COMBATING TUBERCULOSIS IN SOUTHERN AFRICA

HEARING

BEFORE THE

SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, GLOBAL HUMAN RIGHTS, AND INTERNATIONAL ORGANIZATIONS

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COMBATING TUBERCULOSIS IN SOUTHERN AFRICA

THURSDAY, JULY 12, 2018

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH,
GLOBAL HUMAN RIGHTS, AND INTERNATIONAL ORGANIZATIONS,
COMMITTEE ON FOREIGN AFFAIRS,
Washington, DC.

The subcommittee met, pursuant to notice, at 3:00 p.m., in room 2255 Rayburn House Office Building, Hon. Christopher H. Smith (chairman of the subcommittee) presiding.

Mr. SMITH. The subcommittee will come to order, and good afternoon to everyone. Thank you for being here.

Today's hearing will address the persistent and too often underestimated threat to global public health posed by tuberculosis. This brutal contagious disease killed 1.7 million people in 2016—the most recent data available—making it the deadliest infectious disease in the world, killing more than both HIV/AIDS and malaria combined.

TB is devastating for many people globally but it impacts the people of Africa, especially southern Africa, disproportionately.

In 2016, 44 percent of all TB deaths occurred in the Africa region, in spite of accounting for only 25 percent of all new TB cases. Africans die at a rate of 72 per 100,000 infected, compared with 35 per 100,000 in Southeast Asia and 13 per 100,000 in the eastern Mediterranean region.

Those infected with HIV/AIDS are particularly vulnerable to TB and nearly three-quarters of those co-infected with HIV and TB in 2016 lived in sub-Saharan Africa.

Thankfully, most cases of TB are curable if patients are diagnosed and adhere to a proper treated regimen. However, millions of newly-infected people go undiagnosed and without treatment each year, and the global spread of multiple drug resistant, or MDR, or extensively drug resistant—XDR TB—which emerges when patients receive inappropriate or incomplete treatment, poses and even greater and more costly threat.

In 2016, roughly, 490,000 people develop MDR TB. An additional 110 new cases were resistant to the most effective treatment. Not only is treating MDR and XDR TB a grueling process for the patient, it also costs far more to treat than the other manifestation of the disease.

One study by the Stop TB Partnership estimated that drug-resistant TB could kill up to 2.5 million people annually and cost the global economy $16.7 trillion if left unchecked.

The dangerous potential of a drug-resistant TB outbreak is evident in the South African mining sector where exposure to silica dust, crowded poor living conditions, and high HIV prevalence created an incubator for disease and heightened the risk of contracting TB.

Further complicating the problem, approximately 40 percent of mine workers are migrants who frequently move across borders and don't receive consistent medical treatment from public health systems in the region that do not coordinate sufficiently.

This further increases the risk of MDR and XDR TB infections.

I am encouraged to see that U.S. funding for combating TB increased to $261 million in 2018, which is $20 million more than was allocated in 2017, and more than $82 million higher than the administration's request.

This shows that my colleagues and I and all of us are taking this threat seriously and I think that is a positive step on our part.

But we must not stop there or become complacent in any way. The World Health Organization anticipates a $7.4 billion budget shortfall for the global plan to end TB if the international community does not significantly increase funding.

We must encourage our international partners to step up to this challenge and take the opportunity of the U.N. General Assembly high level meeting on ending TB this September to do so.

But even more, we must explore more innovative and holistic approaches to eliminating this disease. We must work from a regional perspective and increase coordination among health systems.

We must pay special attention to the mines in South Africa. We must redouble our efforts to diagnose and treat every person infected with TB and we must pull out all the stops when it comes to preventing MDR or XDR TB infections.

We must also encourage the World Health Organization to stop being overly bureaucratic when it comes to battling TB. There are bottlenecks in the WHO approval process for new treatments and new diagnostic tests which need to be fixed.

I am looking forward to hearing from our very distinguished panel, which I'll introduce shortly. I would like to welcome Tommy and Amanda Russo, distinguished guests who are here visiting, and their parents from Howell Township in my district.

Thank you for coming, Tommy and Amanda, and I would like to yield to my good friend and colleague, the ranking member, Ms. Bass.

Ms. BASS. Thank you, Mr. Chairman.

I want to thank you for convening today's hearing on combating tuberculosis in southern Africa. We know this is an issue that is important to all of us with global dimensions that impact everyone.

I want to thank our witnesses for taking the time to testify before this committee today. We know that you have dedicated your life to addressing the great public health challenges and we thank you.

I also want to thank Ranking Member Engel, who might be here. He has consistently championed several health priorities and, in

particular, the spread of tuberculosis, both multi-drug resistant and extensively drug resistant TB.

In 2016, 25 percent of all new TB cases developed in Africa and 2.5 million people—44 percent of all TB deaths—occurred in the region. Meanwhile, we know that TB cases are both preventable and curable.

But we are here today because the southern African region has the highest incidence of TB in the world. The association with HIV/AIDS and co-infection has made TB one of the leading killers of HIV/AIDS-positive people globally, and southern Africa has one of the highest burdens of TB and the highest burdens of HIV.

Defeating TB requires expanding access to affordable treatment but also prevention of TB in the first place.

I look forward to hearing on how the U.S. is supporting more effective treatment as well as prevention.

Thank you.

Mr. SMITH. Thank you, Ranking Member.

I now would like to introduce our distinguished panel, beginning first with Dr. Rebecca Martin, who is the director of the Center for Global Health at the U.S. Centers for Disease Control and Prevention, CDC.

With over 18 years of experience working with immunization, HIV, and health system strengthening, Dr. Martin is a leading expert in the field of international health.

She has worked extensively in Africa to measure and evaluate the HIV/AIDS epidemic and equip nations to respond effectively. As director of the Center for Global Health, Dr. Martin leads the CDC's global effort to protect and improve health globally through science, policy, partnership, and evidence-based health action. We are delighted that she is here today to provide her expert insights.

Ambassador Deborah Birx, a medical doctor, is the coordinator for the United States Government Activities to Combat HIV/AIDS and U.S. Special Representative for Global Health Diplomacy.

Over her 30-year career, she has focused on HIV immunology, vaccine research, and global health. Ambassador Birx oversees the implementation of the U.S. President's Emergency Plan for AIDS Relief, or PEPFAR, and all U.S. Government engagement with the Global Fund to fight AIDS, tuberculosis, and malaria.

In her role as U.S. Special Representative for Global Health Diplomacy, she works to align the U.S. Government's diplomacy with foreign assistance programs and address global health challenges and move toward achieving goals, including eliminating AIDS, ending preventable child and maternal deaths, and combating infectious disease threats.

We will then hear from Irene Koek, who is the senior deputy assistant administrator in USAID's Global Health Bureau. Previously, she was the senior infectious disease advisor for the Global Health Bureau and the Global Health Security Agenda led at USAID.

From 2010 to 2014, she was director of the Health Office in USAID Indonesia, where she also served as the health attache and PEPFAR coordinator. During her 32-year career with USAID, Ms. Koek has also worked as a health advisor to the Policy and Program Coordination Bureau, and as chief of infectious disease divi-

sion in the Global Health Bureau helped start the President's malaria initiative and served as chair of the Stop TB coordinating board.

Ms. Koek, thank you for being here as well, and without objection, your full resumes will be made a part of the record.

Dr. Martin, the floor is yours.

STATEMENT OF REBECCA MARTIN, PH.D., DIRECTOR, CENTER FOR GLOBAL HEALTH, U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

Ms. MARTIN. Thank you, Chairman Smith and Ranking Member Bass.

My name is Dr. Rebecca Martin and I serve as the director for the Center for Global Health within the U.S. Centers for Disease Control and Prevention.

I appreciate the opportunity to be here today to discuss the global health security threat of drug resistant tuberculosis and CDC's critical role in preventing and stopping it.

It is a pleasure to join my friends and colleagues, Ambassador Birx and Deputy Assistant Administrator Koek.

In 1973, my older sister was exposed to TB and infected and had to undergo 9 months of treatment, a practice still valid today in many countries, nearly 50 years later.

In 1991, I worked in Haiti to set up a cutting-edge laboratory for TB with fluorescent microscopy, still in use nearly 30 years later in resource-constrained countries.

HIV drives the TB epidemic in southern Africa with the co-infection rate of 60 percent. While we have benefitted from innovations to fight HIV, innovations for TB have not kept pace. We must fight these two diseases together.

I want to emphasize three points about CDC's work in combatting TB. First, CDC leads the U.S. domestic TB program that supports states and large cities, and conducts clinical and epidemiologic and laboratory public health research.

Our success in domestic elimination is dependent upon our work in global TB.

Secondly, a disease threat anywhere is a disease threat everywhere, and there is no greater example than this than drug-resistant TB.

Thirdly, to succeed in controlling TB, we need to develop new tools, scale up existing tools in prevention, and enhance political will.

Today, tuberculosis, although preventable and treatable, is the world's leading infectious disease killer, taking the lives of nearly 1.7 million people each year.

Over 25 percent of these deaths occurred in Africa in 2016 with southern Africa as the epicenter. One-quarter of the world's population—nearly 2 billion—is infected with TB.

Among those individuals who become ill with TB disease, approximately 4 million go undiagnosed and untreated. TB drug resistance first develops when patients receive incomplete or inadequate treatment.

Drug-resistant TB can then spread from person to person, making the disease an even greater threat to global health security.

Globally, in 2016, there were 600,000 new TB cases resistant to first line drugs and 80 percent of them were resistant to multiple drugs.

Drug resistant infections are extremely costly to treat and manage, cause intense suffering, strain fragile health systems, and result in death at much higher rates than drug-susceptible TB, with only one in 10 being cured to date.

A hundred and five countries, including the United States, have also reported cases of extensively drug-resistant TB, an even more severe form of the disease, which is at least 17 times more expensive to treat than medication-responsive TB strains.

I want to talk for a moment about the connection between CDC's global and domestic TB efforts. Over the past two decades, TB cases in the United States have decreased by 75 percent, and U.S. now has one of the lowest cases in the world.

Yet, there is still work to be done here and abroad. People born outside the U.S. make up 70 percent of the total TB cases in the U.S. Nearly all of these people arrived in the U.S. over 10 years ago.

To control TB and prevent drug resistance in the United States, we must work outside of our borders. For example, CDC works with our counterparts—ministries of health—in more than 25 countries to combat TB, including those countries from which most U.S. TB cases originate.

In South Africa, CDC has used molecular fingerprinting to determine that multi-drug-resistant TB cases were primarily due to person-to-person spread and not due to problems adhering to treatment regimens.

Also, CDC is a co-lead in addressing TB-HIV co-infection in high burden countries through PEPFAR. Despite recent success, stopping TB will require that we scape up access to existing tools and redouble our efforts to develop the next generation of drugs and technologies to accelerate our impact.

Importantly, expanding TB-preventive therapy, which is up to 90 percent effective in protecting people with latent TB infection from progressing to active disease could change the trajectory of the TB epidemic.

In the coming years, continued U.S. leadership will be essential to eliminating TB domestically and in the international community mobilizes to address this threat.

We have an opportunity to demonstrate our leadership at the upcoming United Nations General Assembly in September and we need champions like the Honorable Minister Motsoaledi, who could not be here with us today, and each of you.

In closing, I'd like to leave you with a quote from Nelson Mandela, who said, "It always seems impossible until it's done."

At CDC, we embrace the impossible.

Thank you for the opportunity to appear before you today and I look forward to answering your questions.

[The prepared statement of Ms. Martin follows:]

HEARING TESTIMONY
House Foreign Affairs Committee
Subcommittee on Africa, Global Health, Human Rights, & International Organizations
The Threat of Drug-Resistant TB in Southern Africa
Dr. Rebecca Martin, Director, Center for Global Health, Centers for Disease Control & Prevention

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.

Mr. SMITH. Dr. Martin, thank you so very much.
Dr. Birx.

STATEMENT OF THE HONORABLE DEBORAH L. BIRX, M.D., U.S. GLOBAL AIDS COORDINATOR, U.S. SPECIAL REPRESENTATIVE FOR GLOBAL HEALTH DIPLOMACY, U.S. DEPARTMENT OF STATE

Dr. BIRX. Thank you, Chairman Smith, Ranking Member Bass. Thank you for your continued incredible vision and support for PEPFAR and let me again thank your staff, who have been really instrumental in the work that we do every day, and to the rows behind me who are so extraordinarily dedicated for TB. There's a lot of people in the audience today who are very much committed to our response globally to TB/HIV.

I am not going to repeat many of the numbers that were just presented. If we can have the first graphic—I think, hopefully, shows you the absolute ramp up of both TB and HIV concomitantly in southern Africa. And so picking this as a focus of southern Africa was really brilliant because it shows if we control the HIV pandemic, we return to those much lower and we control the TB pandemic in southern Africa.

Our goal in PEPFAR has always been to provide the best care, and part of that best care now requires us to dramatically expand our TB activities, which we have done over the last 2 years.

We've invested about $1.5 billion within PEPFAR on TB and TB/HIV but we are really focused on increasing and accelerating our impact.

We've taken a three-prong approach. One is ensuring that all TB cases are tested for HIV and then those cases that are found to be dually infected start on HIV treatment immediately.

We are also focused, number two, on preventing TB from developing in the first place in HIV positive clients and this is by treating them early before their immune system begins to deteriorate.

Third, we are screening our HIV-infected clients for TB and ensuring that those who have active disease are treated immediately and those who don't have active disease are immediately put on TB-preventive therapy, which is a new addition to our program with a clear indicator.

In our first focus area, and, you know, at PEPFAR we always try to be honest with ourselves, so in the first focus area of ensuring that every TB client is tested for HIV. We are at about a 95 percent success rate in our most recent data, and in getting those individuals on treatment we are at a 95 percent success rate.

This makes sense because TB clients are often seen frequently, and so missing that opportunity of getting them on HIV drugs would be inexcusable.

In the second area, which is really preventing deterioration of the immune system, we haven't done as well, and this is—really, we haven't been able to prevent the new cases of TB because countries have been delayed in often starting immediate treatment.

But through sub-Saharan Africa, with the leadership of our Ambassadors in countries and the leaderships of ministers of health, many countries have gone to what we call test and start.

So upon immediate diagnosis of HIV they started on TB—started on HIV therapy. Allowing them to thrive and not transmit the virus but also preventing opportunistic infection and, therefore, TB.

If we can see the next graphic, I wanted to be honest also with who we are missing. The blue bars are men, the green bars are women, divided by age groups.

These are the impact surveys that we have in the field. This is a summary of seven countries in sub-Saharan Africa clearly showing that we are missing men between age zero and 34 and we are missing women between zero and 24.

It makes sense because we implemented what we call B+, to ensure all women that are pregnant immediately have access to lifelong treatment about 4 years ago, and you can see that almost every woman over 25 has been diagnosed and is on treatment.

It's really missing the healthy individuals. We know when people are infected with HIV they have a long prodrome of asymptomatic where their immune system is constantly under destruction.

If we can find them early when they are perceived to be healthy, we can prevent the consequences of these opportunistic infections.

So we are very much dedicated to finding these missing healthy children, missing healthy men, and missing healthy women, long before their immune system deteriorates.

If we are able to do this, we've created a community of practice that not only is strengthening the health system for everyone but also provides the platform to find other communicable, noncommunicable, and future disease threats in the communities because the communities will see themselves within the health system and health-seeking behavior.

Our third area of focus—the early diagnosis and treatment of TB in our HIV positive clients is also slowly improving.

We are now up to about 76 percent of our clients are screened for TB when they come in to our PEPFAR HIV clinics and that has been a big change over the last 2 years.

Where we are failing our clients is taking the ones that have been screened negative for active disease and getting them what we call preventive therapy.

We were in the single digits and we are beginning to make progress quarter over quarter as we measure our progress in that indicator.

We are beginning to see a real impact from our joint efforts of combatting HIV and TB together. The death rates have, remarkably, declined and in Botswana, Namibia, and a whole series of countries who had gone to earlier treatment there's been a dramatic decline in the number of TB cases.

I really—if immediate therapy for anti-retro viral therapy is the cornerstone of PEPFAR, both the active TB case findings and the preventive therapy will be our capstone.

And so although we are behind compared to our other areas of work, we are very much focused on these areas and we'd appreciate your attention to this critical issue for us.

Thank you.

[The prepared statement of Dr. Birx follows:]

Written Testimony

Ambassador-at-Large Deborah L. Birx, M.D.

Coordinator of the United States Government Activities to Combat HIV/AIDS and

U.S. Special Representative for Global Health Diplomacy

House Foreign Affairs Committee

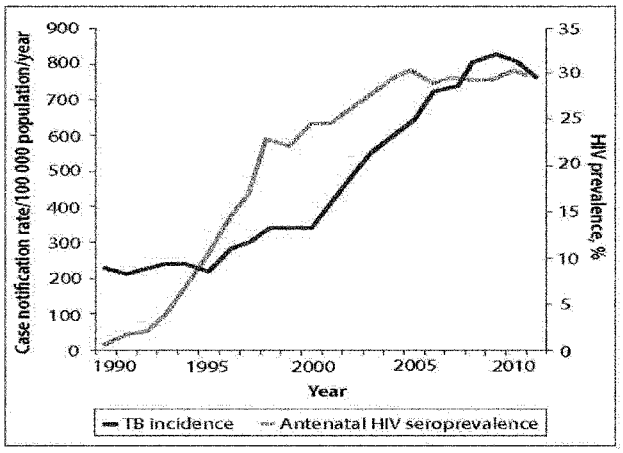
Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations

"The Threat of Drug-Resistant TB in Southern Africa"

July 12, 2018

Thank you Chairman Smith, Ranking Member Bass, and other distinguished members of this Subcommittee. I am deeply honored to appear before the House Foreign Affairs Committee and your Subcommittee, which have provided such visionary leadership and remarkable support for the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) since its inception in 2003. Thank you very much for the opportunity to be here today to discuss global TB/HIV co-infection and PEPFAR's critical role in the fight against this deadly epidemic.

It has been estimated that a quarter of the world's population is infected with Mycobacterium tuberculosis, the organism that causes TB disease. Infection precedes the development of TB disease, sometimes by decades, and is clinically latent. Only about ten percent of infected people with functioning immune systems will develop active, symptomatic TB disease in their lifetimes. People whose immune systems are impaired from conditions like malnutrition and especially HIV infection are at particular risk of, and from, active TB disease. Persons living with HIV are 20-30 times more likely than people without HIV to develop TB disease, and when they do, they are much more likely to die. Your focus on this particular alignment of HIV and TB in Southern Africa is timely and critical for both diseases. In Africa, the prevalence of TB surged dramatically through the 1990s, driven by the HIV epidemic (see graphic).



