Update on Lab services in the African region including new diagnostics

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NTP Manager’s Meeting, Nairobi 14-16 Oct 2013
Scope of presentation

- Mandate for Lab strengthening: WHO (AFR/RCs); Maputo Declaration; ASLM-Ministerial Call for Action, SLIPTA process
- Recommendations from RC for Lab strengthening
- Current data on Lab capacities in the African region
- Plan of action for support to NTP-linked labs
- Quality Control & accreditation drive (SLIPTA process)
- Quality Control for TB Microscopy
- Update on XpertMTB/Rif Roll out
- New Diagnostic tools and Methods
- Update on Expand TB project
- Conclusions
Mandate for TB Lab strengthening

- At its forty-eighth session, the WHO Regional Committee for Africa passed Resolution AFR/RC48/R2(Sept 1998) urging Member States to evaluate the laboratory component of disease control programmes as the first step towards strengthening disease surveillance. The fifty-eighth session (Yaounde, Sept 2008) re-affirmed Regional commitment to Lab strengthening (AFR/RC58/R6)
- The Maputo declaration (Jan 2008)
- ASLM-ministerial call for action (Dec 2012)
Actions proposed

• Develop a comprehensive national laboratory policy.
• Formulate a national laboratory strategic plan.
• Establish or strengthen laboratory leadership.
• Set up a national public health reference laboratory.
• Strengthen the public health laboratory supply and distribution system.
• Improve public health laboratory quality assurance systems.
• Strengthen laboratory staff training at all levels.
Actions proposed 2

• Ensure maintenance of laboratory equipment.
• Strengthen laboratory management information systems.
• Monitor and evaluate laboratory services.
• Ensure adequate funding for public health laboratory services.
State of Labs in the African region 2010¹

- 8,547 laboratories are linked to national TB programmes for microscopy services
- 123 providing culture, 48 providing drug susceptibility testing (DST)
- Laboratory to population ratio of 1 microscopy laboratory to 93,000 population
- 1 culture laboratory to 7.2 million population
- 1 DST laboratory to an average of 18 million population

¹ WHO AFRO Strategic Plan for control of Tuberculosis 2013-17
challenges

• Inequitable distribution of access to lab services
• Only 2 operational SRLs in the African Region
• Poor-non-existent lab networks in most countries
• Lack of well functioning National Lab reference services
• Insufficient trained Lab staff/Old establishments
• Poor equipment
• Poor supplies linked to poor maintenance schedules
• Excessive dependence on donor support linked to poor National ownership and response
Plan of action to support Lab strengthening (WHO/AFR)

• Promote use of GFATM funds and MoHs resources for lab strengthening
• Include operational research for use of new diagnostic tools in GF applications
• Review lab capacity for all NRL through desk reviews, ISTs (FP) and external consultants
• Provide support for development of national lab policy
• Facilitate QC measures for Mic, Cult and DST (External Panel evaluations through SRLs)
• All programme reviews to have a lab review component using new tools
• NRLs should meet expected quality standards (accredited, SLIPTA)
• Ensure functional lab networks from periphery to center
• Ensure sample referral services from periphery to center linked to treatment services and recording formats
• Support the implementation of iLED microscopy policy at all levels
• Support roll out of XpertMTB/Rif technology
• Continue the implementation of EXPAND-TB project
• Training of Lab staff with regular competency reviews
• Maputo Ministerial call for action:
  – Strengthen/establish national PHLS or Ctrs of excellence for disease
detection, monitoring and surveillance to improve DPC efforts
  – Dev entities and units for Lab services with MoHs of African countries
  – Promote policies that support PHLS, standardize lab workforce;
    provide career paths for lab workers
  – Dev thro regional economic blocks, harmonized Lab workforce
developmental strategy and certify lab workers at all levels
  – Establish/dev national Lab professional regulatory councils in all
countries to optimise quality of lab workforce, ethics and facilitate
  legislation
  – Request WHO, AU, ASLM and Regional economic communities to
    promote & coordinate partnerships aimed at improving integrated lab
    services
Lab strengthening

• **QUALITY CONTROL & OVERSIGHT TO OPTIMISE LABORATORY SERVICES IN THE AFRICAN REGION**
• Guidelines and Policy for implementation was finalized and approved in July 2011, in Nairobi

• Following the resolutions and declaration of WHO-AFRO

• Has catalytic effect to enable countries develop their national laboratory strategic and operational plans

• Country owned program
SLIPTA

• A framework for improvement of laboratory quality system in developing countries to fulfill ISO 15189 standards in a stepwise process to achieve accreditation.

