

- UPDATE -
Implementation and roll-out of Xpert MTB/RIF
October 2011

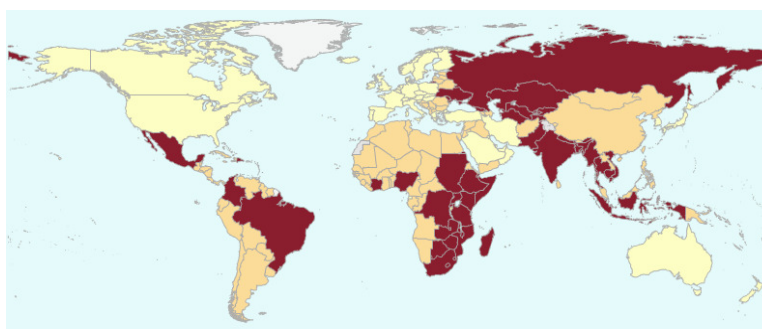
This document provides an update on the global roll-out of Xpert MTB/RIF, the WHO-endorsed test for the rapid and simultaneous detection of TB and rifampicin resistance. Background information on the test, as well as operational considerations, WHO interim recommendations on site selection and positioning of the test, selection of individuals to test and patient management approaches, as well as the key data elements that need to be collected to inform future scale-up, can be found in the **WHO Policy Statement “Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF system”** and the **WHO Rapid Implementation document “Technical and operational ‘How-to’, Practical considerations”**: http://www.who.int/tb/laboratory/policy_statements

Monitoring the roll-out of Xpert MTB/RIF and plans for procurement

The TB Diagnostics and Laboratory Strengthening unit of the WHO Stop TB Department (STB) 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.

As of 30 June 2011, a total of 138 GeneXpert machines (comprising 681 modules) and 191,900 Xpert MTB/RIF test cartridges had been procured in 28 countries under the concessional pricing agreement. Over half of the cartridges (117,580 cartridges) had been procured by South Africa alone. These data, provided by the manufacturer via FIND, are mapped at:
<http://www.stoptb.org/wg/gli/assets/documents/map/1/atlas.html>

Additionally, WHO has collected information from National TB control programmes and partners from 43 countries describing the planned orders, funding sources, placement of machines, and any reported problems with usage reported from the field. Recent additions include orders and plans from USAID-supported partners in 15 countries, describing procurement of over 90 machines. 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 programme and/or partners have shared information on procurements and plans

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 changes. A reporting form can be found at:

<http://www.stoptb.org/wg/gli/assets/documents/map/2/XpertMTBRIFreportingform.doc>

Validation panels

As a complement to the internal validation checks of the Xpert MTB/RIF assay, a validation scheme has been developed under guidance of WHO-STB, in which panels comprised of artificial sputum specimens spiked with non-viable (dead) organisms will be sent to procurers of GeneXpert machines. The panels are intended to be used with each new machine or with recalibrated modules, to validate expected performance of the modules at the time of installation or recalibration. Cepheid, the manufacturer of the Xpert MTB/RIF assay, has agreed to ship the validation panels as part of a pilot scheme to end-users of the technology. Two hundred panel sets have already been produced for the pilot scheme; the usefulness of these panels will first be evaluated by a selected number of sites before being made available more broadly.

Xpert MTB/RIF Research Mapping Tool launched by TREAT TB - Invitation to view and participate

While efforts for implementation of Xpert MTB/RIF are under way, there are still many unanswered questions around the tests' optimal use within country health systems and in different patient populations that warrant further research. The Union, through the USAID-funded TREAT TB initiative, has developed an online tool supported by WHO that allows researchers and policy makers to globally map ongoing research activities around Xpert MTB/RIF. The tool aims to be a comprehensive platform providing information and initiating exchange and discussion in order to optimize research efforts related to implementation and scale-up of Xpert MTB/RIF. Currently the tool shows detailed information on 22 research projects in 15 countries.

