Participant Centers for Disease Control and Prevention (CDC) Susceptibility Testing of *Mycobacterium tuberculosis* and Nontuberculous Mycobacteria Performance Evaluation Program

Subject: Analyses of Participant Laboratory Results for the January 2002 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 *M. kansasii* shipped in January 2002. Participant laboratories received either four *M. tuberculosis* complex strains only or four *M. tuberculosis* strains and a nontuberculous mycobacteria (NTM) culture. Testing results were received and analyzed from 137 of 140 (98%) laboratories participating in this shipment. Nine laboratories did not report results due to internal issues related to equipment, staffing or other problems. Nineteen participating laboratories are located in countries other than the United States. Ten laboratories did not receive shipments due to shipping issues such as import permit concerns.

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

The NTM strain in this performance evaluation is intended to provide an assessment of the various methods, drugs, and interpretations that are reported by laboratories that perform drug susceptibility testing for these different strains. The test results for the NTM strain also provides 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) tentative 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 Public Health Practice Program Office

Enclosures

# Analyses of the January 2002 Performance Evaluation Results for *M. tuberculosis* complex and Nontuberculous Mycobacteria Drug Susceptibility Testing Reported to the Centers for Disease Control and Prevention by Participating Laboratories

This report is an analysis of laboratory test results reported to the Centers for Disease Control and Prevention (CDC) by participant laboratories for the four *Mycobacterium tuberculosis* complex and *M. kansasii* shipped in January 2002. Participant laboratories either received four *M. tuberculosis* only or four *M. tuberculosis* and one NTM strain. Testing results were received and analyzed from 137of 140 (98%) laboratories participating in this shipment.

#### Descriptive Information on Participant laboratories

Figure 1 shows the laboratory classification reported by 133 of the participants. Participants consisted of 71 health departments, 47 hospitals, 12 independents, and 3 "other" type of laboratories.

Figure 2 provides the distribution of the annual volume of *M. tuberculosis* isolates tested for drug susceptibilities by participating laboratories in calendar year 2001.

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 all test methods used. Some methods, such as the proportion method with Lowenstein-Jensen (L-J) media, may reflect procedures used by international participants. The three other methods listed were the E-test, micro dilution MIC, and L-J resistance ratio methods. Figure 5 provides a breakdown of the test procedures used by the participating laboratories testing *M. kansasii.* 

#### M. tuberculosis test results:

The aggregate test results are provided in separate tables, representing strains A, B, C, D and E to facilitate comparison among laboratories. Table 1 for the *M. tuberculosis* complex strains A, B, C, and D is constructed to include the results for the radiometric (BACTEC), agar proportion (AP), Lowenstein Jensen (L-J) proportion, and other methods at each concentration of drug. The results for 3 "other" methods are grouped together and include the E-test, L-J resistance ratio, and micro dilution MIC. 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, p-amino-salicylic acid) antituberculosis drugs are highlighted for the conventional and radiometric methods. Participants should note that the new NCCLS tentative standard (Susceptibility Testing of Mycobacteria, Nocardia, and Other Aerobic Actinomycetes; Tentative Standard-Second Edition, NCCLS document M24-T2 [ISBN 1-56238-423-6] NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA, 2000) recommends testing streptomycin as a secondary drug and also adds ofloxacin and rifabutin to

the list of recommended secondary drugs. Participants should note that these recommended combinations reflect the critical concentrations of antituberculosis drugs in 7H10 agar and those concentrations for the BACTEC method that directly correlate with the critical concentrations in the conventional method (1-4). 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.

**For Strain A**, resistance to rifampin 1.0  $\mu$ g/ml by AP was reported by 71% (29/41) of laboratories, while 78% (82/105) reported resistance by the BACTEC method.

**For Strain B,** 100% (39) laboratories reported resistance to INH 0.2  $\mu$ g/ml with the AP method and 99% (102/103) by BACTEC. High-level resistance (at 0.4 and 1.0  $\mu$ g/ml concentrations of INH) was reported by 97 and 98 percent of laboratories with BACTEC and AP, respectively. The strain was resistant to streptomycin by both BACTEC and AP method.

**Strain C** was resistant to INH at 1.0  $\mu$ g/ml by AP and 0.4  $\mu$ g/ml by BACTEC while 80% (4/5) of laboratories reported resistance at 5.0  $\mu$ g/ml with the AP method. Ninety-seven percent of laboratories found this strain to be resistant to 2.5  $\mu$ g/ml and 5  $\mu$ g/ml of EMB with both the BACTEC and AP methods. However, only 62% of laboratories detected resistance to the higher concentration of EMB at 10  $\mu$ g/ml with AP, but 94% detected resistance with BACTEC at 7.5  $\mu$ g/ml.

**Strain D** was susceptible to primary drugs by all laboratories except 3% (3/90) detected resistance to PZA.

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 *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 the consultation of 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:

The aggregate test results are provided in Tables 2 and 3 for **Strain E**, *M. kansasii*, to facilitate comparison among laboratories. Table 2 represents either single or multiple drug concentrations with "breakpoint" susceptibility test results. Table 3 includes all the quantitative MIC test results.

Of participants who tested **Strain E** (*M. kansasii*), 73% (16/22) reported the isolate resistant to rifampin 1.0 µg/ml with AP; however, 100% (10) reported it susceptible to rifampin 2.0 µg/ml by BACTEC. For *M. kansasii* isolates resistant to 1 µg/ml of rifampin, the recommended secondary drugs for susceptibility testing are ethambutol, isoniazid, streptomycin, clarithromycin, amikacin, ciprofloxacin, trimethoprim sulfamethoxazole or sulfamethoxazole (7). One hundred percent (16) of participants found this isolate (*M. kansasii*) resistant to ethambutol 5.0 µg/ml. One laboratory reported resistance and one reported susceptible with INH 5 µg/ml with AP. Because results are commonly variable with the lower (1.0 µg/ml) concentration, INH 5.0 µg/ml is recommended for testing *M. kansasii* (7).

