HEARING TESTIMONY
House Foreign Affairs Committee
Subcommittee on Africa, Global Health, Human Rights, & International Organizations
The Threat of Drug-Resistant TB in Southern Africa
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Chairman Smith, Ranking Member Bass, and members of the Subcommittee—my name is Dr. Rebecca Martin, and I serve as the Director of the Center for Global Health within the Centers for Disease Control and Prevention (CDC). Thank you very much for the opportunity to be here today to discuss the global threat of drug-resistant tuberculosis (TB) and CDC's critical role in the fight against this deadly epidemic.

Tuberculosis and the Scourge of Drug-Resistant TB

Tuberculosis is a disease caused by the bacterium *Mycobacterium tuberculosis*, which spreads from person to person through the air. As TB disease progresses, it attacks the lungs and can damage the brain, kidneys, and spine. TB can lead to premature death if untreated.

Despite being preventable and treatable, TB has surpassed HIV/AIDS as the world's leading infectious disease killer, taking the lives of 1.7 million people each year. TB is also the leading cause of death among people living with HIV. One quarter of the world's population – nearly 2 billion people – is infected with TB bacteria, and over 10 million of these latent infections progress to active TB disease each year and become transmissible. Among individuals who become ill with TB, approximately four million people go undiagnosed and untreated, allowing further transmission.

TB drug resistance develops when patients receive incomplete or inadequate treatment. Treatment of drug-susceptible TB requires at least six months of treatment with four different antibiotics. This regimen was developed to assure that all the bacteria in the person's system are killed. However, if this regimen is interrupted, only some of those TB bacteria are killed. Other TB bacteria are able to withstand the partial treatment and continue to grow. Patients whose treatment is not completed can relapse, die, or develop drug-resistant strains of bacteria that can then be transmitted to others.

CDC is focused on drug-resistant TB as a leading health security threat to the U.S. and countries around the world. The World Health Organization (WHO) estimates there were 600,000 new cases with resistance to first-line drugs in 2016, of which 490,000 cases were multi-drug resistant (MDR). A total of 105 countries, including the United States, have reported cases of extensively drug-resistant (XDR) TB, an even more severe form of the disease. Drug-resistant infections are extremely costly to treat and manage, cause intense suffering, strain already fragile health systems, and results in mortality at much higher rates than drug-susceptible TB. TB drug resistance accounts for approximately 30 percent of all antimicrobial resistance worldwide.

CDC's Role in Combating TB

CDC is a leader in the fight against TB in the U.S. and around the globe. Our efforts to combat TB are helping to ensure a safer America and a safer world. CDC leads the U.S. national TB program, providing technical and financial support to all state TB programs, and conducting clinical, epidemiologic and

laboratory research. Findings from this research influence treatment, diagnostics, programs, and laboratory services throughout the world. CDC's domestic investment in TB elimination protects Americans' health. Over the past two decades, TB case rates in the United States decreased by 75 percent, and the U.S. now has one of the lowest case rates in the world. Despite these gains, we still have tremendous work ahead.

To eliminate TB in the United States we must work outside of our borders to control TB and prevent drug-resistance. People born outside the U.S. make up 70 percent of the total TB cases in the United States—nearly all of these people came to the U.S. with the bacteria that cause TB living inside them but not causing illness.

CDC works with the State Department to ensure that licensed, and experienced medical doctors practicing overseas screen and treat immigrants and refugees for active TB, according to CDC guidelines, and are cured, before entry into the United States. Under the authority of the *Immigration and Nationality Act (INA)*, the CDC provides the technical instructions for the required medical screening exam. The INA defines medical conditions for inadmissibility, which by regulation, include TB.

