

January 29 1999

Participant
Centers for Disease Control and Prevention (CDC)
Susceptibility Testing of *Mycobacterium tuberculosis* and Nontuberculous Mycobacteria
Performance Evaluation Program

Subject: Analyses of Participant Laboratory Results for the September 1998 Shipment

Dear Participant:

Enclosed are analyses of laboratory test results reported to the Centers for Disease Control and Prevention (CDC) by participant laboratories for the strains of *Mycobacterium tuberculosis*, *M. avium complex*, and *M. marinum* shipped in February 1998. Participant laboratories received either 3 *M. tuberculosis* strains or all five *M. tuberculosis* and nontuberculous mycobacteria (NTM) strains. Testing results were received and analyzed from 136 of 145 (93.8%) of laboratories participating in this shipment. An additional 9 laboratories indicated that they have discontinued *M. tuberculosis* drug susceptibility testing since the last shipments and 5 laboratories outside of the continental U.S. were unable to obtain import permits.

The enclosed aggregate report is prepared in a format that will allow laboratories to compare their results with results obtained by other participants for the same strain using the same method, drug, and concentration. The first *three* pages contain descriptive information about the participant laboratories. We encourage you to circulate this report to all personnel who are involved with drug susceptibility testing, reporting, or interpretation for *M. tuberculosis* and NTM.

The addition of NTM strains to this performance evaluation is intended to provide an assessment of the various methods, drugs, and interpretations that are reported by laboratories that perform drug susceptibility testing for these different strains. The test results for NTM strains also provide information on interlaboratory agreement with different test methods and will assist with efforts to develop standard methods for NTM drug susceptibility testing. By reporting these practices and test results CDC is neither recommending nor endorsing these testing practices. Some of the test results reported by participants, may in fact, provide inappropriate or misleading information to the clinician. A consensus report by the American Thoracic Society is referenced to provide participants with recommendations for NTM test methods and drugs that have clinical relevance.

If you have any comment or suggestions on the results in this report or have questions regarding the changes in this program, you may call me at (770) 488-8076.

Sincerely yours,

John C. Ridderhof, Dr.P.H.
Science Administrator
Division of Laboratory Systems
Public Health Practice Program Office

Enclosures

Analyses of the September 1998 Performance Evaluation Results for *M. tuberculosis* and Nontuberculous Mycobacteria Drug Susceptibility Testing Reported to the Centers for Disease Control and Prevention by Participating Laboratories

This report is an analysis of laboratory test results reported to the Centers for Disease Control and Prevention (CDC) by participant laboratories for the 3 strains of *Mycobacterium tuberculosis*, 1 strain of *M. avium complex*, and 1 strain of *M. marinum* shipped in September 1998. Participant laboratories either received 3 *M. tuberculosis* or all five *M. tuberculosis* and NTM strains. Testing results were received and analyzed from 136 of 145 (93.8%) participating laboratories in this shipment.

Descriptive Information on Participant laboratories

Figure 1 shows the laboratory classification reported by 135 of the participants. Participants consisted of 67 health departments, 58 hospitals, 8 independents, and 2 “other” type of laboratories.

Figure 2 provides the distribution of the annual volume of *M. tuberculosis* isolates tested for drug susceptibilities by participating laboratories in calendar year 1997.

Figure 3 lists the biosafety levels reported by participant laboratories for *M. tuberculosis*. All laboratories are strongly encouraged to consult the CDC/NIH manual, Biosafety in Microbiological and Biomedical Laboratories (3rd edition) for recommendations and to determine their correct biosafety level. Figure 4 lists the biosafety levels reported by participant laboratories for working with rapidly growing NTM cultures and figure 5 lists the biosafety levels reported by participant laboratories for working with slow growing NTM cultures.

Figure 6 provides a breakdown of the test procedures used by the participating laboratories for *M. tuberculosis* drug susceptibility testing. Participants were asked to check all of the test methods used. Figure 7 provides a breakdown of the test procedures used by the participating laboratories for *M. avium complex*. Figure 8 provides a breakdown of the test procedures used by the participating laboratories for *M. marinum*.

M. tuberculosis test results:

Table 1 provides the percentage of laboratories that included the recommended critical concentration of primary antituberculosis drug in their regimen. The aggregate test results are provided in separate tables, representing cultures F, G, H, I, and J, to facilitate comparison among laboratories. Table 2 for the *M. tuberculosis* cultures F, G, and H is constructed to include the results for both the radiometric (BACTEC) and conventional (agar) methods at each concentration of drug. The test results are listed in the appropriate (susceptible or resistant) columns with a corresponding total number of tests (Sum) column provided as 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.

In table 2 the concentrations recommended by CDC and the NCCLS (tentative standard) for the primary (isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin) and secondary (ethionamide, kanamycin, capreomycin, cycloserine, p-amino-salicylic acid) antituberculosis drugs are highlighted for the conventional and radiometric method. Participants should note that these recommended combinations reflect the critical concentrations of antituberculosis drugs in 7H10 agar and those concentrations for the BACTEC method that directly correlate with the critical concentrations in the conventional method (1-6). When two concentrations are highlighted, such as for isoniazid, ethambutol and streptomycin, the lower concentration is the critical concentration that should always be included to determine whether the *M. tuberculosis* isolate is resistant.

Strain F was resistant to pyrazinamide and strain G was resistant to rifampin. For strain A, 100% (2/2) of participants using the conventional method and 97.6% (81/83) using the BACTEC method detected pyrazinamide resistance. For strain G, 100% (44/44) detected rifampin resistance at the critical concentration (1F g/ml) in the conventional method, and 98.1% (105/107) detected rifampin resistance at the equivalent concentration (2 F g/ml) with the BACTEC method.

For strain H, 92.1% (35/38) detected streptomycin resistance at the critical concentration (2 F g/ml) in the conventional method, and 78% (78/100) detected streptomycin resistance at the equivalent concentration (2 F g/ml) with the BACTEC method. Although the results for strain H represent a minor difference in the detection of streptomycin resistance, this difference between the conventional and BACTEC methods has been observed for 3 *M. tuberculosis* isolates in the last two shipments. In the February 1998 shipment, strain A had streptomycin resistance detected by 24% (11/46) in the conventional method and 0% (0/111) detected streptomycin resistance with the BACTEC method. For the February 1998 strain B, 97.7% (43/44) detected streptomycin resistance in the conventional method, and 83.8% (93/111) detected streptomycin resistance with the BACTEC method.

The provision of test results for all drugs that are reported to CDC should not be construed as a recommendation or endorsement for testing particular drugs or concentrations with patient isolates of *M. tuberculosis*. It is assumed that some of the drugs are being tested for the purpose of research or for potential use in the few referral institutions that may treat patients with *M. tuberculosis* isolates resistant to almost all standard drugs. Laboratories should not add drugs to their testing regimen without the consultation of physicians with expertise in the treatment of multi-drug resistant tuberculosis. Laboratories may contact their local TB control program for referrals of physicians with experience and expertise in treating multi-drug resistant tuberculosis.

Nontuberculous Mycobacteria test results:

The aggregate test results are provided in Tables 3 and 5 for culture I, *M. avium* complex and Tables 4 and 6 for culture E, *M. marinum* to facilitate comparison among laboratories. Tables 3 and 4, for *M. avium* complex and *M. marinum* respectively, represent either single or multiple drug concentrations with "breakpoint" susceptibility test results. In tables 3 and 4, the participant laboratories reported an interpretation of either susceptibility or resistance for each drug

concentration that was reported. Tables 5 and 6 represent all minimum inhibitory concentrations (MICs) susceptibility test results, for *M. avium* complex and *M. marinum* respectively, reported by the participant laboratories. Tables 5 and 6 include all the quantitative MIC test results, regardless of whether the laboratory provided a test interpretation of resistant or susceptible for the reported MIC.

