

Analyses of June 2005 *M. tuberculosis* and Nontuberculous Mycobacteria Drug Susceptibility Test Results Reported by Participating Laboratories

This report is the analyses of laboratory test results reported to the Centers for Disease Control and Prevention (CDC) by participant laboratories for the four *Mycobacterium tuberculosis* complex and one *M. kansasii* strain shipped in June 2005. 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 140 of 148 (94.6%) laboratories participating in this shipment. Of the laboratories submitting results, 67 (47.9%) reported via the online data entry system.

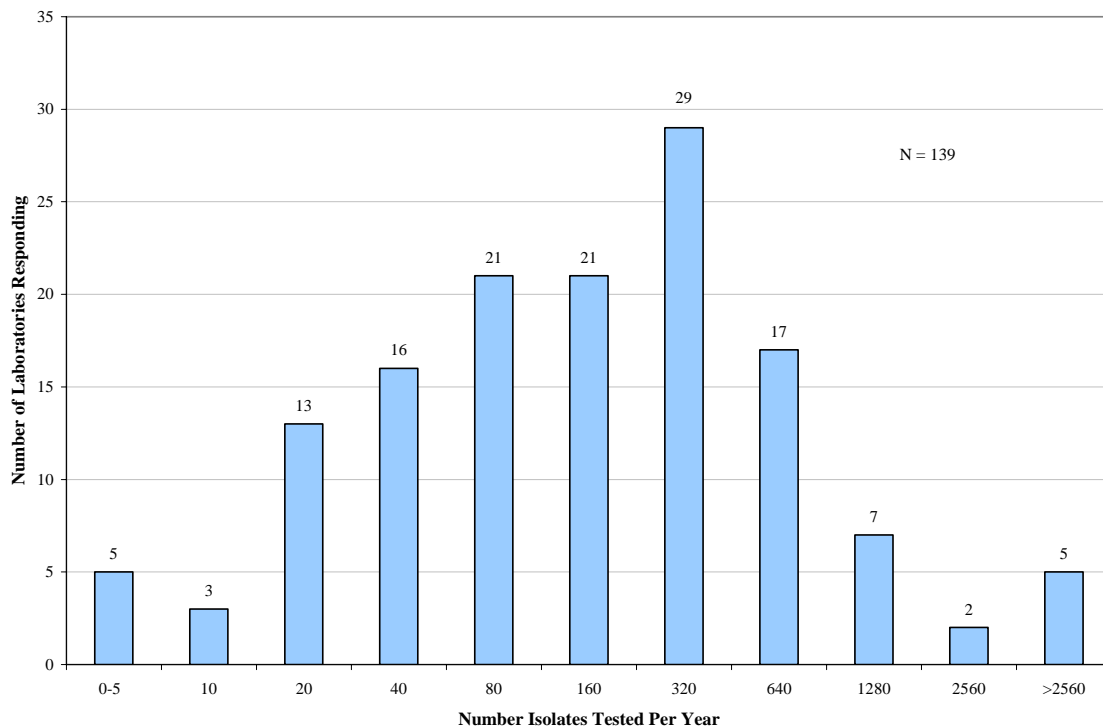
Descriptive Information on Participant Laboratories

Laboratory classifications reported by the 140 participants are

- 83 (59.3%) health departments,
- 40 (28.6%) hospitals,
- 13 (9.3%) independent laboratories, and
- 4 (2.9%) “other” type of laboratories.

Figure 1 shows the distribution of the annual volume of *M.tb* susceptibility testing by participants.

Figure 1: Distribution of the Annual Volume of *M. tuberculosis* Isolates Tested for Drug Susceptibility by Participating Laboratories in Calendar Year 2004.



Based on 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.

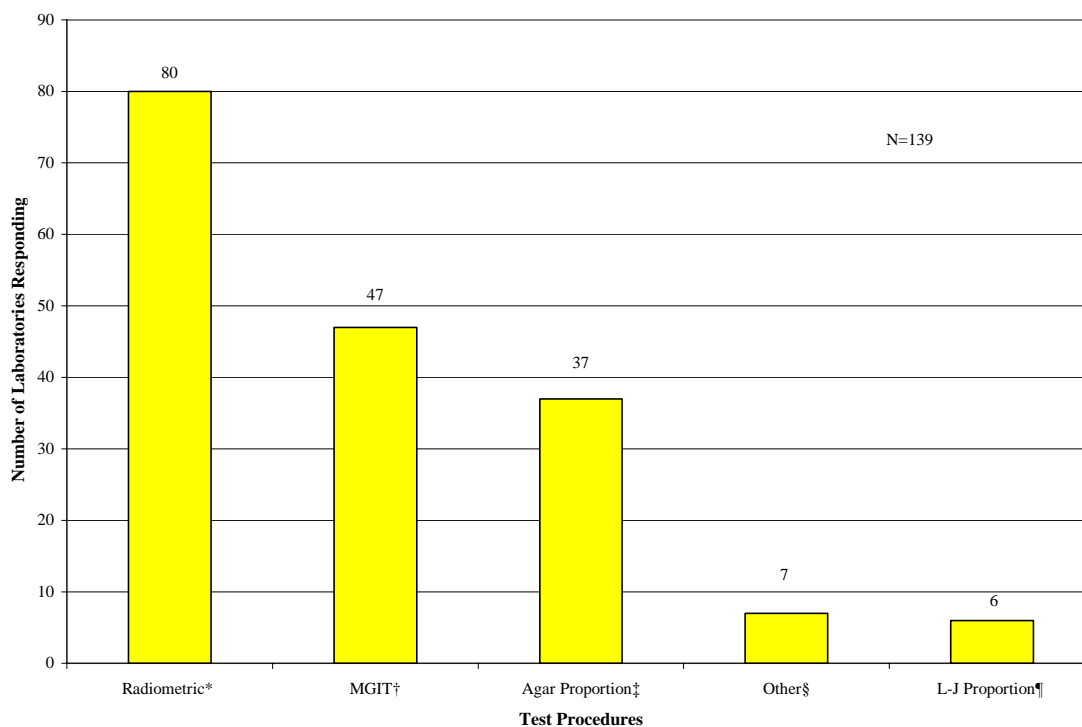
The biosafety levels (BSL) reported by participant laboratories for *M. tuberculosis* are

- BSL-3, 81 participants,
- BSL-2 with facilities with level 3 containment equipment, 46 participants,
- BSL-2, 11 participant,
- BSL-1, one participant, and
- One laboratory reported that they did not know the BSL level of the laboratory.