Churchyard et al, "Tuberculosis control in South Africa: successes, challenges and recommendations." *South African Medical Journal*; 2014

In Southern Africa, the two diseases are so entwined that they are best considered as a syndemic – synergistically interacting epidemics, each worsening the other. In some communities in Africa with high burdens of HIV, rates of TB are literally hundreds of times higher than they are in the United States.

In 2016 alone, an estimated 2.5 million people in Africa developed TB disease, 30 percent of whom were HIV infected, resulting in an estimated 764,000 new cases of TB among persons living with HIV. TB is also a relentless killer of persons with HIV; it is the leading cause of hospitalization, and far and away the leading cause of death, responsible for approximately 40 percent of deaths in people with HIV. In Africa in 2016, there were almost 417,000 TB deaths, 320,000 of which were in persons with HIV. HIV patients are more likely to have extra-pulmonary TB, which is often harder to diagnose, and more likely to develop resistance to TB drugs, which makes TB extremely difficult to treat. The TB case fatality ratio is approximately 20 percent in most African countries – many times higher than in Europe and the United States. This is particularly concerning since we have the tools we need to cure and prevent TB – which means that those deaths arguably could have been avoided.

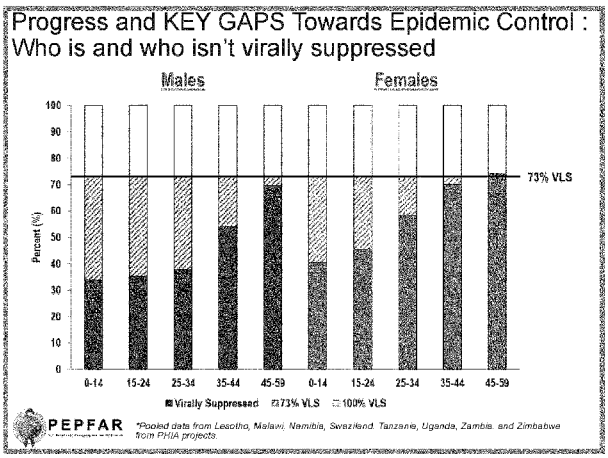
The persistent incidence and mortality of TB disease highlights two things: that TB remains an urgent public health concern in Africa and that we haven't yet done enough. Our goal is to provide the best care possible for our patients living with HIV and we are focused in three areas: (1) ensuring all TB cases are tested for HIV and treated for both infections, (2) preventing TB from developing in our HIV-infected clients by ensuring they are treated for HIV before their immune system deteriorates, and (3) screening our HIV infected clients for TB and

curing them when they are diagnosed or ensuring that they are given a course of TB preventive therapy. These efforts will interrupt transmission, lower TB prevalence, and help end this epidemic. In regions of the world where TB and HIV are tied together, HIV programs play a pivotal role in implementing the strategy to reduce TB through these focused interventions. As I will discuss, PEPFAR has committed to addressing TB in Africa by dramatically increasing HIV/TB investments and activities over the past decade and more recently by aggressively scaling up antiretroviral therapy for all persons living with HIV and accelerating the roll-out of TB preventive therapy.

Since 2005, PEPFAR has invested over 1.5 billion dollars on TB/HIV programming, and as a result, PEPFAR-supported countries around the world have made substantial gains in TB control. So let's review our progress. In focus area (1), testing all TB patients for HIV and ensuring rapid initiation of antiretroviral therapy for those that test positive, we are doing well. This intervention dramatically lowers the risk of death and has been a focus of PEPFAR for several years. In PEPFAR-supported countries in the second quarter of FY 2018, the proportion of TB patients with documented HIV status was approximately 95 percent, and the proportion of those with HIV infection who were started on ART exceeded 95 percent.

In focus area (2), ensuring everyone is begun on antiretroviral treatment immediately upon diagnosis to prevent the destruction of their immune system and prevent opportunistic infections including TB, we have not done as well – and this has been a core focus of the program over the past 2 years. While finding and curing TB in our patients is a critical strategy, preventing TB from developing in the first place is the ultimate goal. Providing antiretroviral therapy to all HIV-infected patients before impairment of their immune systems is the single most impactful intervention possible: antiretroviral therapy for those that are HIV infected bolsters the immune system and reduces the risk of developing TB disease by about 65 percent, and it reduces mortality in those who already have the disease. We have seen that Option B+ – antiretroviral therapy for expectant mothers – when offered to all pregnant women, regardless of CD4 cell count, dramatically reduced the risk of TB reactivation and death in women. Clinical trial and modeled data strongly suggest that wide-scale implementation of antiretroviral therapy will sharply reduce TB incidence and transmission in communities with high burdens of both diseases. Early antiretroviral therapy also protects communities by decreasing both HIV and TB transmission within those communities. By lowering the number of hospitalizations and preventing deaths, we are preserving the integrity and economic capacity of families and communities.

We constantly seek more accurate data, at national and sub-national levels, to better track our progress and more precisely identify and address the key gaps and obstacles. We have conducted comprehensive community-level impact surveys (PHIAS) to better understand the gaps in achieving our goals, as demonstrated in this graphic below:



We are missing HIV-positive individuals among males 0-34 years old and females 0-24 – these are mostly "healthy" individuals infected with HIV, but the virus is quietly destroying their immune system and if we don't find and treat them now, early in their disease, they will present later, sick with opportunistic infections, including TB. This is a core focus of the PEPFAR program; if we meet this challenge, stable health systems in Africa and health-seeking behaviors of communities will follow. Such systems and behaviors are needed to combat all the non-communicable diseases and ensure early identification of new infectious diseases and zoonotic events (critical for the global health security agenda) will be there.

Scaling up antiretroviral therapy is the cornerstone of PEPFAR's TB/HIV efforts, and for the past two years, we have been insisting that programs start antiretroviral therapy in all people living with HIV (PLHIV) as soon as possible after confirmation of HIV status, regardless of CD4 cell count. This Test and Start policy is now the standard of care, and we are aggressively pursuing implementation of this policy and practice in all countries where we work.

We are seeing the effects of the scale-up. Rates of TB increased starkly across Africa after HIV exploded in the 1990s; we are now seeing the reverse of this trend: the World Health Organization has reported falling TB incidence as antiretroviral therapy is expanded where there is a high dual burden, and published data from Eswatini, Kenya, and Malawi clearly show decreases in new TB cases in the areas where HIV scale-up has been most effective. The effect of antiretroviral therapy on mortality is equally evident: UNAIDS has reported that AIDS-related deaths have fallen by 48 percent since the peak in 2005, and deaths specifically attributed to TB among people living with HIV fell by 33 percent. These effects will be amplified as we further scale up antiretroviral therapy to all PLHIV. And this success actually comes with a cost-saving: modeling data from Botswana show that in addition to preventing

tens of thousands of TB cases, antiretroviral therapy given to all PLHIV will save tens of millions of dollars in TB treatment costs over the next 15 years.

In order to accommodate the increase in the number of patients who are being treated with antiretroviral therapy as a result of Test and Start, we are decongesting the healthcare facilities by spacing out follow-up appointments for the vast majority of PLHIV who are doing well and shifting monitoring of adherence and symptoms to community health workers. This will not only free up clinic appointments for those that are newly registering, it will also develop healthcare infrastructure in the communities where TB and HIV patients live, facilitating treatment adherence and diagnostic evaluation of those with symptoms and those who were exposed to either disease.

The third area of focus is the early diagnosis of TB in persons with HIV and increasing access of TB preventive therapy. By emphasizing routine screening for the symptoms of TB disease in all PLHIV at every visit to a PEPFAR-supported facility, we are able to find TB disease early and refer directly for diagnostic workup and treatment, key to preventing drug resistance. Our recent data show that 76 percent of our patients were screened for TB at their last visit. We remain focused on improving the frequency and quality of TB screening and are collecting site-level data to focus our interventions.

We are using sensitive diagnostic technology followed by effective treatment to save more lives and lower TB transmission. The GeneXpert platform is a cartridge-based diagnostic tool that uses molecular technology to diagnose TB disease. It doesn't require a laboratory setting, and can be placed at or near the point of care. It is much more sensitive than traditional diagnostic methods, and the newest cartridge is as sensitive as the best laboratory-based tests. In 2012, PEPFAR partnered with USAID and the Bill and Melinda Gates Foundation to reduce the cost of each test from 17 to 10 dollars, and has directly funded the purchase of more than 500 GeneXpert machines in over 20 countries and well over 100,000 cartridges. The GeneXpert platform can now be leveraged to document and monitor HIV viral load, which is especially important and lifesaving for early infant diagnosis, amplifying the effect of this considerable investment. PEPFAR continues to play a critical role in providing technical assistance to ensure that this platform is efficiently scaled up in a coordinated manner.

PEPFAR is also making treatment more accessible by pushing to integrate clinical care for TB and HIV. In the countries where we work, TB and HIV are often separate programs with separate clinic systems that are frequently not co-located. This means that historically, patients with HIV and TB disease needed to engage two different and often uncoordinated care and treatment systems. As recommended by the World Health Organization, PEPFAR is integrating TB/HIV care by providing care for both diseases in one clinic. We are building capacity in partner governments through effective policy change and focused training, which will allow treatment of HIV in TB clinics, greatly diminishing the burden put on patients and promoting adherence and retention in care.

The risk of TB disease and its attendant mortality can be further reduced by adding TB preventive therapy to antiretroviral therapy. This is a key intervention. The combination of TB

preventative therapty and antiretroviral therapy has been shown to reduce the risk of TB disease by almost 95 percent, and TB preventative therapy has been shown to reduce mortality in PLHIV by 37 percent, independent of antiretroviral therapy and CD4 cell count.

If immediate antiretroviral therapy is the cornerstone of PEPFAR's TB/HIV efforts, then TB infection control and TB preventive therapy are the capstones. We are actively monitoring all PEPFAR-supported facilities to ensure that they each have and are compliant with policies for preventive therapy and infection control. TB preventive therapy for people living with HIV has been a World Health Organization recommendation for years, but with the newer global targets and the ambition to end the TB epidemic, it has become a more prominent component of TB control efforts. PEPFAR has always recommended TB preventive therapy for our patients, but in the past, most countries did not have a specific policy, and we did not closely follow how well preventive therapy programs were implemented. That has changed. Almost all of the countries in which we work now have national guidelines recommending preventive therapy for PLHIV.

In 2016, PEPFAR revised the suite of TB indicators and now mandates reporting on initiation and completion of TB preventive therapy as well as TB screening and initiation of TB therapy in those diagnosed with the disease. These additions were part of a deliberate attempt to drive programming and encourage fully integrated TB/HIV care in PEPFAR countries. In the past year, we have seen a remarkable increase in PEPFAR targets for TB preventive therapy: despite limited advanced planning and no requirements for targets for FY 2018, 21 countries have initiated or expanded TB preventive therapy programming, and the targets for FY 2019 are substantially higher in almost every country.

A number of markedly successful programs have been introduced: the Democratic Republic of Congo, Malawi, Mozambique, and South Africa have all had steady progress incorporating TB preventive therapy into routine care with approaches that are well documented and replicable. More notably, Kenya had tremendous rapid success rolling out TB preventive therapy through a well-designed, carefully crafted collaboration between the country's national TB and HIV programs. Their approach resulted in an increase in the number of PLHIV who initiated TB preventive therapy from a total of 10,000 PLHIV in 2014 to more than 880,000 by this year, with treatment completion rates approximating 90 percent for most implementing partners. We are promoting TB preventive therapy in all of the countries where PEPFAR is implementing programs and will continue to monitor and expand to ensure that all of our patients have been treated.

With correct application of sufficient resources, the fight against TB/HIV is a battle we can win. We must make a commitment to finding and treating all persons with HIV before they have immune impairment and get clinically sick, and we must find and effectively treat all persons with TB disease – we simply cannot afford not to. We need to facilitate effective treatment to unburden our patients. Care should be integrated and mainstreamed, and adherence should be promoted in ways that do not require patients to report for observation. Inadequate or

erratic treatment has led to the development of drug-resistant disease, which now threatens to undermine the progress that is being achieved.

Once it develops, drug-resistant TB spreads exactly the same way as drug-susceptible TB: to anyone who shares air with a sick patient. It is expensive and extremely difficult to treat patients with drug-resistant TB on a large scale – but the financial and public health consequences of our failure to do so will be devastating. It is an imminent and growing threat to public health. Recent reports suggest that by 2050, the consequences of drug-resistant microbes, most importantly multi-drug-resistant TB, could have a more catastrophic impact on global financial mechanisms than the 2008 housing crisis.

But such a crisis can be avoided. All the interventions I've mentioned are proven concepts – none are controversial or questionable, they simply need to be fully scaled. Effective scale-up of these interventions will allow us to gain control of the TB epidemic in high HIV settings. The goal of PEPFAR is to save lives and, by doing so, revive communities afflicted with a high burden of HIV. By greatly expanding antiretroviral and TB preventive therapy, while diminishing the burdens placed on patients, we are cutting transmission of both diseases and getting ever closer to realizing a world free of HIV and TB. The continued focus on effective and innovative TB/HIV programming will help consolidate those achievements and further global efforts to end the TB pandemic.

Chairman Smith, Ranking Member Bass, and other distinguished members of this Subcommittee, thank you for the opportunity to appear before you today. We are profoundly grateful for the ongoing support and engagement of the House Foreign Affairs Committee and this Subcommittee for PEPFAR's work.

Thank you. I look forward to your questions.

Mr. SMITH. Dr. Birx, thank you very much.
Ms. Koek.

STATEMENT OF MS. IRENE KOEK, SENIOR DEPUTY ASSISTANT ADMINISTRATOR, GLOBAL HEALTH BUREAU, U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT

Ms. KOEK. Thank you very much, Chairman Smith, Ranking Member Bass. Thank you very much for your leadership and support for the work the U.S. Government does to advance global health and your commitment to fight tuberculosis.

I am very honored to be here today with my U.S. Government colleagues to discuss our collective efforts against this deadly disease.

TB has long been an important issue for me. As chief of the infectious diseases division I helped start USAID's program 20 years ago and watched it grow the first part of its existence.

Thanks to the support of Congress, the U.S. Government is the single largest donor to TB programs globally. Collectively, we share a vision of a world free from TB.

The collaboration and complementary efforts of USG departments and agencies is reflected in our implementation of U.S. Government global TB strategy and the MDR national action plan.

USAID leads USG global TB efforts through our support for high-quality diagnosis, treatment, prevention, and care services for millions of people who are at risk or suffer from MTB and MDR TB.

We focus in 22 high-burden countries including five in southern Africa. We also support an additional 32 countries through targeted technical assistance primarily in support of Global Fund TB grants.

Our efforts are designed to accelerate and optimize implementation of country-owned and led national TB programs. In order to achieve the greatest impact on the TB epidemic, we focus on the areas with the greatest burden of disease and on ensuring that the innovations with the highest potential are rapidly identified and widely implemented. We focus in countries with the highest burden of TB, of drug-resistant TB, and HIV-associated TB.

We use data to target our interventions to benefit the majority of those suffering from TB. TB predominantly affects the poorest and most vulnerable with approximately 95 percent of TB deaths occurring in low and middle income countries.

Each day, more than 4,600 individuals die from this curable disease. The majority of the TB burden is in Asia. Almost 60 percent of all TB cases are found in India, Indonesia, China, Pakistan, and the Philippines.

Although while HIV-associated TB only accounts for one-tenth of the world's TB cases, it has a disproportionate impact in Africa, which is home to 75 percent of the global TB-HIV cases.

The investments on TB have paid off. Since 2000, our support in USAID priority countries contributed to a 40 percent decrease in TB-related mortality and a 27 percent decrease in TB prevalence.

In the last 2 years, USAID has helped provide high-quality TB treatment for 6 million TB patients including 150,000 MDR TB patients. USAID investments over the past 20 years have dramatically improved global and national TB surveillance systems, which

have enabled better targeting of interventions at the global and country level, and improved data for decision making.

At the country level, USAID works with national TB programs and local partners to scale up and accelerate implementation of new tools and approaches, focusing on four pillars.

The first is person-centered care. TB care has evolved to embrace a human rights approach that is focused on meeting the individual needs of each person so they are able to access timely quality diagnosis, care, and treatment regardless of where they seek services.

Typically, this is through primary health care in community settings. USAID increasingly works with faith-based and community organizations to provide the support needed, improved treatment outcomes, and combat the stigma so often borne by TB patients, particularly among women and children.

Secondly, access to early diagnosis and initiation of quality treatment is one of the best ways to prevent the transmission of active TB disease as well as the development of MDR TB.

We leverage American innovation in industry to scale up new tools for better diagnosis and treatment. With Johnson & Johnson, for example, we've introduced bedaquiline, a new TB option for people with drug resistance in more than 70 countries for 25,000 people often providing the only treatment option.

USAID is also partnering with diagnostic companies such as Cepheid and Becton Dickinson to expand access to rapid TB and drug-resistant testing.

The third pillar is preventing the development of active TB disease. USAID works to prevent both the transmission of TB from one person to another and the progression from latent TB infection to active TB disease.

The combination of TB preventive therapy and anti-retroviral therapy reduced the risk of developing active TB disease and people living with HIV by up to 90 percent.

As Ambassador Birx has already noted, scaling up TB-preventive therapy among people with HIV is critical and requires a strengthened and more focused approach.

Fourth is accelerating research and innovation. USAID's research portfolio has been a key component of our TB program since its inception. In close cooperation with USG partners, USAID has supported several late-stage research cities that have led to major policy changes, including a standardized fixed dose combination TB regimen and a shortened MDR TB treatment regimen.

The U.N. High Level Meeting on TB later this year will provide a much-needed opportunity to bring global attention to a disease that, despite its horrific impact is all too often ignored or unseen.

It is critical that we continue to maximize investments and leverage additional resources to bring self-reliant sustainable TB responses within countries.

We stand at a pivotal juncture, but with your steadfast support, we can help the world take the right path. With increased political commitment, we can and will end TB.

Thank you again for your support. I look forward to your questions.

