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Introduction

Chairman Smith, Ranking Member Bass, and members of the Subcommittee, thank you for inviting me here today to testify on the U.S. Agency for International Development's (USAID) response to the global Tuberculosis and Multi-Drug Resistant Tuberculosis (MDR-TB) epidemic. I would like to express my appreciation for your steadfast support for USAID's TB program and our other global health programs, which have improved and saved lives around the globe and are vital to President Obama's call for ending extreme poverty.

For the past 20 years, the U.S. Government, through USAID, has led the global effort to increase access to TB diagnosis, treatment and care, particularly among those who are most impoverished. The USAID TB program has been a major catalyst in decreasing the TB burden in many countries. Our efforts to build partnerships with National TB Programs, Ministries of Health, multilateral organizations, and departments and agencies across the U.S. Government have developed and strengthened country capacity to control the TB epidemic. These efforts have also contributed to sustainable health systems and made substantial contributions to building the coordinated global community for TB. Since USAID's TB program began almost 20 years ago, together with the critical assistance of its partners 43 million lives have been saved—a tremendous accomplishment for which we should all be proud. Further, investments in TB diagnosis, care and treatment have had a significant impact on the lives of the most impoverished individuals and communities globally. As a result of the united global effort, the world is on track to meet the Millennium Development target of a 50 percent reduction in TB incidence by the end of 2015. This is a remarkable achievement.

Throughout my career, combating TB and MDR-TB has been a personal priority. While living in New York in the 1990s and on faculty at Columbia University, I worked with Dr. Tom Frieden and others on combating the MDR-TB outbreak in New York City. The challenges we faced in New York were in some ways similar to the challenges we face globally: Re-emergence of TB and MDR-TB was due to the decline in attention and resources dedicated to controlling and treating TB. With USAID's support, I led WHO's first global MDR-TB report in 1997 and a second one in 2000. While at The Rockefeller Foundation, I was instrumental in the creation of the Global Alliance for TB Drug Development, the Global TB Drug Facility and the Stop TB Partnership. I care deeply for the fight against TB and I am proud of the work being done today by the U.S. Government. But we need to do more and in new ways.

Global TB Situation

New data released this fall by the WHO shows that tuberculosis is now the leading infectious killer in the world. Each day, more than 4,100 individuals die, each week, more than 28,000—more than twice the total number of deaths from Ebola in West Africa since the outbreak began—and each year, 1.5 million succumb to this preventable disease. In 2014, approximately 9.6 million people developed TB, including 3.2 million women and 1 million children. TB affects individuals in the most economically productive age groups and is one of the top five causes of death among women of reproductive age. TB predominantly affects the poorest and most vulnerable, and approximately 95 percent of TB deaths occur in low- and middle-income countries.

Worldwide, more than two billion people are infected with the bacterium that causes TB *(Mycobacterium tuberculosis*) and are at risk of developing TB disease. While most people infected with the bacterium will not develop TB disease, conditions that suppress an individual's immune system increase the person's risk of progressing from TB infection to TB disease. The most significant among these include medical conditions, such as HIV infection, diabetes, and cancer. In addition, malnutrition, smoking, and immunosuppressive medications are associated with the development of active TB.

Despite the continuing and devastating impact of TB around the globe, considerable progress has been made in the past 25 years. Since 1990, TB deaths have declined by 47 percent and TB prevalence has declined by 42 percent globally. Recent innovations have dramatically expanded our ability to rapidly diagnose all forms of TB and provide appropriate, life-saving treatment and care to those in need. This includes the GeneXpert diagnostic tool that has revolutionized diagnosis of TB drug resistance, shortening the time for laboratory confirmation from a month or more to less than two hours. And new and improved drugs, diagnostic tools, and programmatic approaches are in the pipeline and are expected to be rolled out over the next few years.

The global community has recently developed a new WHO END TB strategy and Stop TB Partnership Global Plan to End TB to accelerate progress and end the TB epidemic by 2030. The strategy identifies intermediate targets for 2025, 2030, and 2035 to stimulate the rate of decline in TB incidence from the current 1.5 percent to 10 percent each year. This acceleration will require all partners to work closely together to optimize the use of existing tools and approaches as well as increase investment in the development and implementation of new and better methods to diagnose, treat, and prevent tuberculosis (including vaccines).

