

## Analyses of January 2007 *M. tuberculosis* and Nontuberculous Mycobacteria Drug Susceptibility Test Results Reported by Participating Laboratories

This report analyzes the laboratory test results reported to the Centers for Disease Control and Prevention (CDC) by participant laboratories for the four *Mycobacterium tuberculosis* complex and one *Mycobacterium abscessus* strains shipped in January 2007. Participant laboratories received either four *M. tuberculosis* complex strains only or four *M. tuberculosis* complex strains and one nontuberculous mycobacteria (NTM) strain. Testing results were received and analyzed from 132 of 141 (93.6%) laboratories participating in this shipment. Of the laboratories submitting results, 81 (61.4%) reported via the online data entry system.

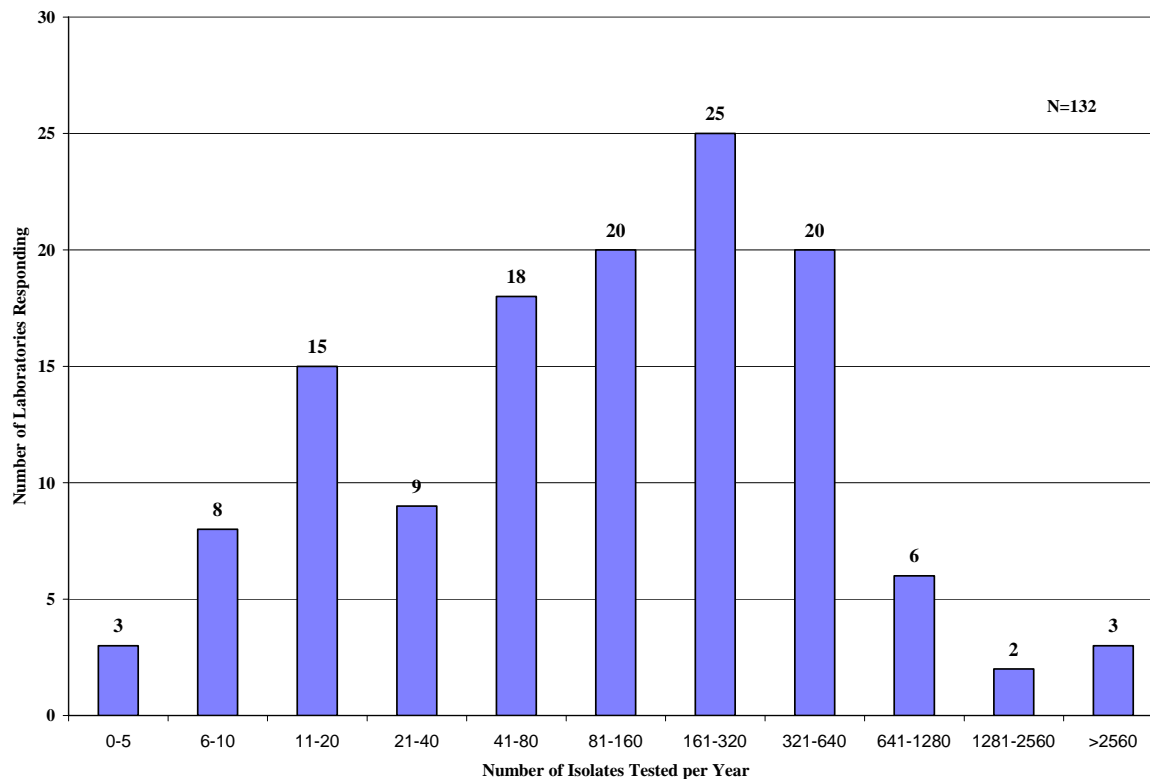
### Descriptive Information on Participant Laboratories

Laboratory classifications reported by the 132 participants are:

- 75 (56.8%) health departments,
- 39 (29.5%) hospitals,
- 13 (9.9%) independent laboratories, and
- 5 (3.8%) other type of laboratories.

Figure 1 shows the distribution of the annual volume of *M. tuberculosis* susceptibility testing performed by participants. The numbers on top of the bars indicate the number of laboratories at the upper limit of that group.

**Figure 1: Distribution of the Annual Volume of *M. tuberculosis* Isolates Tested for Drug Susceptibility by Participating Laboratories in Calendar Year 2006.**



According to the annual volume of testing reported, some laboratories perform less than one drug susceptibility test per month. Laboratories performing these low testing volumes may want to consider referring drug susceptibility tests to other facilities.

## Biosafety Levels of Participant Laboratories

The biosafety levels (BSL) reported by participant laboratories for handling *M. tuberculosis* are:

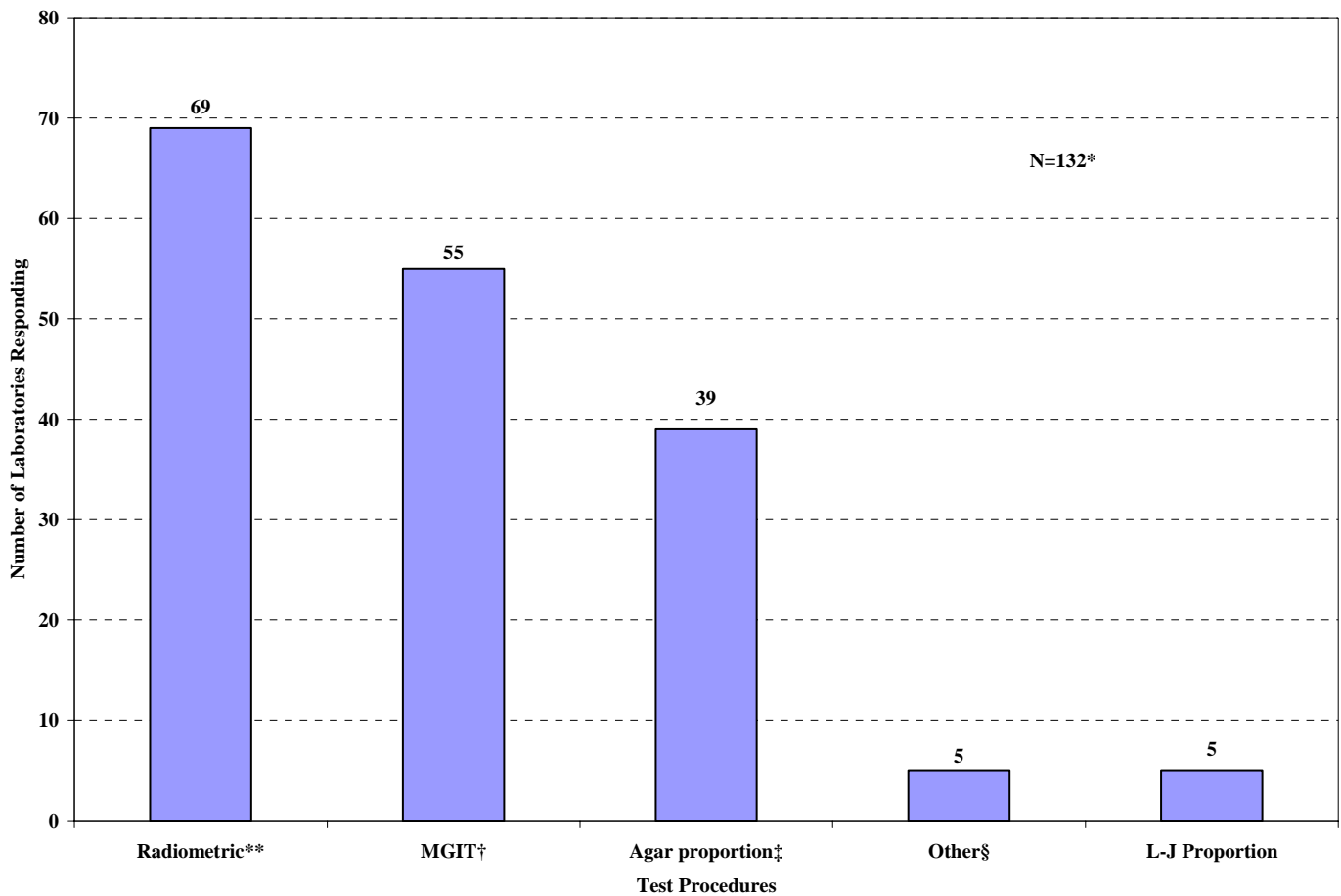
- BSL-3, 81 participants,
- BSL-2 with facilities with level 3 containment equipment, 40 participants,
- BSL-2, 11 participants.

