

**ADDRESSING THE NEGLECTED DISEASES  
TREATMENT GAP**

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**HEARING**

BEFORE THE

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

OF THE

COMMITTEE ON FOREIGN AFFAIRS  
HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRTEENTH CONGRESS

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## **ADDRESSING THE NEGLECTED DISEASES TREATMENT GAP**

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**THURSDAY, JUNE 27, 2013**

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 2:06 p.m., in room 2200, Rayburn House Office Building, Hon. Christopher H. Smith (chairman of the subcommittee) presiding.

Mr. SMITH. Good afternoon.

Today's hearing will examine the neglected diseases that affect a relatively small but a significant number of children around the world. These diseases are not only debilitating for their victims but far too often fatal when untreated. Such diseases largely impact poor people in poor countries.

They are not only small in numbers but those folks who are unable to pay market prices for treatments and are unlikely to lead the social movements to force action on their respective diseases. That means that research on detection, vaccines, and drug treatment for their ailments do not receive the priority that diseases such as HIV/AIDS, often seen in pandemic levels, are given.

The World Health Organization has identified 17 neglected tropical diseases, or NTDs. The list ranges from Chagas to rabies to leprosy to dengue fever. However, there are others not on the list of 17 diseases that also receive less attention. These include such diseases as polio and smallpox, which have largely been eliminated from the planet, and fatal, fortunately rare NTDs such as kuru and Ebola.

I would note parenthetically, back in the early 1980s, when I authored what was known as the Child Survival Reauthorization Amendment for some \$50 million, I traveled to El Salvador, and the polio vaccine was given to upwards of 200,000 children, along with other immunizations to guard against pertussis, diphtheria, and other leading killers of children. Thankfully, some of those diseases are largely gone, but some, sadly, are making a comeback.

I would also point out that we have had hearings in this subcommittee and I have introduced legislation to focus on another problem, particularly in Africa, of the infection-based hydrocephalic condition that is hurting so many children in places like Uganda.

I actually went to CURE International's clinic in Uganda and saw children who got the treatment. Dr. Benjamin Warf has devel-

oped it out of Harvard. There are no shunts involved, and these kids went from very large painful conditions in their head, water on the brain, to very healthy children. And at least 5,000 kids have been saved there. We have been asking, urging, begging practically, that USAID do something administratively to try to address that issue.

This hearing will consider the current U.S. Government's handling of these and other neglected diseases to determine what more can be done or should be done to address this situation. Current U.S. law favors research on those diseases threatening the American homeland, but in today's world diseases can cross borders as easily as those affected by them or the products imported from the United States.

For example, Chagas is most prevalent in Latin America, but it has been identified in patients in Texas. And cases of dengue fever have recently been reported in Florida. We cannot afford to assume that what may have seemed to be an exotic disease only happens to people in other countries.

Ten years ago, West Nile virus, another NTD, was not seen in the United States or anywhere else outside of the East African nation of Uganda, but in less than a decade it has spread across the country and much of the rest of the world. Last year, 286 people died from West Nile virus in the United States alone. As recently as the mid-1990s, this disease was seen only sporadically and was considered a minor risk for human beings.

Generally, NTDs affect the health of the poor in developing countries where access to clean water, sanitation, and health care is limited. Roughly 2 billion people are being treated for at least one NTD, although most individuals are infected with several NTDs at once.

Several NTDs are difficult to control by drug treatment alone because of their complicated transition cycles that involve nonhuman carriers, such as insects. Furthermore, some of the drugs have significant side effects, including death, and cannot be used by young children or pregnant women.

A study done in 2001 found that research and development of drugs to treat infectious diseases had ground to a near standstill. From 1975 to 1999, the report stated 1,393 new drugs were brought to the market globally, but only 16, or 1.1 percent, were for tropical diseases, including malaria and even tuberculosis, although these diseases represented 12 percent of the global disease burden.

A 2012 update of that study found that the gap between the percentage of research and development of NTDs and their percentage of the global disease burden had narrowed, but there is still a long way to go to reach an adequate balance.

Of the 756 new drugs approved between 2000 and 2011, 29, or 3.8 percent, were for neglected diseases, although the global burden of such diseases was estimated at 10.5 percent. Of these, only four were new chemical creations, three of which were for malaria, but none for tuberculosis or neglected tropical diseases.

It is unprofitable for companies to create treatments for diseases with few victims, and especially for few paying victims, and no certain way to recover research and development costs. Our heart goes

out to those who suffer from these neglected diseases, and we want our Government to speed up research and development in cooperation with universities and private companies.

However, research and development takes time and effort and costs money that private companies perhaps cannot easily justify to their stockholders, including many of us, without incentives. We are here today to consider such incentives and to look at the system in place to forge successful efforts to deal with NTDs.

We have with us representatives from the National Institutes of Health, which was established to understand, treat, and ultimately prevent the many infectious immunologic and allergic diseases that threaten millions of human lives. Their government partner in the system for developing solutions to the problem of NTDs and other diseases, of course, is the Food and Drug Administration, which, among other responsibilities, is charged with protecting and promoting public health through the regulation and supervision of prescription and over-the-counter pharmaceutical medications, vaccines, and biopharmaceuticals.

Also joining us today are representatives from a network specializing in providing medicines at the lowest possible price to those suffering from NTDs, a major pharmaceutical company that develops new drugs for the treatment of diseases, rare and otherwise, and a new organization seeking to extend the benefits of proven interventions to improve the lives of the poor in developing countries.

If a solution to the gap between existing research and development and successful strategies to meet the challenges of NTDs is to be found, it will take the collaboration of organizations represented here today, who are all leaders in their field.

I would like to yield to Dr. Bera and then to my friend, Mr. Meadows.

Mr. BERA. Thank you, Chairman.

And I want to applaud you for having a series of hearings on the importance of emerging diseases and the importance of developing new therapeutics and so forth. Return on investment can't just be measured in dollars returned and dividends. Return on investment also is on relief of suffering, lives saved, and so forth, and those are clearly very important measures. And I applaud you for championing that and having these hearings.

You know, I look at this issue as a physician and have to look at it from that perspective of global health. I am excited about hearing the testimony. It is not going to be an easy challenge, elevating the consciousness. And, you know, when I look at a number of the neglected diseases—you know, the last I discussed this was when I took parasitology in medical school.