Every year, more than 3.5 million individuals with active TB are not properly diagnosed or reported to national TB programs. A majority of these "missing" 3.5 million people do not have access to or do not receive appropriate services, resulting in poor outcomes. Many die of TB, and many of those who survive endure long illnesses and significant morbidity. They frequently infect those in close contact in their families and communities. Every person with active TB disease who is not on treatment can infect between 10-15 other people each year. As such, "missing" people with TB is not only a clinical and humanitarian issue, it is a serious public health issue. Most of the individuals who comprise the "missing" cases are from 10 countries: Indonesia, India, Nigeria, Pakistan, Bangladesh, South Africa, Democratic Republic of the Congo, China, Tanzania and Mozambique. USAID is partnering with almost all of these nations to help accelerate TB detection and scale up treatment programs. Intensified efforts to reach and treat every person with active TB are vital to curbing the global TB epidemic. USAID has supported countries to find the TB cases earlier through community based approaches, engaging

all care providers, introducing new tools, and expanding diagnostic networks. This past year, for example, USAID supported countries to improve their community-based TB interventions, ranging from TB education and awareness campaigns, to community-level sputum collection and treatment support.

The recently released Stop TB Partnership's Global Plan estimated that to end TB by 2030 the world collectively will need to invest about $13 billion a year to implement TB control activities and research and development. In 2015, a total of about $6.6 billion was invested in TB worldwide. Yet, despite donor support and domestic resources, there is a major funding gap in reaching the WHO END TB 2030 target. In the future, most resources for implementation will continue to come from domestic country budgets, with additional support from other donors and the private sector. Providing technical support to host country governments to increase and maximize their resources for TB and working with local and international private sector resources to expand private sector commitments for TB are important areas of work for USAID. It is critical to maximize existing U.S. Government investments. As such, USAID will continue to work with other USG agencies to leverage all U.S. Government resources and encourage partner countries and other key stakeholders to increase their country level and research support for TB.

Drug-resistant Tuberculosis

Despite recent gains in combating TB globally, the increase in drug-resistant TB threatens to reverse the progress made. Inadequate TB diagnosis and treatment contribute to the development and spread of MDR-TB, a form of TB that is resistant to two of the most important first-line drugs, and extensively drug-resistant TB (XDR-TB), which is resistant to first-line and some second-line TB drugs.

In October 2015, the G-7 Health Ministers signed the Berlin Declaration for Antimicrobial Resistance (AMR) to address this serious and growing public health issue. In December 2014, the O'Neill Commission AMR Review determined that by 2050, 10 million people will die each year from drug-resistant infections. There is also the potential to devastate economies, with an estimated output loss of $100 trillion from now to 2050. MDR-TB is one of the most common drug resistant diseases. More than half a million people develop MDR-TB each year. If the MDR-TB problem is not rapidly addressed, it will continue to grow, exacting a huge toll in terms of morbidity and mortality and potentially threatening national economies, particularly those of low income countries.

I had the privilege of working with WHO on the first MDR-TB survey nearly 18 years ago. Since then, WHO has updated this data every two years, providing critically important data for countries and the global community. MDR-TB now occurs worldwide, with an estimated 480,000 cases in 2014, making up about 3.3 percent of all new TB cases. XDR-TB has been reported in more than 100 countries. HIV and MDR-TB is a particularly deadly combination—people living with HIV are more likely to develop TB and those with MDR-TB are more likely to die, even if they are diagnosed and receive treatment.

MDR-TB is harder to cure and takes much longer. While more than 85 percent of TB patients who are diagnosed and notified are successfully treated, the WHO reports that globally only 48 percent of individuals diagnosed with and treated for drug-resistant TB (both MDR and XDR-TB) are treated successfully. If the spread of drug-resistant TB is not quickly prevented and controlled, TB-related deaths and treatment costs will increase dramatically. It will reverse the past twenty years of progress. The Obama Administration recognized the urgent need to address antimicrobial resistance, directing the U.S. Government to "work domestically and internationally to reduce the emergence and spread of antibiotic-resistant bacteria," under the Presidential Executive Order *Combating Antibiotic-Resistant Bacteria*.