• Designed based on ISO 15189/17025 Standards and the 12 QSEs of CLSI (GP26:A4)

• The Checklist is developed to monitor and check the progress and improvement of laboratory quality system
SLIPTA Checklist

- Identify areas where improvement is needed
- Develop and implement a work plan
- Monitor laboratory progress
- Conduct re-testing where required
- Continue steps to achieve full accreditation
SLIPTA Checklist (continued)

- The checklist consists of three parts:
  - Part I: Profile of Laboratory
  - Part II: Audit Checklist (Remarks and scoring)
  - Part III: Summary of Findings (Recommendations)

- The checklist has 334 questions divided into 12 sections and a total of 258 scores (100%)
- The 258 points are divided into a five steps that correspond with a Star Level
<table>
<thead>
<tr>
<th>Section</th>
<th>Total Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section 1: Document and Records</td>
<td>25</td>
</tr>
<tr>
<td>Section 2: Management Reviews</td>
<td>17</td>
</tr>
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<td>Section 3: Organization and Personnel</td>
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<td>Section 4: Client Management and Customer Service</td>
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<td>Section 5: Equipment</td>
<td>30</td>
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<td>Section 6: Internal audit</td>
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<td>Section 7: Purchasing and Inventory</td>
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<td>Section 8: Process Control and Internal and External Quality Assessment</td>
<td>33</td>
</tr>
<tr>
<td>Section 9: Information Management</td>
<td>18</td>
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<tr>
<td>Section 10: Corrective Action</td>
<td>12</td>
</tr>
<tr>
<td>Section 11: Occurrence/Incident Management and Process Improvement</td>
<td>12</td>
</tr>
<tr>
<td>Section 12: Facilities and Safety</td>
<td>43</td>
</tr>
<tr>
<td>TOTAL SCORE</td>
<td>258</td>
</tr>
</tbody>
</table>
### No Stars
(0 – 142 pts)
< 55%

### 1 Star
(143 – 165 pts)
55 – 64%

### 2 Stars
(166 – 191 pts)
65 – 74%

### 3 Stars
(192 – 217 pts)
75 – 84%

### 4 Stars
(218 – 243 pts)
85 – 94%

### 5 Stars
(244 – 258 pts)
≥95%

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**End Point**
National, Regional or International Accreditation Body
ENSURING QUALITY CONTROL FOR MICROSCOPY NETWORK AT POC
Microscopy network Accreditation

• Current laboratory accreditation drive
  – complementary to reference lab accreditation
  – huge numbers (WHO 2009)
    • labs: India 13,000; Indonesia 5000; Brasil 4000; DR Congo 1500; ...
    • tests, e.g. DF Bangladesh 700,000 per year (165 labs, 1/6th of population)
  – not individual labs, but network organization and functionality
  – For the first time, establishes a standard to guide assessments and monitor improvements

• Revive interest in microscopy
  – competing multitude of new laboratory priorities
  – no realistic replacement yet at the peripheral level
  – often unclear status, e.g. “100% EQA coverage”??

• Model for other point of care techniques organised as networks
Achievements

• Assessment tool version 1: under publication
• policies questionnaire: national level
  – validation questionnaires: national, intermediate, peripheral levels
  – stratified random site sampling system
  – links to various GLI microscopy guidance documents: http://www.stoptb.org/wg/gli/default.asp
• First pilot test performed: Pakistan NTP
  – has confirmed the needs
• ISO does not address network management
  – proposed standards and measures discussed among partners
    ➔ for GLI endorsement (done)
Standards for accreditation of an AFB-microscopy network

1. The TB microscopy network structure, its services to the NTP, its management, future expansion and appropriate use (balanced with that of other available TB laboratory methods), must be defined in a strategic plan.

   **Measure for standard #1** – A national strategic plan for TB laboratory services exists, either on its own or as part of the general NTP or laboratory services strategic plan. It clearly defines the place of microscopy as the first-line diagnostic and treatment monitoring test, except when Xpert MTB/RIF is available and indicated because of high prevalence of MDR-TB or HIV. The plan includes a gradual switch from Ziehl Neelsen to LED fluorescence technique where feasible.

