
NON-COMMERCIAL CULTURE METHODS AND MYCOBACTERIOPHAGE-BASED ASSAYS FOR RAPID SCREENING OF PATIENTS AT RISK OF DRUG-RESISTANT TUBERCULOSIS

- EXPERT GROUP MEETING -

Date and time: 8 - 9 September 2009, 09:00 – 18:00
Venue: Crowne Plaza Hotel, Geneva, Switzerland

BACKGROUND

Early detection of drug resistance in tuberculosis (TB) allows the use of appropriate treatment regimens for patients, which has an important impact for improved TB control. The development of rapid methods for drug susceptibility testing (DST) is crucial due to increasing rates of multidrug-resistant tuberculosis (MDR-TB) worldwide and the emergence of extensively drug-resistant tuberculosis (XDR-TB), with very high reported HIV-associated mortality. Spread of drug resistant strains of *Mycobacterium tuberculosis* and the management of patients diagnosed with drug resistant disease is one of the most formidable obstacles faced by national tuberculosis control programmes, compounded by a critical lack of appropriate diagnostic tools and vastly inadequate laboratory capacity.

Conventional culture and DST methods require prolonged periods to confirm mycobacterial growth and detect drug resistance, during which time patients may be inappropriately treated, drug resistant strains may continue to spread, and amplification of resistance may occur. Rapid diagnosis of TB and drug resistance will therefore have obvious patient- as well as public health benefits, including better prognosis, increased survival, prevention of acquisition of further drug resistance, and reduced spread of drug resistant strains to vulnerable populations.

Commercially available liquid culture systems and molecular line probe assays for rapid detection of MDR-TB have been endorsed by WHO; however, due to their complexity and cost, as well as the need for sophisticated laboratory infrastructure, uptake has been limited in many resource-constrained settings. Several non-commercial culture and DST methods have been developed at the same time, aimed at use in laboratories that lack access to more sophisticated infrastructure and techniques. Among these methods, microscopic observation of drug susceptibility (MODS), thin layer agar (TLA), colorimetric redox indicator (CRI) method nitrate reductase assay (NRA) and mycobacteriophage-based assays have shown promise as rapid, inexpensive methods.

WORLD HEALTH ORGANIZATION: EVIDENCE-BASED PROCESS FOR POLICY GUIDANCE

In order to facilitate rapid policy guidance on the use of new diagnostic tools, new methods, and/or novel approaches using existing tools, WHO has recently developed a systematic, structured, evidence-based process: The first step constitutes a systematic review and meta-analysis of available data, using standard methods appropriate for diagnostic accuracy studies. The second step involves the convening of an Expert Group to evaluate the strength of the evidence base and recommend operational and logistical considerations for mainstreaming such tools/approaches into national TB control programmes, and/or identify gaps to be addressed in future research. The third and final step involves WHO policy guidance on the use of these tools/approaches, presented to the WHO Strategic and Technical Advisory Group for TB (STAG-TB) for endorsement and subsequent dissemination to member states for implementation.

MEETING OBJECTIVES

- To review the evidence base and evaluate data from systematic reviews commissioned by WHO on the performance characteristics of non-commercial culture methods and mycobacteriophage-based assays for rapid diagnosis of drug-resistant tuberculosis;
- To evaluate preliminary data from field demonstration projects on non-commercial culture methods and mycobacteriophage-based assays for rapid diagnosis of drug-resistant tuberculosis;
- To define the laboratory infrastructure, human resource requirements, and further operational research data needed for programmatic implementation of non-commercial culture methods and mycobacteriophage-based assays for rapid diagnosis of drug-resistant tuberculosis;
- To outline potential issues to be addressed by WHO in subsequent policy recommendations;

EXPECTED OUTCOMES

- Evidence-based recommendations on the use of non-commercial culture methods and mycobacteriophage-based assays for rapid screening of patients with drug-resistant tuberculosis;
- Consensus on laboratory infrastructure, human resource requirements and further research data needed for programmatic implementation of non-commercial culture methods and mycobacteriophage-based assays for rapid diagnosis of drug-resistant tuberculosis;
- Development of WHO policy guidance on the use of non-commercial culture methods and mycobacteriophage-based assays for rapid diagnosis of drug-resistant tuberculosis.

PROVISIONAL AGENDA

Tuesday 8 September 2009

Chair: P Nunn & K Weyer, WHO

Rapporteur: F Cobelens

08:30 - 08:40	Welcome	M Raviglione/R Ridley
08:40 - 08:50	Introduction Meeting scope and objectives	K Weyer
08:50 - 09:00	Declaration of Interest by Expert Group members	Chair
09:00 - 09:15	Grading quality of evidence and strength of recommendations: Brief overview of GRADE	K Steingart
09:15 - 09:45	Systematic review: Microscopic observation of drug susceptibility (MODS) for rapid diagnosis of drug-resistant tuberculosis	J Minion & M Pai
09:45 - 10:15	Discussion	All
BREAK 10:15 - 10:30		
10:30 - 10:50	Laboratory infrastructure, human resource requirements, and research gaps for implementation of MODS	D Moore
10:50 - 11:30	Discussion	All
11:30 - 12:00	Draft recommendations	All
LUNCH 12:00 - 13:00		
13:00 - 13:30	Systematic review: Nitrate reductase assay (NRA) for rapid diagnosis of drug-resistant tuberculosis	A Martin
13:30 - 14:15	Discussion	All
14:15 - 14:35	Laboratory infrastructure, human resource requirements, and research gaps for implementation of NRA	L Barrera
14:35 - 15:00	Discussion	All
15:00 - 15:30	Draft recommendations	All
BREAK 15:30 - 15:45		
15:45- 16:15	Systematic review: Colorimetric redox indicator method (CRI) for rapid diagnosis of drug-resistant tuberculosis	A Martin
16:15 - 16:45	Discussion	All
16:45 - 17:00	Laboratory infrastructure, human resource requirements, and research gaps for implementation of CRI	L Barrera
17:00 - 17:30	Discussion	All
17.30 - 18:00	Draft recommendations	All

Wednesday 9 September 2009

Chair: P Nunn & K Weyer, WHO

Rapporteur: F Cobelens

09:00 – 09:30	Systematic review: Thin-layer agar (TLA) for rapid diagnosis of drug-resistant tuberculosis	J Minion & M Pai
09:30 - 10:15	Discussion	All
10:15 - 10:30	Laboratory infrastructure, human resource requirements, and research gaps for implementation of TLA	J Robledo
BREAK 10:30 - 10:45		
10:45 - 11:30	Discussion	All
11:30 - 12:00	Draft recommendations	All
LUNCH 12:00 - 13:00		
13:00 - 13:30	Systematic review: Mycobacteriophage-based assays for rapid diagnosis of drug-resistant tuberculosis	J Minion & M Pai
13:30 - 14:15	Discussion	All
14:15 - 14:30	Laboratory infrastructure, human resource requirements, and research gaps for implementation of mycobacteriophage-based assays	M Bonnet
14:30 - 15:00	Discussion	All
15:00 - 15:30	Draft recommendations	All
BREAK 15:30 - 16:00		
16:00 - 16:15	GRADE summary	J Minion
16:15 - 17:45	Final recommendations	Chair
16:45 - 17:00	Next steps and closing	Chair

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