Globally, CDC works to find, cure, and prevent TB worldwide, through on-the-ground interventions and global leadership in operational research and technical expertise. CDC works to improve basic TB prevention and infection control efforts to break the cycle of transmission and prevent drug resistance. We are developing innovative approaches to find and treat the roughly 4 million people each year who develop TB disease and go undiagnosed, unreported, or inappropriately treated. Our experts strengthen lab networks and surveillance systems for faster and more accurate diagnosis, and we assist health facilities to implement best practices to end TB transmission. CDC also conducts operational research to identify better, less toxic treatment regimens that cure patients faster and invests in understanding epidemiological factors that drive the spread of TB, HIV-associated TB, and MDR TB. In addition, CDC conducts clinical, epidemiologic, and laboratory research that has led to safer, more effective latent TB regimens, improved tests for latent TB infection, and better methods of detection of drug resistance.

CDC works closely with ministries of health through strong, peer-to-peer working relationships. We work with countries that are most directly connected to our domestic TB epidemics, and we help to strengthen their national TB programs and reduce their TB burden. These global efforts protect U.S. citizens from TB transmission domestically and during travel to foreign countries.

CDC is also a lead implementer of programs to address TB/HIV coinfection in high-burden countries through the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). We provide HIV testing to TB patients and support HIV treatment for people living with HIV/TB co-infection, whose weakened immune systems make them more vulnerable to becoming ill from TB. CDC works in more than 25 countries to combat TB, including ten PEPFAR Priority Countries that account for 80 percent of HIV/TB treatment. In Kenya, India, Mexico, China, and Vietnam, CDC has TB experts in CDC country offices to provide direct technical assistance to governments.

CDC's Collaboration across U.S. Agencies and International Organizations

Globally, fewer than one in five people with MDR TB receive the drugs they need to combat the disease, and less than half of those that do are cured. CDC is a lead implementer of the National Action Plan for Combating Multidrug-Resistant Tuberculosis (NAP), which builds on the National Action Plan to Combat Antibiotic-Resistant Bacteria (CARB). CARB focuses on preventing the spread of resistant pathogens and includes activities to prevent the spread of MDR-TB around the world. The NAP is a five-year plan that builds on and contributes to the U.S. Government's domestic and global TB strategies, as well as the WHO's END TB Strategy. CDC supports, together with the U.S. Agency for International Development (USAID) and the National Institutes of Health (NIH), the three goals of the NAP: 1) Strengthening domestic capacity to combat MDR TB; 2) Improving international capacity and collaboration to combat MDR TB; and 3) Accelerating basic and applied research and development to combat MDR TB.

CDC works closely with our interagency partners to implement PEPFAR and global TB initiatives. The U.S. Global TB Strategy focuses on the comparative advantages and strengths of all federal agencies to control TB globally. For example, CDC coordinates with USAID at headquarters and in the field to strengthen capacity to combat MDR TB in countries with the highest TB burden. In Uganda and other African countries, CDC strengthens national TB laboratory networks to diagnose TB and MDR TB. To accelerate basic and applied research and development to combat MDR TB, CDC works with USAID and the NIH to assess the effectiveness of therapeutic regimens combining licensed and novel drugs that may result in fewer serious side effects and shorter treatment durations for patients with MDR TB. U.S. Government agencies hold monthly Global TB Coordination teleconference calls to share information and plan collective approaches. CDC and USAID field teams also collaborate to support Global Fund TB grants.

CDC's work supports and contributes to the WHO's END TB Strategy (2015-2035), the Stop TB Partnership's Global Plan to End TB (2016-2020), and the USG's Global TB Strategy (2015-2019). CDC collaborates with these technical organizations, ministries of health, the Global Fund to Fight AIDS, Tuberculosis and Malaria, and other U.S. agencies to find, cure, and prevent TB, HIV-associated TB, and drug-resistant TB.

As a new frontier in the fight against TB, CDC focuses on expanding the use of TB preventive therapy (TPT), which works by attacking latent TB bacteria before they can multiply to cause active disease, spread, and develop resistance. TPT can dramatically reduce latent TB cases, preventing TB disease and transmission. In people on TPT, it is 90 percent effective in protecting people with latent TB infection from progressing to TB disease. In the United States, more than 80 percent of active TB cases stem from reactivation of past latent TB infection. Therefore, expanding testing and treatment of persons at risk for latent TB infection, in addition to active case-finding and treatment, is key to eliminating TB. CDC is taking these evidence-based data and implementing programmatic changes to amplify public health impact. Through PEPFAR, CDC is leading the aggressive scale-up to more than triple access to TPT to prevent TB disease among people living with HIV in southern Africa and beyond. CDC also supports innovative operational research to improve diagnosis of TB in persons living with HIV.

