

May 27, 2008

Participant
Centers for Disease Control and Prevention (CDC)

Drug Susceptibility Testing of *Mycobacterium tuberculosis* and Nontuberculous Mycobacteria Performance Evaluation Program

Subject: Analyses of Participant Laboratory Results for the January 2008 Shipment

Dear Participant:

Enclosed are analysis of laboratory test results reported to the Centers for Disease Control and Prevention (CDC) by participant laboratories for strains of *Mycobacterium tuberculosis* complex and the nontuberculous mycobacteria (NTM), *M. chelonae*, shipped in January 2008. Participant laboratories (139) received either four *M. tuberculosis* complex strains only or four *M. tuberculosis* strains and one NTM culture. Testing results were received and analyzed from 133 of 139 (95.7%) laboratories participating in this shipment. Of the laboratories submitting results, 97 (72.9%) reported them via the online data entry system.

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

The NTM strain in this performance evaluation is intended to provide an assessment of the various methods, drugs, and interpretations that are reported by laboratories performing drug susceptibility testing for these different strains. The test results for the NTM strain 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 and the Clinical Laboratory and Standards Institute (CLSI) approved standard are referenced to provide participants with recommendations for NTM test methods and drugs that have clinical relevance.

If you have any comments or suggestions on the results in this report or have questions regarding the changes in this program, you may call me at (404) 718-1062.

Sincerely yours,



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Enclosures

Analyses of January 2008 *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 chelonae* strains shipped in January 2008. 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 133 of 139 (95.7%) laboratories participating in this shipment. Of the laboratories submitting results, 97 (72.9%) reported via the online data entry system.

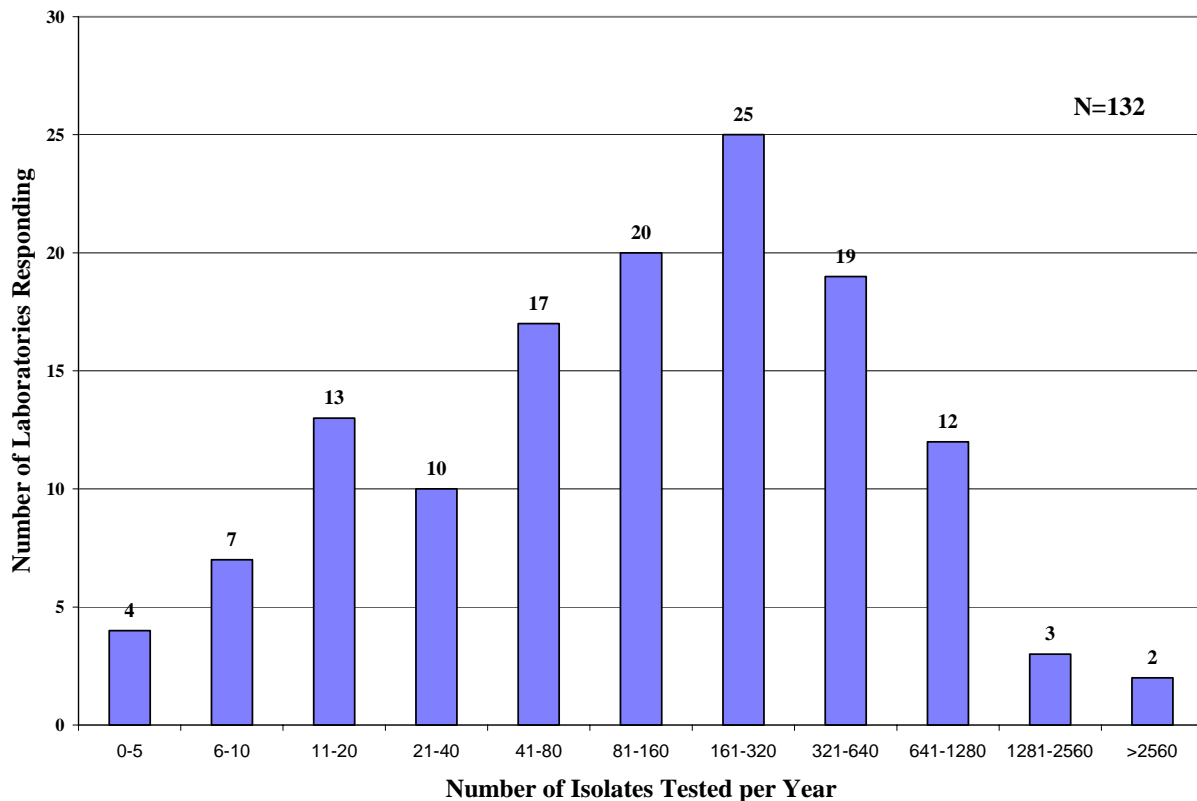
Descriptive Information on Participant Laboratories

Laboratory classifications reported by the 133 participants are:

- 80 (60.1%) health departments,
- 37 (27.8%) hospitals,
- 11 (8.3%) 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 within each group.

Figure 1: Distribution of the Annual Volume of *M. tuberculosis* Isolates Tested for Drug Susceptibility by Participating Laboratories in Calendar Year 2007.



