



Drug resistance in Canada

2003

Reported susceptibility results of the **Canadian Tuberculosis Laboratory Surveillance System**



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Tuberculosis

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INTRODUCTION

Tuberculosis Prevention and Control (TBPC) at the Centre for Infectious Disease Prevention and Control, in collaboration with the Canadian Tuberculosis Laboratory Technical Network and participating laboratories (representing all provinces and territories) in the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) (Appendix 2), established a laboratory-based national surveillance system in 1998 to monitor tuberculosis (TB) drug resistance patterns in Canada.

Laboratories report their results on anti-tuberculous drug susceptibility testing to TBPC for every patient that they receive a specimen or an isolate from each calendar year. TBPC subsequently produces an annual report. This report presents 2003 and adjusted 2002 (to reflect duplicate removal and late reporting) drug susceptibility data for TB isolates across Canada as of March 10, 2004.

METHODOLOGY

TBPC maintains a computerized database containing drug susceptibility test results of *Mycobacterium tuberculosis* (MTB) and MTB complex (MTBC) isolates. Isolates identified as *M.bovis* BCG are included in the CTBLSS but are excluded from this report. Results of susceptibility testing for second-line anti-tuberculous drugs, although reported, are also not included in this report. Data are collected either through manual completion of a standard reporting form (Appendix 3) or by electronic transmission. Information collected includes sex, year of birth, province/territory from which the report originates, province/territory from which the specimen originates and susceptibility results. TBPC makes every effort to eliminate duplicate specimens; only the most recent susceptibility results for a given patient in the current reporting year are included for analysis.

Newfoundland and Labrador identifies the species and tests all isolates for drug resistance in Newfoundland. Some provinces identify the species and test their own isolates and those of other provinces/territories (British Columbia: British Columbia and Yukon Territory isolates; Alberta: Alberta and Northwest Territories isolates; Quebec: Quebec and New Brunswick isolates; Ontario: Ontario and Nunavut isolates; Nova Scotia: Nova Scotia and Prince Edward Island isolates). Saskatchewan tests for drug resistance on all MTBC isolates. Other provinces and territories report results at the species level.

Laboratories generally perform routine susceptibility testing of MTB or MTBC to first-line anti-tuberculous drugs using the radiometric proportion method (Bactec[®]). Saskatchewan uses MGIT[®] 960 and all others use Bactec[®] 460. Table A lists the first-line anti-tuberculosis drugs and the concentrations in mg/L used by the participating laboratories.

As noted in Table A, the number and specific first-line anti-tuberculous drugs that are subject to routine susceptibility testing differ among the provinces and territories. Accordingly, the number of isolates included in the descriptive analyses varies.

Table A: Minimal inhibitory concentrations for routine testing of first-line anti-tuberculosis drugs **Anti-TB drugs** MIC (mg/L) Comments Isoniazid (INH) 0.1 2.0 Rifampin (RMP) Ethambutol (EMB) 2.5 British Columbia uses an MIC of 4.0 mg/L. Routine testing is not performed for isolates from Streptomycin (SM) 2.0 Quebec, Nova Scotia, New Brunswick, Prince Edward Island. Routine testing is not performed for isolates from 100.0 Pyrazinamide (PZA) British Columbia, Saskatchewan and the Yukon Territory.

In 2003, a total of nine laboratories participated in the proficiency for anti-microbial susceptibility testing of *M. tuberculosis* to anti-tuberculous first line drugs conducted by the National Reference Centre for Mycobacteriology. Six strains of *M. tuberculosis* were submitted for testing. Participant results are presented in Appendix 2.

▶ RESULTS

Of the 1,379 isolates in 2003 included for analysis, 173 (12.5%) were resistant to one or more first-line anti-tuberculous drug(s). Resistance to INH was the most common type of drug resistance (9.3%). Twenty isolates (1.5%) were multi-drug resistant tuberculosis (MDR-TB) strains (defined as resistance to at least INH and RMP), of which seven isolates demonstrated resistance to four or five first-line anti-tuberculous drugs tested. Reporting of MDR-TB isolates was from British Columbia, Alberta, Manitoba, Ontario and Quebec. Five provinces and territories (Yukon Territory, Northwest Territories, Nunavut, Nova Scotia and Prince Edward Island,) reported that all isolates tested were susceptible to all the first-line anti-tuberculous drugs.

Demographic information on the individual patients from whom the isolates originated is limited in this laboratory-based surveillance system. Of the 1,354 isolates for which the year of birth and sex reporting was complete, 37% were between the ages 25 and 44. Males accounted for 53% of all the isolates and 57% of the drug resistant isolates.

DISCUSSION

The number of reported TB isolates in 2003 was relatively unchanged from the previous year (1,420 in 2002 to 1379 in 2003 isolates). In addition, the percentage of isolates demonstrating any type of drug resistance was also unchanged between the two reporting years (12.6% in 2002 to 12.5% in 2003) and the proportion of isolates classified as MDR-TB was identical (1.5%) in both years. Overall, levels of TB drug resistance have shown no significant difference since the inception of this reporting system in 1998.

Over 75% of the reported laboratory TB isolates in Canada in 2003 originated from three provinces. Ontario, Quebec and British Columbia have consistently reported the majority of isolates and MDR-TB in the six years of data collection. Since the initiation of this laboratory-based surveillance system Saskatchewan, the Atlantic Provinces, the Yukon and Northwest Territories have not reported any MDR-TB isolates.

The results observed to date in this surveillance system are consistent with international data. In the latest report of the global TB drug resistance surveillance project jointly conducted by the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (IUATLD), the median prevalence of TB drug resistance among the participating countries was 1.1% for new cases and 7% for previously treated cases (as compared with 12.5% overall in Canada). The median prevalence of MDR-TB was 10.2% for new cases and 18.4% for previously treated cases (as compared with 1.5% overall in Canada).

LIMITATIONS

Sensitivity testing for first-line anti-TB drugs is not uniform across the country. Therefore, there are limitations in interpreting the data, particularly the percentage of isolates that are resistant to SM and PZA.

