Approaches to developing a robust TB LAM quality assessment programme

04th May 2023

Anura David

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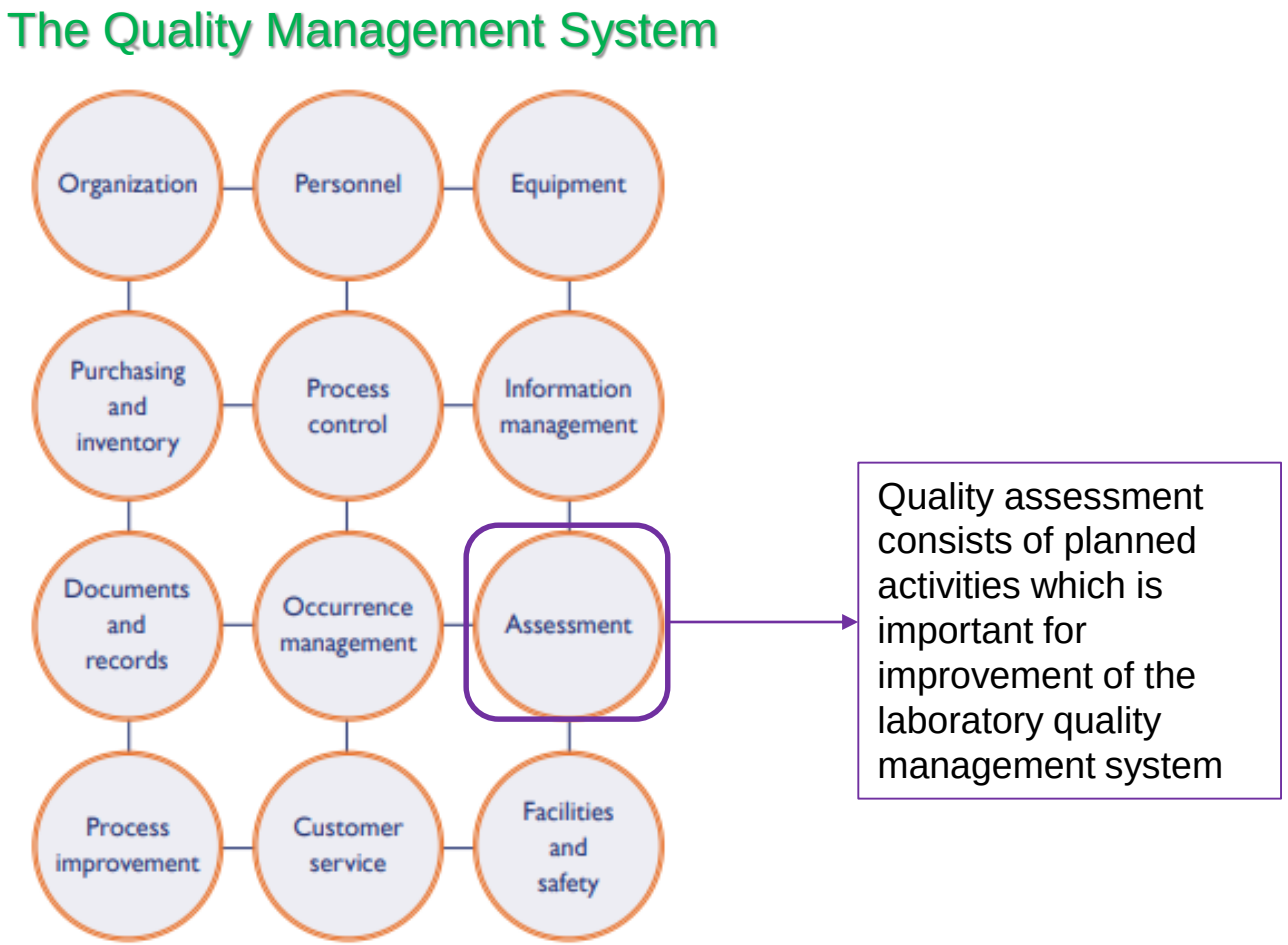
QMS in a laboratory environment

