

July 7, 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 February 1999 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. xenopi*, and *M. abscessus* shipped in February 1999. 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 137 of 150 (91.3%) of laboratories participating in this shipment. An additional 6 laboratories indicated that they have discontinued *M. tuberculosis* drug susceptibility testing or the laboratory has closed since the last shipments.

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 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.

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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 February 1999 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. xenopi*, and 1 strain of *M. abscessus* shipped in February 1999. Participant laboratories either received 3 *M. tuberculosis* or all five *M. tuberculosis* and NTM strains. Testing results were received and analyzed from 137 of 150 (91.3%) 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 69 health departments, 53 hospitals, 10 independents, and 3 “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 1998.

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 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. Some methods, such as the proportion method with Lowenstein-Jensen media, may reflect procedures used by international participants. Figure 5 provides a breakdown of the test procedures used by the participating laboratories for *M. xenopi* complex. Figure 6 provides a breakdown of the test procedures used by the participating laboratories for *M. abscessus*.

M. tuberculosis test results:

The aggregate test results are provided in separate tables, representing cultures K, L, M, N, and O, to facilitate comparison among laboratories. Table 1 for the *M. tuberculosis* cultures K, L, and M 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 1 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 K was resistant to ethambutol, strain L was resistant to rifampin and isoniazid, and strain M was resistant to pyrazinamide. In some instances the level of drug resistance is close to the critical concentration of drug resulting in a lack of consensus. For strain K, 61% (25/41) of participants using the conventional agar proportion method and 87.3% (89/102) using the BACTEC method detected ethambutol resistance.

For strain L, 100% (48/48) detected rifampin resistance at the critical concentration (1F g/ml) in the conventional method, and 98.1% (106/108) detected rifampin resistance at the equivalent concentration (2 F g/ml) with the BACTEC method. There was very little consensus on detection of isoniazid resistance in strain L. Using the agar proportion method, 51.2% (21/41) of participants detected isoniazid resistance and 35.2% (31/88) detected isoniazid resistance with the BACTEC method. Among participants using the BACTEC method, 11 reported borderline results for INH at the equivalent critical concentration of 0.1 ug/ml. One unusual pattern for strain L was the relatively high percentage of participants detecting resistance at the high concentrations of isoniazid in both BACTEC and agar proportion despite the low percentage of laboratories detecting resistance at the lower critical concentrations of drug in both methods.

For strain M, 98.8% (35/38) of participants detected pyrazinamide 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 2 and 4 for culture N, *M. xenopi* and Tables 3 and 5 for culture O, *M. abscessus* to facilitate comparison among laboratories. Tables 2 and 3, for *M. xenopi* and *M. abscessus* 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 4 and 5 represent all minimum inhibitory concentrations (MICs) susceptibility test results, for *M. xenopi* and *M. abscessus* respectively, reported by the participant laboratories. Tables 4 and 5 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 33 participant that provided test results on strain N, *M. xenopi*: 28 participants reported breakpoint test results and 6 participants reported MIC test results. Table 2, representing all of the breakpoint susceptibility test results for *M. xenopi*, includes results reported for the conventional agar proportion, BACTEC, and Disk elution test methods. There are currently no guidelines on appropriate testing for *M. xenopi*. The American Thoracic Society (ATS) recommendations (9) for *M. xenopi* state, “initial therapy should consist of a macrolide, rifampin or rifabutin, and ethambutol with or without initial streptomycin.” The NCCLS Subcommittee on Antimycobacterial Susceptibility testing is currently weighing recommendations for NTM. A preliminary recommendation for *M. xenopi* is that because susceptibility results are generally variable for all the drugs but some susceptibility is evident using antituberculosis concentrations, susceptibility testing to clarithromycin, the quinolones, and the standard antituberculosis drugs would be reasonable. This would include testing rifampin, ethambutol, streptomycin, clarithromycin, isoniazid, and rifabutin (Dr. Richard Wallace, University of Texas Health Center, Tyler). There was a lack of consensus among participant results for rifampin which may represent either difficulty in testing *M. xenopi* or the rifampin MIC for this particular strain.

There were 32 participants that reported testing results for strain O, *M. abscessus*: 21 participants reported breakpoint test results and 12 participants reported MIC test results. Table 3, representing all of the breakpoint susceptibility test results for *M. abscessus*, includes results reported for the agar proportion, BACTEC, E-test, Microtiter, Disk elution, and 5 ‘other’ test methods. The ATS recommendations note that the “rapidly growing mycobacteria (*M. fortuitum*, *M. abscessus*, *M. chelonae*) should not be performed with the antituberculosis agents.” A recent study of reproducibility for microdilution testing provides interpretive guidelines and modification to the ATS recommendations in that *M. abscessus* should be tested against antibacterial drugs including amikacin, doxycycline, imipenem, the fluorinated quinolones, ceftazidime, and clarithromycin (10).

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.

REFERENCES

1. **Inderlied, C. B. and M. Salfinger.** 1995. Antimicrobial Agents and Susceptibility Tests: Mycobacteria, p. 1385-1404. In Murray, Patrick R., Baron, Ellen Jo, Pfaller, Michael A., Tenover, Fred C., Tenover, Robert C. (ed.) Manual of clinical microbiology, 6th ed. American Society for Microbiology, Washington, D.C.
2. **David, H. L.** 1971. Fundamentals of drug susceptibility testing in tuberculosis. DHEW Publication No. (CDC) 712165. Center for Disease Control, Atlanta.
3. **Kent, P.T and G.P. Kubica.** 1985. Public health mycobacteriology: a guide for the level III laboratory. Centers for Disease Control, Atlanta.
4. **Siddiqi, S.H., J.E. Hawkins, and A. Laszlo.** 1985. Interlaboratory drug susceptibility testing of *Mycobacterium tuberculosis* by a radiometric procedure and two conventional methods. J. Clin. Microbiol. 22:919-923.
5. **Hawkins, Jean E., Wallace, Richard J. Jr., Brown, Barbara A.** 1991. Antibacterial Susceptibility Tests: Mycobacteria, p. 1138-1152. In Balows, Albert, Hausler, William J. Jr., Herrmann, Kenneth L., Isenberg, Henry D., Shadomy, H. Jean (ed.) Manual of clinical microbiology, 4th ed. American Society for Microbiology, Washington, D.C.
6. **NCCLS.** Antimycobacterial Susceptibility Testing for *Mycobacterium tuberculosis*; Tentative standard. NCCLS document M24-T, December, 1995
7. **Laszlo, A., Rahman, M. Raviglione, M., Bustreo, F., WHO/IUATLD Network of Supranational Reference Laboratories.** 1997. Quality assurance programme for drug susceptibility testing of *Mycobacterium tuberculosis* in the WHO/IUATLD Supranational Laboratory Network: first round of proficiency testing. Int.J. Tuberc. Lung Dis. 1 (3):231-238
8. **Woods, G.L., F.G.Witebsky.** 1996. Susceptibility testing of *Mycobacterium avium* complex in clinical laboratories: Results of a questionnaire and proficiency test performance by participants in the College of American Pathologist Mycobacteriology E survey. Arch.Pathol.Lab.Med. 120:436-439.
9. **American Thoracic Society.** 1997. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. Am.J.Respir.Crit.Care Med. 156:S1-S25.
10. **Woods, G.L., J.S. Bergmann, F.G.Witebsky, G.A. Fahle, A. Wanger, B. Boulet, M. Plaunt, B.A. Brown, and R.J. Wallace.** 1999. Multi-site reproductibility of results obtained by the broth microdilution method for susceptibility testing of *Mycobacterium abscessus*, *Mycobacterium chelonae*, and *Mycobacterium fortuitum*. J. Clin. Microbiol 37:1676-1682.