[The prepared statement of Ms. Koek follows:]

Irene Koek
Senior Deputy Assistant Administrator
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House Committee on Foreign Affairs

Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations

July 12, 2018

Introduction

Chairman Smith, Ranking Member Bass and members of the Subcommittee, thank you for inviting me to testify on the U.S. Agency for International Development (USAID) response to the tuberculosis (TB) epidemic in southern Africa and globally.

As South Africa Minister of Health Aaron Motsoaledi has so aptly said of death by tuberculosis "[it] happens very slowly, maybe in a corner somewhere, in an isolated hospital ward, with nobody watching, so it doesn't evoke any emotion. Maybe that's what's at play around the entire world."

For more than 20 years, the U.S. Government (USG) has been a leader in the global effort to increase access to TB diagnosis, treatment, prevention and care, particularly in countries with the highest burden of disease. Thanks to the generosity of the American people and the strong support of the U.S. Congress, USAID is the largest bilateral donor in the fight against TB. We work in partnership with national TB programs (NTPs) in Ministries of Health (MoHs), the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), the World Health Organization (WHO), the Stop TB Partnership, technical assistance organizations, civil society including faith-based organizations, as well as affected people and communities. USAID has driven and funded interventions, tools, and technologies that have helped save 53 million lives from 2000 to 2016. Our efforts to build partnerships with national governments, multilateral organizations, and departments and agencies across the US Government have developed and strengthened country capacity to end the TB epidemic around the world.

TB has long been an issue of particular concern for me. Twenty years ago, I was privileged to play a key role in the creation of USAID's TB program. During my tenure as head of the USAID's Infectious Disease Division, the USAID TB program grew to be a major component of USAID's health portfolio. I was also heavily engaged in the creation of the Global Drug Facility (GDF) and the Stop TB Partnership, a unique international organization comprised of 1,500 partners dedicated to work collectively to end TB.

U.S. Government collaborative efforts to end TB globally

The U.S. Government's global TB strategy leverages interagency strengths and innovations to endeavor to reach every person with TB, cure those in need of treatment, and prevent the spread of the disease and new infections.

The vital collaboration and complementary efforts across the USG are reflected in our shared successes through the implementation of the U.S. Government Global TB Strategy (2015-2019) and the National Action Plan for Combating Multidrug-Resistant TB (2016-2020) as we work together to save lives and protect America's global health security. The U.S. Government

Global TB Strategy outlines clear roles and responsibilities for each federal partner. Among them, USAID leads international TB efforts to increase access to high quality, person-centered diagnosis, treatment, and care for TB and multidrug-resistant (MDR) TB. The Office of the Global AIDS Coordinator leads international HIV/AIDS efforts, including TB/HIV. The Centers for Disease Control and Prevention (CDC), within the Department of Health and Human Services (HHS), works domestically and globally on TB, including through PEPFAR, on research, surveillance, diagnostic and laboratory capacity, and treatment. The National Institutes of Health (NIH), specifically the National Institute of Allergy and Infectious Diseases (NIAID), also within HHS, conducts biomedical TB research that informs the overall TB effort; and the Department of Defense supports TB diagnosis and operational research through international laboratories. With the U.S. Government as the largest contributor to the Global Fund, combined with USAID's bilateral efforts, resources dedicated to TB/HIV coinfection efforts through the President's Emergency Plan for AIDS Relief (PEPFAR), and NIH and CDC investments in research, the U.S. is by far the leader in work to end TB worldwide.

The National Action Plan promotes greater coordination to reduce the domestic and global risk of MDR-TB; increases the American public's awareness of the threats posed by the disease; and serves as a call to action to all stakeholders on this worldwide concern. Similar to the U.S. Government Global TB Strategy, the three goals of the National Action Plan are implemented through a collaborative effort by multiple U.S. Government departments and agencies, with USAID leading the second goal of improving international capacity and collaboration to combat MDR-TB.

USAID leads U.S. Government global TB efforts through its support for high-quality diagnosis, treatment, prevention, and care services for millions of people with TB and at risk for TB and MDR-TB. The Agency bilateral TB program works with MoHs in 22 high-burden countries including Malawi, Mozambique, South Africa, Zambia, and Zimbabwe in southern Africa to produce sustainable results. USAID investments in TB save lives by improving the capacity of NTPs to introduce and expand access to new tools and high-quality TB services. In addition to USAID's bilateral programming, the Agency supports an additional 32 countries through targeted technical assistance and support for Global Fund grants including Angola, Botswana, Lesotho, Madagascar, Namibia, and Swaziland in southern Africa. In all, the Agency provides focused assistance to 54 countries, including 11 in southern Africa, to optimize implementation of country-owned and led national TB programs.

Global TB situation

TB is the leading infectious cause of death, ninth leading cause of all deaths worldwide, and the most common cause of death in people with HIV. Each day, more than 4,600 individuals die of this curable disease, culminating in 1.7 million deaths each year--for context, that's more than twice the size of the population of the Chairman's congressional district in New Jersey. In 2016, approximately 10.4 million people developed TB, including 3.7 million women and 1 million children. Worldwide, more than two billion people are infected with *Mycobacterium tuberculosis*, the bacterium that causes TB. Those at greatest risk of developing active TB disease are those with compromised immune systems, including HIV, diabetes, and malnutrition. The disease predominantly affects the poorest and most vulnerable, with about 95 percent of TB deaths occurring in low- and middle- income countries. The majority of the global TB burden is in Asia. More than 55 percent of all TB cases are found in India, Indonesia, China, Pakistan, and the Philippines. If we don't solve TB in these countries, we cannot end TB.

Every year, about 60 percent of individuals with active TB disease are officially reported as

diagnosed and initiated on treatment. The remaining "missing" 40 percent--4.1 million people--do not receive services that meet international standards, which can lead to significant morbidity, drug-resistant (DR) TB, and even death. Unfortunately, the longer people with active TB disease remain untreated, whether it is drug-susceptible (DS) or DR, the more likely they are to spread the disease, infecting their families and communities. People with active TB disease can infect up to 10 to 15 other people over the course of a year.

Africa's estimated 2.6 million annual cases of TB comprise 25 percent of the world's TB burden. In Africa, the TB mortality rate in both those who are HIV-negative and people living with HIV (PLHIV) is, respectively, more than two and six times higher than the global average. The TB epidemic in the African region, as in other regions, is driven by a variety of factors, including weak health systems, but is exacerbated by the high prevalence of HIV, particularly in southern Africa.

TB is the leading killer of PLHIV, accounting for 40 percent of all HIV deaths worldwide. In 2016, almost 400,000 of the one million people with HIV-associated TB died of TB. As one of PEPFAR's main implementers, USAID works to make sure that countries receiving both PEPFAR funds and TB funds are coordinated, to ensure that patients have access to quality services for TB and HIV regardless of where they receive their care

USAID's bilateral TB program is working with countries to make certain every TB patient is being tested for HIV. In 2016, 82 percent of TB patients in the Africa region had a documented HIV test. PEPFAR data indicate that about half of eligible patients on antiretroviral treatment (ART) were screened for TB in 2017. Screening for active TB disease among PLHIV is important not only to identify individuals who would benefit from TB treatment for active disease, but because it can also identify individuals who would benefit from TB preventive therapy (TPT), which can greatly reduce the risk of developing active TB disease. When TPT is used as an adjunct to HIV treatment, the risk of active TB disease in PLHIV can be reduced by up to 90 percent. Screening for TB among PLHIV and scaling up TPT requires a strengthened and more focused response.

While HIV has the greatest impact on the TB epidemic in Africa, DR-TB is a major public health concern globally. DR-TB threatens to reverse progress made in combating the TB epidemic throughout the world. Experts have determined that by 2050, 75 million people will lose their lives to DR-TB and that the disease could cost the global economy $17 trillion.

Weak TB programs contribute to the development and spread of DR-TB which, like DS-TB, is transmitted through the air from person to person. MDR-TB, a form of TB that is resistant to two of the most efficacious medicines used to treat DS-TB, is present in every country in the world; extensively drug-resistant (XDR) TB, which is resistant to even more drugs, has been reported in more than 100 countries. In 2016, there were an estimated 600,000 cases of MDR-TB worldwide, accounting for more than four percent of all new TB cases; 93,000 (16%) were in Africa.

Despite the continuing and devastating impact of TB around the globe, considerable progress is being made. Since 2000, the TB mortality rate decreased by about 37 percent and the incidence rate declined by about 19 percent. 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.

USAID response to the global TB situation

USAID works in most of the countries with the highest burdens of TB, MDR-TB, and TB/HIV to strengthen health systems and increase country capacity to provide high-quality TB services. Since 2000, our contributions have helped priority countries achieve an almost 40 percent decrease in TB-related mortality and a 20 percent decrease in TB incidence. USAID has helped provide high-quality TB treatment for almost 6 million TB patients, including almost 150,000 MDR-TB patients, in just the last two years. Over the past 20 years, USAID investments have also improved international and national TB surveillance systems, which have enabled better targeting of interventions at the global and country level, and identified trends in TB and MDR-TB which have informed policies, research, and response.

USAID has been a catalyst for investment and change in high burden TB countries. Over 80 percent of funding to support the TB response is financed through national domestic resources. With the majority of the world's TB cases in middle income countries, and with the limited international TB resources available, USAID has played a critical role in accelerating and enhancing the TB response in supported countries by influencing national and subnational clinical and technical policies and guidelines to improve the quality of care and introduce new approaches and tools, and has helped ensure coordination to maximize efforts. The Agency continues to work with governments and major partners to mobilize domestic resources and drive quality improvements for sustainable, multisectoral, person-centered TB programs.

The Agency's commitment to a person-centered approach requires a multisectoral response that includes ministries and sectors other than those directly related to health care. For example, USAID engages Ministries of Labor to reach manufacturers and workers, Ministries of Education to reach teachers and children, correctional agencies to reach prisoners and guards, faith-based and community organizations to reach families and communities, and the corporate sector to reach companies ranging from mining enterprises to the pharmaceutical industry and private health care providers. At the country level, USAID works with NTPs and local partners to scale up and accelerate implementation of the following tools and approaches:

Person-centered care: To improve quality of care and TB outcomes, USAID works with a range of organizations to ensure services are tailored to the needs of individuals and their communities. TB care has evolved to embrace a human rights approach that is focused on meeting the individual needs of each person so that they are able to access timely, quality diagnosis, care, and treatment in a supportive environment that is based on respect for patient autonomy, physical comfort, and psychosocial support. Individuals receiving TB treatment face months of therapy; those requiring treatment for DR-TB not only face months of therapy but toxic and often painful regimens. Person-centered care has been shown to reduce stigma, and increase patient satisfaction as well as treatment adherence. USAID has pioneered country- and population-specific interventions in all priority countries.

Public-private partnerships: USAID continues to leverage American innovation and leadership in an effort to scale up new tools to improve the quality of diagnosis and treatment. In a joint effort with Johnson and Johnson, the Agency has introduced bedaquiline, the first new TB drug approved by the Food and Drug Administration (FDA) in more than 50 years. More than 25,000 treatment courses are now available in more than 70 countries to treat people with DR-TB. USAID led the successful effort that resulted in rapid global introduction and scale-up of this new drug regimen. In addition, USAID has been instrumental in the introduction of the shortened MDR-TB treatment regimen (which can reduce the duration of treatment by more than 50 percent, from at least 20 months to 9 months) in all priority countries. Some USAID

countries with intensified support are enrolling almost 80 percent of those eligible on the regimen, improving treatment outcomes and saving precious resources. USAID is also partnering with diagnostic companies such as Cepheid and Becton Dickinson to expand access to quality rapid testing for TB and DR-TB. In FY 2016, USAID reduced the number of "missing" TB cases by 10 percent in priority countries by strengthening screening and the diagnostic network, to find people earlier so that they can initiate treatment more rapidly, not only improving the health of these individuals, but decreasing transmission to others.

Preventing the development of active TB disease: USAID programs work to prevent both the transmission of TB from one person to another, and the progression from latent TB infection (LTBI) to active TB disease in those who become infected. Access to early diagnosis and quality treatment is one of the best ways to prevent the transmission of active TB disease, as well as the development of MDR-TB. In addition, TPT, a critical intervention, particularly for contacts of individuals with active TB disease and PLHIV, is being expanded in countries.

Engaging the private health sector: USAID partners with the private sector and affected communities to expand their engagement in the delivery of TB services. Across our bilateral TB programs, USAID enables providers outside the government system, such as faith-based organizations, to care for patients as recommended by national guidelines, and to facilitate their inclusion in local planning activities. For example, Ethiopia established a new public-private platform within the Federal Ministry of Health to improve the provision of TB care. Through USAID technical support, facility standards were finalized and health facility inspectors trained, and a learning community for private health businesses was created. In India, USAID trained a group of private providers in an urban population of West Bengal to provide quality TB services. Although this urban population represented only 15 percent of the total population of West Bengal, the project was able to double the TB cases detected by the private sector in the state.

Management of drugs and commodities: USAID continues to be a major supporter of the GDF. The GDF is a pooled procurement mechanism that provides a package of services, including technical assistance in TB drug management and monitoring of drug use, as well as procurement of high-quality TB drugs at low cost. As the largest supplier of TB medicines and diagnostics, GDF ensures the availability, affordability and quality of TB medicines. Since 2012, GDF interventions have led to a price reduction in MDR-TB treatment regimens by more than 60 percent and several individual drugs by 70 percent. Earlier this year, the GDF announced 28 newly signed agreements with manufacturers for 83 products that will result in additional savings of approximately $31 million. The price reductions are particularly valuable to high-burden, middle-income countries such as South Africa and India, as it is imperative that they realize high returns on their domestic investments, ensuring increased and continued self-reliance.

Monitoring and Evaluation: USAID provides global technical leadership and country-level support to improve the collection, analysis, and use of TB data to inform policies and programs and customize interventions to those most at risk for TB. Timely, accurate, and complete data are required for NTPs to make strategic decisions and prioritize services. In addition, the Agency provides technical assistance to support the development of global guidance and the implementation of TB prevalence surveys, drug resistance surveys, and quality service assessments. For example, the recent prevalence survey in Kenya showed prevalence was three times higher in males than females. Not only do males have a higher disease burden, but they are also two times more likely to be missed. The survey also revealed that in Kenya, the highest prevalence age group among women was 65 and over. This survey provided essential data that

is being used to inform evidence-based, tailored TB programming.

Research and Innovation: USAID's research portfolio has been a key component of its TB program since inception. In close cooperation with USG partners, the Agency supports late-stage research studies and ensures the uptake of early-stage research supported by departments and agencies. Our research focuses on improving the treatment of DS-TB and MDR-TB, preventing progression from infection to disease as well as transmission from person to person, and building capacity to conduct operational research that improves the performance of TB programs. One of the studies currently supported by USAID is the Standardized Treatment REgimen of Anti-tuberculosis drugs for patients with Multi-drug resistant Tuberculosis (STREAM) study, the first rigorously conducted global trial to test new drug regimens for the treatment of MDR-TB that are that are less than half as long as the current regimen (6-9 vs 20-24 months), eliminate the need for painful injections, and do not cause debilitating conditions such as loss of hearing and psychosis.

Looking ahead

USAID is committed to accelerating progress toward ending tuberculosis. The Agency continues to mobilize increased commitments and funding from high-burden countries and other donors in support of this goal. The United Nations High-Level Meeting on TB (UNHLM) later this year will provide a much needed opportunity to support these objectives and bring global attention to a disease that, despite its horrific impact, is all too often ignored or unseen. It is critical we continue to maximize existing resources and leverage additional resources to build self-reliant TB responses. The first UNHLM on TB in September this year will provide an historic opportunity to galvanize the political commitment needed to step up the battle against TB and put the world and individual countries on the path to ending the epidemic. With increased political commitment, we will have the opportunity to accelerate action on TB, prioritizing domestic resource mobilization, increased early diagnosis and treatment of TB and DR-TB, person-centered care, rapid development and introduction of new tools through collaborative research efforts, and furthering of private sector partnerships.

USAID will continue its work with other USG departments and agencies to maximize our investments by leveraging the collective resources of partner governments as well as other key stakeholders. In particular, the Agency will continue to expand person-centered approaches to TB services; active detection by reaching out to contacts of TB patients; scaling up TB services in coordination with HIV programs; expanding engagement with the private sector including private practitioners and faith-based organizations; and forging partnerships with the corporate sector. In addition, the Agency will continue to advance novel approaches and evidence-based interventions to inform global policy guidelines and improve programs.

USAID remains committed to ending TB. Administrator Mark Green has declared TB, "a fight we can win" and has actively engaged to bring greater attention and resources to the issue. The Agency has been successfully implementing the USG's Global TB Strategy and looks forward to continuing to build upon these achievements.

Thank you again to Chairman Smith, Ranking Member Bass, and the members of the Subcommittee for calling this timely hearing. We stand at a critical juncture in the road between the path of ending the epidemic and letting the disease continue to kill more people than any other infectious disease each year. With your support, we can help the world take the right path, and end TB.

Mr. SMITH. Thank you, Ms. Koek. Thank you very much.

Thank you all for your testimonies and, again, most importantly, for your extraordinary leadership.

Let me just ask you, now, one of those reasons why drug resistance in all diseases including TB has increased across many diseases—infectious diseases—is the misuse of antibiotics, not completing the regimen as prescribed.

How are the physicians and the dispensers, the health care professionals—has the education of those individuals and especially those who are affected then been as robust as it could be to mitigate that problem?

Ms. MARTIN. Thank you for the question. I will start off and happy to hand over. But, definitely, with the work that we have been doing in training health care providers, also working through the clinical trials consortium, which engages other countries as well, the opportunity to create centers of excellence for training is very critical.

CDC's efforts as well in combatting anti-microbial resistance has taken on these efforts and been ensuring that we are working toward the efforts of addressing, as you have mentioned, both the leadership and the use of anti-microbial resistant agents but also the importance of making sure that people complete treatment.

And this is something within TB that we have been working on to ensure looking at how to improve regimens for treatment so that they can be shorter courses and also less harmful side effects so that people will finish and less drug resistance will form.

Mr. SMITH. Yes.

Ms. KOEK. If I could just add to what Dr. Martin just talked about.

One of the areas that's been a real focus for our programs is reaching all clinicians and throughout the system. I mean, very often what we see at a number of countries is people will go to their regular doctor—their private provider, for example—who may or may not be trained on tuberculosis or recognize it right away. So they may just prescribe some antibiotics or a piece of it.

