TB laboratory Diagnosis

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Diagnostics pipeline

Abbreviations: DST Drug susceptibility test; NAAT Nucleic acid amplification test; LTBI Latent TB infection; POC Point of care; MODS Microscopic observation drug-susceptibility; NRA Nitrate reductase assay; CRI Colorimetric redox indicator assay; LED Light-emitting diode; LPA Line probe assay
Policies not recommended

• ‘Negative’ policy (do-not-use)
  – 2011: Commercial serodiagnostics
  – 2011: IGRAs (high TB or HIV burden settings)
Coming in 2012 - 2013

• Laboratory biosafety
  – Procedure (risk)-based, minimum requirements

• Guidance on drug susceptibility testing
  – Update on 2008 guidance; New drugs

• LPA update
  – Improved 1st-line LPA; New 2nd-line LPA (XDR)

• Evaluation of new technologies
  – ........
TB 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
Core elements of laboratory services

- Policy framework for implementing new TB diagnostics
- Laboratory infrastructure and maintenance
- Equipment validation and maintenance
- Specimen referral and transport mechanisms
- Laboratory commodity and supply chain management
- Laboratory information and data management systems
- Laboratory quality management systems
- Laboratory human resource development
Considerations for GF proposals

- Local epidemiology (TB, HIV, MDR-TB)
- NTP priorities for case detection (risk groups)
- National TB laboratory strategic plans
- GLI Roadmap for TB Laboratory Strengthening
- WHO Policy Framework for implementing new TB diagnostics at country level
- Laboratory networks and capacity
  - Placement of different technologies
  - Number and type of laboratories at each service level
- Laboratory staff resources and skills base
- Budget for a comprehensive laboratory network
Common mistakes

• TB laboratory component not linked to country epidemiological assessment or related gap analyses
• Lack of strategic plans for introduction of new TB diagnostics, including country case finding strategies and diagnostic algorithms
• Lack of indication of how and where TB laboratory services fit into overall proposals (e.g. links to HIV-associated TB and MDR-TB components)
• Insufficient gap analyses of TB laboratory services
• Lack of detail on plans for external quality assurance
• Lack of training plans based on human resource needs assessment
• Unclear technical assistance needs and plans
• Incomplete and under-estimated budgets (e.g. focused on laboratory commodities only)
Helpful tools and references (1)

- WHO Briefing Note on TB laboratory strengthening
  [Link to Briefing Note](http://www.stoptb.org/wg/kg/assets/documents/BRIEFING%20NOTE%20LABS%20for%20GC.pdf)

- GLI Roadmap for TB Laboratory Strengthening
  [Link to GLI Roadmap](http://www.stoptb.org/wg/kg/assets/documents/GLI%20Roadmap%20First%20Issue%20201011.pdf)

- WHO policies and supporting documents
  - Microscopy
    - [Link to Microscopy Documents](http://whqlibdoc.who.int/publications/2011/9789241501613_eng.pdf)
    - [Link to Microscopy Documents](http://whqlibdoc.who.int/publications/2011/9789241501606_eng.pdf)
  - Culture, species identification and drug-susceptibility testing
    - [Link to Culture Documents](http://whqlibdoc.who.int/hq/1998/WHO_TB_98.258_(part3).pdf)
    - [Link to Culture Documents](http://whqlibdoc.who.int/publications/2011/9789241501620_eng.pdf)
  - Molecular testing (LPA and Xpert MTB/RIF)
    - [Link to Molecular Testing](http://www.who.int/tb/laboratory/line_probe_assays/en/index.html)
    - [Link to Molecular Testing](http://whqlibdoc.who.int/publications/2011/9789241501545_eng.pdf)
    - [Link to Molecular Testing](http://whqlibdoc.who.int/publications/2011/9789241501569_eng.pdf)
    - [Link to Molecular Testing](http://www.who.int/tb/features_archive/factsheet_xpert_may2011update.pdf)
Helpful tools and references (2)

• Laboratory biosafety

• Training and supporting tools
  http://wwwn.cdc.gov/dls/ila/acidfasttraining/
  http://www.stoptb.org/wg/gli/documents.asp (see GLI laboratory toolbox)

• Quality assurance
  Others: see GLI laboratory toolbox http://www.stoptb.org/wg/gli/documents.asp

• Costing & Budgeting tool

Additional supporting documents can be found on WHO and GLI web sites:
http://www.stoptb.org/wg/gli/default.asp
Transfer of technology: learning by doing

- EXPAND-TB Project: 27 countries including 10 in AFR
  - Liquid culture and Drug Susceptibility Testing (DST)
  - Rapid speciation
  - Line Probe Assay (LPA)

- Xpert MTB RIF roll out
EXPAND-TB progress July 2011

**Laboratory assessment**
- Laboratory assessment
- Memorandum of understanding
- Infrastructure upgrade
- Creation of SOPs policy reform

**Technology transfer**
- Equipment and supplies
- Procurement
- Training
- Quality assurance
- Laboratory validation

**Routine testing and monitoring**
- Monitoring and evaluation
- Impact assessment
- Market dynamics

**Timeline**
- **18–24 months**
  - Bangladesh
  - Belarus
  - Indonesia
  - Peru
  - Kazakhstan
  - Senegal
  - Viet Nam