Figure 1. Primary Classification of Participating Laboratories

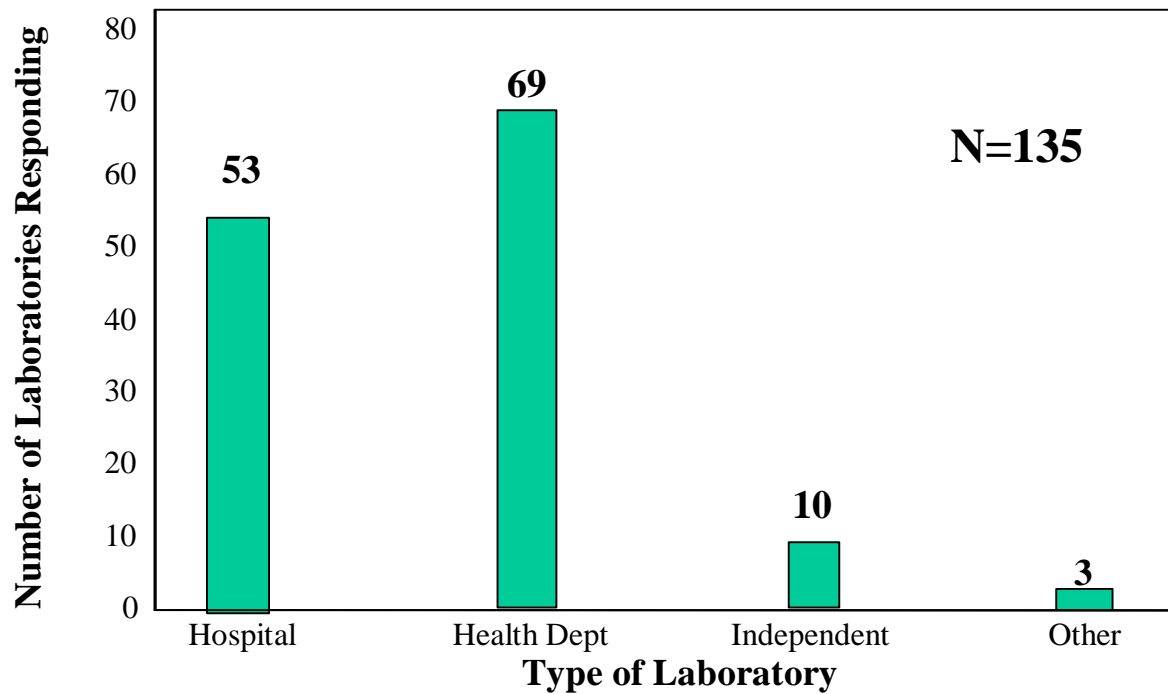
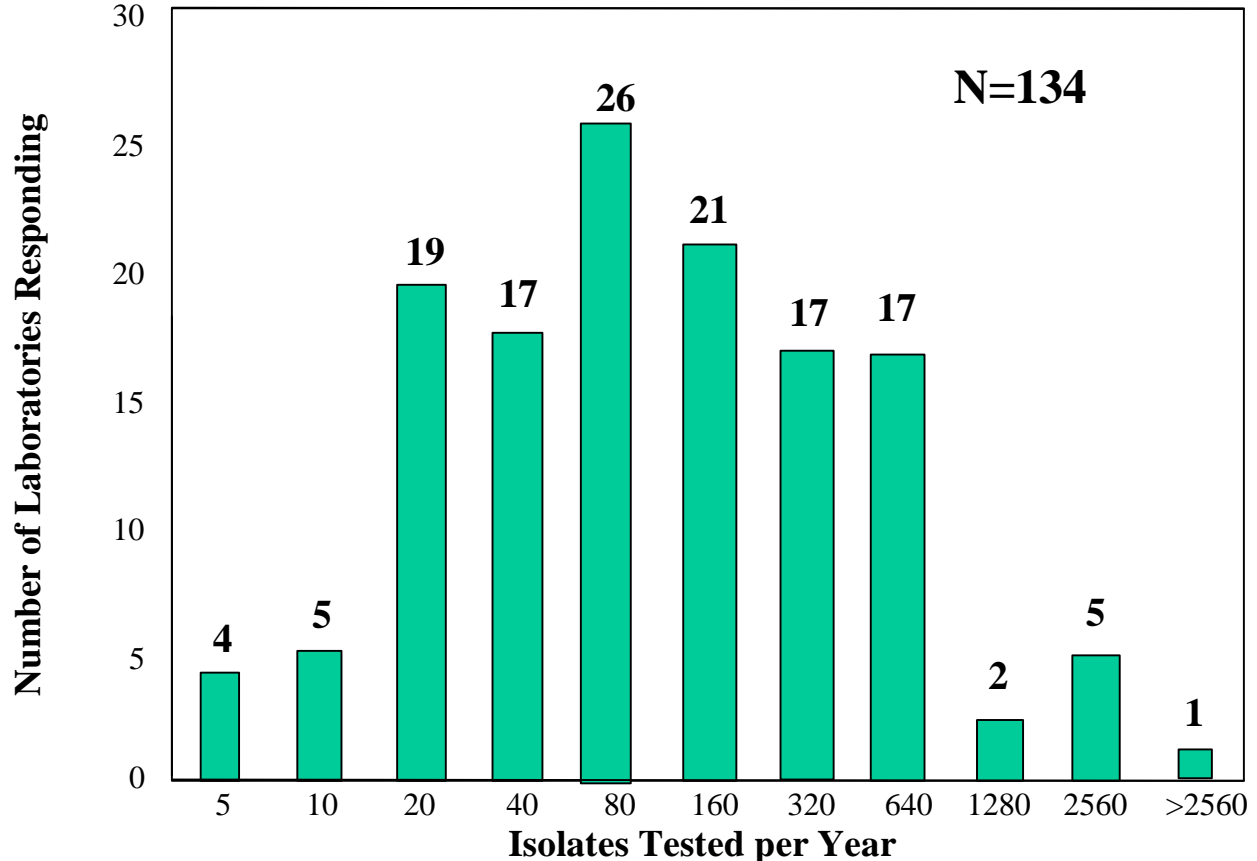
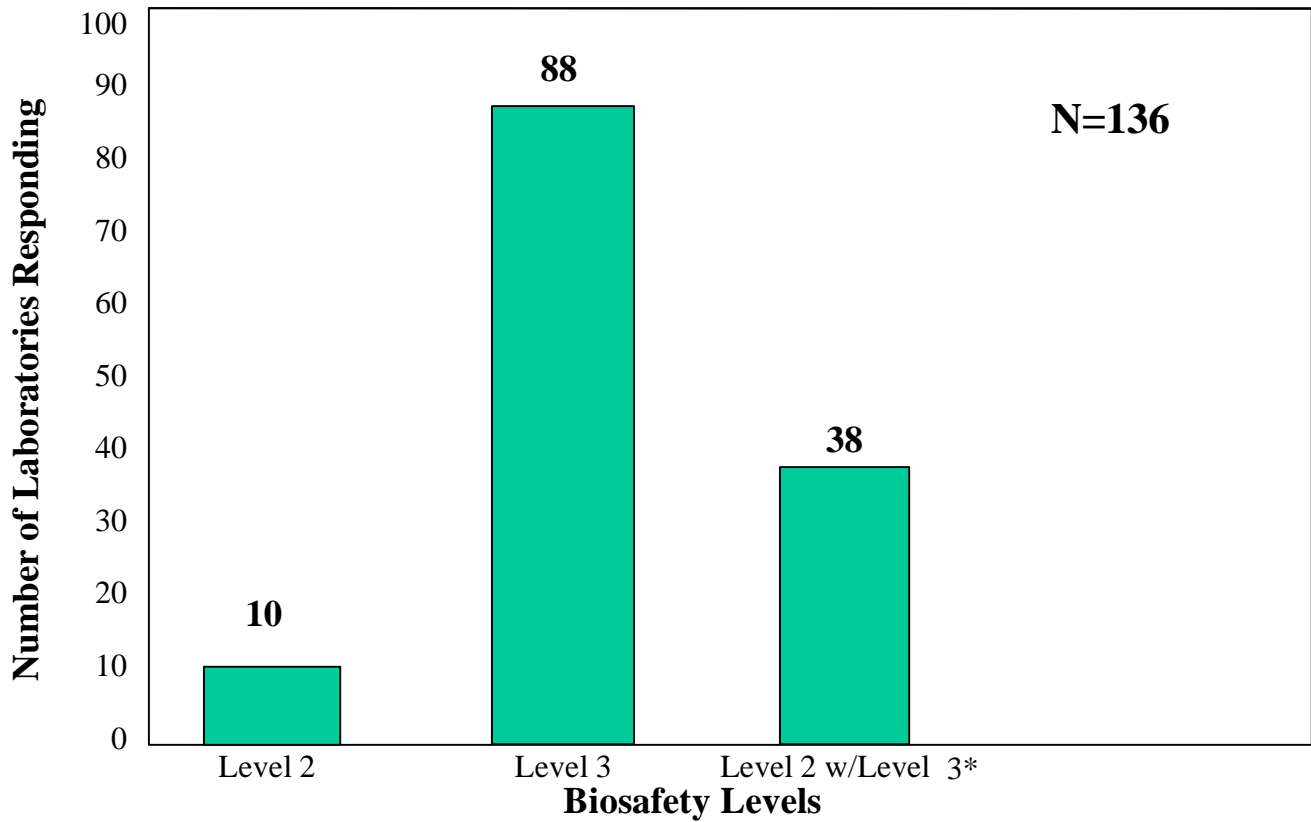