There were 27 participant that provided test results on strain I, *M. avium* complex: 19 participants reported breakpoint test results and 10 participants reported MIC test results. Table 3, representing all of the breakpoint susceptibility test results for *M. avium complex*, includes results reported for the conventional agar proportion, BACTEC, Disk elution, and 1 other (modified agar disk elution) test methods. Some participants reporting results for *M. avium* complex used the conventional method and BACTEC methods and with concentrations of primary drugs recommended for *M. tuberculosis* (8). The American Thoracic Society (ATS) recommendations (9) for *M. avium* complex state, “Susceptibility testing with rifabutin and the antituberculosis drugs is not recommended. Routine testing against clarithromycin should not be performed, but that test should be performed on isolates from patients who have failed prior macrolide therapy or prophylaxis. Minimal inhibitory concentration of >32 Fg/ml is the recommended resistance breakpoint.” For strain I, all of the breakpoint susceptibility and MIC interpretations provided for clarithromycin and azithromycin were reported as resistant. The clarithromycin MICs results reported for strain I ranged from ≥ 2 Fg/ml to ≥ 256 Fg/ml with 5/11 participants reporting an MIC ≥ 32 Fg/ml. Only 3/27 (11.1%) of participants restricted testing to clarithromycin, as recommended by ATS.

There were 35 participants that reported testing results for strain J, *M. marinum*: 28 participants reported breakpoint test results and 12 participants reported MIC test results. Table 3, representing all of the breakpoint susceptibility test results for *M. marinum*, includes results reported for the conventional agar proportion, BACTEC, E-test, Microtiter, and 1 other (Sensititre MIC) test methods. The ATS recommendations for *M. marinum* note that the “desired test drugs are rifampin, ethambutol, doxycycline or minocycline, clarithromycin, and a sulfonamide”. Only 6/35 (17.1%) of participants restricted testing to rifampin, ethambutol, doxycycline or minocycline, clarithromycin, and a sulfonamide, as recommended by ATS.

Many laboratories perform drug susceptibility testing for NTM in the absence of clinical studies demonstrating the efficacy of particular drugs and/or drug concentrations and methods (8,9). The addition of NTM strains to this performance evaluation program should not be interpreted as recommendations for laboratories to adopt NTM drug susceptibility testing, especially if the laboratory has limited experience with these tests and methods. We encourage laboratories that perform NTM drug susceptibility testing to consult recommendations, references, and physicians with expertise in infectious diseases when selecting test methods, drugs, and test interpretations.

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Figure 1. Primary Classification of Participating Laboratories

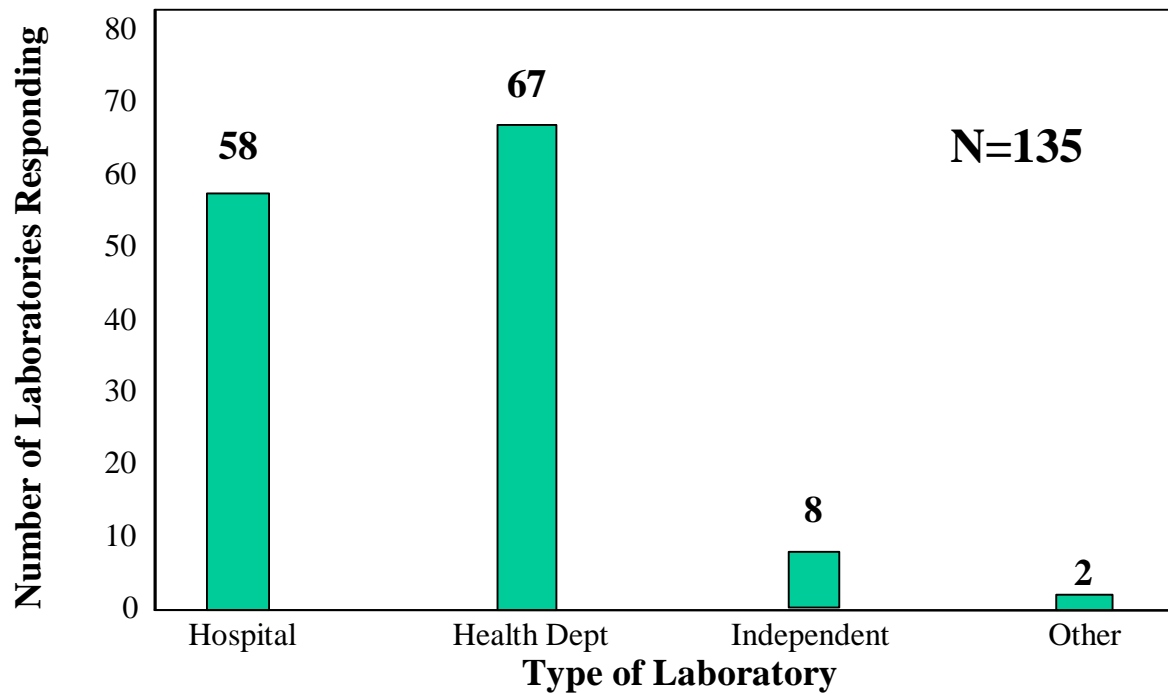
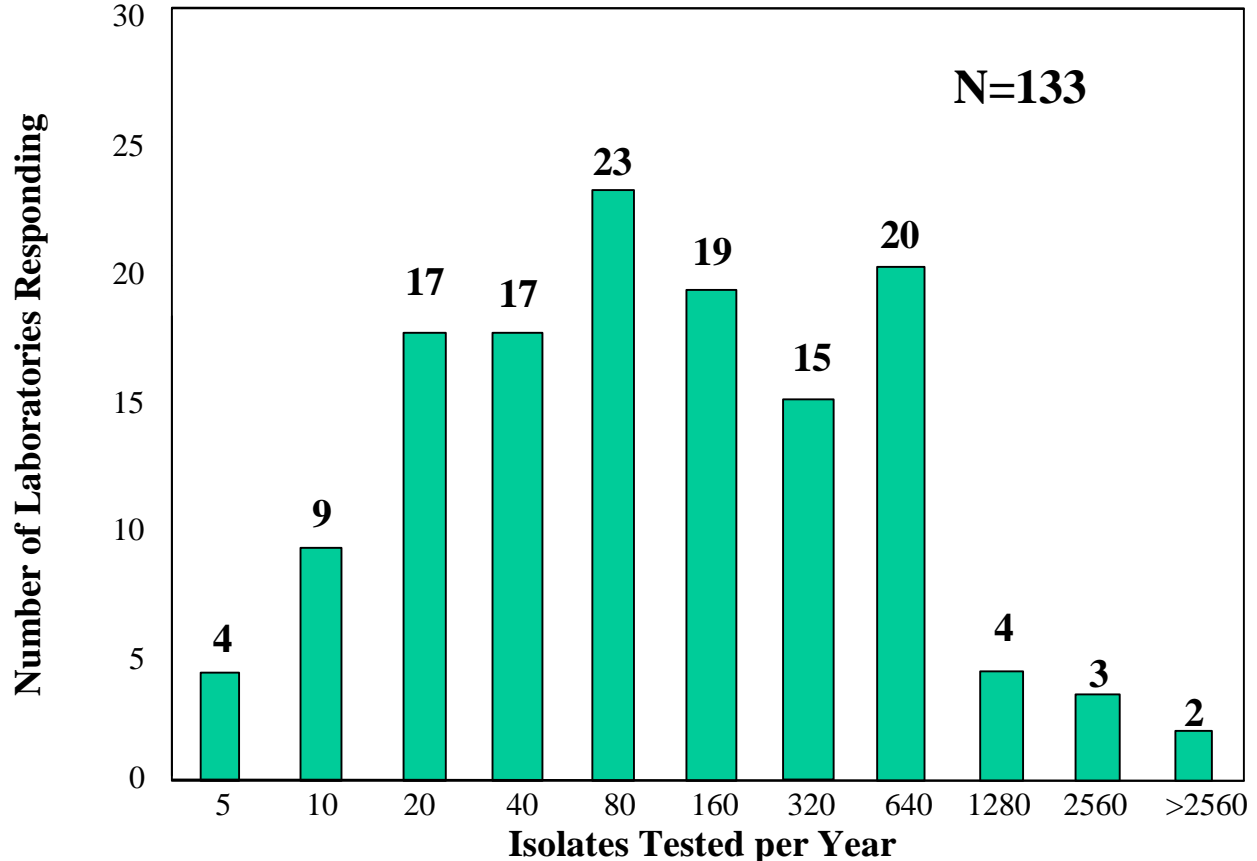
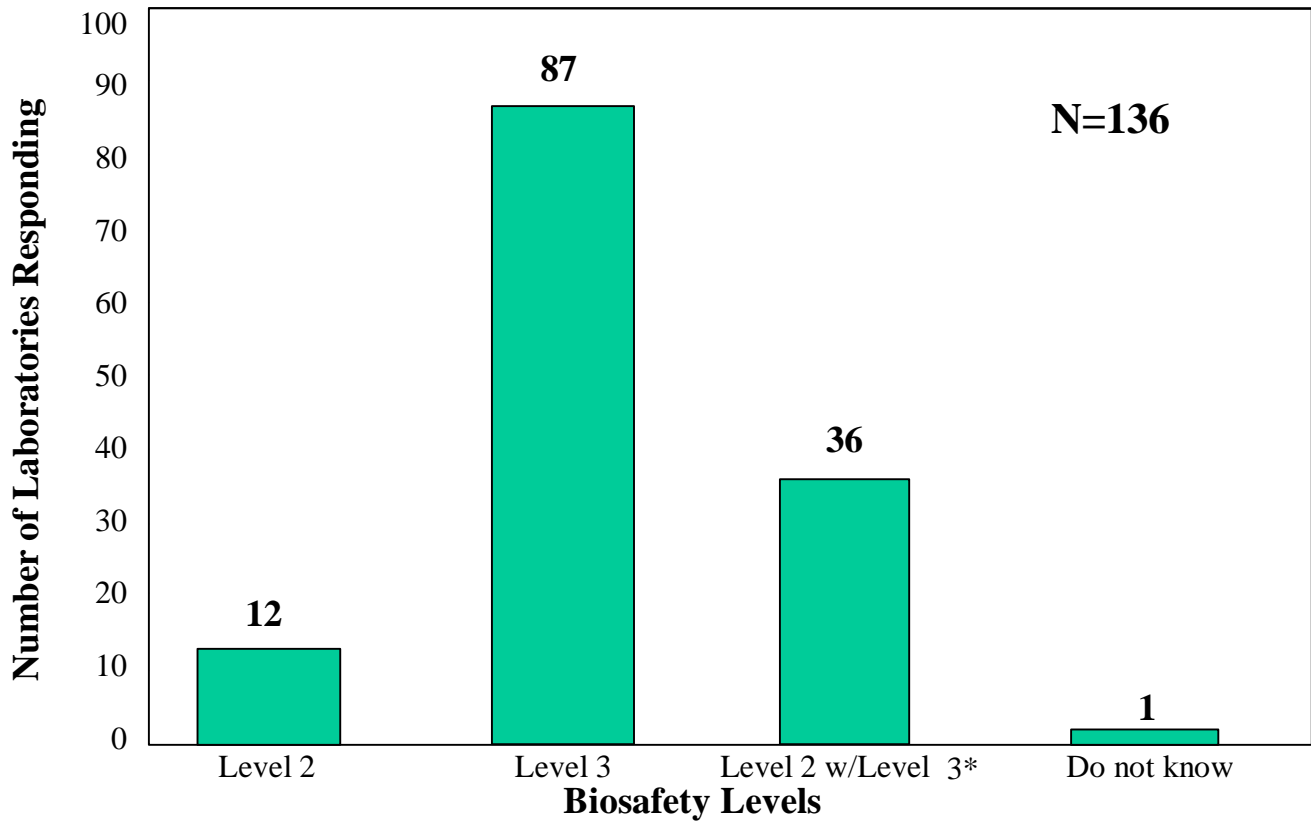