More epidemiological information on the TB cases from which the isolates were submitted would be desirable to critically examine drug resistance patterns in Canada. Demographic information is sparse; only sex and year of birth are routinely reported in this surveillance system. As well, no differentiation can be made between primary and secondary/acquired drug resistance from the data.

CONCLUSIONS

With growing worldwide concern regarding TB drug resistance, this surveillance system is vital in providing the necessary data in a timely fashion to monitor trends in TB drug resistance in Canada. The surveillance data collected to date indicate that the prevalence of TB drug resistance in this country is similar to that in the overall global situation.

REFERENCE

 The WHO/IUATLD Global Project on Anti-tuberculosis Drug Resistance Surveillance (1999-2002). Anti-tuberculosis drug resistance in the world. Report No. 3. (WHO/CDS/TB/2000.278). Geneva: World Health Organization, 2004.

Figure 1 Reported TB drug resistance in Canada by province/territory – 2003

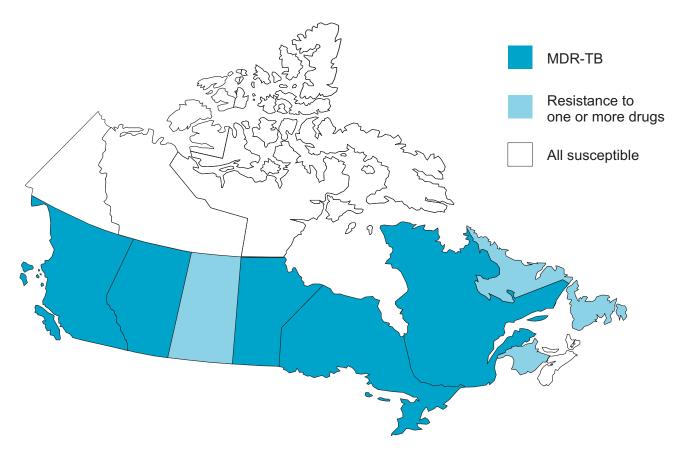
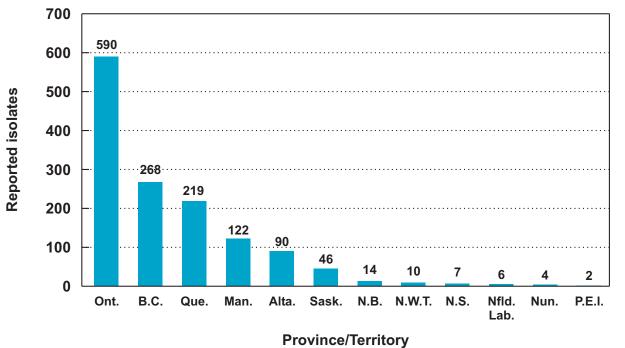
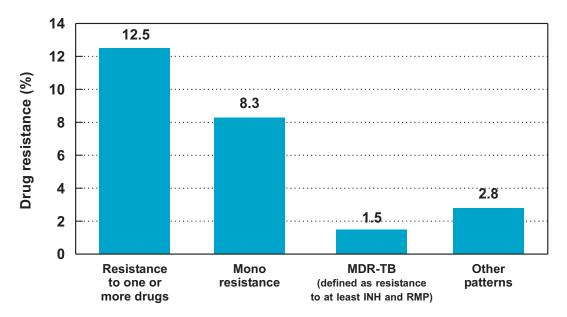


Figure 2 Reported MTB isolates in Canada by province/territory - 2003

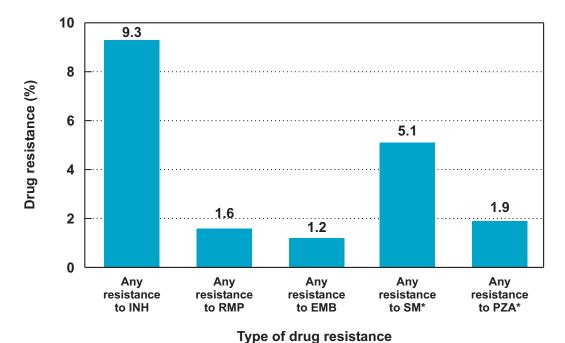


► Figure 3 Overall pattern of reported TB drug resistance in Canada – 2003



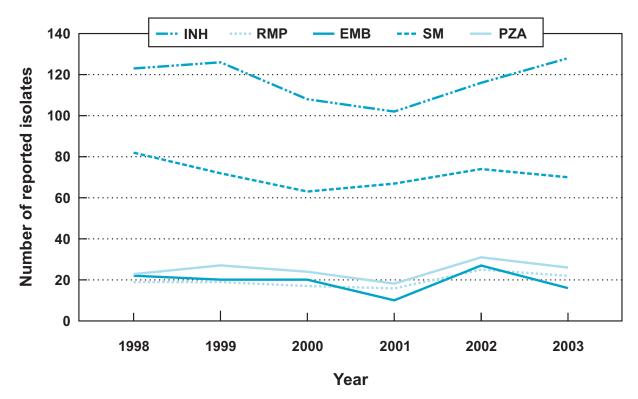
Type of drug resistance

► Figure 4 Reported TB drug resistance in Canada by type of drug – 2003



* SM and PZA are not part of routine first-line drug testing in some provinces/territories.