Find out about research collaborations, patient populations targeted, impact assessment and the main objectives addressed in the different projects by accessing the Xpert Research Mapping Project tool at: <http://xrmt.treattb.org>. Researchers conducting projects assessing Xpert MTB/RIF are invited to add their information via the link provided on the Mapping Tool website. For questions and comments contact xpertmappingproject@theunion.org.

Published evidence on Xpert MTB/RIF

Upon the request of countries and partners, a list of published references about Xpert MTB/RIF with web links to abstracts has been compiled by WHO-STB. Topics include development and evaluation of the assay, detection of extrapulmonary and paediatric TB, cost-effectiveness, and commentary and review. This resource is available at <http://www.stoptb.org/wg/gli/assets/documents/map/XpertPublications.pdf>, and will be regularly updated. The current list is attached as an annex to this Update.

Joining this mailing list

If you have received this email as a forward, and would like to be added directly to our mailing list, please send a request to the contact below.

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Annex. Published evidence and commentary on the Xpert MTB/RIF assay

On development of the assay

- Banada P et al. *Containment of Bioaerosol Infection Risk by the Xpert MTB/RIF Assay and Its Applicability to Point-of-Care Settings*. J Clin Microbiol. 2010 Oct;48(10): 3551-3557.
<http://jcm.asm.org/cgi/content/abstract/48/10/3551?maxtoshow=&hits=10&RESULTFORMAT=&fulltext=mtb%2Frif&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT>
- El-Hajj HH et al. Detection of rifampin resistance in mycobacterium tuberculosis in a single tube with molecular beacons. J. Clin. Microbiol. 39, 4131–4137 (2001).
<http://jcm.asm.org/cgi/content/abstract/39/11/4131>
- Piatek AS et al. *Genotypic analysis of mycobacterium tuberculosis in two distinct populations using molecular beacons: implications for rapid susceptibility testing*. Antimicrob. Agents Chemother. 44, 103–110 (2000).
<http://aac.asm.org/cgi/content/abstract/44/1/103>
- Piatek AS et al. *Molecular beacon sequence analysis for detecting drug resistance in mycobacterium tuberculosis*. Nat. Biotechnol. 16, 359–363 (1998).
<http://www.nature.com/nbt/journal/v16/n4/full/nbt0498-359.html>

On evaluation of the assay

- Zeka AN et al. *Evaluation of the GeneXpert MTB/RIF Assay for the Rapid Diagnosis of Tuberculosis and detection of RIF-resistance in Pulmonary and Extrapulmonary Specimens*. J Clin Microbiol. 2011 Sep 28. [Epub ahead of print]
<http://jcm.asm.org/cgi/content/abstract/JCM.05434-11v1>
- Hanif SN et al. *GeneXpert® MTB/RIF for rapid detection of Mycobacterium tuberculosis in pulmonary and extra-pulmonary samples*. Int J Tuberc Lung Dis. 2011 Sep;15(9):1274-5.
<http://www.ingentaconnect.com/content/iatld/ijtd/2011/00000015/00000009>
- Ioannidis P et al. *Cepheid GeneXpert MTB/RIF Assay for Mycobacterium tuberculosis Detection and Rifampin Resistance Identification in Patients with Substantial Clinical Indications of Tuberculosis and Smear-Negative Microscopy Results*. J Clin Microbiol. 2011 Aug;49(8): 3068-3070.
<http://jcm.asm.org/cgi/content/abstract/49/8/3068>
- Teo J et al. *Comparison of two nucleic acid amplification assays, the Xpert MTB/RIF and the Amplified Mycobacterium Tuberculosis Direct (MTD) assay, for the detection of Mycobacterium tuberculosis in respiratory and non-respiratory specimens*. J Clin Microbiol. 2011 Aug 24. [Epub ahead of print].
<http://jcm.asm.org/cgi/content/abstract/JCM.00211-11v1?maxtoshow=&hits=10&RESULTFORMAT=&fulltext=mtb%2Frif&searchid=1&FIRSTINDEX=10&resourcetype=HWCIT>
- Miller MB et al. *Performance of Xpert MTB/RIF RUO Assay and IS6110 Real-Time PCR for Mycobacterium tuberculosis Detection in Clinical Samples*. J Clin Microbiol. 2011 Oct;49(10):3458-62. Epub 2011 Aug 17.
<http://jcm.asm.org/cgi/content/abstract/49/10/3458>