Figure 2. 1997 Annual Volume of *M. tuberculosis* Isolates for Participating Laboratories



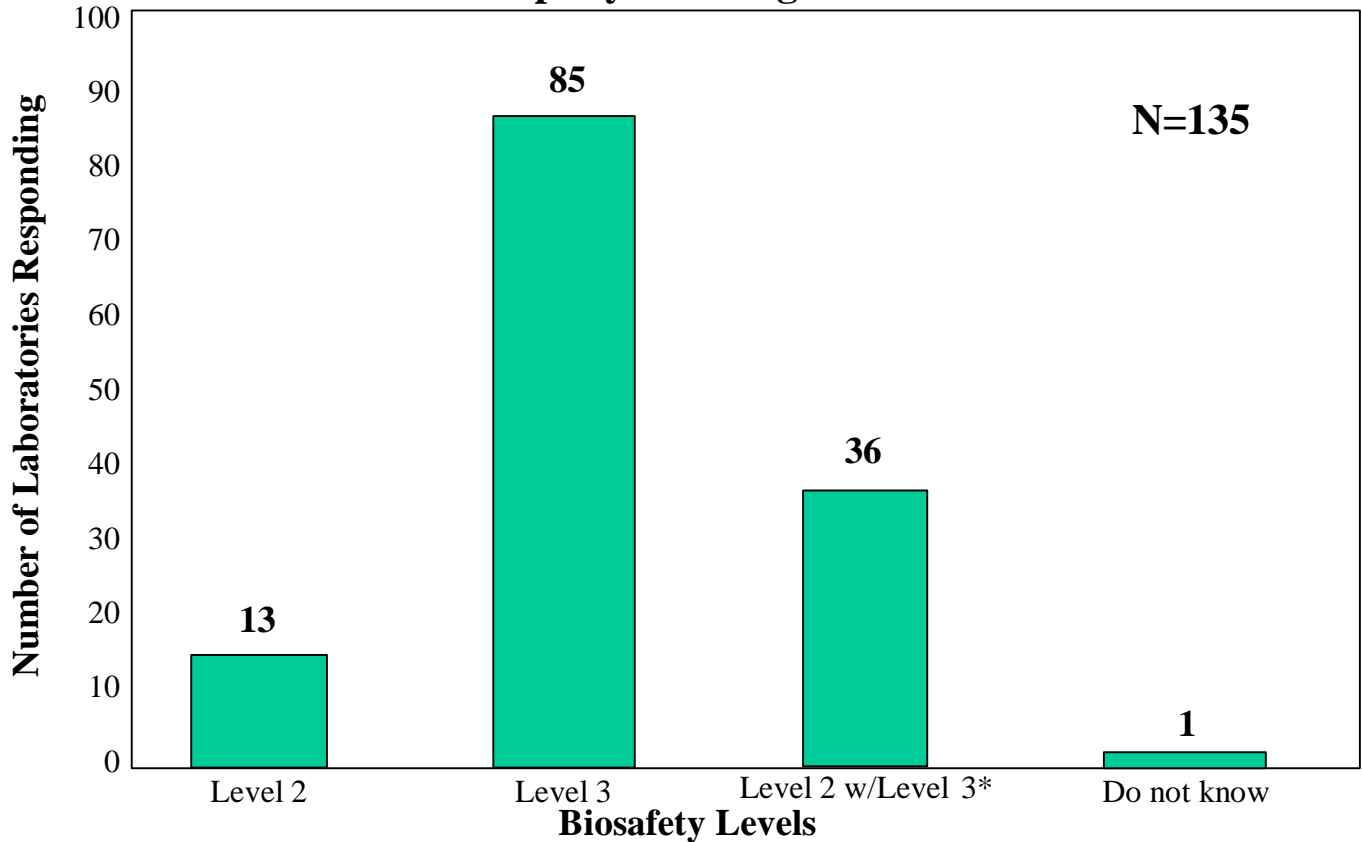
Group labels indicate upper limit of the group.