► Figure 5 Any resistance to first-line anti-TB drugs in Canada – 1998-2003



► Figure 6
Overall pattern of reported TB drug resistance in Canada – 1998-2003

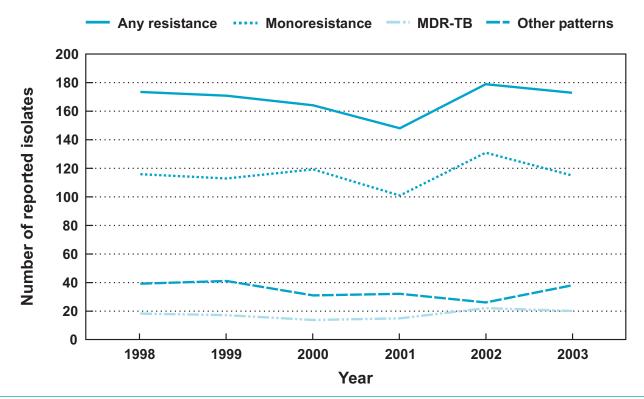


Table 1. Overall pattern of reported TB drug resistance in Canada – 1998-2003	eported TB dru	ıg resistance	in Canada – 19	98-2003		
	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested	1,461 (100.0)	1,415 (100.0)	1,491 (100.0)	1,475 (100.0)	1,420 (100.0)	1,379 (100.0)
Isolates susceptible	1,288 (88.2)	1,243 (87.8)	1,323 (88.7)	1,327 (90)	1,241 (87.4)	1,206 (87.5)
Any resistance to INH	123 (8.4)	127 (9)	111 (7.4)	102 (6.9)	116 (8.2)	128 (9.3)
Any resistance to RMP	19 (1.3)	20 (1.4)	18 (1.2)	16 (1.1)	25 (1.8)	22 (1.6)
Any resistance to EMB	22 (1.5)	20 (1.4)	21 (1.4)	10 (0.7)	27 (1.9)	16 (1.2)
Any resistance to SM	82 (5.6)	72 (5.1)	65 (4.4)	68 (4.6)	74 (5.2)	70 (5.1)
Any resistance to PZA	23 (1.6)	27 (1.9)	24 (1.6)	20 (1.4)	31 (2.2)	26 (1.9)
Resistance to one or more drugs	173 (11.8)	172 (12.2)	168 (11.3)	148 (10)	179 (12.6)	173 (12.5)
Monoresistance	116 (7.9)	113 (8)	121 (8.1)	101 (6.8)	131 (9.2)	115 (8.3)
MDR-TB*	18 (1.2)	18 (1.3)	15 (1)	15 (1)	22 (1.5)	20 (1.5)
Other patterns	39 (2.7)	41 (2.9)	32 (2.1)	32 (2.2)	26 (1.8)	38 (2.8)

 * MDR-TB is defined as resistance to at least INH and RMP.

Table 2. Reported MTB isolates by "reporting" and "originating" province/territory, Canada – 2003	rted MTB	isolate	s by "re	porting	g" and	"origin	ating"	provind	:e/terri	tory, Ca	anada -	- 2003		
						ŏ	iginating	Originating Province/Territory	:e/Territo	2				
Reporting Province	CANADA	Nfld. Lab.	P.E.I	N.S.	Ä.B.	Que	Ont.	Man.	Sask.	Alta.	B.C.	Yukon	T.W.N	Nun.
Number of isolates	1,379	9	7	7	14	219	590	122	46	06	268	7	10	4
Nfid. Lab.	9	9	ı	ı	ı	ı	ı	ı	ı	ı	ı	ı	ı	ı
N.S.	თ	ı	7	7	ı	ı	ı	ı	ı		1	ı	ı	ı
N.B.	41	ı	ı	1	4	ı	ı	ı	ı	ı	1	ı	ı	ı
Que.	219	ı	ı	1	ı	219	1	ı	ı	ı	1	ı	ı	ı
Ont.	593	-	ı	ı	-	-	590		ı	-	ı		1	3
Мап.	122	ı	ı	ı	ı	ı	ı	122	ı	-	1	ı	ı	ı
Sask.	42	ı	ı	ı	ı	ı	ı		42	-	ı	1	ı	
Alta.	104	-	ı	ı	1	ı	ı	1	4	90	ı	ı	10	ı
B.C.	269	ı	ı	ı	ı	ı	ı	ı	ı	-	268	7	ı	ı
Nun.	←	ı	ı	1	ı	ı	ı	ı	ı	ı	1	ı	ı	~

Nun. 4 N.W.T 10 Yukon B.C. 268 2 Alta. 90 Originating Province/Territory Sask. 46 Table 3. Reported MDR-TB* isolates by province/territory, Canada - 2003 Man. 122 Ont. 590 12 က $\overline{}$ 2 4 Que 219 N.B. 4 N.S. _ P.E.I 2 Nfld. Lab 9 CANADA 1,379 20 2 _ α က INH, RMP, SM, EMB & PZA INH, RMP, EMB & PZA Total number of MDR-TB* isolates INH, RMP & EMB INH, RMP & PZA Total number of isolates tested INH, RMP & SM INH & RMP

* MDR-TB is defined as resistance to at least INH and RMP.