Figure 2. 1997 Annual Volume of *M. tuberculosis* Isolates for Participating Laboratories



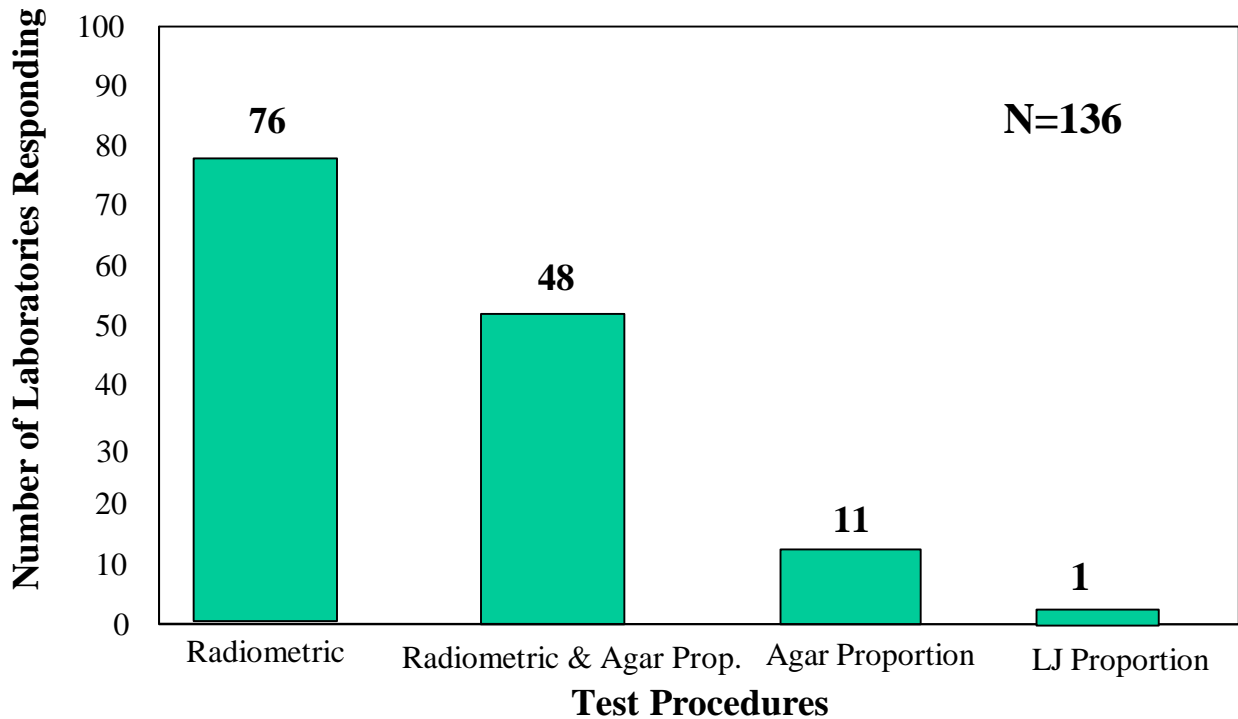
Group labels indicate upper limit of the group.