Figure 3. Biosafety Levels of Participating Laboratories for *M. tuberculosis*



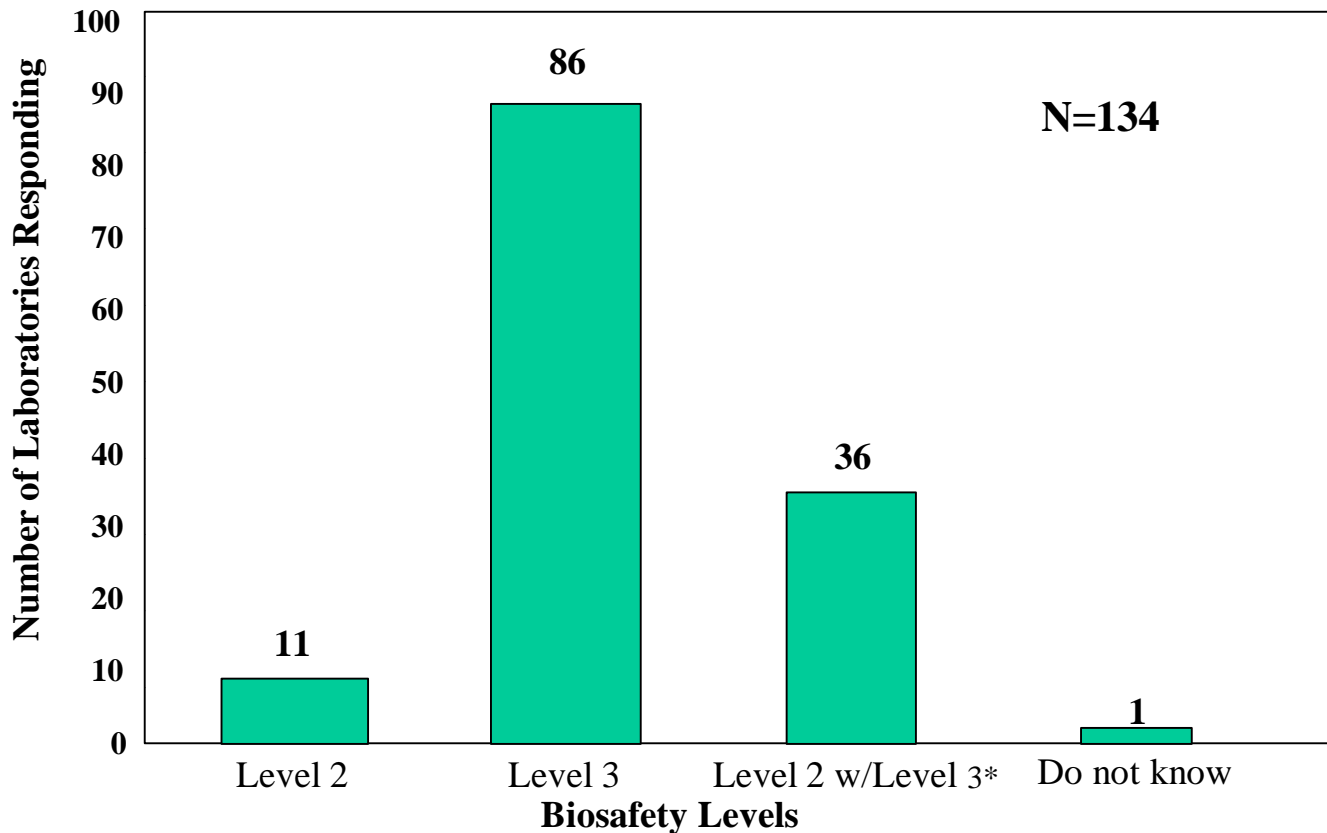
* Biosafety level 2 for facilities with level 3 containment equipment

