
Rifampin	2.00				18		18							
Rifampin	5.00	2		2										
Pyrazinamide	0.00											1		1
Pyrazinamide	5.00							1		1				
Pyrazinamide	20.00				1		1							
Pyrazinamide	100.00				14		14	61	5	66				
Pyrazinamide	300.00				1		1					1	2	3
Ethambutol	0.00											1		1
Ethambutol	2.50				17	1	18							
Ethambutol	5.00	18	1	19	3		3	69		69		3		3
Ethambutol	7.50	2		2	3		3	1		1				
Ethambutol	8.00											4		4
Ethambutol	10.00	7		7										
Streptomycin	1.00				1		1	49	1	50				
Streptomycin	2.00	23		23	16	3	19							
Streptomycin	4.00	1		1				6		6				
Streptomycin	6.00				2		2							
Streptomycin	10.00	19		19										
Ethionamide	1.25					1	1							
Ethionamide	2.50				1		1							
Ethionamide	5.00	17	2 <sup>†</sup>	19	1	1	2	2		2				
Ethionamide	10.00	3		3										
Kanamycin	0.00											1		1
Kanamycin	5.00	10		10	1		1							
Kanamycin	6.00	8		8										
Capreomycin	0.00											1		1
Capreomycin	2.50							1		1				
Capreomycin	3.00							1		1				
Capreomycin	5.00				1		1							
Capreomycin	10.00	17		17										
Cycloserine	30.00	8		8										
Cycloserine	60.00	1		1										

\* VersaTREK<sup>®</sup>, Hain GenoType<sup>®</sup>, XPERT MTB/RIF or Molecular Methods

† Includes borderline results

**Table 4 Continued: Participant results for *M. tuberculosis*, Isolate I– susceptible to first-line and second-line drugs**

Drug	Conc.	Test Method														
		AP Results			BACTEC Results			MGIT Results			Other Results*					
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum			
p-Aminosalicylic acid	2.00	14		14												
p-Aminosalicylic acid	4.00								1		1					
p-Aminosalicylic acid	8.00	2		2												
p-Aminosalicylic acid	10.00	4		4												
Amikacin	0.00											1		1		
Amikacin	1.00								1		1					
Amikacin	1.50								1		1					
Amikacin	2.00	1		1	1		1									
Amikacin	4.00	2		2												
Amikacin	5.00	1		1												
Amikacin	6.00	5		5												
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												
Ofloxacin	0.00											1		1		
Ofloxacin	0.60	1		1												
Ofloxacin	1.00	1		1	1		1									
Ofloxacin	2.00	14		14	4		4									
Ofloxacin	4.00	1		1	1		1									
Ciprofloxacin	0.00											1		1		
Ciprofloxacin	1.00	1		1	1		1		1		1					
Ciprofloxacin	2.00	4		4	1		1									
Ciprofloxacin	4.00				1		1									
Clofazimine	0.06						1		1							
Clofazimine	0.12				1		1									
Clofazimine	0.25				1		1									
Clofazimine	0.50				1		1									
Clofazimine	1.00	1		1												
Gatifloxacin	0.00											1		1		
Levofloxacin	1.50								1		1					
Levofloxacin	2.00				1		1									
Moxifloxacin	0.00											1		1		
Moxifloxacin	0.25								1		1					
Moxifloxacin	1.00	1		1												
Rifabutin	0.50	6		6	1		1									
Rifabutin	1.00	2		2												
Rifabutin	2.00	7		7												

\* VersaTREK®, Hain GenoType®, XPERT MTB/RIF or Molecular Methods

## **Isolate J, *M. tuberculosis*–resistant to Isoniazid at 0.2µg/ml and 1.0µg/ml; Ethambutol at 5.0µg/ml; Amikacin at 4.0µg/ml; Capreomycin at 10.0µg/ml; and Kanamycin at 5.0µg/ml by Agar Proportion 7H10 method**

### **Isoniazid**

As noted in the section for Isolate G, there are two described mechanisms that account for the majority of INH resistance. Mutations in *katG* are generally associated with high-level resistance to INH. Mutations in the promoter region of the *inhA* gene are generally associated with low-level resistance to INH and are less frequent than *katG* mutations. DNA sequence analysis of *inhA* and *katG* of Isolate J revealed a G>C point mutation in the *katG* locus resulting in serine being replaced by threonine at codon 315 (Ser315Thr); *inhA* was wild-type (i.e., no mutations were detected).

Ninety-seven laboratories reported INH results for this isolate at the critical concentration. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 100% (27/27) of the laboratories reporting AP results;
- 100% (20/20) of the laboratories reporting BACTEC™ results; and
- 100% (69/69) of the laboratories reporting MGIT™ results;
- 100% (3/3) of the laboratories reporting VersaTREK® results.