All laboratories are strongly encouraged to consult the CDC/NIH manual, Biosafety in Microbiological and Biomedical Laboratories (5th Edition), which can be accessed on the web at <http://www.cdc.gov/od/ohs/biosfty/bmb15/bmb15toc.htm> for recommendations and to determine their correct biosafety level.

## Laboratory Test Procedures

Figure 2 shows the number of laboratories by the type of procedure used for drug susceptibility testing.

**Figure 2: Procedures Used by the Participating Laboratories for *M. tuberculosis* Drug Susceptibility Testing**



\* Some participants reported more than one test method.

\*\* Radiometric is BACTEC 460TB

† MGIT, Mycobacteria Growth Indicator Tube (BACTEC MGIT 960)

‡ Agar proportion using Middlebrook 7H10 or 7H11 medium.

§ Other methods listed were microtiter, BacT/ALERT, VersaTREK ESP and Colorimetric method for determining MICs with Alamar Blue, Pyrazinamidase test, and resistance ratio method (RRM) on LJ genotype MTBDR HAIN Lifescience.

Some methods, such as the RRM and BacT/ALERT, reflect procedures used by international participants.

### **M. tuberculosis Complex Strains Test Results:**

To facilitate comparison among laboratories, the aggregate test results are provided in Tables 1.0 through 1.3 at the end of this document, representing strains K, L, M, and N. The tables for the *M. tuberculosis* complex strains K, L, M, and N include the results for the radiometric (BACTEC), agar proportion (AP), Lowenstein-Jensen (L-J) proportion, MGIT and other methods at each concentration of drug.

In the tables, the concentrations recommended by CDC and the Clinical and Laboratory Standards Institute (CLSI) for the primary [isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB)] and secondary [streptomycin (SM), ethionamide (THA), kanamycin (KM), capreomycin (CM), and p-amino-salicylic acid (PAS)] antituberculosis drugs are highlighted for the conventional and radiometric methods. 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. When two concentrations are highlighted, such as for isoniazid and ethambutol, the lower concentration is the critical concentration that should always be included to determine whether the *M. tuberculosis* isolate is resistant.

**Strain K, *M. tuberculosis***-Streptomycin resistant at 2.0 µg/ml by agar proportion method.

Streptomycin is a second line drug and has one recommended concentration for AP method (2.0µg/ml) and equivalent concentrations for MGIT and BacT/ALERT MB (1.0 µg/ml and 0.9µg/ml respectively).

Laboratories have shown concordance for streptomycin resistance by AP method 98.7 % (78/79) and by MGIT method 97.7 % (43/44)

**Strain L, *M. tuberculosis*** was fully susceptible.

Among the laboratories performing BACTEC there was small discordance 2.0 % (1/51) for pyrazinamide, however this discordance was more with laboratories performing MGIT 6.5% (3/46) for pyrazinamide. All other susceptibility results were in agreement.

**Strain M, *M. tuberculosis***- INH resistant at 0.2 µg/ml by the agar proportion method.

Isoniazid has two recommended concentrations for the AP method (0.2 µg/ml and 1.0 µg/ml) and equivalent concentrations for BACTEC 460TB and MGIT (0.1 µg/ml and 0.4 µg/ml, respectively).

Among the participant laboratories using agar proportion, 54.2 % (13/24) reported INH resistance at 0.2µg/ml. Laboratories reported 100.00% (25/25) INH susceptible results at 1.0µg/ml concentration.

For participants using BACTEC 460, 42.9 % (24/56) reported INH resistance at 0.1 µg/ml. Laboratories reported 100.00% (18/18) INH susceptible results at 0.4µg/ml concentration.

For participants using MGIT, 76.5 % (39/51) reported INH resistance at 0.1 µg/ml. Laboratories reported 95.8 % (23/24) INH susceptible results at 0.4µg/ml concentration.

**Strain N, *M. tuberculosis***, was resistant to INH at 0.2 µg/ml and 1.0 µg/ml and PZA resistant at 100 µg/ml by the agar proportion method.

Isoniazid has two recommended concentrations for the AP method (0.2 µg/ml and 1.0 µg/ml) and equivalent concentrations for BACTEC 460TB and MGIT (0.1 µg/ml and 0.4 µg/ml, respectively).

Pyrazinamide has recommended concentration for MGIT (100 µg/ml) and an equivalent concentration for BacT/ALERT MB (200 µg/ml).

INH results:

Among the participant laboratories using agar proportion, 100% (28/28) have reported resistance at 0.2µg/ml. Laboratories reported 87.5% (28/32) resistance results at 1.0µg/ml concentration.

For participants using BACTEC 460, 1.8 % (1/57) reported susceptible results at 0.1 µg/ml. Laboratories reported 100.00% (19/19) resistant results at 0.4µg/ml concentration.

