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 June 2004 Shipment

Dear Participant:

Enclosed are analyses 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. xenopi*, shipped in June 2004. Participant laboratories (157) received either four *M. tuberculosis* complex strains only or four *M. tuberculosis* strains and one NTM culture. Testing results were received and analyzed from 149 of 153 (97%) laboratories participating in this shipment. Of the laboratories submitting results, 47 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. The first three pages contain descriptive information about the participant laboratories. We encourage you to circulate this report to personnel who are involved with drug susceptibility testing, reporting, or 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 National Committee for Clinical Laboratory Standards (NCCLS) 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 (770) 488-8133.

Sincerely yours,

Bereneice M. Madison, Ph.D. Division of Laboratory Systems

Enclosures

### Analyses of June 2004 *M. tuberculosis* and nontuberculous mycobacteria drug susceptibility test results reported by participating laboratories

This report is an analysis of laboratory test results reported to the Centers for Disease Control and Prevention (CDC) by participant laboratories for the four *Mycobacterium tuberculosis* complex and one *M. xenopi* strain shipped in June 2004. Participant laboratories received either four *M. tuberculosis* complex strains only or four *M. tuberculosis* complex strains and one NTM strain. Testing results were received and analyzed from 149 of 153 (97%) laboratories participating in this shipment. Of the laboratories submitting results, 47 reported them via the online data entry system.

#### **Descriptive Information on Participant Laboratories**

Figure 1 shows the laboratory classification reported by 149 of the participants. Participants consisted of 83 health departments, 48 hospitals, 13 independent laboratories, and 5 "other" type of laboratories.

Figure 2 provides the distribution of the annual volume of *M. tuberculosis* isolates tested for drug susceptibilities by participating laboratories in calendar year 2003.

Figure 3 lists the biosafety levels reported by participant laboratories for *M. tuberculosis*. All laboratories are strongly encouraged to consult the CDC/NIH manual, <u>Biosafety in</u> <u>Microbiological and Biomedical Laboratories</u> (4th edition), for recommendations and to determine their correct biosafety level.

Figure 4 provides a breakdown of the test procedures used by the participating laboratories for *M. tuberculosis* drug susceptibility testing. Participants were asked to check test methods used. Some methods, such as the proportion method with Lowenstein-Jensen (L-J) media, may reflect procedures used by international participants. The 'other' methods listed were microtiter, BacT/ALERT, TREK ESP and Colorimetric method for determining MICs.

Figure 5 provides information on the test procedures used by the participating laboratories testing *M. xenopi*.

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

The aggregate test results are provided in separate tables, representing strains F, G, H, and I to facilitate comparison among laboratories. Table 1 for the *M. tuberculosis* complex strains F, G, H, and I are constructed to include the results for the radiometric (BACTEC), agar proportion (AP), Lowenstein-Jensen (L-J) proportion, MGIT and other methods at each concentration of drug. The test results are listed in the appropriate (susceptible or resistant) columns with a corresponding total number of tests (Sum) column provided as a denominator for determining the level of consensus. This report contains all results reported by participating laboratories, including many drug concentrations with only one result.

In Table 1 the concentrations recommended by CDC and the NCCLS for the primary (isoniazid, rifampin, pyrazinamide, and ethambutol) and secondary (streptomycin, ethionamide, kanamycin, capreomycin, and p-amino-salicylic acid) antituberculosis drugs are highlighted for the conventional and radiometric methods. Participants should note that the new NCCLS-approved standard (Susceptibility Testing of Mycobacteria, Nocardiae, and Other Aerobic Actinomycetes; Approved Standard, NCCLS document 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. Note that these recommended combinations reflect the critical concentrations of antituberculosis drugs in 7H10 agar and those concentrations for the BACTEC method that directly correlate with the critical concentrations in the conventional

method (1-4). When two concentrations are highlighted, such as for isoniazid and ethambutol, the lower value is the critical concentration to always be included for determining whether the *M. tuberculosis* isolate is resistant.

**Strain F** was a strain of *M. tuberculosis* resistant only to ethambutol. There were some discordances in regard to resistance among different testing methodologies. Of the laboratories performing the AP method, 94.1% (32/34) were in agreement on resistance at the critical concentration (5.0  $\mu$ g/ml), while 97.4% (75/77) were in agreement on BACTEC 460TB using the 2.5  $\mu$ g/ml concentration. However, laboratories performing BACTEC MGIT had 78.4% (29/37) agreement at the 5.0  $\mu$ g/ml concentration, while laboratories (5/7) performing L-J Proportion had 71.4% agreement. There was less agreement on resistance, 89.5% (17/19) among laboratories performing the BACTEC 460TB method at 7.5  $\mu$ g/ml. All (34) laboratories performing INH testing with the AP method at both 0.2 and 1.0  $\mu$ g/ml were in complete agreement on susceptibility of the strain. Similarly, 100% of laboratories performing BACTEC 460TB, 97.6% (81/83) were in agreement on the 0.1  $\mu$ g/ml concentration, while those (21) performing 0.4  $\mu$ g/ml were in complete agreement among laboratories on susceptibility to rifampicin and pyrazinamide among laboratories and test methods.

**Strain G** was a fully susceptible strain of *M. tuberculosis*. Among laboratories performing the BACTEC MGIT method, however, there were minor discordances (reports of resistance): on INH (at 0.1  $\mu$ g/ml), 3.2% (1/31); 9.1% (3/33) on rifampicin; 8% (2/25) on pyrazinamide and 6.3% (2/32) on ethambutol. Seven (7) laboratories reported contamination of L-J culture slants with a gram-positive rod.