All laboratories are strongly encouraged to consult the CDC/NIH manual, [Biosafety in Microbiological and Biomedical Laboratories](http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm) (4th Edition), which can be accessed on the web at <http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4toc.htm>, for recommendations and to determine their correct BSL level.

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

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



* Radiometric is BACTEC 460TB

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

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

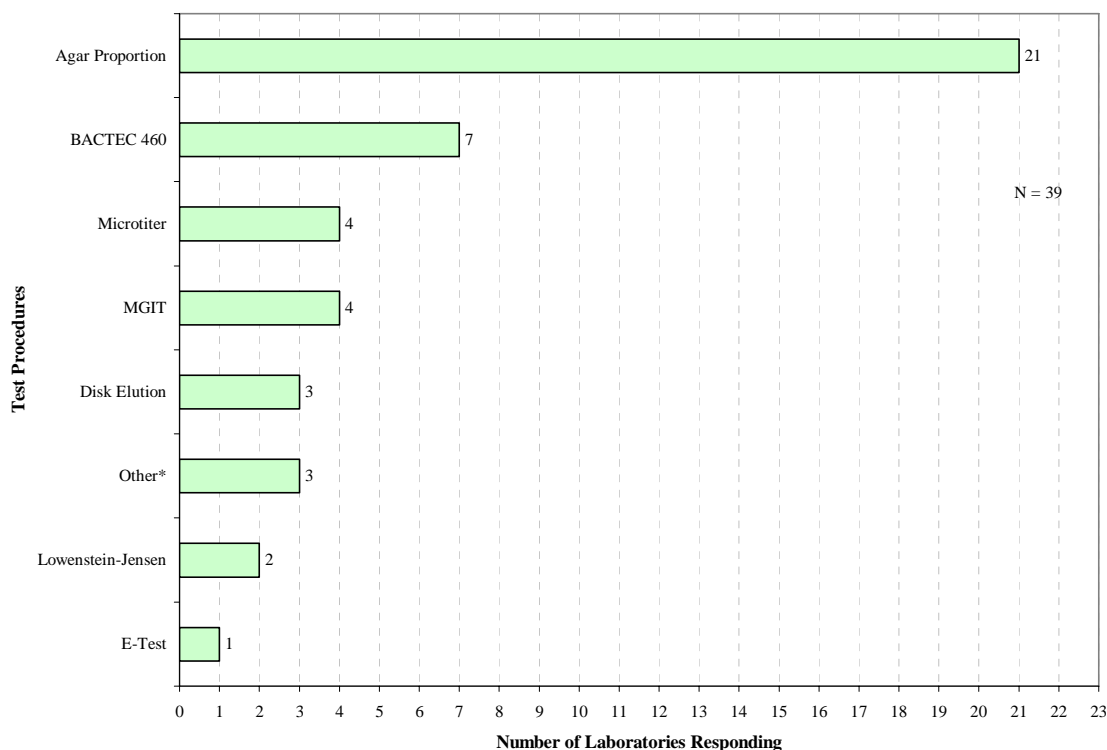
§ Other methods listed were microtiter, BacT/ALERT, TREK ESP and Colorimetric method for determining MICs.

¶ L-J, Lowenstein Jensen medium

Some methods, such as the L-J proportion method media, reflect procedures used by international participants. The number of participants using MGIT has increased steadily since 2003, due in part to its introduction into the United States (U.S.) market.

Thirty-nine laboratories performed susceptibility testing on *M. kansasii*. Figure 3 shows the procedures used.

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



*Other tests include alamar blue, submerged disk, and resistance ratio method (RRM)

Note: some participants reported using more than one test method.

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 P, Q, R, and S. The tables for the *M. tuberculosis* complex strains P, Q, R, and S 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 NCCLS 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.

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, 2, 3, 4} 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.

Strain P, *M. tuberculosis*- resistant to PZA at the recommended concentration, 100 µg/ml. See Table 1.0.

Of the 101 laboratories that tested PZA at 100 µg/ml;

- 98.4% (61/62) detected resistance with BACTEC 460TB, while
- 89.2% (33/37) detected resistance with MGIT,
- One laboratory detected resistance by the L-J proportion method, and
- One laboratory detected resistance by the PZASE biochemical method.

For INH and RIF, at the recommended concentrations for both, there was complete agreement between laboratories using AP and BACTEC. And, there was only minor discordance, 3.1% resistance (2/64) between laboratories testing EMB at the recommended concentration of 2.5 µg/ml using BACTEC 460TB.

When pyrazinamide resistance is detected in a *M. tuberculosis* complex DNA probe-positive isolate, especially if the organism is fully susceptible to the other primary drugs, further testing such as niacin, nitrate reductase, and thiophen-2-carboxylic acid hydrazide (TCH) susceptibility tests should be performed to determine if the isolate is *M. bovis*.²

Streptomycin, a secondary drug, was tested by 89.9% (125/139) of the participants with a high degree of interlaboratory agreement among all methods of susceptibility testing;

- 100% agreement between AP and BACTEC 460TB for the critical concentrations (see Table 1.0 for Culture P), and
- 97.6% (122/125) overall agreement at all concentrations.