For participants using MGIT, 100.0 % (52/52) reported resistance at 0.1 µg/ml and 100.0% (26/26) resistant results at 0.4µg/ml concentration.

Pyrazinamide results:

For participants using BACTEC 460, 98.1 % (52/53) reported resistance results at 100 µg/ml.

For participants using MGIT, 97.8 % (44/45) reported resistance at 100 µg/ml.

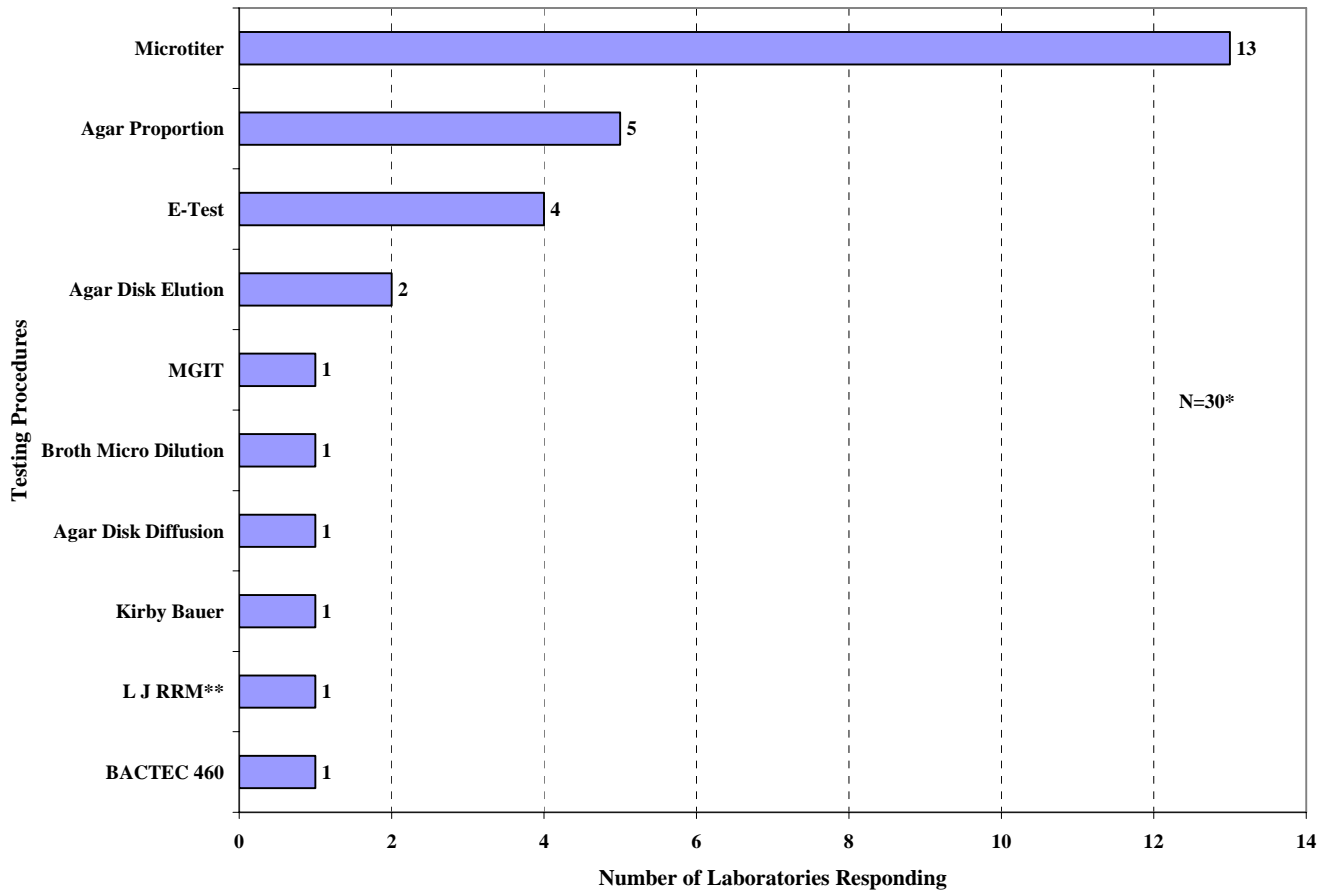
One laboratory reported resistance result by using L-J method.

*Note:* Our providing test results for all drugs that are reported to CDC by participant laboratories should not be construed as a recommendation or endorsement for testing particular drug concentrations with patient isolates of the *M. tuberculosis* complex. 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. Laboratories should not add drugs to their testing regimen without consulting physicians having expertise in treating 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-Strain O, *Mycobacterium abscessus*

Thirty laboratories performed susceptibility testing on *M. abscessus*. Figure 3 shows the procedures used.

**Figure 3: Procedures Used by Participating Laboratories Testing Strain O, *M. abscessus*.**



\*Some participants reported more than one test method. Therefore, the total is greater than the number of laboratories reporting results.

\*\* L J RRM, resistance ratio method

### ***M. abscessus* case history:**

**Patient:** A fifteen year old female with cystic fibrosis developed increased cough and sputum production. High resolution computed tomography of the lung showed bronchiectasis and multiple nodules in the right middle lobe. No cavitation was present. A bronchoscopy was performed and the acid-fast smear was 3+ positive.

**Laboratory Findings:** At four days, many non-pigmented colonies of an acid-fast bacillus grew on routine culture media and on acid-fast culture. The mycobacteria were identified by partial 16S sequence analysis and high performance liquid chromatography (HPLC) as *Mycobacterium chelonae/abscessus* complex and by PCR RFLP analysis of a 444 bp segment of the *hsp65* gene as *M. abscessus*. The patient was treated with a combination of amikacin, cefoxitin, and clarithromycin for 6 months. Cultures continued to be sporadically positive but symptoms abated after 6 months. Periodic administration of the previous multidrug therapy was planned to control the symptoms and progression of the *M. abscessus*.

The prevalence of lung disease caused by rapidly growing mycobacteria is unknown.<sup>1</sup> Underlying disorders that are associated with the disease include lung damage produced by prior mycobacterial infection, gastroesophageal disorders with chronic vomiting, lipid pneumonia, cystic fibrosis, and bronchiectasis. PCR RFLP has shown that *M. abscessus* accounts for approximately 80% of rapidly growing mycobacterial respiratory disease isolates. Isolates of *M. abscessus* are susceptible to clarithromycin (100%), clofazimine, amikacin (90%), and cefoxitin (70%) and imipenem (50%).