But having recently, you know, a few years ago, traveled to Nicaragua with our medical students from UC-Davis to work out there, it is very, you know—we were dealing with a dengue fever epidemic. And, you know, I am going to be curious and certainly ask some questions about developing better surveillance mechanisms, as well, so we are actually better capturing the burden of disease, especially with emerging diseases.

And, you know, I am excited about this testimony. So, again, that is the doctor in me, and that is the public health side of me.

So, with that, I will yield back. And, again, I am looking forward to the testimony.

Mr. SMITH. Thank you.

Mr. Meadows?

Mr. MEADOWS. Thank you, Mr. Chairman.

And thank each of you for coming today.

I want to echo what my colleague, Dr. Bera, just said. The chairman has been a strong, unflinching voice for those that, many times, never have a voice here on Capitol Hill.

And it is an honor to serve with you.

And I certainly look forward to hearing your testimony as we look at this. They have called votes, so I am going to keep my opening remarks brief and hear from the experts here, but thank you so much for being willing to highlight this and help us prioritize and help identify what we can do legislatively and certainly from an appropriations standpoint to make your job easier. Thank you.

With that, I will yield back, Mr. Chairman.

Mr. SMITH. Thank you very much, Mr. Meadows.

I would like to introduce our very distinguished panelists. We do have a vote under way, and I deeply apologize for the inconvenience. I thought I would introduce you and then we would be in brief recess. And hopefully several other members will come back to hear your testimony so there is no rush.

So let me introduce our very distinguished panel, beginning with Dr. Lee Hall, who is chief of Parasitology and International Programs Branch, Division of Microbiology and Infectious Diseases at the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health. He oversees multiple programs that support basic translational and clinical research in development in parasites and vectors responsible for transmission of parasites.

He has developed and provided oversight for a range of research programs and has served on numerous committees for Federal international activities, including vaccine R&D and global health. Dr. Hall has also chaired and participated in numerous scientific symposia and national and international meetings.

And our next witness will then be Dr. Jesse Goodman, who is the chief scientist of the FDA. He has a broad responsibility for and engagement in strategic leadership and coordination of FDA's cross-cutting scientific and public health efforts, including for public health preparedness and medical countermeasures. He led the 2009 H1N1 pandemic response and the medical countermeasure review for the Food and Drug Administration.

Prior to joining FDA, he was a professor of medicine and chief of infectious diseases at the University of Minnesota, where he directed multihospital infectious disease research. He has authored numerous scientific papers and has been elected to the American Society for Clinical Investigation and to the Institute of Medicine.

We will stand in brief recess and then continue with the hearing.  
[Recess.]

Mr. SMITH. The committee will resume its meeting.

And I would like to start with Dr. Hall, if you could, and then go to Dr. Goodman. Thank you.

I do apologize for that very long delay with the votes.

Let me just say, vice chairman of the committee, Mr. Weber, do you have anything to add?

Mr. WEBER. I am good to go.

Mr. SMITH. Okay.

**STATEMENT OF LEE HALL, M.D., PH.D., CHIEF, PARASITOLOGY AND INTERNATIONAL PROGRAMS BRANCH, DIVISION OF MICROBIOLOGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES**

Dr. HALL. Mr. Chairman and members of the committee, thank you for the opportunity to discuss the global and domestic public health threat of neglected tropical diseases, or NTDs, which affect millions of people worldwide and significant numbers in the United States.

I am chief of the Parasitology and International Programs Branch of the National Institute of Allergy and Infectious Diseases, or NIAID, at the National Institutes of Health. I will now present a summary of my written testimony, which has been submitted for the record.

NIAID supports research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases, including the great global killers HIV/AIDS, tuberculosis, and malaria; emerging infectious pathogens, such as West Nile virus, Ebola virus, and the novel coronavirus emerging in the Middle East; and reemerging infectious diseases, such as dengue fever.

NIAID is committed to improving public health through support of basic research, identification of drug and vaccine targets, pre-clinical testing, and clinical trials. NIAID also offers a broad array of preclinical and clinical resources for researchers to help generate the evidence necessary for the review and eventual approval and licensure of diagnostics, therapeutics, and vaccines by the Food and Drug Administration.

The World Health Organization has identified 17 infectious diseases as NTDs. These NTDs are concentrated in impoverished populations in the developing world. Among them are several well-known diseases such as dengue fever, African sleeping sickness, and Hansen's disease, or leprosy.

The global burden of these diseases is high. Over 1 billion people suffer from one or more NTDs, which exact an extraordinary human and economic cost. NTDs both result from and contribute to poverty. And they are often co-endemic with other infectious diseases, such as HIV/AIDS, tuberculosis, and malaria.

Treatment and prevention options for NTDs are currently limited. NIAID is working to strengthen the research and development pipeline for NTDs by leveraging existing clinical research infrastructure and resources. For example, the NIAID Tropical Medicine Research Centers are designed to facilitate research on the cause, diagnosis, prevention, and treatment of NTDs in countries where they are endemic.

NIAID also facilitates research on NTDs by providing access to resources, including repositories of genomic sequences and samples of parasites, transmission vectors, and hosts, as well as services for

early-stage development of NTD countermeasures. NIAID enters into public-private partnerships with a variety of organizations to share the cost and risk of developing new and improved vaccines, treatments, diagnostics, and vector control strategies.

But time does not permit me to describe all of the work we are doing in this area. I will now highlight recent NIAID-supported scientific discoveries on several important NTDs.

Dengue fever affects millions of people every year and is re-emerging as a disease of public health importance in the Americas, including endemic transmission in Puerto Rico and locally acquired cases in Florida. The disease is caused by mosquito-borne viruses that produce high fever, joint and muscle pain, and, in severe cases, death.

NIAID is funding studies on dengue fever, including development of rapid diagnostic tests, therapies, and vaccines. Recently, NIAID scientists identified TetraVax, a promising vaccine candidate that has been licensed by manufacturers in Brazil, India, and Vietnam. Phase two clinical trials to further evaluate TetraVax will begin soon in Brazil and Thailand. If successful, this vaccine could be instrumental in limiting the spread of dengue fever worldwide.