In Table 3, seventy-five percent (3/4) of laboratories reported susceptible MIC results for rifampin. One of these four laboratories reported resistance to rifampin at 4.0 µg/ml by microtiter

while another reported susceptible at the same concentration by AP. A previous study showed that isolates in broth microdilution testing exhibit lower MICs than in agar and several isolates with low level rifampin resistance were missed (8).

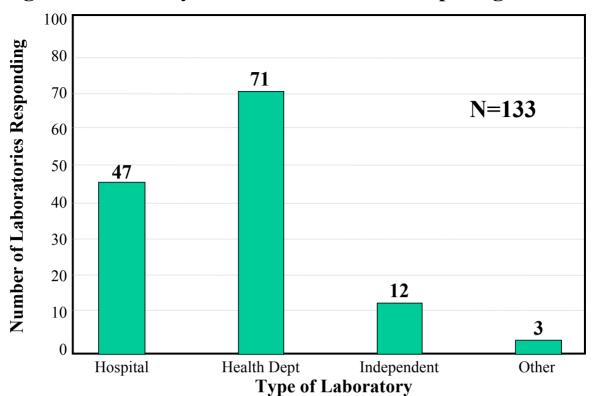
Drugs for treatment of infections with *M. kansasii* include isoniazid, rifampin and ethambutol, but routine susceptibility testing is usually not performed except for rifampin. Rifabutin is used in HIV-infected patients on treatment with protease inhibitors. Patient cultures which remain positive after 3 months of appropriate therapy should have susceptibility tests repeated (6, 8).

Many laboratories perform drug susceptibility testing for NTM in the absence of clinical studies demonstrating the efficacy of particular drugs and/or drug concentrations and methods (6). The addition of NTM strains to this performance evaluation program should not be interpreted as recommendations for laboratories to adopt NTM drug susceptibility testing, especially if the laboratory has limited experience with these tests and methods. We encourage laboratories that perform NTM drug susceptibility testing to consult recommendations, references, and physicians with expertise in infectious diseases when selecting test methods, drugs, and test interpretations.

Special thanks to the following persons for reviewing this report: Nancy G. Warren, Ph.D., Laboratory Corporation of America; Richard Wallace, M.D., Ph.D., and Barbara Brown-Elliott, M.S., University of Texas at Tyler, TX; Gail L. Woods, M.D., Merck Company; Wendy Gross, M.S., TB Reference Laboratory, Westhaven, CT; Beverly Metchock, Dr. P.H., Centers for Disease Control and Prevention.

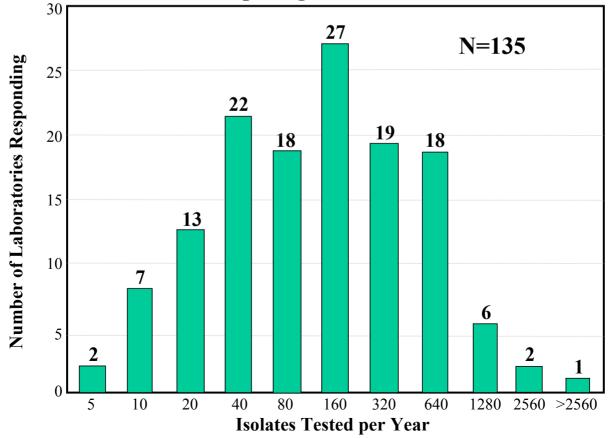
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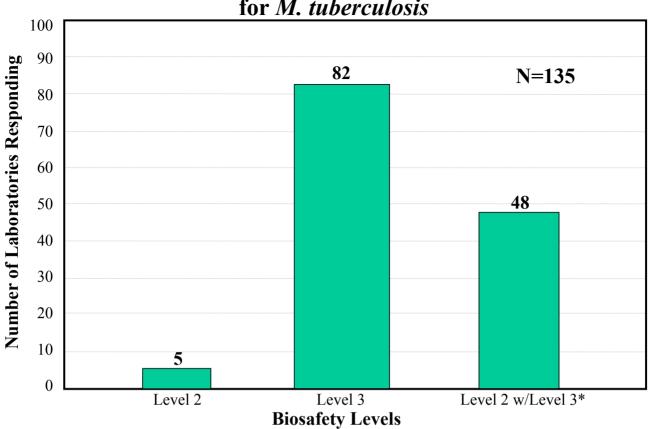
**Figure 1. Primary Classification of Participating Laboratories** 

Figure 2. 2001 Annual Volume of *M. tuberculosis* Isolates for Participating Laboratories



Group labels indicate upper limit of the group.