**Susceptibility results:**

Of the 30 laboratories that reported susceptibility testing for *M. abscessus*, 8 reported drug susceptibility test results for primary and secondary anti-tuberculosis drugs used for *M. tuberculosis* for example rifampicin, and ethionamide. CLSI guidelines do not recommend testing of anti tuberculosis drugs for rapid growers. CLSI recommends testing of amikacin, cefoxitin, ciprofloxacin, clarithromycin, doxycycline, imipenem, linezolid, sulfamethoxazole, and tobramycin only.<sup>2,3</sup> Current guidelines indicate that imipenem and tobramycin should not be reported for *M. abscessus*.

See Tables 2 and 3 for complete susceptibility testing results reported for *M. abscessus*.

*The addition of NTM strains to this performance evaluation program should not be interpreted as a recommendation 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.*

## Tables

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.

The CDC and CLSI recommendations reflect the critical concentrations of anti-tuberculosis drugs in 7H10 agar and those concentrations for the BACTEC 460TB method that directly correlate with the critical concentrations in the conventional method.<sup>4,5,6,7</sup> These critical values are highlighted. When two concentrations are highlighted, such as for isoniazid and ethambutol, the lower value is the critical concentration which should always be included for determining whether the *M. tuberculosis* isolate is resistant.

Participants should note that the Clinical and Laboratory Standards Institute approved standard “Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes,” M24-A (ISBN 1-56238-500-3) CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA, 2003 recommends testing streptomycin as a secondary drug and also adds ofloxacin and rifabutin to the list of recommended secondary drugs.

Concentrations are listed in micrograms per milliliter, µg/ml.

## Acknowledgments

Special thanks to the following persons for reviewing this report: Nancy G. Warren, Ph.D., Pennsylvania Department of Health; Barbara Brown-Elliott, M.S., University of Texas at Tyler, TX; Beverly Metchock, Dr. PH; Pamela H. Robinson, CDC/Atlanta; Wendy Gross, M.S., TB Reference Laboratory, West Haven, CT; G. David Cross, M.S., CDC/Atlanta; and Bereneice Madison, Ph.D., CDC/Lusaka, Zambia.

**Table 1.0:** Participant Results for culture K, *M. tuberculosis* resistant to streptomycin at 2.0 µg/ml.

DRUG	Conc	Test Method															
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
Isoniazid	0.05															1	1
Isoniazid	0.10				57		57					51	1	52		2	2
Isoniazid	0.12	1		1													
Isoniazid	0.20	26		26	4		4	4		4		1		1		2	2
Isoniazid	0.40				17		17					17		17		1	1
Isoniazid	1.00	28		28	2		2	4		4		2		2		1	1
Isoniazid	5.00	4		4													
Isoniazid	10.00							1		1							
Isoniazid	100.00							1		1							
Rifampin	0.50				1		1										
Rifampin	1.00	31		31	7		7		1	1		53		53		2	2
Rifampin	2.00				58		58					1		1			
Rifampin	5.00	3		3				1		1							
Rifampin	8.00															1	1
Rifampin	16.00															1	1
Rifampin	32.00															1	1
Rifampin	40.00							4		4							
Rifampin	50.00							1		1							
Pyrazinamide	64.00															1	1
Pyrazinamide	100.00				51		51	1		1		45	1	46		1	1
Pyrazinamide	300.00				1		1									1	1
Pyrazinamide	400.00							1		1							
Ethambutol	1.00							1		1							
Ethambutol	1.60															1	1
Ethambutol	2.00							4		4							
Ethambutol	2.50				49	1	50					1		1			
Ethambutol	3.20															1	1
Ethambutol	4.00				1		1										
Ethambutol	5.00	27		27	6		6	1		1		50	2	52		2	2
Ethambutol	6.40															1	1
Ethambutol	7.50	3		3	12	1	13					2		2			
Ethambutol	8.00															1	1
Ethambutol	10.00	11		11													
Streptomycin	1.00						1	1		1		1	42	43			
Streptomycin	2.00		28	28	1	48	49						1	1		1	1
Streptomycin	4.00		1	1		2	2		4	4			10	10			
Streptomycin	5.00								1	1							
Streptomycin	6.00				1	13	14										
Streptomycin	7.50															1	1
Streptomycin	10.00		25	25			2	2		1	1		1	1		1	1
Streptomycin	15.00															1	1
Streptomycin	30.00															1	1
Streptomycin	50.00						1	1									
Ethionamide	1.25				1		1										
Ethionamide	2.50				3		3										
Ethionamide	5.00	17		17	2		2					1		1			
Ethionamide	10.00	3		3												1	1
Ethionamide	20.00								1	1						1	1
Ethionamide	40.00								1	1						1	1



**Table 1.0:** Participant Results for culture K, *M. tuberculosis* resistant to streptomycin at 2.0 µg/ml.

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Kanamycin	5.00	8		8	3		3									
Kanamycin	6.00	12		12												
Kanamycin	10.00							1		1						
Kanamycin	20.00							1		1						
Kanamycin	40.00							1		1						
Capreomycin	0.50													1		1
Capreomycin	1.00													1		1
Capreomycin	1.25				1		1									
Capreomycin	3.00										1		1			
Capreomycin	5.00				2		2									
Capreomycin	10.00	14		14												
Capreomycin	14.00														1	1
Capreomycin	28.00													1		1
Capreomycin	40.00							1		1						
Capreomycin	56.00													1		1
Cycloserine	12.00													1		1
Cycloserine	20.00								1	1						
Cycloserine	24.00													1		1
Cycloserine	25.00	1		1												
Cycloserine	30.00	7		7				1		1						
Cycloserine	40.00							1		1						
Cycloserine	48.00													1		1
Cycloserine	60.00	1		1												
p-Aminosalicylic acid	0.50							1		1						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00	15		15												
p-Aminosalicylic acid	4.00				1	1	2									
p-Aminosalicylic acid	8.00	2		2												
p-Aminosalicylic acid	10.00	4		4												
Amikacin	0.50													1		1
Amikacin	1.00				2		2									
Amikacin	1.50										1		1			
Amikacin	2.00	1		1	1		1									
Amikacin	2.50				1		1									
Amikacin	4.00	3		3	1		1									
Amikacin	5.00				1		1									
Amikacin	6.00	6		6												
Amikacin	7.50													1		1
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												
Amikacin	15.00													1		1
Amikacin	30.00													1		1

