- UPDATE -
Implementation and roll-out of Xpert MTB/RIF
May 2012

This document provides an update on the global roll-out of the Xpert MTB/RIF assay, the WHO-endorsed test for the rapid and simultaneous detection of TB and rifampicin resistance. For background and guidance on use of the test, including the WHO Policy Statement, Rapid Implementation document and Checklist of prerequisites to country implementation, as well as published literature, visit http://www.who.int/tb/laboratory/mtbrifrollout.

Outcomes of the Xpert MTB/RIF Early Implementers meeting – Annecy, France, 18-19 April 2012

Implementers of Xpert MTB/RIF gathered with technical partners and donors for a meeting focusing on the roll-out of the technology, as part of the 4th Global Laboratory Initiative (GLI) Partners meeting in Annecy, France. The objectives of the Xpert MTB/RIF Early Implementers meeting were threefold: to provide a platform for sharing up-to-date information and experiences on the use of the diagnostic; for sharing country, partner and donor activities and plans for improved coordination; and for achieving a greater understanding of the needs of implementers.

Major and recurring points raised and discussed at the meeting included:

- **User satisfaction:** Implementers indicated an overall high level of satisfaction with use of the technology, describing it as fast, easy-to-use, modern and much less cumbersome than conventional TB diagnostic techniques.
- **Need for price reduction:** The price of an Xpert MTB/RIF test cartridge (16.86 USD) was repeatedly raised as an obstacle to an accelerated and sustainable roll-out of the technology, in both low- and middle-income settings. Negotiations between the manufacturer and major buyers and donors are ongoing, with the aim of finding a solution that would result in a drop in price, benefiting as many countries as possible.
- **Diagnostic and clinical algorithms:** The time and resources needed to develop and implement effective diagnostic *and* clinical management algorithms incorporating the new technology should not be underestimated. Training of doctors and nurses on interpretation of Xpert MTB/RIF results and clinical management of patients must be included in country roll-out.
- **Errors and invalid results:** In a relatively small but significant number of sites, errors and invalid results in the initial phase of implementation raised anxiety on use of Xpert MTB/RIF. Recurring errors at particular sites were linked to improper procedures in specimen collection and preparation of samples, and faulty modules and cartridges. The South Africa National Health Laboratory Service (NHLS) had an error rate of 3-4% in the initial phase of implementation, which then decreased in the presence of adequate training and troubleshooting; the overall error rate after performing over 300,000 tests was 2.2%. The introduction of the new G4 generation Xpert MTB/RIF cartridge in December 2011 has reduced the number of signal loss (5011) errors, most commonly reported. Going forward, the systematic reporting of information on the frequencies of errors at implementation sites by the WHO data collection website will allow for monitoring of error rates.
- **Scaling up treatment capacity to match diagnostic capacity:** Treatment of rifampicin-resistant TB cases that are diagnosed by Xpert MTB/RIF was a major concern in many sites. While some argue for a cautious roll-out of the diagnostic in order to ensure treatment is available for all rifampicin-resistant cases diagnosed, others argue that diagnosis in the absence of appropriate treatment nevertheless allows for patients to make appropriate life decisions and protect the health of their families, while also facilitating interventions for reduced transmission of drug-resistant strains in healthcare facilities (2010 WHO Guidance on ethics of tuberculosis, prevention care and control).
- **Private sector access:** Adoption of Xpert MTB/RIF by the large private sector in many high-burden countries would be highly beneficial for increasing patient access to rapid and reliable diagnosis, and at the same time replacing technologies that are not endorsed by WHO. The establishment of collaborations between private providers and national TB control programmes would be mutually beneficial, allowing for

private providers to access concessional prices and for national TB control programmes to ensure that patients detected in the private sector are duly reported and subsequently registered for appropriate treatment.

- **Need for innovation:** Continued innovation is needed on several fronts. First, technical innovation will allow for Xpert MTB/RIF to be used in more settings at levels closer to the point of care, where lack of reliable electricity and high temperatures may otherwise prevent the reliable use of the technology. Also, implementation of electronic information management systems and mHealth initiatives (i.e., those using mobile communication devices) will facilitate stronger links between diagnosis and follow-up care. Innovation in financial mechanisms by donors and buyers may result in a decrease in prices with higher volumes of cartridges procured. Lastly, innovation is needed to close the gap between diagnostics and treatment, in particular ensuring proper treatment of those patients diagnosed with rifampicin-resistant TB.