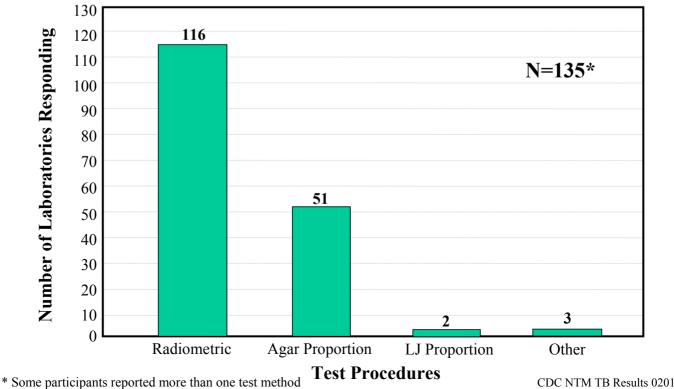
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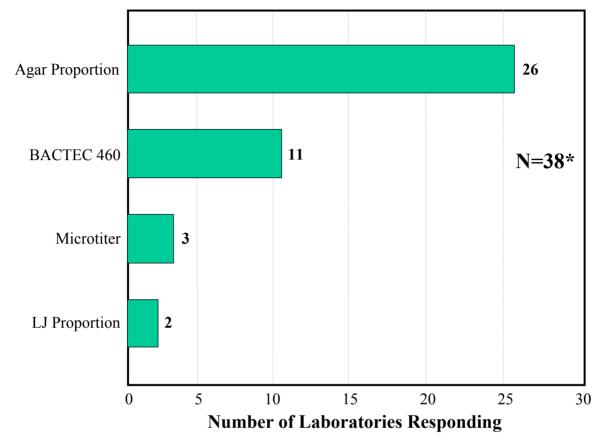


# Figure 3. Biosafety Levels of Participating Laboratories for *M. tuberculosis*

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







# Figure 5. Test Procedures used by Laboratories for Strain E - M. kansasii

\* Some participants reported more than one test method

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

							Test M	1ethod					
		A	gar Pro	p.		BACTE	C		LJ Prop		C	ther Te	sts
			Results	5		Results			Results	5		Result	S
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.01				1		1						
Isoniazid	0.02	1		1									
Isoniazid	0.10				104		104				2		2
Isoniazid	0.12	1		1									
Isoniazid	0.20	36		36	4		4	2		2			
Isoniazid	0.40				25		25				1		1
Isoniazid	1.00			36	3		3						-
Isoniazid	5.00	4		4	-		C C						
Rifampin	0.25	-				1	1						
Rifampin	0.50	4		4	3	2	5						
Rifampin	1.00		29	41	1	6	7				1	1	2
Rifampin	2.00			7	23	82	105				•	•	-
Rifampin	5.00		2	5	1	~~	. Jo 1						
Rifampin	10.00	-	2	U	1		1						
Rifampin	40.00				'		•		1	1			
Pyrazinamide	25.00	1		1						1			
Pyrazinamide	50.00				1		1						
Pyrazinamide	99.00						1						
Pyrazinamide	100.00				91	1	92				1		1
Ethambutol	2.00				<u>.</u>		<u>.</u>	2		2	<u>!</u>		
Ethambutol	2.50	1		1	100	1	101	2		2			
Ethambutol	3.75	1		1	1	ľ	тот 1						
Ethambutol	4.00						1						
Ethambutol	5.00			33	7		7				2		2
Ethambutol	6.00	2+					1				2		2
Ethambutol	7.50			6	15		15						
Ethambutol	8.00			0	IJ		IJ				1		1
Ethambutol	10.00			12							I		I
Streptomycin	1.00			12							1		1
	2.00	41		41	101		101				I		I
Streptomycin	2.00 4.00			41	e ofofofofofofofofofofofofofofof		******************************	2		2			
Streptomycin					1		1 10	Z		2			
Streptomycin	6.00			30	18		18						
Streptomycin Ethionamide	10.00 1.25			ວບ		1	1						
Ethionamide	2.50				1	1							
			A	ററ	1 4		1						
Ethionamide Ethionamide	5.00 10.00		1	26 4	4		4						
Ethionamide				4				4		4			
	40.00				4		4	1		1			
Kanamycin	2.50			40	1		1						
Kanamycin	5.00			12	4		4						
Kanamycin	6.00			18						4			
Kanamycin	40.00							1		1			

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

	[						Test M	1ethod					
		A	gar Pro	p.		BACTE			LJ Prop		0	ther Te	sts
			Results	-		Results	5		Results			Results	5
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Capreomycin	1.25				1		1				-		eam
Capreomycin	2.50				1		1						
Capreomycin	5.00	1		1	7		7						
Capreomycin	10.00	20		20			,						
Capreomycin	40.00	- Y		~~				1		1			
Cycloserine	12.00	1		1				•					
Cycloserine	25.00	1		1									
Cycloserine	30.00	12		12				1		1			
Cycloserine	50.00	1		1	1		1						
Cycloserine	60.00	1		1	•		'						
p-Aminosalicylic acid	0.50	I		I				1		1			
p-Aminosalicylic acid	1.00							1		1			
p-Aminosalicylic acid	2.00	18		18				I		I			
p-Aminosalicylic acid	4.00	ю		10	1		1						
p-Aminosalicylic acid	4.00	3		3	1		1						
	0.00 10.00	3 3											
p-Aminosalicylic acid Amikacin		3 1		3 1									
	1.00						4						
Amikacin	2.00	1		1	1		1						
Amikacin	2.50				1		1						
Amikacin	4.00	4		4			4						
Amikacin	5.00	-		-	1		1						
Amikacin	6.00	6		6									
Amikacin	12.00	1		1									
Ofloxacin	1.00		3	3		1	1						
Ofloxacin	1.25					1	1						
Ofloxacin	2.00		8	8		4	4		1	1			
Ofloxacin	2.50					1	1						
Ofloxacin	4.00		3	3									
Ofloxacin	5.00					1	1						
Ofloxacin	8.00					1	1						
Ciprofloxacin	0.25	1		1									
Ciprofloxacin	0.50	1		1									
Ciprofloxacin	1.00		3	3		1	1						
Ciprofloxacin	2.00	3	5	8		1	1						
Ciprofloxacin	2.50					1	1						
Ciprofloxacin	4.00					1	1						
Ciprofloxacin	5.00					1	1						
Levofloxacin	2.00					1	1						
Levofloxacin	8.00					1	1						
Clofazimine	0.06				1		1						
Clofazimine	0.50				1		1						
Clofazimine	1.00	1		1									
Azithromycin	3.00		1	1									
Clarithromycin	3.00		1	1									