**Table 1.0:** Participant Results for culture K, *M. tuberculosis* resistant to streptomycin at 2.0 µg/ml.

DRUG	Conc	Test Method																
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results				
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum		
Ofloxacin	0.50															1		1
Ofloxacin	1.00	3		3	1		1									1		1
Ofloxacin	1.25															1		1
Ofloxacin	2.00	7		7	7		7	1		1			1		1			
Ofloxacin	2.50															1		1
Ofloxacin	4.00	1		1	1		1									1		1
Ofloxacin	5.00															1		1
Ofloxacin	8.00				1		1											
Clarithromycin	24.00															1		1
Clofazimine	0.06				1		1											
Clofazimine	0.12				1		1											
Clofazimine	0.25				1		1											
Clofazimine	0.50				2		2									1		1
Clofazimine	1.00	1		1														
Clofazimine	17.50															1		1
Clofazimine	70.00															1		1
Rifabutin	0.50	2		2														
Rifabutin	1.00	1		1	1		1										1	1
Rifabutin	2.00	4		4												1		1
Levofloxacin	1.50												1		1			
Levofloxacin	2.00				2		2											
Levofloxacin	4.00				1		1											
Levofloxacin	8.00				1		1											
Moxifloxacin	0.50	1		1														

**Table 1.1:** Participant Results for Culture *L. M. tuberculosis* fully susceptible

DRUG	Conc	Test Method															
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
Isoniazid	0.05															1	1
Isoniazid	0.10				57		57					52		52		2	2
Isoniazid	0.12	1		1													
Isoniazid	0.20	24		24	4		4	4		4		1		1		2	2
Isoniazid	0.40				17		17					17		17		1	1
Isoniazid	1.00	25		25	2		2	4		4		2		2		1	1
Isoniazid	5.00	4		4													
Isoniazid	10.00							1		1							
Isoniazid	100.00							1		1							
Rifampin	0.50				1		1										
Rifampin	1.00	28		28	7		7	1		1		53		53		2	2
Rifampin	2.00				58		58					1		1			
Rifampin	5.00	2		2				1		1							
Rifampin	8.00															1	1
Rifampin	16.00															1	1
Rifampin	32.00															1	1
Rifampin	40.00							4		4							
Rifampin	50.00							1		1							
Pyrazinamide	64.00															1	1
Pyrazinamide	100.00				50	1	51	1		1		43	3	46		1	1
Pyrazinamide	300.00				1		1									1	1
Pyrazinamide	400.00							1		1							
Ethambutol	1.00							1		1							
Ethambutol	1.60															1	1
Ethambutol	2.00							4		4							
Ethambutol	2.50				50		50					1		1			
Ethambutol	3.20															1	1
Ethambutol	4.00				1		1										
Ethambutol	5.00	24		24	6		6	1		1		52		52		2	2
Ethambutol	6.40															1	1
Ethambutol	7.50	3		3	12		12					2		2			
Ethambutol	8.00															1	1
Ethambutol	10.00	9		9													
Streptomycin	1.00				1		1	1		1		42		42			
Streptomycin	2.00	25		25	49		49					1		1		1	1
Streptomycin	4.00	1		1	1		1	4		4		7		7			
Streptomycin	5.00							1		1							
Streptomycin	6.00				11		11										
Streptomycin	7.50															1	1
Streptomycin	10.00	21		21				1		1						1	1
Streptomycin	15.00															1	1
Streptomycin	30.00															1	1
Ethionamide	1.25				1		1										
Ethionamide	2.50				3		3										
Ethionamide	5.00	16		16	2		2					1		1			
Ethionamide	10.00	3		3												1	1
Ethionamide	20.00							1		1						1	1
Ethionamide	40.00							1		1						1	1

**Table 1.1:** Participant Results for Culture L, *M. tuberculosis* fully susceptible

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Kanamycin	5.00	7		7	3		3									
Kanamycin	6.00	10		10												
Kanamycin	10.00							1		1						
Kanamycin	20.00							1		1						
Kanamycin	40.00							1		1						
Capreomycin	0.50													1		1
Capreomycin	1.00													1		1
Capreomycin	1.25				1		1									
Capreomycin	3.00										1		1			
Capreomycin	5.00				2		2									
Capreomycin	10.00	13		13												
Capreomycin	14.00													1		1
Capreomycin	28.00													1		1
Capreomycin	40.00							1		1						
Capreomycin	56.00													1		1
Cycloserine	12.00													1		1
Cycloserine	20.00							1		1						
Cycloserine	24.00													1		1
Cycloserine	25.00	1		1												
Cycloserine	30.00	6		6				1		1						
Cycloserine	40.00							1		1						
Cycloserine	48.00													1		1
Cycloserine	60.00	1		1												
p-Aminosalicylic acid	0.50							1		1						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00	13		13												
p-Aminosalicylic acid	4.00				2		2									
p-Aminosalicylic acid	8.00	2		2												
p-Aminosalicylic acid	10.00	3		3												
Amikacin	0.50													1		1
Amikacin	1.00				2		2									
Amikacin	1.50										1		1			
Amikacin	2.00				1		1									
Amikacin	2.50				1		1									
Amikacin	4.00	2		2	1		1									
Amikacin	5.00				1		1									
Amikacin	6.00	6		6												
Amikacin	7.50													1		1
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												
Amikacin	15.00													1		1
Amikacin	30.00													1		1

**Table 1.1:** Participant Results for Culture L, *M. tuberculosis* fully susceptible

DRUG	Conc	Test Method															
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
Ofloxacin	0.50															1	1
Ofloxacin	1.00	2		2	1		1									1	1
Ofloxacin	1.25															1	1
Ofloxacin	2.00	6		6	7		7	1		1	1		1				
Ofloxacin	2.50															1	1
Ofloxacin	4.00				1		1									1	1
Ofloxacin	5.00															1	1
Ofloxacin	8.00				1		1										
Clarithromycin	6.00															1	1
Clarithromycin	12.00															1	1
Clarithromycin	24.00															1	1
Clofazimine	0.06					1	1										
Clofazimine	0.12				1		1										
Clofazimine	0.25				1		1										
Clofazimine	0.50				2		2								1		1
Clofazimine	1.00	1		1													
Clofazimine	17.50																
Clofazimine	35.00														1		1
Clofazimine	70.00														1		1
Rifabutin	0.50	2		2													
Rifabutin	1.00				1		1								1		1
Rifabutin	2.00	3		3											1		1
Levofloxacin	1.50											1		1			
Levofloxacin	2.00				2		2										
Levofloxacin	4.00				1		1										
Levofloxacin	8.00				1		1										
Moxifloxacin	0.50	1		1													