Strain Q, *M. tuberculosis*-resistant only to low level concentrations (0.1 µg/ml) of INH. See Table 1.1

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

For participants using BACTEC, resistance was reported by

- 70% (49/70) at 0.1 µg/ml and
- 4.30% (1/23) at 0.4 µg/ml.

For participants using MGIT, resistance was reported by

- 73.9% (34/46) at 0.1 µg/ml and
- 11.1% (2/18) at 0.4 µg/ml

For participants using the AP method

- 53.6% (15/28) detected resistance at 0.2 µg/ml, while
- 9.7% (3/31) detected resistance at 1.0 µg/ml.

None of the laboratories using L-J proportion method detected resistance to INH. And, there was complete agreement between laboratories using AP and BACTEC 460TB at the recommended concentrations for RIF, PZA, EMB, and SM.

Strain R, *M. tuberculosis*- fully susceptible. See Table 1.2.

One hundred thirty-nine participants reported results for strain R:

- 100% (39/39) of the participant laboratories using AP reported this isolate to be susceptible to all drugs tested, and
- 98.8% (81/82) using BACTEC 460TB reported fully susceptible.
- Of the participants using MGIT,
 - 4.4% (2/45) reported resistance to INH at 0.1 µg/ml,
 - 2.2% (1/45) reported resistance to RIF at 1.0 µg/ml, and
 - 2.2% (1/46) reported resistance to EMB at 5.0 µg/ml.
- There was only minor discordance (reports of resistance) between laboratories using other methods.

Strain S, *M. bovis*-resistant to PZA at 100 µg/ml. See table 1.3

M. bovis, part of the *Mycobacterium tuberculosis* complex (MBTC) which includes *M. tuberculosis*, *M. africanum*, *M. microti*, and *M. canettii*, is one of the two species of “tubercle bacilli” that is the causative agent of tuberculosis. While *M. bovis* is not usually a human pathogen, from January 2001-2003 New York City reported 35 confirmed cases of *M. bovis*.⁵

In this shipment, of the 98 laboratories that tested PZA at 100 µg/ml,

- 100% (61/61) of the BACTEC 460TB users,
- 94.4% (34/36) for the participants that used MGIT detected resistance, and
- One laboratory detected resistance by the PZASE biochemical method.

Note: Agar proportion is not a satisfactory method for PZA susceptibility testing since many isolates fail to grow when agar has been acidified to the degree necessary for PZA susceptibility testing.⁶

Interestingly, 19.1% (13/68) of BACTEC 460TB users and 13.3% (6/45) reported low-level (0.1 µg/ml) resistance to INH using MGIT. However, there was almost complete agreement between laboratories and methods testing the other primary drugs (RIF, PZA, and EMB) at the critical concentrations. If isolates are resistant only to PZA, other tests should be performed to confirm identification. (*M. bovis* is resistant to PZA, whereas most isolates of *M. tuberculosis* are susceptible.^{6, 7})

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 drugs or 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 Test Results:

Strain T, *M. kansasii*, because of the patient’s history was suspected to be resistant to rifampin and isoniazid. See Tables 2 and 3.

Case History:

The patient is a 60 year old male with pulmonary *Mycobacterium kansasii* disease. He received antimycobacterial treatment with a combination of rifampin and isoniazid for 4 months. The patient had chronic obstructive pulmonary disease and was HIV negative. Three months post-treatment he again developed night sweats and cough and a small lesion in the left lung apex was detected on chest radiograph. Fine needle aspiration of the lesion was performed and no acid-fast bacilli were observed by fluorescence microscopy. Mycobacteria were detected in broth cultures on day 10 and were identified as *M. kansasii* by High Performance Liquid Chromatography.

The drugs routinely used for therapy against *M. kansasii* include INH, RIF, and EMB.⁷ In this survey, 39 laboratories performed susceptibility testing on this isolate:

- 94.4 % (34/36) detected resistance to INH by all methods, at all concentrations tested (One laboratory reported as resistant to >20 µg/ml by microtiter.)
- 100% (39/39) detected resistance to RIF by all methods, at all concentrations. (One participant reported susceptibility to Rifabutin (RBT) by AP at 2.0 µg/ml.)
- 91.2% (31/34) reported susceptibility to ethambutol (EMB) by all methods, at all concentrations.

Participants should review the Clinical and Laboratory Standards Institute Guidelines (CLSI) on pages 20-24, with special attention to section 4.3 “Susceptibility Testing of *Mycobacterium kansasii*.” Antimicrobial agents recommended for testing *M. kansasii* are found in Table 6 in the Clinical and Laboratory Standards Institute (NCCLS) Guidelines.⁶ Some laboratories still continue to test the first line TB drugs which is contrary to the recommendations made by the American Thoracic Society (1997 document)⁷ and the soon to be released new document.

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.

Acknowledgements

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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.

Participants should note that the Clinical and Laboratory Standards Institute (previously known as NCCLS-approved standard “Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes”, M24-A [ISBN 1-56238-500-3] NCCLS, 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.