CDC and TB in Africa

Africa remains a global TB hotspot. WHO reports that over 400,000 people died from TB in Africa in 2016, representing nearly 25 percent of global TB deaths. South Africa, Mozambique, and Zimbabwe are among the highest burden countries in the world for drug-resistant TB. Africa lacks sufficient facilities to provide rapid diagnosis, care, and treatment to patients where they live, and high rates of HIV infection suppress immune systems and fuel TB transmission in all its forms. Mining and other cross-border seasonal work can interrupt TB treatment, leading to resistance and increasing opportunities for transmission.

CDC works closely with ministries of health and other partners to scale-up existing tools. In Uganda, Mozambique, and Kenya, CDC is expanding access to rapid testing and rapid treatment by mapping access points for TB care. Through PEPFAR, CDC works to find and treat those with latent TB infection in Africa and deliver preventive therapy to interrupt the cycle of TB transmission. CDC works with several countries including Botswana, Ethiopia, Mozambique, Nigeria, Rwanda, Zambia, Zimbabwe, and Lesotho to implement innovative and effective TB infection control practices in healthcare settings. CDC partnered with Zimbabwe to implement a national policy for annual TB screening and treatment for all health care workers, which has reduced TB rates.

In Zambia, Lesotho, and Mozambique, CDC is developing novel approaches to provide seasonal mineworkers and their families with diagnosis, care, and treatment services both at work and in home communities. To address the need for better, faster diagnostics and shorter, safer treatment regimens for drug-resistant TB, CDC is working through the AIDS Clinical Trial Group in South Africa to identify the best approach for preventing MDR TB among exposed children and family members.

South Africa has been a pioneer in these efforts. CDC works closely with the Ministry of Health in South Africa to combat TB, and they have been a strong and effective partner. In 2006, an outbreak of XDR TB in KwaZulu-Natal devastated the state's population, demonstrating the catastrophic toll caused by drug-resistant strains. A ground-breaking study revealed that MDR TB spread from person-to-person in hospitals and did not emerge solely from incomplete drug regimens. The outbreak killed 52 of 53 patients who developed TB disease, and we learned more about how easily drug-resistant TB spreads to persons living with HIV and we learned more about the transmissibility and high mortality of drug resistant TB among people living with HIV. Since this experience, South Africa has scaled up testing for drug resistance, tested new drug regimens to cure drug-resistant TB faster with fewer side effects, and implemented effective infection control programs in hospitals. Globally and in its own region, South Africa is leading by example to tackle the enormous challenges of these dual epidemics of HIV and TB.

Momentum in the Fight against TB

Infectious disease threats do not respect borders, so a disease threat anywhere is a threat everywhere. Like other infectious threats, TB (and especially drug-resistant TB) jeopardizes the health, security, and prosperity of America and our partners.

The world has made great strides against TB – with more than 53 million lives saved since 2000 – but we cannot win the battle against this disease unless we find more cases, expand access to diagnosis and treatment, stop transmission, and effectively prevent the development and spread of drug-

resistant TB. Further, we will not eliminate TB in the United States unless we control TB and prevent drug-resistance internationally.

To do this, we must scale up access to the effective tools we have and redouble efforts to develop the next generation of technologies to accelerate our impact. Beyond this, we must look for new ways to hold ourselves and others accountable for progress, which can begin with an effective accountability framework—an independent mechanism to track commitments and progress for all nations.

Political will is critical from every country combatting TB. As the Subcommittee is aware, heads of state will gather in September 2018 at the United Nations General Assembly for the first-ever high-level meeting on TB, which could lead to new commitments from countries and accelerate progress where it is needed most. The world is focused on the TB epidemic, and we must seize the moment together to halt this global threat in its tracks.

Thank you for your support of CDC's global TB efforts, and I would be pleased to answer your questions.