So it's been really important and a real focus to try to reach all providers, whether they be in the public sector or the private sector and try to make sure that particularly private sector providers—and we see this often in a number of countries—may not at the outset provide the right treatment but to make sure they really understand what the appropriate treatment regimen is and do the diagnosis before they begin treatment.

And that's been a really important area of support for us and something we really need to continue to get the word out and make sure all providers are part of the network and are connected to the public system so you can get the reporting up through the—through the systems.

Mr. SMITH. You know, the High Level Meeting that's slated for September 26th at the United Nations—which could be a true pivot point for all governments, including our own, to have a more cohesive plan—could you perhaps fill us in on where we are in terms of—obviously, they will show up—the delegates—on September 26th with a plan largely intact.

How well along are you in those preparations? What does it look like? I don't think this is the Manhattan Project where we've got secrets that can't be conveyed. Could you give us a good insight as to where we are right now?

Ms. KOEK. Let me start and ask my colleagues to add on.

So there's been much, much discussion around what really do we need to get out of the High Level Meeting and this—actually, this meeting is the culmination of years and years of effort to really get it on the agenda, and we really owe a big thanks to Minister Motsoaledi, who's been a tremendous champion, to make this happen.

So what we are really hoping is will come out of this is a very high level goal of getting—targeting 40 million people on treatment by 2022. So 40 by 2022 is the very high level ask.

But part of that, and this is one of the things that is being pushed through the development of the communique is about making sure there's an accountability framework.

So in order to reach that goal, what every country really needs to do and using the kind of data that we've been talking about, that there is an accountability for every country about what they need to do to reach those patients who are not yet diagnosed and put on treatment and supported throughout treatment.

We are also really pushing for an independent body to monitor that, much like has been done for polio and done so successfully to really make sure that there is—that not only is there accountability but there's a oversight about accountability.

And then also working with faith-based and civil society groups, making sure they're part and parcel of the commitment and the instruction and also private sector as well.

Mr. SMITH. Has the outreach to faith-based groups been as robust as it should be?

Ms. KOEK. I think it's underway, and this is where the Stop TB partnership has been playing a really important role of reaching civil society and trying to reach the outreach.

I think that we can do a lot more and that would be a really high priority over the coming months to make sure the faith-based community is absolutely——

Mr. SMITH. I raise that—you know, in my early career in the 1980s—early in the '80s—I authored the Child Survival Amendment, which put $50 million into immunizations, and went to Central America several times including to El Salvador when they had Days of Tranquility and the FMLN and the Duarte government ceased all fighting so kids could be immunized against polio, diphtheria, pertussis, and the like.

And it was the church that made that happen. They admonished mothers, families, to bring their children for the immunization. Many of the vaccination sites were church sites.

I know USAID and Mark Green get it. I know all of you get it, how important it is to have a partner that has such a low cost overhead that can get volunteers.

We've done it with HIV/AIDS for years with PEPFAR. But I just hope in this mobilization there's a full inclusion of faith-based entities.

Ms. KOEK. No, I couldn't agree with you more, sir. The faith-based community is a tremendously important voice on this, and as you have described, they've been so involved. Members of that community have been so involved in health issues but certainly TB as well, and I think can be an extraordinarily powerful force at the U.N. High Level Mission and it's part of our engagement.

And, as you noted, Administrator Green is very, very committed to this and we have regular conversations with that community and continue to make sure that TB is on their agenda as well.

Mr. SMITH. Let me ask you—first of all, I want to thank Dr. Birx for holding that meeting that we had in New York with Dr. Aaron Motsoaledi. We had hoped that he would be here and he had to cancel due to other pressing issues.

But that meeting was extraordinary, so I want to thank Dr. Birx for putting that meeting together.

Let me ask you—for many of our pharmaceutical companies, developing drugs to combat or to, hopefully, cure TB, is a high bar because the rate of return is just not there for them and I am wondering if there are incentives—any recommendation you can make to try to get even further buy-in on the R&D side with our pharmaceuticals who do amazing work.

Like on neglected tropical diseases, I mean, they have been leaders and have provided enormous amount of research with very little or no return because it's the right thing to do, and I am wondering on the TB issue if you could speak to that.

Dr. BIRX. I will just open on this one because I think one of the—the important part we have from the program side is as new drugs—and we saw the new CDC recommendation in the MMWR for a 1-month short course on treatment—our job is that as we have these new drugs new regimens available is to get them into program, because nothing is more encouraging to the pharmaceutical industry to take their hard-earned research and clinical trials and translate that into client care and I think that's part of—that's part of our job to really ensure not only that there's incentives but that the drugs get utilized quickly when they're shown to be effective.

This new preventive therapy going to 1 month will be—it's a huge breakthrough for clients. That's a game changer when they know they only have to take a medicine for 30 days.

We do have supposed to remind people curative drugs available today for each of these different entities, we would love that in HIV if we had a curative drug.

So I think for us not to do everything to utilize them effectively is really a tragedy. So I think we want to be really committed to translating new drugs into action immediately.

Ms. KOEK. Just to add to that, I think the—you know, we—in the last couple of years there finally has been a new drug that has come out for TB—bedaquiline and some other—for the first time in over 40 years.

And so the investments in research that have happened over the last 10 or 15 years are finally paying off after long, long neglect. There are a few more, I think, in the research pipeline and we've been really fortunate for bedaquiline. Johnson & Johnson, which

has been behind this, is really committed to making sure that it's available.

We have a memorandum of understanding with J&J to do donation of bedaquiline as it goes through the final stages of research. It's already been approved actually by WHO even ahead of being approved by the FDA, which is quite a groundbreaking effort, if you will.

So as we go through the donation program and they move to market in the final stages, it will be available and it really has made a huge difference on the treatment of MDR TB.

But there are more drugs needed in the pipeline and we need to continue the research pipeline. I know that NIH and it looks like the TB Alliance for Drug Development are after it and it's a hugely important part of what we do in TB overall.

Mr. SMITH. Yes, Dr. Martin.

Ms. MARTIN. If I could just add to this. I think as well the work that is being done, especially in finding the missing cases so the active case finding, also makes and closes the gap by 40 percent of those who don't complete treatment, and this will also make the market more viable once you see the ability to be able to use the drugs and to close the gap for ensuring people are treated.

Mr. SMITH. Ranking Member Bass.

Ms. BASS. I want to thank the three of you again for testifying today but way more important than that, for your dedication and your work.

Unfortunately, I am doing double duty in two hearings and will have to run out. But I did want to ask just a few quick questions.

You know, you mentioned, Dr. Birx, about diagnosing and treating people right away and I was just curious how is TB diagnosed in Africa? I mean, I certainly know how—I worked in the medical field for many years.

We do a skin test or an x-ray. But that also takes time to get the results back. So you can't just see a patient and then give treatment. So how is it diagnosed?

Dr. BIRX. So we are very fortunate in collaborating both with the TB program and the HIV program to rapidly get gene experts in the field so that we can rapidly diagnosis.

Now, this gene expert machine is molecular in basis and can be used for HPV. It can be used for new zoonotic events. So it is a technology that's now available throughout sub-Saharan Africa.

We spent the last year mapping where every single gene expert machine is, and interestingly, we found that we have more gene expert machines than we need.

So the good news is that the equipment is not the limiting factor. It's utilizing it effectively. So if we want to test every TB client we have enough gene expert machines available in the country and I think that's really reassuring to everybody.

Until we map them, you know, everybody wasn't communicating but we've had this great collaboration between the TB program and the HIV program because we were each buying them, and now when we put them together we see that there's a capacity there to test everyone and provide that rapid diagnosis and get people on treatment immediately. And as you said, that is the key——

Ms. BASS. Right.

Dr. BIRX [continuing]. To the health and welfare of our clients in the long run and also the key to creating nontransmissability at the household level, and to the health care providers, which we have to remember—and thank you for bring that up—it's really not only important that we train the health care provider on how to diagnose TB but also how they can protect themselves with infection control.

Ms. BASS. You were also mentioning a percentage of patients that are diagnosed with TB and you test them immediately for HIV. What's the percent?

Dr. BIRX. Ninety-five. We are up to 95 percent of the TB cases are tested for HIV.

Ms. BASS. No. What's the percent of HIV—that are HIV positive?

Dr. BIRX. It changes by country. In South Africa, some places it's—so that graphic where I showed you where we are missing men, it's higher the more people you're missing early in the early stages.

So as we find ways to find men and well children early, the TB cases should plummet. So a TB case and that percentage—having a high percentage of HIV and the TB is a reference point for us not doing as well as we should——

Ms. BASS. I see.

Dr. BIRX [continuing]. Because that shouldn't happen. So we want that to be zero. But right now, it's everywhere from 5 percent to probably 60 percent.

Ms. BASS. Wow.

Dr. BIRX. But that's our failure on the HIV side to not getting people on HIV treatment early so that there's no dual infection.

Ms. BASS. And you mentioned—thank you. Thank you.

And, Dr. Martin, you were mentioning other countries. You said that there are several countries where people come into the United States and TB is spread.

I am used to seeing in Los Angeles a lot of our TB cases were in the homeless population. It didn't impact—it wasn't from people coming in the country but what are those countries that you were referring to?

Ms. MARTIN. Thank you, and just to note too, while they may not be U.S. born, it's not that it's they're first arriving with TB. It's more that we are seeing that after a year or 50 percent after 10 years may move on to active TB disease.

Ms. BASS. I see.

Ms. MARTIN. And those countries that we are seeing them are India, Vietnam, China, Philippines—I am missing one—Mexico.

Ms. BASS. Oh, the countries that Dr. Koek was mentioning. I see.

Ms. MARTIN. And we are seeing, as Irene Koek mentioned, it's with the middle income countries where they're seeing these as well. It's not just low income countries but middle income countries that need to be able to stop and detect diseases where they are occurring—the TB—and stop it before it comes and be able to spread or create drug resistance.

Thank you.

Ms. BASS. I see. Dr. Koek, did you want to respond to that as well?

Ms. KOEK. Yes, just to add on to that, because I think the burden is indeed in a number of those countries and in addition to a very high burden in southern Africa, particularly where the co-infection issue is, as Dr. Birx talked about, but there is a big burden in other countries in Africa, which is less driven by HIV, and then as we talked about earlier, also in Asia where you do have the largest number—countries with the largest numbers and they are these lower middle income countries.

And so our work in those countries is really catalytic because the resources to pay for the TB programs or pay for the health systems is really coming from the countries but our work is catalytic to make sure that—to get the right treatment, make sure the right treatment and diagnosis is happening.

Mr. SMITH. Mr. Garrett.

Mr. GARRETT. So, obviously, a little late getting to the table here. But on the subject matter of tuberculosis, I pulled up the Chemonics site. I want to thank you all and your staff.

I believe that Dr. Birx, you were present on the Chemonics hearing and we got a wonderfully detailed series of responses from you all, which I would like to pretend happens all the time that we ask for them, but it doesn't, and I am grateful for that.

And as soon as I got it, I sat down and looked up Chemonics to see if they were doing TB work in sub-Saharan Africa, which they're not. So that abates a potential line of questioning.

But, you know, I guess what I am most interested in is the cost-benefit analysis as it relates to fostering desirable outcomes for global stability, minimum basis global human opportunity as within the scope of this committee and how addressing something that was largely eradicated, largely, in the United States three generations ago—my father's mother had tuberculosis that she contracted as a nurse during the Great Depression—what the cost benefit analysis is for us getting involved in this realm now.

What's the good that we are—and this is in no way, shape, or form a skeptical question but just an opportunity to tell the story that we are able to do and at what cost and are we having success—and, again, I apologize for my tardiness—bang-for-the-buck wise.

Again, PEPFAR is a success story as it relates to HIV in Africa, et cetera. We talked about that in a previous hearing.

What are we doing in this realm that we need to know about, that we need to trumpet? When I go tell my constituents of why foreign aid dollars matter, why U.S. global health involvement matters?

Dr. BIRX. I just want to thank you for your line of questioning during the Chemonics group to really talking about efficiencies and effectiveness in programming because that is a very critical component to our work at all times.

And I think the work that we described within the tuberculosis field is—we've done analysis not only cost savings for the United States but cost savings to the health programs in every one of these countries so they can invest dollars in their new and burgeoning issues that are going to come up.

We know that there's this youth bulge, and so if we have co-infection of TB or HIV—we had a slide up before you came in about

the undiagnosed HIV cases are all in healthy people now and those healthy people are all under 35, and 60 percent of sub-Saharan Africa will be under 20 by 2020.

So we see that confluence of those two pieces that by preventing the next cycle of either HIV or TB the cost savings not only to us but to the health system in general for sub-Saharan Africa so that they can invest more and more dollars into their new and burgeoning, we hope, growing age expectancy into the 60s in the NCDs.

Ms. MARTIN. Could I add to that question.

Thank you very much, Congressman. I wanted to just add for our analysis we've done. For every $1 invested there's $43 return on the investment for investing in reduction of mortality for TB.

In addition, we do see multi drug-resistant in TB as one of the largest global health security threats in national security to countries both economically and in terms of trade. So I just wanted to mention that. Thank you.

Mr. GARRETT. Yes, ma'am.

Ms. KOEK. If I could just add one——

Mr. GARRETT. I knew you were ready.

Ms. KOEK. I hate to beat this horse to death, but just one more piece. The other thing about TB is a part of the global efforts and the global assistance that the U.S. does provide is more—our resources are relatively small to what countries are putting into their own TB programs.

So our pieces of money, they are really catalytic and it really is that 80 percent of the costs are borne by countries——

Mr. GARRETT. And you're—you're literally getting buy-in and, again, I am a fiscal hawk who leans toward shrinking government but I am a big advocate for foreign aid where it's done properly.

And so what I want to see, and I think we are seeing here—and PEPFAR, again, is the great example—is the good will that we can export by virtue of, for lack of a better expression, giving a darn that manifests itself, and there are a lot of things that need to happen. That 60 percent of sub-Saharan Africa under the age of 20 by 2020 is scary in and of itself.

Having said that, with increased education, for example, you see decreased birth rates. Right now, the United States can't, with $21 trillion in debt, shoulder this entire burden.

But somebody's got to lead. The Chinese foreign aid model is give money to the oligarchs and the dictators and ours is to help people.

But we need to brand it so it's clear I am asking—there's a question mark coming—that these are the efforts of the United States—that this leadership, this seed money, this 20 percent that begets the 80 percent, is—essentially got a red, white, and blue USAID—not literally—label on it.

Ms. KOEK. Yes, it is, and there's a lot of recognition for the work we do at country level through the TB programs, in addition, that's complementary to the work through PEPFAR because it really is recognized that this is coming from the American people and the engagement from the U.S. Government.

Mr. GARRETT. I would commend that to continue and that you guys are not the enemy. We are on the same team here.

Ms. KOEK. Yes.

Mr. GARRETT. That's so important. I think you stem radicalization and there's certainly a lot of messaging, some of it within this country. Have you gone all this time without talking about Russian meddling?

I am trying to identify us as something that I hope we are not. We need to be clear on what we are and this is a good way to do it. And, again, when I get with my fiscal sort of budget hawk crowd, I need to be able to say here's why this matters—that we are quantifying lives saved not just in sub-Saharan Africa but around the world by virtue of creating outcomes wherein there's hope, right, I would argue, and Chris has probably heard me do this 100 times, that a young person who wants to go to med school usually doesn't strap on a bomb vest.

But when there's no hope, the 14-year-old will pick up the AK-47 for a meal. So thank you, and please continue to make sure that folks know not that we are, you know, hegemonic and all-knowing, because arrogance precedes resentment, right, but that we give a darn.

So thank you.

Ms. MARTIN. If I could add on that, too. I think the other value is the lessons that we've learned here in the U.S., being one of the lowest cases—countries in the world—the lessons we've learned in how to deal with latent TB infection and how we've been able to test and how to be able to identify.

These are practices and opportunities we can share with other countries as well our experiences that can then be tailored, and this is something as well that gives us an opportunity to share this information. Thank you.

Mr. GARRETT. Thanks for what you do.

Thank you, Mr. Chairman.

Mr. SMITH. Thank you.

Dr. Martin, you had said in an article that you published on World Tuberculosis Day that every dollar spent on TB results in a $43 economic benefit to society. And, of course, if you're disease- or parasite-free—that's incalculable and we all want to be healthy.

But in the actual dollars and cents world, we often have to make an argument as to why spending that next dollar or dollars is justifiable and that kind of analysis is helpful in prying loose those additional dollars.

So if you could speak to that calculation, if you would. Secondly, let me ask, if I could, you know, more than half of the funds—roughly, $16 billion—for the global plan to eliminate TB by 2035 are anticipated to be raised by affected countries, and I am wondering if you could speak to—you know, are we talking about greater burden sharing and those countries picking up more of a piece?

If they don't, obviously, there has to be a safety net so that sick people don't continue to be sick. So if you could speak to that.

What countries are doing the best? I mean, we know some of the countries are doing the worst. We look at North Korea where the President just visited just recently.

I remember being in South Korea many years ago meeting with a priest who actually had access to Pyongyang to treat and help tuberculosis patients including those who were suffering from drug resistance. Our Government was supportive—not to overtly be-

cause—but it was like an open secret that they're there just to help the people, and I am wondering, a country like North Korea where the health care grid is invisible.

It doesn't get much worse, and the prioritization given by Kim is probably nonexistent. But, you know, as this drug resistance breaks out, obviously there are pockets. Speak to the worst countries of the world, if you would, as well as this idea of the burden sharing to meet the goals by 2035.

Let me also ask you, if I could, what would you like to see included in new TB legislation? Where are the gaps, what haven't we met before?

You do so much and do it so extraordinarily well by administrative action when there are gaps. But there probably are some authorities and statutory changes that you would find to be helpful.

What needs to be updated in the national action for combatting MDR TB of 2015? Again, that would be a similar issue of what we can do—and what you're doing that we need to catch up on—if you would.

And, again, I did ask before—maybe you can elaborate a little further, if you would, for the upcoming U.N. meeting, what does it look like? What will the plan, in your view—if you can share that with us—look like or is it still in a stage where it's not ready for publication?

Ms. MARTIN. Maybe you answer this.

Okay. I will start with the first question. On that, as we've said, in terms of doing the analysis of looking, that for every $1 that's invested in reducing mortality due to TB we do find a $43 savings.

Now, this—in looking at return on investments for other infectious diseases, this is very comparable, but actually one of the higher ones in terms of being able to invest.

And I think as Irene Koek has mentioned, we do see that countries are shouldering most of the burden and the cost of this—of 80 percent of the cost for TB are paid for by the countries that have the disease burden as well and that this will continue.

