

# Molecular Detection of Drug Resistance (MDDR)

Centers for Disease Control and Prevention (CDC)  
 Mycobacteriology Laboratory Branch (MLB)  
 1600 Clifton Road, NE, MS F08  
 Atlanta, GA 30333

MDDR Contact Information:

Telephone: 404-639-2455

FAX: 404-639-5491

Email: TBLab@cdc.gov

Intended use	Rapid detection of drug resistance in <i>Mycobacterium tuberculosis</i> isolates			
Assay	DNA sequencing will be performed using the ABI 3130xl. Sequencing will be performed from PCR products amplified from genetic loci associated with resistance to first- and second-line anti-tuberculosis drug. DNA sequencing was chosen as the platform due to its automation, high-throughput and potential for expansion (additional loci can be added to the panel).			
Loci to be sequenced and associated drug resistance	First-line MDDR to detect MDR-TB <ul style="list-style-type: none"> <li>▪ <i>rpoB</i> (Rifampin)</li> <li>▪ <i>inhA</i> and <i>katG</i> (Isoniazid)</li> </ul> Second-line MDDR to detect XDR-TB <ul style="list-style-type: none"> <li>▪ <i>gyrA</i> (Fluoroquinolones)</li> <li>▪ <i>rrs</i> (Kanamycin, Amikacin, Capreomycin)</li> <li>▪ <i>eis</i> (Kanamycin)</li> <li>▪ <i>tlyA</i> (Capreomycin)</li> </ul>			
Performance	<b><u>Drug</u></b>	<b><u>Gene</u></b>	<b><u>Sensitivity</u></b> <b><u>(%)</u></b>	<b><u>Specificity</u></b> <b><u>(%)</u></b>
	RIF	<i>rpoB</i>	96.1	97
	INH	<i>inhA</i> + <i>katG</i>	88.6	98.7
	FQ	<i>gyrA</i>	82.2	97
	KAN	<i>rrs</i> + <i>eis</i>	86.8	96.9
	AMK	<i>rrs</i>	87.9	99
	CAP	<i>rrs</i> + <i>tlyA</i>	44.6	85.9
Limitations	<ul style="list-style-type: none"> <li>▪ Potential to identify mutations that do not confer phenotypic resistance</li> <li>▪ Not all genetic loci associated with resistance are known, therefore, a susceptible molecular result does not rule out resistance</li> </ul>			
Submission criteria	Must meet one of the following criteria: <ul style="list-style-type: none"> <li>▪ High Risk of RIF-R or MDR-TB (e.g. previous TB, MDR-TB contact, foreign born)</li> <li>▪ Known Rif-R</li> </ul>			

	<ul style="list-style-type: none"> <li>▪ High profile patient (e.g. daycare worker, nurse)</li> <li>▪ Adverse reaction (e.g. RIF allergy)</li> <li>▪ Mixed or non-viable culture</li> <li>▪ Others may be accepted on case by case basis</li> </ul>
Sample types accepted	<p><b>Isolates only</b> (one per patient)</p> <ul style="list-style-type: none"> <li>▪ Solid Media (e.g. LJ or Middlebrook)</li> <li>▪ MGIT cultures</li> <li>▪ Bactec460 vials <u>will not</u> be accepted</li> </ul>
Submission guidelines	<ul style="list-style-type: none"> <li>▪ Isolates must be shipped Monday-Thursday</li> <li>▪ Submit MLB MDDR request form by email <a href="mailto:TBLab@cdc.gov">TBLab@cdc.gov</a></li> <li>▪ Wait for approval and further instructions</li> <li>▪ Submit isolate, attach DASH and MDDR request form</li> </ul>
Conventional DST	All isolates submitted for MDDR will also undergo conventional DST by the agar proportion method (PZA by MGIT 960)
Reporting	<ul style="list-style-type: none"> <li>▪ Interim Report: MDDR results</li> <li>▪ Final Report: MDDR and Conventional DST results with “conclusion”/”final interpretation”</li> </ul>
References	<ul style="list-style-type: none"> <li>▪ S.Ramaswamy and J.M. Musser. Tubercle and Lung Disease. 79(1):3-29, 1998.</li> <li>▪ C. Maus et al. AAC. 49(8):3192-3197, 2005.</li> <li>▪ S. Feuerriegel et al. AAC. Epub, 2009.</li> <li>▪ M. Zaunbrecher et al., submitted</li> </ul>

(09/06/2009)