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* were:

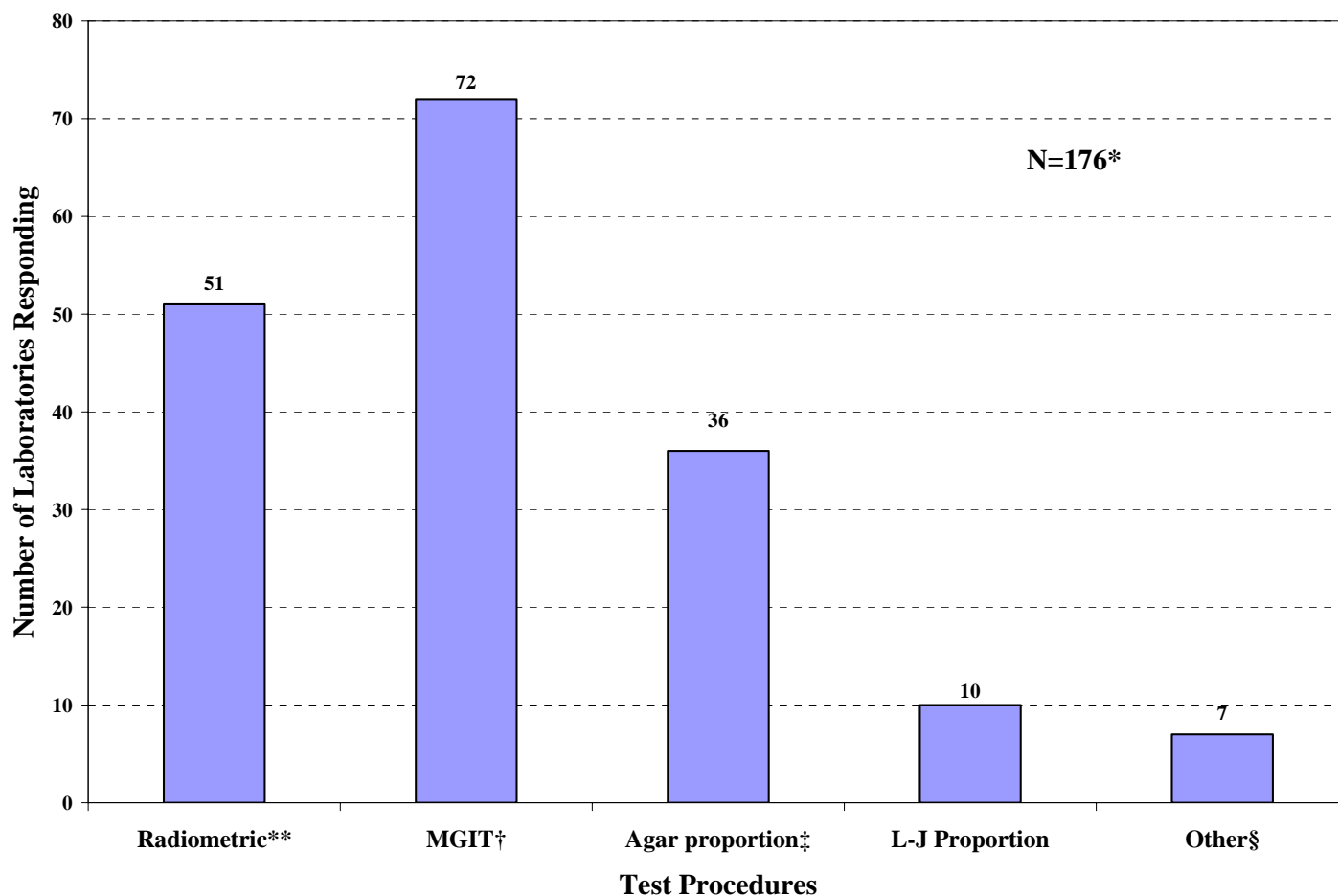
- BSL-3, 78 participants,
- BSL-2 with facilities with level 3 containment equipment, 40 participants,
- BSL-2, 15 participants.

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.

39 laboratories reported using 2 methods and 2 laboratories reported using 3 methods. Some methods, such as the RRM reflect procedures used by international participants only.

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 A, B, C, and D. The tables for the *M. tuberculosis* complex strains A, B, C, and D 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)¹ 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 A, *M. tuberculosis*, was fully susceptible to first line of drugs by the agar proportion method. Among the participant laboratories INH resistance was shown by 2.9% (2/70) at 0.1 µg/ml by MGIT method and 2.4% (1/41) by BACTEC method.

Among the participating laboratories 83.3% (10/12) reported resistance to capreomycin by agar proportion method.

Strain B, *M. tuberculosis* –Rifampin resistant at 1.0 µg/ml by agar proportion method. Rifampin is a first line drug and has one recommended concentration for agar proportion method (1.0 µg/ml) and equivalent concentrations for BACTEC, MGIT and BacT/ALERT MB (2.0 µg/ml, 1.0 µg/ml and 0.9 µg/ml respectively).

Laboratories showed concordance for Rifampicin resistance by agar proportion method 96.4% (27/28), BACTEC 460 method 100% (39/39), and by MGIT method 98.3% (58/59)

Strain C, *M. tuberculosis*- INH resistant at 0.2 µg/ml by 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, 95.8% (23/24) reported INH resistance at 0.2 µg/ml.

For participants using BACTEC, 75% (30/40) reported INH resistance at 0.1 µg/ml.

For participants using MGIT, 65.2% (45/69) reported INH resistance at 0.1 µg/ml.

Strain D, *M. tuberculosis*- INH resistant at 0.2 µg/ml and 1.0 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 and MGIT (0.1 µg/ml and 0.4 µg/ml, respectively).

Among the participant laboratories using agar proportion, 100% (25/25) reported INH resistance at 0.2 µg/ml and 96.6% (28/29) reported INH resistance at 1.0 µg/ml;

Participants using BACTEC, reported 97.4% (38/39) resistance for INH at 0.1 µg/ml and 100% (15/15) resistance at 0.4 µg/ml respectively.