**Strain H** was resistant only to low level concentrations of INH. Testing by AP at the critical concentration (0.2 µg/ml), 65.6% (21/32) of laboratories detected resistance. Similarly, at the critical concentration (0.1 µg/ml) using the BACTEC 460TB method, 79.0% (64/81) of laboratories detected resistance; at the same concentration of INH using MGIT, 83.3% (30/36) detected resistance. Resistance was reported at the higher concentration of INH (1.0 µg/ml) with the AP method by 12.9% (4/31) of laboratories. Laboratories testing 0.4 µg/ml INH reported resistance with BACTEC 460TB and MGIT - 12.5% (3/24) and 30.8% (4/13), respectively. Of the seven laboratories performing the L-J Proportion method, none detected resistance for INH. There was almost complete agreement among laboratories on the susceptibility of strain H for the other primary drugs - rifampicin, pyrazinamide, and ethambutol. Of the 36 laboratories performing MGIT at 5.0 µg/ml of ethambutol, 11.1% (4/36) reported resistance.

**Strain I** was resistant to the high concentrations of INH. Participants performing AP, BACTEC 460TB, L-J Proportion and MGIT methods were in agreement on resistance at the higher concentrations. On the critical concentration of  $(0.1 \ \mu g/ml)$  INH, there was 100% (36/36) agreement among participants using MGIT 960 and 98.8% (82/83) agreement among participants using BACTEC 460TB. Agreement among participants using AP was 97.1% (34/35) at 0.2  $\mu$ g/ml, while among laboratories using L-J proportion, agreement was 87.5% (7/8). There was complete agreement among participants on all methods on the susceptibility of rifampicin. There was, however, some disagreement among users of MGIT - 75.0% (21/28) and BACTEC 460TB - 98.6% (71/72) for susceptibility to 100  $\mu$ g/ml pyrazinamide. All participants were also in agreement on the susceptibility of **Strain I** to the critical concentration of ethambutol with AP (35/35), BACTEC 460TB (77/77) and L-J proportion (7/7), with slight discordance seen with MGIT, 97.2% (35/36). Similar agreement was observed among methods and participant results for streptomycin.

Note: There was a recall of the Becton Dickinson BACTEC 960TB MGIT SIRE Supplement Lot # 3351099 shipped between February 10 and July 16, 2004. The supplement was reported as contaminated with a fungus. We were not able to determine if results in this shipment were affected by this recall.

Our providing test results for all drugs that are reported to CDC should not be construed as a recommendation or endorsement for testing particular drugs or concentrations with patient isolates of 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 J** was isolated from a 60-year-old patient with a history of chronic obstructive pulmonary disease. He complained of weight loss, cough, dyspnea and chest pain. His radiograph findings were abnormal, showing extensive pulmonary infiltrates and right upper lobe cavity. Multiple sputum cultures were positive for *M. xenopi*.

Antimicrobial agents recommended for testing *M. xenopi* (Strain J) are found in Table 6 in the NCCLS Guidelines (6) and are the same as for testing *M. kansasii*. Strain J was resistant to ethambutol (refer to Tables 2 and 3) and to ofloxacin and minocycline by microtiter MICs (Table 3). Most laboratories reported it to be susceptible to rifampicin and isoniazid, as well as to rifabutin, streptomycin, and clarithromycin (Tables 2 and 3). A few laboratories reported 'no growth' for the strain for several drugs.

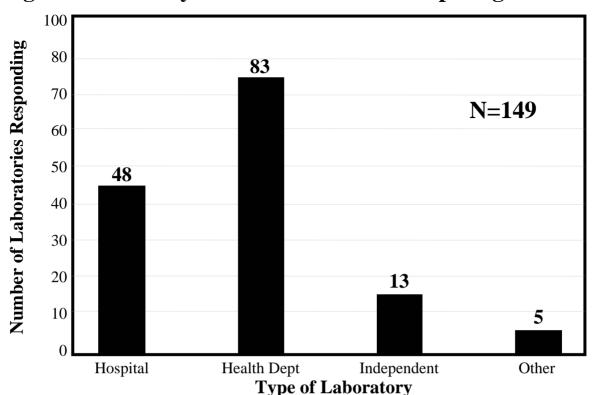
**Mycobacterium xenopi** is a slow-growing non-tuberculous mycobacterium. Although *M. xenopi* was first recovered from a cold-blooded animal (*Xenopus laevis*, a South African toad), it is a thermophile (optimum temperature is 43°C). The organism is found in fresh water and has been isolated in water samples collected from water systems in homes and hospitals (9). *Mycobacterium xenopi* was isolated infrequently and only occurred in clusters prior to the epidemic of Acquired Immunodeficiency syndrome. **Mycobacterium xenopi** is one of the most common NTM in parts of England and Canada. A classic chest x-ray from infection with *M. xenopi* mimics tuberculosis. The organism has also been associated with cases resembling pulmonary and colonic metastases (4, 5, 7, 8).

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.

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

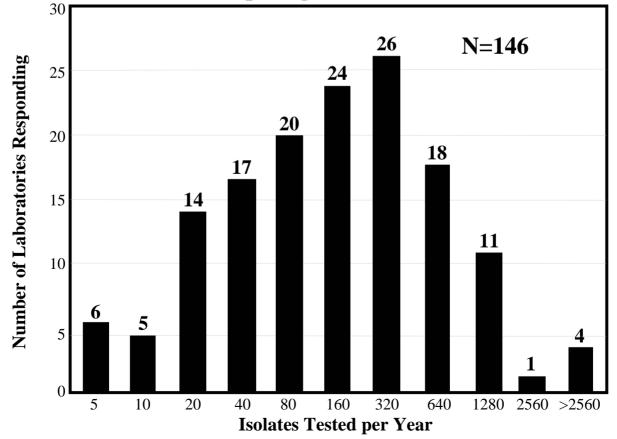
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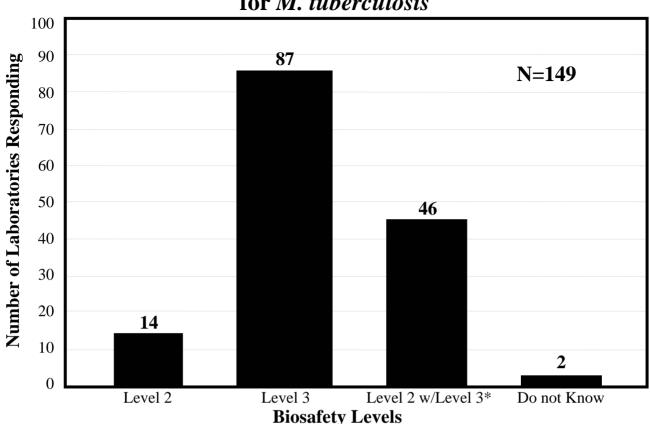
**Figure 1. Primary Classification of Participating Laboratories** 