Table 4. Reported TB drug resistance by gender and age group, Canada - 2003 **Number of Isolates Any Resistance** MDR-TB* Age Group No. (%) No. (%) No. (%) 1,379 (100) 173 (100) 20 (100) Total Males 2 (0.1)(0.0)(0.0)Females (0.7)2 (1.2) (0.0)0-4 Unknown (0.0)-(0.0)(0.0)**Total** 11 (0.8) 2 (1.2) (0.0)Males 4 (0.3)-(0.0)(0.0)**Females** (0.6)(0.0)(0.0)8 5-14 (0.0)Unknown -(0.0)(0.0)Total (0.9)- (0.0) (0.0)12 Males 75 (5.4)10 (5.8) (0.0)**Females** 76 (5.5) (20.0)15 (8.7) 15-24 Unknown 3 (0.2) -(0.0)(0.0)Total 154 (11.2) 25 (14.5) 4 (20.0) Males 126 21 (12.1) 6 (9.1)(30.0)**Females** 135 (9.8) 20 (11.6) 3 (15.0) 25-34 Unknown 14 (1.0) -(0.0)(0.0)Total 275 (19.9) 41 (23.7) (45.0)Males 19 (11.0) 131 (9.5)2 (10.0)**Females** 1 (5.0) 99 (7.2) 13 (7.5) 35-44 Unknown 3 (0.2) -(0.0)(0.0)3 (15.0) **Total** 233 (16.9) 32 (18.5) Males 118 (8.6)17 (0.0)(9.8)**Females** 53 (3.8) 6 (3.5) (0.0)45-54 Unknown 6 (0.4) 1 (0.6)(0.0)**Total** 177 (12.8) 24 (13.9) (0.0)Males 76 (5.5)8 (4.6)1 (5.0)**Females** 61 (4.4) 4 (2.3) 1 (5.0)55-64 Unknown 3 (0.2)(0.0)(0.0)**Total** 140 (10.2) 12 (6.9) 2 (10.0) Males 88 (6.4)11 (6.4)2 (10.0) **Females** 55 (4.0)6 (3.5)(0.0)65-74 Unknown 6 (0.4)(0.0)(0.0)Total 149 (10.8) 17 (9.8) (10.0)Males 110 (8) 12 (6.9) (0.0)**Females** (0.0)83 (6)7 (4) 75+ (0.0)Unknown 10 (0.7)(0.0)Total 203 (14.7) 19 (11.0) -(0.0)Males 6 (0.4)(0.0)(0.0)**Females** 8 (0.6)(0.0)(0.0)Unknown Unknown 11 (8.0)1 (0.6)(0.0)**Total** 25 1 (1.8)(0.6)(0.0)Males 736 (53.4)98 (56.6) 11 (55.0)Total **Females** 587 (42.6) 73 (42.2) 9 (45.0)Unknown 2 (1.2) 0 (0.0) 56 (4.1) * MDR-TB is defined as resistance to at least INH and RMP.

Table 5. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Alberta – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, SM, EMB and PZA	119 (100.0)	118 (100.0)	104 (100.0)	91 (100.0)	108 (100.0)	90 (100.00)
Isolates susceptible	107 (89.9)	111 (94.1)	92 (88.5)	79 (86.8)	94 (87.0)	74 (82.2)
Isolates resistant to one or more drugs	12 (10.1)	7 (5.9)	12 (11.5)	12 (13.2)	14 (13.0)	16 (17.8)
Monoresistance	9 (7.6)	6 (5.1)	7 (6.7)	8 (8.8)	12 (11.1)	10 (11.1)
INH	4 (3.4)	2 (1.7)	2 (1.9)	5 (5.5)	6 (5.6)	5 (5.6)
EMB	- (0.0)	- (0.0)	1 (1.0)	- (0.0)	- (0.0)	- (0.0)
SM	5 (4.2)	4 (3.4)	3 (2.9)	3 (3.3)	6 (5.6)	3 (3.3)
PZA	- (0.0)	- (0.0)	1 (1.0)	- (0.0)	- (0.0)	2 (2.2)
MDR-TB*	1 (0.8)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (1.1)
INH & RMP	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (1.1)
INH, SM, EMB, RMP & PZA	1 (0.8)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
Other Patterns	2 (1.7)	1 (0.8)	5 (4.8)	4 (4.4)	2 (1.9)	5 (5.6)
INH & SM	1 (0.8)	1 (0.8)	3 (2.9)	2 (2.2)	1 (0.9)	4 (4.5)
INH, SM & EMB	- (0.0)	- (0.0)	1 (1.0)	- (0.0)	- (0.0)	1 (1.1)
INH, SM & PZA	1 (0.8)	- (0.0)	1 (1.0)	2 (2.2)	1 (0.9)	- (0.0)
* MDR-TB is defined as resistance to at least IN	IH and RMP.					

Table 6. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, British Columbia – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, SM and EMB**	237 (100.0)	244 (100.0)	277 (100.0)	331 (100.0)	259 (100.0)	268 (100.0)
Isolates susceptible	212 (89.5)	224 (91.8)	245 (88.4)	296 (89.4)	228 (88.0)	239 (89.2)
Isolates resistant to one or more drugs	25 (10.5)	20 (8.2)	32 (11.6)	35 (10.6)	31 (12)	29 (10.8)
Monoresistance	17 (7.2)	15 (6.1)	23 (8.3)	22 (6.6)	25 (9.7)	17 (6.3)
INH	14 (5.9)	11 (4.5)	13 (4.7)	12 (3.6)	12 (4.6)	11 (4.1)
EMB	- (0.0)	1 (0.4)	1 (0.4)	- (0.0)	2 (0.8)	1 (0.4)
RMP	1 (0.4)	1 (0.4)	1 (0.4)	1 (0.3)	- (0.0)	- (0.0)
SM	2 (0.8)	2 (0.8)	8 (2.9)	9 (2.7)	8 (3.1)	5 (1.9)
PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
MDR-TB*	2 (0.8)	1 (0.4)	5 (1.8)	8 (2.4)	2 (0.8)	5 (1.9)
INH & RMP	- (0.0)	- (0.0)	- (0.0)	4 (1.2)	- (0.0)	1 (0.4)
INH, RMP & EMB	- (0.0)	- (0.0)	1 (0.4)	- (0.0)	- (0.0)	- (0.0)
INH, RMP & SM	1 (0.4)	- (0.0)	2 (0.7)	2 (0.6)	- (0.0)	1 (0.4)
INH, RMP & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.4)
INH , RMP, EMB & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.4)	1 (0.4)
INH, RMP, SM & EMB	1 (0.4)	1 (0.4)	2 (0.7)	1 (0.3)	- (0.0)	- (0.0)
INH, RMP, SM, EMB & PZA	- (0.0)	- (0.0)	- (0.0)	1 (0.3)	1 (0.4)	1 (0.4)
Other Patterns	6 (2.5)	4 (1.6)	4 (1.4)	5 (1.5)	4 (1.5)	7 (2.6)
INH & EMB	1 (0.4)	1 (0.4)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
INH & SM	5 (2.1)	2 (0.8)	2 (0.7)	5 (1.5)	3 (1.2)	6 (2.2)
INH & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.4)	1 (0.4)
INH, SM & EMB	- (0.0)	1 (0.4)	2 (0.7)	- (0.0)	- (0.0)	- (0.0)

^{*} MDR-TB is defined as resistance to at least INH and RMP.