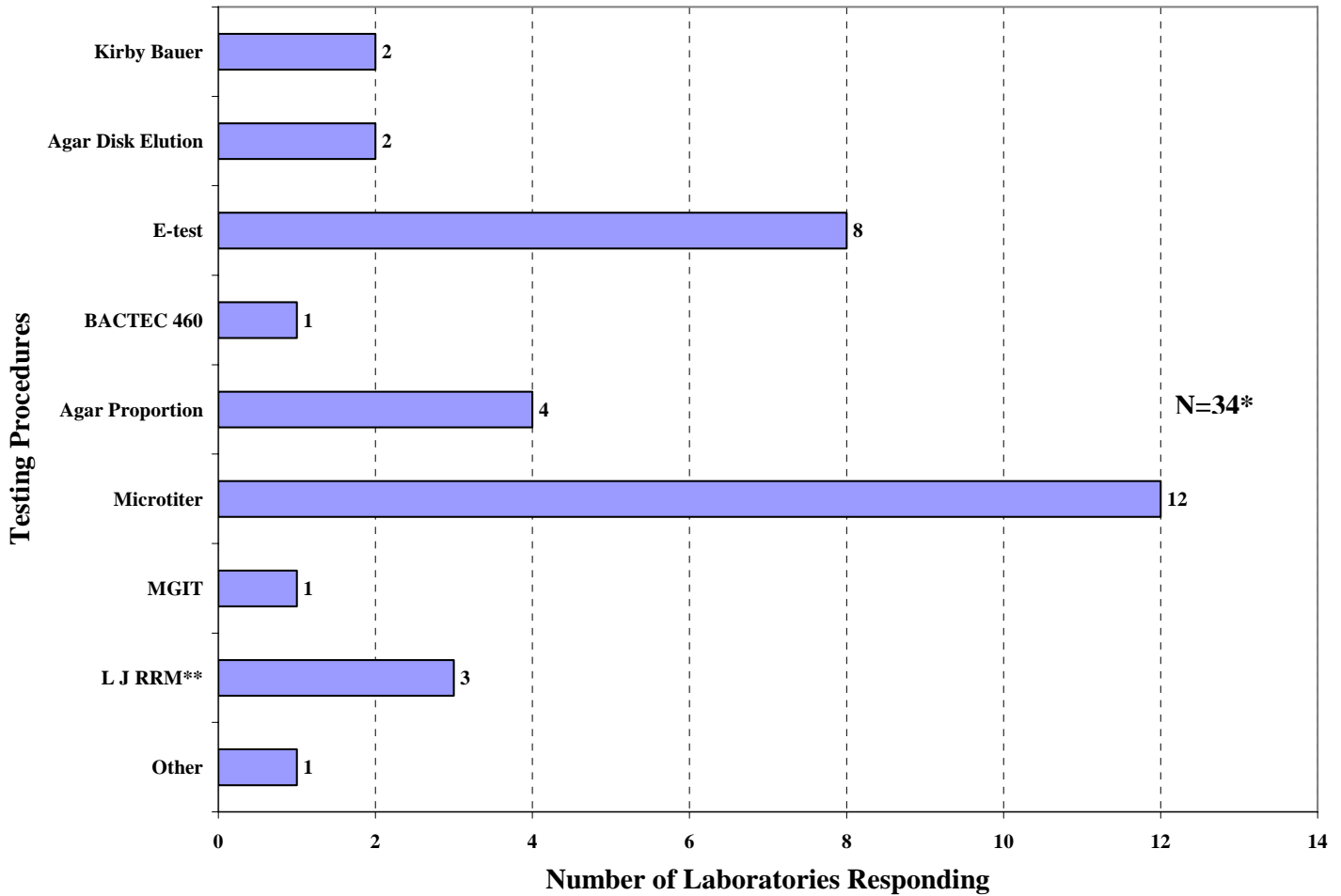
Participants using MGIT reported 98.6% (68/69) resistance for INH at 0.1 µg/ml and 100% (32/32) resistance for INH at 0.4 µg/ml;

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 E, *Mycobacterium chelonae*

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

Figure 3: Procedures Used by Participating Laboratories Testing Strain T, *M. chelonae*.



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

** LJ RRM, resistance ratio method

***M. chelonae* case history:**

Patient: A 59 year old man was referred by a dermatologist to the infectious disease doctor with a chronic wound on his left foot, specifically the big toe near to the nail. Any attempt of treatment with “conventional” anti-microbial agents was unsuccessful. The wound penetrated the skin and toe all the way to the bone and joint and produced a small amount of pus.

Laboratory Findings: Examination of a smear made from the pus was stained by the Ziel-Nielsen method and revealed a substantial number of acid fast bacilli. The Lowenstein-Jensen slant showed growth within seven (7) days. The culture was submitted to a reference laboratory for identification and drug susceptibilities. The isolate was identified as *Mycobacterium chelonae* and drug susceptibility testing was performed.

Mycobacterium chelonae is a rapidly growing nontuberculous mycobacterium that can cause skin, bone and soft tissue infections. Disseminated disease can occur in immunocompromised patients. Epidemic and sporadic cases of keratitis associated with contact lens wear have been reported. It is less frequent in pulmonary disease. It is important to differentiate the isolate as *M. abscessus/chelonae* because both can cause similar infections in skin but *M. chelonae* is easier to treat than *M. abscessus*. *M. chelonae* isolates are resistant to ceftiofloxacin. Drug susceptibility testing is important to initiate mono or combination therapy to avoid the development of macrolide resistance in serious cases.

Susceptibility results:

Of the 34 laboratories that reported susceptibility testing for *M. chelonae*, 6 laboratories also reported drug susceptibility test results for primary and secondary anti-tuberculosis drugs used for *M. tuberculosis*, for example rifampicin, and isoniazid.

Participants should note that the CLSI recommends (CLSI, M24-A, 2003) that NO first line antituberculous agents be tested against the RGM.