Figure 2. 2003 Annual Volume of *M. tuberculosis* Isolates for Participating Laboratories



Group labels indicate upper limit of the group.

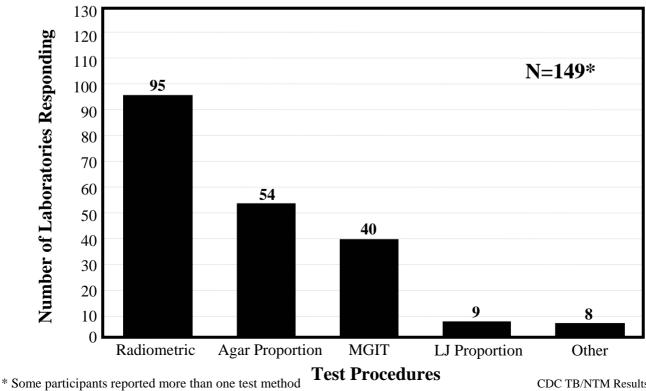
CDC TB/NTM Results 0406



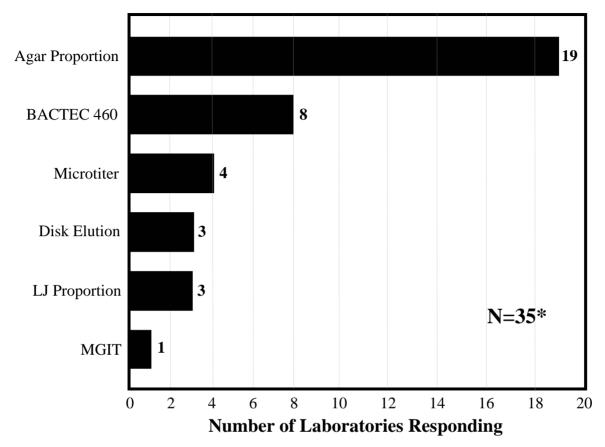
## Figure 3. Biosafety Levels of Participating Laboratories for *M. tuberculosis*

\* Biosafety level 2 for facilities with level 3 containment equipment





CDC TB/NTM Results 0406



# Figure 5. Test Procedures used by Laboratories for Strain J - M. xenopi

\* Some participants reported more than one test method

#### Table 1. Participant Results for Culture F, M. tuberculosis

	Ī							Tes	st Me	thod						
		Ac	jar Pr	op.	B	ACTE	С		J Pro			MGI	Т	Ot	her T	ests
		-	, Result	-		Result			Resul	•		Resu			Resu	
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.01	0		oum	1		1	0		Oum	0		Oum	0		oum
Isoniazid	0.03				'		1							1		1
Isoniazid	0.05															1
Isoniazid	0.00													1		1
Isoniazid	0.03				81	2	83	1		1	36		36	2		2
Isoniazid	0.10				U.	4	υJ	•		1	50		50	1		1
Isoniazid	0.12	34		34	2		2	8		8	1		1	1		1
Isoniazid	0.20	1		1	2		2	0		0	· ·		1	1		1
Isoniazid	0.20				21		21				8		8	2		2
Isoniazid	0.40	1		1	<u> </u>		<u> </u>	1		1	0		0	1		1
Isoniazid	1.00	34		34	3		3	5		5				1		1
Isoniazid	5.00	4		4	5		5	5		5						1
Isoniazid	10.00	4		1				2		2				'		1
Isoniazid	100.00			1				2 1		1						
Rifampin	0.06	-						- 1		I				1		1
Rifampin	0.00													1		1
Rifampin	0.12													1		1
Rifampin	0.25				1		1									1
Rifampin	0.50				'		I							1		1
Rifampin	1.00	37		37	7		7		1	1	38		38	3		3
Rifampin	2.00	37		J	, 84		, 84		I	I	30		30	2		2
Rifampin	2.00 5.00	4		4	04		04	1		1				2		2
Rifampin	20.00	4		4				1		1						
Rifampin	40.00							8		8						
Rifampin	40.00 50.00							0 1		0 1						
Pyrazinamide	1.00							1		1						
-	2.00							1		1						
Pyrazinamide Pyrazinamide	2.00				1		1	I		I						
-	99.00 100.00				72		י 72	4		4	30		30	2		2
Pyrazinamide	200.00				12		12	1 1		1	30		30	2		Z
Pyrazinamide					4		4	I		1						
Pyrazinamide	300.00				1		1	4		4						
Pyrazinamide Ethambutol	400.00							1 1	4	2					4	4
Ethambutol	1.00 1.80							I	1	2					1	1 1
Ethambutol								2	5	7					1 1	1
	2.00 2.50		1	4	2	76	77	2	Э	1					I	I
Ethambutol Ethambutol			1	1	4	75	77		4	4						
Ethambutol Ethambutol	3.00 3.75					4	4		1	1						
						1	1								4	4
Ethambutol	4.00		00	<b>ი</b> 4		1	1	A	4	0	_		07		1 3	1 3
Ethambutol	5.00	0+0+0+0+0+0+0+0+0+0+0	32	34	· ·	8	8	1	1	2	8	29	37		3	3
Ethambutol	7.50		1	4	2	17	19									~
Ethambutol	8.00													2		2
Ethambutol	10.00		4	11												
Ethambutol	16.00													1		1
Ethambutol	32.00													1		1

