Background

Earlier and improved tuberculosis (TB) case detection - including smear-negative disease often associated with HIV - as well as expanded capacity to diagnose multidrug-resistant tuberculosis (MDR-TB) are global priorities for TB control. MDR-TB poses formidable challenges due to its complex diagnostic and treatment options, while HIV-associated TB largely goes undetected due to the limitations of current diagnostic techniques. Alarming increases in MDR-TB, the global emergence of extensively drug-resistant TB (XDR-TB), documented institutional transmission, and rapid mortality in MDR-TB and XDR-TB patients with HIV co-infection have highlighted the urgency for rapid diagnostic methods.

Genotypic (molecular) methods have considerable advantages for scaling up programmatic management of drug-resistant and HIV-associated TB, offering speed of diagnosis, standardized testing, potential for high throughput, and fewer requirements for laboratory bio-safety. Since the development in the early 1980s of the polymerase chain reaction (PCR), the first and most familiar method to amplify nucleic acid sequences, molecular diagnostics have been widely expected to have a major impact on clinical medicine. However, despite several theoretical advantages, the use of molecular tests for TB has been limited, largely due to the complexities of DNA extraction, amplification and detection, and the bio-safety concerns related to manipulating *Mycobacterium tuberculosis* organisms.

Over the past five years, and with support from the US National Institutes of Health (NIH), the Foundation for Innovative New Diagnostics (FIND) has partnered with Cepheid, Inc. (Sunnyvale, CA) and the University of Medicine and Dentistry of New Jersey (UMDNJ, Newark, NJ) to develop an automated, cartridge-based NAAT for TB based on the GeneXpert multi-disease platform. The GeneXpert system was launched in 2004 and simplifies molecular testing by fully integrating and automating the three processes (sample preparation, amplification and detection) required for real-time PCR-based molecular testing. The development of the Xpert MTB/RIF assay for the GeneXpert platform was completed in 2009 and is considered an important breakthrough in the fight against TB. For the first time, a molecular test is simple and robust enough to be introduced outside of conventional laboratories. Xpert MTB/RIF detects *M. tuberculosis* as well as rifampicin resistance-conferring mutations directly from sputum, in an assay providing results within 100 minutes.

In December 2010, WHO endorsed the Xpert MTB/RIF assay and recommended that roll-out of the technology be phased in by country health authorities within the context of national plans for appropriate management of TB, MDR-TB and HIV-associated TB. A Global Consultation subsequently convened by WHO outlined consensus on interim diagnostic algorithms, patient management approaches, and operational/logistical aspects to be addressed during Xpert MTB/RIF implementation. These aspects are contained in a Rapid Implementation document recently issued by WHO, aimed at guiding systematic roll-out of Xpert MTB/RIF in varying epidemiological and resource settings, with a view towards large-scale implementation based on programmatic data collected during the roll-out phase.

This Workshop aims to bring together representatives from country health programmes planning to start implementation of the Xpert MTB/RIF assay, international institutions and agencies, and non-governmental organizations involved in providing support to country programmes. The overall goal of the Workshop is to provide participants with the science behind Xpert MTB/RIF, assay performance characteristics, and the potential impact on diagnostic access in different epidemiological and resource settings. The Workshop will focus on the practical application of the WHO Implementation Document within country-specific context.

Meeting Objectives

- To provide country health programmes and their local and international technical partners with the science behind Xpert MTB/RIF, assay performance characteristics and the need to link diagnosis with treatment and care in different epidemiological and resource settings;
- To discuss with countries and partners the practical considerations for roll-out of Xpert MTB/RIF using the WHO Implementation Document, including interim diagnostic algorithms, patient management approaches, and key data elements to be collected to inform future scale-up;
- To map country and technical partner plans for roll-out of Xpert MTB/RIF in order to maximize resources and avoid duplication and overlap.