Also note that when *M. chelonae* is isolated, tobramycin MIC should be reported as this is the preferred aminoglycoside for this species.

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

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^{4,5,6,7}. 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 CLSI 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 A, *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				40	1	41				68	2	70	4		4	4
Isoniazid	0.20	20		20	2		2	6		6	1		1	2		2	2
Isoniazid	0.40				12		12				21		21	3		3	3
Isoniazid	0.50							1		1							
Isoniazid	1.00	22		22	1		1	4	1	5							
Isoniazid	5.00	3		3										1		1	1
Isoniazid	10.00							2		2							
Isoniazid	20.00								1	1							
Isoniazid	100.00							1		1							
Rifampin	0.10										1		1				
Rifampin	0.50										1		1				
Rifampin	1.00	21		21	4		4		1	1	64	2	66	4		4	4
Rifampin	2.00				42		42				2		2				
Rifampin	5.00	3		3				1		1							
Rifampin	8.00													1		1	1
Rifampin	16.00													1		1	1
Rifampin	32.00													1		1	1
Rifampin	40.00							8		8							
Rifampin	50.00							1		1							
Pyrazinamide	64.00										54	2	56	1		1	1
Pyrazinamide	100.00				35		35	1		1				1		1	1
Pyrazinamide	300.00													3		3	3
Pyrazinamide	400.00							1		1							
Ethambutol	1.00							1		1							
Ethambutol	1.60													1		1	1
Ethambutol	2.00							9		9							
Ethambutol	2.50				35		35				2		2				
Ethambutol	3.20													1		1	1
Ethambutol	5.00	20		20	4		4	1		1	68	2	70	3		3	3
Ethambutol	6.40													1		1	1
Ethambutol	7.50	1		1	9		9				2		2				
Ethambutol	8.00													3		3	3
Ethambutol	10.00	8		8													
Ethambutol	25.00													1		1	1
Streptomycin	1.00							1		1	51	1	52				
Streptomycin	2.00	19		19	38		38				2		2	1		1	1
Streptomycin	4.00							6	1	7	9		9				
Streptomycin	5.00							1		1							
Streptomycin	6.00				8		8										
Streptomycin	7.50													1		1	1
Streptomycin	8.00							1		1							
Streptomycin	10.00	19		19				1		1				1		1	1
Streptomycin	15.00													1		1	1
Streptomycin	30.00													1		1	1
Ethionamide	1.25				1		1										
Ethionamide	2.50				3		3										
Ethionamide	5.00	15		15	1		1										
Ethionamide	10.00	3		3										1		1	1
Ethionamide	20.00							1		1				1		1	1
Ethionamide	40.00							1		1				1		1	1

Table 1.0: Participant Results for Culture A, *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	4.00				1		1									
Kanamycin	5.00	7		7	3		3									
Kanamycin	6.00	8		8												
Kanamycin	10.00							1		1						
Kanamycin	20.00							1		1						
Kanamycin	40.00							1		1						
Capreomycin	0.50													1		1
Capreomycin	1.25				1	2	3									
Capreomycin	5.00					1	1									
Capreomycin	10.00	2	10	12												
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	50.00	1		1												
p-Aminosalicylic acid	0.50							2		2						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00	11		11												
p-Aminosalicylic acid	4.00				2	1	3									
p-Aminosalicylic acid	8.00	1		1												
p-Aminosalicylic acid	10.00	3		3												
Amikacin	0.50													1		1
Amikacin	1.00				2		2									
Amikacin	2.00				1		1									
Amikacin	4.00	2		2												
Amikacin	5.00				1		1									
Amikacin	6.00	4		4												
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												
Amikacin	15.00													1		1
Amikacin	30.00													1		1
Ofloxacin	0.20	1		1												
Ofloxacin	0.50														1	1
Ofloxacin	1.00	1		1										1		1
Ofloxacin	1.25													1		1
Ofloxacin	2.00	8		8	4		4	1		1	1		1			
Ofloxacin	2.50													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

Table 1.0: Participant Results for Culture A, *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
Clofazimine	0.06				1	1										
Clofazimine	0.12										1		1			
Clofazimine	0.50				1		1							1		1
Clofazimine	1.00	1		1												
Clofazimine	17.50													1		1
Clofazimine	35.00													1		1
Clofazimine	70.00													1		1
Rifabutin	0.50	4		4										1		1
Rifabutin	2.00	3		3												
Ciprofloxacin	0.50													1		1
Ciprofloxacin	1.00	1		1	2		2							1		1
Ciprofloxacin	1.60													1		1
Ciprofloxacin	2.00	6		6	1		1							1		1
Ciprofloxacin	3.20													1		1
Ciprofloxacin	4.00										1		1			
Ciprofloxacin	6.40													1		1
Levofloxacin	2.00				1		1									
Levofloxacin	8.00				1		1									
Moxifloxacin	1.00	1		1												