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

							Test M	lethod					
		A	gar Pro	pp.	E	BACTE	С		LJ Prop	).	C	ther Te	sts
			Results			Results			Results			Result	5
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.01			00		1	1			00	-		00
Isoniazid	0.02		1	1		•	•						
Isoniazid	0.10		·	•	1	102	103					2	2
Isoniazid	0.20		39	39		.5	.ce 5		2	2		-	-
Isoniazid	0.40		~~	ΥΥ	1	30	31		-	-		1	1
Isoniazid	1.00	1	39	40		4	9. 4					•	
Isoniazid	2.00		~~	• •	1	1	2						
Isoniazid	5.00	4	1	5	2	•	2						
Rifampin	0.50	3		3	4		4						
Rifampin	1.00	44		44	7		7				2		2
Rifampin	2.00	7		7	106	1	, 107				2		2
Rifampin	5.00	5		5	100		107						
Rifampin	40.00	5		5				2		2			
Pyrazinamide	25.00	1		1				2		2			
Pyrazinamide	50.00	1		1	1		1						
Pyrazinamide	99.00				1		1						
Pyrazinamide	100.00				89	2	91				1		1
Ethambutol	2.00				UU UU	4	U I	2		2	<u> </u>		
Ethambutol	2.50	1		1	101		101	2		2			
Ethambutol	3.75	1		1	1		101 1						
Ethambutol	4.00				1		1						
Ethambutol	5.00	34	1	35	7		7				2		2
Ethambutol	6.00	1	I		· ·		'				2		2
Ethambutol	7.50	6		6	15		15						
Ethambutol	8.00	0		0	١J		ι.J				1		1
Ethambutol	10.00	12		12							1		I
Streptomycin	1.00	14		14								1	1
Streptomycin	2.00	2	40	42		99	99					1	I
Streptomycin	4.00	<u> </u>	πv	74		2	2	1	1	2		1	1
Streptomycin	6.00				1	20	21	1	I	2		1	I
Streptomycin	10.00	1	29	30		<u>ح</u> ن 1	۰ <del>د</del> ا						
Ethionamide	1.25		<b>-</b> V	00		2	2						
Ethionamide	2.50				2	<u>~</u>	2						
Ethionamide	5.00	22	3	25	6		6						
Ethionamide	10.00	5	4	<u>-</u> -9 5	Ĭ		J						
Ethionamide	40.00	Ŭ		U				1		1			
Kanamycin	2.50				1		1	•					
Kanamycin	5.00	13		13	5		5						
Kanamycin	6.00	19		19	Ĭ		U						
Kanamycin	40.00			10				1		1			
Capreomycin	1.25				2		2						
Capreomycin	2.50				2		2						
Capreomycin	5.00				7		7						
Capreomycin	10.00	19		19	'		'						
Capreomycin	40.00			13				1		1			
Capiconiyon	-10.00							I		I			

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

								Test N	1ethod							
		A	gar Pro	op.		ΒA	CTEC	;		LJ	Prop	).	C	Other	Tes	sts
			Result	S		Re	esults			Re	sult	5		Res	sults	;
DRUG	Conc.	S	R	Sum	S		R	Sum	S		R	Sum	S		R	Sum
Cycloserine	12.00	1	-	1												-
Cycloserine	25.00	1		1												
Cycloserine	30.00	12		12					1			1				
Cycloserine	50.00	1		1	1			1								
Cycloserine	60.00	2		2												
p-Aminosalicylic acid	0.50								1			1				
p-Aminosalicylic acid	1.00								1			1				
p-Aminosalicylic acid	2.00	18		18												
p-Aminosalicylic acid	4.00				2			2								
p-Aminosalicylic acid	8.00	4		4												
p-Aminosalicylic acid	10.00	3		3												
Amikacin	1.00	1		1	1			1								
Amikacin	2.00	1		1	1			1								
Amikacin	2.50				1			1								
Amikacin	4.00	3		3												
Amikacin	5.00				1			1								
Amikacin	6.00	6		6												
Amikacin	12.00	1		1												
Ofloxacin	1.00	2	1	3	1			1								
Ofloxacin	1.25				1			1								
Ofloxacin	2.00	7		7	6			6	1			1				
Ofloxacin	4.00	3		3												
Ciprofloxacin	0.25	1		1												
Ciprofloxacin	0.50	1		1												
Ciprofloxacin	1.00			3	3			3								
Ciprofloxacin	2.00	9		9	1			1								
Ciprofloxacin	2.50				1			1								
Levofloxacin	2.00				2			2								
Clofazimine	0.06				1			1								
Clofazimine	0.50				2			2								
Clofazimine	1.00	1		1												