Laboratories also reported 100% (68/68) resistance when tested at recommended higher concentrations for INH.

Laboratories using molecular methods (Hain GenoType® MTBDRplus, and Laboratory Developed Tests) reported INH resistance.

### **Ethambutol**

Ethambutol (EMB) is an important first-line drug for the treatment of tuberculosis and is used in combination with INH, RMP, and PZA to prevent emergence of drug resistance. EMB is a bacteriostatic agent that is active against growing bacilli and has no effect on non-replicating bacilli [5]. EMB targets the arabinosyl transferases (*embCAB* operon), thereby inhibiting the biosynthesis of the cell wall components arabinogalactan and lipoarabinomannan [5, 9].

Conventional culture based methods of EMB susceptibility testing are problematic [10, 11]. Sequence analysis of EMB-resistant clinical isolates has shown that EMB resistance is associated primarily with missense mutations within the EMB resistance determining region of the gene *embB* at codons 306, 406, and 497[4, 9].

DNA sequence analysis of *embB* of Isolate J revealed a mutation resulting methionine replaced by isoleucine at codon 306 (Met306Ile). This mutation is highly associated with EMB resistance [12].

Ninety-five laboratories reported EMB results for this isolate at the critical concentration. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 80% (20/25 ) of the laboratories reporting AP results;

- 93.8% (15/16) of the laboratories reporting BACTEC™ results;
- 79.7% (55/69) of the laboratories reporting MGIT™ results;
- 0.0% (0/3) of the laboratories reporting VersaTREK® results.

The laboratory using Hain GenoType® MTBDRsl also reported EMB resistance.

### **Second- line drugs**

Isolate J was also resistant to Amikacin, Capreomycin, and Kanamycin by the AP method. Mutations in the 16S *rRNA* gene (*rrs*) have been associated with resistance to second-line injectable drugs [13]. DNA sequence analysis of the *rrs* gene of Isolate J revealed a mutation resulting alanine replaced by glycine at codon 1401 (Ala1401Gly) which is highly associated with resistance to second line injectable drugs.

#### **Amikacin**

Fourteen laboratories reported Amikacin results for this isolate. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 100% (3/3) of the laboratories reporting AP results at the recommended critical concentration.

The laboratory using Hain GenoType® MTBDRsl also reported Amikacin resistance.

#### **Capreomycin**

Twenty-five laboratories reported Capreomycin results for this isolate. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 80% (16/20) of the laboratories reporting AP results at the recommended critical concentration.

The laboratory using Hain GenoType® MTBDRsl also reported Capreomycin resistance.

#### **Kanamycin**

Twenty-three laboratories reported Kanamycin results for this isolate. (Some laboratories submitted results from more than one method.) This isolate was reported resistant by:

- 100% (21/21) of the laboratories reporting AP results at the recommended critical concentration.

The laboratory using Hain GenoType® MTBDRsl also reported Kanamycin resistance.

See Table 5 for the complete results submitted by all participants for Isolate J.

**Table 5: Participant results for Isolate J, *M. tuberculosis*–resistant to Isoniazid at 0.2µg/ml and 1.0µg/ml; Ethambutol at 5.0µg/ml; Amikacin at 4.0µg/ml; Capreomycin at 10.0µg/ml; and Kanamycin at 5.0µg/ml by Agar Proportion 7H10 method**

Drug	Conc.	Test Method											
		AP Results			BACTEC Results			MGIT Results			Other Results*		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.00											3	3
Isoniazid	0.10					20	20		69	69		3	3
Isoniazid	0.20		27	27		1	1		1	1			
Isoniazid	0.40					5	5		36	36		3	3
Isoniazid	1.00		27	27		2	2						
Isoniazid	2.00					1	1						
Isoniazid	5.00	2	2	4		1		1					
Isoniazid	10.00		1	1									
Rifampin	0.00											5	5
Rifampin	1.00	26		26		4		4	70		70	3	3
Rifampin	2.00					18		18					
Rifampin	5.00	3		3									
Pyrazinamide	5.00								1		1		
Pyrazinamide	20.00					1		1					
Pyrazinamide	100.00					13	1	14	65	2	67		
Pyrazinamide	300.00					1		1				4	4
Ethambutol	0.00											1	1
Ethambutol	2.50					1	15	16					
Ethambutol	5.00	5	20 <sup>†</sup>	25		1	3	4	14	55 <sup>†</sup>	69	3	3
Ethambutol	7.50	1	1 <sup>†</sup>	2		4		4		1	1		
Ethambutol	8.00											3	3
Ethambutol	10.00	11		11		1		1					
Streptomycin	1.00					1		1	50	1	51		
Streptomycin	2.00	26		26		18	2	20					
Streptomycin	4.00	1		1					7		7		
Streptomycin	6.00					2		2					
Streptomycin	10.00	21		21									
Ethionamide	1.25					1	1	2					
Ethionamide	2.50					2		2					
Ethionamide	5.00	14	8 <sup>†</sup>	22		1	1	2		2	2		
Ethionamide	10.00	3	1 <sup>†</sup>	4									
Kanamycin	0.00											1	1
Kanamycin	2.50						1	1					
Kanamycin	5.00		11	11			3	3					
Kanamycin	6.00		10	10									
Kanamycin	10.00						1	1					
Capreomycin	0.00											1	1
Capreomycin	1.25						1	1					
Capreomycin	2.50						1	1		1	1		
Capreomycin	3.00									1	1		
Capreomycin	5.00					1	2 <sup>†</sup>	3					
Capreomycin	10.00	4	16	20		1		1					
Cycloserine	30.00	9	1	10									
Cycloserine	60.00	1		1									