#### Table 1. Participant Results for Culture F, M. tuberculosis

	[							Tes	t Me	thod						
		Ac	gar Pi	rop.	В	ACT	EC		J Pro			MGI	т	Oth	ner T	ests
			Resul	-		Resul			Resul			Resu			Resul	
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Streptomycin	0.25	3	Γ	Sum	3	N	Sum	3	Л	Sum	3	Γ	Sum	3	Γ	Sum 1
	0.25													1		1
Streptomycin								4		4	20		20	-		-
Streptomycin	1.00			~~				1		1	29		29	1		1
Streptomycin	2.00	*****************		35	77		77	-		_			~	3		3
Streptomycin	4.00	1		1	1		1	7		7	3		3	1		1
Streptomycin	5.00							1		1						
Streptomycin	6.00				15		15	_								
Streptomycin	8.00							3		3				1		1
Streptomycin	10.00	23		23				1		1						
Ethionamide	1.25				2		2									
Ethionamide	2.00	1		1												
Ethionamide	2.50				2		2									
Ethionamide	5.00	20	1	21	5		5									
Ethionamide	10.00	5		5												
Ethionamide	20.00								1	1						
Ethionamide	40.00							2		2						
Kanamycin	4.00	1		1												
Kanamycin	5.00	11		11	2		2									
Kanamycin	6.00	17		17												
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	5.00				4		4									
Capreomycin	10.00	18		18	-		-									
Capreomycin	20.00	ιU		ιv				1		1						
Capreomycin	40.00							1		1						
Cycloserine	20.00							1	1	1						
Cycloserine	30.00	11		11				2	I	2						
Cycloserine								2 1		2 1						
	40.00			4				I		I						
Cycloserine	60.00			1				2		2						
p-Aminosalicylic acid	0.50							3		3						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00		1	16			4									
p-Aminosalicylic acid	4.00			~		1	1									
p-Aminosalicylic acid	8.00			3												
p-Aminosalicylic acid	10.00			4												
Amikacin	0.50													1		1
Amikacin	1.00			_	1		1							1		1
Amikacin	2.00			2	1		1									
Amikacin	2.50			1	1		1									
Amikacin	4.00			3												
Amikacin	5.00				1		1									
Amikacin	6.00			5												
Amikacin	8.00				1		1									
Amikacin	12.00	2		2												

#### Table 1. Participant Results for Culture F, M. tuberculosis

								Tes	t Me	thod						
		Ag	jar Pr	op.	В	ACTEC		L	J Pro	p.		MGI	Т	Ot	her T	ests
		F	Result	ts	F	Results		R	lesul	ts	I	Resu	lts		Resu	lts
DRUG	Conc.	S	R	Sum	S	R Su	m	S	R	Sum	S	R	Sum	S	R	Sum
Ofloxacin	0.50														1	1
Ofloxacin	1.00	3		3	1	1										
Ofloxacin	2.00	9		9	6	6		1		1				1		1
Ofloxacin	4.00	3		3	1	1										
Ofloxacin	8.00				1	1										
Ciprofloxacin	0.50													1		1
Ciprofloxacin	1.00	1		1	2	2								1		1
Ciprofloxacin	2.00	10		10	3	3										
Ciprofloxacin	4.00				1	1										
Levofloxacin	0.16		1	1												
Levofloxacin	0.30		1	1												
Levofloxacin	0.60	1		1												
Levofloxacin	1.00	1		1												
Levofloxacin	2.00				4	4										
Levofloxacin	8.00				1	1										
Rifabutin	0.50	2		2	1	1										
Rifabutin	1.00	1		1	1	1										
Rifabutin	2.00	4		4												
Clofazimine	0.50				1	1									1	1
Clofazimine	1.00													1		1

				Test	Method					
		Agar Prop.	BACTEC		Prop.		MGI	Т	Ot	ner Tests
		Results	Results		esults	I	Resu			Results
DRUG	Conc.	S R Sum	S R Sum	S	R Sum	S	R	Sum	S	R Sum
Isoniazid	0.01			<u> </u>	IX Oum	0		Ouiii	0	
Isoniazid	0.03								1	1
Isoniazid	0.06								1	1
Isoniazid	0.00								1	1
Isoniazid	0.03		81 81	1	1	30	1	31	1	1
Isoniazid	0.10		01		Ĩ	50	1	51	1	1
Isoniazid	0.12	29 29	2 2	7	7	1		1	1	1
Isoniazid	0.20	20 20	2 2	'	'			1	1	1
Isoniazid	0.20		20 20			8		8	1	1
Isoniazid	0.40		20 20	1	1	0		0	1	1
Isoniazid	1.00	27 27	3 3	4	4				1	1
Isoniazid	5.00	4 4	5 5	4	4				1	1
Isoniazid	10.00			2	2					'
Isoniazid	100.00			2	2 1					
Rifampin	0.06			1	I				1	1
Rifampin	0.06								1	1
									1	1
Rifampin Bifampin	0.25		1 4						1	1
Rifampin Bifampin	0.50 0.90		1 1						1	1
Rifampin					4	00	~	00	1	-
Rifampin	1.00	30 30	7 7	1	1	30	3	33	2	2
Rifampin	2.00	0 0	82 82		4				2	2
Rifampin	5.00			1	1					
Rifampin	20.00			1	1					
Rifampin	40.00			7	7					
Rifampin	50.00			1	1				-	
Pyrazinamide	1.00			1	1					
Pyrazinamide	2.00			1	1					
Pyrazinamide	99.00		1 1				-	~-	-	
Pyrazinamide	100.00		69 69	1	1	23	2	25	2	2
Pyrazinamide	200.00			1	1					
Pyrazinamide	300.00		1 1							
Pyrazinamide	400.00			1	1					
Ethambutol	1.00			2	2				1	1
Ethambutol	1.80				o –				1	1
Ethambutol	2.00			4	37				1	1
Ethambutol	2.50	1 1	75 75							
Ethambutol	3.75		1 1							
Ethambutol	4.00		1 1		-		-		1	1
Ethambutol	5.00		6 6	2	2	30	2	32	2	2
Ethambutol	7.50	3 3	15 15							
Ethambutol	8.00								1	1
Ethambutol	10.00	8 8								
Ethambutol	16.00								1	1
Ethambutol	32.00								1	1
Streptomycin	0.25								1	1
Streptomycin	0.50								1	1
Streptomycin	1.00			1	1	24	1	25	1	1
Streptomycin	2.00		75 75						3	3
Streptomycin	4.00	1 1	1 1	6	6	3		3	1	1
Streptomycin	5.00			1	1					
Streptomycin	6.00		15 15							
Streptomycin	8.00			2	1 3				1	1
Streptomycin	10.00	20 20		1	1					

