WHO support to the evolving TB Diagnostic Landscape

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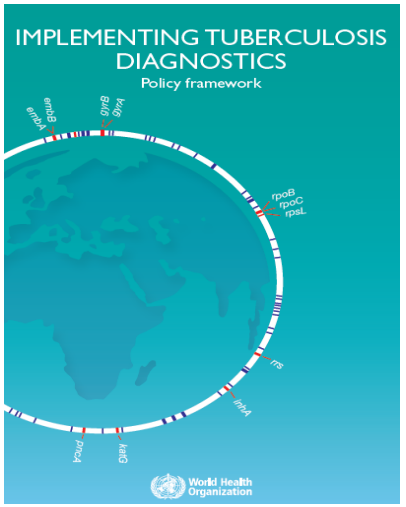
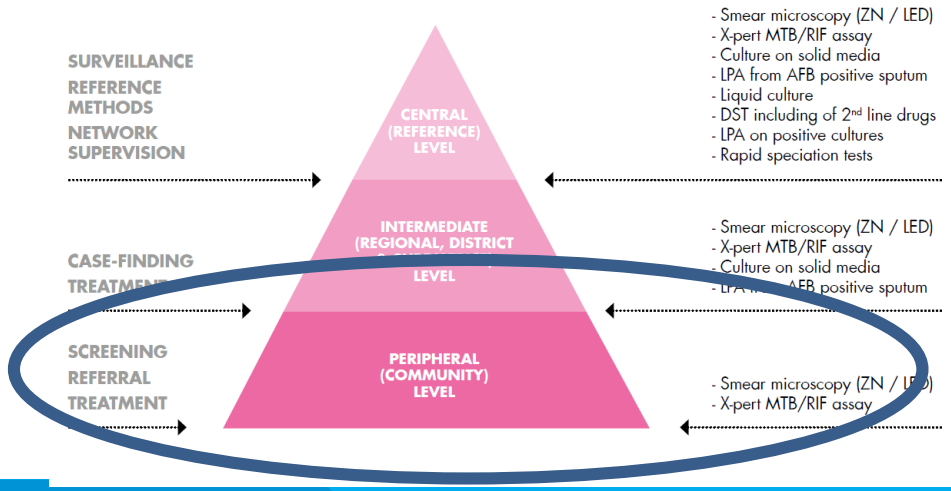
Content

- Diagnostic techniques recommended by WHO
- WHO policy development process for new TB diagnostics
- Target product profiles and support to diagnostic developers
- Planned work on diagnostic policy development