2. A national AFB-microscopy manual with standard operating procedures must exist, and be available in some format at all the microscopy labs.

   **Measure for standard #2** - The national SOPs or guidelines are available and followed at all levels. Internal and external quality assurance policies and procedures are covered in this manual or separately, clearly stating the process and responsibilities at various levels. The operating procedures and policies respect global guidelines on the main points.

3. There must be documented and recent evidence of complete coverage of the population by AFB-microscopy labs, organized as a network.

   **Measure for standard #3** – There is at least one functional AFB-microscopy lab per 50,000 to 150,000 population, depending on population density. Except in the smallest countries, intermediate level laboratories assure an important part of the required training, external quality assessment (EQA) and supplies management for the peripheral level.
4. Qualifications and number of staff required for performing AFB-microscopy and its EQA must be appropriate and complemented by job descriptions and training curricula with sufficient emphasis on practice.

5. EQA must target all labs, including regular supervision visits.

6. Globally standardized recording and reporting formats for AFB-microscopy and its quality assurance must be used at all levels of the network.

7. The NRL or lab specialist of the NTP must assure excellent control over microscopy network supplies and equipment, including estimates and specifications for procurement, balanced distribution, provision for buffer stocks and stock management at all levels.

8. A policy regarding the place of the private sector and its microscopy labs within the NTP must exist and should be functional.

9. There must be a dedicated budget for the microscopy network, assuring continuous and country-wide availability of free, quality assured AFB-microscopy.

10. AFB-microscopy laboratories must be safe for the staff and the community.
SRL to enhance TB diagnostics in Africa
• An SRL is a centre of excellence that achieves high technical and programmatic standards.

• In Africa such labs are rare and many times we depend on Western countries for support.
The TB laboratory network
## Functions

<table>
<thead>
<tr>
<th>Facility</th>
<th>Serves</th>
<th>Services Provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRL</td>
<td>Multiple NRLs</td>
<td>Quality control (e.g. panel testing), TA, training, support with Drug-resistance surveys, higher-level testing (e.g. second line DST, molecular diagnostics),</td>
</tr>
<tr>
<td>NRL</td>
<td>Country, Intermediate Labs (IL)</td>
<td>Quality control, quality assurance/supervision, diagnostic services (e.g. culture, DST), operations research, training</td>
</tr>
<tr>
<td>IL</td>
<td>Peripheral diagnostic centers</td>
<td>Quality control, quality assurance/supervision, diagnostic services (culture, microscopy)</td>
</tr>
</tbody>
</table>
"The chain is only as strong as the weakest link"

- A functional, efficient network depends on each level having the capacity to fulfill its proper functions.

- If one level lacks that capacity, the level above is compelled to deliver replacement services.

- This leads to longer diagnostic delays, inefficient use of resources, and limited capacity to perform higher level functions.
Rationale for Regional SRL

• African country laboratories face similar problems:
  – Human resource
  – Infrastructure
  – Quality services
  – Access
  – Biosafety
  – Financial matters
  – Etc etc

• A regional SRL has potential to connect better
Support to other countries

• In Africa, not all countries have a TB reference laboratory.

• Those who have, are generally very weak while others have limited strength in a few areas.

• Because of this, countries rely on highly proficient TB laboratories in other countries (Supranational Reference Laboratories – SRL) for support.

• The purpose of SRL is to ensure that the TB reference laboratory in the other country are functional.
Business case for having a regional SRL

- TB is a global problem (TB anywhere is TB everywhere)

- There are only 6 SRLs for the 45 countries in Africa, and some countries are not covered

- The few SRLs are overburdened, can’t be sufficient

- SRLs in Africa will serve as models to emulate

- They will be a test-case

- African SRLs will serve as demonstration sites compared to SRLs in the North.

- Training and TA will also be more efficient because of the cultural similarities.