The focus of our precious global TB resources has always been to develop strong TB diagnosis, treatment, and care programs to "turn off the tap" or stop the transmission of new cases, as well as prevent the development of MDR-TB. Countries have started to address their MDR-TB programs only after their national TB programs were established and achieved high TB treatment success rates. Countries that were successful in developing strong national TB programs have been able to keep their MDR-TB rates low. In many countries throughout the world, however, the breakdown in health service delivery systems, the poor quality of services in the private sector, and a lack of regulations on TB drugs has created MDR-TB.

Unfortunately, the tools to address MDR-TB diagnosis and treatment have been sub-optimal. It was only a few years ago that quality diagnosis of MDR-TB in high burden countries was even possible and even then it took months to diagnosis. Recently, new diagnostic techniques have given us the ability to diagnose MDR-TB within hours, such as Xpert MTB/RIF. USAID has made a significant investment in the scale-up of Xpert. In collaboration with CDC and PEPFAR, USAID provides a comprehensive technical approach to help countries successfully utilize Xpert. USAID partnered with PEPFAR, the Bill and Melinda Gates Foundation, and the manufacturer Cepheid to lower the price of Xpert cartridges for the developing world.

While significant gains have been made in rolling out this new technology, it is not fully available at the point of care—that is, it is not readily available at the clinics where individuals at risk seek care. Due to funding constraints, the test, despite being cost-effective, is still thought to be relatively expensive, and often "saved" for special circumstances rather than used as intended. As a result, many who might have been diagnosed are still missed. As seen in the global report released a few weeks ago, however, substantial progress has occurred in the diagnosis of MDR-TB, largely attributable to new molecular diagnostics. In 2014, 58 percent of previously treated patients (and therefore at highest risk of having MDR-TB), and 12 percent of new cases were tested, compared to just 17 percent and 8.5 percent, respectively, in 2013, an increase of 300 percent and 50 percent, respectively. Of the 123,000 cases detected globally, 111,000 started on MDR-TB treatment in 2014, an increase of almost 15 percent over the previous year. While MDR-TB treatment success remains unacceptably low at 50 percent, 43 of the 127 countries and territories that report treatment outcomes to WHO successfully treated more than 75 percent of patients.

I am very proud to note that USAID's support has been a key factor in much of this progress. In many of our priority countries, including Indonesia, Kenya, DR Congo, India and others, our partnership and technical support to National TB Programs has helped establish effective MDR-TB diagnosis and treatment capacities, including scaling up of the use of the GeneXpert

diagnostic tool. In Indonesia, for example, USAID worked in partnership with the Ministry of Health and the Global Fund to stand up MDR-TB diagnosis and treatment centers. There are now more than 30 in-patient MDR-TB treatment facilities and 900 MDR-TB treatment satellite sites across the country.

While the number of patients on treatment has doubled and tripled over the past several years, treatment scale-up is still much slower than desired for several reasons. First, until recently, diagnosis was lengthy and complicated, and individuals were lost to follow-up. Second, many programs felt ill-equipped to address a complicated disease that required toxic drugs for long periods of time. Initially, many countries believed that adequate treatment could only be delivered in clinic or hospital settings that had limited capacity. Great strides have been made in the past couple of years. Treatment is now being brought to the community level to provide patient-centered care. Community health workers and volunteers are being trained and are delivering care, and quality of care by private practitioners has improved. Progress has occurred in locally adapted treatment guidelines, and with the procurement of appropriate supplies of quality drugs. New, shorter and less toxic regimens are now being tested widely. The prospect is for a much more rapid scale-up in the near future.