**Table 1.2:** Participant Results for Culture M, *M. tuberculosis*, INH resistant at 0.2µg/ml

DRUG	Conc	Test Method															
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results			
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	
Isoniazid	0.05															1	1
Isoniazid	0.10				32	24	56				12	39	51	1	1	2	
Isoniazid	0.12		1	1													
Isoniazid	0.20	11	13	24	3	1	4	3	1	4		1	1	2		2	
Isoniazid	0.25		1	1													
Isoniazid	0.40				18		18				23	1	24				
Isoniazid	0.50	1		1													
Isoniazid	1.00	25		25	2		2	3		3	1	1	2	1		1	
Isoniazid	2.00				1		1										
Isoniazid	5.00	4		4													
Isoniazid	10.00							1		1							
Isoniazid	100.00							1		1							
Rifampin	0.50				1		1										
Rifampin	1.00	28		28	7		7	1		1	53		53	2		2	
Rifampin	2.00				57	1	58				1		1				
Rifampin	5.00	2		2				1		1							
Rifampin	8.00													1		1	
Rifampin	16.00													1		1	
Rifampin	32.00													1		1	
Rifampin	40.00							4		4							
Rifampin	50.00							1		1							
Pyrazinamide	64.00															1	1
Pyrazinamide	100.00				50	1	51	1		1	43	3	46	1		1	
Pyrazinamide	300.00				1		1							1		1	
Pyrazinamide	400.00							1		1							
Ethambutol	1.00							1		1							
Ethambutol	1.60													1		1	
Ethambutol	2.00							4		4							
Ethambutol	2.50				50		50				1		1				
Ethambutol	3.20													1		1	
Ethambutol	4.00				1		1										
Ethambutol	5.00	24		24	6		6	1		1	52		52	2		2	
Ethambutol	6.40													1		1	
Ethambutol	7.50	2		2	12		12				1		1				
Ethambutol	8.00													1		1	
Ethambutol	10.00	8		8													
Streptomycin	1.00	1		1	1		1		1	1	41		41				
Streptomycin	2.00	26		26	49		49				1		1	1		1	
Streptomycin	4.00	1		1	1		1	4		4	6		6				
Streptomycin	5.00							1		1							
Streptomycin	6.00				11		11										
Streptomycin	7.50													1		1	
Streptomycin	10.00	20		20				1		1				1		1	
Streptomycin	15.00													1		1	
Streptomycin	30.00													1		1	

**Table 1.2:** Participant Results for Culture M, *M. tuberculosis*, INH resistant at 0.2µg/ml

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Ethionamide	1.25				1		1									
Ethionamide	2.00	1		1												
Ethionamide	2.50				2		2									
Ethionamide	5.00	15	1	16	2		2				1		1			
Ethionamide	10.00	3		3											1	1
Ethionamide	20.00							1		1					1	1
Ethionamide	40.00							1		1					1	1
Capreomycin	1.25				1		1									
Capreomycin	3.00											1		1		
Capreomycin	5.00				2		2									
Capreomycin	10.00	13		13												
Capreomycin	14.00														1	1
Capreomycin	28.00														1	1
Capreomycin	40.00							1		1					1	1
Capreomycin	56.00														1	1
Cycloserine	12.00														1	1
Cycloserine	20.00							1		1						
Cycloserine	24.00														1	1
Cycloserine	25.00	1		1												
Cycloserine	30.00	6		6				1		1						
Cycloserine	40.00							1		1						
Cycloserine	48.00														1	1
Cycloserine	60.00	1		1												
p-Aminosalicylic acid	0.50							1		1						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00	13		13												
p-Aminosalicylic acid	4.00				2		2									
p-Aminosalicylic acid	8.00	2		2												
p-Aminosalicylic acid	10.00	3		3												
Amikacin	0.50														1	1
Amikacin	1.00				2		2									
Amikacin	1.50											1		1		
Amikacin	2.00				1		1									
Amikacin	2.50	1		1	1		1									
Amikacin	2.50															
Amikacin	4.00	2		2	1		1									
Amikacin	5.00				1		1									
Amikacin	6.00	6		6												
Amikacin	7.50														1	1
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												
Amikacin	15.00														1	1
Amikacin	30.00														1	1

**Table 1.2:** Participant Results for Culture M, *M. tuberculosis*, INH resistant at 0.2µg/ml

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Ofloxacin	0.50													1		1
Ofloxacin	1.00	2		2	1		1									
Ofloxacin	1.20	1		1												
Ofloxacin	1.25													1		1
Ofloxacin	2.00	5		5	7		7	1		1	1		1			
Ofloxacin	2.50													1		1
Ofloxacin	4.00				1		1									
Ofloxacin	5.00													1		1
Ofloxacin	8.00				1		1									
Clarithromycin	12.00													1		1
Clarithromycin	24.00													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										1		1
Clofazimine	17.50													1		1
Clofazimine	35.00													1		1
Clofazimine	70.00													1		1
Rifabutin	0.50	2		2												
Rifabutin	1.00				1		1							1		1
Rifabutin	2.00	3		3												
Levofloxacin	1.50											1		1		
Levofloxacin	2.00				2		2									
Levofloxacin	4.00				1		1									
Levofloxacin	8.00				1		1									
Moxifloxacin	0.16	1		1												
Moxifloxacin	0.50	1		1												
Moxifloxacin	1.00	1		1												



**Table 1.3:** Participant Results for Culture N, *M. tuberculosis*, resistant to INH at 0.2 µg/ml and 1.0µg/ml and PZA resistant at 100µg/ml by the agar proportion method

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.05														1	1
Isoniazid	0.10				1	56	57					52	52		2	2
Isoniazid	0.12		1	1												
Isoniazid	0.20		28	28		5	5	4	4		1	1		2	2	
Isoniazid	0.25		1	1												
Isoniazid	0.40				19	19					26	26		1	1	
Isoniazid	0.50		1	1												
Isoniazid	1.00	4	28	32		4	4	4	4		2	2		1	1	
Isoniazid	2.00				2		2									
Isoniazid	3.00				1		1									
Isoniazid	5.00	4		4	1		1									
Isoniazid	10.00				1		1	1		1						
Isoniazid	100.00							1		1						
Rifampin	0.50				1		1									
Rifampin	1.00	34		34	7		7	1	1		53		53	2		2
Rifampin	2.00				58		58				1		1			
Rifampin	5.00	3		3				1		1						
Rifampin	8.00													1		1
Rifampin	16.00													1		1
Rifampin	32.00													1		1
Rifampin	40.00							4		4						
Rifampin	50.00							1		1						
Pyrazinamide	64.00														1	1
Pyrazinamide	100.00				1	52	53	1	1		1	44	45	1	1	1
Pyrazinamide	300.00					1	1								1	1
Pyrazinamide	400.00							1	1							
Ethambutol	1.00							1		1						
Ethambutol	1.60													1		1
Ethambutol	2.00							4		4						
Ethambutol	2.50				50		50				1		1			
Ethambutol	2.50															
Ethambutol	3.20													1		1
Ethambutol	4.00				1		1									
Ethambutol	5.00	30		30	6		6	1		1	50	2	52	2		2
Ethambutol	6.40													1		1
Ethambutol	7.50	3		3	12		12				2		2			
Ethambutol	8.00													1		1
Ethambutol	10.00	13		13												
Streptomycin	1.00				1		1	1	1		30	12	42			
Streptomycin	2.00	21	14	35	27	24	51				1		1	1		1
Streptomycin	4.00	1		1	1		1	3	1	4	8		8			
Streptomycin	5.00								1	1						
Streptomycin	6.00				13	1	14									
Streptomycin	7.50														1	1
Streptomycin	10.00	24	1	25	1		1	1		1				1		1
Streptomycin	15.00													1		1
Streptomycin	30.00													1		1
Streptomycin	50.00				1		1									