Table 1.0: Participant Results for culture P, *M. tuberculosis* PZA resistant at 100 µg/ml

DRUG	Conc	Test Method															
		Agar Prop 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	0.09															1	1
Isoniazid	0.10				71		71					44	2	46	2		2
Isoniazid	0.12	1		1													
Isoniazid	0.20	29		29	1		1	6		6	1		1	2		2	2
Isoniazid	0.40				18		18				11	1	12	2		2	2
Isoniazid	0.50							1		1							
Isoniazid	1.00	29		29	2		2	3		3	1		1	1		1	1
Isoniazid	5.00	4		4													
Isoniazid	10.00							2		2							
Isoniazid	100.00							1		1							
Rifampin	0.06															1	1
Rifampin	0.12															1	1
Rifampin	0.25															1	1
Rifampin	0.50				2		2									1	1
Rifampin	0.90															1	1
Rifampin	1.00	31		31	5		5	1		1	45		45	3		3	3
Rifampin	2.00				71		71				2		2	1		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							5		5							
Rifampin	50.00							1		1							
Pyrazinamide	64.00															1	1
Pyrazinamide	99.00						1	1									
Pyrazinamide	100.00				1	61	62		1	1	4	33	37		1	1	1
Pyrazinamide	200.00							1		1							
Pyrazinamide	300.00						1	1									
Pyrazinamide	400.00							1		1							
Ethambutol	1.00							1		1						1	1
Ethambutol	1.60															1	1
Ethambutol	1.80															1	1
Ethambutol	2.00							5		5						1	1
Ethambutol	2.50				62	2	64	1		1	1		1			1	1
Ethambutol	3.20															1	1
Ethambutol	3.75				1		1										
Ethambutol	4.00				2		2									1	1
Ethambutol	5.00	29		29	5		5	1		1	44	2	46	2		2	2
Ethambutol	6.40															1	1
Ethambutol	7.50	2		2	12		12				1		1				
Ethambutol	8.00															2	2
Ethambutol	10.00	9		9													
Ethambutol	16.00															1	1
Ethambutol	32.00															1	1

Table 1.0: Participant Results for Culture P, *M. tuberculosis* PZA resistant at 100 µg/ml

DRUG	Conc	Test Method														
		Agar Prop 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
Streptomycin	0.25														1	1
Streptomycin	0.50														1	1
Streptomycin	1.00							1		1		34	2	36	1	1
Streptomycin	2.00	28		28	65		65					1		1	2	2
Streptomycin	2.50														1	1
Streptomycin	4.00	1		1	2		2	5		5		4		4	1	1
Streptomycin	5.00							1		1						
Streptomycin	6.00				13		13					1		1		
Streptomycin	8.00														1	1
Streptomycin	10.00	21		21				1		1					1	1
Streptomycin	15.00														1	1
Streptomycin	30.00														1	1
Ethionamide	1.00		1	1		1	1									
Ethionamide	1.25				1		1									
Ethionamide	2.00	1		1	1		1									
Ethionamide	2.50				2		2				1		1			
Ethionamide	4.00				1		1									
Ethionamide	5.00	18	1	19	3		3									
Ethionamide	10.00	4		4											1	1
Ethionamide	20.00							1	1	2					1	1
Ethionamide	30.00							1		1						
Ethionamide	40.00							2		2					1	1
Kanamycin	4.00	1		1												
Kanamycin	5.00	8		8	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	1.00														1	1
Capreomycin	1.25				2		2									
Capreomycin	5.00				2		2									
Capreomycin	10.00	15		15												
Capreomycin	12.50														1	1
Capreomycin	20.00							1		1						
Capreomycin	25.00														1	1
Capreomycin	40.00							1		1						
Capreomycin	50.00														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				2		2						
Cycloserine	40.00							1		1						
Cycloserine	48.00														1	1
Cycloserine	60.00	1		1												

Table 1.0: Participant Results for Culture P, *M. tuberculosis*, PZA resistant at 100 µg/ml

DRUG	Conc	Test Method														
		Agar Prop 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	0.50									2		2				
p-Aminosalicylic acid	1.00									2		2				
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	3		3												
Amikacin	0.50													1		1
Amikacin	1.00				2		2							1		1
Amikacin	2.00	1		1	2		2									
Amikacin	2.50	1		1												
Amikacin	4.00	2		2	1		1									
Amikacin	5.00				1		1									
Amikacin	6.00	5		5												
Amikacin	7.50													1		1
Amikacin	8.00				2		2									
Amikacin	12.00	2		2												
Amikacin	15.00													1		1
Amikacin	30.00													1		1
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	8		8	7		7	1		1	1	1		1		1
Ofloxacin	2.50													1		1
Ofloxacin	4.00				2		2									
Ofloxacin	5.00													1		1
Ofloxacin	8.00				2		2									
Ciprofloxacin	0.50													1		1
Ciprofloxacin	1.00	1		1	3		3							1		1
Ciprofloxacin	1.60													1		1
Ciprofloxacin	2.00	9		9	2		2									
Ciprofloxacin	3.20													1		1
Ciprofloxacin	4.00				2		2									
Ciprofloxacin	6.40													1		1
Ciprofloxacin	10.00	1		1												
Levofloxacin	0.30	1		1												
Levofloxacin	1.00											1		1		
Levofloxacin	2.00				1		1									
Levofloxacin	8.00				1		1									
Rifabutin	0.50	2		2												
Rifabutin	1.00	1		1	1		1									
Rifabutin	2.00	2		2												
Clofazimine	0.06				1	1	2									
Clofazimine	0.12				1		1									
Clofazimine	0.25				1		1									
Clofazimine	0.50				1		1							1		1
Clofazimine	1.00	1		1										1		1
Clofazimine	17.50													1		1
Clofazimine	35.00													1		1
Clofazimine	70.00													1		1
Clarithromycin	12.00													1		1

Table 1.1: Participant Results for Culture Q, *M. tuberculosis*-isoniazid resistant at 0.1 µg/ml

