A roadmap for TB laboratory strengthening within WHO policy frameworks and national laboratory strategies

Karin Weyer, WHO
On behalf of the GLI Core Group
Outline

- Addressing diagnostic and laboratory gaps
- Rationale for a Roadmap
- Process, purpose, scope
- Core elements
- TB diagnostic algorithm (what/where/when)
Global TB estimates - 2007
(Updated February 2009)

All forms of TB
Greatest number of cases in Asia; greatest rates per capita in Africa

Estimated number of cases
9.27 million (139 per 100,000)

Estimated number of deaths
1.77 million (27 per 100,000)

Multidrug-resistant TB (MDR-TB)
511,000
150,000

Extensively drug-resistant TB (XDR-TB)
50,000
30,000

HIV-associated TB
1.4 million
456,000

Greatest number of cases in Asia; greatest rates per capita in Africa
Overall problem: MDR-TB diagnostic and treatment levels far too low

511,000 estimated cases annually

- Diagnosed and treated in Green Light Committee programmes: 3%
- Countries report diagnosis and treatment, standard unknown
- No diagnosis and treatment reported. Some treatment probably obtained, quality unknown
Laboratory scale-up

Driven by

- Case detection moving towards universal access
- HIV-associated and drug resistant TB

Challenged by

- Weak health systems
- Inadequate human resources
- Insufficient programmatic and managerial capacity
- Inadequate infrastructure (biosafety)
- Problems of availability and access
- Slow technology transfer
- Lack of recognition of laboratory importance in TB control, weak communication between NTPs and laboratory services
Acceleration

Recent developments:

• At least 20 new technologies in various stages of development and evaluation

• Distinct target areas for drug-resistant TB being addressed

• WHO policy formulation
  – Liquid culture, rapid speciation and line probe assays endorsed by WHO 2007-2008;*
  – LED microscopy and selected non-commercial culture and drug susceptibility testing methods expected in 2009

• Expanded access to new diagnostics and laboratory strengthening

*Available at: http://www.who.int/tb/dots/laboratory/policy/en
Why a Roadmap?
Process

• May 08: GLI CG meeting
  – GLI strategic objectives defined
• May 08: 1st annual GLI meeting
  – Consultant findings on stakeholder interviews and country fact finding visits
  – Break-out group discussions to identify gaps and next steps
• Oct 08: Dedicated TBCAP funding
• Oct 08 - Jun 09:
  – Conceptual framework defined
  – Country case studies pursued and common themes identified
  – Stakeholder interviews continued
  – WHO policy recommendations incorporated
• Jun 09 – Aug 09
  – Intensive revision by Writing Committee, GLI CG and external laboratory experts
Purpose and scope

- **Structured framework** for TB laboratory strengthening based on WHO-GLI norms and standards, documented best-practices at country level, growing lessons from the field (‘learning by doing’)
- **Generic document** encompassing managerial, operational and technical aspects of TB laboratory strengthening within the context of national laboratory strategic plans
- **Broad user base** including NTP and NRL managers, technical agencies, donor agencies, implementing partners, programme budgeting and planning officers
- **Living document**, responsive to changes in TB diagnostic landscape and WHO policy frameworks

- Supported by resource list for tools and technical procedures
Core elements

- Laboratory infrastructure and maintenance
- Equipment validation and maintenance
- Specimen referral and transport mechanisms
- Policy framework for implementing new TB diagnostics
- Laboratory commodity and supply chain management
- Laboratory information and data management systems
- Laboratory quality management systems
- Laboratory human resource development
Policy change at country level, based on

- Local epidemiology (TB, HIV, MDR-TB)
- NTP priorities for case detection (risk groups)
- Laboratory networks and capacity
- Laboratory staff resources and skills base
- Treatment policies for drug-resistant TB
- Financial resources
Expansion of laboratory services based on

- Tiered system (peripheral, intermediate, central)
- Available technologies
- Ancillary laboratory needs related to specialised treatment (e.g. ART, second-line anti-tuberculosis drugs)
  - General microbiology, biochemistry, haematology, etc.
- Integrated approach
Stepwise approach (3)

• Phase 1: Laboratory preparedness
  – Assessment of TB laboratory networks and diagnostic policies
  – Upgrade of laboratory infrastructure and biosafety
  – Development and implementation of GLP, SOPS, QA, etc.
  – Training of core laboratory staff
  – Initiation of NTP policy reform on diagnostics

• Phase 2: Introduction of new diagnostics
  – Integration of new diagnostics into NTP policies and procedures
  – Procurement and installation of instruments, reagents, supplies
  – Validation of new tools and laboratory performance
  – Adjustment of NTP policy based on local data

• Phase 3: Impact assessment
  – Continued mentoring, technical support and oversight
  – Assessment of impact on NTP outcomes
Analytical process

- Quantify or estimate TB, TB-HIV and MDR-TB burden
- Identify and target patient risk groups, eg.
  - Treatment failures
  - Non-converting patients
  - HIV+ individuals
- Quantify or estimate diagnostic need to identify cases
  - Number of suspects to be screened
  - Number and type of laboratories at each service level
- Estimate budget for comprehensive laboratory services
  - All core components
  - Capacity for diagnosis and monitoring
  - Ancillary laboratory tests
Laboratory algorithm

Starts with

• Screening policy for suspects
• Microscopy services as entry point
MDR-TB diagnosis using conventional solid culture and DST

<table>
<thead>
<tr>
<th>Microscopy</th>
<th>Solid culture</th>
<th>1st line DST</th>
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<tbody>
<tr>
<td>24h</td>
<td>6-8w</td>
<td>3-4w</td>
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MDR-TB diagnosis after 9 to 12 weeks

MDR-TB diagnosis using liquid culture and DST

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<thead>
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<th>Microscopy</th>
<th>Liquid culture</th>
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MDR-TB diagnosis after 3 to 5 weeks

MDR-TB diagnosis using line probe assay, liquid culture and DST

<table>
<thead>
<tr>
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<th>Line probe assay</th>
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MDR-TB diagnosis after 1 to 2 days

MDR-TB diagnosis after 3 to 5 weeks
### XDR-TB diagnosis using conventional solid culture and DST

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<thead>
<tr>
<th>Microscopy</th>
<th>Solid culture</th>
<th>1st line DST</th>
<th>2nd line DST*</th>
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* Methods not validated or standardised

XDR-TB diagnosis after 12 to 16 weeks

### XDR-TB diagnosis using liquid culture and DST

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XDR-TB diagnosis after 4 to 9 weeks

### XDR-TB diagnosis using line probe assay, liquid culture and DST

<table>
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<th>Microscopy</th>
<th>LPA</th>
<th>Liquid culture</th>
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XDR-TB diagnosis after 4 to 9 weeks
Policy considerations

- Current technologies not mutually exclusive
  - Conventional culture capacity required for SM- specimens
  - Conventional DST capacity required to detect XDR-TB
- Liquid culture and line probe assay as gold standards, to be phased in without loss of existing culture and DST capacity
- LED microscopy as alternative for both fluorescence and conventional light microscopy (pending STAG endorsement)
- Selected non-commercial culture and DST methods not alternatives for gold standards, but may provide interim solution (pending STAG endorsement)
Strengthening TB laboratories

‘From unimaginable...to indispensable’
Acknowledgements

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• **And with apologies for any unintended oversight…**