To your point then about what's going to be needed and looking at to shoulder this, going forward, and what are we expecting countries to do, I think one of the biggest things that's important, and it leads into the U.N. General Assembly, is the political will—creating that political will and having that—those champions to be able to make sure that this is taken on as a serious issue and brought forward.

We've seen this in some countries and you asked for some good examples. Looking at India—one country where we work—we've been working at looking at how to improve air control and air quality in some of the facilities.

The model that was seen did lead to good success for infection prevention and control and the states has now been expanded to an additional seven states in India. But the government is picking this up and doing it themselves.

So as we see good practices and the governments being able to take them on and to scale them up, our funds are seen—our activities are catalytic in moving forward a lot of these efforts.

In thinking about what are some of the—what post-UNGA looks like and thinking about this, I think Irene Koek has mentioned

very well the need for an accountability framework, and this is to look at progress being made globally but also the resources that are being tracked and being followed.

The mention of an independent monitoring board such as exists for polio eradication is one example of moving this effort forward. But it would have to make sure that there is some accountability and I think U.S. leadership in this is critical and appreciate you keeping this on the agenda to move these efforts forward, and thank you for your work in that.

The other big piece, I think, as we've mentioned, is engaging the civil society, the faith-based organizations, and really looking at well, how U.S. commitment can be leveraged by other countries to get them more engaged as well as to step up and ensure that we continue our resources globally for the efforts that are needed.

I will stop there for now. Thank you.

Ms. KOEK. Just building on some of your questions, on the $16 billion I don't have the global plan in front of me and we'd be happy to share that. But exactly as Dr. Martin said, 80 percent of it does come from countries.

Now, a significant share from the administrative health budget, if you will, but there's also a concern that a fair bit of that also comes from out-of-pocket expenditures, and since TB really does affect the poorest of the poor, we want to make sure that they're not being driven into complete poverty by TB.

So looking at those details at a country level is really, really important. But I would be happy to share what we have on that, as we go forward.

Mr. GARRETT. Yes, if you don't mind. You have really given me a great segue. So we know that TB affects the poorest of the poor and we know that we try to tie our aid to the economic achievement in a country because it's more reasonable to demand that, say, South Africa chip in than maybe one of their neighbors to the north who might not have the opportunity toward economic prosperity that, say, the mining has perpetually sort of brought to South Africa.

But all fruit aren't apples and so in South Africa, for example, in the Rand buildup around Pretoria you have got sort of a transient population based on economic opportunity that exists within the mining employment community and therefore a heightened risk of transmission and then travelling outward.

How do you make sure we are not doing a one-size-fits-all and saying well, South Africa has achieved this level of economic achievement, therefore, they need to carry this burden, when perhaps we might be more effective in addressing the spread if we target sort of the hotbeds of transmission, right, which exists there.

And then, secondarily and tangentially, I've been—the health minister in South Africa has kind of taken a role here. If you can sort of tie that in in your response. I was going to say Aaron's last name but then I would say it wrong and——[laughter]—we learned it by reading.

Ms. KOEK. Thank you, because that actually leads into an answer to one of Chairman Smith's other questions because——

Mr. GARRETT. Teamwork.

Ms. KOEK [continuing]. South Africa is a really good example both of a success story and given the strong leadership we've seen from Mr. Motsoaledi in the government and even courteous I've had practice, sir, on it—[laughter]—and they've worked—the government and the minister of health has worked really closely with the mining industry to make sure that because it is—mines are a hotbed of TB, right, and miners do go back to their homes where—which might be much poorer—so making sure they're—the miners are tested and started on treatment and the treatment is followed as they go home so they're not taking TB back to their communities. So we have a very, very strong program on that partnership with the mining industry.

Our work in South Africa is, you know, minuscule compared to—in terms of dollar amount. You know, it builds on the work that Ambassador Birx is doing through PEPFAR around TB—that it really is that kind of partnership Ambassador Birx talks about before—that it is meant to catalyze what the Government of South Africa is doing.

And exactly as you say, that work in South Africa is much more catalytic and much smaller relative to what we might need to do in a much more poorer country. We are trying to work also with the global fund grants in those countries to make sure they're——

Mr. GARRETT. And one of the problems of government inherently, in my experience—and I think you guys do a bang-up job here—but is that we do create a one-size-fits-all paradigm wherein sometimes we let things fall out.

So that's to be commended you have identified really the problem and—because, yeah, I mean, on an economic achievement scale and by virtue of natural resources that are really, in certain areas, unparalleled, but and—so yes.

Ms. KOEK. Just on that——

Mr. GARRETT. Avoiding the "this is the way we do it so this is the way we should do it" thing, which I think you're doing.

Ms. KOEK. On that point because it's really an important one, and one-size-fits-all really doesn't work for something like TB as it does for anything else.

So we work really closely with our counterparts at country for—they'll have a strategy for how to deal with TB—where are the—where is the burden the greatest—where are the patients most—where do we need to do the most work. So working within that——

Mr. GARRETT. Now if we could just get you guys——

Ms. KOEK [continuing]. Country level strategy is what happens, and it really does vary from one country to another.

Mr. GARRETT. We just need to get you guys to work on K-12 out here in the states.

Dr. BIRX. Just quickly, because I think it ties some of your pieces together and you talk about what things should look like.

I mean, what we've learned in PEPFAR is this political will and transcending that political and to really focusing domestic and global resources where the need is the greatest. And I think you point out a really critical issue.

Oftentimes, in opposition areas, in informal settlements, there is not that same attention to the most vulnerable who are at higher risk for HIV and TB, and we need to link our catalytic funds to

these kind of policy changes and investments that are linked to where the need is the greatest and I think holding countries accountable to investing in this accountability framework needs to be linking where diseases are and where investments are because we often see that those aren't always in complete alignment and I think that's really important.

And I think when you talked about education of the health care workers and that importance, the piece of this within the FBOs that I think we haven't paid enough attention to in the last decade is the alignment with the churches and engagement with the churches.

We have to get education back into the churches around these core diseases. They can be critical and identify the most vulnerable in the community that aren't getting adequate access to either health care or the resources that they need and I think the FBOs have been tremendous but we need to engage directly the pastors in the churches in a real way.

Mr. SMITH. Before I yield to Mr. Castro, on that point—on one trip to Nigeria that I made during the previous administration, we had about $500 million health care budget. So I asked how much of that in Nigeria, like much of Africa if not all of sub-Saharan Africa is being allocated toward faith-based entities.

I had just left Jos, where churches have been firebombed and Archbishop Kaigama had a HIV/AIDS or a PEPFAR program pulled from him, which was absolutely inexplicable for orphans—100 orphans—and all of a sudden there's no more money.

I never got an answer, ever. But I asked how much of that money—the $500 million—has been broken out for faith-based work in Nigeria, and it was about 7 percent, 8 percent. Just that has to change and is changing, like I know.

I would like to yield to Mr. Castro.

Mr. CASTRO. Thanks. Thank you for your testimony and thank you for being here and for all the work that you're doing in Africa and, I am sure, in different parts of the world.

I am told by my grandmother—I was told back then that her mother died of tuberculosis in Mexico around 1922—early 1920, and I notice that there has been about a 26 percent cut in the President's budget request in 2018 from 2017.

And so let me ask you what would be the impact—the human impact of the work that you do and how many more people wouldn't get served if that in fact ends up being the cut that we sustain?

Ms. KOEK. Thank you, sir, and I really do want to appreciate and thank the strong support we've received from Congress for the TB program. So I think you're aware the budget request did reflect an overall constrained budget environment.

However, the resources that were in that even reduced request would be targeted to the highest priority countries for us where the biggest burden is.

So I can't quite do the calculation on how many people would not do services, but given that our work really is catalytic, meant to be for—at country level, we would really try to prioritize among those high burden countries and try to really make sure that the resources went as far as they could.

Mr. CASTRO. But you agree that less people will get served?

Ms. KOEK. I would imagine so. It would have to be a calculation. We'd have to.

Mr. CASTRO. Sure. Yes, I guess I can submit for the record an analysis, I mean, if there's 400,000 people each year in Africa that die from tuberculosis. So I will submit a question for the record on the human impact of the 26 percent cut if it in fact goes through.

Let me ask you, the chairman sent out a memo that has the rankings of the top 10 causes of death worldwide and but do you know with respect to Africa where TB ranks? This is a worldwide ranking, but do you know where it ranks in terms of Africa?

Dr. BIRX. Right now, it's the primary infectious disease cause of death because of the high HIV-driving component to that. So we believe, as we control the HIV pandemic, we will control the TB pandemic in sub-Saharan Africa in those countries where it's being dual driven.

Ms. MARTIN. I was just going to add as well, I think the other piece that we see is that the increased drug resistance occurring as well and also the importance of as we see it being one of the leading causes that as well is if people are not treated and if people don't finish treatment, the opportunity for drug resistance to grow and to increase and the impact of that as well increases in terms of being able to treat them and the cost to treat them as well.

Mr. CASTRO. All right. Thank you.

I yield back.

Mr. SMITH. Thank you, Mr. Castro.

Let me just ask one final question. You know, there is an enhanced vulnerability of women who are pregnant to TB and, you know, from my point of view, I believe that there are two patients when the woman is pregnant—both the unborn child and the mother—and everything humanly possible should be done to enhance their health.

That's why this committee and I and my staff are so absolutely committed to the first 1,000 days from conception to the second birthday so the children and the women—the mothers—are as healthy as humanly possible.

And I am wondering, is there any special protocol necessary to ensure that the woman's health is protected and strengthened if she were to get TB while she's pregnant?

And, of course, what are the vulnerabilities to the baby in terms of transfer of the disease?

Dr. BIRX. I will start. I am glad you picked up on that because we've also noticed that within HIV. There's a unique high rate of susceptibility—it was just published in an abstract at CROI just a few months ago—of women in their last tri semester and in those first 6 months after delivery, and we are trying to really understand that.

And so this increased intensity of oversight and screening both for TB and HIV will be absolutely critical because, obviously, it's much more important to the pregnant woman to prevent the disease from ever occurring because the drugs, as all drugs, have toxicity across the board and, certainly, MDR drugs have particularly toxicity.

So it's more about making sure that women remain healthy be ensuring they come into the pregnancy healthy and their immune system is intact so that you can prevent the occurrence of reactivation of TB.

Mr. SMITH. Thank you. Okay.

Anything further any of you would like to say? And, again, your recommendations on legislation would be very well appreciated.

Yes, Dr. Martin.

Ms. MARTIN. Thank you.

I just wanted to respond to Congressman Garrett's question too about not one-size-fits-all and how do you identify those areas, and I think this is the importance of surveillance and the importance of being able to hone in and know what's happening, having those data to be able to use in real time to know where those hot spots are—to know what we can then do to focus as opposed to blanketing everywhere how you can really hone in, and that requires that we have and that countries have those data available and the importance of surveillance to be able to detect and the laboratory work to be able to know the confirmation.

Thank you.

Mr. SMITH. I just—oh, yes, Ms. Koek.

Ms. KOEK. I would just say one thing on legislation. I think the most important thing from legislation would be it's the signal it sends of the importance of something like TB, and just as this hearing has been a really important signal about why this is such an issue that requires the attention.

So we very much appreciate your time on that.

Mr. SMITH. Thank you.

Your testimonies and the information as well as the questions and those that we'll submit we do share with the appropriators who are always looking for insights, so we will expand this to other Members of Congress so that they know just how important this is.

But, again, thank you for your leadership. I would just conclude by saying that sustainable political will coupled with compassion and competent leadership is the reason, I believe, why the HIV/AIDS pandemic, which Henry Hyde, the author of that legislation—it was George Bush and Henry Hyde and all of us behind them, but they were the leaders—I remember Henry Hyde telling all of us in a Republican caucus that he did it frequently from the chair that this is the equivalent of bubonic plague—that unless very, very aggressive actions are taken, this will get—it's already awful—it will get far worse.

And he was a driver like no other, as Bush was right there, of course, leading, and it shows that where there's a political will, where that compassion exists and you have competent leadership like you, it makes all the difference in the world.

So thank you. You have friends here on the Hill. It's bipartisan, and we'll do everything we can to support you, following your lead.

The hearing is adjourned.

[Whereupon, at 4:08 p.m., the committee was adjourned.]

APPENDIX

Material Submitted for the Record

SUBCOMMITTEE HEARING NOTICE
COMMITTEE ON FOREIGN AFFAIRS
U.S. HOUSE OF REPRESENTATIVES
WASHINGTON, DC 20515-6128

Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations
Christopher H. Smith (R-NJ), Chairman

July 9, 2018

TO: MEMBERS OF THE COMMITTEE ON FOREIGN AFFAIRS

You are respectfully requested to attend an OPEN hearing of the Committee on Foreign Affairs to be held by the Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations in **Room 2255** of the Rayburn House Office Building (and available live on the Committee website at http://www.ForeignAffairs.house.gov):

DATE: Thursday, July 12, 2018

TIME: 3:00 p.m.

SUBJECT: Combating Tuberculosis in Southern Africa

WITNESSES: The Honorable Deborah L. Birx, M.D.
U.S. Global AIDS Coordinator
U.S. Special Representative for Global Health Diplomacy
U.S. Department of State

Ms. Irene Koek
Senior Deputy Assistant Administrator
Global Health Bureau
U.S. Agency for International Development

Rebecca Martin, Ph.D.
Director
Center for Global Health
U.S. Centers for Disease Control and Prevention

By Direction of the Chairman

The Committee on Foreign Affairs seeks to make its facilities accessible to persons with disabilities. If you are in need of special accommodations, please call 202/225-5021 at least four business days in advance of the event, whenever practicable. Questions with regard to special accommodations in general (including availability of Committee materials in alternative formats and assistive listening devices) may be directed to the Committee.

COMMITTEE ON FOREIGN AFFAIRS

MINUTES OF SUBCOMMITTEE ON *Africa, Global Health, Global Human Rights, and International Organizations* HEARING

Day *Thursday* Date *July 12, 2018* Room *2255*

Starting Time *3:00pm* Ending Time *4:08pm*

Recesses [ ] (____to____) (____to____) (____to____) (____to____) (____to____) (____to____) (____to____)

Presiding Member(s)

Chairman Smith

Check all of the following that apply:

Open Session [☑]
Executive (closed) Session [ ]
Televised [ ]

Electronically Recorded (taped) [ ]
Stenographic Record [☑]

TITLE OF HEARING:

Combating Tuberculosis in Southern Africa

SUBCOMMITTEE MEMBERS PRESENT:

Ranking Member Bass, Rep. Garrett, Rep. Castro

NON-SUBCOMMITTEE MEMBERS PRESENT: *(Mark with an * if they are not members of full committee.)*

HEARING WITNESSES: Same as meeting notice attached? Yes [✓] **No** [ ]
(If "no", please list below and include title, agency, department, or organization.)

STATEMENTS FOR THE RECORD: *(List any statements submitted for the record.)*

Rep. Smith: Statement by Ranking Member of the House Foreign Affairs Committee, Eliot Engel

Rep Smith: Statement of the American Thoracic Society

TIME SCHEDULED TO RECONVENE _____
or
TIME ADJOURNED _____

Subcommittee Staff Associate

MATERIAL SUBMITTED FOR THE RECORD BY THE HONORABLE CHRISTOPHER H. SMITH, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY, AND CHAIRMAN, SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, GLOBAL HUMAN RIGHTS, AND INTERNATIONAL ORGANIZATIONS

RANKING MEMBER ELIOT L. ENGEL
REMARKS ON GLOBAL ANTI-TUBERCULOSIS EFFORTS
HOUSE FOREIGN AFFAIRS SUBCOMMITTEE ON AFRICA AND GLOBAL HEALTH
WASHINGTON, D.C.
THURSDAY, JULY 12, 2018

Thank you Mr. Chairman and Ranking Member Bass.

As a co-chair of the House TB Elimination Caucus, I have long been active in the fight to end tuberculosis. So, I'm happy to see this Subcommittee looking at this issue that, I think, gets far too little attention.

Tuberculosis kills more people worldwide than any other infectious disease. This is especially tragic, because we know how to diagnose and cure it. We need to make sure patients—especially the poor and marginalized populations hit hardest by this disease—can access better, more affordable treatment.

It's also a threat to American security. Most drug-resistant TB cases are now caused by transmission from person to person, making it easier for this terrible disease to spread to new geographic areas. Moreover, cases of these aggressive strains are becoming more frequent, and they are much costlier to treat than TB that responds to medication. Diseases don't respect borders, so it's essential that we meet this challenge where it exists now—before we have to grapple with new cases on our own shores.

Failure to tackle TB also threatens the substantial gains we've made in the fight against HIV/AIDS. TB is the leading killer of people living with HIV/AIDS. So, if left unchecked, the TB pandemic could erase decades of global progress to end both of these diseases, much of which has been achieved thanks to American support.

Retreating from the world won't stop the spread of infectious diseases. If we want to wipe out TB for good, we need to engage and invest in TB prevention, treatment, and control.

We also need to work closely with our global partners. In September, the United Nations General Assembly will hold a High-Level Meeting on TB. This gathering is an opportunity for the Administration to engage and demonstrate American leadership on this issue—and I urge officials to do so. Ending the TB pandemic is

an essential global health priority—for the United States and our partners around the world.

Thank you to our witnesses for being here, and I look forward to hearing from you.

MATERIAL SUBMITTED FOR THE RECORD BY THE HONORABLE CHRISTOPHER H. SMITH, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY, AND CHAIRMAN, SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, GLOBAL HUMAN RIGHTS, AND INTERNATIONAL ORGANIZATIONS

Polly Parsons, MD
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Washington, DC 20036

Statement of the American Thoracic Society

Submitted for

the House Africa, Global Health, Human Rights and International Organizations

Subcommittee of the House Foreign Affairs Committee hearing, Combating Tuberculosis

in Southern Africa

July 12, 2018

The American Thoracic Society is a 16,000 member international professional and scientific society dedicated to the prevention and treatment of lung diseases, critical illness and sleep disorders. The Society was founded in 1905 as the American Sanitorium Association focused on the prevention and treatment of tuberculosis and maintains a strong area of interest in domestic and global tuberculosis control and related research The ATS thanks Chairman Smith and Ranking Member Bass for this important hearing on tuberculosis in Southern Africa.

