REPORT TO CONGRESS

Health-Related Research and Development Activities at USAID

An Update on the Five-Year Strategy, 2006–2010

TUBERCULOSIS

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Tuberculosis

Issues and Rationale

Tuberculosis (TB) is a major global health threat that kills approximately 1.8 million people each year; more than one-third of the world's population is thought to be infected with TB. While TB is found in almost every country in the world, it disproportionately affects poor countries and marginalized populations. Eighty percent of estimated cases occur in just 22 developing and/or transitioning countries. Despite advances in TB prevention and treatment, multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB threaten to undermine recent progress in controlling this disease.

Over the past two decades, the global HIV epidemic has caused tremendous increases in the burden of TB in regions of high HIV prevalence, especially in sub-Saharan Africa. Not only are HIV-positive individuals at a higher risk of becoming infected with TB, but among people with latent TB infection, HIV infection is the strongest known risk factor for progressing to active TB disease. An estimated 30 to 40 percent of HIV-related deaths are due to TB.

Areas of Research and Introduction

The translation of research and development into programmatic norms is of strategic importance to USAID. The Agency has been a leading supporter of research activities that aim to have a direct effect on country-level TB programs while mitigating the risks of drug resistance by (1) reducing diagnostic delay; (2) reducing the duration and improving efficacy of treatment (including care of persons infected with TB and HIV); (3) preventing disease; and (4) increasing access to Directly Observed Treatment, Short-course (DOTS). USAID brings its field presence to TB research within these targeted areas by informing the research community about field-based needs and priorities, enabling field-based trials of new technologies, preparing the field for the introduction of new technologies, addressing barriers to access services, and translating the results of research into policy and practice.

New Drugs/Improved Regimens

Research to investigate new anti-TB drugs is critical because more effective, better tolerated, shortened regimens can dramatically improve patient outcomes, reduce the toll of TB on patients and their families, decrease the strain on health systems, and slow the development of MDR-TB. Approximately 20 percent of USAID's research funding for TB is used to support the evaluation of promising new drugs. USAID's comparative advantage is to contribute to research at the stage where it has direct implications for the field (clinical trials at Phase IIB and beyond). USAID is providing ongoing support to the Global Alliance for TB Drug Development (a public-private partnership) to continue Phase IIB and Phase III clinical trials of three novel anti-TB compounds designed to shorten the duration of TB treatment. A fourth drug is being evaluated through the WHO's Special Programme for Research and Training in Tropical Diseases. USAID-led clinical trials also aim to revise, refine, and maximize the impact of current treatment standards and regimens.

USAID currently is supporting a study that will test the efficacy of a nine-month, standardized regimen that uses existing drugs for MDR-TB treatment; a nine-month treatment regimen is significantly shorter in duration than the current standard regimen of 18 to 24 months. This Standardized Treatment Regimen of Anti-TB Drugs for Patients with MDR-TB study will generate the evidence to inform new MDR-TB treatment recommendations from global technical agencies regarding the use of affordable drugs to treat TB. Technical assistance is under way to carry out this clinical trial in Kenya, South Africa, Vietnam, Indonesia, India, and Peru, and an evaluation protocol has been developed.

USAID is supporting the CDC to carry out the Preserving Effective TB Treatment Study, which compares the effectiveness of WHO's Green Light Committee (GLC)-approved MDR-TB treatment programs with non-GLC-approved programs in preventing resistance to second-line anti-TB drugs used in the treatment of MDR-TB. In FY 2009, the target enrollment of 1,802 patients in the Preserving Effective TB Treatment Study was completed, and baseline specimens and data were collected. By comparing acquired resistance to second-line anti-TB drugs among MDR-TB patients in GLC and non-GLC programs, the study aims to inform global policy and country decision makers on the future direction of these programs.

New Diagnostics

USAID research targets the development of innovative diagnostic tools and approaches that accelerate TB case detection, provide enhanced diagnostic sensitivity and specificity, and are feasible for use in low-resource settings, in addition to supporting the improvement of currently existing diagnostic methods.

As a result of USAID-supported research, light-emitting diode fluorescence microscopy and front-loaded diagnosis have been adopted into global policy by WHO and endorsed for use in country programs. Light-emitting diode fluorescence microscopy increases ease of use while simplifying maintenance compared to traditional fluorescent microscopy. "Front-loading" or "same-day diagnosis" allows for the collection and examination of consecutive sputum specimens as well as the provision of test results in one day, compared with the current practice of two to three sputum examinations taken over two days or more. These new tools may reduce laboratory workloads and turnaround time for test results as well, facilitating earlier initiation of treatment. USAID currently is supporting evaluations on the implementation and scale-up of light-emitting diode fluorescence microscopy in countries with a high burden of TB. A recent evaluation of light-emitting diode fluorescence microscopy in Tanzania resulted in the introduction of this tool in high-volume laboratories throughout the country.

Line Probe Assays recently have been recommended by WHO for the detection of drug-resistant TB in sputum smear-positive samples. USAID currently is supporting operational research around the implementation of Line Probe Assays in epidemiologically different field settings (South Africa, Brazil, and India). This study will use an impact assessment framework that was developed to simplify the evaluation of health system requirements for effective implementation of Line Probe Assays to define, group, and link the outcomes that will be addressed in the research. The study aims to produce useful information for national TB programs in countries that are undertaking or are planning to undertake rollout of Line Probe Assays technology and is expected to be completed by July 2012.

Along with its partners, USAID is using novel approaches to diagnostic modeling, which blend transmission modeling with health system modeling concepts to accelerate the introduction of TB diagnostic tools. By assessing the impact of new tools on transmission dynamics within different epidemiological settings in conjunction with health system impacts and requirements, this comprehensive modeling approach will provide targeted guidance for national-level decision makers in high-TB-burden countries regarding the packages of diagnostic tools most suitable for their specific needs and budgets. A prototype model that focuses on diagnostics for drug-sensitive TB has been designed using this new approach and will be submitted for publication by the end of 2010.

Improved Performance of and Accessibility to DOTS Programs

Country-level operational research is central to the improved performance of TB programs. USAID supports operations research to assess country-specific barriers to implementation, develop innovative approaches, and guide the adoption and use of new tools in the context of a national TB program.

In India, USAID-supported studies that resulted in significant changes to the national TB control policy – a change from the definition of a TB suspect from having a cough for a period of three weeks to having a cough for a period of two weeks, as well as a reduction in the number of sputum specimens required for diagnosis of TB from three to two. The study findings demonstrated an increase in the identification of persons with symptoms of TB. Launched nationwide in 2009, the new policy will not only help to detect TB cases sooner, but it will also reduce the laboratory workload and make diagnostic testing more convenient for patients.

Improve the Care of Persons Infected with TB and HIV

USAID-supported research is addressing challenges to coordinated TB-HIV care and poor treatment compliance. An evaluation of adherence rates among patients with TB/MDR-TB and HIV/AIDS who are on concurrent or overlapping treatments is currently under way in South Africa. A separate review is examining epidemiological trends, risk factors, and treatments related to poor outcomes among children and adolescents with drug-resistant TB. The study results will be used to develop more effective programs for pediatric and adolescent TB patients, especially those with HIV infection.

New Vaccines

USAID is committed to providing support to promising vaccines that have the potential to have the greatest impact on TB control. USAID will work closely with the National Institutes of Health and the vaccine community to support field trials of vaccines that have progressed to late phases of development research. Clinical vaccine candidates for TB have emerged only recently, and it is expected that this support may occur as soon as 2011.