^{**} Routine testing for PZA not conducted

Table 7. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Manitoba – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB, SM and PZA**	106 (100.0)	100 (100.0)	102 (100.0)	110 (100.0)	114 (100.0)	122 (100.0)
Isolates susceptible	98 (92.5)	89 (89.0)	94 (92.2)	101 (91.8)	106 (93.0)	114 (93.4)
Isolates resistant to one or more drugs	8 (7.5)	11 (11.0)	8 (7.8)	9 (8.2)	8 (7.0)	8 (6.6)
Monoresistance	4 (3.8)	6 (6.0)	6 (5.9)	6 (5.5)	4 (3.5)	7 (5.7)
INH	2 (1.9)	3 (3.0)	6 (5.9)	2 (1.8)	3 (2.6)	3 (2.5)
SM**	2 (1.9)	3 (3.0)	- (0.0)	4 (3.6)	- (0.0)	3 (2.5)
PZA***	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.9)	1 (0.8)
MDR-TB*	2 (1.9)	2 (2.0)	- (0.0)	2 (1.8)	3 (2.6)	1 (0.8)
INH & RMP	- (0.0)	1 (1.0)	- (0.0)	1 (0.9)	1 (0.9)	1 (0.8)
INH, EMB, RMP & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.9)	- (0.0)
INH, EMB & RMP	1 (0.9)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
INH, SM, EMB, RMP & PZA	1 (0.9)	- (0.0)	- (0.0)	1 (0.9)	1 (0.9)	- (0.0)
INH, SM, RMP & PZA	- (0.0)	1 (1.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
Other Patterns	2 (1.9)	3 (3.0)	2 (2.0)	1 (0.9)	1 (0.9)	- (0.0)
INH & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.9)	- (0.0)
INH & SM	2 (1.9)	1 (1.0)	2 (2.0)	1 (0.9)	- (0.0)	- (0.0)
INH, SM & EMB	- (0.0)	1 (1.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
INH, SM & PZA	- (0.0)	1 (1.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)

^{*} MDR-TB is defined as resistance to at least INH and RMP

^{**} Routine testing for SM not conducted for 2002.

^{***} Includes *M. bovis* isolates: 1 for 2002

Table 8. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, New Brunswick – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB and PZA*	10 (100.0)	12 (100.0)	9 (100.0)	10 (100.0)	10 (100.0)	14 (100.0)
Isolates susceptible	9 (90.0)	12 (100.0)	9 (100.0)	10 (100.0)	9 (90.0)	13 (92.9)
Isolates resistant to one or more drugs	1 (10.0)	- (0.0)	- (0.0)	- (0.0)	1 (10.0)	1 (7.1)
Monoresistance	1 (10.0)	- (0.0)	- (0.0)	- (0.0)	1 (10.0)	1 (7.1)
INH	1 (10.0)	- (0.0)	- (0.0)	- (0.0)	1 (10.0)	1 (7.1)
* Routine testing for SM not conducted.						

Table 9. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Newfoundland and Labrador – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB, SM and PZA	8 (100.0)	9 (100.0)	11 (100.0)	9 (100.0)	4 (100.0)	6 (100.0)
Isolates susceptible	8 (100.0)	9 (100.0)	11 (100.0)	9 (100.0)	4 (100.0)	4 (66.7)
Isolates resistant to one or more drugs	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	2 (33.3)
Monoresistance	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	2 (33.3)
INH	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (16.7)
RMP	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (16.7)

Table 10. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Northwest Territories – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB, SM and PZA	27 (100.0)	11 (100.0)	8 (100.0)	6 (100.0)	3 (100.0)	10 (100.0)
Isolates susceptible	27 (100.0)	11 (100.0)	8 (100.0)	6 (100.0)	3 (100.0)	10 (100.0)

Table 11. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Nova Scotia – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB and PZA*	9 (100.0)	8 (100.0)	4 (100.0)	7 (100.0)	10 (100.0)	7 (100.0)
Isolates susceptible	8 (88.9)	7 (87.5)	4 (100.0)	7 (100.0)	9 (90.0)	7 (100.0)
Isolates resistant to one or more drugs	1 (11.1)	1 (12.5)	- (0.0)	- (0.0)	1 (10.0)	- (0.0)
Monoresistance	1 (11.1)	1 (12.5)	- (0.0)	- (0.0)	1 (10.0)	- (0.0)
INH	1 (11.1)	1 (12.5)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (10.0)	- (0.0)
* Routine testing for SM not conducted.						

Table 12. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Nunavut* – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, SM, EMB and PZA***	N/A	15 (100.0)	29 (100.0)	31 (100.0)	22 (100.0)	4 (100.0)
Isolates susceptible	N/A	15 (100.0)	28 (96.6)	30 (96.8)	22 (100.0)	4 (100.0)
Isolates resistant to one or more drugs	N/A	- (0.0)	1 (3.4)	1 (3.2)	- (0.0)	- (0.0)
Monoresistance	N/A	- (0.0)	1 (3.4)	- (0.0)	- (0.0)	- (0.0)
INH		- (0.0)	1 (3.4)	- (0.0)	- (0.0)	- (0.0)
MDR-TB**	N/A	- (0.0)	- (0.0)	1 (3.2)	- (0.0)	- (0.0)
INH & RMP		- (0.0)	- (0.0)	1 (3.2)	- (0.0)	- (0.0)

^{*} Note: Nunavut began reporting in 1999.