Table 1.1: Participant Results for culture B, *M. tuberculosis*, resistant to rifampin at 1.0 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				37	1	38						63		63	4	4
Isoniazid	0.20	24		24	2		2	5		5			1		1	2	2
Isoniazid	0.40				11		11						20		20	3	3
Isoniazid	1.00	27		27				5		5							
Isoniazid	5.00	4		4											1		1
Isoniazid	10.00							2		2							
Isoniazid	20.00							1		1							
Isoniazid	100.00							1		1							
Rifampin	0.10												1		1		
Rifampin	0.50												1		1		
Rifampin	1.00	1	27	28		3	3		1	1		1	58	59		4	4
Rifampin	2.00					39	39						2	2			
Rifampin	5.00	1	3	4		2	2		1	1							
Rifampin	8.00															1	1
Rifampin	10.00					1	1						1	1			
Rifampin	16.00															1	1
Rifampin	32.00															1	1
Rifampin	40.00							2	5	7							
Rifampin	50.00								1	1			1	1			
Pyrazinamide	64.00														1		1
Pyrazinamide	100.00				33		33	1		1		53		53	1		1
Pyrazinamide	300.00														3		3
Pyrazinamide	400.00							1		1							
Ethambutol	1.00							1		1							
Ethambutol	2.00							8		8							
Ethambutol	2.50				34		34										
Ethambutol	2.50											2		2			
Ethambutol	3.20														1		1
Ethambutol	5.00	24		24	3		3	1		1		61	2	63	3		3
Ethambutol	6.40														1		1
Ethambutol	7.50	2		2	7		7					2		2			
Ethambutol	8.00														3		3
Ethambutol	10.00	11		11													
Ethambutol	25.00														1		1
Streptomycin	1.00							1		1		45	1	46			
Streptomycin	2.00	27		27	36		36					2		2	1		1
Streptomycin	4.00							6		6		8		8			
Streptomycin	5.00							1		1							
Streptomycin	6.00				6		6										
Streptomycin	7.50														1		1
Streptomycin	8.00							1		1							
Streptomycin	10.00	24		24				1		1					1		1
Streptomycin	15.00														1		1
Streptomycin	30.00														1		1
Ethionamide	1.25				2		2										
Ethionamide	2.50				2		2										
Ethionamide	5.00	23		23	2		2										
Ethionamide	10.00	4		4											1		1
Ethionamide	20.00							1		1					1		1
Ethionamide	40.00							1		1					1		1

Table 1.1: Participant Results for culture B, *M. tuberculosis*, resistant to rifampin at 1.0 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	2.50				1		1									
Kanamycin	5.00	10		10	3		3									
Kanamycin	6.00	13		13												
Kanamycin	10.00							1		1						
Kanamycin	20.00							1		1						
Kanamycin	40.00							1		1						
Capreomycin	0.50													1		1
Capreomycin	1.25				1		1									
Capreomycin	2.50				1		1									
Capreomycin	5.00				3		3									
Capreomycin	10.00	17		17												
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	10		10				1		1						
Cycloserine	40.00							1		1						
Cycloserine	48.00													1		1
Cycloserine	50.00	1		1												
Cycloserine	60.00	1		1												
p-Aminosalicylic acid	0.50							2		2						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00	17		17												
p-Aminosalicylic acid	4.00				2		2									
p-Aminosalicylic acid	8.00	1		1												
p-Aminosalicylic acid	10.00	4		4												
Amikacin	0.50													1		1
Amikacin	2.00	1		1												
Amikacin	2.00				1		1									
Amikacin	2.50				1		1									
Amikacin	4.00	3		3												
Amikacin	5.00	1		1												
Amikacin	5.00				1		1									
Amikacin	6.00	5		5												
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
Ofloxacin	0.20	1		1												
Ofloxacin	0.50														1	1
Ofloxacin	1.00	1		1	1		1							1		1
Ofloxacin	1.25				1		1							1		1
Ofloxacin	2.00	12		12	4		4	1		1	2		2			
Ofloxacin	2.50													1		1
Ofloxacin	4.00	1		1												
Ofloxacin	5.00													1		1
Ofloxacin	8.00										1		1			

Table 1.1: Participant Results for culture B, *M. tuberculosis*, resistant to rifampin at 1.0 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
Clarithromycin	3.00		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	0.50				2		2							1		1
Clofazimine	1.00	1		1												
Clofazimine	17.50													1		1
Clofazimine	35.00													1		1
Clofazimine	70.00													1		1
Rifabutin	0.05					1	1									
Rifabutin	0.25					1	1									
Rifabutin	0.50		6	6		2	2									
Rifabutin	1.00					1	1									
Rifabutin	2.00		4	4											1	1
Rifabutin	4.00													1		1
Ciprofloxacin	0.50														1	1
Ciprofloxacin	1.00	1		1	2		2									
Ciprofloxacin	1.25				1		1									
Ciprofloxacin	1.60													1		1
Ciprofloxacin	2.00	7		7	1		1									
Ciprofloxacin	2.50				1		1									
Ciprofloxacin	3.20													1		1
Ciprofloxacin	4.00										1		1			
Ciprofloxacin	5.00	1		1	1		1									
Ciprofloxacin	6.40													1		1
Levofloxacin	2.00				2		2									
Levofloxacin	8.00				1		1									
Moxifloxacin	1.00	2		2												
Azithromycin	3.00		1	1												