Seven million to eight million people have Chagas disease. As many as 300,000 people in the United States may have Chagas disease, most having been infected in endemic countries and then traveling to the United States. The growing pipeline of treatments for Chagas disease includes a promising drug candidate, K777. NIAID-funded basic research identified this drug. NIAID also supported preclinical studies and will continue clinical development of K777 to determine its safety and efficacy for treating Chagas disease. NIAID-supported researchers also are exploring innovative designs for Chagas disease vaccines. Such interventions are showing great promise in limiting Chagas disease worldwide.

Schistosomiasis is a chronic disease caused by parasitic worms. Though its mortality is relatively low, tens of millions of people worldwide suffer chronic and debilitating consequences. NIAID supported the genome sequencing of multiple species of worms responsible for different forms of schistosomiasis, including one that causes a form associated with bladder cancer. This genomic information has helped to identify potential cancer-causing genes in this organism as well as targets for new antiparasitic therapies.

NIAID also pursues the development of schistosomiasis vaccines. Recently, NIAID-supported researchers identified a promising vaccine candidate, and NIAID is partnering with a small business under NIH's Small Business Innovation Research Program to further preclinical development of this vaccine. Together with the Bill and Melinda Gates Foundation, NIAID sponsored a meeting this year to assess schistosomiasis vaccine candidates and provide guidance for future vaccine research.

Hansen's disease, also known as leprosy, is a chronic bacterial disease that often leads to lifelong disability. Hansen's disease has long been associated with social stigma and discrimination. Nearly 230,000 new cases of Hansen's disease were identified globally in 2010. In the United States, 213 cases were reported in 2009, including some thought to result from transmission to humans from armadillos.

NIAID research efforts on Hansen's disease are focused on early detection, prevention of nerve damage, and discovery of emerging drug resistance. Armadillos, the only animal known to be susceptible to Hansen's disease, are an important tool for research on this disease. NIAID has supported the only globally available research reagents from Hansen's disease propagated in armadillos and also supported the development of the armadillo as an animal model to evaluate the efficacy of new drugs and vaccines.

In conclusion, NIAID will continue its longstanding investment in improved diagnostics, therapeutics, and vaccines to control the global and domestic threat of NTDs by capitalizing on public-private partnerships and fruitful collaborations with academia, non-profit organizations, and industry.

Thank you for the opportunity to testify about this important issue. I would be pleased to answer the committee's questions.

Mr. SMITH. Thank you very much, Dr. Hall.

[The prepared statement of Dr. Hall follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
NATIONAL INSTITUTES OF HEALTH

The Role of the National Institute of Allergy and Infectious Diseases Research  
in Addressing Neglected Tropical Diseases

Testimony before the  
House Committee on Foreign Affairs  
Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations  
Hearing on “Addressing the Neglected Diseases Treatment Gap”

B. Fenton (“Lee”) Hall, M.D., Ph.D.  
Chief, Parasitology & International Programs Branch  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases

June 27, 2013

Mr. Chairman and Members of the Committee:

Thank you for the opportunity to discuss the global public health threat of infectious diseases, focusing on neglected tropical diseases (NTDs) that affect millions of people worldwide and significant numbers in the United States. I am the Chief of the Parasitology and International Programs Branch in the Division of Microbiology and Infectious Diseases of the National Institute of Allergy and Infectious Diseases (NIAID). NIAID is the lead institute at the National Institutes of Health (NIH) for infectious diseases and supports research and development on medical countermeasures to address these debilitating and sometimes deadly infections.

#### **NIAID OVERVIEW**

NIAID conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases. As part of its mission, NIAID must address the dynamic scientific challenges that arise from HIV/AIDS, tuberculosis, diarrheal diseases, pneumonia, and malaria; emerging infectious pathogens such as West Nile virus, Ebola virus, and the novel coronavirus emerging in the Middle East (MERS-CoV); and re-emerging infectious diseases such as dengue fever.

NIAID's statutory mandate enables us to conduct and support the research necessary to combat infectious diseases worldwide via our intramural research program and the extramural research community. NIAID is committed to discovering and moving biomedical products along the research and development pathway from "bench to bedside" through support of basic research, identification of drug and vaccine targets, pre-clinical testing, and clinical trials. Critical to this effort are NIAID's public-private partnerships with organizations including non-profits and philanthropies such as the Bill & Melinda Gates Foundation, global research and

development initiatives including the multi-sector “Decade of Vaccines” collaboration, academic institutions, and biotechnology and pharmaceutical companies, as well as coordination and collaboration with Federal agencies such as the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), and the Department of Defense. NIAID offers a broad array of pre-clinical and clinical resources to facilitate research and development partnerships in infectious diseases and to help generate the evidence necessary for FDA's review and approval and licensure of diagnostics, therapeutics, and vaccines.

#### **NIAID EFFORTS AGAINST NEGLECTED TROPICAL DISEASES**

The World Health Organization (WHO) has identified 17 infectious diseases as NTDs<sup>1</sup> and has stated that NTDs persist under conditions of poverty and are concentrated almost exclusively in impoverished populations in the developing world. Among these 17 NTDs are several well-known diseases such as dengue fever, African sleeping sickness, schistosomiasis, and Hansen’s disease (leprosy). NIAID’s mission includes research on these and other infectious diseases that have a disproportionate impact on people worldwide living in resource-poor settings. The NIH contributes the vast majority of the funds that make the United States the largest public funder of NTD-related research and development in the world.<sup>2</sup> We make this effort because the global burden of these neglected diseases is high: over one billion people currently suffer from one or more NTDs. In more than 100 countries, multiple NTDs are endemic and exact an extraordinary human and economic cost in terms of disability and death

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<sup>1</sup>The WHO defines the following as neglected tropical diseases: Buruli ulcer, Chagas’ disease, dengue, dracunculiasis (guinea-worm disease), echinococcosis, foodborne trematodiasis, human African trypanosomiasis (sleeping sickness), leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis (river blindness), rabies, schistosomiasis, soil-transmitted helminthiasis, taeniasis/cysticercosis, trachoma, and yaws (endemic treponematoses).

<sup>2</sup>G-finder survey, 2012

every year.<sup>3</sup> NTDs both result from, and contribute to, poverty and they are often co-endemic with other infectious diseases such as HIV/AIDS, tuberculosis, and malaria.