DRUG	Conc	Test Method														
		Agar Prop 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	0.09														1	1
Isoniazid	0.10				21	49	70				12	34	46	2		2
Isoniazid	0.12		1	1												
Isoniazid	0.20	13	15	28	2		2	6		6		1	1	2		2
Isoniazid	0.25	1		1												
Isoniazid	0.40				22	1	23				16	2	18	2		2
Isoniazid	0.50							1		1						
Isoniazid	1.00	28	3	31	2		2	3		3		1	1	1		1
Isoniazid	2.00				1		1									
Isoniazid	5.00	3		3												
Isoniazid	10.00							2		2						
Isoniazid	100.00							1		1						
Rifampin	0.06													1		1
Rifampin	0.12													1		1
Rifampin	0.25													1		1
Rifampin	0.50				2		2							1		1
Rifampin	0.90													1		1
Rifampin	1.00	31		31	5		5	1		1	44	1	45	3		3
Rifampin	2.00				71		71				2		2	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							5		5						
Rifampin	50.00							1		1						
Pyrazinamide	64.00													1		1
Pyrazinamide	99.00				1		1									
Pyrazinamide	100.00				61		61	1		1	37		37	1		1
Pyrazinamide	200.00								1	1						
Pyrazinamide	300.00				1		1									
Pyrazinamide	400.00							1		1						
Ethambutol	1.00							1		1				1		1
Ethambutol	1.60													1		1
Ethambutol	1.80													1		1
Ethambutol	2.00							5		5				1		1
Ethambutol	2.50				64		64	1		1	1		1			
Ethambutol	3.20													1		1
Ethambutol	3.75				1		1									
Ethambutol	4.00				2		2							1		1
Ethambutol	5.00	30		30	5		5	1		1	44	2	46	1	1	2
Ethambutol	6.40													1		1
Ethambutol	7.50	2		2	12		12				1		1			
Ethambutol	8.00													2		2
Ethambutol	10.00	9		9												
Ethambutol	16.00													1		1
Ethambutol	32.00													1		1

Table 1.1: Participant Results for Culture Q, *M. tuberculosis*-isoniazid resistant at 0.1 µg/ml

DRUG	Conc	Test Method														
		Agar Prop 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
Streptomycin	0.25														1	1
Streptomycin	0.50														1	1
Streptomycin	1.00							1		1		32	4	36	1	1
Streptomycin	2.00	29		29	65		65					1		1	2	2
Streptomycin	2.50														1	1
Streptomycin	4.00	1		1	2		2	5		5		4		4	1	1
Streptomycin	5.00							1		1						
Streptomycin	6.00				13		13					1		1		
Streptomycin	8.00														1	1
Streptomycin	10.00	22		22				1		1					1	1
Streptomycin	15.00														1	1
Streptomycin	30.00														1	1
Ethionamide	1.00	1		1	1		1									
Ethionamide	1.25				1		1									
Ethionamide	2.00				1		1									
Ethionamide	2.50				3		3				1		1			
Ethionamide	4.00				1		1									
Ethionamide	5.00	21		21	3		3									
Ethionamide	10.00	3		3											1	1
Ethionamide	20.00							1	1	2					1	1
Ethionamide	30.00							1		1						
Ethionamide	40.00							2		2					1	1
Kanamycin	4.00	1		1												
Kanamycin	5.00	9		9	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	1.00														1	1
Capreomycin	1.25				2		2									
Capreomycin	5.00				3		3									
Capreomycin	10.00	17		17												
Capreomycin	12.50														1	1
Capreomycin	20.00							1		1						
Capreomycin	25.00														1	1
Capreomycin	40.00							1		1						
Capreomycin	50.00														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	11		11				2		2						
Cycloserine	40.00							1		1						
Cycloserine	48.00														1	1
p-Aminosalicylic acid	0.50							2		2						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00	16		16												
p-Aminosalicylic acid	4.00				2		2									
p-Aminosalicylic acid	8.00	1		1												
p-Aminosalicylic acid	10.00	4		4												

Table 1.1: Participant Results for Culture Q, *M. tuberculosis*-isoniazid resistant at 0.1 µg/m

DRUG	Conc	Test Method															
		Agar Prop 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				2		2								1		1
Amikacin	2.00	2		2	2		2										
Amikacin	2.50	1		1	1		1										
Amikacin	4.00	3		3	1		1										
Amikacin	5.00				1		1										
Amikacin	6.00	4		4													
Amikacin	7.50														1		1
Amikacin	8.00				2		2										
Amikacin	12.00	2		2													
Amikacin	15.00														1		1
Amikacin	30.00														1		1
Ofloxacin	0.50															1	1
Ofloxacin	1.00	3		3	2		2										
Ofloxacin	1.00																
Ofloxacin	1.20	1		1													
Ofloxacin	1.25														1		1
Ofloxacin	2.00	9		9	7		7	1		1	1		1		1		1
Ofloxacin	2.50														1		1
Ofloxacin	4.00				2		2										
Ofloxacin	5.00														1		1
Ofloxacin	8.00				2		2										
Ciprofloxacin	0.50														1		1
Ciprofloxacin	1.00	1		1	4		4								1		1
Ciprofloxacin	1.00																
Ciprofloxacin	1.00																
Ciprofloxacin	1.60														1		1
Ciprofloxacin	2.00	9		9	2		2										
Ciprofloxacin	3.20														1		1
Ciprofloxacin	4.00				2		2										
Ciprofloxacin	6.40														1		1
Levofloxacin	0.30	1		1													
Levofloxacin	1.00											1		1			
Levofloxacin	2.00				2		2										
Levofloxacin	8.00				1		1										
Rifabutin	0.50	3		3													
Rifabutin	1.00	2		2	2		2										
Rifabutin	2.00	3		3													
Clofazimine	0.06				1	1	2										
Clofazimine	0.06																
Clofazimine	0.12				1		1										
Clofazimine	0.25				1		1										
Clofazimine	0.50				2		2									1	1
Clofazimine	0.50																
Clofazimine	1.00	1		1											1		1
Clofazimine	17.50														1		1
Clofazimine	35.00														1		1
Clofazimine	70.00														1		1
Clarithromycin	12.00														1		1