\* VersaTREK<sup>®</sup>, Hain GenoType<sup>®</sup>, XPERT MTB/RIF or Molecular Methods

† Includes borderline results

**Table 5 Continued: Participant results for Isolate J, *M. tuberculosis*–resistant to Isoniazid at 0.2µg/ml and 1.0µg/ml; Ethambutol at 5.0µg/ml; Amikacin at 4.0µg/ml; Capreomycin at 10.0µg/ml; and Kanamycin at 5.0µg/ml by Agar Proportion 7H10 method**

Drug	Conc.	Test Method														
		AP Results			BACTEC Results			MGIT Results			Other Results*					
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum			
p-Aminosalicylic acid	2.00	18		18												
p-Aminosalicylic acid	4.00								1		1					
p-Aminosalicylic acid	8.00	2		2												
p-Aminosalicylic acid	10.00	4		4												
Amikacin	0.00												1		1	
Amikacin	1.00									1		1				
Amikacin	1.50									1		1				
Amikacin	2.00		1	1		1	1									
Amikacin	2.50					1	1									
Amikacin	4.00		3	3												
Amikacin	5.00		1	1												
Amikacin	6.00	1	5	6												
Amikacin	8.00					1	1									
Amikacin	12.00		2	2												
Ofloxacin	0.00												1		1	
Ofloxacin	0.60	1		1												
Ofloxacin	1.00	2		2	2		2									
Ofloxacin	1.25				1		1									
Ofloxacin	2.00	15		15	5		5									
Ofloxacin	4.00	1		1	1		1									
Ciprofloxacin	0.00												1		1	
Ciprofloxacin	1.00	2		2	2		2		1		1					
Ciprofloxacin	2.00	6		6	1		1									
Ciprofloxacin	4.00				1		1									
Clofazimine	0.06					1	1									
Clofazimine	0.12				1		1									
Clofazimine	0.25				1		1									
Clofazimine	0.50				3		3									
Clofazimine	1.00	1		1												
Gatifloxacin	0.00												1		1	
Levofloxacin	1.50								1		1					
Levofloxacin	2.00				2		2									
Moxifloxacin	0.00												1		1	
Moxifloxacin	0.25								1		1					
Moxifloxacin	1.00	1		1												
Moxifloxacin	5.00	1		1												
Rifabutin	0.50	6		6	2		2									
Rifabutin	1.00	2		2	1		1									
Rifabutin	2.00	8		8												

\* VersaTREK®, Hain GenoType®, XPERT MTB/RIF or Molecular Methods

## Abbreviations Used in This Report

AMK	amikacin
AP	agar proportion
BACTEC™	BACTEC™ 460TB
bp	base pair
BSL	Biosafety Level
CDC	Centers for Disease Control and Prevention (CDC)
CIP	ciprofloxacin
CLF	clofazimine
CLSI	Clinical Laboratory and Standards Institute
CM	capreomycin
CS	cycloserine
DNA	deoxyribonucleic acid
DST	Drug Susceptibility Testing
EMB	ethambutol
ETH	ethionamide
HMO	Health Maintenance Organization
INH	isoniazid
KM	kanamycin
LEV	levofloxacin
MGIT™	BACTEC™ MGIT™ 960 (Mycobacteria Growth Indicator Tube)
MOX	moxifloxacin
MPEP MTB NTM DST	Model Performance Evaluation Program for <i>Mycobacterium tuberculosis</i> and Nontuberculous Mycobacteria Drug Susceptibility Testing
NIH	National Institutes of Health
NTM	Nontuberculous Mycobacteria
OFX	ofloxacin
PAS	p-aminosalicylic acid
PPO	Preferred Provider Organization
PZA	pyrazinamide
QRDR	quinolone-resistance-determining region
RBT	rifabutin
RMP	rifampin
RNA	ribonucleic acid
SM	streptomycin
VersaTREK®	VersaTREK® Myco Susceptibility Kit

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