Treatment and prevention options for NTDs are currently limited, and useful point-of-care diagnostics are lacking for many of them. NIAID is working to strengthen the research and development pipeline of such countermeasures by leveraging existing clinical research infrastructure and resources. For example, the NIAID Tropical Medicine Research Centers (TMRCs) are designed to build in-country research capacity and facilitate research on the cause, diagnosis, prevention, and treatment of NTDs. The TMRCs, which are located in disease-endemic areas such as Brazil, the Philippines, Mali, and Ghana, conduct field studies and laboratory research on a variety of infectious diseases including leishmaniasis, schistosomiasis, Chagas' disease, and soil-transmitted helminthiasis. Among other advances, TMRC-supported investigators have identified proteins that may ultimately lead to new, less invasive, point-of-care diagnostics for visceral leishmaniasis, a disease that is currently diagnosed by an aspirate of the spleen and is fatal if left untreated for severe cases.

NIAID also supports research to develop improved tools for diagnosis, prevention, and treatment of NTDs by providing researchers with resources they might not otherwise be able to access. These resources include repositories of genomic sequences and samples of parasites, transmission vectors, and hosts as well as services to facilitate early-stage development of countermeasures against NTDs. In addition, NIAID enters into public-private partnerships with host country governments, academic institutions, industry, and global organizations, to leverage opportunities and share the cost—and risk—of developing new and improved vaccines, treatments, diagnostics, and vector control strategies. NIAID research and partnerships leading to recent scientific discoveries related to several important NTDs are highlighted below.

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<sup>3</sup> WHO

#### Dengue fever

Dengue fever affects 50 to 100 million people worldwide every year and is re-emerging as a disease of public health importance in the Americas, including endemic transmission in Puerto Rico and locally acquired cases in Florida. The disease is caused by mosquito-borne viruses that produce high fever, joint and muscle pain, and in severe cases, death. No specific medication exists for dengue fever, and NIAID is working to identify better ways to prevent and treat this infection.

NIAID is funding studies on effective community-based prevention programs, improved laboratory-based surveillance, rapid diagnostic tests and therapies, and the development and testing of several formulations for dengue vaccines. Recently, early-stage clinical trials of dengue vaccines developed by NIAID scientists have identified a lead candidate that was safe and stimulated a strong immune response in most recipients after just one dose. The NIAID vaccine, called TetraVax, was designed to protect against all four dengue viruses and has been licensed by manufacturers in Brazil, India, and Vietnam for production and further evaluation. Phase II clinical trials to evaluate further the safety of TetraVax and its ability to evoke an immune response will begin soon in Brazil and Thailand. If successful, this vaccine could be instrumental in limiting the spread of dengue fever worldwide.

#### Chagas' disease

Due to increasing migration of populations from endemic areas, Chagas' disease, once confined to the Americas, is now being seen on other continents. The WHO estimates that seven to eight million people worldwide are currently infected with *Trypanosoma cruzi*, the parasite that causes Chagas' disease. Over one-third of those chronically infected suffer serious cardiac,

digestive, or neurological complications. CDC estimates that as many as 300,000 people in the United States are infected with *T. cruzi*, most having acquired their infections in endemic countries, and that 300 infected babies are born each year in the United States. If detected and treated promptly, the disease is curable, so there is an urgent need for better ways to prevent, detect, and more rapidly treat this disease.

The growing pipeline of treatments for Chagas' disease includes a promising drug candidate that has been supported by NIAID. NIAID-funded basic research identified K777, a drug that inhibits an enzyme essential for parasite survival, as a promising treatment for Chagas' disease. NIAID also supported pre-clinical toxicity studies and advanced development including manufacturing, formulation, and pharmacokinetic studies, and will continue clinical development of K777 to determine its safety and efficacy for treating Chagas' disease.

NIAID basic and pre-clinical research is also contributing to efforts toward development of a vaccine against Chagas' disease. NIAID-supported researchers are exploring innovative vaccine designs in the laboratory and in animal models. These include vaccines composed of molecules called glycolipids; vaccines that activate T cells, important components of the immune response; and whole parasite vaccines that have been inactivated so they cannot cause disease but can still generate immunity to Chagas' disease. Together with NIAID's ongoing research to develop and evaluate promising candidates for therapeutics and blood-based diagnostic tests, these efforts show great promise in limiting Chagas' disease worldwide.

### Schistosomiasis

Schistosomiasis is a chronic, parasitic disease caused by trematode worms that infected more than 243 million people in 2011.<sup>4</sup> Though mortality from schistosomiasis is relatively low, tens of millions of people worldwide suffer chronic and debilitating consequences. NIAID grantees and scientists are working diligently to identify better ways to treat and prevent various forms of this disease.

NIAID provided resources enabling the sequencing of the genomes of multiple species of *Schistosoma* responsible for different forms of schistosomiasis, including *Schistosoma haematobium*, which causes a form of disease associated with bladder cancer and increased susceptibility to HIV infection. The genome sequence has helped to identify potential cancer-causing genes in this organism as well as targets for new anti-parasitic therapies.

Schistosomes are long-lived parasites that survive for many years in their host and are capable of repairing themselves when damaged. Recent basic biologic studies have provided insight into schistosomes' mechanisms of cellular regeneration that may have far-reaching implications beyond schistosomiasis. NIAID intramural studies of fibrosis, or scarring, resulting from tissue damage caused by schistosomes also provide insights for other diseases that result in harmful fibrosis, such as liver cirrhosis. NIAID scientists are partnering with several companies to study fibrosis and to develop new therapeutic strategies targeting the pathways that lead to fibrotic tissue damage.

NIAID also supports research on the organisms that serve as environmental reservoirs of schistosome parasites. For example, NIAID-supported scientists recently investigated the environmental conditions that facilitate growth of *S. mansoni* within the snail *Biomphalaria glabrata*. The parasites multiply within freshwater snails and are released into the water, where

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<sup>4</sup> WHO

people engaged in agricultural, domestic, and recreational activities are infected. The scientists found that temperature influences whether the parasites can grow within the snail. This finding contributes to understanding of how these parasites survive in the environment and may help uncover methods to prevent the spread of *S. mansoni* and other schistosome parasites.