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

	ſ						Test M	lethod					
		A	gar Pro	op.		BACTE	С		LJ Prop	).	0	ther Te	sts
			Result	•		Results	6		Results			Result	5
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Isoniazid	0.01			e u	-	1	1			••••		1	••••
Isoniazid	0.02		1	1		-	-						
Isoniazid	0.10		-	-	2	102	104					2	2
Isoniazid	0.20		39	39		5	5		2	2		_	_
Isoniazid	0.40					31	31		_	_		1	1
Isoniazid	1.00	1	39	40		4	4					-	-
Isoniazid	2.00		~ ~	17		2	2						
Isoniazid	5.00	1	4	5		2	2						
Rifampin	0.50	4		4	4		4						
Rifampin	1.00	44		44	6		6				2		2
Rifampin	2.00	7		7	107		107				_		-
Rifampin	5.00	5		5									
Rifampin	40.00	Ũ		Ū				2		2			
Pyrazinamide	25.00	1		1				_		-			
Pyrazinamide	50.00	•			1		1						
Pyrazinamide	99.00				1		1						
Pyrazinamide	100.00				90	1	91				1		1
Ethambutol	2.00				~~		Υ.		2	2	•		•
Ethambutol	2.50		1	1	3	99	102		-	-			
Ethambutol	3.75		•		Y	1	.u– 1						
Ethambutol	4.00					1	1						
Ethambutol	5.00	1	35	36		9	9					2	2
Ethambutol	6.00		1	 1		Ũ	Ũ					-	-
Ethambutol	7.50		6	6	1	17	18					1	1
Ethambutol	8.00		0	Ũ			10					1	1
Ethambutol	10.00	5	8	13		1	1						
Streptomycin	1.00	v	v	ιv		1					1		1
Streptomycin	2.00	35	5	40	101	1	102						
Streptomycin	4.00	υU	Y	TΥ	1 1		יט <i>ב</i> 1	2		2			
Streptomycin	6.00				18		18	2		2			
Streptomycin	10.00	30	1	31	10		10						
Ethionamide	1.25			Ų,	1	2	3						
Ethionamide	2.50				2	2	2						
Ethionamide	5.00	25	1	26	6		6						
Ethionamide	10.00			20 5	Ĭ		J						
Ethionamide	40.00	Ŭ		0				1		1			
Kanamycin	2.50				1		1	- '					
Kanamycin	5.00	13		13	6		6						
Kanamycin	6.00	19		13 19	Ĭ		v						
Kanamycin	40.00	10		10				1		1			
Capreomycin	1.25				3		3	1		I			
Capreomycin	2.50				2		2						
Capreomycin	5.00				7		7						
Capreomycin	10.00	20		20	'		'						
Capreomycin	40.00			20				1		1			
Capieomycin	+0.00							I		I			

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

								lethod					
		A	gar Pr	op.		BACTE	0		LJ Prop		0	ther Te	sts
			Result	S		Results	3		Results	;		Result	S
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
Cycloserine	12.00	1	-	1			-		-				-
Cycloserine	25.00	1		1									
Cycloserine	30.00	12		12				1		1			
Cycloserine	50.00	1		1	1		1						
Cycloserine	60.00	2		2									
p-Aminosalicylic acid	0.50							1		1			
p-Aminosalicylic acid	1.00							1		1			
p-Aminosalicylic acid	2.00	19		19	1		1						
p-Aminosalicylic acid	4.00				2		2						
p-Aminosalicylic acid	8.00	4		4									
p-Aminosalicylic acid	10.00	3		3									
Amikacin	1.00	1		1									
Amikacin	2.00	1		1	1		1						
Amikacin	2.50				1		1						
Amikacin	4.00	4		4									
Amikacin	5.00				1		1						
Amikacin	6.00	6		6									
Amikacin	12.00	1		1									
Ofloxacin	1.00	1	1	2		1	1						
Ofloxacin	1.25					1	1						
Ofloxacin	2.00	8		8	7		7	1		1			
Ofloxacin	2.50				1		1						
Ofloxacin	4.00	3		3									
Ofloxacin	5.00				1		1						
Ciprofloxacin	0.25	1		1									
Ciprofloxacin	0.50	1		1									
Ciprofloxacin	1.00	2		2	2		2						
Ciprofloxacin	2.00	9		9	1		1						
Ciprofloxacin	2.50				1		1						
Levofloxacin	2.00				2		2						
Clofazimine	0.06				1		1						
Clofazimine	0.50				2		2						
Clofazimine	1.00	1		1									