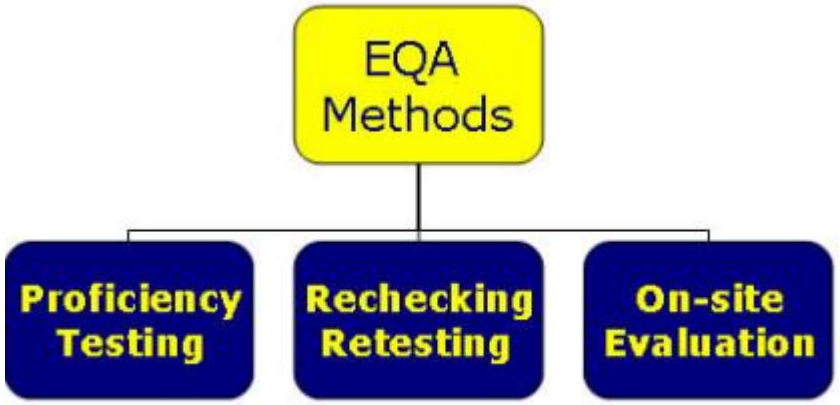
Quality management systems in laboratories assure the **reliability** of all aspects of the **operations**.



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

WHO Laboratory quality management system: handbook (2011)

QA Overview



WHO Laboratory quality management system: handbook (2011)

- 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
  - 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**
  - Proper training, SOPs and quality control and required to ensure **quality results**
  - Challenges
    - **limitations of the assay** itself

- Field setting
  - Testing (and therefore QA) performed by **non-lab personnel**, including nurses and other healthcare workers – offers the advantage of **reduced patient waiting time**
  - 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)
  - Concerns about performance of Alere LAM assay
  - Regulatory delays
  - Waste disposal
  - 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)

TB LF LAM QA Package development stakeholders sensitization meeting (Sep 2022)

LAM QA material development

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

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

0 = unacceptable
1 = acceptable
* acceptable for up to 4 months storage
**liquid evaporated after 25 week storage

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

Considerations for LAM QA

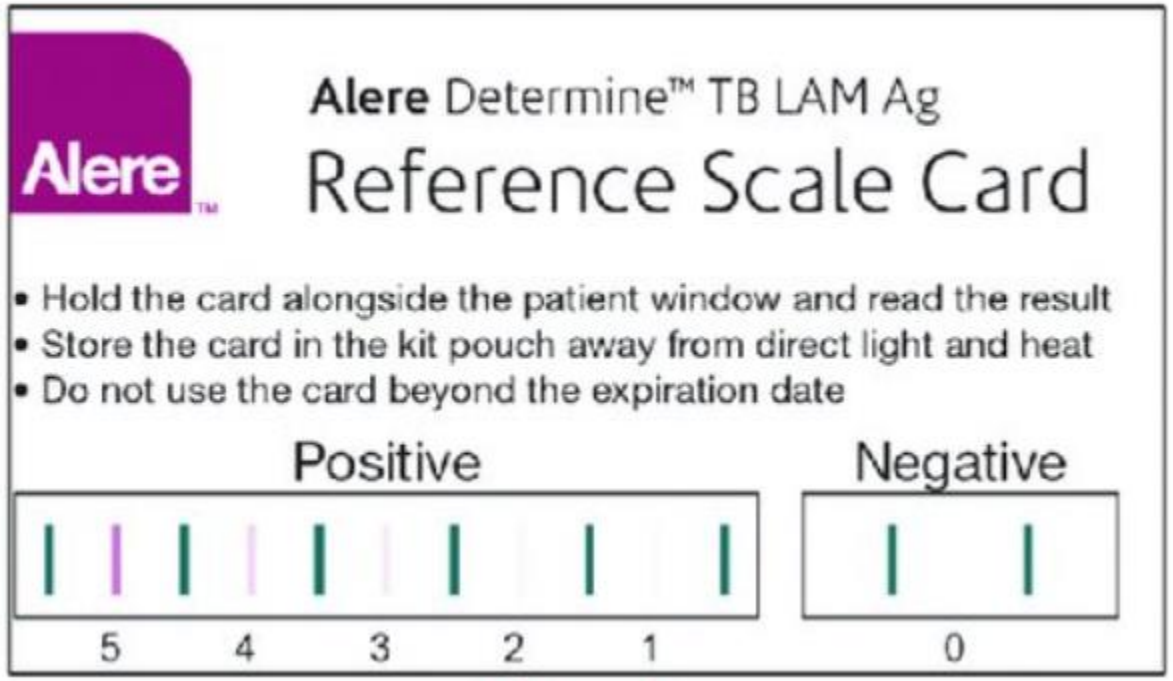
- Urine = ideal sample type but…
  - Not sterile
  - Contains bacteria and other pathogens