Figure 4. Biosafety Levels of Participating Laboratories for Rapidly Growing NTM



* Biosafety level 2 for facilities with level 3 containment equipment

Figure 5. Biosafety Levels of Participating Laboratories for Slow Growing NTM



* Biosafety level 2 for facilities with level 3 containment equipment

Figure 6. Test Procedures used by Laboratories for *M. tuberculosis*

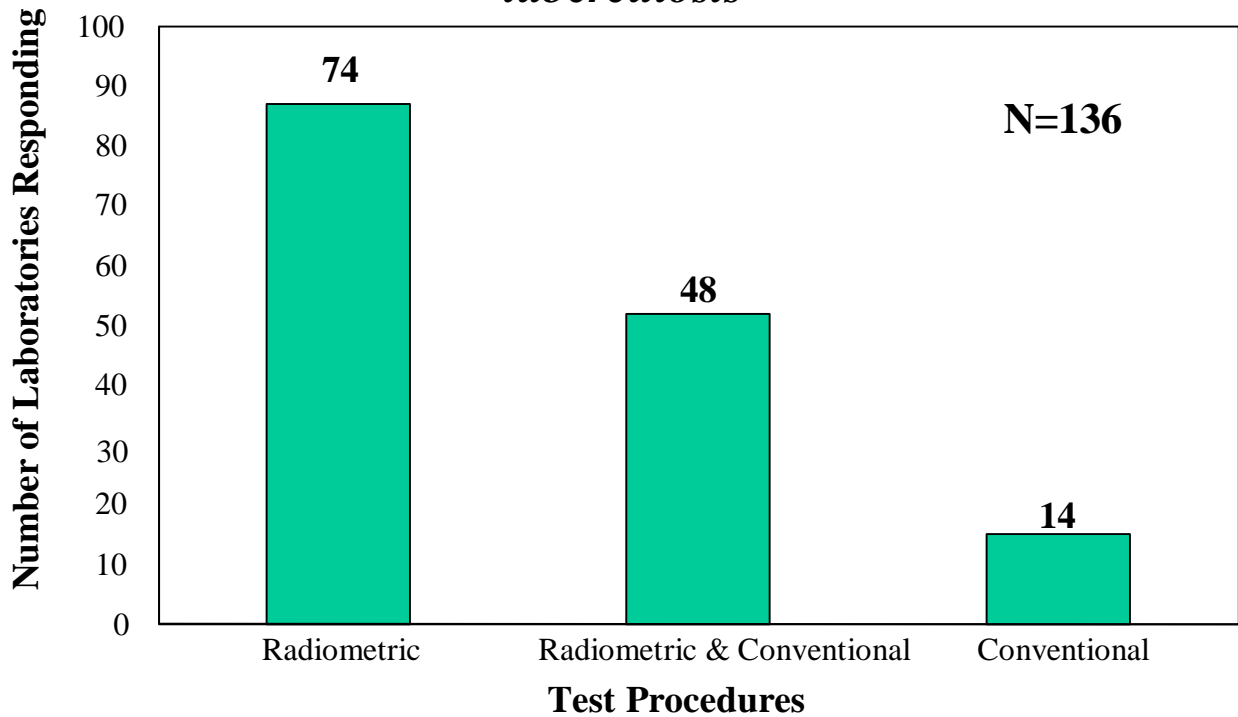
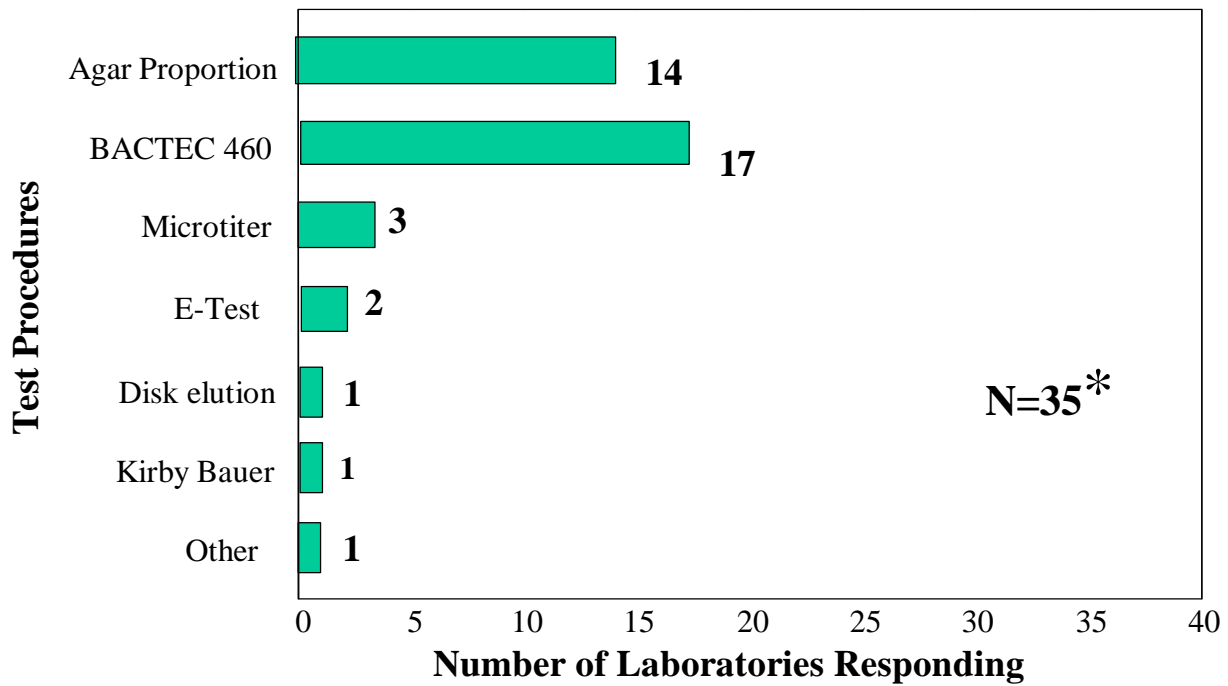
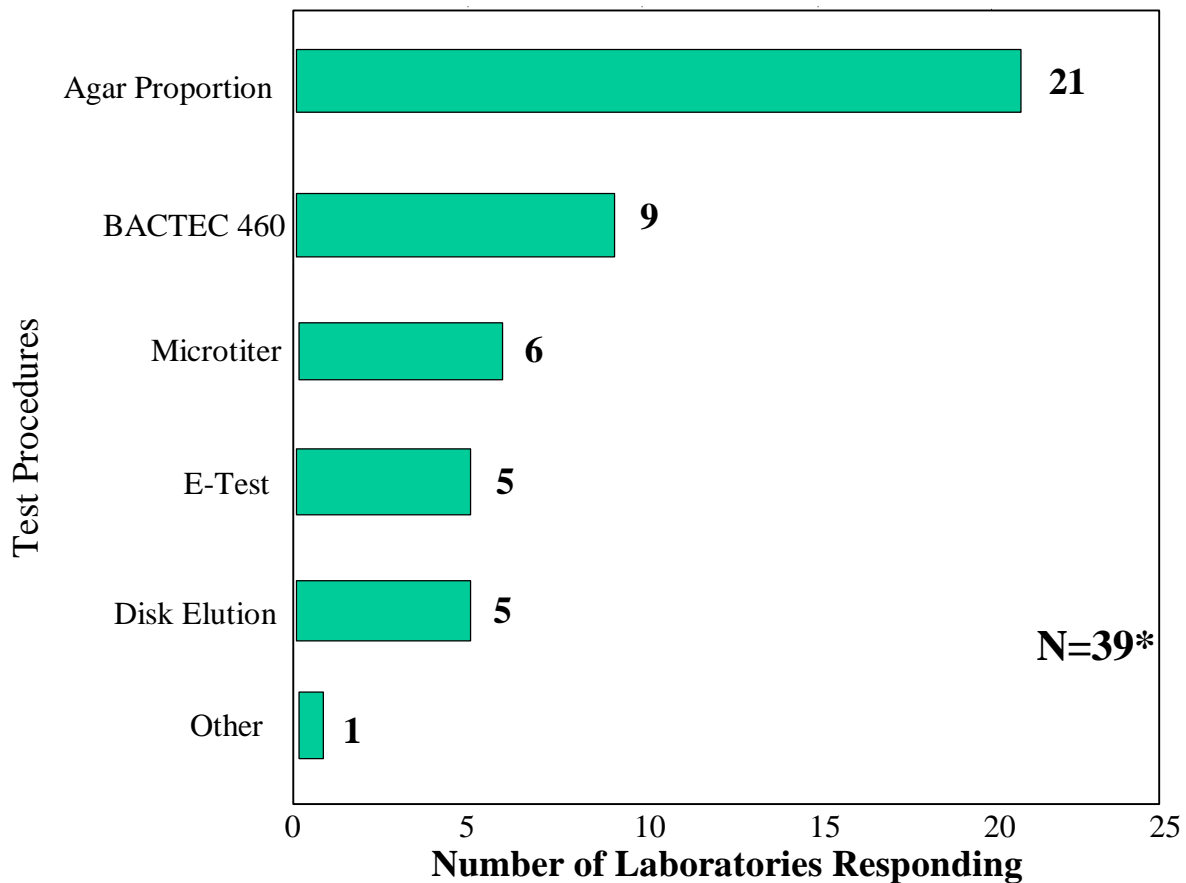


Figure 7. Test Procedures used by Laboratories for Strain I - *M. avium* complex



* Some participants reported >1 test method

Figure 8. Test Procedures used by Laboratories for Strain J - *M. marinum*



* Some participants reported >1 test method

Percentage of Participating Laboratories Performing *M. tuberculosis* Drug Susceptibility Tests with the Recommended Critical Concentrations

Drug	Conventional		BACTEC	
	Recommended Critical Concentration	Labs Performing Critical Concentration	Equivalent Concentration	Labs Performing Critical Concentration
Isoniazid	0.2 Fg/ml	85.7% (42/49)	0.1 Fg/ml	90.4% (103/114)
Rifampin	1 Fg/ml	93.6% (44/47)	2 Fg/ml	95.5% (108/113)
Pyrazinamide	25 Fg/ml	100% (2/2)	100 Fg/ml	97.6% (84/86)
Ethambutol	5 Fg/ml	85.1% (40/47)	2.5 Fg/ml	90.2% (101/112)
Streptomycin	2 Fg/ml	88.8% (40/45)	2 Fg/ml	95.3% (101/106)