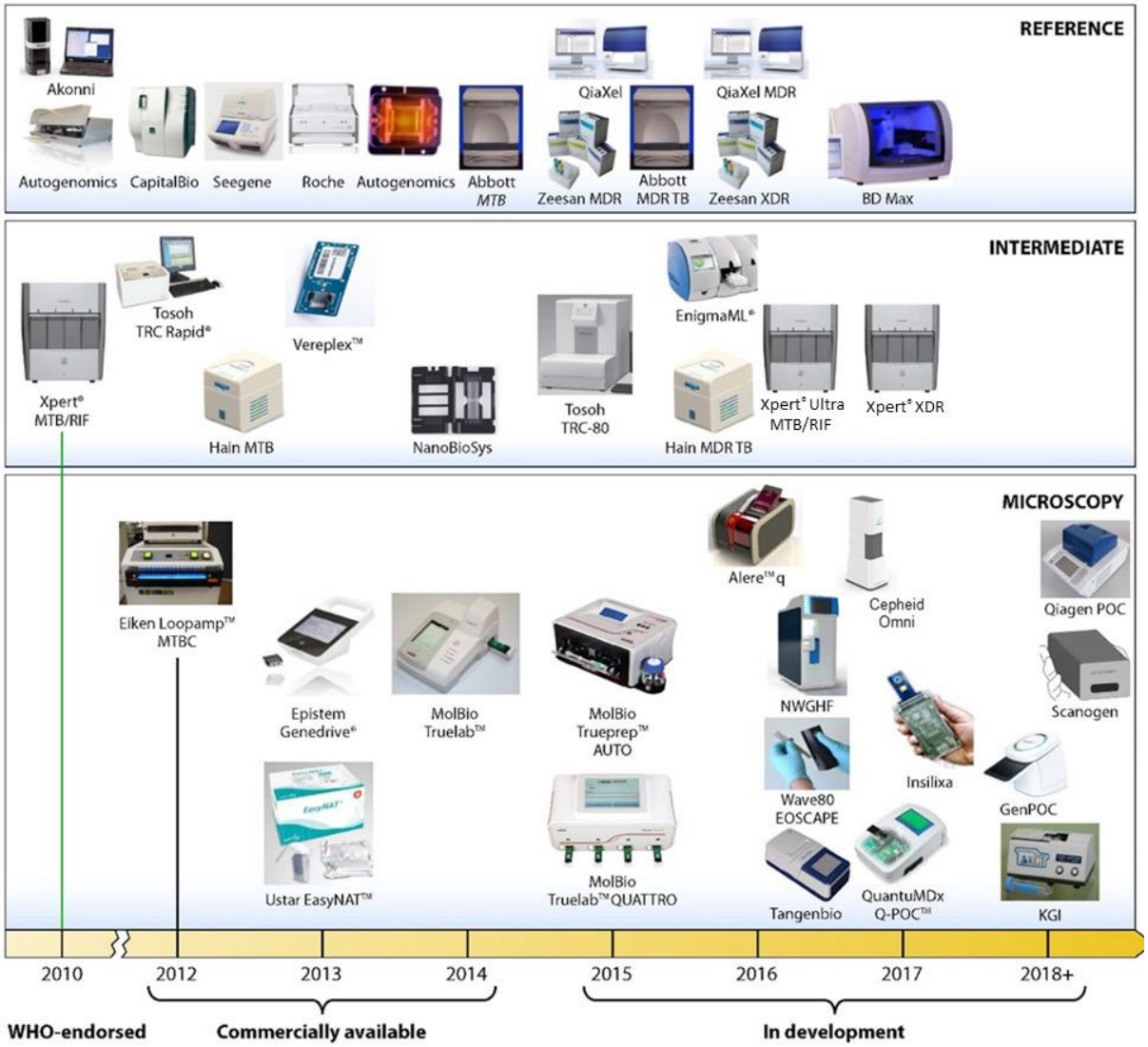
WHO's recommended techniques for diagnosing TB

- **Microscopy**
  - Conventional light microscopy
  - Light-emitting diode fluorescent microscopy
- **Culture**
  - Culture on solid media
  - Commercial liquid culture systems and rapid speciation
- **Drug-susceptibility testing**
  - DST first-line anti-TB agents
  - DST for second-line anti-TB agents
  - Non-commercial methods
- **Molecular testing**
  - LPA (first and second-line)
  - TB-LAMP
  - Xpert MTB/RIF assay (Ultra)
- **LF-LAM Urine test for PLHIV**





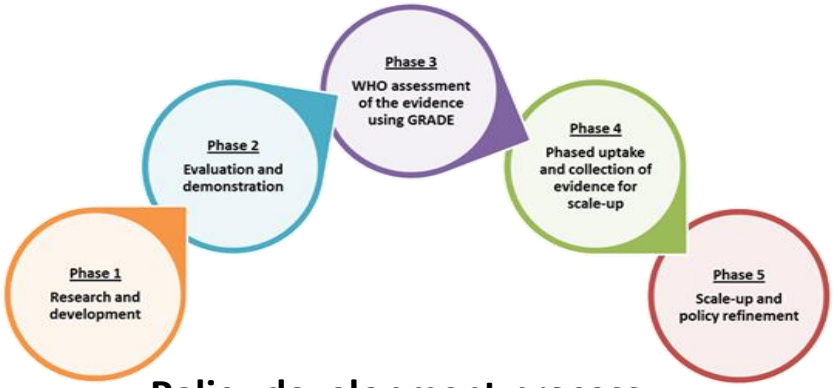
Interest in TB is at an all time high and the pipeline of technologies is robust



