Quality assurance / proficiency testing for Xpert MTB/RIF and other molecular methods

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Presentation outline

• EQA/PT for Xpert MTB/RIF

• Verification for Xpert MTB/RIF

• PATH experience – partnership with Wits University/NHLS for the commercialization of EQA/verification panel production

• Ways forward
External Quality Assessment/Proficiency Testing
Xpert MTB/RIF
Why is it important?

* EQA is a specialized form of assessment * focused on assuring accuracy and reliability of examination methods * PT is only one method used for EQA

* EQA /PT is an effective tool to promote continual improvement!

EQA/PT can identify occurrences/nonconforming events

PT programs offer external assessment of process output

CLSI, 2011: GP26-A4
EQA/PT for Xpert MTB/RIF

• “There is a scarcity of established PT programs for molecular diagnostics...though PT is even more important when technologies are evolving”  CLSI: MM14-A:2005

• No established EQA/PT programs specific for Xpert MTB/RIF

• Pilot EQA programs currently underway: CDC, NHLS

• EQA/PT programs for general molecular testing available from CAP, UKNEQAS, SNRL’s (DST for MDR incl. LPA), RCPA, others?
Criteria for Xpert MTB/RIF Specific EQA/PT

- Testing material must contain whole *M. tb* for capture of bacteria by filter in the cartridge (0.8um)
- Panel composition: Sensitive: RIF resistant: NTM: Neg. 3 x annual
- Testing procedure must be safe and compatible with Xpert MTB/RIF testing protocol
- Non-laboratory skilled HCW’s must be able to perform testing in non-lab setting
- Cost-effective and sustainable for large scale National programs
- Easy to transport
## Comparison of Xpert MTB/RIF PT materials

<table>
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<tr>
<th>Program</th>
<th>Advantage</th>
<th>Disadvantages</th>
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| **Heat inactivated M.tb** | **Liquid:**  
• Same sample format as patient specimens  
• Same amount of SR to add as patient specimen (2ml)  
• No additional consumables. | • Shipping cost – weight of liquid (n=48/infinity).  
• Leakage during transport |
|                       | **Lyophilized:**  
• Weight for transportation is reduced compared to liquid equivalent. | • Cost to prepare is increased compared to liquid?  
• Format for testing different to patient sample specimen.  
• Amount of SR to add is different to patient specimen (~2.8ml)  
• May require additional consumables. |
| **DCS**               | • Easy to prepare  
• Easy to ship  
• Perforated spots easier than cutting spots | • Format for testing different to patient sample specimen.  
• Requires additional consumables for processing on site.  
• Amount of SR to add is different to patient specimen (~2.8ml) |
What can we learn from other TB EQA programs?
What can we learn from other TB EQA programs?

- It takes time and resources!

- EQA program introduction needs to be tailored to the readiness level of country

- *M.tb* necessitates special considerations related to;
  - Labor intensive growth process
  - Shipping permission/regulations
  - High costs (shipping etc)
  - Resistance profiles
Remote monitoring as a tool for EQA

• EQA/PT is more than just proficiency panels!

• Remote monitoring allows real-time performance indicator monitoring

• Allows prompt corrective action

NHLS, 2013
Verification
Xpert MTB/RIF
Why is it important?

Verification needed to demonstrate performance specifications for examinations on new instruments

CLSI, 2011: GP26-A4
Why is it important?

- Gives assurance to users that the Xpert MTB/RIF instrument is functioning properly at the time of installation.
- Checks to verify that users can correctly interpret and report results.
- Verifies that there are no major errors in the process control system and that samples are identified correctly, tested correctly and reported correctly.
- Quickly recognizes major problems with an instrument or user at installation.
Verification for Xpert MTB/RIF

Pilot verification programs currently underway;

• GLI – verification panels sent to 172 sites in 27 countries. Have also been sent to 31 sites using LPA

• NHLS – 1,880 modules verified, 152 instruments from 142 sites. DCS showed compatibly for use with LPA MTBDRplus2
Criteria for Xpert MTB/RIF specific verification

- As per EQA criteria
- New SRLN guidance recommends unblinded panels
- Performed upon installation and recalibration
- 1 x pansusceptible strain (?)
An EQA/verification panel commercialization initiative

Our experiences
The need

- Partnership with Wits University/NHLS (South Africa) grew out of projected domestic Xpert MTB/RIF EQA/verification panel demands, and later additional demands

- Sustainable solution required that focused on local capacity and manufacture

- Part of PATHs technology transfer and African diagnostics manufacturing initiative

- Discussion underway with GLI regarding production of GLI liquid verification panel
Activities to date

• Working with Wits/NHLS, WHO/GLI, FIND, CDC, USAID and other partners to collaboratively address standards related to Xpert MTB/RIF (& other molecular tests) comprehensive QMS

• Wits University developed attenuated non-cording WT MTB strains – RIF resistant derivative (Centre of TB Excellence)

• Patent has been approved for entire Wits U/NHLS DCS QA process

• Currently the full commercialization plan has been finalized in collaboration with Wits U/NHLS
Ways forward

• How can we ensure quality management for fast-followers?

• How often to perform EQA/PT?
  • 3/year/per module/per site?

• Ideal panel composition? (RIF resistant/sensitive/NTM/negative)

• Do current programs assess the entire workflow process adequately? (incl. pre & post examination)
Ways forward

- Which quality performance indicators need to be commonly agreed upon?

- EQA/PT and verification are only two of the tools needed for quality management. What Xpert MTB/RIF specific guidance is required for each component of a total quality management approach? What is realistic?

- Web/network real time vs. paper systems?

- How can we ensure synergy with existing EQA programs for TB? e.g: harmonization of on-site supervision schedule

- Consensus is required!
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- FIND