- Cheaper services. For example, it is cheaper to train, have TA and refer samples to an African country than an off continent country.
DR-TB and HIV-Infected TB

• XpertMTB/RIF project
TBXpert Project

• 25.9 million USD UNITAID-funded project for procurement and implementation of GeneXperts and Xpert MTB/RIF cartridges
  • Consortium: **WHO Global TB Programme, Stop TB Partnership,**
    Global Laboratory Initiative (GLI), TB REACH, Global Drug Facility (GDF), EXPAND-TB, African Society for Laboratory Medicine (ASLM),
    Interactive Research and Development (IRD)

• Goal: To increase rapid diagnosis of TB, HIV-associated TB and drug-resistant TB in low- and middle-income countries

• Key expected outcomes:
  – Increases in incident bacteriologically-positive TB and TB/HIV cases detected
  – Increases in rifampicin-resistant TB cases detected
  – Reductions in diagnostic delay
  – Decentralized positioning of GeneXperts
  – Increased market penetration in private and public non-NTP sectors
TBXpert Project

230 GeneXperts and 1.4 million Xpert MTB/RIF cartridges in 21 countries, from 2013-2015
TBXpert Project

- 21 recipient countries selected based on TB, MDR-TB, TB/HIV burden; capacity to provide further diagnostic testing and care; UNITAID priorities (low-income countries prioritized)
- TB REACH contributing 10-12 million USD for support of implementation at selected sites (according to the TB REACH Proposal Review Committee)
  - Supporting all sites in 7 countries and some of the sites in another 7 countries
- IRD to establish sustainable social business models in Jakarta, Dhaka and Karachi (<25 GeneXperts in each city)
- ASLM to coordinate technical assistance support in Congo, Ethiopia, Tanzania, Mozambique, Kenya
- Cooperation with PEPFAR, USAID, CDC, Global Fund, Supranational Reference Laboratories and other partners to ensure provision of technical assistance and treatment of patients diagnosed with rifampicin resistance
<table>
<thead>
<tr>
<th>Country</th>
<th>GeneXperts</th>
<th>Xpert MTB/RIF cartridges (tentative)</th>
<th>Total sites receiving cartridges</th>
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</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>25</td>
<td>165,000</td>
<td>25</td>
</tr>
<tr>
<td>Belarus</td>
<td>4</td>
<td>26,000</td>
<td>4</td>
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<tr>
<td>Cambodia</td>
<td>8</td>
<td>46,000</td>
<td>9</td>
</tr>
<tr>
<td>Congo</td>
<td>1</td>
<td>7,000</td>
<td>1</td>
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<tr>
<td>Ethiopia</td>
<td>8</td>
<td>46,000</td>
<td>8</td>
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<tr>
<td>India</td>
<td>40</td>
<td>202,000</td>
<td>40</td>
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<tr>
<td>Indonesia</td>
<td>25</td>
<td>165,000</td>
<td>25</td>
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<tr>
<td>Kenya</td>
<td>11</td>
<td>73,000</td>
<td>13</td>
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<tr>
<td>Kyrgyzstan</td>
<td>1</td>
<td>8,000</td>
<td>1</td>
</tr>
<tr>
<td>Malawi</td>
<td>8</td>
<td>63,000</td>
<td>8</td>
</tr>
<tr>
<td>Moldova</td>
<td>0</td>
<td>53,000</td>
<td>23</td>
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<tr>
<td>Mozambique</td>
<td>12</td>
<td>84,000</td>
<td>16</td>
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<tr>
<td>Myanmar</td>
<td>4</td>
<td>23,000</td>
<td>4</td>
</tr>
<tr>
<td>Nepal</td>
<td>13</td>
<td>56,000</td>
<td>22</td>
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<tr>
<td>Pakistan</td>
<td>25</td>
<td>165,000</td>
<td>28</td>
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<tr>
<td>Philippines</td>
<td>10</td>
<td>62,000</td>
<td>10</td>
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<tr>
<td>Swaziland</td>
<td>2</td>
<td>15,000</td>
<td>2</td>
</tr>
<tr>
<td>Tanzania</td>
<td>10</td>
<td>62,000</td>
<td>10</td>
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<tr>
<td>Uganda</td>
<td>8</td>
<td>46,000</td>
<td>8</td>
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<tr>
<td>Uzbekistan</td>
<td>6</td>
<td>26,000</td>
<td>6</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>9</td>
<td>52,000</td>
<td>9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>230</strong></td>
<td><strong>1,445,000</strong></td>
<td><strong>272</strong></td>
</tr>
</tbody>
</table>
Xpert MTB/RIF roll-out: global progress