Link: Agenda of the Xpert MTB/RIF Early Implementers meeting and all presentations

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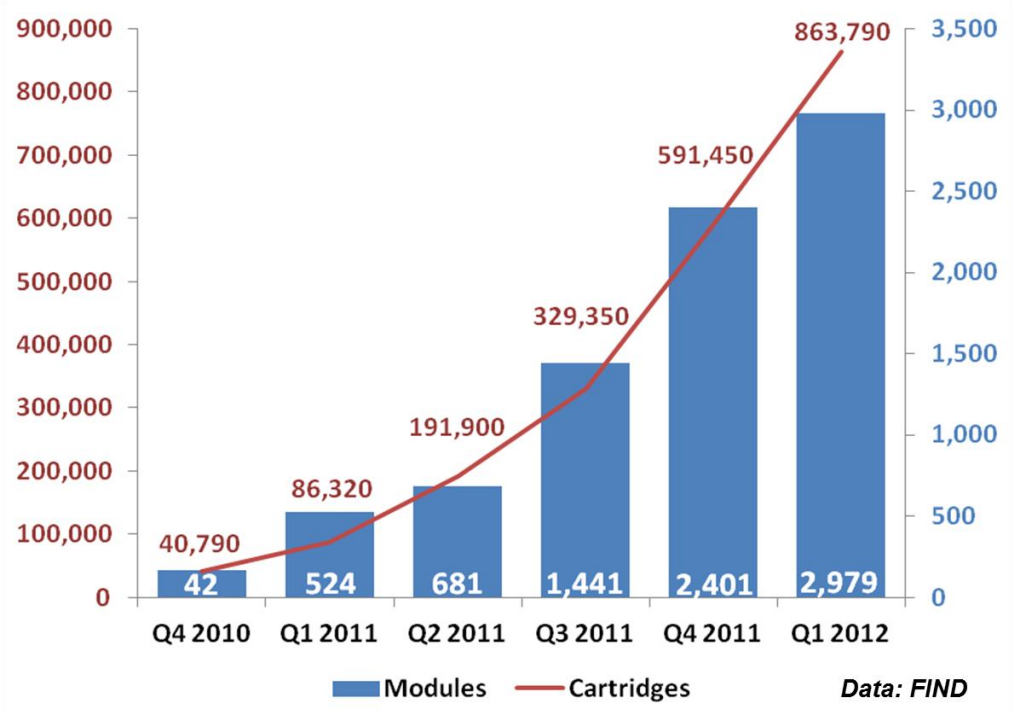
Monitoring the global roll-out of Xpert MTB/RIF

The Laboratories, Diagnostics and Drug Resistance Unit of the WHO Stop TB Department maintains a website (http://www.who.int/tb/laboratory/mtbrifrollout) monitoring the roll-out of Xpert MTB/RIF, in order to facilitate coordination among implementers, including countries, technical agencies, nongovernmental agencies, and other partners.

By the end of March 2012, a total of 611 GeneXpert instruments (comprising 2,979 modules) and 863,790 Xpert MTB/RIF test cartridges had been procured in 61 countries under concessional pricing.

Cumulative number of GeneXpert modules and Xpert MTB/RIF cartridges procured under concessional pricing



Over half of the Xpert MTB/RIF cartridges (478,980 cartridges) have been procured for use in South Africa alone, followed by Kenya (34,310), India (25,640), Pakistan (22,440), Zimbabwe (21,570), Tanzania (20,370), Nigeria (18,160), Philippines (17,440) and Brazil (16,730). Data by country, provided by the manufacturer via FIND, are mapped at: http://www.stoptb.org/wg/gli/assets/documents/map/1/atlas.html

WHO has also collected information from National TB control programmes and partners from 50 countries describing the planned orders, funding sources, placement of instruments, and any problems with usage reported from the field. This information, including detailed information by country, is available at: http://www.stoptb.org/wg/gli/assets/documents/map/2/atlas.html

Countries for which the National TB control programme and/or partners have shared detailed information on placement of instruments, funding, and planned orders

In order to have the most comprehensive and up-to-date information to facilitate coordination, we rely on all country implementers, partners, and funders to notify us of any updates/changes. A reporting form can be found at: http://www.stoptb.org/wg/gli/assets/documents/map/2/XpertMTBRIFreportingform.doc

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Collection of evidence on use of Xpert MTB/RIF

The WHO Stop TB Department's Laboratories, Diagnostics and Drug Resistance Unit continues to ask early implementers of Xpert MTB/RIF to kindly share some basic information on the ongoing use of their GeneXpert instruments, via the website: https://extranet.who.int/xpertmtbrif. Collectively this information would be invaluable to provide more effective guidance for the wider global scale-up in use of Xpert MTB/RIF. For more information on this initiative, visit: http://www.who.int/tb/features_archive/xpert_use_web

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Validation panels: Initial results

As a complement to the internal validation checks of the Xpert MTB/RIF assay, a pilot GLI validation scheme has been developed under guidance of WHO, in which panels comprised of artificial sputum specimens spiked with non-viable organisms have been produced. To date, results have been received for 192 tests performed at 49 sites in 10 countries. Three occurrences of false MTB detection (3 sites) and 1 occurrence of false rifampicin susceptibility (1 site) have been recorded. While such discrepancies could be the result of transcription errors when recording results or cross-contamination, follow-up testing and review of run files will be performed. Going forward, the manufacturer has agreed to include these panels when shipping a new instrument or with recalibrated modules.

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