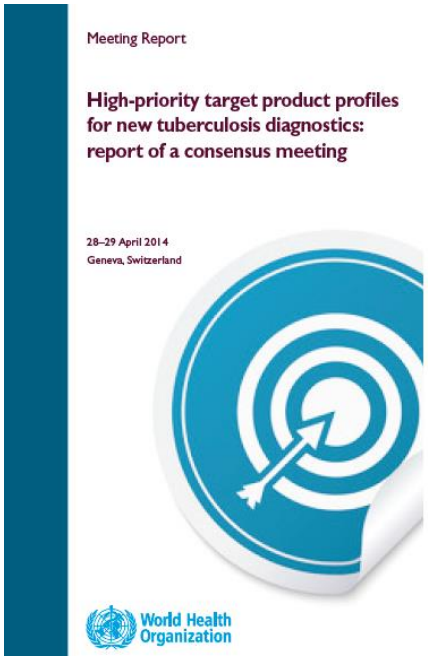
- Majority of technologies developed for the intermediate and central level laboratories
- More technologies suitable for the peripheral level as are replacement for microscopy are needed
- Greater investment in conducting the field evaluation and demonstration studies in high burden setting is needed

UNITAID 2015 Tuberculosis Diagnostics Technology And Market Landscape 4th Edition

WHO's process for developing policies on TB diagnostics



Policy development process



- The developers of diagnostic tests are encouraged to engage in early discussions with WHO to ensure that the new technology will be appropriate for the end-users.

- Priority target product profiles (TPP) for new diagnostics, developed following a consensus building process, are described in the TPP meeting report

Prioritizing the Products

Evaluation Criteria

Prioritization By Key Stakeholders | **Impact** | **Market** | **Implementation And Scalability**

Product Ideas

	Target product profiles for potential new TB diagnostic tests	Prioritization by key stakeholders: Patients and community advocates	Prioritization by key stakeholders: National tuberculosis programmes	Prioritization by key stakeholders: Field practitioners	Prioritization by key stakeholders: Researchers	Impact: Potential to reduce TB incidence	Impact: Potential to reduce TB morbidity and mortality	Market: Potential (global) market size	Market: Potential to reach the market in the next 5 years	Implementation and scalability: Potential use as a point-of-care test	Implementation and scalability: Potential to get scaled-up	Score	Priority rank
	TRIAGE, RULE OUT AND SYSTEMATIC SCREENING TEST												
A	Triage test for those seeking care	high	high	high	medium	high	medium	high	low	high	high	26	3
B	An HIV/ART clinic-based test to rule out active TB	high	high	high	high	low	high	medium	medium	high	high	26	3
C	Systematic screening test for active case finding	high	high	medium-high	medium	high	medium	medium	low	high	high	24.5	5
	RAPID TB DIAGNOSIS TEST (WITH OPTIONAL DRUG SUSCEPTIBILITY TESTING)												
D	Rapid, sputum-based, cartridge-based, molecular test for microscopy centers (with the option of add-on drug susceptibility testing cartridge)	medium-high	high	high	high	high	high	high	high	high	high	29.5	1
E	Rapid biomarker-based instrument-free test for non-sputum samples (which can also detect childhood and extrapulmonary TB)	high	high	high	high	high	high	high	low	high	high	28	2
F	Multiplexed test for TB and other infectious diseases	high	medium-high	low	medium	medium	medium-high	medium-high	low	high	medium	19	8
	NEXT-GENERATION DRUG SUSCEPTIBILITY TEST												
G	Centralized, high-throughput, drug susceptibility test (incorporating new drugs to support the roll out of new TB treatment regimens post 2014)	medium	high	medium	medium	low	medium	low	high	low	medium	18	9
	TREATMENT MONITORING TEST												
H	Treatment monitoring test (test for cure)	high	high	medium	medium	low	medium	low-medium	low	low	high	19.5	7
	PREDICTIVE TEST FOR LATENT TB INFECTION												
I	Predictive test for latent TB infection at high risk of active TB	high	high	medium	high	high	high	high	low	low	low	23	6

Prioritized Need for TPPs

- Triage/rule-out test
- Sputum-based, smear replacement
- Biomarker-based, non-sputum
- Rapid DST at the peripheral level
- Test of progression

Kik S *et al.* ERJ 2014

WHO supporting manufacturers' to bring products to the market

Manufacturers are encouraged to engage with WHO early in the development process to ensure that once a design-locked product is developed it can be properly evaluated to meet WHO requirements