NIAID also pursues the development of vaccines against schistosomiasis to help prevent schistosome infections. Recently, NIAID-supported researchers identified a promising vaccine candidate targeting the Sm-p80 antigen of *S. mansoni*. The Sm-p80 vaccine generated robust immune responses when tested in an animal model of schistosomiasis. NIAID is partnering with a small business under NIH's Small Business Innovation Research program to continue the pre-clinical development of this vaccine candidate. NIAID will continue to seek collaborations and partnerships to support vaccine development for schistosomiasis and other NTDs. Together with the Bill & Melinda Gates Foundation, NIAID co-sponsored a meeting earlier this year to assess the landscape of schistosomiasis vaccine candidates and to provide strategic guidance for future vaccine research and development priorities.

#### Amebiasis

Amebiasis, caused by the parasite *Entamoeba histolytica*, is acquired through contaminated food and water, and generates symptoms that range from mild diarrhea to dysentery. More than 50 million people worldwide are affected each year, leading to as many as 100,000 deaths.<sup>5</sup> Emerging resistance to the current treatment for amebiasis has generated great interest in the development of new therapeutics for amebiasis and related infections. In response, NIAID provided funding to academic partners to screen a library of FDA-approved drugs for activity against *E. histolytica*. The screen identified auranofin, a drug currently used to treat

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<sup>5</sup> CDC

rheumatoid arthritis, as a potential drug for amebiasis. Follow-up tests in animals confirmed its promise. Auranofin has been designated as an orphan drug by FDA for the treatment of amebiasis, which will facilitate its testing for efficacy in humans. NIAID will continue to support clinical development of this promising drug. In addition, NIAID also has provided early-stage research support for amebiasis vaccine candidates.

#### Trachoma

Trachoma, caused by the bacterium *Chlamydia trachomatis*, is a leading cause of blindness worldwide. The disease affects more than 20 million individuals and continues to be hyperendemic in many of the poorest areas of Africa, Asia, Central and South America, Australia, and the Middle East.<sup>6</sup> NIAID conducts and supports research on vaccines to prevent this debilitating infection. NIAID researchers developed a vaccine candidate shown to be safe and effective in an animal model. If this vaccine is efficacious in planned human studies, epidemiological models indicate that it could significantly reduce the prevalence of trachoma and could help limit the spread of the disease in endemic areas.

#### Hansen's disease (leprosy)

Hansen's disease (also known as leprosy) is a chronic bacterial disease caused by *Mycobacterium leprae* that affects the skin, peripheral nerves and upper airway and often leads to life-long disability. Hansen's disease has long been associated with social stigma and discrimination, contributing to the negative effects of this disfiguring disease. The WHO reports that nearly 230,000 new cases of Hansen's disease were identified globally in 2010. The National Hansen's Disease (Leprosy) Registry reported 213 cases of Hansen's disease in the

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<sup>6</sup> WHO

United States in 2009. This number includes cases in Texas and Louisiana thought to result from transmission to humans from nine-banded armadillos living in the region. NIAID has been supporting Hansen's disease research around the world for many years. Research efforts are focused on early detection, prevention of nerve damage, and development of genomic tools to aid in the surveillance of emerging drug resistance to current treatments. Furthermore, NIAID has been supporting the development of novel diagnostics for Hansen's disease to identify the disease prior to the development of symptoms and disability.

NIAID also works to provide critical research resources to facilitate study of Hansen's disease. Armadillos, the only animal known to be susceptible to Hansen's disease, are an important tool for research on the disease. Since 1978, NIAID has supported the only globally available contracts for the preparation of research reagents from *M. leprae* that is propagated in armadillos to produce sufficient quantities of the bacteria. These NIAID-funded efforts also support the development of the armadillo as an animal model of Hansen's disease and associated nerve damage to evaluate the efficacy of new drugs and vaccines.

#### Onchocerciasis and filarial infections

NIAID conducts and supports research on infections caused by parasitic filarial worms. These filarial infections include NTDs such as onchocerciasis and lymphatic filariasis. Onchocerciasis, or river blindness, is caused by the parasite *Onchocerca volvulus*, which is transmitted to humans via the bite of *Simulium* blackflies. The parasite is currently estimated to infect at least 25 million people, primarily in sub-Saharan Africa, leading to 300,000 cases of blindness.<sup>7</sup> Technology to detect the OV-16 antigen of *O. volvulus*, initially developed by NIAID researchers in the early 1990s, is moving forward to commercial development as a

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<sup>7</sup> CDC

diagnostic tool. Using NIAID's technology, the non-profit organization PATH will partner with Standard Diagnostics, Inc., to manufacture and distribute a rapid test to detect the parasite. PATH plans additional public-private partnerships with the WHO and others to assess the diagnostic test at field sites in Africa. Such technologies can expand our capability to detect and treat river blindness and other NTDs.

NIAID supports a broad range of activities for filarial infections, including a research resource center that provides critical reagents to the scientific community. NIAID researchers have developed improved treatment regimens for filarial infections and have advanced the molecular diagnosis of blood- and skin-borne filarial infections. In particular, NIAID researchers have worked to uncover the genetic sequence of *Brugia malayi*, one of the causes of the disfiguring disease lymphatic filariasis. The WHO estimates that 120 million people in tropical regions of the world have this disease, which can lead to elephantiasis, or disfiguring swelling of the limbs. NIAID scientists are using genetic information to map the expression of *B. malayi* proteins at various stages of the parasite's life cycle. This research contributes to better understanding of the parasite and could be used to identify targets in the parasite for new drugs or vaccines. NIAID scientists also are examining the response of the human hosts of *B. malayi* to understand the progression of the disease and develop treatments to prevent its debilitating effects. In addition, NIAID is currently supporting development of a recombinant fusion protein vaccine for lymphatic filariasis, which could help prevent many cases of this devastating disease.

NIAID scientists also are conducting clinical trials on loiasis, a filarial infection caused by the *Loa loa* parasite that affects several million individuals in West and Central Africa. While mass drug administration of deworming agents has been used to control other filarial infections,

these treatment campaigns have led to serious adverse effects in individuals infected with *Loa loa*. The goal of the NIAID clinical studies is to understand and prevent the adverse drug reactions, which will ultimately allow the restoration of mass drug administration to limit the effects of loiasis in these regions.