TB Globally

Tuberculosis (TB), an airborne infectious disease, is the leading global infectious killer, ahead of HIV/AIDS, claiming 1.7 million lives each year.[1] In 2016, 10.4 million people became ill with TB, 10 percent of whom were children. TB is among the top five causes of death for women of reproductive age in low-income countries. While most TB cases are both preventable and curable when international guidelines are used, many parts of the world -- such as Africa -- are struggling to implement global recommendations, giving rise to drug resistant TB. As the top killer of people living with HIV/AIDS, TB is also undermining the substantial contributions in controlling AIDS made by the US government through PEPFAR.

TB in the US

In the U.S., every state reports cases of TB annually and in 2017, twenty states reported TB increases.[2] California, Texas, New York, Hawaii and Alaska are the most highly burdened states. TB outbreaks continue to occur across the U.S., outstripping local public health department budgets. There are also an estimated 13 million people in the U.S. with latent TB infection.[3] In 2013, drug resistant tuberculosis was identified as a serious public health threat to the U.S. in CDC's 2013 report on antimicrobial resistance.[4] Drug-resistant TB poses a particular challenge to domestic TB control due to the high costs of treatment, intensive health care resources and burden on patients.

Drug Resistant TB

Globally there are about 500,000 cases of multi-drug resistant (MDR) annually but only about 25% of persons with MDR-TB are identified and treated.[5] MDR-TB is very complex and expensive to treat and as a result of these factors, fatality rates from MDR-TB in developing countries are high. Extensively drug resistant (XDR) TB, which has been identified in most countries, most strikingly in South Africa, is even deadlier. The prevention of new MDR and XDR-TB cases as well as finding and successfully treating current cases must be a top priority to reduce further deaths and disability.

TB in the Southern African Development Community (SADC)

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[1] World Health Organization (WHO). Global TB Report 2016.www.who.int.

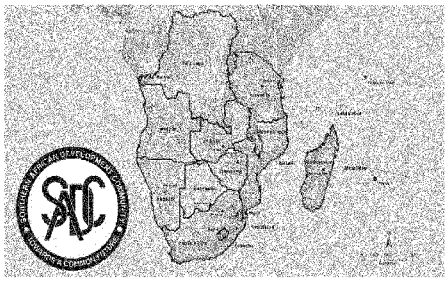
[2] Stewart RJ, Tsang CA, Pratt RH, Price SF, Langer AJ. Tuberculosis — United States, 2017. MMWR Morb Mortal Wkly Rep 2018;67:317–323. DOI: http://dx.doi.org/10.15585/mmwr.mm6711a2

[3] National Health and Nutrition Examination Survey, 2011-2012. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4633161/

[4] Antibiotic Resistance Threats in the United States, 2013. U.S. Dept. of Health and Human Services, Centers for Disease Control and Prevention. https://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf#page=112

[5] Ibid.

The countries in the SADC, especially South Africa, have long had very high rates of TB, and more recently, have also been hard hit by HIV/AIDS, causing TB rates to increase enormously.



Of the 30 high TB burden countries globally, based on either the absolute number of TB cases or rates per 100,000 population in 2016, 9 are SADC countries. South Africa has the largest number of new cases, 438,000, of whom 59% have HIV/AIDS, and a case rate of 781/100,000 population. South Africa also has the largest number of MDR cases, 19,000 or an MDR rate of 34/100,000. Case rates among the other SADC countries range from 728/100,000 in Lesotho to 208/100,000 in Zimbabwe. In addition to HIV/AIDS, an important risk factor for TB in SDAC countries is underground mining. Again, South Africa has the largest number of cases among miners.

South Africa As a Model for TB Care and Investment

XDR-TB was brought to the world's attention by a 2005 outbreak in rural KwaZulu-Natal, South Africa. The strain, which was resistant to almost all anti-TB drugs in the country, occurred in an HIV-positive population and had a shocking mortality rate, killing 52 out of 53 patients, half of them within one month of diagnosis. By late 2006, XDR-TB cases were increasing throughout South Africa. In response, clinicians and public health staff in KwaZulu-Natal and at the local Church of Scotland Hospital developed and implemented a set of community-based care interventions that have become a global best practices model for drug –resistant TB care. The province's "Community Management of MDR-TB Programme" used intensive case-finding of household contacts of patients and in congregate settings such as prisons and schools and specialist outreach teams to care for patients in their homes and screen and educate family members. South Africa's first MDR-TB decentralized hospital was opened in KwaZulu-Natal region in 2007. This followed the opening of other specialized MDR-TB hospitals throughout South Africa with the goals of alleviating hospital bed shortages for MDR and XDR-TB patients and discharging patients to intensive community-based care within weeks.

Very much to its credit, the South African government and researchers within the country have taken a proactive approach to addressing the TB epidemic and in this regard, are providing global leadership in research and in implementation of programmatic innovations. For example, South Africa now the majority of providers use rapid molecular testing to diagnose TB and to identify drug resistance. Moreover, the country has officially implemented one of the 2 new anti-

TB drugs, bedaquiline, in the drug regimen for MDR TB, thereby avoiding the use of a highly toxic injectable drug.

Although South Africa continues to be one of the most highly burdened countries, including for drug resistant TB, under the leadership of Minister of Health Aaron Motsoaledi, the development and implementation of best practices throughout the country coupled a high level of political commitment and significant increase in funding for TB control and research and development, South Africa is a leader in global efforts to halt the TB pandemic.

Internationally, as the Chair of the Stop TB Partnership Coordinating Board, Minister Motsoaledi was in large part responsible for a remarkable convening of ministers of health from most of the world's countries to focus on TB in Moscow in November 2017. This was an important step leading to the UN High Level Meeting on TB on September 26, 2018. Thus, South Africa is proving to be a leader not only of SADC countries but of the world in its aggressive approach to the TB epidemic.

Need for New TB Tools

Although effective drugs, and accurate diagnostic tests for TB exist, these technologies are inadequate for controlling the global epidemic. The World Health Organization, though the "End TB Strategy" has set the ambitious goal of ending TB as a disease of public health significance by 2035. This goal will not be reached without new tools, especially drug regimens for preventing TB that can be implemented in low resource settings and a vaccine that will protect against the disease. In addition there is an urgent need for new anti-TB treatments, particularly for shorter drug regimens with less toxic drugs for both drug-sensitive and especially drug resistant TB. Patients with MDR and XDR TB must be treated for up to two years with toxic drugs that can cause hearing loss and other severe side effects leading to low treatment success rates Although rapid molecular tests are available for diagnosing TB, their deployment has been limited by cost and complexity; thus, what is needed is a rapid, accurate point-of-care test suited to use in first level facilities where persons seek care.

UN High Level Meeting on Tuberculosis

The September 26, 2018 United Nations High-Level Meeting on Tuberculosis (UNHLM), the first-ever such meeting to be focused on the TB, is a unique opportunity to obtain commitments from heads of state to the ambitious global targets set by WHO to eliminate TB by 2035. The commitment requires that there be sufficient funding and high-level accountability to achieve the global goals. The ATS urges the U.S. to ensure robust funding commitments from countries, including for TB research and development and a strong accountability framework including the appointment of an independent eminent individual or panel appointed by the U.N. to oversee the publishing of an annual report on progress towards goals. Additionally, we urge the U.S. to send a high level U.S. delegation to the UNHLM, that will include the Secretary of Health and Human Services and Directors of the National Institute of Allergy and Infectious Diseases and Centers for Disease Control and Prevention.

Funding

The U.S. is providing strong global leadership on tuberculosis through the U.S. Agency for International development (USAID), Centers for Disease Control and Prevention (CDC), PEPFAR and the National Institutes of Health. But TB's position as a global health security threat requires increased commitment and investment. TB control, including research and development efforts, has historically been severely underfunded. FY2018 USAID global TB funding is $261 million, which is disproportionally low relative to other global health priorities and TB's burden as the leading infectious killer. The Lantos-Hyde PEPFAR reauthorization, passed in 2008, authorized $4 billion over 5 years for TB, but annual funding appropriated has not come close to this.

In December, 2015, the U.S. government released the inter-agency National Action Plan to Combat Multi-Drug Resistant (MDR) Tuberculosis (National Action Plan). The National Action Plan provides a comprehensive plan for combating drug resistant TB in the U.S. and abroad and for accelerating research and development to develop new TB diagnostic, treatment and prevention tools, but no funding was ever appropriated for its implementation. USAID has reached the key MDR-TB treatment targets for years one and two of the plan but has indicated that reaching year three to year five goals is not achievable under current funding. The continued global pandemic of this airborne infectious disease and spread of drug resistant TB demand that the U.S. strengthen our investment in global and domestic TB control and research to develop new TB diagnostic, treatment and prevention tools through USAID, CDC and NIH.

Recommendations

The ATS recommends the following:

1) The U.S. should provide leadership to secure robust global targets for the detection, treatment and prevention of TB and funding and accountability political commitments from countries in the political declaration to be finalized at the September 26 2018 United Nations High-Level Meeting on Tuberculosis, including the appointment of an independent eminent individual or panel appointed by the U.N. to oversee the publishing of an annual report on progress towards the TB Political Declaration's goals.
2) In order to begin to halt the TB pandemic and implement the National Action Plan we urge Congress to provide $400 million for USAID's TB program in FY2019.
3) In order to provide a coordinated global TB investment, we recommend that Congress provide $21 million in specific line-item funding for CDC's global TB program
4) Accelerate research and development efforts, including research goals under the National Action Plan, to develop new TB diagnostic, treatment and prevention tools by providing increased funding for NIH and CDC TB research efforts.
5) Congress should direct the Biomedical Advanced Research and Development Authority (BARDA) to support late-stage TB diagnostic, treatment and prevention tool development.
6) Enact the Comprehensive TB Elimination Act, H.R. 5794/S. 2506, to strengthen U.S. TB control and implement the U.S. goals of the National Action Plan and put the U.S. on the path to TB elimination.

The ATS appreciates the opportunity to submit this statement to the subcommittee. For more information, please contact Nuala S. Moore with the American Thoracic Society at (202) 296.9770 or Nmoore@thoracic.org

Questions for the Record – Ranking Member Eliot Engel
Combatting Tuberculosis in Southern Africa
July 12, 2018

Answered by Ms. Irene Koek

1. Is the U.S. on track to meet the goals of the U.S. Government Global TB Strategy (2015-2019) and the National Action Plan for Combating Multidrug-Resistant TB (2016-2020)? If not, what obstacles remain?

   Between 2000-2016, a 20% reduction in the TB incidence rate and a 30% reduction in the TB mortality rate was achieved in USAID's TB priority countries. These are significant achievements towards meeting the goals of the U.S. Government Global TB Strategy and the National Action Plan for Combating Multidrug-Resistant TB (MDR-TB). However, there are a number of obstacles that will likely prevent us from fully realizing all of the goals set forth in these strategies. One of the main obstacles is the lack of access to TB services beyond the government facilities to find all of the people with TB, MDR-TB, and TB/HIV quickly, particularly in the private, non-governmental and community sectors. Another obstacle is the lack of tools and technologies to better address the epidemic such as a point-of-care diagnostic, new and less toxic drugs, and a vaccine. USAID continues its efforts to address these challenges.

2. You note in your testimony that "[TB] predominantly affects the poorest and most vulnerable, with about 95 percent of TB deaths occurring in low- and middle- income countries," and "the longer people with active TB disease remain untreated, whether it is drug-susceptible (DS) or DR, the more likely they are to spread the disease, infecting their families and communities." Is it fair to say that the absence of affordable treatments could hinder efforts to control TB?

   Current efforts to control TB are hindered by insufficient access to services and the appropriate tools to diagnosis and treat the disease. Treatment has become more affordable. Through the Global Drug Facility (GDF), supported by USAID, countries have access to high-quality and affordable TB treatment. GDF has worked diligently to negotiate price reductions in treatment for both drug-susceptible and drug-resistant TB. Last month, GDF announced 28 newly-signed agreements with manufacturers for 83 products that will result in a savings of approximately $31 million in one year. The price of MDR-TB treatment regimens has declined more than 60 percent since 2012, while the price of some of the medicines to treat MDR-TB has fallen by 70 percent. By the end of 2017, GDF had delivered more than 30 million treatment courses to 139 countries. GDF is the largest global provider of quality-assured tuberculosis medicines, diagnostics, and laboratory supplies to the public sector.

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USAID's partnerships with the private sector have also played a key role in increasing rapid access to the few promising new tools entering the TB market. For example, USAID has partnered with Johnson and Johnson to introduce bedaquiline, the first new TB drug approved by the Food and Drug Administration (FDA) in more than 50 years. USAID is also partnering with diagnostic companies such as Cepheid and Becton Dickinson to expand access to quality rapid testing for TB and drug resistant TB.

3. You note in your testimony that "In 2016, 82 percent of TB patients in the Africa region had a documented HIV test. PEPFAR data indicate that about half of eligible patients on antiretroviral treatment (ART) were screened for TB in 2017." What are the barriers to scaling these rates up to 100%?

   There has been remarkable progress in scaling up HIV testing of TB patients in the African region. In the last ten years, HIV testing among TB patients has increased from 40 percent to 82 percent. We expect this number to continue to increase as we continue to prioritize testing, especially in areas of high burdens of HIV and TB.

   As an implementing agency of PEPFAR, USAID is addressing the key barriers to scaling up TB screening and treatment of people living with HIV (PLHIV), as approximately half of PLHIV on ART are currently screened for TB. All PLHIV that present for HIV care should be screened for TB and, if diagnosed with active TB disease, referred for immediate initiation of TB treatment. PLHIV that do not have active TB disease should be immediately started on TB preventive treatment and then subsequently screened at every HIV care visit. TB, as the leading killer of PLHIV, requires intensive screening and treatment to reduce HIV mortality.

4. According to the World Health Organization, there is an annual $2.3 billion gap between the resources needed for successful implementation of tuberculosis programs and what is currently being spent worldwide. However, the President's FY 2019 budget request included an $83 million cut to bilateral tuberculosis funding (compared with the FY 2018 enacted level). How many fewer people would USAID be able to test for tuberculosis or treat for tuberculosis if this cut went into effect?

   USAID has been a catalyst for investment and change in high burden TB countries. Over 80 percent of funding to support the TB response is financed through these countries' national domestic resources. We continue to work with all partners, including ministries of health; multilateral, private, non-profit, and faith-based organizations; and civil society to provide resources, expertise, and services to individuals with TB and those at risk of

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TB. USAID views the control of TB as an important milestone on the journey to country self-reliance, and will be seeking opportunities to raise additional private capital to match USAID's investments.

The focus of our available funding even in constrained scenarios is to provide support for the 22 high priority countries. With fewer resources, USAID would invest less in non-priority countries, the roll-out of new tools, research and development, and direct less funding to enhance efforts by national governments to find missing TB patients among vulnerable and hard-to-reach populations.

Answered by the Honorable Deborah L. Birx

1. You note in your testimony that "PEPFAR has committed to addressing TB in Africa by dramatically increasing HIV/TB investments and activities over the past decade and more recently by aggressively scaling up antiretroviral therapy for all persons living with HIV and accelerating the roll-out of TB preventive therapy." Will the PEPFAR Strategy for Accelerating HIV/AIDS Epidemic Control (2017-2020) allow for these scale-ups to continue in all countries served by the PEPFAR program?

   PEPFAR remains committed to addressing TB as a top policy and programmatic priority. There has been an increase in the provision of TB preventive therapy to persons newly enrolling in HIV care, driven largely by the programmatic activities of PEPFAR-supported countries. PEPFAR continues efforts to support the scale-up of the Cepheid GeneXpert MTB/RIF test, a fully automated, molecular diagnostic test for TB. This test enables programs to diagnose TB quickly, which can help reduce transmission and decrease mortality.

   PEPFAR recently revised its suite of TB indicators and now requires our country teams to report on initiation and completion of TB preventive therapy as well as TB screening and initiation of TB therapy in those diagnosed with the disease. These additions were part of a deliberate attempt to drive programming and encourage fully integrated TB/HIV care in PEPFAR countries. Encouragingly, despite no requirements for targets or advanced planning, 17 countries initiated or expanded TB preventive therapy programming in FY 2017.

   We can prevent cases of TB in the first place by scaling up antiretroviral therapy (ART), which reduces the risk that a person living with HIV will develop TB by around 65 percent, and the addition of TB preventive therapy to ART reduces the risk by 97 percent.

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Among people living with HIV who do develop TB, early ART can halve the mortality rate, which is why testing for HIV and initiating ART are key interventions.

2. You note in your testimony that "As recommended by the World Health Organization, PEPFAR is integrating TB/HIV care by providing care for both diseases in one clinic." In the event that integrated services are scaled back, or clinics that provide integrated care are closed, how might patient adherence to treatment regimens and care retention be affected?

   We are working to ensure that these integrated services are not scaled back. From a country perspective, integration makes sense as care is provided in one of the two existing national program clinics (HIV or TB), so no new facilities are required; overall costs are lower and patient satisfaction is higher. Patient adherence for both HIV and TB is also supported by community healthcare workers and family members who are sometimes enlisted to support treatment adherence. We are developing cost-effective interventions to help promote HIV adherence and community treatment, such as Community ART Refills Groups and Viremia clinics that focus on improving adherence in those with unsuppressed viral loads. These interventions will decongest clinics, allowing for greater numbers of patients enrolled into care within the same infrastructure. These interventions can also be used to support adherence to TB treatment.

3. You note in your testimony that "People whose immune systems are impaired from conditions like malnutrition and especially HIV infection are at particular risk of, and from, active TB disease." Is it fair to say that activities to prevent HIV infections may have the added effect of reducing rates of active TB disease?

   Yes. HIV makes it much more likely that a person who is infected with the Mycobacterium tuberculosis (the organism that causes TB) will develop TB disease. This has epidemiologic implications; in Southern Africa, the HIV epidemic was a dramatic driver of the TB epidemic. Anything that reduces HIV transmission would be expected to lower the incidence of TB disease. Scale-up of antiretroviral therapy (ART) would lower the overall TB incidence rates by bolstering immune system functioning in those with HIV, thereby reducing the individual risk of developing TB disease, and by lowering HIV transmission, reducing the overall pool of people at enhanced risk. Our focus on dramatic scale-up of ART would be expected to reduce the incidence rates of all opportunistic infections.

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4. You have made the use of data a cornerstone of your stewardship of PEPFAR – specifically, using data to pinpoint areas of greatest need and allocating funds accordingly. Is it fair to say that this use of data has helped improve the allocation of funds for TB/HIV care?