TB and poverty

People living in poverty are more likely to develop TB and individuals with TB are more likely to be driven further into poverty. This year was a historic moment when world leaders adopted the 2030 Agenda for Sustainable Development, which provided the path to poverty elimination. Today, roughly 1 billion people live in extreme poverty. While that is still an overwhelming number of people—great progress has been made. Compared to 1990, today nearly one billion fewer people live in extreme poverty. By 2012, the poverty rate in the developing world had fallen to 15 percent from 44 percent in 1990. Together with our partners, President Obama has called for Ending Extreme Poverty and USAID has incorporated it into its overall mission of partnering to end extreme poverty and promote resilient, democratic societies while advancing our security and prosperity. USAID's TB program is critically important to achieving the SDGs for eliminating poverty and ending the TB epidemic.

TB disproportionately affects people living in poverty and imposes further financial hardships on TB patients and their families. Even when TB diagnosis and treatment are available free of charge, the cost of accessing care can be difficult for families to bear. On average, TB patients in low- and middle-income countries lose three to four months of work and up to 30 percent of their annual income. This financial burden is greater for persons with MDR-TB and for the extreme poor. Households affected by TB often resort to coping mechanisms that can cause further hardship. Children may be taken out of school to help an ailing parent or to seek paid work to support the family. Patients themselves may take out a loan, sell household items, or seek financial help from relatives. This healthcare-related impoverishment increases the future risk of TB for the entire affected family, thus continuing or worsening the cycle of poverty.

TB resource mobilization

TB is one of the key priorities of the Global Health Bureau at USAID. In FY2015, USAID's planned contribution was over $240 million towards the effort to combat TB. In fact, the U.S. Government is the single largest donor to TB programs globally through the TB portion of our contribution to the Global Fund to Fight AIDS, TB and Malaria (Global Fund), USAID bilateral funds, and PEPFAR TB/HIV funds. Further, the NIH, led by NIAID, supports a comprehensive biomedical research program in TB. These complementary efforts ensure the maximum impact to save countless lives and prevent the further development of MDR-TB.

The majority of the TB burden is in the BRICS countries (Brazil, Russia, India, China, and South Africa), consisting of almost 50 percent of all TB cases and 60 percent of the MDR-TB cases. While domestic resources make up 80 percent of all the funding in high burden countries, it is important for these countries to continue to devote resources to addressing this problem within their borders so that we can collectively achieve the global targets in TB. Over the past eight years, China has tripled and India has doubled its domestic TB budget. Many of the high burden TB countries are expected to continue on an economic growth trajectory of up to 9 percent per year. However, out of pocket health expenditures are above 30 percent for most of the high burden countries. As can be expected, government health spending improves with income level. Of the 22 high burden TB countries, there are 10 countries that have doubled their domestic TB investments over the past eight years, including Ethiopia with an eight fold increase over this time period. USAID will continue to work with countries to mobilize domestic resources for TB through a multi-pronged approach, as well as reduce out-of-pocket costs for those individuals that can't afford to pay.

USAID's TB Vision

Preventing the spread of TB and the development of resistant strains globally is vital to safeguarding U.S. national interests. Reducing TB morbidity and mortality is an important element of the USAID's efforts to improve global health and reduce poverty. The USAID's investments in combating TB have yielded impressive health dividends. Working in the highest burden countries that often provide limited access to quality healthcare, we have played a pivotal role in achieving global targets on TB prevalence and mortality. Since 2000, our contributions have helped these countries achieve a 43 percent decrease in TB-related mortality and a 42 percent decrease in TB prevalence.

USAID's efforts focus on: preventing the spread of TB through earlier detection of individuals with TB; support to develop high-quality TB treatment and care programs; creation and development of MDR-TB diagnostic and treatment services; and expansion of research and innovation capacity. USAID provides significant support for strengthening and expanding high quality TB programs in 23 priority countries. We provide focused assistance to an additional 31 countries to implement their national TB programs and Global Fund grants. Across its programs, USAID works closely with government, private sector, academia, and community partners to increase the impact and sustainability of USAID investments. With FY 2014 funding, USAID helped provide high-quality TB treatment for over 2.7 million TB patients, including 60,000 multidrug-resistant TB (MDR-TB) patients. USAID also worked closely with global country partners to improve TB surveillance and estimates of TB burden. USAID and CDC worked with WHO to support TB prevalence surveys in high priority countries, which resulted in a better

understanding of the TB burden. USAID also partners with the Global Fund, international donors, and affected countries to maximize the impact of the Global Fund's TB and TB/HIV grant portfolio of almost $4.5 billion disbursed across 100 countries since 2002.