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

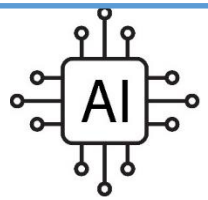
- No template for reporting of results
- Currently recorded in patient file – Negative result not always documented
- EQA will require a reporting tool
  - Training videos or other
- Challenges with result interpretation – faint bands



https://www.researchgate.net/publication/221859142_Diagnostic_accuracy_of_a_urine_LAM_strip-test_for_TB_detection_in_HIV-infected_hospitalized_patients/figures?lo=1

Role of Digital Health Technologies

Digital Health Applications



Software

Tablet

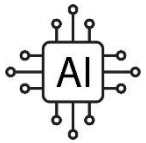
Mobile

Reader

Significance:

Capture + store results digitally

+



Automated interpretation

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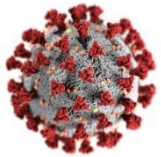
CQM and surveillance

Use Case



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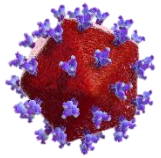


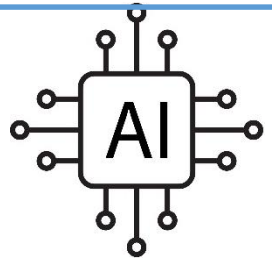
COVID-19 HIV

Proof of Concept:

Operator

Visual Read

V/S



Interpretation

Documents Accessible:

- **WHO (2016)**. Monitoring and evaluating digital health interventions: a practical guide to conducting research and assessment.
- **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

University of the Witwatersrand WITS DIH Diagnostic Innovation Hub

iLEAD

Bill & Melinda Gates foundation

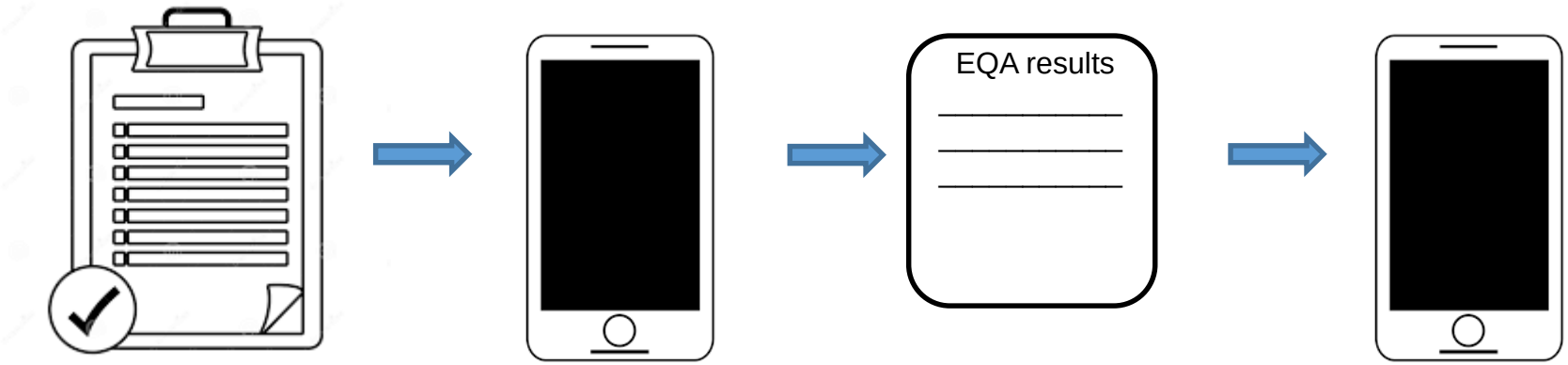
audere

Fio Corporation

Slide courtesy of Dr Vidya 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



Testing site

EQA provider

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:

	Urine TB LF-LAM EQA Panel *(Pilot)*	4 Vials *(Not yet accredited)*	SSQ-LFLAM-MTB-EQA

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

HSRO Health Sciences Research Office

health Department: Health REPUBLIC OF SOUTH AFRICA

iLEAD INNOVATION: LAB ENGINEERED ACCELERATED DIAGNOSTICS

NATIONAL HEALTH LABORATORY SERVICE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | Wits Enterprise

BILL & MELINDA GATES foundation

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PHRU IMPROVING LIFE THROUGH RESEARCH Perinatal HIV Research Unit of the University of the Witwatersrand

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