From Dream to Reality Check
On MDR-TB Management Scale-up

Stop TB Partnership's
MDR-TB Working Group Meeting 2007

Dr Mario Raviglione
Director, Stop TB Department
Tbilisi, Georgia, 20 September 2007
<table>
<thead>
<tr>
<th>Estimated number of cases (in million)</th>
<th>Estimated number of deaths (in million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All forms of TB</td>
<td>8.8</td>
</tr>
<tr>
<td>Multidrug-resistant TB (MDR-TB)</td>
<td>116,000</td>
</tr>
<tr>
<td>Extensively drug-resistant TB (XDR-TB)</td>
<td>16,000</td>
</tr>
</tbody>
</table>

(Zignol M et al. Global Incidence of Multidrug-Resistant Tuberculosis, JID 2006:194)
MDR-TB prevalence in new TB cases, 1994-2003

- Estonia: 5.0
- Uzbekistan: 13.2
- Kazakhstan: 14.2
- Israel: 14.2
- Russia (Tomsk): 13.7
- China (Liaoning): 10.4
- Lithuania: 9.4
- Latvia: 9.3
- Russia (Ivanovo): 9.0
- China (Henan): 7.8
- Dominican Rep: 6.6
- Ivory Coast: 5.3
- Iran: 5.0
- Ecuador: 4.9
Estimated number of MDR-TB cases by regions, 2005

- South-east Asia, 114,967
- Western Pacific Region, 152,018
- Eastern Mediterranean Region, 18,330
- Eastern Europe, 65,853
- Latin America, 11,301
- Africa high HIV incidence, 48,141
- Africa low HIV incidence, 10,449
- Central Europe, 1,462
- Established Market Economies, 1,681

Global burden: 424,203 cases
XDR-TB – Extensive Drug Resistance
The new threat

XDR = Resistance to at least INH and RIF (MDR) PLUS resistance to any fluoroquinolone, AND any one of the second-line injectable drugs (amikacin, kanamycin, or capreomycin)

Of 17,690 isolates from 49 countries during 2000-2004 20% were MDR and 2% were XDR

XDR found in:
USA: 4% of MDR
Latvia: 4% of MDR
S Korea: 15% of MDR

XDR found in South Africa associated with HIV
Countries with XDR-TB confirmed cases as of September 2007

Based on information provided to WHO Stop TB Department 13 September 2007
Treating MDR-TB in the bush of Swaziland – St Philip's, 8-2007
Will drug-resistant strains replace drug-susceptible ones?

Observed and expected spread of MDR-TB

Can MDR-TB case management generate additional XDR-TB?

Message: the higher the % of MDR-TB managed with current poor outcomes, the higher the % of XDR-TB generated

Figure: Dynamics of the emergence and transmission of multiple strains of tuberculosis resistant to a variety of first-line and second-line drugs

Predicted data generated using the Amplifier model and uncertainty analysis. To generate these predictions we assumed that extensively drug-resistant tuberculosis (XDR-TB) cases could not be cured, and that the cure rates of multidrug-resistant tuberculosis (MDR-TB) cases were not increased substantially above their current rates. The figure shows the quantitative relationship between the percentage of MDR tuberculosis cases that are XDR tuberculosis and the percentage of MDR tuberculosis cases that are detected and treated. The fitted curve is exponential ($y=3.912e^{0.005x}$; $R^2=0.76$).

Blower S, Supervie V. Predicting the future of XDR tuberculosis. Lancet 2007
The Stop TB Strategy to achieve the 2015 MDGs

1. PURSUE HIGH-QUALITY DOTS EXPANSION AND ENHANCEMENT
   - Political commitment with increased and sustained financing
   - Case detection through quality-assured bacteriology
   - Standardized treatment with supervision and patient support
   - An effective drug supply and management system
   - Monitoring and evaluation system, and impact measurement

2. ADDRESS TB/HIV, MDR-TB AND OTHER CHALLENGES
   - Implement collaborative TB/HIV activities
   - Prevent and control multidrug-resistant TB
   - Address prisoners, refugees and other high-risk groups and special situations

3. CONTRIBUTE TO HEALTH SYSTEM STRENGTHENING
   - Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery, and information systems
   - Share innovations that strengthen systems, including the Practical Approach to Lung Health (PAL)
   - Adapt innovations from other fields

4. ENGAGE ALL CARE PROVIDERS
   - Public-Public, and Public-Private Mix (PPM) approaches
   - International Standards for TB Care (ISTC)

5. EMPOWER PEOPLE WITH TB, AND COMMUNITIES
   - Advocacy, communication and social mobilization
   - Community participation in TB care
   - Patients’ Charter for Tuberculosis Care

6. ENABLE AND PROMOTE RESEARCH
   - Programme-based operational research
   - Research to develop new diagnostics, drugs and vaccines
What needs to be done to address MDR-TB and XDR-TB effectively?