   Yes, we use our data to identify programs and specific sites that are performing below par and that require additional support and focused intervention. We are also able to identify programs (and sites) that are performing well in similar contexts, which allow us to elicit and share "best practices" with under-performing sites. We have also conducted mapping exercises to enable us to strategically place diagnostic equipment, enhancing capacity across all PEPFAR-supported countries.

Answered by Dr. Rebecca Martin

1. You note in your testimony that "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." However, it is my understanding that the Biomedical Advanced Research and Development Authority (BARDA) and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) have never offered funding opportunities to product developers working on MDR-TB medical countermeasures, including drugs, diagnostics or vaccines. How could CDC work with BARDA to ensure that DR-TB is included as part of BARDA's essential work on medical countermeasure development?

   The Centers for Disease Control and Prevention (CDC) is a lead implementer of the National Action Plan to Combat Antibiotic-Resistant Bacteria (CARB) alongside many operating divisions and agencies across the Department of Health and Human Services and the U.S. Government. In 2013, CDC published the Antibiotic Resistance Threats in the United States, 2013 report (https://www.cdc.gov/drugresistance/threat-report-2013/index.html), which provides information on the burden and threats posed by the antibiotic-resistant germs having the most impact on human health. Drug-resistant TB is highlighted in this report as a serious threat to the United States.

   The Office of the Assistant Secretary for Preparedness and Response (ASPR), through the Biomedical Advanced Research and Development Authority (BARDA) invests in the development of products to address antimicrobial resistance. BARDA has largely

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focused on the research and development of novel antibiotics to stem the tide of antimicrobial resistant infections in both hospitals and in communities across the United States. These antibiotics are typically derivatives of existing classes of antibiotics that overcome known drug resistance mechanisms while also targeting one or more of the bioterrorism agents BARDA is tasked with addressing as part of its core mission. Additionally, the overall strategy is to leverage the development of products for routine clinical use as a means of having products "at the ready" in the event of a bioterrorism event.

Many of the products that would be developed to prevent or treat TB do not possess the dual purpose of also addressing a bioterrorism pathogen. For example, bedaquilin, the most recently approved TB drug, is not predicted to have any activity against the five bioterrorism bacteria (anthrax, plague, tularemia, glanders, melioidosis) for which BARDA is tasked with developing medical countermeasures.

Re-directing resources to address TB would come from an expense to other programs that address chemical, biological, radiological, and nuclear threats, pandemic influenza, and other emerging infectious diseases.

In regard to CARB-X, TB is not currently in the scope of CARB-X. However, in addition to substantial research investments by NIAID, there are other important groups with particular expertise addressing this challenge, including the Bill and Melinda Gates Foundation and TB Alliance.

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Answered by Ms. Irene Koek:

1. Deputy Administrator Koek: The continued spread of drug resistant TB is a threat to global health security, with 480,000 cases of multi-drug resistant TB reported globally. Yet the WHO estimates that only about 25% of people with multi-drug (MDR) resistant TB globally are getting appropriately treated. Drug resistant TB is a problem for the U.S. too as in 2017 my state of CA reported 29 cases of MDR-TB. The National Action Plan to Combat MDR-TB, released in December 2015, provides a comprehensive roadmap for combating TB in the US., internationally and for accelerating research and development of new TB diagnostic, treatment and prevention tools. Is USAID on track to meet its overall target for treating 200,000 MDR-TB cases by 2020? What challenges exist that might make meeting this target difficult?

   While we have seen some progress, the proportion of people infected with MDR-TB who have not yet been diagnosed remains below what it should be, as are the number of patients who successfully completing their treatment. The National Action Plan to Combat MDR-TB target is to treat an additional 200,000 MDR-TB builds upon a target of treating 360,000 MDR-TB patients in the U.S. Government Global TB Strategy. In the past year, USAID has seen a significant increase in improving the quality of MDR-TB treatment with the rapid uptake of new drugs and the shortened TB regimen. USAID did meet the Year 1 milestones but observed detection and treatment rates remained relatively unchanged in Year 2, in line with the global trends observed in 2017. Increased political will within the target countries and access to additional resources will be required for the rapid scale-up needed in 2018, and through the rest of the Plan to achieve the milestones laid out for Year 3.

   We are working with our partners to reach the goals developed in a collaborative effort across the U.S. Government. Our work is focused on finding the missing TB cases globally, scaling up access to rapid MDR-TB diagnostic services, and enrolling patients on effective treatment. In India, USAID piloted and scaled-up the first-ever use of GeneXpert to diagnose TB and MDR-TB in adults and children, leading to a new national policy. The support to pediatric case finding with GeneXpert in India showed a 4-fold increase in case detection of MDR-TB in children - a disease that would otherwise have never been detected or detected too late for these children. USAID designed and implemented a Joint TB Diagnostic Network Assessment to identify interventions and priorities to assist the Government of India in operationalizing the diagnostic targets and goals in their National TB Strategic Plan. In addition, this assessment supports India's MDR-TB infrastructure expansion plan. On the treatment side, USAID supported the introduction of bedaquiline for MDR- and XDR-TB patients in India. The introduction of

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this life-saving medicine was done through a comprehensive package of support to clinicians and patients in facilities throughout India. The lack of access to quality TB services as well as the lack of point-of-care diagnostics and shorter and less toxic treatment are key barriers that prevent us from meeting our targets. We are working with partners including Cepheid and Becton Dickinson to address these challenges through increasing access to TB diagnostic services. For example, in India, our new Partnership with Becton Dickinson is helping to optimize testing for second-line drug resistance which is critically important to ensure that MDR-TB patients are placed on appropriate treatment. Our partnership with Johnson and Johnson supports the roll-out of new treatments.

2. A subsequent May 2018 report from USAID on the National Action Plan for Combating Multi-Drug Resistant Tuberculosis states that in 2017 the rate of increase in expanding access to MDR-TB diagnosis and treatment has "remained relatively unchanged" and that "additional resources will be required" to reach further milestones. This is very concerning, since MDR-TB is a global health security threat. For FY 18, Congress has provided an 8% increase to USAID's TB program, a boost of $20 million. For all the witnesses: What can be done to accelerate access to diagnosis and treatment for drug resistant TB, and what level of resources is required?

   Diagnosing MDR-TB starts with finding TB cases. Globally, we are only finding about two-thirds of estimated TB cases. The remaining one-third of TB cases are either not diagnosed or diagnosed but not reported. With the resources that are already available, USAID is supporting interventions to accelerate the detection of MDR-TB, starting with finding the missing cases and improving access to drug susceptibility testing (DST). Through our person-centered approach, we are increasing awareness and addressing factors that are preventing persons with TB symptoms from accessing TB diagnostic and treatment services. We are increasing active screening of TB and MDR-TB among vulnerable groups using different strategies, including community-based screening, universal screening, and DST at health facilities using GeneXpert. Even though GeneXpert is not a point-of-care diagnostic test, countries can improve systems to allow every person with signs and symptoms of MDR-TB access to GeneXpert testing. Improvements in systems like specimen referral and transport and diagnostic data management enable countries to use existing rapid molecular tests, like GeneXpert, to accurately diagnose MDR-TB and start appropriate treatment in much less time than traditional tests. By investing in these supportive systems, countries will be prepared to introduce new MDR-TB diagnostic tools, like sequencing, when they become available. However, in the long run, given the cost and infrastructure requirements of Xpert, there is

a need to continue to invest in new, rapid and practical point-of-care TB screening and diagnostic tools.

People with drug-resistant TB (DR-TB) can be deterred from starting treatment as DR-TB treatment regimens are long, difficult and can involve serious side effects. To address this issue, USAID is supporting the development of new TB treatment regimens which are shorter and more tolerable to patients. These regimens are expected to result in increased treatment adherence and higher cure rates. Additional funds will continue to support clinical trials to evaluate new drugs and ensure that the drugs are accessed by those most in need.

3. When a woman becomes pregnant her chance of developing TB doubles. People who are malnourished, including children, are also known to be much more vulnerable to TB. For Ambassador Birx and Deputy Administrator Koek, how are your agencies working to integrate TB screening and other TB services into programs meeting the needs of orphans and vulnerable children and pregnant women? How are your programs working to break down siloed health programs and integrate TB into other global health programs?

Finding all people without access to services (the missing TB patients) is a priority for USAID's TB program. We are supporting interventions to reach vulnerable and marginalized populations including people living with or affected by HIV, mine workers, pregnant women and children.

We have integrated TB screening services within primary health care services and maternal and child health services, including antenatal clinics and child and well-baby clinics. Diagnosis of TB in children remains more difficult than in adults. However, we are using evidence from recent studies to improve our ability to identify the disease in children, and we have supported the development of new pediatric formulations to make appropriate treatment widely available.

With regard to pregnant women, we have engaged with partners from USAID's reproductive health programs to advocate and promote TB screening during pregnancy and after childbirth. We are supporting the gathering of evidence on the efficacy and safety of new TB drugs to inform future treatment guidelines for this population.

We are supporting the screening of people living with HIV (PLHIV) for TB as part of ongoing, routine care and addressing barriers/challenges to TB screening for PLHIV. Current guidelines delineate procedures for PLHIV who screen positive for TB. If further evaluation indicates active TB disease, treatment is initiated as soon as possible.

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If the evaluation does not indicate active disease, providers are directed to begin TB preventive therapy.

We are working with a wide range of faith-based and community organizations to reach families and communities, and prioritizing finding "missing" TB patients among vulnerable, hard-to-reach and marginalized populations, including people living with HIV, mineworkers, pregnant women, and children. And we are reaching beyond Ministries of Health to include Ministries of Labor to reach manufacturers and workers, Education for teachers and children, correctional agencies for prisoners and guards, faith-based and community organizations to reach families and communities, and the corporate sector to include mining enterprises, the pharmaceutical industry and private healthcare providers.

4. Private sector companies have been reluctant to make risky investments in researching new TB cures. The market dynamics of TB – a disease that afflicts mainly the poor – make it likely that companies won't be able to recoup their R&D investments.

   For all the witnesses, given this situation, what more should we do to incentivize private sector companies to invest in TB research?

   USAID continues to leverage American innovation and leadership to improve the quality of diagnosis and treatment through the scale-up of new tools. In a joint effort with Johnson and Johnson, the Agency has utilized its extensive delivery platform to increase the introduction and scale-up of bedaquiline in over 70 countries. In addition, Johnson and Johnson is utilizing USAID's research platform for the Phase III clinical trial of bedaquiline, maximizing limited TB funding. USAID is also partnering with diagnostic companies, such as Cepheid and Becton Dickinson, to expand access to quality, rapid testing for TB and drug resistant -TB. These type of partnerships are a win-win for the private and the public sectors.

5. For all the witnesses, to what degree do you think the price of medicines is a factor driving the overall cost of treating TB? How significant are drug costs compared to other barriers to access of treatment?

   With significant USAID support, the Global Drug Facility has changed the landscape of TB care since its creation in 2001 by increasing access to high quality and affordable TB treatments and diagnostics for populations in need. By the end of 2017, GDF delivered more than 30 million treatment courses to 139 countries. The average price for a six-month course of quality-assured drug-susceptible TB treatment from GDF is

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$35. The price of some medicines for drug-susceptible TB has fallen by 70 percent. GDF is the largest global provider of quality-assured tuberculosis medicines, diagnostics, and laboratory supplies to the public sector. The GDF is a pooled procurement mechanism that provides a package of services, including technical assistance in TB drug management and monitoring of drug use, as well as procurement of high-quality TB drugs at low cost. As the largest supplier of TB medicines and diagnostics, GDF ensures the availability, affordability and quality of TB medicines.

The MDR-TB drug supply is considered a fragile and orphan market because of its small size and low profit. It is further hampered by the fact that each patient requires many drugs for a long period of time. Despite this, last month GDF announced 28 newly-signed agreements with manufacturers for 83 products that will result in a savings of approximately $31 million in one year. The price of MDR-TB treatment regimens has declined by more than 60 percent since 2012. These price reductions are only possible because GDF serves as a pooled procurement mechanism for quality-assured tuberculosis medicines, diagnostics, and laboratory supplies globally. By the end of 2017, GDF delivered more than 30 million treatment courses to 139 countries.

The small number of new TB drugs coming to market in recent decades is very concerning, and I would like to know how it affects your programmatic work.

6. For all the witnesses, how would you describe and characterize the current situation of available TB treatments as well as what you see as the prospects for new treatments and their availability?

The current TB treatment landscape has been composed of old and toxic generic drugs for many years. Particularly for MDR-TB, the situation has been quite dire, since most of the drugs, until recently, were not initially developed for that purpose. The long duration of MDR-TB treatment and severe adverse events associated with these drugs are major barriers to treatment success. There have been two new drugs developed (bedaquiline and delamanid) and until recently they were only internationally recommended for a small number of drug-resistant patients. The broader availability of these drugs and their use have offered life-saving treatment options to those with the worst types of drug resistance. USAID's support has made these drugs available through the Global Drug Facility (GDF). As more data become available, countries will update their treatment guidelines to recommend broader use for these new drugs. In addition, USAID and others are supporting clinical trials to determine the most optimal regimen using existing and new drugs.

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There has been a decrease in the number of private pharmaceutical companies that are investing in developing new TB drugs given that the TB market is considered to be less profitable. Nevertheless, we are seeing a small increase in the number of new compounds that are being evaluated for their efficacy against TB, though these compounds will likely take more than 5 years to be approved for use in TB treatment.

Answered by the Honorable Deborah L. Birx

1. A subsequent May 2018 report from USAID on the National Action Plan for Combatting Multi-Drug Resistant Tuberculosis states that in 2017 the rate of increase in expanding access to MDR-TB diagnosis and treatment has "remained relatively unchanged" and that "additional resources will be required" to reach further milestones. This is very concerning, since MDR-TB is a global health security threat. For FY 18, Congress has provided an 8% increase to USAID's TB program, a boost of $20 million. For all the witnesses: What can be done to accelerate access to diagnosis and treatment for drug resistant TB, and what level of resources is required?

   PEPFAR collaborates with USAID on TB programming, and we can leverage efforts to maximally impact the MDR-TB epidemic. Access to diagnosis and access to effective treatment are two critical bottlenecks. Molecular testing that can detect both TB disease and rifampicin-resistance, the hallmark of MDR-TB, is an important focus for PEPFAR, and we are currently working with USAID to improve access to, and maintenance of, such platforms in all of our countries. We are optimizing the use of these platforms (e.g., the GeneXpert platform), but still need to ensure that all HIV facilities have access to molecular testing, and this will require strategic development of specimen transportation systems as well as procurement of additional machines – both of which require resources. Based on results from USAID-supported studies, PEPFAR supports the use of the shorter, less expensive and less toxic treatment regimens for MDR-TB, and we will be promoting these regimens for our patients with MDR-TB.

2. When a woman becomes pregnant her chance of developing TB doubles. People who are malnourished, including children, are also known to be much more vulnerable to TB. For Ambassador Birx and Deputy Administrator Koek, how are your agencies working to integrate TB screening and other TB services into programs meeting the needs of orphans and vulnerable children and pregnant women? How are your programs working to break down siloed health programs and integrate TB into other global health programs?

   All persons living with HIV, including and especially pregnant women, are regularly screened for symptoms of TB disease at each visit. We follow this indicator closely, and

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work to improve screening when performance is sub-par. Outside of those in HIV treatment, we include educational programming on TB for orphans and vulnerable children and for the adolescent girls and young women who participate in our DREAMS programs. We are actively working to integrate TB and HIV programs, which are still separate, even at the clinical level, in many of the countries where we work.

3. Private sector companies have been reluctant to make risky investments in researching new TB cures. The market dynamics of TB – a disease that afflicts mainly the poor – make it likely that companies won't be able to recoup their R&D investments. For all the witnesses, given this situation, what more should we do to incentivize private sector companies to invest in TB research?

   There is a potentially robust market for TB diagnostics, and we should try to incentivize the development of new products by demonstrating the size of the market (~20 million people living with HIV [PLHIV] on treatment, and growing). It is also worth highlighting that both PEPFAR and Global Fund funding can be used for TB diagnosis and treatment among PLHIV. Additional support for non-profit enterprises could greatly accelerate progress in both TB diagnosis and treatment.

4. For all the witnesses, to what degree do you think the price of medicines is a factor driving the overall cost of treating TB? How significant are drug costs compared to other barriers to access of treatment?

   The drug costs for drug-resistant TB are indeed prohibitive, and probably one of the biggest barriers to treatment. The drug costs for drug-susceptible TB (DS-TB) are not a significant barrier; for DS-TB, the biggest barrier is finding the undiagnosed cases that are in the community. Many patients, particularly men, do not come to care unless they are disabled or unremittingly ill; those that have TB often have infectious disease for many months before they come for care. The cost of community screening and case-finding is significantly higher and more prohibitive than the drug costs for DS-TB treatment.

5. The small number of new TB drugs coming to market in recent decades is very concerning, and I would like to know how it affects your programmatic work. We are somewhat encouraged to see a handful of new drugs making their way through development, but certainly the pace has not kept up with the need. We still have 60-year-old regimens that require 6 months of up to 4 drugs, and we are in urgent need of shorter,

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more effective regimens. The pill burden introduced by TB disease can diminish treatment adherence for both TB and HIV, as patients get overwhelmed and weary from taking so many medicines, and this has impacted our programmatic work in the TB/HIV population. Furthermore, there is a growing concern about multidrug-resistant TB, which is an increasing threat in Southern Africa. Without new drugs, we will most certainly have an increasing number of patients demonstrating resistance to all available drugs who we will not be able to treat. These patients are at very high risk of death and pose immediate threats to their families and communities.

6. For all the witnesses, how would you describe and characterize the current situation of available TB treatments as well as what you see as the prospects for new treatments and their availability? How does the environment for new TB drugs challenge the programs you oversee in Southern Africa? Finally, how do these same challenges affect our own ability to treat TB, including virulent and drug resistant strains?

   Response: TB is, by far, the biggest killer of people living with HIV (PLHIV), especially in Southern Africa; this presents a direct challenge for PEPFAR, the purpose of which is to save the lives of PLHIV and restore communities devastated by the HIV. Unless we have shorter, more effective regimens against TB disease, TB will remain an enormous obstacle to achieving our goals. It is encouraging that there are a number of TB drugs in the pipeline, and there is emerging evidence that new combinations of currently available drugs are highly effective, and may allow for all oral, short duration treatment for many patients with drug resistant TB. But almost all of the new drugs are years away from being widely available, and we have patients with extensive drug resistance patterns that are untreatable by currently available drugs. These patients are often actively transmitting disease, so the current situation of drug-resistant TB is an urgent one. We need additional research to bring more drugs under investigation and to accelerate the timeline to drug availability and we need pricing that makes these drugs accessible to countries with limited financial capacity.