#### Table 1. Participant Results for Culture G, M. tuberculosis

	]					Τe	est N	/lethod						
		Agar	Prop.	В	ACTEC			Prop.		MGI	Г	Ot	her T	ests
		-	sults		Results			sults		Resul			Resu	
DRUG	Conc.		R Sum	S	R Su	n S		R Sum	S	R	Sum	S	R	Sum
Ethionamide	1.25	<u> </u>	( Joann	1	1		·	( Ouin			oum			Cam
Ethionamide	2.50			1	1									
Ethionamide	5.00	14	14	2	2									
Ethionamide	10.00		 5	-	-									
Ethionamide	20.00		U			1		1						
Ethionamide	40.00					2		2						
Kanamycin	4.00	1	1			2		L						
Kanamycin	5.00		8	1	1									
Kanamycin	6.00	14	0 14	•										
Kanamycin	10.00	1-7	17			1		1						
Kanamycin	20.00					1		1						
Kanamycin	40.00							1						
Capreomycin	0.50					+		I				1		1
Capreomycin	1.00											1		1
Capreomycin	1.00			1	1							1		I
Capreomycin	1.25 5.00			1	1									
Capreomycin	10.00	13	13	1	1									
Capreomycin	20.00	เง	IJ			1		1						
	40.00							1						
Capreomycin	20.00					1		1						
Cycloserine		~	0											
Cycloserine	30.00	9	9			2		2						
Cycloserine	40.00					1		1						
Cycloserine	60.00	1	1					0						
p-Aminosalicylic acid	0.50					2		2 2						
p-Aminosalicylic acid	1.00		<b>.</b>			2		Z						
p-Aminosalicylic acid	2.00	0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1	11											
p-Aminosalicylic acid	8.00		3											
p-Aminosalicylic acid	10.00	3	3									4		4
Amikacin	0.50											1		1
Amikacin	1.00			1	1							1		1
Amikacin	2.00		1	1	1									
Amikacin	4.00		2											
Amikacin	6.00	3	3											
Amikacin	8.00			1	1									
Amikacin	12.00	1	1			_								
Ofloxacin	0.50												1	1
Ofloxacin	1.00		1											
Ofloxacin	2.00		7	4	4			1 1				1		1
Ofloxacin	4.00		2	1	1									
Ofloxacin	8.00			1	1									
Ciprofloxacin	0.50												1	1
Ciprofloxacin	1.00		1	1	1							1		1
Ciprofloxacin	2.00	8	8	2	2									
Ciprofloxacin	4.00			1	1									
Levofloxacin	1.00	1	1											
Levofloxacin	2.00			3	3									
Levofloxacin	8.00			1	1									
Rifabutin	0.50	2	2											
Rifabutin	1.00		1											
Rifabutin	2.00	2	2											
Clofazimine	0.50												1	1
Clofazimine	1.00											1		1

#### Table 1. Participant Results for Culture H, M. tuberculosis

								Tes	t Me	thod						
		Ac	gar Pr	op.	В	ACTE	EC		J Pro			MGI	-	Ot	ner T	ests
		-	, Resul	-	F	Result	ts		Resul	•		Resul			Resu	
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.01	0		oum	1		1	<u> </u>		Cum	Ŭ		ouiii	<u> </u>		Cam
Isoniazid	0.03				•										1	1
Isoniazid	0.06													1	•	1
Isoniazid	0.10				17	64	81	1		1	6	30	36	1	1	2
Isoniazid	0.12					V I	Υ.	•		1	Ŭ	00	00	1	•	1
Isoniazid	0.20	11	21	32	2	1	3	7		7		1	1	•	1	1
Isoniazid	0.25		- ' 1	1	~	•	0			,				1	•	1
Isoniazid	0.20			1	21	3	24				9	4	13	2		2
Isoniazid	0.50	1		1	<u>د</u> ا	J	<u>4</u> π 1				5	7	10	1		1
Isoniazid	1.00	27	4	31	3		3	3		3				1		1
Isoniazid	5.00	4		31 4	1		1	5		5				1		1
Isoniazid	10.00	4	1	4	I		I	1		1				I		1
Isoniazid	100.00		I	I				1								
	0.06							I		1				4		4
Rifampin Bifampin	0.06													1		1 1
Rifampin																-
Rifampin	0.25													1		1
Rifampin	0.50				1		1							1		1
Rifampin	0.90	20		~~	~		•				~~~		~~	1		1
Rifampin	1.00	33		33	6		6		1	1	38		38	3		3
Rifampin	2.00	_			84		84							2		2
Rifampin	5.00	3		3				1		1						
Rifampin	20.00							1		1						
Rifampin	40.00							7		7						
Rifampin	50.00							1		1						
Pyrazinamide	1.00							1		1						
Pyrazinamide	2.00							1		1						
Pyrazinamide	99.00				1		1									
Pyrazinamide	100.00				70	1	71	1		1	30		30	2		2
Pyrazinamide	300.00				1		1									
Pyrazinamide	400.00							1		1						
Ethambutol	1.00							2		2				1		1
Ethambutol	1.80													1		1
Ethambutol	2.00							6		6				1		1
Ethambutol	2.50	1		1	76		76									
Ethambutol	3.00							1		1						
Ethambutol	3.75				1		1									
Ethambutol	4.00				1		1							1		1
Ethambutol	5.00	30		30	6		6	2		2	32	4	36	2		2
Ethambutol	7.50	3		3	15		15									
Ethambutol	8.00													2		2
Ethambutol	10.00	9		9												
Ethambutol	16.00													1		1
Ethambutol	32.00													1		1