Table 2. Participant Results for Culture F --
M. tuberculosis

DRUG	Conc.	Test Method						DRUG	Conc.	Test Method					
		Agar Proportion Results			BACTEC Results					Agar Proportion Results			BACTEC Results		
		S	R	Sum	S	R	Sum			S	R	Sum	S	R	Sum
Isoniazid	0.01				2		2	Cycloserine	25.00	2		2			
Isoniazid	0.10	1		1	103		103	Cycloserine	30.00	14		14			
Isoniazid	0.20	39		39	7		7	Cycloserine	50.00	1		1			
Isoniazid	0.40				23		23	Cycloserine	60.00	1		1			
Isoniazid	1.00	40		40	5		5	p-Aminosalicylic	2.00	13		13			
Isoniazid	5.00	5		5				p-Aminosalicylic	5.00	1		1			
Rifampin	1.00	41		41	7		7	p-Aminosalicylic	8.00	2		2			
Rifampin	2.00	1		1	107		107	p-Aminosalicylic	10.00	4		4			
Rifampin	5.00	8		8				Amikacin	2.00	1		1	1		1
Pyrazinamide	25.00		2	2		1	1	Amikacin	2.50				1		1
Pyrazinamide	100.00		1	1	2	81	83	Amikacin	4.00	4		4			
Pyrazinamide	300.00					1	1	Amikacin	5.00	1		1			
Ethambutol	2.00				1		1	Amikacin	6.00	4		4			
Ethambutol	2.50	1		1	100	1	101	Amikacin	8.00	1		1			
Ethambutol	3.75				1		1	Amikacin	12.00	1		1			
Ethambutol	4.00				1		1	Ofloxacin	1.00	4		4	2		2
Ethambutol	5.00	38		38	6		6	Ofloxacin	2.00	2		2	4		4
Ethambutol	6.00	1		1				Ofloxacin	4.00	1		1			
Ethambutol	7.50	3		3	14		14	Ciprofloxacin	1.00	3		3	3		3
Ethambutol	10.00	15		15				Ciprofloxacin	2.00	14		14	1		1
Streptomycin	2.00	37		37	101		101	Clofazamine	0.12				1		1
Streptomycin	4.00				1		1	Clofazamine	0.25	1		1			
Streptomycin	6.00				16		16	Clofazamine	0.50				1		1
Streptomycin	10.00	30		30				Rifabutin	0.50	1		1			
Ethionamide	1.25				1		1	Rifabutin	1.00	1		1	2		2
Ethionamide	2.50				1		1	Rifabutin	2.00	5		5			
Ethionamide	5.00	27	1	28	3		3								
Ethionamide	10.00	4	1	5											
Kanamycin	5.00	12		12	2		2								
Kanamycin	6.00	20		20											
Capreomycin	1.25				1		1								
Capreomycin	5.00				4		4								
Capreomycin	10.00	19		19	1		1								

Table 2. Participant Results for Culture G --
M. tuberculosis

DRUG	Conc.	Test Method						DRUG	Conc.	Test Method						
		Agar Proportion			BACTEC					Agar Proportion			BACTEC			
		S	R	Sum	S	R	Sum			S	R	Sum	S	R	Sum	
Isoniazid	0.01				2		2	Cycloserine	25.00	2		2				
Isoniazid	0.10	1		1	102		102	Cycloserine	30.00	14		14				
Isoniazid	0.20	41		41	7		7	Cycloserine	50.00	1		1				
Isoniazid	0.40				23		23	Cycloserine	60.00	1		1				
Isoniazid	1.00	42		42	6		6	p-Aminosalicylic	2.00	14	1	15				
Isoniazid	5.00	5		5				p-Aminosalicylic	4.00				2		2	
Rifampin	1.00		44	44		7	7	p-Aminosalicylic	5.00	1		1				
Rifampin	2.00		1	1	2	105	107	p-Aminosalicylic	8.00	2		2				
Rifampin	5.00		10	10		1	1	p-Aminosalicylic	10.00	4		4				
Pyrazinamide	25.00	2		2	1		1	Amikacin	1.00				1		1	
Pyrazinamide	100.00	1		1	81	1	82	Amikacin	2.00	1		1	2		2	
Pyrazinamide	300.00				1		1	Amikacin	2.50				1		1	
Ethambutol	2.00				1		1	Amikacin	4.00	4		4				
Ethambutol	2.50	1		1	99	1	100	Amikacin	5.00	1		1				
Ethambutol	3.75				1		1	Amikacin	6.00	4		4				
Ethambutol	4.00				1		1	Amikacin	8.00	1		1				
Ethambutol	5.00	39		39	6		6	Amikacin	12.00	1		1				
Ethambutol	6.00	1		1				Ofloxacin	1.00	5	1	6	2		2	
Ethambutol	7.50	4		4	15		15	Ofloxacin	2.00	3	1	4	5		5	
Ethambutol	10.00	16		16				Ofloxacin	4.00	1		1				
Streptomycin	2.00	39		39	100		100	Ciprofloxacin	1.00	4	1	5	4		4	
Streptomycin	4.00				1		1	Ciprofloxacin	2.00	14	1	15	1		1	
Streptomycin	6.00				16		16	Clofazamine	0.12				1		1	
Streptomycin	10.00	32		32				Clofazamine	0.25	1		1	1		1	
Ethionamide	1.25				1		1	Clofazamine	0.50				1		1	
Ethionamide	2.50				1		1	Rifabutin	0.50		1	1				
Ethionamide	5.00	31		31	4		4	Rifabutin	1.00		2	2		3	3	
Ethionamide	10.00	5		5				Rifabutin	2.00		5	5				
Kanamycin	5.00	13		13	4		4									
Kanamycin	6.00	21		21												
Capreomycin	1.25				1		1									
Capreomycin	2.50				1		1									
Capreomycin	5.00				4		4									
Capreomycin	10.00	20	1	21	1		1									

Table 2. Participant Results for Culture H --
M. tuberculosis

DRUG	Conc.	Test Method						DRUG	Conc.	Test Method					
		Agar Proportion			BACTEC					Agar Proportion			BACTEC		
		S	R	Sum	S	R	Sum			S	R	Sum	S	R	Sum
Isoniazid	0.01				2		2	Cycloserine	25.00	2		2			
Isoniazid	0.10	1		1	103		103	Cycloserine	30.00	14		14			
Isoniazid	0.20	40		40	7		7	Cycloserine	50.00	1		1			
Isoniazid	0.40				23		23	p-Aminosalicylic acid	2.00	13		13			
Isoniazid	1.00	41		41	5		5	p-Aminosalicylic acid	4.00				1	1	2
Isoniazid	5.00	5		5				p-Aminosalicylic acid	5.00	1		1			
Rifampin	1.00	42		42	7		7	p-Aminosalicylic acid	8.00	1		1			
Rifampin	2.00	1		1	106		106	p-Aminosalicylic acid	10.00	4		4			
Rifampin	5.00	8		8				Amikacin	2.00	1		1	1		1
Pyrazinamide	25.00	2		2	1		1	Amikacin	2.50				1		1
Pyrazinamide	100.00	1		1	82	2	84	Amikacin	4.00	3		3			
Pyrazinamide	300.00				1		1	Amikacin	5.00	1		1			
Ethambutol	2.00				1		1	Amikacin	6.00	4		4			
Ethambutol	2.50	1		1	99		99	Amikacin	8.00	1		1			
Ethambutol	3.75				1		1	Amikacin	12.00	1		1			
Ethambutol	4.00				1		1	Ofloxacin	1.00	4		4	2		2
Ethambutol	5.00	37		37	6		6	Ofloxacin	2.00	3		3	5		5
Ethambutol	6.00	1		1				Ofloxacin	4.00	1		1			
Ethambutol	7.50	4		4	14		14	Ciprofloxacin	1.00	3		3	4		4
Ethambutol	10.00	15		15				Ciprofloxacin	2.00	14		14	1		1
Streptomycin	2.00	3	35	38	22	78	100	Clofazamine	0.12				1		1
Streptomycin	4.00				2		2	Clofazamine	0.25	1		1	1		1
Streptomycin	6.00				15	2	17	Clofazamine	0.50				1		1
Streptomycin	10.00	29	2	31	1		1	Rifabutin	0.50	1		1			
Ethionamide	1.25				1		1	Rifabutin	1.00	1		1	3		3
Ethionamide	2.50				1		1	Rifabutin	2.00	5		5			
Ethionamide	5.00	29		29	4		4								
Ethionamide	10.00	4		4											
Kanamycin	5.00	13		13	4		4								
Kanamycin	6.00	19		19											
Capreomycin	1.25				1		1								
Capreomycin	2.50				1		1								
Capreomycin	5.00				4		4								
Capreomycin	10.00	19		19	1		1								