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



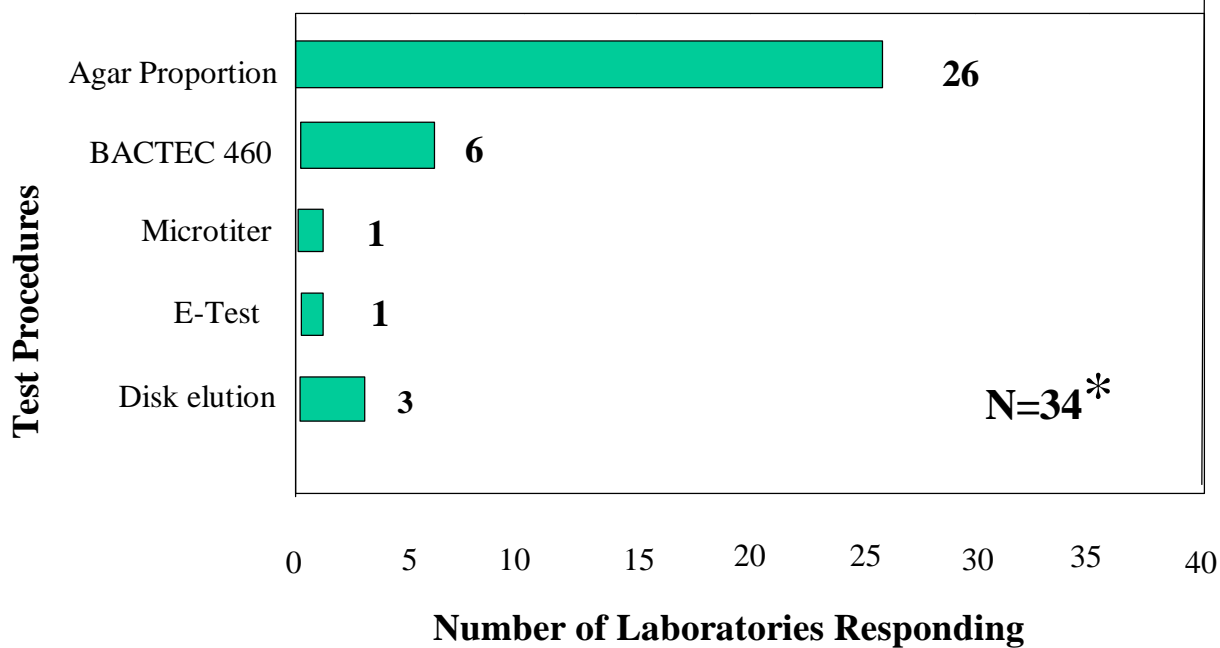
* Biosafety level 2 for facilities with level 3 containment equipment

Figure 4. Test Procedures used by Laboratories for *M. tuberculosis*



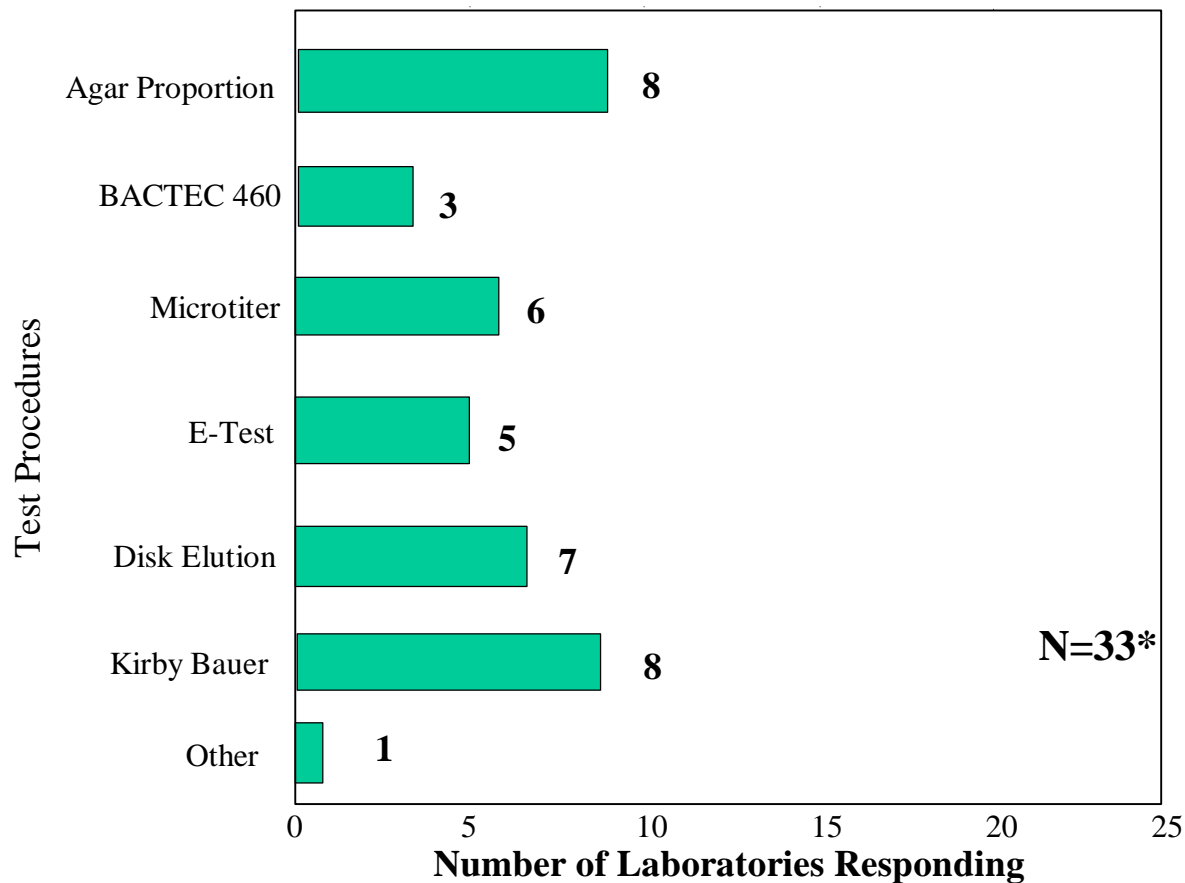
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Figure 5. Test Procedures used by Laboratories for Strain N - *M. xenopi*