#### Table 1. Participant Results for Culture H, M. tuberculosis

	ſ							Tes	t Me	thod						
		Ac	jar Pr	op.	В	ACTE	С		J Pro			MGI	Γ	Ot	ner T	ests
		-	Resul	•		Result			Resul	•		Resul			Resul	
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Streptomycin	0.25	5	IX.	Sum	3	IX.	Sum	0	N	Sum	3	IX.	Sum	5	1	30m
Streptomycin	0.20													1	1	1
Streptomycin	1.00							1		1	29	1	30	1		1
Streptomycin	2.00	31		31	75		75	I		1	29	I	30	3		3
	2.00 4.00	ਤ। 1		ਹ। 1	75 1			5	1	G	3		3	3 1		3 1
Streptomycin				I	I		1	5 1	I	6	3		3	I		1
Streptomycin	5.00				15		45	I		1						
Streptomycin	6.00				15		15	2		2				4		4
Streptomycin	8.00	00		00				3		3				1		1
Streptomycin	10.00	22		22			4	1		1	-			-		
Ethionamide	1.25				1		1									
Ethionamide	2.00	1		1												
Ethionamide	2.50				1		1									
Ethionamide	5.00	17		17	3		3									
Ethionamide	10.00	4		4												
Ethionamide	20.00							1		1						
Ethionamide	40.00							2		2						
Kanamycin	5.00	10		10	1		1									
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	1.00													1		1
Capreomycin	1.25				1		1									
Capreomycin	5.00				2		2									
Capreomycin	10.00	15		15												
Capreomycin	40.00							1		1						
Cycloserine	20.00							1		1						
Cycloserine	30.00	10		10				1		1						
Cycloserine	40.00			-				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	13		13				_		_						
p-Aminosalicylic acid	8.00			3												
p-Aminosalicylic acid	10.00			4												
Amikacin	0.50			•										1		1
Amikacin	1.00				1		1							1		1
Amikacin	2.00	2		2	1		1									'
Amikacin	4.00	2		2			'									
Amikacin	4.00 6.00			2												
Amikacin	8.00			3	1		1									
				1	I		I									
Amikacin	12.00	1		1												

#### Table 1. Participant Results for Culture H, M. tuberculosis

								Tes	t Me	thod						
		Ag	gar Pr	op.	В	ACTE	С	L	J Pro	p.		MGI	Т	Oth	ner Te	ests
		F	Resul	ts	F	Result	s	F	Resul	ts	F	Resu	lts	F	Result	ts
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Ofloxacin	0.50													1		1
Ofloxacin	0.60	1		1												
Ofloxacin	1.00	1		1												
Ofloxacin	1.20	1		1												
Ofloxacin	2.00	7		7	5		5	1		1				1		1
Ofloxacin	4.00	3		3	1		1									
Ofloxacin	8.00				1		1									
Ciprofloxacin	0.50													1		1
Ciprofloxacin	1.00	1		1	1		1							1		1
Ciprofloxacin	2.00	7		7	2		2									
Ciprofloxacin	4.00				1		1									
Levofloxacin	0.16		1	1												
Levofloxacin	0.30	1		1												
Levofloxacin	0.60	1		1												
Levofloxacin	1.00	1		1												
Levofloxacin	2.00				3		3									
Levofloxacin	8.00				1		1									
Rifabutin	0.50	3		3												
Rifabutin	1.00	1		1	1		1									
Rifabutin	2.00	4		4												
Clofazimine	0.50														1	1
Clofazimine	1.00													1		1