Table 3. Participant Results for Culture I, *M. avium* complex

DRUG	Conc.	Test Method											
		Agar Proport.			BACTEC			Disk Elution			Other*		
		Results			Results			Results			Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Amikacin	1.00					1	1						
Amikacin	2.00				1	1	2						
Amikacin	4.00				1		1						
Amikacin	6.00	3	2	5									
Amikacin	8.00				1		1						
Amikacin	12.00	2		2									
Amikacin	32.00	1		1									
Azithromycin	3.00		2	2									
Clofazamine	0.06				1		1						
Clofazamine	1.00	3	1	4									
Clofazamine	2.00				1		1						
Clarithromycin	2.00					1	1						
Clarithromycin	3.00		5	5									
Clarithromycin	4.00		1	1		1	1						
Clarithromycin	6.00		2	2									
Clarithromycin	9.00		1	1									
Clarithromycin	32.00										1		1
Capreomycin	5.00					1	1						
Ciprofloxacin	1.00		2	2	1		1						
Ciprofloxacin	1.25				1		1						
Ciprofloxacin	2.00	4	1	5									
Ciprofloxacin	8.00	1		1	1		1						
Cycloserine	25.00	1		1									
Cycloserine	30.00	2		2									
Cycloserine	50.00	1		1									
Cefoxitin	32.00		1	1									
Ethambutol	2.50					4	4						
Ethambutol	5.00		7	7	1		1						
Ethambutol	7.50	1		1									
Ethambutol	8.00				1	1	2						
Ethambutol	10.00		4	4									
Imipenem	8.00		1	1									
Isoniazid	0.10					2	2						
Isoniazid	0.20		4	4									
Isoniazid	0.40					1	1						
Isoniazid	1.00		6	6									
Isoniazid	2.00		1	1									
Isoniazid	5.00								1	1			
Kanamycin	2.50				1		1						
Kanamycin	5.00					1	1						
Kanamycin	6.00	2	1	3					1	1			
Ofloxacin	1.00		1	1									
Ofloxacin	1.25		1	1									

Table 3. Participant Results for Culture I, *M. avium* complex (Continued)

DRUG	Conc.	Test Method											
		Agar Proport.			BACTEC			Disk Elution			Other*		
		Results			Results			Results			Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Ofloxacin	2.00		2	2									
Pyrazinamide	25.00		1	1									
Rifabutin	0.25				1		1						
Rifabutin	0.50				1		1						
Rifabutin	1.00	2	1	3	1		1						
Rifabutin	2.00	3		3	2		2						
Rifampin	0.50				1		1						
Rifampin	1.00	3	7	10	1		1		1	1			
Rifampin	2.00				2	1	3						
Rifampin	5.00	2		2									
Streptomycin	2.00	2	6	8	4	1	5		1	1			
Streptomycin	6.00				1		1						
Streptomycin	10.00	3		3					1	1			
Ethionamide	5.00		3	3		1	1						
Ethionamide	10.00		1	1					1	1			

Table 4. Participant Results for Culture I, *M. marinum*

DRUG	Conc.	Test Method											
		Agar Proport.			BACTEC			E-Test			Disk Elution		
		Results			Results			Results			Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Amikacin	1.00				1		1						
Amikacin	2.00				1		1						
Amikacin	3.00										1		1
Amikacin	4.00	1		1									
Amikacin	6.00	2		2							1		1
Amikacin	12.00	1		1									
Amikacin	32.00	1		1									
Clofazamine	1.00		1	1									
Clarithromycin	1.00	1		1									
Clarithromycin	3.00	5		5							2		2
Clarithromycin	4.00	1		1									
Capreomycin	5.00				1		1						
Capreomycin	10.00	1		1									
Ciprofloxacin	1.00	2		2	1		1						
Ciprofloxacin	2.00	4		4									
Cycloserine	30.00	1		1									
Cefoxitin	30.00	1		1									
Cefoxitin	32.00	1		1									
Doxycycline	6.00	2	1	3							2		2
Ethambutol	2.50				4		4						
Ethambutol	5.00	15		15							2		2
Ethambutol	7.50	2		2									
Ethambutol	10.00	3		3									
Imipenem	8.00		1	1									
Isoniazid	0.10					2	2						
Isoniazid	0.20		11	11								1	1
Isoniazid	0.40					1	1						
Isoniazid	1.00		12	12									
Kanamycin	5.00	1		1	1		1						
Kanamycin	6.00	5	1	6							1		1
Minocycline	6.00	2		2							1	1	2
Ofloxacin	1.00	1	2	3									
Ofloxacin	2.00	2	1	3									
p-Aminosalicylic acid	2.00		2	2									
Pyrazinamide	25.00		1	1									
Rifabutin	1.00	2		2									
Rifabutin	2.00	1		1									
Rifampin	1.00	19	1	20							3		3
Rifampin	2.00				5		5						
Rifampin	5.00	1		1									

Table 4. Participant Results for Culture I, *M. marinum*

DRUG	Conc.	Test Method											
		Agar Proport.			BACTEC			E-Test			Disk Elution		
		Results			Results			Results			Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Streptomycin	2.00	11	5	16	3		3					1	1
Streptomycin	6.00				1		1						
Streptomycin	10.00	7		7									
Ethionamide	5.00	4	1	5		1	1					1	1
Trimethoprim-Sulfamethoxazole	0.09							1		1			
Trimethoprim-Sulfamethoxazole	0.50											1	1
Trimethoprim-Sulfamethoxazole	5.00	1		1									
Trimethoprim-Sulfamethoxazole	9.50	1		1									
Trimethoprim-Sulfamethoxazole	25.00											1	1
Trimethoprim-Sulfamethoxazole	30.00	2		2									
Tobramycin	8.00		1	1									

Table 5. Participant Minimum Inhibitory Concentrations (MIC)
Test Results for Strain I, *M. avium* complex