#### Leishmaniasis

Leishmaniasis is a poverty-related disease that in some settings is associated with increasing urbanization and associated migration. The WHO estimates that 12 million people around the world are currently infected with *Leishmania* parasites. The parasites, transmitted by the bites of infected sand flies, cause various forms of disease. Cutaneous leishmaniasis causes skin sores, and the more severe visceral leishmaniasis affects internal organs such as the spleen, liver, and bone marrow. NIAID conducts leishmaniasis research in the laboratory and at field sites in Mali, where NIAID scientists are studying cutaneous leishmaniasis in two villages endemic for *Leishmania major* infection. This field research will contribute to a better understanding of the epidemiology of the disease and immune protection against infection. NIAID also has supported pre-clinical development of a vaccine for visceral leishmaniasis, and is currently supporting a clinical trial of a leishmaniasis vaccine. In addition, funding from the Bill & Melinda Gates Foundation is supporting NIAID researchers' assessment of the efficacy of leishmania vaccines against visceral leishmaniasis. NIAID scientists also have partnered with the animal health company Merial Ltd. to develop a canine leishmania vaccine. Dogs in some regions can be an important reservoir of infection, and sand flies can transmit leishmania parasites to humans after biting an infected dog. Such vaccines, if successful, could help prevent *Leishmania* infections and limit the spread of this disease.

**CONCLUSION**

NIAID conducts critical basic and translational research on numerous neglected tropical diseases that is leading to new interventions to improve global health. NIAID will continue its longstanding investment throughout the product development pipeline from basic to pre-clinical and clinical research to tools to diagnose, treat, prevent, and control NTDs. The effective transition from basic research to product development to implementation of global infection control programs requires that we focus on research and development of improved diagnostics, therapeutics, and vaccines, and capitalize on public-private partnerships and fruitful collaborations with academia, non-profit organizations, and industry.

Mr. SMITH. Dr. Goodman?

**STATEMENT OF JESSE GOODMAN, M.D., CHIEF SCIENTIST,  
FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF  
HEALTH AND HUMAN SERVICES**

Dr. GOODMAN. Mr. Chairman and members of the subcommittee, I am Jesse Goodman, chief scientist at the Food and Drug Administration. I, too, want to thank you for this opportunity to discuss rare and neglected diseases and the progress that is being made to accelerate development of products needed to diagnose, prevent, and treat them.

Rare and neglected diseases taken together are a major public health concern. For example, in the United States, rare diseases together affect 30 million Americans. Around the world, most often in impoverished areas, over 1 billion people are affected by at least one neglected disease. As a practicing infectious disease physician, much like you have mentioned, Dr. Bera, I have personally witnessed the devastating toll of these diseases on humans infected with them.

This hearing is also a great opportunity to remind our Nation, as the chairman did, that infectious diseases know no boundaries and that threats to health anywhere are threats to everyone. For example, in recent months, we have seen outbreaks of avian flu in China and of coronavirus, a SARS-like coronavirus in the Middle East that have alarmed the world and spurred preparedness efforts here in the United States.

As you also noted, in 2010 our colleagues at CDC reported dengue, a mosquito-borne infection common throughout the world, for the very first time in United States residents who had not traveled abroad. So this is what we would consider a tropical disease now occurring in our country. Dengue is also a potential threat to blood safety, as also is Chagas disease. So there are both compelling humanitarian reasons but also U.S. national security and health reasons to work together to protect against these diseases.

For all of these reasons, we engage in close collaborations to accelerate development and availability of needed products. I also want to recognize the innovative efforts of many in industry and nongovernmental organizations such as those that Drs. Siegel, Zwane, and Hotez are going to talk about here today.

Our efforts at FDA depend on strong science and a highly interactive review process and utilize a variety of novel tools and incentives. While the need remains great, these approaches have led to important successes, particularly in rare diseases, and I am optimistic that many of them can be applied to neglected diseases.

The Orphan Drug Act provides important incentives to encourage development of drugs to treat rare diseases. Neglected diseases almost always will qualify for orphan drug designation. When drug sponsors apply for and obtain orphan drug designation, they get a number of benefits: Tax credits and grant opportunities for clinical trials, waivers of their user fees, and a period of market exclusivity if the drug is approved.

The FDA Safety and Innovation Act, passed by Congress just last year, provides additional new incentives for certain drugs intended

to treat serious or life-threatening infections, including drug-resistant infections. So we are very interested in that.

Just this week, we issued new draft guidance for industry that puts together all of our different programs for expediting development of products for serious and life-threatening conditions. They are discussed in detail in my written testimony, but one program I wanted to highlight is what we call accelerated approval, which allows approval of a drug or vaccine based on what we call a surrogate endpoint, such as a lab finding or a clinical finding, that is scientifically shown to be likely to predict an ultimate benefit on a serious outcome. This can allow much earlier assessment and approval of likely effectiveness, particularly for chronic diseases.

FDA also recognizes the importance of global collaboration and engagement. While it is a resource challenge, FDA, NIH, and CDC are very involved in global health. We played an important role working together in developing what is called the Global Vaccine Action Plan, which was recently adopted by the World Health Assembly. Lee and I both worked on that.

FDA is also a key partner with the WHO in what we call diagnostics and vaccine prequalification programs. We help them evaluate products for global use, which is particularly important in collaborative efforts to build regulatory capacity in other parts of the world. We work, for example, at something called the African Vaccine Regulatory Forum. The idea here is to help our colleagues in regulatory agencies around the world and potentially get access to countries that need products sooner.

It is also important to make sure, though, that for the products we have now that people have access to them and that they are safe. And there is a big problem with the substandard and counterfeit medicines that are common in many parts of the world. For example, malaria kills more than 600,000 people globally every year, mostly children, but compromised or fake antimalarial medicines have been found to make up 10–50 percent of the drug supply in a number of countries. Such medicines will not cure patients. Sometimes their use results in death or serious injury, and they can lead to resistant strains.

This April, FDA announced a unique public-private partnership to identify counterfeit or substandard antimalarial medications with the development and testing of a device developed in our laboratories called CD-3, or the Counterfeit Detection Device. This partnership includes the Skoll Global Threats Fund, the United States Pharmacopeia, our colleagues at NIH and CDC, the President's Malaria Initiative, as well as the Corning company.