- Blakemore R et al. *A Multi-Site Assessment of the Quantitative Capabilities of the Xpert(R) MTB/RIF Assay*. Am J Respir Crit Care Med. 2011 Aug 11. [Epub ahead of print]
<http://ajrccm.atsjournals.org/cgi/content/abstract/201103-0536OCv1>
- Scott LE et al. 2011 *Comparison of Xpert MTB/RIF with Other Nucleic Acid Technologies for Diagnosing Pulmonary Tuberculosis in a High HIV Prevalence Setting: A Prospective Study*. PLoS Med 8(7): e1001061.
<http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001061>
- Theron G et al. *Evaluation of the Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in a high HIV prevalence setting*. Am J Respir Crit Care Med. 2011 Jul 1;184(1):132-40. Epub 2011 Apr 14. <http://ajrccm.atsjournals.org/cgi/content/abstract/184/1/132>
- Lawn S et al. *Screening for HIV-Associated Tuberculosis and Rifampicin Resistance before Antiretroviral Therapy Using the Xpert MTB/RIF Assay: A Prospective Study*. PLoS Med 8(7): e1001067.
<http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001067>
- Bowles EC et al. *Xpert MTB/RIF®, a novel automated polymerase chain reaction-based tool for the diagnosis of tuberculosis*. Int J Tuberc Lung Dis. 2011 Jul;15(7):988-9.
<http://www.ingentaconnect.com/content/iatld/ijtld/2011/00000015/00000007>
- Rachow A et al. *Rapid and accurate detection of Mycobacterium tuberculosis in sputum samples by Cepheid Xpert MTB/RIF assay--a clinical validation study*. PLoS One. 2011;6(6):e20458. Epub 2011 Jun 29.
<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0020458>
- Armand S et al. *Comparison of the Xpert MTB/RIF test with an IS6110-TaqMan real-time PCR assay for direct detection of Mycobacterium tuberculosis in respiratory and nonrespiratory specimens*. J Clin Microbiol. 2011 May;49(5):1772-6. Epub 2011 Mar 16.
<http://jcm.asm.org/cgi/content/abstract/49/5/1772>
- Malbruny B et al. *Rapid and efficient detection of Mycobacterium tuberculosis in respiratory and non-respiratory samples*. Int J Tuberc Lung Dis. 2011 Apr;15(4):553-5.
<http://www.ingentaconnect.com/content/iatld/ijtld/2011/00000015/00000004>
- Boehme C et al. *Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study*. Lancet. 2011 Apr 30;377(9776):1495-505.
<http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2811%2960438-8/abstract>
- Marlowe EM et al. *Evaluation of the Cepheid Xpert MTB/RIF assay for direct detection of Mycobacterium tuberculosis complex in respiratory specimens*. J Clin Microbiol. 2011 Apr;49(4):1621-3. Epub 2011 Feb 2.
<http://jcm.asm.org/cgi/content/abstract/49/4/1621>
- Moure R et al. *Rapid detection of Mycobacterium tuberculosis complex and rifampin resistance in smear-negative clinical samples by use of an integrated real-time PCR method*. J Clin Microbiol. 2011 Mar;49(3):1137-9. Epub 2010 Dec 29.
<http://jcm.asm.org/cgi/content/abstract/49/3/1137>
- Boehme C et al. *Rapid Molecular Detection of Tuberculosis and Rifampin Resistance*. N Engl J Med 2010 Sep 9; 363(11):1005-1015. <http://www.nejm.org/doi/full/10.1056/NEJMoa0907847>