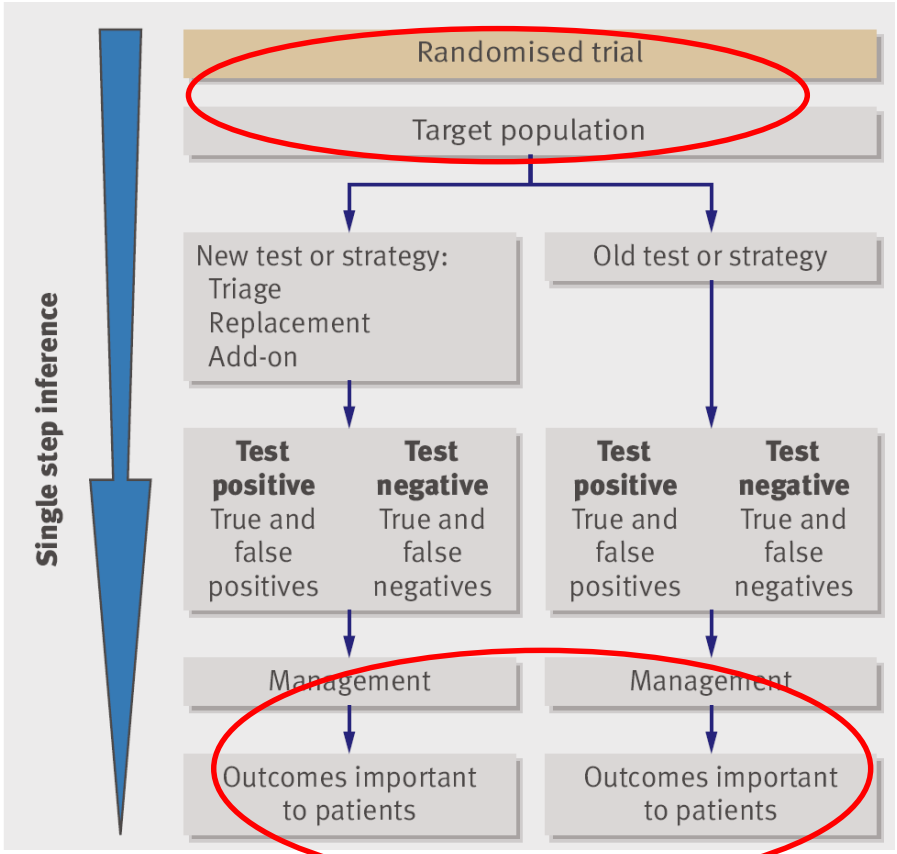
- Reference standards are appropriate
- Appropriate samples are tested
- Ensure study design appropriate with statistical power
- Evaluations are performed in different epidemiological and geographical settings
- FIND as a WHO collaborating centre can facilitate independent evaluation

Much greater investment in the field evaluation studies is needed to expedite new tests from the pipeline