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

Streptomycin         10.00         22         22         1 <th1< th="">         1         1</th1<>		ſ						Test M	lethod					
Results         Results         Results         Results         Results         Results         Results         Non-200         S         R         Sum         Sum         S         R         Sum         Sum <th< td=""><td></td><td></td><td>A</td><td>gar Pro</td><td>op.</td><td>E</td><td>BACTE</td><td>С</td><td></td><td>LJ Pro</td><td>p.</td><td>0</td><td>ther Te</td><td>sts</td></th<>			A	gar Pro	op.	E	BACTE	С		LJ Pro	p.	0	ther Te	sts
DRUG         Conc.         S         R         Sum         Sum         Sum         S         R         Sum         S         R         Sum         S				-										
isoniazid         0.01         1 <th1< th="">         1         <th1< th="">         1         <th1< td=""><td>DRUG</td><td>Conc</td><td></td><td></td><td>-</td><td>S</td><td></td><td></td><td>S</td><td></td><td>-</td><td>S</td><td></td><td></td></th1<></th1<></th1<>	DRUG	Conc			-	S			S		-	S		
Isoniazid       0.10       104       104       104       22       2         Isoniazid       0.20       30       30       30       4       4       2       2       1       1         Isoniazid       0.40       0.00       30       30       3       3       1					Oum						Oum	0		Oum
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$												2		2
Isoniazid       0.20       30       30       4       4       2       2         Isoniazid       1.00       30       30       30       3       3       1       1       1         Isoniazid       5.00       3       3       3       1       1       1       1       1         Isoniazid       5.00       3       3       3       -       2       2       2       3       3       -       2 <td></td> <td></td> <td>1</td> <td></td> <td>1</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>-</td> <td></td> <td>2</td>			1		1							-		2
Isoniazid       0.40       25       25       1       1       1         Isoniazid       5.00       3       3       3       3       1       1       1         Isoniazid       5.00       3       3       3       3       1       1       1       1         Rifampin       0.50       2       2       3       3       3       2       2       2       3       3       3       1						Л		Λ	2		2			
Isoniazid       1.00       30       30       3       3       3         Isoniazid       5.00       3       3       -       -       -         Rifampin       0.50       2       2       3       3       -       -         Rifampin       1.00       35       35       7       7       2       2         Rifampin       5.00       5       5       106       106       -       2       2         Pyrazinamide       50.00       5       5       -       2       2       2         Pyrazinamide       100.00       -       1			JU		JU				2		2	1		1
isoniazid         5.00         3         3			20		30									I
Rifampin       0.50       2       2       3       3       7       7       7       2       2       2         Rifampin       2.00       5       5       106       106       2						5		5						
Rifampin     1.00     35     35     7     7     7       Rifampin     2.00     5     5     106     106     106       Rifampin     40.00     2     2     2       Pyrazinamide     50.00     5     5     2     2       Pyrazinamide     50.00     1     1     1       Pyrazinamide     100.00     87     3     90     1     1       Pyrazinamide     100.00     87     3     90     1     1       Ethambutol     2.00     1     1     1     1       Ethambutol     2.00     1     1     1     1       Ethambutol     2.00     1     1     1     1       Ethambutol     5.00     26     26     7     7     2     2       Ethambutol     5.00     5     1     6     15     15       Ethambutol     7.00     5     1     6     15     15       Streptomycin     1.00     8     8     1     1     1       Streptomycin     1.00     2     2     2     2       Streptomycin     1.00     2     2     2       Streptomycin     1.00 <td></td> <td></td> <td></td> <td></td> <td></td> <td>2</td> <td></td> <td>2</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>						2		2						
Rifampin         2.00         5         5         106         106           Rifampin         40.00         5         5         5         2         2           Pyrazinamide         50.00         1         1         1         1         1           Pyrazinamide         99.00         87         3         90         1         1           Pyrazinamide         100.00         87         3         90         1         1           Ethambutol         2.00         2         2         2         1         1           Ethambutol         3.75         1 <td></td> <td>2</td> <td></td> <td>2</td>												2		2
Rifampin         5.00         5         5         2         2           Rifampin         40.00         1         1         1         2         2           Pyrazinamide         50.00         1         1         1         1         1           Pyrazinamide         100.00         87         3         90         1         1           Pyrazinamide         100.00         87         3         90         1         1           Ethambutol         2.50         1         1         102         102         1         1           Ethambutol         3.75         1         1         1         1         1         1         1         1           Ethambutol         5.00         26         26         7         7         2         2         2           Ethambutol         6.00         1         1         1         1         1         1         1         1           Ethambutol         7.00         5         1         6         15         15         1         1         1         1         1         1         1         1         1         1         1         1         1<												2		2
Rifampin         40.00         2         2         2           Pyrazinamide         50.00         1<						100		100						
Pyrazinamide         50.00         1 <th1< th="">         1         1</th1<>			Э		Э				0		0			
Pyrazinamide         99.00         1 <th1< th="">         1         1</th1<>								4	2		2			
Pyrazinamide         100.00         87         3         90         1         1           Ethambutol         2.50         1         1         102         102         2	,													
Ethambutol         2.00         2         2         2           Ethambutol         2.50         1         1         102         102         1	5						~							
Ethambutol         2.50         1         1         102         102           Ethambutol         3.75         1						87	3	90				1		1
Ethambutol       3.75       1       <									2		2			
Ethambutol       4.00			1		1									
Ethambutol       5.00       26       26       7       7       7       2       2         Ethambutol       6.00       1 <t< td=""><td></td><td></td><td></td><td></td><td></td><td>-</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>						-								
Ethambutol       6.00       1       1       1       15       15       1												_		_
Ethambutol       7.50       5       1       6       15       15       1			fofofofofofofofofofofofofofofof			7		7				2		2
Ethambutol       8.00       8       8       1       1       1         Streptomycin       1.00       33       33       99       99       1       1       1       1         Streptomycin       2.00       33       33       99       99       1														
Ethambutol         10.00         8         8         1 <th1< th="">         1         1         &lt;</th1<>			5	1	6	15		15						
Streptomycin         1.00         1												1		1
Streptomycin         2.00         33         33         99         99           Streptomycin         4.00         1         1         2         2           Streptomycin         6.00         18         18         18         2           Streptomycin         10.00         22         22         2         2           Ethionamide         1.25         1         1         1         1           Ethionamide         10.00         3         3         -         1         1           Ethionamide         10.00         3         3         -         1         1           Ethionamide         10.00         3         3         -         1         1           Kanamycin         5.00         8         8         4         4         -           Kanamycin         6.00         16         16         16         -			8		8									