- **6–12 months**
  - Azerbaijan
  - Cameroon
  - Côte d’Ivoire
  - Djibouti
  - Georgia
  - Haiti
  - Kenya
  - Kyrgyzstan
  - Republic of Moldova
  - Swaziland
  - Tajikistan
  - UR Tanzania

- **Up to year 5**
  - Ethiopia
  - India
  - Lesotho
  - Myanmar
  - Uganda
  - Uzbekistan
Cases of MDR-TB reported by selected countries participating in the EXPAND-TB project, 2008–2010

- **India**
  - 2008: 342
  - 2009: 1660
  - 2010: 2967

- **Uzbekistan**
  - 2008: 308
  - 2009: 654
  - 2010: 1023

- **Uganda**
  - 2008: 26
  - 2009: 57
  - 2010: 93
Xpert MTB/RIF

- Coordination of initial roll-out
  - 35 countries as of Q2 2011
  - Multiple partners

- Monitoring of sales & price reduction
  - Cartridge sales doubling by quarter
  - 600,000 sales expected by end 2011

- Scale-up via UNITAID
  - Early price reduction
  - Increased access
  - Market penetration (private sector)
  - Innovation
Xpert MTB/RIF roll-out

Progress in the roll-out of Xpert MTB/RIF, as of June 2011

GeneXpert modules ordered:
- 0
- 1–4
- 5–14
- 15–29
- ≥30
- Not eligible for preferential pricing
- No data
- Not applicable
Considerations for Xpert MTB/RIF

• Diagnostic algorithm

• Operational conditions
  • stable electricity supply
  • operating temperatures
  • storage space for cartridges
  • Testing capacity of 4 module system per working day is 15-20 tests
  • annual calibration
  • bio-safety conditions similar to smear microscopy

• Preferential prices for eligible countries
  • GeneXpert system, 4 module with desktop: 17’000 $
  • GeneXpert system, 4 module with desktop: 17’500 $
  • Cartridge: 16.86 $

• Installation and running costs
Selection of individuals to test based on risk assessment: summary

A. Individuals at risk of MDR-TB
   - Diagnosed with TB or
   - Suspected of having TB

B. HIV (+) individuals (or HIV unknown in high HIV settings) suspected of having TB
   - HIV (-) individuals not at risk of MDR-TB with either:
     - Abnormal CXR
     - Sputum smear (-) but still suspected of having TB

Primary considerations

Secondary considerations

Xpert MTB/RIF

TB, Rif resistance
   - Enrol on MDR-TB regimen
   - DST FLD and SLD
   - ART if HIV +

TB, no Rif resistance
   - Treatment regimen based on patient history
   - ART if HIV +

No TB detected
   - Appropriate further clinical management
   - IPT if HIV +
### Practical considerations: installation and running costs

#### Sample annual itemized budget

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> Equipment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GeneXpert 4 module with laptop (Ex-Works price)</td>
<td>$17,500.00</td>
<td>&gt;60% price reduction compared to EU/US</td>
</tr>
<tr>
<td>Shipment</td>
<td>$1,000.00</td>
<td>Depends on destination</td>
</tr>
<tr>
<td>Uninterruptible Power Source</td>
<td>$500.00</td>
<td>Local purchase, depends on the market</td>
</tr>
<tr>
<td>Printer</td>
<td>$200.00</td>
<td>Local purchase, depends on the market</td>
</tr>
<tr>
<td><strong>B</strong> Maintenance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual calibration costs</td>
<td>$1,800.00</td>
<td>Highest price if done in Cepheid Toulouse</td>
</tr>
<tr>
<td><strong>C</strong> Consumables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost per cartridge</td>
<td>$16.86</td>
<td>75% price reduction compared to EU</td>
</tr>
<tr>
<td>Number of working days per year</td>
<td>250</td>
<td>Number can vary depending on local context</td>
</tr>
<tr>
<td>Average number of tests per instrument /day</td>
<td>15</td>
<td>Number can vary depending on working hours</td>
</tr>
<tr>
<td>Number of tests/1 year/ full load 1 instrument</td>
<td>3750</td>
<td>G*H</td>
</tr>
<tr>
<td><strong>D</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Losses due to damage/incorrect use (high estimate 10%)</td>
<td>375</td>
<td>10% of I</td>
</tr>
<tr>
<td><strong>E</strong> HR costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technician annual salary</td>
<td>$5,000.00</td>
<td>Country-specific</td>
</tr>
<tr>
<td>Training and TA</td>
<td>$5,000.00</td>
<td>Depends on the needs</td>
</tr>
<tr>
<td><strong>F</strong> Installation costs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$19,200.00</td>
<td>A+B+C+D</td>
</tr>
<tr>
<td><strong>G</strong> Running costs (annual, 1 instrument)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$71,347.50</td>
<td>E+F*(I+J)</td>
</tr>
<tr>
<td><strong>O</strong> GRAND TOTAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>$100,547.50</td>
<td>N+M+L+K</td>
</tr>
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