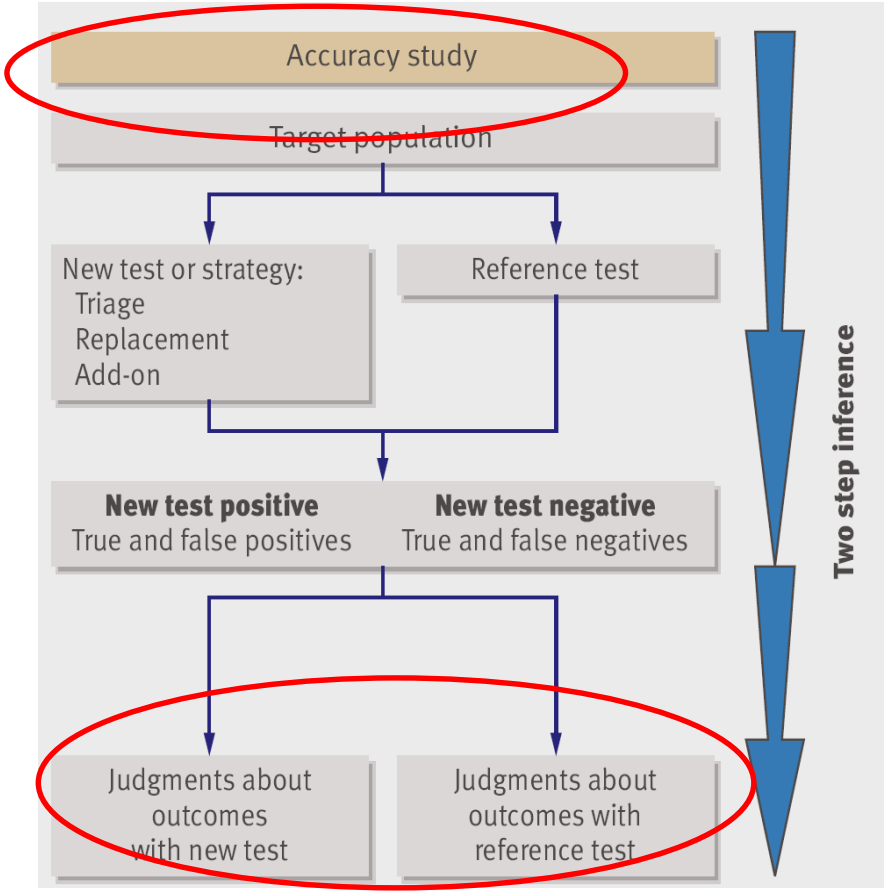
*Grades of Recommendation Assessment, Development and Evaluation