Streptomycin       4.00       1       1       1       2       2         Streptomycin       10.00       22       22       18       11       <												1		1
Streptomycin         6.00         18         18         18           Streptomycin         10.00         22         23         24 <td< td=""><td></td><td></td><td>33</td><td></td><td>33</td><td>99</td><td></td><td>99</td><td></td><td></td><td></td><td></td><td></td><td></td></td<>			33		33	99		99						
Streptomycin         10.00         22         22           Ethionamide         1.25         1         1           Ethionamide         5.00         19         19         6         6           Ethionamide         10.00         3         3         1         1           Ethionamide         10.00         3         3         1         1           Ethionamide         40.00         1         1         1         1           Kanamycin         5.00         8         8         4         4         1         1           Kanamycin         6.00         16         16         1         1         1         1           Capreomycin         1.25         1         1         1         1         1         1           Capreomycin         5.00         6         6         6         6         6         6         6         6         6         1 <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>2</td> <td></td> <td>2</td> <td></td> <td></td> <td></td>									2		2			
Ethionamide       1.25       1       1       1         Ethionamide       5.00       19       19       6       6         Ethionamide       10.00       3       3       1       1         Ethionamide       40.00       1       1       1         Kanamycin       5.00       8       8       4       4         Kanamycin       6.00       16       16       1       1         Kanamycin       40.00       1       1       1       1         Capreomycin       1.25       1       1       1       1         Capreomycin       5.00       14       14       1       1       1         Capreomycin       10.00       14       14       1       1       1       1         Cycloserine       25.00       1       1       1       1       1       1       1         Cycloserine       30.00       7       7       1       1       1       1	Streptomycin	6.00				18		18						
Ethionamide       5.00       19       19       6       6       6         Ethionamide       10.00       3       3       1       1       1         Ethionamide       40.00       8       8       4       4       1       1         Kanamycin       5.00       8       8       4       4       1       1         Kanamycin       6.00       16       16       1       1       1         Kanamycin       40.00       1       1       1       1         Capreomycin       1.25       1       1       1       1         Capreomycin       5.00       14       14       1       1       1         Capreomycin       10.00       14       14       1       1       1       1         Cycloserine       25.00       1       1       1       1       1       1       1         Cycloserine       30.00       7       7       1       1       1       1	Streptomycin	10.00	22		22									
Ethionamide       10.00       3       3       1       1       1         Ethionamide       40.00       8       8       4       4       1       1         Kanamycin       5.00       8       8       4       4       4       4       4         Kanamycin       6.00       16       16       16       1       1       1         Kanamycin       40.00       16       16       1       1       1       1         Capreomycin       1.25       1       1       1       1       1       1         Capreomycin       5.00       14       14       14       1       1       1       1         Capreomycin       10.00       14       14       14       1       1       1       1         Cycloserine       25.00       1       1       1       1       1       1       1         Cycloserine       30.00       7       7       1       1       1       1	Ethionamide	1.25				1		1						
Ethionamide         40.00         1         1         1           Kanamycin         5.00         8         8         4         4         4           Kanamycin         6.00         16         16         1         1         1           Kanamycin         40.00         16         16         1         1         1           Kanamycin         40.00         1         1         1         1         1           Capreomycin         1.25         1         1         1         1         1           Capreomycin         5.00         6         1	Ethionamide	5.00	19		19	6		6						
Kanamycin         5.00         8         8         4         4           Kanamycin         6.00         16         16         1         1         1           Kanamycin         40.00         16         16         1         1         1         1           Kanamycin         40.00         1         1         1         1         1         1           Capreomycin         1.25         1         1         1         1         1         1           Capreomycin         5.00         6         7         7         1	Ethionamide	10.00	3		3									
Kanamycin       6.00       16       16       16       1       1         Kanamycin       40.00       1       1       1       1       1         Capreomycin       1.25       1       1       1       1       1         Capreomycin       5.00       6       6       6       6       6         Capreomycin       10.00       14       14       14       14       14       14       1       <	Ethionamide	40.00							1		1			
Kanamycin       6.00       16       16       16       1       1         Kanamycin       40.00       1       1       1       1       1         Capreomycin       1.25       1       1       1       1       1         Capreomycin       5.00       6       6       6       6       6         Capreomycin       10.00       14	Kanamycin	5.00	8		8	4		4						
Kanamycin       40.00       1       1       1         Capreomycin       1.25       1       1       1         Capreomycin       5.00       6       6       6         Capreomycin       10.00       14       14       14       14         Capreomycin       40.00       1       1       1       1         Cycloserine       25.00       1       1       1       1       1         Cycloserine       30.00       7       7       1       1       1         Cycloserine       50.00       1       1       1       1       1       1	Kanamycin		16		16									
Capreomycin         1.25         1         1         1           Capreomycin         5.00         6         6         6           Capreomycin         10.00         14         14         14         1           Capreomycin         10.00         14         14         1         1         1           Capreomycin         40.00         1         1         1         1         1           Cycloserine         25.00         1         1         1         1         1         1           Cycloserine         30.00         7         7         1         1         1         1           Cycloserine         50.00         1         1         1         1         1         1         1         1	Kanamycin	40.00							1		1			
Capreomycin         5.00         6         6         6         6         6         7         7         1 <th1< th="">         1         <th1< th=""> <t< td=""><td></td><td></td><td></td><td></td><td></td><td>1</td><td></td><td>1</td><td></td><td></td><td></td><td></td><td></td><td></td></t<></th1<></th1<>						1		1						
Capreomycin         10.00         14         14           Capreomycin         40.00         1         1           Cycloserine         25.00         1         1         1           Cycloserine         30.00         7         7         1         1           Cycloserine         50.00         1         1         1         1						6		6						
Capreomycin         40.00         1         1           Cycloserine         25.00         1         1         1           Cycloserine         30.00         7         7         1         1           Cycloserine         50.00         1         1         1         1			14		14									
Cycloserine         25.00         1         1           Cycloserine         30.00         7         7         1         1           Cycloserine         50.00         1         1         1         1         1									1		1			
Cycloserine         30.00         7         7         1         1           Cycloserine         50.00         1         1         1         1         1			1		1									
Cycloserine 50.00 1 1 1 1 1									1		1			
			1			1		1	•		•			
	Cycloserine	60.00	1		1									

