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TAG Treatment Action Group

Partners In Health

CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES

Expert Meeting on Defining Test Specifications for a point-of-care TB test

Paris, 17 –18 March, 2009

- Objective: reach agreement on minimum specifications for a point-of-care TB diagnostic test that meets medical needs
- 34 participants including clinicians, laboratory experts and test developers
- 'Expert Opinion Check' survey conducted prior to the meeting:
  - 30 participants from 17 different countries surveyed by phone, inc. TB practitioners involved at all levels of care, professionals in charge of TB programmes at national level or working in a research institution

Towards TB POC test specifications

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Meeting Outcomes - Test Specifications Required

	Minimum specifications required
Medical decision	Treatment Initiation
Sensitivity - Adults (regardless of HIV status)	Pulmonary TB: Smear pos., culture positive: 95% Smear neg., culture positive: *[60-]80% *[Detection of Extrapulmonary TB being a preferred but not a minimal requirement]*
Sensitivity - children (**incl. EPTB; regardless of HIV status**)	80% compared to culture of any specimen and 60% of probable TB [noting problems of gold standard]
Specificity	Adults: 95% compared to culture Children: - 95% compared to culture - 90% for culture neg., probable TB [problem of gold standard]
Time to results	Max. 3 hours (patient must get result the same day) *[Desirable would be <15min]*

*：The group could not decide on a definite minimal value

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	Minimum specifications required
Throughput	Min 20 test/day by 1 lab staff
Sample collection	Adult: urine, oral, breath, venous blood, sputum *[Desired: NON-sputum based sample type and use of finger prick instead of venous blood]* Child: urine, oral, finger/heel prick
Sample preparation	• Safe – biosafety level 1 • Max. 3 steps • Approximate volumes of samples & reagents (no precise pipetting) • Preparation not highly time sensitive
Number of samples	One sample per test
Read out	• Easy, unambigous to read with qaulitative and simple ‘yes’, ‘no’, ‘invalid’ answer. • Read out stays permanent for at least 1 hour

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	Minimum specifications required
Waste disposal	Simple burning or dispose in sharp pit; no glass Environmentally acceptable disposal
Controls	Positive control included in the kit Quality control simpler and easier than with SSM
Reagents	All reagents contained in a self-contained kit Kit contains sample collection device, H^2O (if needed)
Storage/stability	Shelf life 24 months incl. for reagents Stable at 30°C,higher temp for shorter time periods [to be defined] Stable in high humidity environments
Instrumentation	If instrument needed, no maintenance required Instrument works in tropical conditions Acceptable replacement cost Must fit in backpack, shock resistant
Instrument Design	Can work on battery
Training time	1 day max. training time Can be performed by any health worker
Cost	Below US$10 per test after scale up

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The group could not take a final decision on:

- Diagnosis of EPTB in adults as a minimal requirement for a new TB POC test.

  (interim decision was to define EPTB Dx as highly desirable but not minimal requirement)

- Rejection of use of sputum as sample.

  (interim decision was to define the exclusion of sputum sample as highly desirable but not minimal requirement)

Broader consultation is needed to reach a final decision on those points

Stimulating R&D for a TB POC – next steps

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Best options for rapid TB POC development

- To use existing POC platforms and identify a new biomarker
- To use an identified biomarker and build a new platform
- To assess the adequacy and accessibility of existing specimen sample banks.
- Increase funding for diagnostics fourfold.

	Ag/Ab	**Molecular**
Biomarker:	Unknown	Specific genes IDed
POC Platform:	Lateral flow	Nonexistent

Test Development Limitations Outlined

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- All biomarkers tested on lateral flow devices to date have shown insufficient performance to properly diagnose active TB.
- It is clear that a combination of biomarkers will be needed to achieve good test performance.
- No biomarkers have to date been clearly identified as suitable
- Several potential candidates were mapped out
- Absence of an entity to validate or screen the potential candidate at a very early stage of identification.
- Need for a ‘proof-of-principle’ screening facility testing all biomarker candidates on clinical specimens.
- Need for a facility to test the various combinations of verified markers and aiming at using these combination on a lateral flow platform.

Test Development Limitations Outlined

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•DNA detection using molecular methods seems to show very good performance so far (similar to culture) but a field-adapted portable platform device is as yet inexistant.

•DNA detection could allow the use of alternative specimen types for example urine, but more R&D is needed to define better and optimise its real potential (EPTB, children, HIV+, overall performance etc).

•Need a better assessment of the current and coming portable molecular platforms, in all fields of research.

•Need to bring R&D efforts towards adapting/creating portable molecular plaform with methods specific for TB diagnosis.

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Next Steps

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- To perform a **broader field expert consultation** in order to:
  - To strengthen and validate the agreed specification table
  - To finalise decisions regarding the importance for a new TB POC test to diagnose EPTB and not to be based on sputum specimens.

- To establish a '**clearing house' with open access to information** and regular, rigorous evaluation of progress of different areas (biomarkers, platforms etc)

- To assess and document the **adequacy AND accessibility of existing specimen banks**. If assessment reveals needs, the establishment of a high-quality and open-access specimen banking system will be crucial.

- Current candidate biomarkers need to be systematically evaluated at early stage of R&D.

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Next Steps

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- Develop methodologies for systematic and standardized evaluations and validations new diagnostic tests prior to commercialization.

- Need for more actors to become involved at all levels.

- Need for at least fourfold increase in investment in TB **diagnostics** R&D as well as new funding mechanisms, incl. a prize fund for a TB point-of-care test