Diagnostic study dilemmas

What we want …

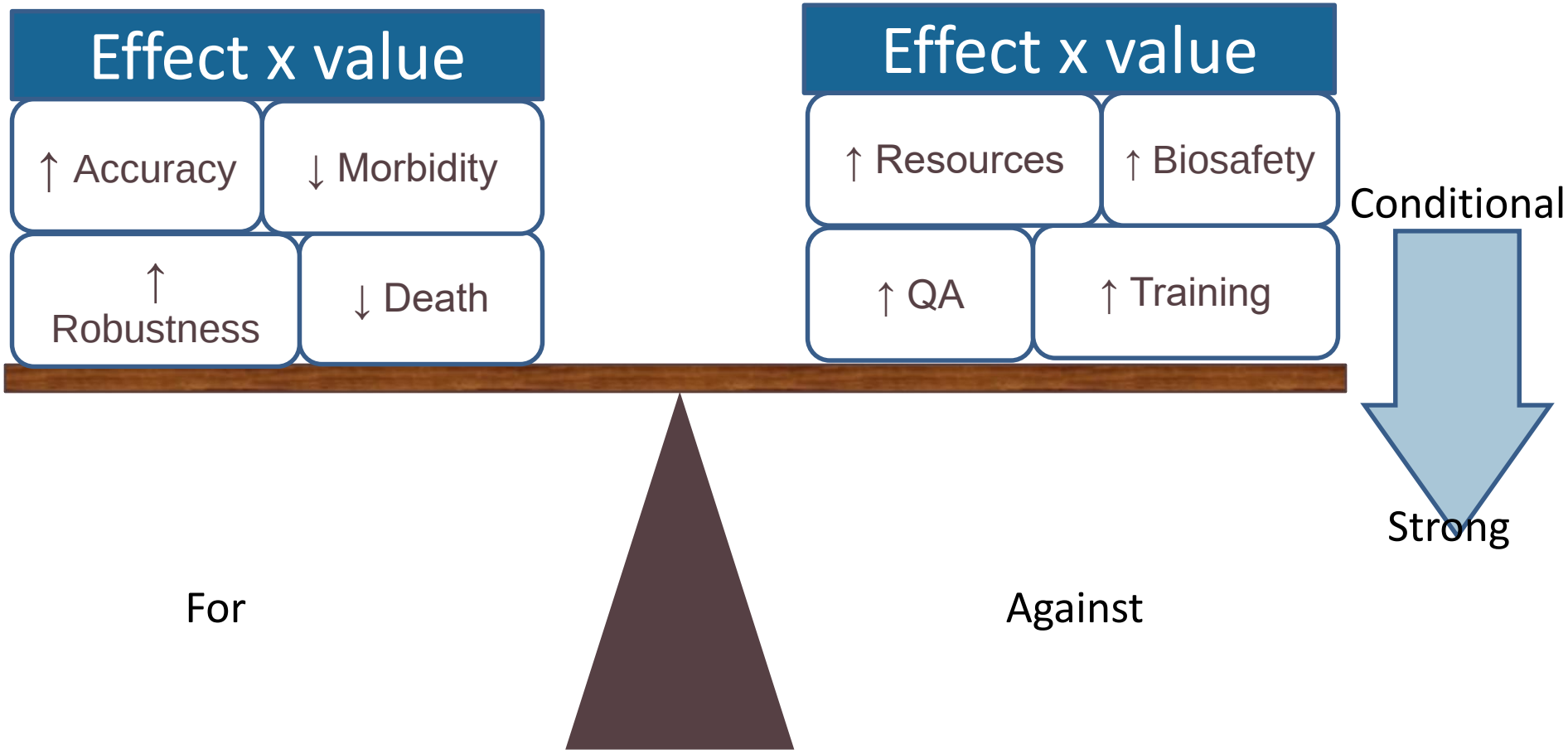


What we have …



Schunemann et al. BMJ, 2008

Desirable vs undesirable consequences



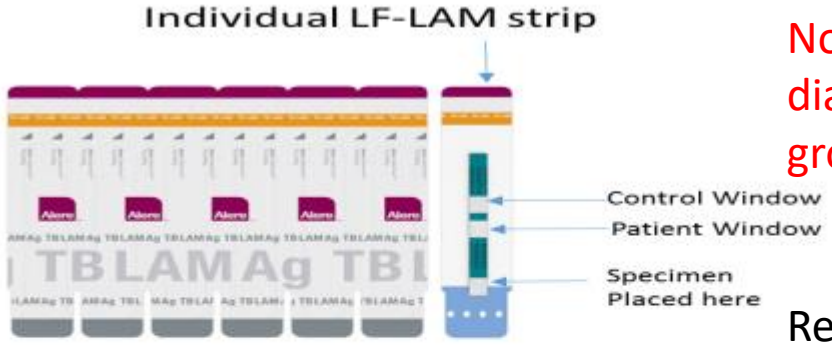
Essential considerations

Since no diagnostic test has perfect accuracy…

Assessing the use of a diagnostic needs to consider the sensitivity and specificity of the test, the level of the health system, the target population and the prevalence of the condition being detected

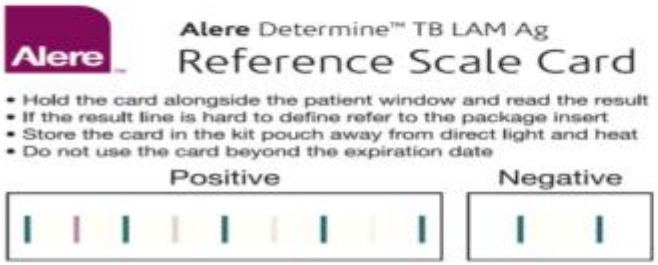
Lateral flow-
Urine Lipoarabinomannin assay (LF-LAM)

A.



Not recommended by WHO for TB screening or diagnosis of active TB disease in most population groups

B.



Recommended to help with the diagnosis of TB in two specific population groups:

- People living with HIV who have signs or symptoms of TB and a CD4 cell count less than or equal to 100 cells/µL
- People living with HIV who are “seriously ill” regardless of CD4 count or if the CD4 count is unknown.

Future work on diagnostics

1. Review of critical concentrations for performing DST and establish methods for new and re-purposed drugs

WHO Technical Expert Group April 24-26 2017

2. Evaluation of the use of sample transport solutions for improved recovery of MTB from culture or detection using molecular methods

WHO Technical Expert consultation planned for May 29 2017

3. Review of centralized high-throughput platforms for the detection MTBC and drug resistance

Guideline Development Group Meeting planned for Q4 2017

GeneXpert Omni and Xpert Ultra

- Small and Portable
- Durable
- Low Power Consumption
- Automatic Connectivity
- Solid State
- Integrated Battery

Expert MTB/RIF Ultra has been evaluated in a non-inferiority diagnostic accuracy study as a replacement for the Xpert MTB/RIF cartridge – Guidance available 24th March 2017

Evaluation the Omni instrument delayed until end of 2017

THANK YOU

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