* Some participants reported >1 test method

Figure 6. Test Procedures used by Laboratories for Strain O - *M. abscessus*



* Some participants reported >1 test method

Table 1. Participant Results for Culture K, *M. tuberculosis*

DRUG	Conc.	Test Method									DRUG	Conc.	Test Method									
		Agar Prop. Results			BACTEC Results			LJ Prop. Results					Agar Prop. Results			BACTEC Results			LJ Prop. Results			
		S	R	Sum	S	R	Sum	S	R	Sum			S	R	Sum	S	R	Sum	S	R	Sum	
Isoniazid	0.01				1		1				p-Aminosalicylic	1.00								1		1
Isoniazid	0.10				105		105				p-Aminosalicylic	2.00	13		13							
Isoniazid	0.12	1		1							p-Aminosalicylic	4.00	1		1							
Isoniazid	0.20	40	1	41	7		7	1		1	p-Aminosalicylic	5.00	1		1							
Isoniazid	0.40				23		23				p-Aminosalicylic	8.00	3		3							
Isoniazid	1.00	38		38	9		9				p-Aminosalicylic	10.00	5		5							
Isoniazid	1.10	1		1							Amikacin	2.00	1		1	1		1				
Isoniazid	5.00	4		4	1		1				Amikacin	2.50				1		1				
Rifampin	1.00	45		45	8	1	9				Amikacin	4.00	3		3							
Rifampin	2.00				104	2	106				Amikacin	5.00	1		1							
Rifampin	5.00	9		9							Amikacin	6.00	6		6							
Rifampin	40.00							1		1	Amikacin	12.00	1		1							
Pyrazinamide	0.10				1		1				Amikacin	18.00	1		1							
Pyrazinamide	10.00				1		1				Amikacin	30.00	1		1							
Pyrazinamide	25.00	1		1	1		1				Ofloxacin	1.00	6		6	1		1				
Pyrazinamide	99.00				1		1				Ofloxacin	1.25				1		1				
Pyrazinamide	100.00				82		82				Ofloxacin	2.00	5		5	4		4	1		1	
Pyrazinamide	300.00				1		1				Ofloxacin	4.00	1		1	1		1				
Ethambutol	2.00									1	1	Ofloxacin	8.00	1		1						
Ethambutol	2.50				13	89	102				Ciprofloxacin	0.50		1	1							
Ethambutol	3.75					1	1				Ciprofloxacin	1.00	4		4	2		2				
Ethambutol	4.00					1	1				Ciprofloxacin	2.00	11		11	1		1				
Ethambutol	5.00	16	25	41	1	7	8				Levofloxacin	2.00				1		1				
Ethambutol	6.00		1	1							Rifabutin	0.25	1		1							
Ethambutol	7.50	4	2	6	17		17				Rifabutin	0.50	2		2							
Ethambutol	10.00	15		15	1		1				Rifabutin	1.00	1		1	2		2				
Streptomycin	2.00	43		43	101		101				Rifabutin	2.00	4		4							
Streptomycin	4.00				1		1	1		1	Clofazamine	0.12				1		1				
Streptomycin	6.00				18		18				Clofazamine	0.50				1		1				
Streptomycin	10.00	30		30																		
Ethionamide	1.25				1		1															
Ethionamide	2.50				1		1															
Ethionamide	5.00	32		32	3		3															
Ethionamide	10.00	4		4																		
Ethionamide	30.00							1		1												
Kanamycin	2.50				1		1															
Kanamycin	5.00	15		15	1		1															
Kanamycin	6.00	20		20																		
Kanamycin	40.00							1		1												
Capreomycin	1.25				1		1															
Capreomycin	2.50				1		1															
Capreomycin	5.00	2		2	4		4															
Capreomycin	10.00	18		18																		
Cycloserine	25.00	2		2																		
Cycloserine	30.00	12	1	13				1		1												
Cycloserine	50.00	1		1																		
Cycloserine	60.00	2		2																		