Research has been a key part of USAID's portfolio since the program's creation. New treatment regimens that are safer and shorter are urgently needed. USAID supports projects designed specifically to explore ways to improve the diagnosis and treatment of MDR-TB. One example of a USAID-supported activity is the Standardized Treatment REgimen of Anti-tuberculosis drugs for patients with Multi-drug resistant Tuberculosis (STREAM) study, the first randomized clinical trial to evaluate standardized MDR-TB treatment regimens. STREAM was developed to determine whether a nine-month treatment regimen as opposed to a 20-month or longer regimen for MDR-TB is both better for patients and more cost effective for health systems. The Phase II of STREAM study will determine whether two standardized regimens for 6 and 9 month containing bedaquiline, with and without injectables are better than the current WHO recommended 20 month or longer regimen. In addition, in several countries, CDC and USAID have worked side by side on select TB research projects.

In another example, USAID and the Gates Foundation, through the Global Alliance for TB Drug Development, contributes to the development and testing of novel drug compounds and new drug combinations. One of these, the Nix-TB study, is the world's first clinical trial to study an XDR-TB drug regimen with only pills, no injections. The Nix-TB regimen consists of a combination of three drugs with the goal of curing XDR-TB in six to nine months. If successful, the injection-free regimen being tested in Nix-TB could transform XDR-TB treatment, with patients being cured by taking a relatively short, simple, and effective regimen. Importantly, the regimen being tested could reduce the complexity and cost of the treatment to a fraction of what it is today, facilitating the global implementation of XDR-TB treatment in resource-poor nations.

USAID also invests in strengthening TB diagnostic networks. Quality diagnostic networks enable health facilities to provide rapid, accurate diagnoses for individuals with all forms of TB. This in turn enables providers to initiate appropriate treatment for TB patients quickly, thereby improving patient outcomes and reducing the spread of TB. At the national level, USAID helps countries strengthen laboratory and diagnostic networks to increase access to services, such as culture, molecular testing, and drug susceptibility testing. USAID also works with ministries of health to help them map and develop clear plans to strengthen key diagnostic services, such as developing algorithms for introducing new diagnostic tools along with quality-assured smear microscopy. USAID and CDC have worked together in several countries to optimize new tools and strengthen national reference labs.

Conclusion

The U.S. Government is committed to directing its future investments in high-burden TB countries to achieve even greater global health progress. As laid out in the U.S. Government Global TB Strategy (2015 – 2019) , the U.S. Government will work with affected countries and international partners in an effort to reach every person with TB, cure those in need of treatment, and prevent new infections and curb the spread of the disease. Under this strategy, the U.S. Government will work to reduce TB incidence by 25 percent from the 2015 levels, successfully treat at least 13 million TB patients, initiate appropriate treatment for at least 360,000 MDR-TB patients, and provide antiretroviral therapy (ART) to 100 percent of registered HIV-infected TB

patients by 2019. USAID will lead the implementation of this strategy, in close coordination with other U.S. Government agencies involved in global TB care.

Healthy, productive citizens are essential for global economic growth and regional security. USAID is committed to working with partners and high burden countries to combat this leading infectious killer. We will optimize our investments to make the most impact towards the objectives of the 2030 Agenda for Sustainable Development, WHO END TB Strategy and the Stop TB Partnership's Global Plan to end TB by 2030. Achieving these ambitious targets cannot be done by the U.S. government alone – even if we are a significant partner – but will require substantial domestic and private sector resource mobilization and increased global attention. Millions of lives have been saved from this terrible disease through concerted and coordinated effort. I am confident that together we can End TB by 2030.

Thank you very much for giving me the opportunity to share some perspectives on USAID's fight against TB. I look forward to your questions.