**Table 1.3:** Participant Results for Culture N, *M. tuberculosis*, resistant to INH at 0.2 µg/ml and 1.0µg/ml and PZA resistant at 100µg/ml by the agar proportion method

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Ethionamide	1.25				4	4										
Ethionamide	2.00		1	1												
Ethionamide	2.50				4	4										
Ethionamide	5.00	1	22	23	1	1	2				1	1				
Ethionamide	10.00	2	1	3											1	1
Ethionamide	20.00							1	1						1	1
Ethionamide	40.00							1	1						1	1
Kanamycin	5.00	11		11	6	6										
Kanamycin	6.00	14		14												
Kanamycin	10.00							1	1							
Kanamycin	20.00							1	1							
Kanamycin	40.00							1	1							
Capreomycin	0.50														1	1
Capreomycin	1.25				4	4										
Capreomycin	3.00										1	1				
Capreomycin	5.00				2	2										
Capreomycin	10.00	19		19												
Capreomycin	14.00														1	1
Capreomycin	28.00													1	1	1
Capreomycin	40.00							1	1							
Capreomycin	56.00														1	1
Cycloserine	12.00														1	1
Cycloserine	20.00							1	1							
Cycloserine	24.00														1	1
Cycloserine	25.00	1		1												
Cycloserine	30.00	9		9				1	1							
Cycloserine	40.00							1	1							
Cycloserine	48.00														1	1
Cycloserine	60.00	2		2												
p-Aminosalicylic acid	0.50							1	1							
p-Aminosalicylic acid	1.00							2	2							
p-Aminosalicylic acid	2.00	20		20												
p-Aminosalicylic acid	4.00				2	1	3									
p-Aminosalicylic acid	8.00	3		3												
p-Aminosalicylic acid	10.00	4		4												

**Table 1.3:** Participant Results for Culture N, *M. tuberculosis*, resistant to INH at 0.2 µg/ml and 1.0µg/ml and PZA resistant at 100µg/ml by the agar proportion method

DRUG	Conc	Test Method																
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results				
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum		
Amikacin	0.50															1		1
Amikacin	1.00					3		3										
Amikacin	1.50											1		1				
Amikacin	2.00	1		1		1		1										
Amikacin	2.50	1		1		1		1										
Amikacin	4.00	3		3		1		1										
Amikacin	5.00					1		1										
Amikacin	6.00	6		6														
Amikacin	7.50															1		1
Amikacin	8.00					1		1										
Amikacin	12.00	2		2														
Amikacin	15.00															1		1
Amikacin	30.00															1		1
Ciprofloxacin	2.00	10		10		4		4										
Ciprofloxacin	3.20															1		1
Ciprofloxacin	4.00					1		1										
Ciprofloxacin	6.40															1		1
Clarithromycin	6.00															1		1
Clarithromycin	12.00															1		1
Clarithromycin	24.00															1		1
Clofazimine	0.06					1		1										
Clofazimine	0.12					1		1										
Clofazimine	0.25					1		1										
Clofazimine	0.50					3		3								1		1
Clofazimine	1.00	1		1												1		1
Clofazimine	17.50															1		1
Clofazimine	35.00															1		1
Clofazimine	70.00															1		1
Rifabutin	0.50	3		3		3		3										
Rifabutin	1.00	1		1		1		1								1		1
Rifabutin	2.00	5		5		1		1										
Levofloxacin	1.50											1		1				
Levofloxacin	2.00					4		4										
Levofloxacin	4.00					1		1										
Levofloxacin	8.00					1		1										
Moxifloxacin	0.16	1		1														
Moxifloxacin	0.50	1		1														
Moxifloxacin	1.00	1		1														

**Table 2:** Participant Results for Culture O, *M. abscessus*

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Amikacin	2.00				1		1									
Amikacin	4.00				1		1									
Amikacin	6.00		1	1												
Amikacin	7.50													1		1
Amikacin	8.00				1		1									
Amikacin	12.00		2	2												
Amikacin	20.00		1	1												
Amikacin	30.00		1	1										1		1
Clofazimine	0.06				1		1									
Clofazimine	0.12				1		1									
Clofazimine	0.25				1		1									
Clofazimine	1.00		1	1												
Clarithromycin	1.20	1		1												
Clarithromycin	3.00		1	1												
Clarithromycin	4.00		1	1												
Clarithromycin	9.00		1	1												
Clarithromycin	15.00													1		1
Ciprofloxacin	2.00		1	1												
Ciprofloxacin	8.00		1	1												
Ciprofloxacin	15.00													1		1
Cycloserine	40.00							1		1						
Cefoxitin	20.00		1	1												
Cefoxitin	30.00	2	1	3										1		1
Doxycycline	6.00		2	2												
Ethambutol	1.60													1		1
Ethambutol	4.00				1		1									
Ethambutol	5.00		2	2				1		1		1		1		
Ethambutol	7.50				1		1									
Gentamicin	4.00		1	1												
Gentamicin	10.00		1	1												
Imipenem	10.00		1	1										1		1
Isoniazid	0.05													1		1
Isoniazid	0.10				1		1					1		1		
Isoniazid	0.20		1	1												
Isoniazid	1.00		1	1												
Isoniazid	100.00							1		1						
Kanamycin	10.00							1		1						
Kanamycin	12.00		1	1												
Kanamycin	30.00		1	1												
Minocycline	6.00		1	1												
Minocycline	30.00													1		1
Moxifloxacin	1.00		1	1												
Moxifloxacin	20.00	1		1												
Ofloxacin	1.00				1		1									
Ofloxacin	1.25													1		1
Ofloxacin	2.00				1		1									
Ofloxacin	4.00				1		1									