Table 1. Participant Results for Culture L, *M. tuberculosis*

DRUG	Conc.	Test Method									DRUG	Conc.	Test Method										
		Agar Prop. Results			BACTEC Results			LJ Prop. Results					Agar Prop. Results			BACTEC Results			LJ Prop. Results				
		S	R	Sum	S	R	Sum	S	R	Sum			S	R	Sum	S	R	Sum	S	R	Sum		
Isoniazid	0.01				1		1				Cycloserine	25.00	3		3								
Isoniazid	0.10				57	31	88				Cycloserine	30.00	12	1	13					1		1	
Isoniazid	0.12	1		1							Cycloserine	50.00	1		1								
Isoniazid	0.20	20	21	41	5	2	7		1	1	Cycloserine	60.00	2		2								
Isoniazid	0.40				11	6	17				p-Aminosalicylic	1.00								1		1	
Isoniazid	1.00	20	17	37	6	2	8				p-Aminosalicylic	2.00	15		15								
Isoniazid	1.10	1		1							p-Aminosalicylic	4.00				1	1						
Isoniazid	2.00				2		2				p-Aminosalicylic	5.00	1		1								
Isoniazid	5.00	4		4	2		2				p-Aminosalicylic	8.00	3		3								
Rifampin	1.00		48	48	1	8	9				p-Aminosalicylic	10.00	5		5								
Rifampin	2.00				2	106	108				Amikacin	0.60	1		1								
Rifampin	5.00		11	11		2	2				Amikacin	2.00	1		1	1		1					
Rifampin	10.00					1	1				Amikacin	2.50				1		1					
Rifampin	40.00							1	1		Amikacin	4.00	3		3								
Pyrazinamide	0.10				1		1				Amikacin	5.00	1		1								
Pyrazinamide	10.00				1		1				Amikacin	6.00	6		6								
Pyrazinamide	25.00	1		1	1		1				Amikacin	12.00	1		1								
Pyrazinamide	99.00					1	1				Amikacin	18.00	1		1								
Pyrazinamide	100.00				78	4	82				Amikacin	30.00	1		1								
Pyrazinamide	300.00				1		1				Ofloxacin	0.60	1		1								
Ethambutol	2.00							1	1		Ofloxacin	1.00	7		7	1		1					
Ethambutol	2.50				94	8	102				Ofloxacin	1.25				1		1					
Ethambutol	3.75				1		1				Ofloxacin	2.00	4		4	5		5	1		1		
Ethambutol	4.00				1		1				Ofloxacin	4.00	1		1	1		1					
Ethambutol	5.00	36	3	39	8		8				Ofloxacin	8.00	1		1								
Ethambutol	6.00	1		1							Ciprofloxacin	0.50	1		1								
Ethambutol	7.50	5		5	14		14				Ciprofloxacin	0.60	1		1								
Ethambutol	10.00	14	1	15							Ciprofloxacin	1.00	5		5	3		3					
Streptomycin	2.00	43		43	102		102				Ciprofloxacin	2.00	10	1	11	1		1					
Streptomycin	4.00				1		1	1	1		Ciprofloxacin	2.50				1		1					
Streptomycin	6.00				18		18				Levofloxacin	2.00				1		1					
Streptomycin	10.00	31		31							Rifabutin	0.25		1	1								
Ethionamide	1.00	1		1							Rifabutin	0.50		2	2								
Ethionamide	2.50				2		2				Rifabutin	1.00		1	1	3		3					
Ethionamide	5.00	32		32	3		3				Rifabutin	2.00		4	4								
Ethionamide	10.00	3		3	1		1				Clofazamine	0.12				1		1					
Ethionamide	30.00							1	1		Clofazamine	0.25				1		1					
Kanamycin	2.50				1		1				Clofazamine	0.50				1		1					
Kanamycin	5.00	14		14	2		2																
Kanamycin	6.00	21		21																			
Capreomycin	1.00	1		1																			
Capreomycin	1.25				1		1																
Capreomycin	2.50				3		3																
Capreomycin	5.00	1		1	4		4																
Capreomycin	10.00	18		18																			

Table 1. Participant Results for Culture M, *M. tuberculosis*

Drug	Conc.	Test Method									Drug	Conc.	Test Method								
		Agar Prop. Results			BACTEC Results			LJ Prop. Results					Agar Prop. Results			BACTEC Results			LJ Prop. Results		
		S	R	Sum	S	R	Sum	S	R	Sum			S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.01				1		1				p-Aminosalicylic	1.00							1		1
Isoniazid	0.10				104		104				p-Aminosalicylic	2.00	12		12						
Isoniazid	0.12	1		1							p-Aminosalicylic	5.00	1		1						
Isoniazid	0.20	40		40	6		6	1		1	p-Aminosalicylic	8.00	3		3						
Isoniazid	0.40				23		23				p-Aminosalicylic	10.00	3		3						
Isoniazid	1.00	36		36	8		8				Amikacin	2.00	1		1	1		1			
Isoniazid	1.10	1		1							Amikacin	2.50				1		1			
Isoniazid	5.00	4		4							Amikacin	4.00	3		3						
Rifampin	1.00	44		44	9		9				Amikacin	5.00	1		1						
Rifampin	2.00				105	1	106				Amikacin	6.00	6		6						
Rifampin	5.00	9		9							Amikacin	12.00	1		1						
Rifampin	40.00							1		1	Amikacin	18.00	1		1						
Pyrazinamide	0.10					1	1				Amikacin	30.00	1		1						
Pyrazinamide	10.00					1	1				Ofloxacin	1.00	6		6	1		1			
Pyrazinamide	25.00	1		1		1	1				Ofloxacin	2.00	4		4	4		4	1		1
Pyrazinamide	99.00					1	1				Ofloxacin	4.00	1		1	1		1			
Pyrazinamide	100.00				1	82	83				Ofloxacin	8.00	1		1						
Pyrazinamide	300.00					1	1				Ciprofloxacin	0.50	1		1						
Ethambutol	2.00							1		1	Ciprofloxacin	1.00	4		4	2		2			
Ethambutol	2.50				101	2	103				Ciprofloxacin	2.00	11		11	1		1			
Ethambutol	3.75				1		1				Levofloxacin	2.00				1		1			
Ethambutol	4.00				1		1				Rifabutin	0.25	1		1						
Ethambutol	5.00	40		40	8		8				Rifabutin	0.50	2		2						
Ethambutol	6.00	1		1							Rifabutin	1.00	1		1	2		2			
Ethambutol	7.50	4		4	15		15				Rifabutin	2.00	4		4						
Ethambutol	10.00	14		14							Clofazamine	0.12				1		1			
Streptomycin	2.00	41		41	101		101				Clofazamine	0.50				1		1			
Streptomycin	4.00				1		1	1		1											
Streptomycin	6.00				18		18														
Streptomycin	10.00	29		29																	
Ethionamide	1.25				1		1														
Ethionamide	2.50				1		1														
Ethionamide	5.00	30		30	3		3														
Ethionamide	10.00	4		4																	
Ethionamide	30.00							1		1											
Kanamycin	5.00	14		14	1		1														
Kanamycin	6.00	20		20																	
Kanamycin	40.00							1		1											
Capreomycin	1.25				1		1														
Capreomycin	5.00	1		1	4		4														
Capreomycin	10.00	18		18																	
Cycloserine	25.00	2		2																	
Cycloserine	30.00	12		12				1		1											
Cycloserine	50.00	1		1																	
Cycloserine	60.00	1		1																	