99 GeneXperts (524 modules) in the public sector in 23 countries

1,402 GeneXperts (7,553 modules) in the public sector in 88 countries

Data: FIND
Xpert MTB/RIF global landscape today

• 3,196,920 Xpert MTB/RIF cartridges procured, as of June 2013 (public sector in eligible countries)

Top procurers:
1,916,200 South Africa
146,360 India
71,250 Swaziland
66,940 Kenya
62,750 Zimbabwe
56,910 Tanzania
52,340 Pakistan
47,130 Malawi
44,320 Mozambique
42,960 DR Congo
38,760 Nigeria
37,430 Philippines

Data: FIND
Cumulative number of GeneXpert modules and Xpert MTB/RIF cartridges procured under concessional pricing

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<tr>
<td>Modules</td>
<td>40,790</td>
<td>86,320</td>
<td>191,900</td>
<td>329,350</td>
<td>591,450</td>
<td>863,790</td>
<td>1,107,330</td>
<td>1,482,550</td>
<td>1,891,970</td>
<td>2,315,380</td>
<td>3,196,920</td>
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<tr>
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<td>0</td>
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</tbody>
</table>

August 2012: “Buy-down” with the manufacturer by PEPFAR, USAID, UNITAID and Bill & Melinda Gates Foundation — the price of the cartridge dropped to 9.98 USD in 145 eligible countries.
WHO policy guidance on Xpert MTB/RIF: current recommendations and updates
Summary of WHO recommendations
(December 2010)

1. Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (Strong recommendation)

2. Xpert MTB/RIF may be considered as a follow-on test to microscopy in settings where MDR-TB or HIV is of lesser concern, especially in further testing of smear-negative specimens (Conditional recommendation acknowledging major resource implications)

Of note:
- Recommendations currently apply to sputum specimens only
- Recommendations apply to children, but based on generalisation of data
WHO commissioned reviews of the evidence (early 2013):
  - Diagnosis of pulmonary TB and rifampicin resistance in adults
  - Diagnosis of extrapulmonary TB
  - Diagnosis of TB in children
  - Affordability and cost-effectiveness

Expert Group Meeting was organized to evaluate evidence and propose recommendations to WHO (May 2013)

Approval by WHO Strategic and Technical Advisory Group (STAG-TB, June 2013), and pending approval of WHO Guidelines review committee (August/Sept 2013)

Updated recommendations to be published Q4 2013
WHO Implementation guide to be updated

Including:

- Updated and enhanced diagnostic algorithms
- Improved budgeting guidance
- Annex of SOPs for processing extrapulmonary specimens
- What to do when Xpert detects rifampicin resistance in a patient not at risk?
Boda Boda Referral mechanisms improves access to Xpert - 2012

<table>
<thead>
<tr>
<th></th>
<th>Referring health facilities</th>
<th>GX SITES</th>
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</thead>
<tbody>
<tr>
<td><strong>Total tests</strong></td>
<td>4034</td>
<td>3508</td>
</tr>
<tr>
<td><strong>MTB NOT DETECTED</strong></td>
<td>3214</td>
<td>2689</td>
</tr>
<tr>
<td><strong>MTB DETECTED</strong></td>
<td>429</td>
<td>614</td>
</tr>
<tr>
<td><strong>INDETERMINATE</strong></td>
<td>391</td>
<td>214</td>
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$\frac{7542}{6} \times 250 = 5$

$\frac{7542}{6} \times 365 = 3.4$
Xpert diagnosed patients on Treatment

<table>
<thead>
<tr>
<th></th>
<th>Q4/2011</th>
<th>Q1/2012</th>
<th>Q2/2012</th>
<th>Q3/2012</th>
<th>Q4/2012</th>
<th>Total</th>
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<tr>
<td><strong>Total treated</strong></td>
<td>62</td>
<td>69</td>
<td>261</td>
<td>216</td>
<td>196</td>
<td>804</td>
</tr>
<tr>
<td><strong>Total Diagnosed</strong></td>
<td>102</td>
<td>215</td>
<td>277</td>
<td>222</td>
<td>197</td>
<td>1013</td>
</tr>
</tbody>
</table>
Other global resources and activities for facilitating the roll-out of Xpert MTB/RIF
Global Forum of Xpert MTB/RIF Implementers
(16-17 April, 2013)

• As part of the annual GLI Partner meeting, 140 representatives from countries, technical agencies, donors
• Sharing up-to-date information, country experiences and plans
• Focus on impact
Global Forum of Xpert MTB/RIF Implementers (16-17 April, 2013)