To further promote development or treatments for rare and neglected diseases, we also strive to bridge the gap between basic scientific research and getting to products that people can use. This gap, in fact, can be filled through enhanced regulatory science, for example, the development of those surrogate endpoints I mentioned that can speed product development, or through disease models. One example, just to mention one of many, is a new model developed at FDA to develop drugs and vaccines against leishmaniasis, which infects 12 million people around the world.

Another remarkable accomplishment is the development of a new vaccine to protect people against serogroup A meningitis, which

causes devastating epidemics in Africa. Working through a unique public-private partnership, the Meningitis Vaccine Project, FDA scientists developed and made available an innovation that allowed a safe and effective meningitis vaccine to be manufactured efficiently at greatly reduced cost. As a result, over 100 million people in Africa have now been vaccinated, and that disease has been beaten back dramatically.

While much remains to be done, recent FDA approvals highlight the success and promise of these kinds of proactive approaches. For example, Sirturo, or bedaquiline, was granted accelerated approval as an orphan drug just this last December to be used as part of combination therapy for multidrug-resistant pulmonary tuberculosis when there are no other treatment options. Similarly, FDA used expedited approaches to approve Kalydeco to treat a rare form of cystic fibrosis. This drug was approved within 3 months, a near record time.

So, in conclusion, thank you for this opportunity to testify about our work with others in combating rare and neglected diseases. Your engagement and support, including the strong science at FDA, has been and will remain important in helping to solve problems in developing these needed products. I am frankly optimistic that, with so many people working together so well, we will continue to see progress.

I look forward to working with you and welcome your questions.  
Mr. SMITH. Dr. Goodman, thank you so very much.  
[The prepared statement of Dr. Goodman follows:]



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Silver Spring MD 20993

**STATEMENT OF  
JESSE L. GOODMAN, M.D., M.P.H.  
CHIEF SCIENTIST  
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DEPARTMENT OF HEALTH AND HUMAN SERVICES  
BEFORE THE  
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, GLOBAL HUMAN  
RIGHTS, AND INTERNATIONAL ORGANIZATIONS  
COMMITTEE ON FOREIGN AFFAIRS  
U.S. HOUSE OF REPRESENTATIVES  
JUNE 27, 2013  
RELEASE ONLY UPON DELIVERY**

**INTRODUCTION**

Good afternoon, Chairman Smith, Ranking Member Bass, and Members of the Subcommittee. I am Dr. Jesse L. Goodman, Chief Scientist at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services. I appreciate the opportunity to be here today to discuss FDA's role with respect to rare and neglected diseases.

There are approximately 7,000 rare diseases, generally defined by the Orphan Drug Act (ODA) as diseases affecting fewer than 200,000 people in the United States, and numerous neglected diseases that predominantly affect impoverished or disenfranchised populations of the developing world. In addition, the World Health Organization (WHO) has identified 17 neglected tropical diseases globally. While the number of people affected with each rare disease is small, collectively, rare diseases affect approximately 1 in 10 people in the United States (around 30 million Americans), and around the world, more than 1 billion people are affected by at least one neglected disease. For these reasons, rare and neglected diseases are a major public health concern. As a practicing physician and researcher specializing in infectious diseases and also trained in oncology, I have personally witnessed the devastating human face of diseases like these.

Infectious diseases know no boundaries. Threats to health anywhere are threats to everyone. For example, in recent months, outbreaks of avian influenza in China and of Middle East Respiratory Syndrome coronavirus have captured global attention and spurred preparedness efforts in the United States. Witness the risks to the United States from extensively drug-resistant TB and the disruption that a single infected traveler caused in 2007. In May 2010, the Centers for Disease Control and Prevention (CDC) reported that, for the first time, cases of dengue, the most

common mosquito-borne viral disease causing 50 to 100 million infections and 25,000 deaths each year around the world, were identified in Florida residents who had not traveled overseas.<sup>1</sup> These compelling global humanitarian needs, as well as our desire to do all we can to protect our own nation's health and national security, require us to bring the best possible science to bear against rare and neglected diseases. For all of these reasons, the needs and opportunities are enormous and FDA, working with government partners, industry, and non-governmental organizations, can help make a real difference.

I appreciate the opportunity to briefly highlight some of FDA's many activities in encouraging and speeding the development of drugs, vaccines, devices, and diagnostic tests for rare and neglected diseases.

#### The Orphan Drug Act (ODA)

ODA, passed in 1983, created financial incentives, including grants, to support the development of new drugs for people with rare diseases. Under this system, developers of promising drugs, including biologics, can apply to receive "orphan designation." Orphan designation provides three main financial incentives for the development of products for qualifying rare diseases. First, the sponsor can receive tax credits of up to 50 percent on clinical trial costs associated with studying the designated drug for that rare disease. Second, the sponsor is eligible for a waiver of the user fee associated with that marketing application. Third, if a designated drug is subsequently shown to be safe and effective and receives marketing approval, the sponsor may be eligible to receive market exclusivity for seven years. This program also benefits those affected by neglected diseases, as drugs for the treatment of the neglected diseases of the

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<sup>1</sup> <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5919a1.htm>

developing world often also qualify as orphan drugs because they affect fewer than 200,000 people in the United States.

Since its passage 30 years ago, ODA has been extremely successful. In the decade prior to passage of ODA, there were fewer than 10 drug approvals for orphan diseases that were sponsored by industry, but since passage, more than 2,800 drugs and biologics have been officially designated as “orphans,” and approximately 440 have gone on to full marketing approval.

ODA also established the Orphan Products Grant Program to encourage clinical development of products for use in rare diseases. Since the grant program’s inception 30 years ago, over \$290 million has been used to fund over 530 clinical trials. Approximately 10 percent of all approvals of products for rare diseases have been supported, in part, by the Orphan Products Grants Program. This program also can help support important work on diseases that predominantly affect impoverished populations of the developing world. Currently, for example, we are funding a study of rifapentine for pulmonary tuberculosis and a study of AQ-13 for the treatment of drug-resistant malaria.

ODA’s fundamental principles have been adopted by many other countries, most notably by the European Medicines Agency (EMA) in 1999. While FDA remains a world leader in orphan drug regulation, this international attention to orphan drugs, combined with Internet linkages among patient groups and a pharmaceutical industry without borders, has made global harmonization an important component of the work at FDA. EMA and FDA now have a joint application form for orphan designation.