Table 2. Participant Results for Culture N, *M. xenopi*

DRUG	Conc.	Test Method								
		Agar Proportion Results			BACTEC Results			Disk Elution Results		
		S	R	Sum	S	R	Sum	S	R	Sum
Amikacin	4.00	1		1						
Amikacin	6.00	2		2				1		1
Amikacin	12.00	1		1						
Clofazamine	1.00	1		1						
Clarithromycin	3.00	3		3						
Capreomycin	5.00				1		1			
Capreomycin	10.00	3	1	4						
Ciprofloxacin	1.00	2		2						
Ciprofloxacin	2.00	3		3				1		1
Cycloserine	30.00	2	2	4						
Cycloserine	36.00	1		1						
Cycloserine	60.00	1		1						
Ethambutol	2.50					3	3			
Ethambutol	5.00	2	15	17					3	3
Ethambutol	7.50	1	1	2		1	1			
Ethambutol	10.00	1	3	4					2	2
Isoniazid	0.10					2	2			
Isoniazid	0.20	1	13	14					3	3
Isoniazid	0.40					1	1			
Isoniazid	1.00	13	2	15				2	1	3
Isoniazid	2.00		1	1						
Isoniazid	5.00	1		1				1		1
Kanamycin	5.00	3		3	1		1			
Kanamycin	6.00	5		5				1		1
Ofloxacin	1.00		1	1						
Ofloxacin	2.00	1		1						
Ofloxacin	8.00	1		1						
p-Aminosalicylic acid	2.00	2	1	3						
p-Aminosalicylic acid	5.00	1		1						
p-Aminosalicylic acid	8.00	1		1						
Rifabutin	1.00	2		2						
Rifabutin	2.00	1		1						
Rifampin	1.00	11	10	21				1	2	3
Rifampin	2.00				2	1	3			
Rifampin	5.00	2		2					1	1
Streptomycin	2.00	16	3	19	2	1	3	2	1	3
Streptomycin	6.00					1	1			
Streptomycin	10.00	9		9				2		2
Ethionamide	5.00	6		6		1	1	1		1
Ethionamide	10.00	2		2	1		1	1		1

Table 3. Participant Results for Culture O, *M. abscessus*

DRUG	Conc.	Test Method															
		Agar Proportion			BACTEC			Microtiter			Disk Elution			Other			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
Amikacin	4.00							1		1							
Amikacin	6.00		1	1								1	1	2			
Amikacin	12.00		2	2								1		1			
Amikacin	30.00	2		2								5		5	5	5	
Augmentin	30.00												1	1			
Augmentin	64.00								1	1							
Azithromycin	8.00							1		1							
Clarithromycin	1.00							1		1							
Clarithromycin	3.00	2		2								3		3			
Clarithromycin	4.00	1		1													
Clarithromycin	9.00		1	1													
Clarithromycin	15.00											1		1	2	2	
Capreomycin	10.00		1	1													
Cefmetazole	30.00												1	1			
Ciprofloxacin	0.50		1	1													
Ciprofloxacin	2.00		2	2									4	4			
Ciprofloxacin	4.00								1	1							
Ciprofloxacin	5.00														4	4	
Ciprofloxacin	8.00		1	1													
Cefoxitin	16.00							1		1							
Cefoxitin	30.00	2	2	4								4	3	7	1	1	2
Doxycycline	5.00	1		1													
Doxycycline	6.00	2		2								3	1	4			
Doxycycline	30.00											1		1	3	1	4
Ethambutol	2.50		1	1		2	2										
Ethambutol	5.00		2	2													
Ethambutol	10.00		1	1													
Erythromycin	15.00												1	1		3	3
Erythromycin	16.00								1	1							
Gentamycin	4.00							1		1							
Gentamycin	10.00											1		1	2		2
Imipenem	4.00							1		1							
Imipenem	8.00		1	1								1	3	4			
Imipenem	10.00		1	1									1	1	1	2	3
Isoniazid	0.10					2	2										
Isoniazid	0.20		2	2													
Isoniazid	1.00		3	3													
Isoniazid	5.00		1	1													
Kanamycin	1.00							1		1							
Kanamycin	6.00		1	1													
Kanamycin	30.00											1		1	2		2
Minocycline	0.25							1		1							
Minocycline	6.00	1		1								1		1			
Minocycline	10.00											1		1			
Minocycline	30.00											2		2		1	1

Table 3. Participant Results for Culture O, *M. abscessus*

DRUG	Conc.	Test Method															
		Agar Proportion			BACTEC			Microtiter			Disk Elution			Other			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
Ofloxacin	5.00											1	1				
p-Aminosalicylic acid	5.00		1	1													
Polymyxin B	300.00											1	1				
Pyrazinamide	25.00		1	1													
Rifampin	1.00		4	4													
Rifampin	2.00					2	2										
Sulfisoxazole	50.00											1	1				
Streptomycin	2.00		3	3		2	2										
Streptomycin	10.00		3	3								1	1		2	2	
Sulfamethoxazole	0.25											1	1				
Sulfamethoxazole	20.00											1	1				
Sulfamethoxazole	250.00														1	1	
Sulfamethoxazole	256.00								1	1							
Tetracycline	6.00											1		1			
Tetracycline	30.00											1		1			
Ethionamide	5.00		1	1													
Trimethoprim-Sulfamethoxazole	1.50												1	1			
Trimethoprim-Sulfamethoxazole	10.00		1	1													
Trimethoprim-Sulfamethoxazole	20.00														2	2	
Trimethoprim-Sulfamethoxazole	30.00		1	1									3	3			
Tobramycin	2.00							1		1							
Tobramycin	6.00		1	1													
Tobramycin	8.00		1	1								2	2	4			
Tobramycin	10.00											1		1			
Tobramycin	30.00														1	1	
Vancomycin	30.00											1	1		2	1	3

**Table 4. Participant Minimum Inhibitory Concentrations (MIC)
Test Results for Strain N, *M. xenopi***

DRUG	Test Method	MIC	Interpretation			Sum
			S	R	None	
Amikacin	BACTEC 460	≤2.00	2			2
Amikacin	Microtiter	4.00			1	1
Azithromycin	BACTEC 460	256.00			1	1
Azithromycin	BACTEC 460	≤4.00	1			1
Azithromycin	BACTEC 460	≤32.00	1			1
Clofazamine	Microtiter	0.50			1	1
Clarithromycin	BACTEC 460	8.00			1	1
Clarithromycin	BACTEC 460	≤2.00	3			3
Clarithromycin	Microtiter	0.50			1	1
Capreomycin	Agar proportion	16.00	1			1
Ciprofloxacin	Agar proportion	1.20	1			1
Ciprofloxacin	Microtiter	0.50			1	1
Cefoxitin	E-test	≥256.00		1		1
Doxycycline	Agar proportion	≥5.00		1		1
Doxycycline	BACTEC 460	≥16.00		1		1
Ethambutol	Agar proportion	≥5.00		1		1
Ethambutol	Agar proportion	≥8.00		1		1
Ethambutol	Microtiter	4.00			1	1
Imipenem	E-test	≥32.00		1		1
Isoniazid	Agar proportion	1.00	1			1
Isoniazid	Agar proportion	4.00	1			1
Isoniazid	BACTEC 460	0.50			1	1
Isoniazid	Microtiter	4.00			1	1
Kanamycin	Agar proportion	16.00	1			1
Levofloxacin	BACTEC 460	≤2.00	1			1
Ofloxacin	Agar proportion	1.20	1			1
Ofloxacin	BACTEC 460	2.00	1			1
Rifabutin	BACTEC 460	≤0.05	2			2
Rifabutin	Microtiter	0.06			1	1
Rifampin	Agar proportion	≥1.00		1		1
Rifampin	Agar proportion	≥4.00		1		1
Rifampin	BACTEC 460	2.00	1			1
Rifampin	BACTEC 460	≤2.00	1			1
Rifampin	Microtiter	0.06			1	1
Streptomycin	Agar proportion	≥2.00		1		1
Streptomycin	Agar proportion	≤8.00	1			1
Streptomycin	BACTEC 460	≤2.00	1			1
Ethionamide	Agar proportion	≤4.00	1			1
Trimethoprim-Sulfamethoxazole	Agar proportion	≤0.06	1			1
Trimethoprim-Sulfamethoxazole	E-test	≥32.00		1		1