- **Key findings and recurring points:**
  - High burden countries and multi-national initiatives highlighted impact found in piloting or wide-scale implementation:
    - Increases in bacteriologically positive TB case detection and rifampicin-resistant TB cases
    - Reduction in time to diagnosis; less evidence in reduction of time to treatment
  - Many countries have **ambitious scale-up plans**
  - **Cartridge shortages** as a result of manufacturing problems threaten efficient functioning of programmes and may introduce delay to new large-scale country plans and multi-national initiatives; need to improve forecasting
Global Forum of Xpert MTB/RIF Implementers
(16-17 April, 2013)

• **Key findings and recurring points: (continued)**
  
  – **Diagnostic and treatment capacity** for rifampicin-resistant TB need to be matched
  
  – **Engaging the private sector**: Innovative PPM initiatives forming to provide Xpert to private sector at concessional prices in selected Asian countries
  
  – **Electronic recording and reporting**: a panel of partners and Cepheid described their advancements
  
  – **In-country partner collaboration must be led by NTPs** and is critical to ensure a unified strategy and efficient use of resources
NTPs and partners in 56 countries have shared information on sites of instruments and plans for procurement

www.who.int/tb/laboratory/mtbrifrollback
NTPs and partners in 56 countries have shared information on sites of instruments and plans for procurement.
Quarterly updates on Xpert MTB/RIF implementation and roll-out, sent to WHO mailing list (750+ external recipients)

Online list of published literature on Xpert MTB/RIF linked to abstracts, updated monthly (by category: paediatric TB, extra-pulmonary TB, cost-effectiveness, etc.)

www.who.int/tb/laboratory/mtbrifrollout

Information note promoting Xpert MTB/RIF for improving TB case detection among people living with HIV: Joint product between WHO TB and HIV Departments
Revised WHO definitions and reporting framework

• Prompted largely by the need to accommodate Xpert MTB/RIF into revised case and outcome definitions

• New 2013 WHO guidance:
  – Examples of revised forms and lab registers (Xpert results recorded in same register as smear)
  – Quarterly reporting focuses on bacteriological confirmation (smear, culture or Xpert-positive) instead of smear positivity

• Revised definitions will be used by WHO as the basis for global data collection starting in 2014 for year 2013 data
Coming soon

• Publication of updated **WHO recommendations** and accompanying implementation guidance

• As a TB CARE I project and in collaboration with GLI partners, a **training package** on Xpert MTB/RIF is being developed, combining modules and products of KNCV (TB CARE I), FIND and Cepheid
  - expected finalization: Q4 2013 / Q1 2014

• Union Conference on Lung Health, Paris (Oct 2013)
  - Symposia: Critical issues and challenges for maximising the impact of Xpert; Innovative PPM approaches for Xpert
Diagnostic Tools and Methods

Developmental trajectory
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
Acceleration

- **Tools development**: At least 20 new technologies in various stages of development and evaluation in last 10 years

- **WHO policies**: *
  - 2007: New SS+ case definition, two-specimen approach, liquid culture, rapid speciation
  - 2008: Line probe assay
  - 2009: LED microscopy, ‘same-day diagnosis’, selected non-commercial culture and drug susceptibility testing methods
  - 2010: Xpert MTB-RIF
  - 2011: IGRAs, commercial serodiagnostics

- **Access** to new diagnostics and laboratory strengthening (GLI, EXPAND-TB and Xpert MTB/RIF)

*Available at: [http://www.who.int/tb/dots/laboratory/policy/en](http://www.who.int/tb/dots/laboratory/policy/en)
Tools/methods not recommended

• Evidence base too weak, to be reassessed
  – 2009: Sputum processing methods
  – 2009: Thin Layer Agar method for rapid DST
  – 2012: LPA for XDR-TB

• ‘Negative’ policy (do-not-use)
  – 2011: Commercial serodiagnostics
  – 2011: IGRAs (high TB or HIV burden settings)
Tools in tiered health services

