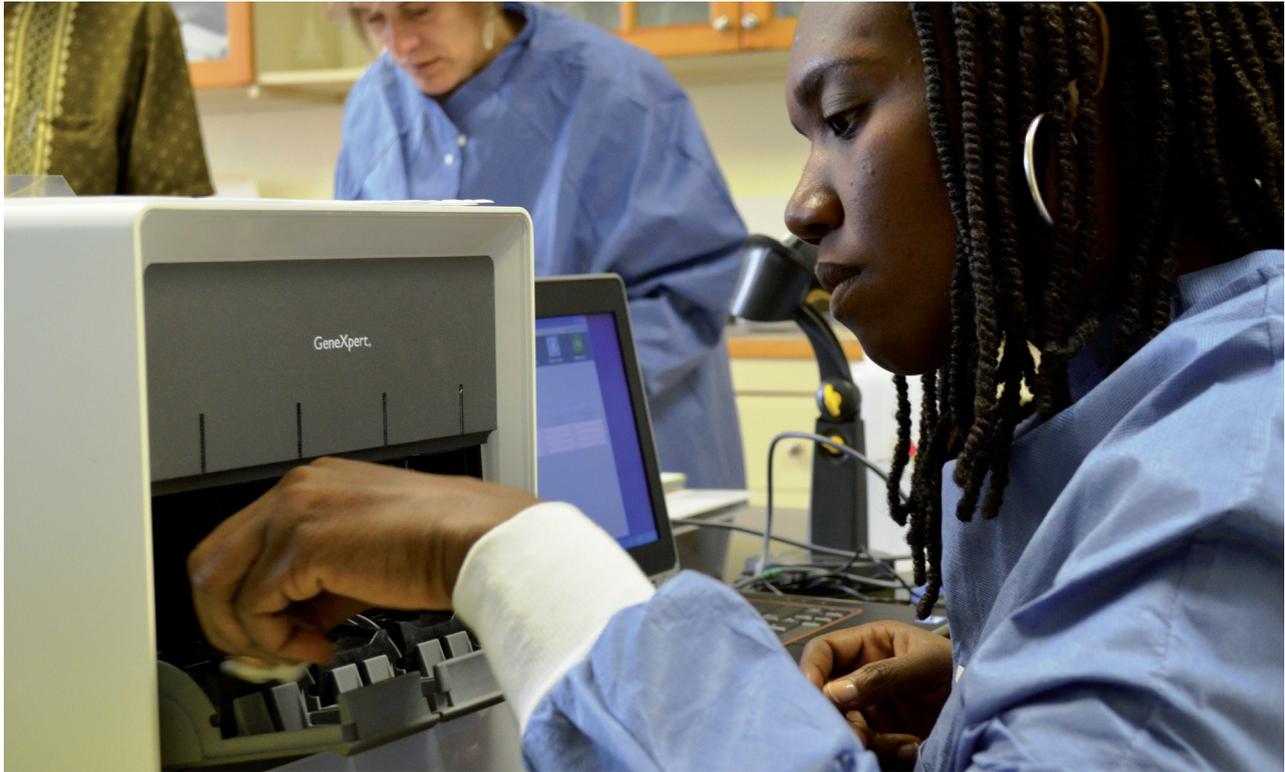


Catalysing success through partnerships:

## DETECTION OF TUBERCULOSIS AND DRUG RESISTANCE BECOMES FASTER AND SIMPLER



Until four years ago, diagnosing tuberculosis (TB) mainly relied on microscopy, a method providing poor accuracy, while detection of drug resistance using culture was lengthy, with patients waiting up to four months for their test results. Since the introduction of the Xpert MTB/RIF<sup>®</sup> test, a fully automated cartridge-based assay that runs on the GeneXpert platform, health care providers can now diagnose TB within 90 minutes and at the same time determine whether the patient has a drug-resistant form of the disease. This assay can be used in decentralized settings and is revolutionizing TB diagnosis in low-income countries.

### About TB and Xpert MTB/RIF

- Tuberculosis is the second most common cause of death from an infectious disease in adults in resource-constrained countries. In 2012, there were an estimated 8.6 million TB cases and 1.3 million deaths, the majority of which were likely preventable with existing treatments.
- FIND is working to improve diagnosis of TB and testing for drug resistance to increase adequate treatment for individual patients, control the disease at the population level and prevent the spread of drug resistance. Our work is focused on supporting the development, validation, demonstration and

implementation of diagnostics for diseases of poverty, such as the Xpert MTB/RIF test, that can be used at different levels of the health care system.