Table 1.2: Participant Results for culture *C. M. tuberculosis*, resistant to isoniazid at 0.2 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				10	30	40						24	45	69	4	4
Isoniazid	0.20	1	23	24	1	2	3	2	4	6		1		1	1	1	1
Isoniazid	0.40				14		14					29		29	3		3
Isoniazid	0.50							1		1							
Isoniazid	1.00	26	1	27	2		2	4		4							
Isoniazid	5.00	3		3	1		1										
Isoniazid	10.00							2		2							
Isoniazid	20.00							1		1							
Isoniazid	100.00							1		1							
Rifampin	0.10											1		1			
Rifampin	0.50											1		1			
Rifampin	1.00	25		25	4		4	1		1		64	1	65	3		3
Rifampin	2.00				42		42					2		2			
Rifampin	5.00	4		4				1		1							
Rifampin	10.00											1		1			
Rifampin	16.00														1		1
Rifampin	32.00														1		1
Rifampin	40.00							8		8							
Rifampin	50.00							1		1		1		1			
Pyrazinamide	64.00															1	1
Pyrazinamide	100.00				34		34					55		55	1		1
Pyrazinamide	300.00														3		3
Ethambutol	1.00							1		1							
Ethambutol	1.60														1		1
Ethambutol	2.00							8	1	9							
Ethambutol	2.50				36		36					2		2			
Ethambutol	3.20														1		1
Ethambutol	5.00	22	1	23	4		4	1		1		66	2	68	3		3
Ethambutol	6.40														1		1
Ethambutol	7.50	2		2	9		9					2		2			
Ethambutol	8.00														3		3
Ethambutol	10.00	10		10													
Streptomycin	1.00								1	1		52		52			
Streptomycin	2.00	24		24	38		38					2		2			
Streptomycin	4.00							7		7		10		10			
Streptomycin	5.00							1		1							
Streptomycin	6.00				8		8										
Streptomycin	8.00							1		1							
Streptomycin	10.00	23		23				1		1							
Streptomycin	15.00														1		1
Streptomycin	30.00														1		1
Ethionamide	1.25				1		1										
Ethionamide	2.50				2	1	3										
Ethionamide	5.00	17	3	20	2		2										
Ethionamide	10.00	3		3				1		1					1		1
Ethionamide	20.00							1		1					1		1
Ethionamide	40.00							1		1					1		1

Table 1.2: Participant Results for culture *C. M. tuberculosis*, resistant to isoniazid at 0.2 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	4.00				1		1									
Kanamycin	5.00	9		9	3		3									
Kanamycin	6.00	11		11												
Kanamycin	10.00							1		1						
Kanamycin	20.00							1		1						
Kanamycin	40.00							1		1						
Capreomycin	0.50													1		1
Capreomycin	1.25				3		3									
Capreomycin	5.00				2		2									
Capreomycin	10.00	15		15												
Capreomycin	14.00													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	9		9				1		1						
Cycloserine	40.00							1		1						
Cycloserine	48.00													1		1
Cycloserine	50.00	1		1												
p-Aminosalicylic acid	0.50							2		2						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00	14		14												
p-Aminosalicylic acid	4.00				3		3									
p-Aminosalicylic acid	8.00	1		1												
p-Aminosalicylic acid	10.00	3		3												
Amikacin	0.50													1		1
Amikacin	1.00				2		2				1		1			
Amikacin	2.00	1		1	1		1									
Amikacin	4.00	3		3												
Amikacin	5.00	1		1	1		1									
Amikacin	6.00	4		4												
Amikacin	8.00				1		1									
Amikacin	10.00										1		1			
Amikacin	12.00	2		2												
Amikacin	15.00													1		1
Amikacin	30.00													1		1
Ofloxacin	0.20	1		1												
Ofloxacin	0.50														1	1
Ofloxacin	1.00	2		2										1		1
Ofloxacin	1.25													1		1
Ofloxacin	2.00	10		10	5		5	1		1	2		2			
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

Table 1.2: Participant Results for culture *C. M. tuberculosis*, resistant to isoniazid at 0.2 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
Clofazimine	0.06				1		1									
Clofazimine	0.12											1		1		
Clofazimine	0.50				1		1							1		1
Clofazimine	1.00	1		1												
Clofazimine	17.50													1		1
Clofazimine	35.00													1		1
Clofazimine	70.00													1		1
Rifabutin	0.50	5		5												
Rifabutin	1.00														1	1
Rifabutin	2.00	3		3										1		1
Ciprofloxacin	0.50														1	1
Ciprofloxacin	1.00	1		1	2		2									
Ciprofloxacin	1.60													1		1
Ciprofloxacin	2.00	7		7	1		1									
Ciprofloxacin	3.20													1		1
Ciprofloxacin	4.00											1		1		
Ciprofloxacin	6.40													1		1
Levofloxacin	2.00				1		1									
Levofloxacin	8.00				1		1									
Moxifloxacin	1.00	2		2												

Table 1.3: Participant Results for culture D, *M. tuberculosis*, resistant to isoniazid at 0.2 and at 1.0 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				1	38	39				1	68	69		4	4
Isoniazid	0.20		25	25		3	3	1	3	4		1	1		1	1
Isoniazid	0.40					15	15					32	32		3	3
Isoniazid	0.50							1		1						
Isoniazid	1.00	1	28	29		2	2	3		3		1	1			
Isoniazid	2.00					2	2									
Isoniazid	3.00											1	1			
Isoniazid	5.00	1	1	2		1	1									
Isoniazid	10.00							1		1		1	1			
Isoniazid	20.00							1		1						
Rifampin	0.10										1		1			
Rifampin	0.50										1		1			
Rifampin	1.00	26	1	27	4		4				65		65	3		3
Rifampin	2.00				39	1	40				2		2			
Rifampin	5.00	4		4												
Rifampin	8.00													1		1
Rifampin	16.00													1		1
Rifampin	32.00													1		1
Rifampin	40.00							7		7						
Pyrazinamide	64.00													1		1
Pyrazinamide	100.00				35		35				54	1	55	1		1
Pyrazinamide	300.00													3		3
Ethambutol	1.60													1		1
Ethambutol	2.00							5	2	7						
Ethambutol	2.50				14	21	35				2		2			
Ethambutol	3.20													1		1
Ethambutol	5.00	22	3	25	3	2	5				61	7	68	3		3
Ethambutol	6.40													1		1
Ethambutol	7.50	2		2	10		10				2		2			
Ethambutol	8.00													3		3
Ethambutol	10.00	10		10	1		1									
Streptomycin	1.00										51	1	52			
Streptomycin	2.00	26		26	38	1	39				2		2			
Streptomycin	4.00							6		6	10		10			
Streptomycin	6.00				7		7									
Streptomycin	7.50													1		1
Streptomycin	8.00							1		1						
Streptomycin	10.00	22		22												
Streptomycin	15.00													1		1
Streptomycin	30.00													1		1
Ethionamide	1.25				2	2	4									
Ethionamide	2.50				3		3									
Ethionamide	5.00	22	1	23	2		2									
Ethionamide	10.00	2		2										1		1
Ethionamide	20.00													1		1
Ethionamide	40.00													1		1
Kanamycin	2.50				1		1									
Kanamycin	4.00				1		1									
Kanamycin	5.00	9		9	5		5									
Kanamycin	6.00	13		13												
Kanamycin	40.00							1		1						