Answered by Dr. Rebecca Martin

1. A subsequent May 2018 report from USAID on the National Action Plan for Combatting Multi-Drug Resistant Tuberculosis states that in 2017 the rate of increase in expanding access to MDR-TB diagnosis and treatment has "remained relatively unchanged" and that "additional resources will be required" to reach further milestones. This is very concerning, since MDR-TB is a global health security threat. For FY 18, Congress has provided an 8% increase to USAID's TB program, a boost of $20 million. For all the

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witnesses: What can be done to accelerate access to diagnosis and treatment for drug resistant TB, and what level of resources is required?

The U.S. Government released the National Action Plan for Combating Multidrug-Resistant (MDR) TB in 2015, laying out ambitious targets for accelerating efforts to find, cure, and prevent MDR TB through on-the-ground service delivery, technical support to Ministries of Health, and through research and innovation. The National Action Plan identifies areas where the U.S. Government can leverage its demonstrated experience and expertise to have the highest impact on the global epidemic.

Fighting TB is considered one of the "best buys" in public health and development because of the expected $43 return on investment in improved health outcomes for every dollar spent. Governments of high-burden countries have recognized this, contributing 80 percent of the total global funding for addressing TB. The U.S. Government remains the largest international donor through bilateral and multilateral funding arrangements. However, there remains a global funding shortfall for all forms of TB. The World Health Organization (WHO) estimates that there is an annual funding gap for TB interventions of $2.3 billion. If filled, this gap would enable full treatment for 17 million TB and MDR-TB patients and save six million lives over three years.

2. Dr. Martin, given the ongoing TB challenge within the US, with more than 9,000 cases this past year, are the CDC resources for both global and domestic TB adequate?

Funding for global and domestic TB supports the priority areas of enhancing TB treatment, diagnostic tools, prevention, and program delivery. Global Tuberculosis activities are supported by funding from CDC'S HIV/AIDS, Viral Hepatitis, Sexually Transmitted Infections, and Tuberculosis budget. In addition, CDC leverages its work in PEPFAR to address HIV/TB coinfection. CDC will continue to strategically direct its resources to seek new innovative activities to advance the priority areas and prevent the spread of TB. CDC will target funding for global TB to finding cases, particularly for high-risk populations, and improving diagnostic algorithms; curing TB by optimizing TB and MDR-TB treatment regimens; improve linkage to care and treatment, especially among people living with HIV and preventing TB through implementing effective TB infection control practices in health facilities and congregate settings and scaling-up preventive therapy for people living with HIV and children.

3. Private sector companies have been reluctant to make risky investments in researching new TB cures. The market dynamics of TB – a disease that afflicts mainly the poor – make it likely that companies won't be able to recoup their R&D investments. For all the

witnesses, given this situation, what more should we do to incentivize private sector companies to invest in TB research?

The major disincentives to TB drug development are a small domestic market, a reasonably large global market but with most of the disease occurring in low income individuals in developing countries and a fixed treatment course (usually months as compared to lifetime treatment for other diseases such as diabetes and asthma). As indicated in the question, the high costs of R&D coupled with the high costs of regulatory approval relative to potential revenue in the current market make it difficult to recoup these investments. Directly or indirectly subsidizing R&D and regulatory approval costs could make TB drug development more attractive. Indirect subsidization through government funding of clinical trials and other research already occurs. For example, the CDC Tuberculosis Trials Consortium conducts clinical treatment trials of TB drugs that have led to new treatment regimens and have been used as evidence necessary for regulatory approval. Continuing these types of activities could help to increase opportunities for private sector development.

4. For all the witnesses, to what degree do you think the price of medicines is a factor driving the overall cost of treating TB? How significant are drug costs compared to other barriers to access of treatment?

Overall, TB is costly to treat. In the U.S., a case of drug susceptible TB costs $18,000 to treat; multidrug-resistant TB costs $160,000 to treat, and extensively drug-resistant TB costs $513,000. Drug costs are a significant driver of the treatment costs for multidrug and extensively drug-resistant TB compared to drug-susceptible TB. Local and state health departments serve as the provider of last resort for these drugs. The cost of drugs for drug-resistant TB can have a substantial impact on health department budgets. The cost to treat TB internationally varies by location.

The length of TB treatment (6-9 months) requires substantial public health resources to ensure completion of treatment. Additional services and testing necessary to ensure treatment to cure, including clinic visits, directly observed therapy, transportation, housing, hospitalization, x-rays, blood tests, cultures and drug susceptibility testing, account for the remainder of costs beyond drugs. Drug-resistant treatment is even longer (18-24 months).Toxicity of current drugs also adds to costs by causing interruption and extension of TB treatment, potential need to change to more costly second-line drugs and interventions to address the toxicity that could include hospitalization. Local and state health departments work to overcome barriers to access domestically by ensuring necessary treatments and services are available regardless of a patient's financial or social

situation. Without this dedicated public health infrastructure, the burdens for access to care would likely include more barriers in addition to cost (drugs and other) as mentioned above. In many low and middle-income countries, other factors such as stigma, lack of knowledge about TB, extreme poverty, opportunity cost to access health services, lack of high quality drugs and diagnostics, inequality in access to the health services, and distrust with the health system become critical barriers to treatment.

5. The small number of new TB drugs coming to market in recent decades is very concerning, and I would like to know how it affects your programmatic work. For all the witnesses,

   a) How would you describe and characterize the current situation of available TB treatments as well as what you see as the prospects for new treatments and their availability?

   Both domestically and globally, the treatment for drug-susceptible TB is very effective if administered correctly, achieving 95% cure. However, the regimen is relatively long, at least 6 months, and requires multiple drugs that have potential significant toxicity, such as liver damage. The length and complexity of the regimen require substantial ancillary services to ensure completion and cure because treatment failure is often associated with acquisition of drug resistance and transmission of disease to others. Regimens for multidrug-resistant TB are less effective, more toxic, take much longer (18-24 months) and are substantially more expensive. Therefore, patients and TB programs would benefit greatly from new drugs that allowed a much shorter treatment with less toxicity, which ideally could be used for drug-susceptible and drug-resistant TB. Also of concern, many TB drugs have a single U.S. manufacturer, making them vulnerable to shortages. When patents expire, manufacturers may sell the license or discontinue making the drug altogether.

   There are several new regimens that are being studied by various research entities including CDC. Studies include new drugs, new combinations of drugs and repurposing of older drugs. It is hoped that some new regimens will be available within the next five years. However, the overall pipeline of potential new drugs is sparse and clinical trials capacity is limited. More candidate drugs and research capacity are needed to transform TB treatment as happened with HIV treatment.

   CDC has ongoing activities addressed at both the development of new drug regimens and mitigating drug shortages. The former activity includes research on both treatment for latent TB infection to prevent progression to TB disease and treatment of TB disease.

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- CDC conducts clinical, operational, and laboratory research to develop better tools and operationalizing their use in TB programs. For example, CDC's TB Trials Consortium identified a shortened regimen for preventing TB disease among people who have latent TB infection and is now being used in the US and globally. In June 2018, based on new CDC research, CDC updated guidelines for expanding use of this regimen for children over 2, people with HIV infection, and delivery by either self-administration or directly observed therapy.
- CDC is working with TB programs and private healthcare providers to offer short-course LTBI treatment to people at risk for developing TB disease. The regimen is easier to tolerate and more likely to be completed by patients and is far less costly than treating a case of TB disease ($600 for testing and treatment of latent TB infection as opposed to $18,000 to treat TB disease.)
- CDC is currently conducting a study of two new regimens for TB disease that would cut the duration of treatment by one third to 4 months. Enrollment in the study should be completed at the end of 2018 with results being available in 2020.

b) How does the environment for new TB drugs challenge the programs you oversee in Southern Africa?

The standard treatment regimen for drug-resistant TB is long, toxic, and costly. The treatments often can last up to two years with daily injections that can cause severe side effects at a cost of up to $500,000 for a single case in the United States. Such treatments also drain health resources, requiring long hospital stays and years-long community care. Recently approved new drugs – Delaminid and Bedaquiline – offer the potential for shorter regimens with higher treatment success rates. Several clinical trials, including most recently in South Africa, have shown regimens including Bedaquiline to be more efficacious with fewer side effects, higher completion, and lower mortality rates than the standard regimen. These drugs have not been tested for use in children, and there remain no pediatric formulations for the 33,000 children globally who develop drug-resistant TB each year. Moreover, overall treatment costs remain a challenge in high-burden countries -- even though the individual drugs are generally available at low cost at present. Because treatment involves multiple drugs, and also involves careful supervision, in part due to concerns that widespread use could lead to resistance if not administered properly, quality care can be a relatively expensive proposition in many settings. Clinicians and TB programs worldwide are weighing the risk of widespread use of these new drugs. In June 2018, South Africa, working with international partners, became the first country to replace the standard MDR-TB regimen with the shorter MDR-TB regimen incorporating Bedaquiline. These are promising developments in addressing treatment for drug-resistant TB, but

further research and development efforts for new innovative tools for both prevention and treatment is needed.

c) Finally, how do these same challenges affect our own ability to treat TB, including virulent and drug resistant strains?

Most domestic TB programs have faced challenges obtaining drugs for treating patients with drug resistant TB. These include nationwide shortage, shipping delays, and expense to programs and patients. Locating the appropriate drugs as rapidly as possible is imperative in order to halt transmission of drug resistant TB and to cure the patient. CDC established a TB emergency drug stockpile to aid TB programs affected by drug shortages. CDC activated this stockpile in March 2018 in response to a rupture in rifapentine supply at several U.S. distributors that threatened to interrupt treatment for patients on latent TB infection therapy. Since partial treatment is ineffective these patients would have needed to restart their regimens once supplies were re-established--a net loss for them and the TB programs. Partial treatment also could lead to the development of resistance to these first line treatments. Therefore, CDC provided rifapentine from the stockpile to affected programs, enabling over 530 patients in 12 states to complete therapy, alleviating this critical shortage.

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Answered by Ms. Irene Koek

1. How many individuals do current U.S. global health programs support?

   Multiple agencies contribute to the implementation of U.S. global health programs. Currently, CDC works in more than 60 countries with over 1700 staff, collaborating with a wide array of partners to coordinate global health strategies, tactics and priorities with a sole focus on global health. Our global programs are run by world experts in epidemiology, surveillance, informatics, laboratory systems, and other essential disciplines to provide strong global health leadership capacity. The work of these experts strengthen critical public health services around the world. Our global programs address more than 400 diseases, health threats, and conditions that are a major source of death, disease, and disability – building upon our U.S. public health program expertise and knowledge of these diseases to help protect Americans from major health threats, wherever they arise. CDC's National Center for Immunization and Respiratory Diseases cooperates with more than 50 countries to improve surveillance and response for influenza, both seasonal viruses and novel viruses with pandemic potential, and works in dozens of countries to promote introduction of vaccines for diseases including HPV and rotavirus. Within the CDC's Center for Global Health (CGH), the Global Immunization Division (GID) works through partners across the world to protect against contagious and life-threatening vaccine-preventable diseases - saving an estimated 2 to 3 million lives each year. The Division of Global Health Protection (DGHP) collaborates with global partners to protect the U.S. from deadly and costly public crises by strengthening the capacity of other countries to prevent, detect, and respond to disease threats. Moreover, the Division of Parasitic Diseases and Malaria (DPDM) works to reduce the threat of parasitic diseases and to eliminate the global burden of malaria and neglected tropical diseases. This includes co-implementation of the President's Malaria Initiative (PMI). In addition, through PEPFAR, CDC and the Division of Global HIV/TB (DGHT) has supported 7.3 million people on antiretroviral therapy, TB screening for 4.7 million people living with HIV (PLHIV), including 400,000 children. In 2017, PEPFAR provided 650,000 PLHIV with TB Preventive Treatment (TPT).

2. How many fewer individuals would U.S. global health programs support, if funding levels and prioritization reflected the President's budget request?

   CDC works to provide the highest quality global health programs to achieve the greatest impact on reducing uncontrolled outbreaks of infectious diseases. Should the funding levels and prioritization reflected in the 2019 President's Budget become enacted, CDC

will continue to leverage its resources and support critical global health programs at a reduced scope.

3. Which individual at your agency currently coordinates your agency's participation in the Global Health Security Agenda (GHSA) and with which individual and office at NSC does your agency coordinate with on matters related to the GHSA?

   In partnership with U.S. government agencies, other nations, international organizations, public and private stakeholders, CDC seeks to accelerate progress toward a world safe and secure from infectious disease threats. CDC has a number of staff across programs that work on GHSA. Within the Center for Global Health (CGH), the Associate Director for Global Health Security coordinates with subject matter and technical experts throughout the agency to implement GHSA. It is the role of the Associate Director for Global Health Security to coordinate both efforts within CGH and across the agency. The Associate Director for Global Health Security also coordinates CDC cooperation with the Weapons of Mass Destruction & Biodefense office within the NSC.

4. What efforts, if any, do you cooperate or collaborate with the Global Development Lab at USAID on?

   CDC currently does not collaborate with USAID's Global Development Lab.

Answered by the Honorable Deborah L. Birx

1. How many individuals do current U.S. global health programs support?

   Today, after 15 years, PEPFAR supports more than 14 million men, women, and children with lifesaving HIV treatment – more than twice as many as 4.5 years ago. When PEPFAR began, only 50,000 people in Africa were on lifesaving HIV treatment.

   PEPFAR is not only saving lives by treating HIV, but also by stopping transmission before it happens, including through three primary prevention interventions:

   PEPFAR continues to be the driving force in preventing mother-to-child transmission. To date, PEPFAR has enabled more than 2.2 million babies to be born HIV-negative to HIV-positive mothers and kept their mothers alive through t provision of lifesaving antiretroviral treatment.

   To prevent new infections in boys and men, PEPFAR has supported more than 15.2 million of them through the provision of voluntary medical male circumcision (VMMC),

including through the largest single-year increase (nearly 3.5 million) in VMMC results during fiscal year (FY) 2017, since the beginning of PEPFAR.

To prevent infection in adolescent girls and young women, PEPFAR designed the groundbreaking DREAMS (Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe) public-private partnership. In nearly two-thirds of PEPFAR-supported DREAMS districts in 10 African countries, new HIV diagnoses are down 25-40 percent or more among adolescent girls and young women since 2015.

2. How many fewer individuals would U.S. global health programs support, if funding levels and prioritization reflected the President's budget request?

   With the President's budget request the United States will continue to be the single largest donor to global HIV/AIDS relief efforts. The requested levels will allow PEPFAR to maintain all patients currently on antiretroviral treatment (ART). It will support the continuation of U.S. HIV/AIDS relief efforts in more than 50 countries through direct bilateral and regional programs, and the Global Fund.

   In addition to maintaining the current ART service delivery levels across PEPFAR countries, PEPFAR will continue to work toward achieving epidemic control in 13 high HIV/AIDS burden countries, in line with the Administration's new PEPFAR Strategy for Accelerating HIV/AIDS Epidemic Control (2017-2020). In addition to saving millions of lives, this strategy will reduce the future costs required to sustain the HIV/AIDS response.

3. Which individual at your agency currently coordinates your agency's participation in the Global Health Security Agenda (GHSA) and with which individual and office at NSC does your agency coordinate with on matters related to the GHSA?

   In my role as Coordinator of the United States Government Activities to Combat HIV/AIDS and U.S. Special Representative for Global Health Diplomacy I work closely with the Bureau of Oceans and International Environmental Scientific Affairs and Department leadership to ensure all Global Health Security issues are coordinated with the NSC.

   The health systems supported by PEPFAR are on the front lines of "detect" within the global health security agenda. PEPFAR has built health infrastructure and strengthened

capacity through an emphasis on sustainability. This infrastructure and capacity not only support people living with HIV/AIDS, but also are leveraged for maternal and child health, tuberculosis, malaria, immunizations, and emergency disease outbreak responses. We invest in robust laboratories and well-trained laboratory specialists critical to well-functioning health systems, enabling clinicians and health workers to better diagnose and treat a range of diseases and conditions. PEPFAR has trained nearly 250,000 health care workers to deliver and improve HIV care and other health services, creating a lasting infrastructure that enables partner countries to address all health challenges of today and tomorrow.

In 2017 alone, through PEPFAR's COPs/ROPs, we invested nearly $600 million in health system strengthening investments, including nearly $100 million to strengthen laboratory systems. These efforts have also strengthened the ability of countries with sizable HIV/AIDS burdens to swiftly address other outbreaks, such as Ebola, avian flu, and cholera, ultimately enhancing global health security and protecting America's borders. These critical health systems investments have enabled PEPFAR to directly support the global health security agenda.

4. What efforts, if any, do you cooperate or collaborate with the Global Development Lab at USAID on?

PEPFAR has cooperated over the years in a variety of capacities with the Global Development Lab. A few years ago when PEPFAR convened subject-specific interagency Technical Working Groups (TWGs), there was a representative from the Lab on the Public Private Partnership TWG. While the TWG structure is no longer active, we often still consult with the Lab on various partnerships and innovations. More recently, when PEPFAR was in the early stages of launching the DREAMS Innovation Challenge, we consulted with the Lab on the structure, design, process, criteria, and timelines of running an innovation challenge/prize competition.

Additionally, PEPFAR is an active participant every year in Global Partnership Week (GPW), which is co-hosted by the Secretary's Office of Global Partnerships at the U.S. Department of State, the Global Development Lab, Concordia, and PeaceTech Lab. GPW brings together leaders and practitioners from multilateral organizations, civil society, and corporations to celebrate uncommon solutions to accelerating public-private partnerships from start to scale. Finally, PEPFAR has participated in several events hosted by the Lab, including those related to the Global Innovation Exchange. Overall,

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the relationship between PEPFAR and the Global Development Lab is strong and we look forward to continued collaboration.

Answered by Dr. Rebecca Martin

1. How many individuals do current U.S. global health programs support?

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3. Which individual at your agency currently coordinates your agency's participation in the Global Health Security Agenda (GHSA) and with which individual and office at NSC does your agency coordinate with on matters related to the GHSA?

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