^{**} MDR-TB is defined as resistance to at least INH and RMP

^{***} Routine testing for SM not conducted when isolate tested by Quebec (n=13 for 1999, n=28 for 2000, n=30 for 2001 and n=11 for 2002)

Table 13. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Ontario – 1998-2003

to mot-fine an		logis arag.	3, Ontario			
	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB, SM and PZA	629 (100.0)	589 (100.0)	599 (100.0)	589 (100.0)	586 (100.0)	590 (100.0)
Isolates susceptible	538 (85.5)	489 (83.0)	519 (86.6)	521 (88.5)	492 (84.0)	506 (85.8)
Isolates resistant to one or more drugs	91 (14.5)	100 (17.0)	80 (13.4)	68 (11.5)	94 (16.0)	84 (14.2)
Monoresistance	55 (8.7)	57 (9.7)	52 (8.7)	44 (7.5)	61 (10.4)	46 (7.8)
INH	34 (5.4)	34 (5.8)	23 (3.8)	20 (3.4)	30 (5.1)	24 (4.1)
EMB	4 (0.6)	- (0.0)	1 (0.2)	1 (0.2)	1 (0.2)	- (0.0)
SM	11 (1.7)	19 (3.2)	16 (2.7)	16 (2.7)	25 (4.3)	18 (3.1)
RMP	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.2)
PZA**	6 (1.0)	4 (0.7)	12 (2.0)	7 (1.2)	5 (0.9)	3 (0.5)
MDR-TB*	11 (1.7)	13 (2.2)	9 (1.5)	3 (0.5)	16 (2.7)	12 (2.0)
INH & RMP	2 (0.3)	3 (0.5)	1 (0.2)	- (0.0)	2 (0.3)	3 (0.5)
INH, RMP & EMB	- (0.0)	1 (0.2)	2 (0.3)	1 (0.2)	1 (0.2)	1 (0.2)
INH, RMP & SM	1 (0.2)	3 (0.5)	3 (0.5)	- (0.0)	2 (0.3)	1 (0.2)
INH, RMP & PZA	- (0.0)	1 (0.2)	- (0.0)	- (0.0)	- (0.0)	2 (0.3)
INH, RMP, EMB & PZA	- (0.0)	- (0.0)	- (0.0)	1 (0.2)	1 (0.2)	1 (0.2)
INH, RMP, SM & EMB	2 (0.3)	- (0.0)	2 (0.3)	- (0.0)	5 (0.9)	- (0.0)
INH, RMP, SM & PZA	- (0.0)	- (0.0)	1 (0.2)	- (0.0)	- (0.0)	- (0.0)
INH, RMP, SM, EMB & PZA	6 (1.0)	5 (0.8)	- (0.0)	1 (0.2)	5 (0.9)	4 (0.7)
Other Patterns	25 (4.0)	30 (5.1)	19 (3.2)	21 (3.6)	17 (2.9)	26 (4.4)
INH & EMB	2 (0.3)	4 (0.7)	2 (0.3)	- (0.0)	1 (0.2)	2 (0.3)
INH & PZA**	- (0.0)	- (0.0)	- (0.0)	2 (0.3)	- (0.0)	- (0.0)
INH & SM	20 (3.2)	20 (3.4)	14 (2.3)	16 (2.7)	13 (2.2)	18 (3.1)
SM & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.2)
EMB & RMP	- (0.0)	- (0.0)	2 (0.3)	- (0.0)	- (0.0)	- (0.0)
INH, SM & EMB	2 (0.3)	4 (0.7)	1 (0.2)	3 (0.5)	2 (0.3)	3 (0.5)
INH, SM & PZA	1 (0.2)	2 (0.3)	- (0.0)	- (0.0)	- (0.0)	1 (0.2)
INH, EMB & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.2)
INH, SM, EMB & PZA	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.2)	- (0.0)

^{*} MDR-TB is defined as resistance to at least INH and RMP

^{**} Includes 1 M. Bovis isolate for 1999, 2 M. Bovis isolates for 2000, 2 M. Bovis isolates for 2001, 1 M. Bovis isolate for 2002 and 1 M. Bovis isolate for 2003.

Table 14. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Prince Edward Island – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB and PZA*	2 (100.0)	2 (100.0)	3 (100.0)	2 (100.0)	1 (100.0)	2 (100.0)
Isolates susceptible	2 (100.0)	2 (100.0)	3 (100.0)	1 (50.0)	1 (100.0)	2 (100.0)
Isolates resistant to one or more drugs	- (0.0)	- (0.0)	- (0.0)	1 (50.0)	- (0.0)	- (0.0)
Monoresistance	- (0.0)	- (0.0)	- (0.0)	1 (50.0)	- (0.0)	- (0.0)
PZA**	- (0.0)	- (0.0)	- (0.0)	1 (50.0)	- (0.0)	- (0.0)

^{*} Routine testing for SM not conducted.

Table 15. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Québec – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, EMB and PZA	264 (100.0)	268 (100.0)	278 (100.0)	221 (100.0)	247 (100.0)	219 (100.0)
Isolates susceptible	231 (87.5)	236 (88.1)	249 (89.6)	202 (91.4)	222 (89.9)	187 (85.4)
Isolates resistant to one or more drugs	33 (12.5)	32 (11.9)	29 (10.4)	19 (8.6)	25 (10.1)	32 (14.6)
Monoresistance	28 (10.6)	28 (10.4)	28 (10.1)	18 (8.1)	23 (9.3)	31 (14.2)
INH	9 (3.4)	17 (6.3)	19 (6.8)	14 (6.3)	13 (5.3)	25 (11.4)
RMP	- (0.0)	1 (0.4)	- (0.0)	- (0.0)	1 (0.4)	- (0.0)
SM**	13 (4.9)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
PZA***	6 (2.3)	10 (3.7)	9 (3.2)	4 (1.8)	9 (3.6)	6 (2.7)
MDR-TB*	2 (0.8)	2 (0.7)	1 (0.4)	1 (0.5)	1 (0.4)	1 (0.5)
INH & RMP	- (0.0)	1 (0.4)	- (0.0)	1 (0.5)	- (0.0)	1 (0.5)
INH, RMP & EMB	1 (0.4)	- (0.0)	1 (0.4)	- (0.0)	1 (0.4)	- (0.0)
INH, RMP & SM	1 (0.4)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
INH, RMP, EMB & PZA	- (0.0)	1 (0.4)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
Other Patterns	3 (1.1)	2 (0.7)	- (0.0)	- (0.0)	1 (0.4)	- (0.0)
INH & SM	2 (0.8)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)
INH & EMB	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (0.4)	- (0.0)
INH & PZA	1 (0.4)	2 (0.7)	- (0.0)	- (0.0)	- (0.0)	- (0.0)

^{*} MDR-TB is defined as resistance to at least INH and RMP

^{**} Includes M. bovis isolates: 1 for 2001

^{**} Routine testing for SM not conducted in Quebec effective January 1, 1999 (NT = not tested)

^{***} Includes *M. Bovis* isolates: 1 for 1999, 2 for 2000, 1 for 2001, and 1 for 2003.