- Strengthen basic TB and HIV/AIDS control, to avoid creation of MDR-TB and XDR-TB
- Scale-up programmatic management of MDR-TB and XDR-TB
- Strengthen laboratory services for adequate and timely diagnosis of MDR-TB and XDR-TB
- Expand MDR-TB and XDR-TB surveillance
- Introduce infection control, especially in high HIV prevalence settings
- Strengthen advocacy, communication and social mobilization (e.g., Response Plan)
- Pursue resource mobilization at global, regional and country levels
- Promote research and development into new diagnostics, drugs and vaccines
# 2007-2008 XDR & MDR Tuberculosis Global Response Plan

## MILESTONES

<table>
<thead>
<tr>
<th>Indicator</th>
<th>2007</th>
<th>2008</th>
<th>Total</th>
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<tbody>
<tr>
<td>Cultures performed</td>
<td>1,800,000</td>
<td>2,200,000</td>
<td>4,000,000</td>
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<tr>
<td>Drug susceptibility tests performed</td>
<td>750,000</td>
<td>900,000</td>
<td>1,650,000</td>
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<tr>
<td>New laboratories established</td>
<td>21</td>
<td>22</td>
<td>43</td>
</tr>
<tr>
<td>MDR-TB cases enrolled on treatment (excluding XDR-TB)</td>
<td>60,000</td>
<td>100,000</td>
<td>160,000</td>
</tr>
<tr>
<td>XDR-TB cases enrolled on treatment</td>
<td>6,000</td>
<td>10,000</td>
<td>16,000</td>
</tr>
<tr>
<td>% of estimated MDR-TB cases enrolled in treatment per year (excluding XDR-TB)</td>
<td>15%</td>
<td>28%</td>
<td>16,000</td>
</tr>
<tr>
<td>% of estimated XDR-TB cases enrolled in treatment per year</td>
<td>25%</td>
<td>43%</td>
<td></td>
</tr>
<tr>
<td>Lives Saved</td>
<td>49,000</td>
<td>85,000</td>
<td>134,000</td>
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## COSTS (US$ millions estimated)

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<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>Total</th>
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<tbody>
<tr>
<td>Resources needed by countries</td>
<td>673</td>
<td>1,046</td>
<td>1,719</td>
</tr>
<tr>
<td>Drugs for treatment</td>
<td>391</td>
<td>445</td>
<td>756</td>
</tr>
<tr>
<td>Hospitalization costs</td>
<td>81</td>
<td>121</td>
<td>202</td>
</tr>
<tr>
<td>Capacity building and other operational costs</td>
<td>193</td>
<td>288</td>
<td>481</td>
</tr>
<tr>
<td>Infection control costs</td>
<td>40</td>
<td>72</td>
<td>112</td>
</tr>
<tr>
<td>Laboratory costs</td>
<td>68</td>
<td>100</td>
<td>168</td>
</tr>
<tr>
<td>Technical assistance from partners at global, regional and national levels</td>
<td>42</td>
<td>60</td>
<td>102</td>
</tr>
<tr>
<td>Research and Development (including operational research)</td>
<td>167</td>
<td>167</td>
<td>334</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$882m</strong></td>
<td><strong>$1,273m</strong></td>
<td><strong>$2,155m</strong></td>
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</tbody>
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MDR-TB Projects approved by GLC
September 2007

MDR-TB projects in 48 countries approved by GLC
27 of them GF-supported
A total of 30'000 cases to be treated
Gap between requests to GLC and revised Global Plan, 2006-2015

Thousands

- **Response Plan**
- **GLC**
Conclusions

• XDR-TB is a powerful and threatening alarm call for all of us. Status quo or slow pace are no options.

• Scaling-up of interventions must be massive, well-thought, and rapid. Governments and donors must react now.

• GLC is now ready to accommodate more proposals, but all depends on demand from national TB control programmes.

• Response Plan is for 2007-8 only. WG needs to think now about the future.

• True bottlenecks must be addressed systematically: drug regulations, drug procurement, pre-qualification, lab capacity, and overall human resource capacity of programmes, including community engagement.