



RAPID DIAGNOSIS AND TREATMENT OF MDR-TB

FORMING PARTNERSHIPS TO STRENGTHEN
THE GLOBAL RESPONSE TO MDR-TB - WHERE IT MATTERS MOST

“I am delighted that this initiative will improve both the technology needed to diagnose TB quickly, and increase the availability of drugs to treat highly resistant TB”

British Prime Minister Gordon Brown

Each year, more than 1.5 million people die from TB and nearly 9 million people fall seriously ill with the disease, becoming a source of further contagion. This health challenge has been amplified by the HIV/AIDS epidemic, as people living with HIV are up to 50 times more likely to develop TB than those who are HIV negative.

Furthermore, it is estimated that almost half a million people a year develop MDR-TB, a form of the disease that is difficult to treat with standard drugs because of resistance to isoniazid and rifampicin, the first-line drugs of choice.

Lack of laboratory diagnostic capacity is a crucial barrier preventing an effective response to early and appropriate case detection and treatment of MDR-TB. Today, less than 5% of the estimated number of MDR-TB patients are being detected, and just 2% are receiving the appropriate treatment.

Laboratory capacity varies widely in developing countries...

In the best-case scenario countries have a functional national reference laboratory capable of performing TB culture and drug-susceptibility testing (DST). But in reality, most countries have little or no diagnostic capacity for MDR-TB. In Africa only six countries had the necessary lab equipment and trained personnel to provide data for WHO's 2008 Anti-TB Drug Resistance report, despite the region having the highest incidence of the TB in the world.

For countries facing high proportions of drug resistance, those carrying the largest absolute burden of MDR-TB, and those with a population heavily co infected with HIV, developing rapid detection and improving management of patients with drug-resistant TB is an urgent priority.

This new project, funded by UNITAID, goes some way to addressing the challenges. And through collaborative effort with all partners, it is expected the initiative will achieve a substantial increase in the proportion of cases being diagnosed and treated to more than 15% of cases - equal to a seven-fold increase - over the next four years. This means more lives saved, more cases treated and more TB cases prevented.

PROJECT GOALS

The project's activities will narrow the huge diagnostic gap needed to confront the MDR-TB epidemic by expanding and accelerating access to new diagnostic equipment, supported by adapted laboratory services in 16 selected countries. These efforts will be bolstered by ensuring that the necessary 'know-how' is in place for the technology transfer to happen smoothly and is sustained. All the project's partners will work together to ensure

that this know-how is properly integrated within TB control programmes.

Adequate investment in the new TB diagnostic instruments, reagents, and other essential supplies needed to establish laboratory capacity should result in equitable access by countries and patients to modern, rapid and effective diagnosis, reducing MDR-TB morbidity, mortality and risk of transmission.

UNITAID's financing will be used to secure access at the lowest possible price to diagnostic instruments, reagents and supplies.

GRANT

The project is supported by a large funding agreement that will directly benefit men, women and children at risk - the most vulnerable - in some of the world's poorest countries.

Through the \$26 million grant from UNITAID, partners will work with national TB control programmes to roll out the technology for TB liquid culture and first line drug-susceptibility testing, species confirmation through a rapid immunoassay, and the implementing a molecular line probe assay or DNA polymerase-based method. This method has never used before outside of research settings to diagnose MDR-TB. Currently it takes two to three months to obtain a diagnosis of MDR-TB. The new line probe assay method will dramatically cut this to less than two days.

The project countries will receive the new diagnostic tests through the procurement services and support of the Stop TB Partnership's Global Drug Facility (GDF).

The overall budget is US\$ 26,129,897 over 3 years.

MONITORING AND EVALUATION

Technical monitoring and evaluation will be performed by the Global Laboratory Initiative (GLI) together with the Foundation for Innovative New Diagnostics (FIND), under specific and context-related terms of reference.

Reports will include findings and a list of identified gaps and problems, plus recommendations on corrective steps. The management of supply chain issues and follow-up on related issues will be performed, as needed, by the Global Drug Facility's management experts, either as part of the technical monitoring missions or on a separate basis.

A list of project indicators will include:

- number of culture and DSTs performed
- number of MDR-TB patients detected
- progress in sales volumes towards the trigger point for further price reductions from diagnostics manufacturers
- price reduction per culture and DST

Partner roles will provide complementarities



UNITAID is based on a stable, predictable and innovative form of funding, such as a solidarity contribution on air tickets, together with multi-year budget commitment. This long term, predictable funding is used to scale up the access to drugs and diagnostics for the treatment of HIV/AIDS, malaria and tuberculosis in low and middle income countries by leveraging price reductions. For tuberculosis, UNITAID focuses on markets which are nascent or experiencing supply or demand (price) bottlenecks.

For this project, UNITAID's support will be utilized to procure laboratory equipment, reagents, and consumables, and will be leveraged against the complementary resources needed for laboratory infrastructure development, knowledge sharing and technical assistance.