Table 1.2: Participant Results for Culture R, *M. tuberculosis*-fully susceptible

DRUG	Conc	Test Method															
		Agar Prop 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	0.09															1	1
Isoniazid	0.10				70	1	71					43	2	45	2	2	
Isoniazid	0.12	1		1													
Isoniazid	0.20	27		27	1		1	6		6	1		1		2	2	
Isoniazid	0.40				17		17				12		12		2	2	
Isoniazid	0.50							1		1							
Isoniazid	1.00	25		25	2		2	3		3	1		1		1	1	
Isoniazid	5.00	3		3													
Isoniazid	10.00							2		2							
Isoniazid	100.00							1		1							
Rifampin	0.06															1	1
Rifampin	0.12															1	1
Rifampin	0.25															1	1
Rifampin	0.50				2		2									1	1
Rifampin	0.90															1	1
Rifampin	1.00	29		29	5		5	1		1	44	1	45	3	3		
Rifampin	2.00				71		71				2		2	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	1	5							
Rifampin	50.00							1		1							
Pyrazinamide	64.00															1	1
Pyrazinamide	99.00				1		1										
Pyrazinamide	100.00				61		61	1		1	37		37	1	1		
Pyrazinamide	200.00							1		1							
Pyrazinamide	300.00				1		1										
Pyrazinamide	400.00							1		1							
Ethambutol	1.00							1		1						1	1
Ethambutol	1.60															1	1
Ethambutol	1.80															1	1
Ethambutol	2.00							4		4						1	1
Ethambutol	2.50				64		64	1		1	1		1				
Ethambutol	3.20															1	1
Ethambutol	3.75				1		1										
Ethambutol	4.00				2		2									1	1
Ethambutol	5.00	27		27	5		5	1		1	45	1	46	2	2		
Ethambutol	6.40															1	1
Ethambutol	7.50	2		2	12		12				1		1				
Ethambutol	8.00															2	2
Ethambutol	10.00	7		7													
Ethambutol	16.00															1	1
Ethambutol	32.00															1	1

Table 1.2: Participant Results for Culture R, *M. tuberculosis*-fully susceptible

DRUG	Conc	Test Method															
		Agar Prop 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	
Streptomycin	0.25															1	1
Streptomycin	0.50															1	1
Streptomycin	1.00							1		1		35	1	36		1	1
Streptomycin	2.00	26		26	65		65					1		1		2	2
Streptomycin	2.50															1	1
Streptomycin	4.00	1		1	2		2	5		5		4		4		1	1
Streptomycin	5.00							1		1							
Streptomycin	6.00				13		13					1		1			
Streptomycin	8.00															1	1
Streptomycin	10.00	19		19				1		1						1	1
Streptomycin	15.00															1	1
Streptomycin	30.00															1	1
Ethionamide	1.00				1		1										
Ethionamide	1.25				1		1										
Ethionamide	2.00				1		1										
Ethionamide	2.50				2		2					1		1			
Ethionamide	4.00				1		1										
Ethionamide	5.00	16		16	2		2										
Ethionamide	10.00	3		3												1	1
Ethionamide	20.00							1	1	2						1	1
Ethionamide	20.00																
Ethionamide	20.00																
Ethionamide	30.00							1		1							
Ethionamide	40.00							2		2						1	1
Kanamycin	4.00	1		1													
Kanamycin	5.00	7		7	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	1.00															1	1
Capreomycin	1.25				2		2										
Capreomycin	5.00				1		1										
Capreomycin	10.00	13		13													
Capreomycin	12.50															1	1
Capreomycin	20.00							1		1							
Capreomycin	25.00															1	1
Capreomycin	40.00							1		1							
Capreomycin	50.00															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	8		8				2		2							
Cycloserine	40.00							1		1							
Cycloserine	48.00															1	1
Cycloserine	60.00	1		1													

Table 1.2: Participant Results for Culture R, *M. tuberculosis*-fully susceptible

DRUG	Conc	Test Method														
		Agar Prop 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	0.50								2		2					
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	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	2		2									
Amikacin	4.00	2		2	1		1									
Amikacin	5.00				1		1									
Amikacin	6.00	4		4												
Amikacin	7.50													1		1
Amikacin	8.00				2		2									
Amikacin	12.00	2		2												
Amikacin	15.00													1		1
Amikacin	30.00													1		1
Ofloxacin	0.50														1	1
Ofloxacin	1.00	2		2	1		1									
Ofloxacin	1.25													1		1
Ofloxacin	2.00	8		8	6		6	1		1	1		1		1	1
Ofloxacin	2.50													1		1
Ofloxacin	4.00				2		2									
Ofloxacin	5.00													1		1
Ofloxacin	8.00				2		2									
Ciprofloxacin	0.50													1		1
Ciprofloxacin	1.00	1		1	3		3							1		1
Ciprofloxacin	1.60													1		1
Ciprofloxacin	2.00	8		8	2		2									
Ciprofloxacin	3.20													1		1
Ciprofloxacin	4.00				2		2									
Ciprofloxacin	6.40													1		1
Levofloxacin	1.00											1		1		
Levofloxacin	2.00				1		1									
Levofloxacin	8.00				1		1									
Rifabutin	0.50	2		2												
Rifabutin	1.00	1		1												
Rifabutin	2.00	2		2												
Clofazimine	0.06				1	1	2									
Clofazimine	0.12					1	1									
Clofazimine	0.25				1		1									
Clofazimine	0.50				1		1								1	1
Clofazimine	1.00	1		1										1		1
Clofazimine	17.50													1		1
Clofazimine	35.00													1		1
Clofazimine	70.00													1		1
Clarithromycin	12.00													1		1