Surveillance
Reference methods
Network supervision

Case finding
Treatment

Screening
Referral

Central Reference Level

District & Sub-district Level

Community Level
## Tools in combination

<table>
<thead>
<tr>
<th>Year</th>
<th>Technology</th>
<th>Turnaround time</th>
<th>Sensitivity gain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Baseline</td>
</tr>
<tr>
<td><strong>Before 2007</strong></td>
<td>ZN microscopy</td>
<td>2-3 days</td>
<td>+10% compared to LJ</td>
</tr>
<tr>
<td></td>
<td>Solid Culture</td>
<td>30-60 days</td>
<td></td>
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<tr>
<td><strong>2007</strong></td>
<td>Liquid Culture / DST</td>
<td>15-30 days</td>
<td>S+ only</td>
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<tr>
<td></td>
<td>Rapid speciation</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2008</strong></td>
<td>Line Probe Assay</td>
<td>2-4 days</td>
<td>+10% compared to ZN</td>
</tr>
<tr>
<td></td>
<td>(1st line, Rif &amp; INH)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2009</strong></td>
<td>LED-based FM</td>
<td>1-2 days</td>
<td>1st line only</td>
</tr>
<tr>
<td><strong>2009</strong></td>
<td>In house DST</td>
<td>15-30 days</td>
<td>+40% compared to ZN</td>
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<tr>
<td></td>
<td>(MODS, CRI, NRA)</td>
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</tr>
<tr>
<td><strong>2010</strong></td>
<td>Xpert MTB/RIF</td>
<td>100 minutes</td>
<td></td>
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<tr>
<td></td>
<td>(TB, R resistance)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **early diagnosis & care**
- **smear-negative TB**
- **rapid resistance detection**
Policy uptake at country level (1)

- **Rapid uptake**
  - SS+ case definition

- **Limited or no uptake**
  - Two-specimen strategy
  - Same-day-diagnosis
  - Non-commercial culture and DST methods

- **Gradual uptake**
  - LED microscopy
  - Liquid culture and DST
  - Rapid speciation
  - Line probe assay
  - Xpert MTB/RIF test
EXPAND-TB project

Expanding Access to New diagnostics For Tuberculosis
WHO/GLI/FIND/GDF
Funded by UNITAID
Background

- To expand TB and MDR-TB diagnostic capacity
  - by introducing rapid, quality-assured WHO-endorsed tests
  - by supporting 105 reference labs in 27 countries
  - by increasing market size and decreasing test price

- Unique Diagnostic Project worth more than $350M

- Formal country requests for participation

- Only 5 year project but lasting impact on the implementation of new technologies as it provides essential laboratory capacity
Partners

- **UNITAID**
  - Funding for commodities and assistance

- **gli**
  - Policy framework, standards & monitoring

- **FIND**
  - Main implementer, knowledge transfer

- **GLOBAL DRUG FACILITY**
  - Procurement
2009

1810 cases detected in 4 laboratories in 3 countries

2 to 3 months needed for case detection and DST
2012

Roll-out of new technologies and reduced time to diagnosis:

- MGIT: 3-4 weeks
- LPA: 3 days
- GeneXpert: 2 hours
June 2013

53,739 cases detected in 81 laboratories in 25 countries
Most observed challenges

Specimen referral

Human Resources

Commodity management

Maintenance for infrastructure and equipment

Laboratory Information Management Systems
Conclusion

• Overall Goal - the diagnostics should have an impact on TB control

• Approach – Health system strengthening through improving PHLS
  • Improve quality (accuracy - QMS, timeliness etc)
  • Access (appropriate tools, Distribution, Referral systems and awareness etc)

• Strategy
  • (Policies, strategic plans, EQA for Xcopy for HBCs to expand through Regional focal points/ISTs etc)

• Implementation:

  {Partners (donors and implementers), GLI, EXPAND TB, SRLs, T/As, NRLs, network, PPP, Government - to take more ownership}
THANKS FOR LISTENING!!
New diagnostics and implementation plans

- Discuss roll out plans for Xpert MTB/RIF
- New Molecular diagnostics
- Plans for Phasing-in iLED microscopy to replace conventional Fluorescence microscopy
- Discussions of EXPAND-TB project
- Improvement in detection of DR-TB
- Implementation of improved sample referral pathways
Outline

• Current WHO-endorsed TB diagnostics/approaches

• Policy transfer and uptake

• Policy innovation

• Expand-TB project
Outline

• Current WHO-endorsed TB diagnostics/approaches

• Policy transfer and uptake

• Policy innovation

• EXPAND-TB project