**Table 2:** Participant Results for Culture O, *M. abscessus*

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			MGIT Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
p-Aminosalicylic acid	1.00								1	1						
p-Aminosalicylic acid	2.00	1	1													
Pyrazinamide	400.00							1	1							
Rifabutin	2.00	1	1													
Rifampin	0.50				1	1										
Rifampin	1.00	2	2								1	1				
Rifampin	2.00				1	1										
Rifampin	8.00				1	1								1	1	
Rifampin	50.00							1	1							
Streptomycin	1.00											1	1			
Streptomycin	2.00	1	1													
Streptomycin	4.00				1	1										
Streptomycin	6.00				1	1										
Streptomycin	7.50													1	1	
Streptomycin	10.00	2	2													
Streptomycin	100.00							1	1							
Sulfamethoxazole	100.00														1	1
Ethionamide	1.00				1	1										
Ethionamide	2.00				1	1										
Ethionamide	4.00				1	1										
Ethionamide	5.00	2	2													
Ethionamide	40.00							1	1							
Trimethoprim-Sulfamethoxazole	1.00	1	1													
Trimethoprim-Sulfamethoxazole	2.50	1	1													
Trimethoprim-Sulfamethoxazole	25.00													1	1	
Trimethoprim-Sulfamethoxazole	30.00	1	1													
Tobramycin	6.00	1	1													
Tobramycin	8.00	1	1													
Tobramycin	10.00													1	1	
Vancomycin	30.00	1	1													

**Table 3:** Minimum Inhibitory Concentrations for Culture O, *M. abscessus*

DRUG	Test Method	MIC	Susceptible	Resistant	Intermediate	Sum
Amikacin	Microtiter	≤0.50		1		1
Amikacin	Microtiter	≥1.00	1			1
Amikacin	Microtiter	2.00	1			1
Amikacin	Microtiter	32.00			5	5
Amikacin	E-test	4.00	1			1
Amikacin	E-test	8.00	1			1
Amikacin	E-test	32.00			1	1
Amikacin	E-test	≥64.00		1		1
Amikacin	E-test	≥256.00		1		1
Amikacin	Microtiter	8.00	2			2
Amikacin	Microtiter	16.00	3			3
Amikacin	Agar proportion	≤20.00		1		1
Amikacin	Other	32.00			1	1
Augmentin	Microtiter	>64.00*				0
Azithromycin	Microtiter	≤2.00		1		1
Azithromycin	Microtiter	≥4.00	1			1
Azithromycin	Microtiter	<16.00	1			1
Clofazimine	Agar proportion	<1.00		1		1
Clarithromycin	E-test	0.12	1			1
Clarithromycin	E-test	0.13	1			1
Clarithromycin	E-test	0.25	2			2
Clarithromycin	E-test	1.00	1			1
Clarithromycin	Microtiter	≤0.12	1			1
Clarithromycin	Microtiter	≤0.25	3	1		4
Clarithromycin	Microtiter	0.50	4			4
Clarithromycin	Microtiter	1.00	2			2
Clarithromycin	Microtiter	≤2.00	2			2
Clarithromycin	Microtiter	16.00		1		1
Clarithromycin	Agar proportion	≥1.20	1			1
Clarithromycin	Other	>8.00		1		1
Ciprofloxacin	E-test	1.00	1			1
Ciprofloxacin	E-test	≥32.00		3		3
Ciprofloxacin	Microtiter	≥1.00	1			1
Ciprofloxacin	Microtiter	2.00			2	2
Ciprofloxacin	Microtiter	4.00		4		4
Ciprofloxacin	Microtiter	8.00		2		2
Ciprofloxacin	Microtiter	≥16.00		3		3
Ciprofloxacin	Other	<1.00	1			1
Cefoxitin	E-test	8.00	1			1
Cefoxitin	E-test	16.00	1			1
Cefoxitin	E-test	≥256.00		3		3
Cefoxitin	Agar proportion	≤20.00		1		1
Cefoxitin	Microtiter	32.00			5	5
Cefoxitin	Microtiter	≤64			6	6
Cefoxitin	Microtiter	256.00		1		1
Cefoxitin	Other	64.00			1	1
Doxycycline	Microtiter	≥16.00		3		3
Doxycycline	Microtiter	≥32.00		1		1
Doxycycline	Microtiter	≥64.00		1		1
Doxycycline	Microtiter	≥128.00		1		1
Doxycycline	E-test	≥256.00		5		5

**Table 3:** Minimum Inhibitory Concentrations for Culture O, *M. abscessus*

DRUG	Test Method	MIC	Susceptible	Resistant	Intermediate	Sum
Ethambutol	Agar proportion	<5.00		1		1
Erythromycin	Microtiter	64.00		1		1
Gatifloxacin	Microtiter	≥8.00		1		1
Gatifloxacin	Microtiter	16.00		1		1
Imipenem	Microtiter	4.00	1			1
Imipenem	Microtiter	≥16.00*		2		2
Imipenem	E-test	>32.00		5		5
Levofloxacin	E-test	>32.00		2		2
Linezolid	E-test	8.00	1			1
Linezolid	Microtiter	2.00	1			1
Linezolid	Microtiter	16.00	1	1	7	9
Minocycline	Microtiter	≥8.00		1		1
Minocycline	Microtiter	≥32.00*				0
Minocycline	Microtiter	≥64.00		3		3
Minocycline	Microtiter	≥256.00		1		1
Minocycline	E-test	>4.00		1		1
Moxifloxacin	Microtiter	≥16.00		2		2
Moxifloxacin	Agar proportion	>20.00	1			1
Ofloxacin	Microtiter	≤8.00		1		1
Ofloxacin	Microtiter	>16.00	1			1
Rifabutin	Agar proportion	≤2.00		1		1
Rifabutin	Microtiter	>32.00		1		1
Rifampin	Agar proportion	1.00		1		1
Sulfamethoxazole	Microtiter	≥64.00		1		1
Sulfamethoxazole	Other	>64.00		1		1
Ethionamide	Agar proportion	<1.00		1		1
Trimethoprim-Sulfamethoxazole	Agar proportion	≥2.50	1			1
Trimethoprim-Sulfamethoxazole	Microtiter	≥4.00		2		2
Trimethoprim-Sulfamethoxazole	Microtiter	≥8.00*		2		2
Trimethoprim-Sulfamethoxazole	Microtiter	≥16.00	1	3		4
Trimethoprim-Sulfamethoxazole	E-test	>32.00		5		5
Tobramycin	Microtiter	8.00	1		2	3
Tobramycin	Microtiter	16.00		2		2
Tobramycin	E-test	128.00		1		1

\*one lab gave no interpretation

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