Table 16. Reported results for routine drug susceptibility testing of MTB isolates to first-line anti-tuberculosis drugs, Saskatchewan – 1998-2003

	1998 Total (%)	1999 Total (%)	2000 Total (%)	2001 Total (%)	2002 Total (%)	2003 Total (%)
Total number of isolates tested for INH, RMP, SM and EMB*	49 (100.0)	40 (100.0)	64 (100.0)	68 (100.0)	56 (100.0)	46 (100.0)
Isolates susceptible	47 (95.9)	39 (97.5)	58 (90.6)	65 (95.6)	51 (91.1)	45 (97.8)
Isolates resistant to one or more drugs	2 (4.1)	1 (2.5)	6 (9.4)	3 (4.4)	5 (8.9)	1 (2.2)
Monoresistance	1 (2.0)	- (0.0)	4 (6.3)	2 (2.9)	4 (7.1)	1 (2.2)
INH	1 (2.0)	- (0.0)	2 (3.1)	2 (2.9)	3 (5.4)	1 (2.2)
EMB	- (0.0)	- (0.0)	1 (1.6)	- (0.0)	1 (1.8)	- (0.0)
SM	- (0.0)	- (0.0)	1 (1.6)	- (0.0)	- (0.0)	- (0.0)
Other Patterns	1 (2.0)	1 (2.5)	2 (3.1)	1 (1.5)	1 (1.8)	- (0.0)
INH & EMB	- (0.0)	- (0.0)	1 (1.6)	- (0.0)	1 (1.8)	- (0.0)
INH & SM	1 (2.0)	1 (2.5)	1 (1.6)	1 (1.5)	- (0.0)	- (0.0)
* Routine testing for PZA not conducted.	·					

Table 17. Reported results for routine drug susceptibility testing of MTB isolates
to first-line anti-tuberculosis drugs, Yukon Territory – 1998-2003

	otal (%)	Total (%)				
Total number of isolates tested for INH, RMP, SM and EMB*	(100.0)	- (0.0)	3 (100.0)	1 (100.0)	- (0.0)	1 (100.0)
Isolates susceptible 1	(100.0)	- (0.0)	3 (100.0)	1 (100.0)	- (0.0)	1 (100.0)

^{*} Routine testing for PZA not conducted.

► Appendix 1

Proficiency panel results for anti-microbial susceptibility testing of *M. tuberculosis* to first-line drugs

Antibiotic	Strains A & B	Strain C	Strain D	Strain E	Strain F
SM 2.0 µg/ml	Sensitive 7/7 (100% consensus)	Resistant 7/7 (100% consensus)	Resistant 6/7 (86% consensus)	Sensitive 7/7 (100% consensus)	Sensitive 7/7 (100% consensus)
INH 0.1 μg/ml	Sensitive 9/9 (100% consensus)	Resistant 9/9 (100% consensus)	Resistant 8/9 (89% consensus)	Resistant 9/9 (100% consensus)	Sensitive 9/9 (100% consensus)
RMP 2.0 µg/ml	Sensitive 9/9 (100% consensus)				
EMB 2.5 μg/ml	Sensitive 9/9 (100% consensus)	Resistant 9/9 (100% consensus)	Resistant 8/9 (89% consensus)	Sensitive 9/9 (100% consensus)	Sensitive 9/9 (100% consensus)
PZA 100 µg/ml	Resistant 6/6 (100% consensus)	Resistant 5/7 (71% consensus)	Resistant 4/7 (57% consensus)	Resistant 5/6 (83% consensus)	Sensitive 5/6 (83% consensus)

Phase I: Susceptibility testing of M. tuberculosis - Comments

Eight laboratories are using the radiometric BACTEC TB460 system. One laboratory is using the MGIT 960 system. All laboratories are testing appropriate concentrations of first line drugs.

Streptomycin: Most laboratories that test streptomycin (7 out of 9) are accurately identifying sensitivity and resistance. Current NCCLS approved guidelines (1) consider streptomycin as a second-line drug and suggest the laboratory director should consult with pulmonary/infectious disease specialist and TB control officer to decide if streptomycin should be routinely tested based on the following:

- 1. Patient population
- 2. Prevalence of drug resistance
- 3. Use in community
- 4. Availability and timeliness of testing if resistance or intolerance is encountered

Isoniazid: Most laboratories accurately identified sensitivity and resistance to INH at 0.1 μg/ml. Resistance and sensitivity to INH at 0.4 μg/ml was accurately reported for laboratories testing the higher concentration of INH. Currently, 3 out of 9 laboratories are testing the higher concentration of INH. NCCLS (1) recommends testing a higher concentration of INH when resistance is encountered. Although clinicians may not agree on the usefulness of this data, information of the level of resistance can be provided and used at their discretion. When an isolate exhibits resistance to 0.1 μg/ml and sensitivity to 0.4 μg/ml, NCCLS recommends the following comment to be added to the report: "These test results indicate low-level resistance to INH. Some experts believe that patients infected with strains exhibiting this level of INH resistance may benefit from continuing therapy with INH. A specialist in the treatment of tuberculosis should be consulted concerning the appropriate therapeutic regimen and dosages."