- Blakemore R et al. *Evaluation of the analytical performance of the Xpert MTB/RIF assay*. J Clin Microbiol. 2010 Jul;48(7):2495-501. Epub 2010 May 26.
<http://jcm.asm.org/cgi/content/abstract/48/7/2495>
- Helb D et al. Rapid detection of Mycobacterium tuberculosis and rifampin resistance by use of on-demand, near-patient technology. J Clin Microbiol. 2010 Jan;48(1):229-37. Epub 2009 Oct 28.
<http://jcm.asm.org/cgi/content/abstract/48/1/229>

On detection of extrapulmonary TB

- Causse M et al. *Comparison of Two Molecular Methods for Rapid Diagnosis of Extrapulmonary Tuberculosis*. J Clin Microbiol. 2011 Aug;49(8): 3065-3067.
<http://jcm.asm.org/cgi/content/abstract/49/8/3065>
- Ligthelm LJ et al. *Xpert® MTB/RIF for the rapid diagnosis of tuberculous lymphadenitis from Fine Needle Aspiration biopsy specimens*. J Clin Microbiol. 2011 Aug 31. [Epub ahead of print]
<http://jcm.asm.org/cgi/content/abstract/JCM.01310-11v1?maxtoshow=&hits=10&RESULTFORMAT=&fulltext=mtb%2Frif&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT>
- Vadwai V et al. *Xpert MTB/RIF: a New Pillar in Diagnosis of Extrapulmonary Tuberculosis?* J Clin Microbiol. 2011 Jul;49(7):2540-5. <http://jcm.asm.org/cgi/content/abstract/49/7/2540>
- Hillemann D et al. *Rapid molecular detection of extrapulmonary tuberculosis by the automated GeneXpert MTB/RIF system*. J Clin Microbiol. 2011 Apr;49(4):1202-5.
<http://jcm.asm.org/cgi/content/abstract/49/4/1202>
- See above: Zeka AN et al.; Ioannidis P et al.; Teo J et al.; Hanif et al.; Miller et al. ; Armand S et al. ; Malbruny B et al. ; Moure R et al.

On detection of paediatric TB

- Nicol M et al. *Accuracy of the Xpert MTB/RIF test for the diagnosis of pulmonary tuberculosis in children admitted to hospital in Cape Town, South Africa: a descriptive study*. Lancet Infect Dis. 2011 Jul 15 [Epub ahead of print]. [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(11\)70167-0/fulltext](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(11)70167-0/fulltext)

On cost-effectiveness of the assay

- Dowdy DW et al. *Is Scale-Up Worth It? Challenges in Economic Analysis of Diagnostic Tests for Tuberculosis*. PLoS Med 8(7): e1001063.
<http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001063>
- Meyer-Rath G et al. *The incremental cost of introducing Xpert® MTB/RIF into the South African national tuberculosis programme: Results of the National TB Cost Model 2011/12 - 2016/17*. Johannesburg: Health Economics and Epidemiology Research Office, 2011.
<http://www.tbonline.info/media/uploads/documents/hero-costofgenexpert.pdf>

Commentary and review

- Lawn SD and MP Nicol. *Xpert® MTB/RIF assay: development, evaluation and implementation of a new rapid molecular diagnostic for tuberculosis and rifampicin resistance*. Future Microbiol. 2011 Sep;6:1067-82. http://www.futuremedicine.com/doi/abs/10.2217/fmb.11.84?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed
- Evans CA. *GeneXpert—A Game-Changer for Tuberculosis Control?* PLoS Med 8(7): e1001064. <http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.1001064>
- Van Rie A et al. *Xpert® MTB/RIF for point-of-care diagnosis of TB in high-HIV burden, resource-limited countries: hype or hope?* Expert Rev Mol Diagn. 2010 Oct;10(7):937-46. <http://www.expert-reviews.com/doi/abs/10.1586/erm.10.67>
- Small P and M Pai. *Tuberculosis Diagnosis - Time for a Game Change*. N Engl J Med 2010; 363:1070-1071. <http://www.nejm.org/doi/full/10.1056/NEJMe1008496>

Note: a periodically-updated version of this list can be found at:

<http://www.stoptb.org/wg/gli/assets/documents/map/XpertPublications.pdf>