- FIND's support of Xpert MTB/RIF has helped catalyse its development, regulatory approval, country uptake and sustainability. Immediate and long-term impacts of this test promise faster and more accurate diagnosis with potential reductions in the incidence of TB and drug-resistant TB worldwide.<sup>1</sup>
- FIND's future projects will improve our ability to diagnose TB so that it can be treated and eventually eliminated including: supporting biomarker discovery; catalysing development of much-needed new tests (for example, molecular tests that can be deployed in health clinics instead of referral hospitals or central laboratories, tests with expanded drug susceptibility capabilities, tests to triage patients for referral, improved latent TB testing); and implementation strategies (electronic data reporting, improved linkage to care, improved uptake in country health systems).

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## Addressing the global burden of TB: improving diagnostic capacity

TB is a curable disease when accurately diagnosed and treated in a timely way with appropriate antibiotics. In countries with the heaviest TB burden, there is often very limited access to adequate diagnosis and treatment. Conventional diagnostic tools are imprecise and/or time-consuming – it can take up to two months to test for drug sensitivity – leading to delayed treatment initiation and further spread of the disease<sup>2</sup>. Improper diagnosis and treatment can also lead to development and spread of multidrug-resistant forms of TB (MDR-TB)<sup>3</sup>.

One of the ways that FIND has tackled the urgent need for better diagnostics over the past decade

has been through the role we have played in the development, endorsement, implementation and scale-up of Xpert MTB/RIF, helping to shape the market in the process. This fully automated molecular test can rapidly and accurately diagnose both TB and DR-TB in less than two hours. The test was first endorsed by the World Health Organization (WHO) in 2010. The head of the TB Programme at FIND, Dr. Claudia Denking, emphasizes that “FIND's activities focus on addressing a gap in diagnostic needs for global health, identifying a potential diagnostic solution, providing a platform to support manufacturers in product development, and leading the products through clinical trials to WHO approval”.

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## FIND's commitment: developing and implementing rapid diagnostic solutions for TB

The rapid and accurate Xpert MTB/RIF assay operates on the GeneXpert system. The test works by looking for DNA specific to TB bacteria found in a patient's sputum sample. The test can also identify DNA mutations associated with resistance to rifampicin, which can indicate a multidrug-resistant form of TB.

FIND has been instrumental in **catalysing the development** of Xpert MTB/RIF. In 2006, FIND signed a joint agreement with stakeholders from academia and industry (University of Medicine and Dentistry of New Jersey, now Rutgers and Cepheid

Inc.) to develop a novel TB test with financial support from multiple donors. FIND played a key role in defining prototype specifications in response to conditions encountered in developing countries.

The compelling evidence from multiple studies supporting Xpert MTB/RIF led to the WHO's endorsement of this technology in 2010. FIND conducted multi-country evaluation studies on the effectiveness of the test<sup>4,5</sup>. Results from these studies showed that Xpert MTB/RIF is both sensitive (it can correctly detect 98% of patients with TB) and specific (it can detect 99% of patients without TB).

In comparison to other TB tests, the Xpert test has a higher sensitivity than smear microscopy, similar sensitivity as phenotypic drug-susceptibility testing, and a slightly lower sensitivity than liquid culture<sup>6</sup>. The Xpert test outshines these alternate tests in terms of ease of use, time to diagnosis, and resistance to contamination<sup>2</sup>.

FIND provided crucial support for **country uptake** by designing and funding a multi-country implementation study which showed that the test could be used effectively in low-income settings<sup>7</sup>. In 2012, Xpert MTB/RIF detected 10,000 cases of drug-resistant TB<sup>8</sup>. In 2013, the WHO issued a policy update and recommendations that Xpert MTB/RIF be used as the initial diagnostic test in adults and children presumed to have MDR-TB or HIV-associated TB, and extrapulmonary TB meningitis<sup>9</sup>. At the end of October 2013, there were 887 laboratories across 103 countries using Xpert MTB/RIF<sup>8</sup>. As of June 2014, 3,269 GeneXpert machines and more than 7.5 million

Xpert MTB/RIF cartridges were distributed across high-burden, low-income countries<sup>10</sup>.

**Sustainability** of the Xpert MTB/RIF test in low-income countries is made possible by cost reductions for eligible countries negotiated by FIND via a joint agreement in 2006 and by other stakeholders in 2012. FIND also supported the development of the Calibration kit which allows the modules to be regulated remotely, thus reducing maintenance costs for the system.