Ethambutol: Most laboratories correctly identified ethambutol sensitivity and resistance. One laboratory reported conflicting results between radiometric and agar proportion with strains C/D.

PZA: Six out of 9 laboratories reported results for PZA. All laboratories accurately identified PZA mono-resistance in strains A/B. One laboratory misidentified PZA resistance in strain F. Based on the radiometric method, 5 out of 6 laboratories identified strain C as resistant and one laboratory identified the isolate as sensitive. One laboratory identified strains C/D as sensitive based on the amidase test. Strain D was identified as resistant by 4 laboratories and sensitive by 2 laboratories using the radiometric method. Strain E was reported as resistant by 5 out of 6 laboratories including the laboratory utilizing the amidase test.

- Strains C/D and E repeatedly produced resistance results with radiometric testing at the NRCM. Final percentage results (PZA/control) were generally 20-30%. The stains grew well in the acidic media and decreasing the inoculum also produced resistant results.
- Strains C/D and E produced positive 4 day pyrazinamidase results consistent with a functional enzyme and sensitivity to PZA (2).
- The complete *pncA* gene was sequenced for strains C/D and E. No mutations were found which is consistent with the pyrazinamidase result and sensitivity to PZA (3).
- The lack of a functional pyrazinamidase and mutations in the *pncA* gene have been correlated to PZA resistance (2, 3, 4, 5, 6), however not all PZA resistant strains display these characteristics (4). The percentage of PZA resistant isolates with *pncA* mutations can range from 40% to >90% and appears to be dependent upon geographical area (4, 5, 6, 7). Unknown mechanisms of PZA resistance exist and may be significant.
- The lack of pyrazinamidase activity and *pncA* mutations may confirm PZA resistance however the presence of pyrazinamidase activity and wild type pncA cannot confirm PZA sensitivity.

► Appendix 2

Participating Laboratories of the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS)

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► Appendix 3



Health Santé Canada Canada

Serial No. - N° de série

The Canadian Tuberculosis Laboratory Surveillance System
M. TUBERCULOSIS COMPLEX ANTIMICROBIAL
SUSCEPTIBILITY REPORTING FORM

Système de surveillance des laboratoires de tuberculose au Canada RAPPORT SUR LA SENSIBILITÉ DES SOUCHES DU COMPLEXE M TUBERCUL OSIS AUX ANTIMICRORIENS

	SUSCEPTIBILITY REPORTING FO		WI. TUBE	ERCULUSIS /	AUX ANTIMICROBIENS			
	R INTERNAL USE ONLY - POUR USAGE INTERNE SE	ULEMENT Unique So	urce Laboratory II	D No Identific	ateur unique du laboratoire déclarant:			
	Rec'd at TBPC: Y/A M D ate de réception au LATB:	/ J						
	TBPC Number:	Date specimen / cu	Iture <u>received</u> at la	aboratory:	Y/A M D/J			
N	uméro du LATB:	Date de réception é	echantillon / cultur	re au laboratoire:				
Spe Esp	cie: (may include M. africa		bovis	И. BCG bovis	MTB Complex (species unknown) Complexe MTB (espèce inconnu)			
Have	susceptibility test results been previously reported for		d'antibiogramme o	ont-ils déjà été fo	urnis pour ce patient?			
	No Yes What is the previous Unique Identificateur antérieur ?	ue Source Laboratory ID No.?						
	What is the previous Form N° de formulaire antérieur		Lili	1 1 1				
Note	Note: Only DRUG TESTING RESULTS OF ONE ISOLATE are to be reported. Note: Ne fournir que les RÉSULTATS POUR UNE SEULE SOUCHE par							
	No subsequent drug testing results for the s reported unless the sensitivity pattern chan-	same patient are to be			angement du profil de sensibilité.			
	Province / territory from which this report originates:	I I I (see	code list)		PROV / TERR CODES PROV / TERR			
1	Province / territoire qui soumet ce rapport :		r liste de codes)		10 = NFLD / TN 46 = MAN			
	Province / territory from which specimen originated:	I I (see	code list)		11 = PEI / IPÉ 47 = SASK			
2	Province / territoire d'où provient l'échantillon :	(voir	r liste de codes)		12 = NS / NÉ 48 = ALTA / ALB			
	Patient's date of birth:	D/J (CCYY/MM/DD)	1	I Unknown	13 = NB 59 = BC / BC			
3	Date de naissance du patient :	(SSAA/MM/JJ)		Inconnu	24 = QUÉ / Qc 60 = YUK			
4	Patient's gender: Male		nown		35 = ONT 61 = NWT / TNO			
	Sexe du patient : Masculin	Féminin	nnu		62 = NUN			
5	LABORATORY RESULTS	Concentration		Results (check	appropriate box for every drug)			
	RÉSULTATS DE LABORATOIRE	(if different from on file)	Résultats (cocher la case pertinente pour chaque antibiotique)					
	Antituberculous Drugs Agents Antituberculeux	(si autre que spécifiée)	Sensitive Sensible	Resistant Résistant	Other (specify) Autre (préciser)			
	SM (Streptomycin) (Streptomycine)	mg / L						
	INH (Isoniazid) (Isoniazide)	mg / L						
	RMP (Rifampin) (Rifampicine)	mg / L						
	EMB (Ethambutol)	mg / L						
	PZA (Pyrazinamide)	mg / L						
	2nd line drugs (specify) Antibiotiques de 2º ligne (préciser)	Concentration	Sensitive Sensible	Resistant Résistant	Other (specify) Autre (préciser)			
	1.	mg / L						
	2.	mg / L						
	3.	mg / L						
	4.	mg / L						
	5.	mg / L						
	6.	mg / L						
6	Comments - Commentaires							

HC/SC 9061 (07-2000) Copy 1 (White) - Reporting Laboratory
Copie 1 (Blanche) - Laboratoire déclarant

Copy 2 (Yellow) - Tuberculosis Prevention and Control (TBPC) Copie 2 (Jaune) - Lutte anti-tuberculeuse (LATB)