Table 1.3: Participant Results for culture D, *M. tuberculosis*, resistant to isoniazid at 0.2 and at 1.0 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
Capreomycin	1.25				4		4									
Capreomycin	2.50				1		1									
Capreomycin	5.00				3		3									
Capreomycin	10.00	15		15												
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	24.00													1		1
Cycloserine	25.00	1		1												
Cycloserine	30.00	10		10				1		1						
Cycloserine	48.00													1		1
Cycloserine	50.00	1		1												
Cycloserine	60.00	1		1												
p-Aminosalicylic acid	0.50							1		1						
p-Aminosalicylic acid	1.00							1		1						
p-Aminosalicylic acid	2.00	15		15												
p-Aminosalicylic acid	4.00				2		2									
p-Aminosalicylic acid	8.00	1		1												
p-Aminosalicylic acid	10.00	4		4												
Amikacin	1.00				2		2									
Amikacin	2.00	1		1	1		1									
Amikacin	2.50				1		1									
Amikacin	4.00	2		2												
Amikacin	5.00	1		1	1		1									
Amikacin	6.00	4		4												
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
Ofloxacin	0.20		1	1												
Ofloxacin	1.00		2	2	1		1									
Ofloxacin	1.25					1	1								1	1
Ofloxacin	2.00	2	8	10	6		6	1	1		2	2				
Ofloxacin	2.50				1		1								1	1
Ofloxacin	4.00		1	1												
Ofloxacin	5.00					1	1								1	1
Ofloxacin	8.00											1	1			
Ofloxacin	10.00											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	0.50				3		3									
Clofazimine	1.00	1		1												
Clofazimine	17.50														1	1
Clofazimine	35.00														1	1
Clofazimine	70.00														1	1

Table 1.3: Participant Results for culture D, *M. tuberculosis*, resistant to isoniazid at 0.2 and at 1.0 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
Rifabutin	0.50	5		5	3		3									
Rifabutin	1.00				1		1									
Rifabutin	2.00	3		3												
Ciprofloxacin	1.00		1	1	1	1	2									
Ciprofloxacin	1.60													1		1
Ciprofloxacin	2.00	1	6	7	1		1									
Ciprofloxacin	3.20													1		1
Ciprofloxacin	4.00										1		1			
Ciprofloxacin	6.40													1		1
Levofloxacin	2.00				1	2	3									
Levofloxacin	8.00				1		1									
Moxifloxacin	1.00	1	1	2												

Table 2. Participant Results for Culture E, *M. chelonae*

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			D-Test 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	8.00				1		1									
Amikacin	12.00	1		1												
Amikacin	20.00								1	1						
Amikacin	30.00		1	1										1	1	2
Clofazimine	0.06					1	1									
Clofazimine	0.12					1	1									
Clofazimine	0.25					1	1									
Clarithromycin	3.00	1		1												
Clarithromycin	4.00	1		1												
Clarithromycin	15.00													1		1
Ciprofloxacin	1.00	1		1												
Ciprofloxacin	2.00	1		1												
Ciprofloxacin	5.00														1	1
Ciprofloxacin	20.00								1		1					
Cycloserine	30.00									1	1					
Cycloserine	40.00									1	1					
Cefoxitin	30.00		2	2											1	1
Doxycycline	6.00	2		2												
Ethambutol	2.00								2	2						
Ethambutol	4.00					1	1									
Ethambutol	5.00		1	1					1	1			1	1		
Ethambutol	7.50					1	1									
Erythromycin	15.00														1	1
Gentamicin	4.00		1	1												
Imipenem	10.00														1	1
Isoniazid	0.10					1	1						1	1		
Isoniazid	0.20		1	1												
Isoniazid	1.00		1	1						2	2					
Isoniazid	20.00									1	1					
Kanamycin	12.00	1		1												
Kanamycin	20.00									2	2					
Minocycline	6.00	1		1												
Ofloxacin	1.00					1	1									
Ofloxacin	2.00					1		1								
Ofloxacin	4.00					1		1								
p-Aminosalicylic acid	0.50								1	1						
p-Aminosalicylic acid	1.00									1	1					
p-Aminosalicylic acid	2.00		1	1												
Pyrazinamide	400.00									1	1					
Rifampin	0.50					1	1									
Rifampin	1.00												1	1		
Rifampin	2.00					1	1									
Rifampin	8.00					1	1									
Rifampin	40.00									2	2					
Rifampin	50.00									1	1					

Table 2. Participant Results for Culture *E. M. chelonae*

DRUG	Conc	Test Method														
		AP Results			BACTEC Results			LJ Prop Results			D-Test Results			Other Tests Results		
		S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Streptomycin	1.00											1	1			
Streptomycin	2.00		1	1												
Streptomycin	4.00					1	1		1	1						
Streptomycin	6.00					1	1									
Streptomycin	8.00								1	1						
Streptomycin	10.00		1	1												
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	1		1												
Ethionamide	20.00								1	1						
Ethionamide	40.00							1		1						
Trimethoprim-Sulfamethoxazole	1.00		1	1												
Trimethoprim-Sulfamethoxazole	7.50		1	1												
Trimethoprim-Sulfamethoxazole	25.00														1	1
Tobramycin	8.00		1	1												
Tobramycin	10.00													1		1