#### Table 1. Participant Results for Culture I, M. tuberculosis

								Tes	t Me	thod						
		Ac	jar Pr	ор.	В	ACTE	C	L	J Pro	p.		MGI	Т	Ot	her T	ests
		_	Resul	-	F	Resul	ts	F	Resul	ts		Resu	lts		Resu	lts
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.01				_	1	1									
Isoniazid	0.03														1	1
Isoniazid	0.06														1	1
Isoniazid	0.09														1	1
Isoniazid	0.10				1	82	83	1		1		36	36		2	2
Isoniazid	0.12							-		-					1	1
Isoniazid	0.20	1	34	35		3	3	1	7	8		1	1		1	1
Isoniazid	0.25		1	1		•	Ū	•	-	Ū		•	•		1	1
Isoniazid	0.40		-	-		27	27					14	14		2	2
Isoniazid	0.50		1	1		1	1		1	1					1	1
Isoniazid	1.00	1	36	37		4	4		4	4		1	1		1	1
Isoniazid	2.00		• •	T		1	1		•	-		•	•		•	
Isoniazid	5.00	4	1	5	1	•	1							1		1
Isoniazid	10.00		1	1			•	2		2						•
Isoniazid	100.00		•	•				1		1						
Rifampin	0.06							•		•					1	1
Rifampin	0.12													1		1
Rifampin	0.12															1
Rifampin	0.50				1		1									1
Rifampin	0.90				'		'									1
Rifampin	1.00	38		38	7		7		1	1	38		38	3		3
Rifampin	2.00	JU		JU	84		, 84		1		50		50	2		2
Rifampin	5.00	4		4	ο <del>π</del>		υŦ	1		1				<u> </u>		2
Rifampin	20.00	-		7				1		1						
Rifampin	40.00							8		8						
Rifampin	50.00							1		1						
Pyrazinamide	1.00							1		1						
Pyrazinamide	2.00							1		1						
Pyrazinamide	99.00				1		1									
Pyrazinamide	100.00				71	1	72	1		1	21	7	28	2		2
Pyrazinamide	200.00				11		12	1		1	21	'	20	2		2
Pyrazinamide	300.00				1		1	1		1						
Pyrazinamide	400.00						1	1		1						
Ethambutol	1.00							2		2					1	1
Ethambutol	1.80							~		~				1		1
Ethambutol	2.00							7		7				1		1
Ethambutol	2.50	1		1	77		77	'		'				l '		
Ethambutol	3.00			1	* *			1		1						
Ethambutol	3.75				1		1	1		1						
Ethambutol	4.00				1		1							1		1
Ethambutol	4.00 5.00			35	7		7	2		2	35	1	36	2		2
Ethambutol	5.00 7.50			30 3	/ 15		7 15	2		2	30	I	30	<b>_</b>		2
Ethambutol	7.50 8.00			ა	10		ιÜ							2		2
Ethambutol				12										<sup>∠</sup>		2
	10.00			12										4		4
Ethambutol Ethambutol	16.00													1		1 1
Ethambutol	32.00															1

#### Table 1. Participant Results for Culture I, M. tuberculosis

								Tes	t Me	thod						
		Ag	gar Pr	op.	B	ACTE	С	L	J Pro	p.		MGI	Т	Ot	ner T	ests
		F	Resul	ts	F	Resul	ts	F	Resul	ts		Resu	lts		Resu	lts
DRUG	Conc.	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	29	1	30	1		1
Streptomycin	2.00	36		36	77		77							3		3
Streptomycin	4.00	1		1	1		1	7		7	3		3	1		1
Streptomycin	5.00							1		1						
Streptomycin	6.00				15		15									
Streptomycin	8.00							3		3				1		1
Streptomycin	10.00	25		25				1		1						
Ethionamide	1.25			**********************	1	1	2									
Ethionamide	2.00		1	1												
Ethionamide	2.50				2		2									
Ethionamide	5.00	18	2	20	5		5									
Ethionamide	10.00	5		5												
Ethionamide	20.00							1		1						
Ethionamide	40.00							2		2						
Kanamycin	4.00	1		1												
Kanamycin	5.00	11		11	3		3									
Kanamycin	6.00	18		18												
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				4		4									
Capreomycin	10.00	18		18												
Capreomycin	20.00							1		1						
Capreomycin	40.00							1		1						
Cycloserine	20.00							1		1						
Cycloserine	30.00	11		11				2		2						
Cycloserine	40.00							1		1						
Cycloserine	60.00			1												
p-Aminosalicylic acid	0.50							3		3						
p-Aminosalicylic acid	1.00							2		2						
p-Aminosalicylic acid	2.00			16												
p-Aminosalicylic acid	4.00				1		1									
p-Aminosalicylic acid	8.00			3												
p-Aminosalicylic acid	10.00			4												

#### Table 1. Participant Results for Culture I, M. tuberculosis

										thod								
		Ag	gar Pi	rop.	В	ACT	EC	L	J Pro	p.		Μ	GIT	Γ	0	the	r Te	ests
		I	Resul	ts	F	Resu	lts	F	Resul	ts		Re	sult	ts		Re	sult	ts
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S		R	Sum	S		R	Sum
Amikacin	0.50														1			1
Amikacin	1.00				1		1								1			1
Amikacin	2.00	2		2	1		1											
Amikacin	2.50	1		1	1		1											
Amikacin	4.00	3		3														
Amikacin	5.00				1		1											
Amikacin	6.00	6		6														
Amikacin	8.00				1		1											
Amikacin	12.00	2		2														
Ofloxacin	0.50																1	1
Ofloxacin	0.60		1	1														
Ofloxacin	1.00	3		3		1	1											
Ofloxacin	1.20	1		1														
Ofloxacin	2.00	9		9	7		7	1		1					1			1
Ofloxacin	4.00	3		3	1		1											
Ofloxacin	8.00				1		1											
Ciprofloxacin	0.50																1	1
Ciprofloxacin	1.00	1		1	2		2								1			1
Ciprofloxacin	2.00	10		10	3		3											
Ciprofloxacin	4.00				1		1											
Levofloxacin	0.16		1	1														
Levofloxacin	0.30		1	1														
Levofloxacin	0.60	1		1														
Levofloxacin	1.00	1		1														
Levofloxacin	2.00				4		4											
Levofloxacin	8.00				1		1											
Rifabutin	0.50	3		3	2		2											
Rifabutin	1.00	1		1	1		1											
Rifabutin	2.00	5		5														
Clofazimine	0.50				2		2										1	1
Clofazimine	1.00														1			1