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

							Test N	/lethod					
		A	Agar Pro	op.		BACTE	0		LJ Prop		0	ther Te	sts
			Result	S		Results	;		Results	i		Results	6
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum	S	R	Sum
p-Aminosalicylic acid	0.50							1		1			
p-Aminosalicylic acid								1		1			
p-Aminosalicylic acid	2.00	12		12									
p-Aminosalicylic acid					2		2						
p-Aminosalicylic acid	8.00	3		3									
p-Aminosalicylic acid				2									
Amikacin	1.00				1		1						
Amikacin	2.00				1		1						
Amikacin	4.00	2		2									
Amikacin	5.00				1		1						
Amikacin	6.00	5		5									
Amikacin	12.00	1		1									
Ofloxacin	1.00		1	1									
Ofloxacin	2.00	6		6	3	2	5		1	1			
Ofloxacin	4.00	2		2									
Ciprofloxacin	1.00	1		1	2		2						
Ciprofloxacin	2.00			6	1		1						
Levofloxacin	2.00				2		2						
Clofazimine	0.06				1		1						
Clofazimine	1.00	1		1									

					Те	est Meth	nod			
			Agar Pro	p.		BACTE		LJ	Propor	tion
			Results	-		Results		-	Result	
DRUG	Conc.	S	R	Sum	S	R	Sum	S	R	Sum
Amikacin	4.00	0	1	1	5		Sum	0		Sum
Amikacin	<del>4</del> .00 5.00	1	I	1						
Amikacin	6.00	1		1						
Amikacin	12.00	1		1						
Clarithromycin	0.12	1		1						
Clarithromycin	1.00	I		I				1		1
-					4		4	1		1
Clarithromycin	2.00	0		0	1		1			
Clarithromycin	3.00	3	4	3						
Capreomycin	8.00		1	1						
Ciprofloxacin	1.00	_	2	2						
Ciprofloxacin	2.00	5		5						
Ethambutol	2.00					_	_		1	1
Ethambutol	2.50		1	1		5	5			
Ethambutol	5.00		16	16					1	1
Ethambutol	7.50		1	1		2	2			
Ethambutol	10.00	1	3	4						
Isoniazid	0.10					5	5			
Isoniazid	0.20		16	16					2	2
Isoniazid	1.00		1	1						
Isoniazid	5.00	1	1	2						
Kanamycin	6.00	1		1						
Kanamycin	8.00		1	1						
Levofloxacin	0.60	1		1						
Ofloxacin	1.00	2		2						
Ofloxacin	2.00	1		1						
p-Aminosalicylic acid	2.00		1	1						
Pyrazinamide	100.00								1	1
Pyrazinamide	400.00							1		1
Rifabutin	0.10	1		1						
Rifabutin	1.00	2		2						
Rifabutin	2.00	1		1	1		1			
Rifabutin	40.00							1		1
Rifampin	1.00	6	16	22						•
Rifampin	2.00	•			10		10			
Rifampin	5.00	3		3					1	1
Rifampin	40.00	Ũ		5					1	1
Rifampin	50.00								1	1
Streptomycin	2.00	9	9	18	6	1	7		•	•
Streptomycin	4.00	Ũ	Ŭ		5	•	·		1	1
Streptomycin	10.00	2		2				1		1
Streptomycin	16.00	1		1				'		
Ethionamide	1.00	1		1						
Ethionamide	5.00	1		1						
Ethionamide	5.00 8.00	1		1						
	0.00	I		I						

## Table 2. Participant Results for Culture E, M. kansasii

# Table 3. Minimum Inhibitory Concentrations for Culture E, M. kansasii

DRUG	Test Method	MIC	S	R	Other	Sum
Amikacin	Agar proportion	<5.00	1			1
Amikacin	Microtiter	<0.50	1			1
Amikacin	Microtiter	<1.00	1			1
Amikacin	Microtiter	4.00	1			1
Azithromycin	Microtiter	>4.00		1		1
Azithromycin	Microtiter	<8.00	1			1
Capreomycin	Agar proportion	16.00	1			1
Ciprofloxacin	Microtiter	<u>&lt;</u> 1.00	2			2
Ciprofloxacin	Microtiter	2.00			1	1
Clarithromycin	Agar proportion	<0.12	1			1
Clarithromycin	Microtiter	<u>&lt;</u> 0.25	2			2
Clarithromycin	Microtiter	>0.13		1		1
Clarithromycin	Microtiter	<0.50	1			1
Clofazimine	Microtiter	0.50			1	1
Ethambutol	Agar proportion	>2.50		1		1
Ethambutol	Microtiter	4.00			1	1
Ethambutol	Microtiter	8.00		1		1
Ethionamide	Agar proportion	<1.00	1			1
Ethionamide	Agar proportion	<4.00	1			1
Isoniazid	Agar proportion	<1.00	1			1
Isoniazid	Microtiter	<0.12	1			1
Isoniazid	Microtiter	1.00	1			1
Kanamycin	Agar proportion	16.00	1			1
Levofloxacin	Agar proportion	<0.60	1			1
Levofloxacin	Microtiter	<0.25			1	1
Minocycline	Microtiter	2.00			1	1
Minocycline	Microtiter	4.00			1	1
Ofloxacin	Microtiter	>0.50		1		1
Ofloxacin	Microtiter	<1.00	1			1
Rifabutin	Agar proportion	<0.10	1			1
Rifabutin	Microtiter	>4.00		1		1
Rifabutin	Microtiter	<0.06	1			1
Rifabutin	Microtiter	<0.12	1			1
Rifabutin	Microtiter	<8.00	1			1
Rifampin	Agar proportion	<1.00	1			1
Rifampin	Agar proportion	4.00	1			1
Rifampin	Microtiter	0.50	1			1
Rifampin	Microtiter	4.00		1		1
Streptomycin	Agar proportion	<8.00	1			1
Sulfamethoxazole	Microtiter	<4.00	1			1
Trimethoprim-Sulfamethoxazole	Microtiter	< 0.06	1			1