Expected outcomes

- Participants informed of the outcomes of the Global Consultation on Xpert MTB/RIF and key aspects of the WHO Implementation Document;
- Agreement on the practical considerations for Xpert MTB/RIF roll-out, including patient risk assessment and placement of the Xpert MTB/RIF assay in diagnostic pathways;
- A planning matrix for coordinated roll-out of Xpert MTB/RIF in different epidemiological and resource settings

Participants

The meeting will include representatives from country health programmes planning to start implementation of the Xpert MTB/RIF assay, international institutions and agencies, and non-governmental organizations providing support to these country programmes.

Implementation and roll-out of the Xpert MTB/RIF system for rapid diagnosis of tuberculosis and multidrug-resistance

Workshop for Early Implementers

Hotel Starling, Geneva, Switzerland
7 - 8 April 2011

World Health Organization

THURSDAY, 7 APRIL 2011

8:00-9:00	Registration	
Session 1:	**Introduction**	**Chair: K Weyer**
9:00-9:15	Welcome	K Weyer
9:15-9:30	Workshop scope and objectives	F Mirzayev
9:30-9:45	Introduction of participants	
Session 2:	**Xpert MTB/RIF and the science behind it**	**Chair: R Hassan**
9:45-10:15	Xpert MTB/RIF: Development, analytical performance, and evidence from field evaluation studies	C Boehme
10:15-10:45	*Coffee break*	
10:45-11:15	Xpert MTB/RIF: Operational considerations	C Gilpin
11:15-12:00	GeneXpert System and Xpert MTB/RIF practical demonstration	C Boehme
12:00-12:30	Discussion	
12:30-13:45	*Lunch*	
Session 3:	**Positioning of Xpert MTB/RIF and selection of individuals to test**	**Chair: T Shinnick**
13:45-14:00	Risk assessment	F Mirzayev
14:00-14:30	Primary considerations: individuals at risk of MDR-TB	E Jaramillo
14:30-15:00	Primary considerations: people living with HIV	D Sculier
15:00-15:30	Secondary considerations: where MDR or HIV-associated TB is of lesser concern	K Lonnroth
15:30-16:00	*Coffee break*	
16:00-16:15	Site selection	C Gilpin
16:15-17:00	Discussion	
18:00	Cocktail reception	

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Session 4:	**Practical considerations**	**Chair: G Coetzee**
9:00-9:30	Preferential pricing, installation and start-up costs	G Roscigno
9:30-9:45	Post-marketing surveillance	G Roscigno
9:45-10:00	Involvement of the private sector	M Uplekar
10:00-10:15	Uganda experience using Xpert MTB/RIF	M Joloba
10:15-10:30	Discussion	
10:30-11:00	*Coffee break*	
Session 5:	**Management of patients, R&R and monitoring of treatment response**	**Chair: R O'Brien**
11:00-11:15	Interim case definitions	M Grzemska
11:15-11:30	Registration and reporting of TB and MDR-TB cases, and key data elements for implementation	D Falzon
11:30-11:45	Management of patients with rifampicin resistance	D Falzon
11:45-12:00	Management of persons with HIV-associated TB	H Getahun
12:00-12:30	Discussion	
12:30-13:30	*Lunch*	
Session 6:	**Plans of early implementing partners for Xpert MTB/RIF roll-out**	**Chair: F Mirzayev**
13:30-15:00	Presentations by invited partners and discussion	F.Varaine (MSF); A.Piatek (USAID); O.Gorbacheva (IOM); G.Coetzee (NHLS); A.Nyaruhirira (ICAP); T.Phiri-Nkhoma (MANERELA+); E.Adam (EXPAND-TB)
15:00-15:30	Way forward and next steps: Development of a planning matrix for coordinated roll-out of Xpert MTB/RIF	K Weyer
15:30-16:00	*Coffee break*	
Session 7:	**Operational research**	**Chair: F Varaine**
16:00-16:25	Operational research opportunities and priorities	C Lienhardt
16:25-16:45	Operational research and implementation of new TB diagnostics	B Squire
16:45-17:00	Summary and final remarks	