**Table 5. Participant Minimum Inhibitory Concentrations (MIC)
Test Results for Strain O, *M. abscessus***

DRUG	Test Method	MIC	Interpretation			Sum
			S	R	None	
Amikacin	Agar proportion	≥10.00		1		1
Amikacin	BACTEC 460	16.00			1	1
Amikacin	E-test	4.00	1			1
Amikacin	E-test	1.50	1			1
Amikacin	E-test	16.00	1			1
Amikacin	E-test	24.00			1	1
Amikacin	E-test	≥256.00		1		1
Amikacin	Microtiter	4.00			1	1
Amikacin	Microtiter	2.00	1			1
Amikacin	Microtiter	4.00	1			1
Amikacin	Microtiter	8.00	2			2
Amikacin	Microtiter	≤16.00	1			1
Augmentin	Microtiter	64.00			1	1
Azithromycin	BACTEC 460	≥64.00		1		1
Azithromycin	Microtiter	8.00			1	1
Clarithromycin	Agar proportion	16.00	1			1
Clarithromycin	E-test	1.00	1			1
Clarithromycin	E-test	0.06	1			1
Clarithromycin	E-test	0.13	1			1
Clarithromycin	E-test	3.00			1	1
Clarithromycin	E-test	≥256.00		1		1
Clarithromycin	Microtiter	1.00			1	1
Clarithromycin	Microtiter	0.12	1			1
Clarithromycin	Microtiter	0.50	1			1
Clarithromycin	Microtiter	1.00	2			2
Cefmetazole	Microtiter	32.00			1	1
Ciprofloxacin	Agar proportion	≥10.00		1		1
Ciprofloxacin	E-test	≥32.00			1	1
Ciprofloxacin	E-test	≥32.00		3		3
Ciprofloxacin	Microtiter	4.00			1	1
Ciprofloxacin	Microtiter	32.00		1		1
Ciprofloxacin	Microtiter	≥2.00		1		1
Ciprofloxacin	Microtiter	≥2.00		1		2
Ciprofloxacin	Microtiter	≥16.00		1		1
Cefoxitin	Agar proportion	≥20.00		1		1
Cefoxitin	E-test	128.00		1		1
Cefoxitin	E-test	≥32.00		1		1
Cefoxitin	E-test	≥256.00		4		4
Cefoxitin	Microtiter	16.00			1	1
Cefoxitin	Microtiter	6.00	1			1
Cefoxitin	Microtiter	16.00	1			1
Cefoxitin	Microtiter	32.00			2	2
Cefoxitin	Microtiter	32.00		1		1

**Table 5. Participant Minimum Inhibitory Concentrations (MIC)
Test Results for Strain O, *M. abscessus***

DRUG	Test Method	MIC	Interpretation			Sum
			S	R	None	
Doxycycline	Agar proportion	≥5.00		1		1
Doxycycline	BACTEC 460	4.00		1		1
Doxycycline	E-test	1.00	1			1
Doxycycline	E-test	3.00			1	1
Doxycycline	E-test	4.00		1		1
Doxycycline	Microtiter	0.50	2			2
Doxycycline	Microtiter	1.00	1			1
Doxycycline	Microtiter	2.00			1	1
Doxycycline	Microtiter	≤1.00	1			1
Ethambutol	Agar proportion	≥5.00		1		1
Erythromycin	Microtiter	16.00			1	1
Erythromycin	Microtiter	32.00		1		1
Gentamycin	Microtiter	4.00			1	1
Imipenem	E-test	≥32.00		4		4
Imipenem	Microtiter	4.00			1	1
Imipenem	Microtiter	4.00	1			1
Imipenem	Microtiter	6.00		1		1
Imipenem	Microtiter	8.00			3	3
Kanamycin	Microtiter	1.00			1	1
Levofloxacin	E-test	≥32.00			1	1
Levofloxacin	E-test	≥32.00		2		2
Levofloxacin	Microtiter	≥4.00			1	1
Minocycline	E-test	0.03	1			1
Minocycline	E-test	≥256.00		1		1
Minocycline	Microtiter	0.25			1	1
Minocycline	Microtiter	0.50	1			1
Minocycline	Microtiter	4.00	1			1
Minocycline	Microtiter	≤1.00	1			1
Ofloxacin	BACTEC 460	16.00		1		1
Rifabutin	Agar proportion	≥2.00		1		1
Rifabutin	BACTEC 460	≥2.00		1		1
Rifampin	Agar proportion	≥1.00		1		1
Rifampin	BACTEC 460	≥8.00		1		1
Rifampin	E-test	≥256.00		1		1
Rifampin	Microtiter	≥4.00		1		1
Streptomycin	Agar proportion	≥2.00		1		1
Sulfamethoxazole	Microtiter	256.00			1	1
Sulfamethoxazole	Microtiter	64.00			1	1
Sulfamethoxazole	Microtiter	≥64.00		1		1
Sulfamethoxazole	Microtiter	≥128.00		1		1
Tetracycline	Microtiter	2.00	1			1
Tetracycline	Microtiter	4.00	1			1
Trimethoprim-Sulfamethoxazole	E-test	≥32.00		2		2
Trimethoprim-Sulfamethoxazole	Microtiter	≥4.00		1		1
Trimethoprim-Sulfamethoxazole	Microtiter	≥8.00		1		1
Tobramycin	E-test	3.00	1			1
Tobramycin	Microtiter	2.00			1	1
Tobramycin	Microtiter	2.00	1			1
Tobramycin	Microtiter	8.00			1	1