Table 3. Minimum Inhibitory Concentrations for Culture E, *M. chelonae*

DRUG	Test Method	MIC	Susceptible	Resistant	Intermediate	Sum
Amikacin	AP	<2.50		1		1
Amikacin	AP	>5.00	1			1
Amikacin	E-test	1.00	1			1
Amikacin	E-test	4.00	1			1
Amikacin	E-test	<16.00	1			1
Amikacin	E-test	256.00		1		1
Amikacin	Microtiter	<1.00		1		1
Amikacin	Microtiter	>2.00	1			1
Amikacin	Microtiter	8.00	1			1
Amikacin	Microtiter	≤16.00	3			3
Amikacin	Microtiter	32.00			2	2
Azithromycin	Microtiter	<0.50		1		1
Azithromycin	Microtiter	>1.00	1			1
Clarithromycin	AP	>0.60	1			1
Clarithromycin	E-test	0.02	1			1
Clarithromycin	E-test	0.09	1			1
Clarithromycin	E-test	0.50	2			2
Clarithromycin	E-test	<1.00	1			1
Clarithromycin	E-test	1.50	1			1
Clarithromycin	Microtiter	0.12	1			1
Clarithromycin	Microtiter	>0.13	1			1
Clarithromycin	Microtiter	≤0.25	5			5
Clarithromycin	Microtiter	0.50	2			2
Clarithromycin	Microtiter	1.00	1			1
Clarithromycin	Microtiter	<2.00	1			1
Clarithromycin	Microtiter	4.00			1	1
Ciprofloxacin	AP	<0.16	1			1
Ciprofloxacin	E-test	0.06	1			1
Ciprofloxacin	E-test	0.38	2			2
Ciprofloxacin	E-test	<1.00	1			1
Ciprofloxacin	E-test	>32.00		1		1
Ciprofloxacin	Microtiter	>0.50	1			1
Ciprofloxacin	Microtiter	≤1.00	3			3
Ciprofloxacin	Microtiter	2.00			4	4
Ciprofloxacin	Microtiter	4.00		2		2
Ciprofloxacin	Microtiter	>16.00		1		1
Cefoxitin	AP	<20.00		1		1
Cefoxitin	E-test	>64.00		1		1
Cefoxitin	E-test	>256.00		5		5
Cefoxitin	Microtiter	>128.00		2		2
Cefoxitin	Microtiter	>256.00		8		8
Cefoxitin	Microtiter	>512.00		1		1
Doxycycline	AP	>5.00	1			1
Doxycycline	E-test	0.25	1			1
Doxycycline	E-test	0.38	1			1
Doxycycline	E-test	≤1.00	2			2
Doxycycline	Microtiter	0.25	2			2
Doxycycline	Microtiter	≤1.00	2			2
Doxycycline	Microtiter	2.00			1	1
Doxycycline	Microtiter	>64.00		1		1

Table 3. Minimum Inhibitory Concentrations for Culture E, *M. chelonae*

DRUG	Test Method	MIC	Susceptible	Resistant	Intermediate	Sum
Ethambutol	E-test	>256.00		1		1
Erythromycin	Microtiter	4.00			1	1
Gatifloxacin	Microtiter	1.00	1			1
Gatifloxacin	Microtiter	>8.00		1		1
Imipenem	AP	>20.00		1		1
Imipenem	E-test	8.00			1	1
Imipenem	E-test	>16.00		1		1
Imipenem	E-test	>32.00		3		3
Imipenem	Microtiter	8.00			1	1
Isoniazid	E-test	4.00		1		1
Levofloxacin	E-test	>32.00		2		2
Linezolid	AP	>10.00	1			1
Linezolid	E-test	6.00	1			1
Linezolid	Microtiter	1.00	1			1
Linezolid	Microtiter	4.00	1			1
Linezolid	Microtiter	≤8.00	4			4
Linezolid	Microtiter	16.00			2	2
Minocycline	E-test	0.38	1			1
Minocycline	Microtiter	≤0.50	2			2
Minocycline	Microtiter	1.00	1			1
Moxifloxacin	AP	>1.20	1			1
Moxifloxacin	Microtiter	1.00	1			1
Ofloxacin	Microtiter	<2.00		1		1
Ofloxacin	Microtiter	>4.00	1			1
Rifabutin	Microtiter	>32.00		1		1
Rifampin	E-test	>32.00		1		1
Sulfamethoxazole	Microtiter	>64.00		3		3
Trimethoprim-Sulfamethoxazole	AP	>5.00	1			1
Trimethoprim-Sulfamethoxazole	E-test	2.00	1			1
Trimethoprim-Sulfamethoxazole	E-test	>4.00		1		1
Trimethoprim-Sulfamethoxazole	E-test	>32.00		2		2
Trimethoprim-Sulfamethoxazole	Microtiter	4.00		2		2
Trimethoprim-Sulfamethoxazole	Microtiter	≥8.00		3		3
Trimethoprim-Sulfamethoxazole	Microtiter	>16.00		1		1
Tobramycin	AP	>5.00	1			1
Tobramycin	E-test	0.38	1			1
Tobramycin	E-test	2.00	1			1
Tobramycin	E-test	<4.00	1			1
Tobramycin	E-test	16.00		1		1
Tobramycin	Microtiter	0.50	1			1
Tobramycin	Microtiter	1.00	2			2
Tobramycin	Microtiter	2.00	5			5
Tobramycin	Microtiter	≤4.00	2			2

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