Table 1.3: Participant Results for Culture *S. M. bovis*- resistant PZA at 100 µg/ml

DRUG	Conc	Test Method																
		Agar Prop 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	0.09															1		1
Isoniazid	0.10				55	13	68						39	6	45	1		1
Isoniazid	0.12	1		1														
Isoniazid	0.20	27	1	28	1		1	5		5			1		1	1		1
Isoniazid	0.40				17		17						13		13	2		2
Isoniazid	0.50							1		1								
Isoniazid	1.00	26	1	27	2		2	2		2			1		1	1		1
Isoniazid	5.00	2		2														
Isoniazid	10.00							1		1								
Rifampin	0.50				2		2											
Rifampin	0.90															1		1
Rifampin	1.00	29		29	5		5						45		45	2		2
Rifampin	2.00				70		70						2		2			
Rifampin	5.00	3		3														
Rifampin	8.00																1	1
Rifampin	16.00															1		1
Rifampin	32.00															1		1
Rifampin	40.00							5		5								
Rifampin	50.00																	
Pyrazinamide	64.00																1	1
Pyrazinamide	99.00					1	1											
Pyrazinamide	100.00				61		61						2	34	36	1		1
Pyrazinamide	200.00							1		1								
Pyrazinamide	300.00					1	1											
Ethambutol	1.60															1		1
Ethambutol	1.80															1		1
Ethambutol	2.00							4		4								
Ethambutol	2.50				61	1	62	1		1			1		1			
Ethambutol	3.20															1		1
Ethambutol	3.75				1		1											
Ethambutol	4.00				2		2											
Ethambutol	5.00	27	1	28	5		5						45	1	46	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												35	1	36			
Streptomycin	2.00	27		27	65		65						1		1	1		1
Streptomycin	2.50															1		1
Streptomycin	4.00	1		1	2		2	5		5			4		4			
Streptomycin	5.00																	
Streptomycin	6.00				14		14						1		1			
Streptomycin	10.00	20		20												1		1
Streptomycin	15.00															1		1
Streptomycin	30.00															1		1

Table 1.3: Participant Results for Culture S, *M. bovis*- resistant PZA at 100 µg/ml

DRUG	Conc	Test Method														
		Agar Prop 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				2	2										
Ethionamide	2.00		1	1	1	1										
Ethionamide	2.50				1		1				1		1			
Ethionamide	4.00				1		1									
Ethionamide	5.00	18	1	19	1	2	3									
Ethionamide	10.00	3		3											1	1
Ethionamide	20.00								1		1				1	1
Ethionamide	30.00								1		1					
Ethionamide	40.00								1		1				1	1
Kanamycin	4.00	1		1												
Kanamycin	5.00	7		7	4		4									
Kanamycin	6.00	13		13												
Kanamycin	40.00								1		1					
Capreomycin	1.25				3		3									
Capreomycin	5.00				2		2									
Capreomycin	10.00	15		15												
Capreomycin	12.50														1	1
Capreomycin	20.00								1		1					
Capreomycin	25.00														1	1
Capreomycin	40.00								1		1					
Capreomycin	50.00														1	1
Cycloserine	12.00														1	1
Cycloserine	24.00														1	1
Cycloserine	25.00	1		1												
Cycloserine	30.00	9		9					1	1	2					
Cycloserine	48.00														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	3		3												
Amikacin	1.00				2		2									
Amikacin	2.00	1		1	2		2									
Amikacin	2.50	1		1												
Amikacin	4.00	2		2	1		1									
Amikacin	5.00				1		1									
Amikacin	6.00	4		4												
Amikacin	7.50														1	1
Amikacin	8.00				2		2									
Amikacin	12.00	2		2												
Amikacin	15.00														1	1
Amikacin	30.00														1	1

Table 1.3: Participant Results for Culture S, *M. bovis*- resistant PZA at 100µg/ml

DRUG	Conc	Test Method														
		Agar Prop 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	1.00	2		2	1		1									
Ofloxacin	1.20	1		1												
Ofloxacin	1.25															
Ofloxacin	2.00	8		8	8		8	1		1	1		1		1	
Ofloxacin	2.50														1	1
Ofloxacin	4.00				2		2								1	1
Ofloxacin	5.00														1	1
Ofloxacin	8.00				2		2									
Ciprofloxacin	1.00				3		3									
Ciprofloxacin	1.60														1	1
Ciprofloxacin	2.00	9		9	2		2									
Ciprofloxacin	3.20														1	1
Ciprofloxacin	4.00				2		2									
Ciprofloxacin	6.40														1	1
Levofloxacin	0.30	1		1												
Levofloxacin	1.00										1		1			
Levofloxacin	2.00				1		1									
Levofloxacin	8.00				1		1									
Rifabutin	0.50	2		2	1		1									
Rifabutin	1.00	1		1	1		1									
Rifabutin	2.00	2		2												
Clofazimine	0.06				2		2									
Clofazimine	0.12				1		1									
Clofazimine	0.25				1		1									
Clofazimine	0.50				1		1									
Clofazimine	1.00	1		1												
Clofazimine	17.50														1	1
Clofazimine	35.00														1	1
Clofazimine	70.00														1	1
Clarithromycin	12.00														1	1

