Approaches to developing a robust TB LAM quality assessment programme

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Anura David
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QMS in a laboratory environment

Quality management systems in laboratories assure the **reliability** of all aspects of the **operations**.

In a laboratory environment, all 12 components are usually implemented as part of routine processes and quality assessment is one of them.

**Quality assessment** consists of planned activities which is important for improvement of the laboratory quality management system.

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WHO Laboratory quality management system: handbook (2011)
QA Overview

EQA Methods

- Proficiency testing—external provider sends unknown samples for testing to a set of laboratories, and the results of all laboratories are analyzed, compared, and reported to the laboratories.
- Rechecking or retesting—slides that have been read are rechecked by a reference laboratory; samples that have been analyzed are retested, allowing for inter-laboratory comparison.
- On-site evaluation—usually done when it is difficult to conduct traditional proficiency testing or to use the rechecking/retesting method.

Benefits of EQA
- allows comparison of performance and results among different test sites;
- provides early warning for systematic problems associated with kits or operations;
- provides objective evidence of testing quality;
- indicates areas that need improvement;
- identifies training needs.

What about POC tests and field settings? Do the same rules apply?
Importance of QA

• Laboratory
  o For lateral flow (LF) assays in particular, **quality assessment** is of paramount importance, due to the nature of result interpretation which relies on **operator competency**
  o Proper training, SOPs and quality control and required to ensure **quality results**
  o **Challenges**
    ➢ **limitations of the assay** itself

• Field setting
  o Testing (and therefore QA) performed by **non-lab personnel**, including nurses and other healthcare workers – offers the advantage of **reduced patient waiting time**
  o **Challenges**
    ➢ **Training and competency** is usually **inadequate** in these settings
    ➢ **inappropriate storage** of reagents
    ➢ reagent **stock-outs** and
    ➢ **lack of supportive supervision**

*Lessons learnt from HIV LF QA Programmes*
• Poor participation from HCWs
• Lack of focus on ensuring the quality of HIV tests performed at community level
But… can be improved through provision of additional resources (trainers, supervisors, co-ordinators)
CDC EQA survey

• Initial discussions raised concerns about LF LAM implementation

• Poor uptake of LAM (~20 countries implemented/implementing LAM)
  o Concerns about performance of Alere LAM assay
  o Regulatory delays
  o Waste disposal
  o Ease of urine collection in decentralized centres
    ➢ Feasibility study (OSA and urine) at a PHCF in Jhb
    ➢ >95% of participants reported a clean, safe and suitable space to produce urine (n=330)

• No guidelines available for QA of LAM testing

• TB LF LAM QA Package development survey sent out in late 2022
  (https://www.surveymonkey.com/r/3PH93WB)
LAM QA material development

Wits Biomedical Innovation Award (Scott, David and Stevens) for development of an EQA for LF-TB LAM assay

<table>
<thead>
<tr>
<th>Inactivation method</th>
<th>Control band intensity</th>
<th>Storage temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neat 1:10 1:50 1:100</td>
<td>-20°C ambient 2-8°C 37°C</td>
</tr>
<tr>
<td>Heat (95°C) for 4 hours</td>
<td>0 1∗ 1 1</td>
<td>1 1 1 1**</td>
</tr>
<tr>
<td>Chemical inactivation</td>
<td>0 not done 0 0</td>
<td>1 1 1 1**</td>
</tr>
<tr>
<td>Bruker-Hain Genolyse buffer and heat</td>
<td>0 0 not done 0</td>
<td>not done not done not done not done</td>
</tr>
<tr>
<td>Sonication using a tube-sonicator</td>
<td>0 0 not done 0</td>
<td>not done not done not done not done</td>
</tr>
<tr>
<td>STR buffer (Cepheid)</td>
<td>0 0 0 0</td>
<td>not done not done not done not done</td>
</tr>
<tr>
<td>Heat (95°C) for 4 hours with glass beads</td>
<td>0 1 1 1</td>
<td>not done 1 not done not done</td>
</tr>
<tr>
<td>Heat inactivation using an autoclave</td>
<td>0 1 1 1</td>
<td>not done 1 not done not done</td>
</tr>
</tbody>
</table>

Outcomes:
- Heat inactivation worked well and was more cost-effective than chemical inactivation
- Specimens evaporated at 37°C after 25 weeks of storage
- Pilot testing of material in the field (HCW) and lab testing produced expected results
- ~2% of LAM strips produced invalid results
- Material used for weekly QC testing

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Considerations for LAM QA

• Urine = ideal sample type but…
  o Not sterile
  o Contains bacteria and other pathogens

• Other considerations
  o Material should be stable for transportation to remote areas
  o Biosafety considerations
  o Should mimic clinical specimen
  o Should be packaged so that pipette provided with the LAM kit can be used for testing
  o Volume should be sufficient for repeat testing
  o No of samples and panels required per cycle to ensure that all testing personnel participate
  o Cost effectiveness
  o “Train-the-trainer” initiatives
  o Should be able to be adapted for new LAM technologies

Robust and cost-effective EQA for quality POC testing to support a sustainable EQA programme.
Result reporting

- No template for reporting of results
- Currently recorded in patient file – Negative result not always documented
- EQA will require a reporting tool
  - Training videos or other
- Challenges with result interpretation – faint bands

Role of Digital Health Technologies

Digital Health Applications

- Software
- Tablet
- Mobile
- Reader

**Significance:**

Capture + store results digitally + Automated interpretation + CQM and surveillance

**Use Case:**

COVID-19 + HIV

**Proof of Concept:**

Operator → Visual Read → Interpretation

**Documents Accessible:**

- FDA (2022) The Software Precertification (Pre-Cert) Pilot Program: Tailored Total Product Lifecycle Approaches and Key Findings
- WHO (2023) Target product profile for readers of rapid diagnostic tests
- Concerns regarding Data storage and Data security - WitsDIH team has developed self-declaration form

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Slide courtesy of Dr Vidy Keshav
Result return

• Online result submission – smart device and internet access in remote location?
• Assistance with trouble-shooting
• Ideally would want to photograph results and upload – smart device and internet access
Summary

• Field testing - what level of support can be offered by labs?

• More questions than answers on some aspects of LAM testing

• A quick search for available EQA for LF-TB LAM assay found one:

3 EQA panels for 3 submissions per participant per annum

Each panel contains 4 Liquid Vials each containing 75ul of sample per panel consisting of either MTB which is inactivated and stable at room temperature & MTB negative material (info courtesy of Dean Sher (SSQ)
Acknowledgements