DRUG	Test Method	MIC	Interpretation			Sum
			S	R	None*	
Amikacin	BACTEC 460	≤ 2.00	1			1
Amikacin	BACTEC 460	≤ 4.00	2			2
Amikacin	BACTEC 460	2.00	1			1
Amikacin	BACTEC 460	4.00			2	2
Amikacin	E-test	1.50			1	1
Amikacin	Microtiter	4.00			1	1
Clofazamine	BACTEC 460	≤ 0.06	3			3
Clofazamine	BACTEC 460	≤ 0.12	1			1
Clofazamine	Microtiter	0.50			1	1
Clarithromycin	BACTEC 460	≥ 2.00		1		1
Clarithromycin	BACTEC 460	≥ 8.00		1	1	2
Clarithromycin	BACTEC 460	≥ 16.00		1		1
Clarithromycin	BACTEC 460	≥ 32.00		3	1	4
Clarithromycin	E-test	≥ 256.00			1	1
Clarithromycin	Microtiter	≥ 4.00			1	1
Clarithromycin	Microtiter	≥ 32.00		1		1
Capreomycin	Agar proportion	≥ 16.00		1		1
Ciprofloxacin	BACTEC 460	≤ 1.00	1			1
Ciprofloxacin	BACTEC 460	2.00			1	1
Ciprofloxacin	BACTEC 460	4.00	1			1
Ciprofloxacin	E-test	24.00			1	1
Ciprofloxacin	Microtiter	0.50			1	1
Ciprofloxacin	Microtiter	2.00			1	1
Cycloserine	Agar proportion	≥ 32.00		1		1
Cefoxitin	E-test	≤ 256.00			1	1
Ethambutol	Agar proportion	≥ 8.00		1		1
Ethambutol	BACTEC 460	8.00		2	1	3
Ethambutol	BACTEC 460	≥ 8.00		2		2
Ethambutol	Microtiter	16.00			1	1
Imipenem	E-test	≥ 256.00			1	1
Isoniazid	Agar proportion	≥ 4.00		1		1
Isoniazid	Microtiter	≥ 32.00			1	1
Kanamycin	Agar proportion	≥ 16.00		1		1
Kanamycin	BACTEC 460	4.00			1	1
Minocycline	E-test	50.00			1	1
Rifabutin	BACTEC 460	≤ 0.50	3			3
Rifabutin	BACTEC 460	0.50		1	1	2
Rifabutin	BACTEC 460	≥ 2.00			1	1
Rifabutin	Microtiter	≤ 0.03			1	1

*Some participants reported MIC results without a corresponding interpretation of susceptible or resistant.

Table 5. Participant Minimum Inhibitory Concentrations (MIC)
Test Results for Strain I, *M. avium* complex

DRUG	Method	REL MIC Conc.	Interpretation			Sum
			S	R	None*	
Rifampin	Agar proportion	≥ 4.00		1		1
Rifampin	BACTEC 460	≤ 0.50	2			2
Rifampin	BACTEC 460	2.00			2	2
Rifampin	BACTEC 460	4.00			1	1
Rifampin	BACTEC 460	≥ 2.00		1		1
Rifampin	Microtiter	0.13			1	1
Rifampin	Microtiter	≥ 2.00			1	1
Streptomycin	Agar proportion	≥ 16.00		1		1
Streptomycin	BACTEC 460	≤ 2.00	5			5
Streptomycin	Microtiter	2.00			1	1
Ethionamide	Agar proportion	≥ 8.00		1		1

*Some participants reported MIC results without a corresponding interpretation of susceptible or resistant.

Table 6. Participant Minimum Inhibitory Concentrations (MIC)
Test Results for Strain I, *M. marinum*

DRUG	Test Method	MIC	Interpretation			Sum
			S	R	None*	
Amikacin	E-test	1.00	1			1
Amikacin	E-test	≤ 1.00	1			1
Amikacin	E-test	0.25			1	1
Amikacin	E-test	4.00	1			1
Amikacin	Microtiter	≤ 0.50	1			1
Amikacin	Microtiter	0.25			1	1
Amikacin	Microtiter	0.50	1			1
Amikacin	Microtiter	≥ 8.00		1		1
Clarithromycin	BACTEC 460	≤ 1.00	1			1
Clarithromycin	BACTEC 460	8.00			1	1
Clarithromycin	E-test	0.03	1			1
Clarithromycin	E-test	0.12	1			1
Clarithromycin	E-test	≥ 256.00			1	1
Clarithromycin	Microtiter	1.00	1			1
Clarithromycin	Microtiter	2.00	1			1
Clarithromycin	Microtiter	4.00			2	2
Clarithromycin	Microtiter	≥ 2.00		1		1
Capreomycin	Agar proportion	≥ 16.00		1		1
Ciprofloxacin	BACTEC 460	≤ 1.00	1			1
Ciprofloxacin	E-test	0.12	1			1
Ciprofloxacin	E-test	1.00			1	1
Ciprofloxacin	Microtiter	0.25	1			1
Ciprofloxacin	Microtiter	1.00			2	2
Ciprofloxacin	Microtiter	2.00			1	1
Ciprofloxacin	Microtiter	8.00		1		1
Cycloserine	Agar proportion	≥ 32.00		1		1
Cefoxitin	E-test	0.12			1	1
Cefoxitin	E-test	≥ 256.00		1		1
Cefoxitin	Microtiter	64.00		1		1
Cefoxitin	Microtiter	128.00		1		1
Doxycycline	E-test	4.00			1	1
Doxycycline	Microtiter	≤ 0.25	1			1
Doxycycline	Microtiter	4.00	1		1	2
Ethambutol	Agar proportion	≤ 4.00	1			1
Ethambutol	BACTEC 460	≤ 2.00	1			1
Ethambutol	Microtiter	2.00			1	1
Imipenem	E-test	0.01			1	1
Imipenem	E-test	≥ 32.00		1		1
Imipenem	Microtiter	≤ 1.00	1			1
Imipenem	Microtiter	0.50	1			1
Imipenem	Microtiter	4.00			1	1
Imipenem	Microtiter	≥ 32.00		1		1
Isoniazid	Agar proportion	≥ 4.00		1		1
Isoniazid	Microtiter	≥ 32.00			1	1
Kanamycin	Agar proportion	≤ 8.00	1			1

*Some participants reported MIC results without a corresponding interpretation of susceptible or resistant.

Table 6. Participant Minimum Inhibitory Concentrations (MIC)
Test Results for Strain I, *M. marinum*

DRUG	Test Method	MIC	Interpretation			Sum
			S	R	None*	
Minocycline	E-test	≤ 2.00	1			1
Minocycline	Microtiter	2.00	1			1
Rifabutin	BACTEC 460	2.00			1	1
Rifampin	Agar proportion	≥ 4.00		1		1
Rifampin	BACTEC 460	≤ 2.00	1			1
Rifampin	E-test	0.03	1			1
Rifampin	Microtiter	≤ 1.00	1			1
Rifampin	Microtiter	0.25			1	1
Rifampin	Microtiter	0.50	1			1
Rifampin	Microtiter	1.00			1	1
Streptomycin	Agar proportion	≤ 8.00	1			1
Streptomycin	Microtiter	1.00			1	1
Sulfamethoxazole	Microtiter	16.00		1		1
TCH	Microtiter	≥ 64.00		1		1
Tetracycline	E-test	1.00	1			1
Tetracycline	Microtiter	8.00			1	1
Ethionamide	Agar proportion	≤ 4.00	1			1
Trimethoprim-Sulfamethoxazole	E-test	0.01	1			1
Trimethoprim-Sulfamethoxazole	E-test	0.09	1			1
Trimethoprim-Sulfamethoxazole	Microtiter	≤ 0.50	1			1
Trimethoprim-Sulfamethoxazole	Microtiter	0.25			1	1
Tobramycin	Microtiter	4.00	1			1

*Some participants reported MIC results without a corresponding interpretation of susceptible or resistant.