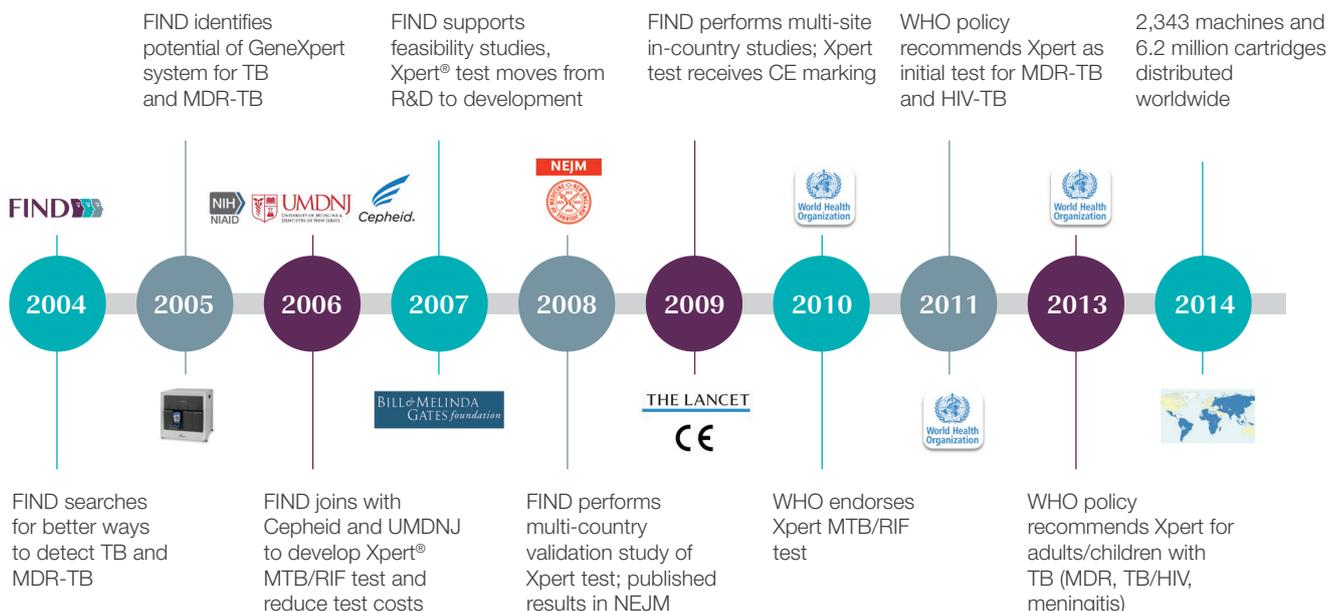
The **immediate impact** of FIND's multifaceted support is improved access to a robust, reliable and accurate test for TB and MDR-TB in developing countries. FIND's implementation activities also provide a better understanding of local and community health care systems and their requirements for successful testing of TB. Rapid and accurate diagnosis of TB followed by appropriate treatment leads to **long-term impacts** such as reduction in mortality, prevalence and incidence of TB in developing countries.

## Helping TB patients worldwide: the diagnostic solution

The Xpert MTB/RIF test is remarkable with respect to the relatively short time frame from product development to market availability. With project

oversight through FIND, this new diagnostic test was developed and on the market in record time (2006-2009).

### Timeline for rapid development and implementation of a diagnostic solution: Xpert® MTB/RIF.



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## Our next steps

- Develop a “next generation” Xpert MTB/RIF test that will analyze non-respiratory specimens (such as stool) rather than variable sputum specimens, which are difficult to obtain
- Support refinement of the GeneXpert system to include a diagnostic test for HIV and Neisseria/ Gonorrhea
- Enable development and deployment of national electronic databases in low-income countries to improve data reporting of TB
- Reduce the number of diagnosed TB patients not receiving treatment by locating those patients who are diagnosed but do not return for treatment through e-Health solutions
- Decrease the time between a positive test result and a treatment programme; the current goal for treatment initiation is within 24 hours of diagnosis
- Ensure project sustainability via improved coordination with local ministries of health

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## Summary

FIND has helped to make the Xpert MTB/RIF test a success story in the fight against tuberculosis. Experts have referred to this test as a game-changer with the potential to revolutionize the diagnosis of TB<sup>2,6</sup>. Xpert MTB/RIF is only one example of what can be achieved through fostering

the development of diagnostic solutions. FIND's efforts strive to create a world where diagnosis guides the way to health for all people by turning complex diagnostic challenges into simple solutions to overcome diseases of poverty and transform lives.

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