Challenges in TB Diagnostics

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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**
## Prioritizing the Products

### Product Ideas

### Evaluation Criteria

<table>
<thead>
<tr>
<th>Prioritization By Key Stakeholders</th>
<th>Implementation And Scalability</th>
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<tbody>
<tr>
<td><strong>Impact</strong></td>
<td><strong>Market</strong></td>
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<tr>
<th>Product Ideas</th>
<th>Prioritized Need for TPPs</th>
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<tbody>
<tr>
<td>Triage/rule-out test</td>
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<tr>
<td>Sputum-based, smear replacement</td>
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<td>Biomarker-based, non-sputum</td>
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<td>Rapid DST at the peripheral level</td>
<td>Rapid DST at the peripheral level</td>
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<td>Test of progression</td>
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**Kik S et al. ERJ 2014**
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
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*
Diagnostic study dilemmas

What we want ...

Randomised trial
Target population

New test or strategy: Triage Replacement Add-on
Test positive True and false positives
Test negative True and false negatives
Management
Outcomes important to patients

What we have ...

Accuracy study
Target population

New test or strategy: Triage Replacement Add-on
Reference test
New test positive True and false positives
New test negative True and false negatives
Judgments about outcomes with new test
Judgments about outcomes with reference test

Schunemann et al. BMJ, 2008
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.