The market demand created through this funding is expected to stimulate the entry of new suppliers and to secure access to diagnostics tools at the lowest possible price.

www.unitaid.eu

The Global Laboratory Initiative (GLI), with the secretariat hosted by WHO Stop TB Department, provides an extensive network of globally available best-practice expertise in TB laboratory infrastructure development, norms and standards, good laboratory practice and quality management.

For this project, GLI will provide technical guidance and facilitate relations with national TB programmes and technical agencies involved in laboratory strengthening to harmonize collaborative efforts and ensure maximal utilization of available resources and expertise.

GLI will also assume overall administration and oversight of the project, working closely with FIND and GDF in implementation, monitoring and evaluation, and eventual impact assessment.

WHO Stop TB Department is playing an instrumental role in strengthening the response to drug-resistant TB.

In October 2006, its XDR-TB Task Force recommended that WHO and partners urgently evaluate new technologies for the rapid diagnosis of MDR-TB and deploy them in the field as soon as possible.

In 2007, a World Health Assembly resolution called on WHO to support Member States in developing laboratory capacity for rapid drug-susceptibility testing (DST), develop consensus guidelines for rapid DST methods and appropriate measures for laboratory strengthening, and to mobilize funding.

The WHO Stop TB Department has also reinforced its laboratory strengthening team and assisted FIND to carry out field evaluations of line probe assays.

Along with the WHO Special Programme for Research and Training in Tropical Disease, the Stop TB Department convened an Expert Group in March 2008 to systematically review and analyse the available evidence on line probe assays. The Expert Group concluded that there was sufficient evidence to justify a recommendation on the use of these methods for rapid detection of MDR-TB.

On 23 June 2008, the Stop TB Department issued a WHO policy statement with recommendations to Member States recommending the use of line probe assays.

www.who.int/tb

FIND, established in 2003, drives the development and implementation of accurate and affordable diagnostic tests for poverty-related diseases that are appropriate to patient care in low-resource settings.

The Foundation will work with its partners to assure access to new diagnostic tools at the lowest possible price, including customer support which is critical for sustainability.

The proposed initial list of diagnostics for this project includes new tests from FIND's pipeline: a liquid TB culture system, a rapid immunoassay for TB species identification, a molecular line probe assay for rapid molecular diagnosis of MDR-TB, and the components needed to perform conventional TB solid culture and drug susceptibility testing.

FIND has experience negotiating large price discounts and establishing agreements with manufacturing partners to cover initial training, customer support, and market vigilance.

FIND will also provide the knowledge sharing and mentoring needed to ensure that these diagnostics are operational.

As additional comparable diagnostic products become available on the market, a competitive tender process will be used to select supply partners according to agreed quality standards.

FIND and GLI are currently involved in building laboratory capacity in three countries – Lesotho, Ethiopia, and Côte d'Ivoire - demonstrating the benefit of optimizing resources through a coordinated partner approach.

www.finddiagnostics.org

The Global Drug Facility (GDF) ensures access to quality anti-TB drugs and diagnostics for countries in need, at the lowest possible price.

For this project, GDF will be responsible for coordinating and managing procurement and delivery of diagnostics for eligible countries, engaging industry to meet the projected and significant market volumes to be funded by UNITAID over the project's three years, and collaborating with WHO to support prequalification of diagnostics.

The Stop TB Partnership whose secretariat is hosted by the World Health Organization in Geneva, is a network of more than 700 international organizations, countries, donors from the public and private sectors, and non-governmental and governmental organizations that are working together to eliminate TB.

The Partnership's Global Plan to Stop TB (2006-2015) sets forth a roadmap for treating 50 million people for TB and enrolling 3 million patients who have both TB and HIV on antiretroviral therapy over the next 10 years, saving about 14 million lives.

It aims to halve TB prevalence and deaths compared with 1990 levels by 2015.

www.stoptb.org/gdf

LINE PROBE ASSAY AND MDR-TB

A molecular line probe test can be used directly from sputum in patients with advance (microscopy-positive) disease and provides results indicating resistance to rifampicin and isoniazid in one day. This is a tremendous breakthrough for dramatically speeding the detection of drug resistance. Conventional solid culture, which is currently the most common method used to detect drug resistance in developing countries, may take two to three months to produce results.

An initial evaluation study of the test was conducted at the National Health Laboratory Service (NHLS) TB laboratory in Cape Town. The study results, which were published in the American Journal of Respiratory and Critical Care Medicine, indicated that the overall performance of the test was superior to conventional TB culture and drug susceptibility testing and had the potential to revolutionize diagnosis of MDR-TB. In collaboration with the South African Medical Research Council and the NHLS, large scale demonstration studies were initiated in South Africa, screening up to 20,000 patients at risk of MDR-TB over a 12-month period.

Rapid diagnosis of MDR-TB will have several benefits. These include earlier treatment of patients which will undoubtedly save more lives, reducing the time spent on inappropriate and ineffective patient treatment (thereby reducing the development of further drug resistance), and controlling the spread of MDR-TB in congregate settings. Most importantly, early identification of MDR-TB will allow much faster investigation into the possibility that patients may have XDR-TB, speeding up the time to diagnose MDR-TB patients who should then be fast-tracked for XDR-TB laboratory tests.