#### Table 2. Participant Results for Culture J, M. xenopi

	Ī	Test Method														
		Ag	op.	BACTEC			LJ Proportion			Di	sk Elu	ition		MGI	Т	
		Results			Results			Results			Results			Results		
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Amikacin	1.00	0		oum	1		1	0		Oum	<u> </u>		Oum	<u> </u>		oum
Amikacin	2.00	1		1			•									
Amikacin	2.50	1		1												
Amikacin	6.00	1		1												
Amikacin	10.00	2		2												
Amikacin	12.00	2		2 1												
Clarithromycin	1.00	I		1				1		1						
Clarithromycin	3.00	3		3				1		I	2		2			
Clarithromycin	4.00	5		5	2		2				2		2			
Clarithromycin	4.00				2 1		2 1									
Clarithromycin	32.00	2		2	I		1									
Clarithromycin	52.00 64.00	2		Z	1		1									
		3		2	I		I	-								
Capreomycin	10.00	3		3												
Ciprofloxacin	1.00										4		4			
Ciprofloxacin	2.00	4		4						4	1		1			
Cycloserine	20.00							1		1						
Cycloserine	60.00	1		1												
Doxycycline	0.60	1		1												
Ethambutol	2.00					_	_	1		1						
Ethambutol	2.50	-		. –		5	5						-			
Ethambutol	5.00	2	13	15								3	3		1	1
Ethambutol	7.50	1		1												
Ethambutol	10.00	2	4	6												
Ethambutol	50.00				1		1									
Isoniazid	0.10				1	4	5								1	1
Isoniazid	0.12		1	1												
Isoniazid	0.20	1	10	11					1	1						
Isoniazid	0.25		1	1												
Isoniazid	0.50	1		1												
Isoniazid	1.00	12		12							2		2			
Isoniazid	2.00	1		1												
Isoniazid	5.00	2		2												
Kanamycin	5.00	2		2												
Kanamycin	6.00	3		3												
Kanamycin	10.00							1		1						
Levofloxacin	0.16		1	1												
Levofloxacin	0.30		1	1												
Levofloxacin	0.60	1		1												
Moxifloxacin	1.00	1		1												
Ofloxacin	1.00	1		1												
Ofloxacin	2.00	4		4												
p-Aminosalicylic acid		2	2	4												
p-Aminosalicylic acid			1	1												
Pyrazinamide	25.00		1	1												

#### Table 2. Participant Results for Culture J, M. xenopi

	Γ															1
					Test Method											
		Agar Prop.			BACTEC			LJ Proportion			Disk Elution			MGIT		
		Results		Results			Results			Results			Results			
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Rifabutin	0.10	1		1	1		1									
Rifabutin	0.50	2		2												
Rifabutin	1.00	1		1										1		1
Rifabutin	2.00	2		2												
Rifampin	1.00	13	4	17				1	1	2	2		2			
Rifampin	2.00				5		5									
Rifampin	5.00	2		2					1	1						
Streptomycin	1.00													1		1
Streptomycin	2.00	13		13	5		5				2		2			
Streptomycin	5.00							1		1						
Streptomycin	10.00	11		11							2		2			
Ethionamide	5.00	5	1	6												
Ethionamide	10.00	2		2												
Ethionamide	40.00								1	1						
Trimethoprim-Sulfam	0.60	1		1												
Trimethoprim-Sulfam	2.00	1		1												

#### Table 3. Minimum Inhibitory Concentrations for Culture J, M. xenopi

DRUG	Test Method	MIC	Susceptible	Resistant	No Growth	Sum
Amikacin	Agar proportion	4.00	1			1
Amikacin	BACTEC 460	<2.00	1			1
Amikacin	Microtiter	>128.00		1		1
Amikacin	Microtiter	<0.50	1		1	2
Amikacin	Microtiter	<1.00	1			1
Azithromycin	Microtiter	< 0.25	1			1
Azithromycin	Microtiter	< 0.50	1			1
Ciprofloxacin	Agar proportion	<0.50	1			1
Ciprofloxacin	Microtiter	<0.06	1			1
Ciprofloxacin	Microtiter	<0.00	I		1	1
Ciprofloxacin	Microtiter	<0.12	1		1	1
Ciprofloxacin	Microtiter	2.00	I		1*	1
Clarithromycin	Agar proportion	<0.06	1		1	1
Clarithromycin	BACTEC 460	<0.00	1			1
	MGIT	<2.00 8.00	1			1
		0.00 <0.12	1			-
Clarithromycin	Microtiter Microtiter	<0.12	1			1
Clarithromycin			1			1
Clarithromycin	Microtiter	< 0.25	2		4	2
Clarithromycin	Microtiter	< 0.50			1	1
Ethambutol	Agar proportion	4.00	1			1
Ethambutol	BACTEC 460	>8.00		1		1
Ethambutol	Microtiter	4.00			1	1
Ethambutol	Microtiter	10.00		1		1
Ethambutol	Microtiter	>16.00		1		1
Gatifloxacin	Microtiter	<0.06			1	1
Isoniazid	BACTEC 460	<0.50	1			1
Isoniazid	Microtiter	0.25	1			1
Isoniazid	Microtiter	<0.30	1			1
Levofloxacin	BACTEC 460	<2.00	1			1
Linezolid	Microtiter	<0.50			1	1
Minocycline	Microtiter	2.00			1	1
Minocycline	Microtiter	8.00		1		1
Moxifloxacin	Microtiter	<0.06			1	1
Ofloxacin	Microtiter	>0.50		1		1
Ofloxacin	Microtiter	<1.00	1			1
Rifabutin	Agar proportion	1.00	1			1
Rifabutin	BACTEC 460	<0.12	1			1
Rifabutin	Microtiter	<0.06			1	1
Rifabutin	Microtiter	<0.12	1			1
Rifabutin	Microtiter	<0.25	1			1
Rifabutin	Microtiter	>4.00		1		1
Rifabutin	Microtiter	<8.00	1			1
Rifampin	BACTEC 460	<0.50	1			1
Rifampin	Microtiter	<0.06			1	1
Rifampin	Microtiter	<0.12	1			1
Rifampin	Microtiter	1.00	1			1
Streptomycin	BACTEC 460	<2.00	1			1
Streptomycin	Microtiter	< 0.30	=			1
Streptomycin	Microtiter	<0.50			1	1
Sulfamethoxazole	Microtiter	<2.00	1			1
Sulfamethoxazole	Microtiter	<4.00				1
Trimethoprim-Sulfamethoxazole		0.12	1		1	1
*Intermediate		0.12				1

\*Intermediate