Table 2: Participant Results for Culture T, *M. kansasii*

DRUG	Conc.	Test Method														
		Agar Prop. 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	1.00				1		1									
Amikacin	2.50	1		1												
Amikacin	6.00	2		2												
Amikacin	7.50													1		1
Amikacin	10.00	1		1	1		1									
Amikacin	12.00	1		1												
Amikacin	15.00													1		1
Amikacin	32.00	1		1												
Clarithromycin	0.16	1		1												
Clarithromycin	3.00	2		2												
Clarithromycin	4.00				1		1									
Clarithromycin	6.00													1		1
Clarithromycin	12.00													1		1
Clarithromycin	15.00	1		1												
Clarithromycin	24.00													1		1
Clarithromycin	32.00	1		1												
Clarithromycin	64.00				1		1									
Capreomycin	10.00	1		1												
Capreomycin	12.50														1	1
Capreomycin	25.00													1		1
Ciprofloxacin	1.60													1		1
Ciprofloxacin	2.00	5		5												
Ciprofloxacin	3.20													1		1
Ciprofloxacin	6.40													1		1
Cycloserine	12.00													1		1
Cycloserine	24.00													1		1
Cycloserine	40.00							1		1						
Cycloserine	48.00													1		1
Ethambutol	1.00							1		1						
Ethambutol	1.60													1		1
Ethambutol	2.50				1	1	2									
Ethambutol	3.20													1		1
Ethambutol	5.00	14	1	15	1		1				3		3			
Ethambutol	6.40													1		1
Ethambutol	7.50	1	1	2												
Ethambutol	10.00	4		4												
Isoniazid	0.10					2	2						2	2		
Isoniazid	0.20		10	10												
Isoniazid	0.20														1	1
Isoniazid	0.40					1	1									
Isoniazid	1.00		11	11					1	1						
Isoniazid	5.00	2	2	4												
Kanamycin	5.00		1	1												
Kanamycin	6.00		2	2												
Kanamycin	20.00								1	1						
Moxifloxacin	0.16	1		1												

Table 2: Participant Results for Culture T, *M. kansasii*

DRUG	Conc.	Test Method														
		Agar Prop. 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	1.00	1		1												
Ofloxacin	1.25													1		1
Ofloxacin	2.00	2		2	1		1									
Ofloxacin	2.00															
Ofloxacin	2.50													1		1
Ofloxacin	5.00													1		1
Ofloxacin	20.00				1		1									
p-Aminosalicylic acid	2.00		4	4												
Pyrazinamide	100.00											1	1			
Rifabutin	0.10					1	1									
Rifabutin	0.50		1	1												
Rifabutin	1.00		1	1		1	1					1	1			
Rifabutin	2.00	1	3	4												
Rifabutin	2.00															
Rifampin	1.00		18	18		2	2					2	2		2	2
Rifampin	2.00					5	5									
Rifampin	5.00		3	3					1	1						
Rifampin	8.00														1	1
Rifampin	10.00					1	1									
Rifampin	16.00														1	1
Rifampin	32.00														1	1
Rifampin	40.00								1	1						
Rifampin	50.00								1	1						
Streptomycin	1.00											1	1	2		
Streptomycin	2.00	10	4	14	2		2									
Streptomycin	4.00	1		1												
Streptomycin	5.00								1	1						
Streptomycin	7.50														1	1
Streptomycin	10.00	12		12												
Streptomycin	15.00														1	1
Streptomycin	30.00													1		1
Sulfamethoxazole	32.00	1		1												
Ethionamide	5.00	5		5												
Ethionamide	10.00	1		1											1	1
Ethionamide	40.00								1	1						
Trimethoprim-Sulfamethoxazole	2.00	1		1												

Table 3: Minimum Inhibitory Concentrations for Culture T, *M. kansasii*

DRUG	Test Method	MIC	Susceptible	Resistant	Intermediate	Sum
Amikacin	E-test	≤16.00	1			1
Amikacin	Microtiter	≤0.50	1			1
Amikacin	Microtiter	≤1.00	1			1
Amikacin	Microtiter	8.00	2			2
Azithromycin	Microtiter	≥1.00		1		1
Azithromycin	Microtiter	≤2.00	1			1
Clarithromycin	Agar proportion	0.25	1			1
Clarithromycin	E-test	≤1.00	1			1
Clarithromycin	Microtiter	≤0.13	1			1
Clarithromycin	Microtiter	≤0.25	2			2
Clarithromycin	Microtiter	<0.50	2			2
Ciprofloxacin	E-test	≥4.00		1		1
Ciprofloxacin	Microtiter	≤0.50	1			1
Ciprofloxacin	Microtiter	2.00	1			1
Ciprofloxacin	Microtiter	≥4.00		2		2
Cefoxitin	E-test	≥64.00		1		1
Doxycycline	E-test	<1.00	1			1
Ethambutol	Microtiter	2.00	2			2
Ethambutol	Microtiter	8.00		1		1
Ethambutol	Other	≥32.00		1		1
Gatifloxacin	Microtiter	0.25	1			1
Imipenem	E-test	≥16.00		1		1
Isoniazid	Microtiter	≥20.00		1		1
Minocycline	Microtiter	2.00			1	1
Moxifloxacin	Microtiter	0.12	1			1
Ofloxacin	Microtiter	≥0.50		1		1
Ofloxacin	Microtiter	<1.00	1			1
Rifabutin	Microtiter	2.00	1	1		2
Rifabutin	Microtiter	8.00		1		1
Rifabutin	Microtiter	≥32.00		1		1
Rifampin	Microtiter	≥8.00		1		1
Rifampin	Microtiter	≥16.00		2		2
Rifampin	Other	≥2.00		1		1
Streptomycin	Microtiter	8.00	1			1
Streptomycin	Microtiter	16.00		1		1
Streptomycin	Other	0.50	1			1
Sulfamethoxazole	Microtiter	≤4.00	1			1
Trimethoprim-Sulfamethoxazole	E-test	≥4.00		1		1
Trimethoprim-Sulfamethoxazole	Microtiter	0.12	1			1

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