FDA's Office of Orphan Products Development (OOPD) serves as a focal point for FDA's efforts to address rare diseases, including efforts on global harmonization for orphan drugs. OOPD was created shortly before the passage of ODA, and it administers the orphan drug designation program, among others. OOPD also fosters inter-agency collaboration to further the development of medical products for rare diseases and to help address the needs of rare disease patients. To facilitate this interaction, in 2012, OOPD spearheaded the creation of the FDA Rare Disease Council. This Council, which consists of representatives from all of the Centers and Offices within the Agency who work on rare disease issues, meets regularly to ensure appropriate communication, coordination, and collaboration on rare disease issues.

#### Generating Antibiotics Incentives Now (GAIN)

There is now also new support for stimulating the development of new antibiotics, which are often important for neglected diseases. FDA is implementing Title VIII of the Food and Drug Administration Safety and Innovation Act (FDASIA) entitled "Generating Antibiotics Incentives Now" or GAIN. The new law provides an additional five years of exclusivity to be added to certain exclusivity periods already provided by the Federal Food, Drug, and Cosmetic Act for certain antibacterial and antifungal drugs intended to treat serious or life-threatening infections, including serious or life-threatening infections caused by antibacterial- or antifungal-resistant pathogens (including new or emerging pathogens), and serious or life-threatening infections caused by qualifying pathogens; these drugs are designated as "qualified infectious disease products." Under GAIN, an application for a qualified infectious disease product is eligible for both Priority Review and Fast Track designation, programs for expediting drug development that are described below. As of the beginning of the month, FDA had designated 17 products (12 distinct active moieties) as qualified infectious disease products under GAIN.

The list of qualifying pathogens will be listed and revised by FDA through regulation; the proposed list of qualifying pathogens published recently and includes *Mycobacterium tuberculosis*.

Expediting Drug Development for Serious or Life-threatening Conditions

FDA has a number of programs intended to facilitate and expedite development and review of new drugs, including biologics, to address unmet medical needs in the treatment of serious or life-threatening conditions. These expedited programs help ensure that therapies for serious conditions are available as soon as it can be concluded that the therapies' benefits justify the risks, taking into account the seriousness of the condition and the availability of alternative treatment.

Fast Track designation is intended to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. Designation may be granted on the basis of preclinical or clinical data. Fast Track designation typically supports both early and more frequent interactions with FDA during drug development. In addition, sponsors can submit portions of a Fast Track marketing application as they are ready and before submitting the complete application, using a practice that is known as rolling review.

The Accelerated Approval pathway can be used to expedite the development and approval of promising therapies that treat a serious or life-threatening condition and provide meaningful therapeutic benefit over available therapies. Accelerated Approval allows approval of a drug that demonstrates an effect on a "surrogate endpoint" that is reasonably likely to predict clinical benefit, or on the basis of an effect on a clinical endpoint that can be measured earlier than effect on survival or irreversible morbidity, that is reasonably likely to predict an effect on irreversible

morbidity or mortality or other clinical benefit. One of the major goals of FDA's regulatory science efforts and collaborations is to help develop better clinical or biologic markers that can predict benefit, which can help both in drug and vaccine development and speed product approval.

FDA has long had in place a review system to ensure that the most critical medical products are reviewed on a priority basis. The goal for Priority Review applications for products that offer major advances in treatment, or provide a treatment when no adequate therapy exists, is to complete them within a six-month period, compared to the 10-month goal for standard review of other products.

The Food and Drug Administration Amendments Act of 2007 (FDAAA) granted FDA the authority, beginning in 2009, to award Priority Review vouchers to a company that submits and, after review, receives marketing approval for certain products for one of 16 neglected "tropical" diseases listed in the legislation. If transferred to apply to a blockbuster drug, the four months of earlier market access available when a Priority Review voucher is redeemed could, in some circumstances, be very valuable. Two such vouchers have been granted for two rare diseases: Sirturo for the treatment of multi-drug resistant tuberculosis and Coartem for the treatment of acute, uncomplicated malaria infections. These approvals are discussed below.

More recently, to further encourage the development of drugs and biologics for the prevention and treatment of rare pediatric diseases, FDASIA authorized FDA to award Priority Review vouchers to sponsors upon approval of certain rare pediatric disease product applications that meet specific criteria that the law enumerates.

FDASIA also established another program, intended to expedite the development and review of drugs for serious or life-threatening conditions, known as Breakthrough Therapy designation. To obtain a Breakthrough Therapy designation, a drug must be intended to treat a serious or life-threatening condition, and preliminary clinical evidence must demonstrate that the drug may provide substantial improvement on at least one clinically significant endpoint over available therapy. A Breakthrough Therapy designation conveys all of the Fast Track program features, as well as more intensive FDA guidance for an efficient drug development program, including an organizational commitment to involve senior managers and experienced review staff.

The Humanitarian Use Device Designation (HUD) and Humanitarian Device Exemption (HDE) Programs

The HDE pathway refers to a premarket approval application submitted seeking an exemption from the otherwise applicable effectiveness requirements for devices. In order to be eligible for marketing approval under the HDE pathway, devices must first be designated as a HUD. This first step, performed by OOPD, evaluates whether the device benefits patients in the treatment or diagnosis of a disease or condition that affects fewer than 4,000 individuals in the United States per year. To receive approval from FDA under the HDE marketing pathway, the device must meet certain criteria, including a determination by FDA that the probable benefits outweigh the risks of injury or illness from use of the device and that there is no comparable device. Recent examples of devices granted an HDE include the Berlin Heart EXCOR Pediatric Ventricular Assist Device and the Argus II Retinal Prosthesis System. The Berlin Heart is designed to assist pediatric patients with heart failure while they await a heart transplant. The Argus II Retinal Prosthesis System is a device implanted in the eye to improve the visual function of patients with advanced retinitis pigmentosa, a rare genetic eye disease that often leads to total blindness.

#### Diagnostic Tests for Tropical Diseases

FDA's Center for Devices and Radiological Health (CDRH) has worked with manufacturers, other government agencies, and WHO to successfully foster the development of diagnostics for tropical diseases, including those considered neglected. CDRH is an active consultant to WHO for its pre-qualification program to help assess and make available effective new diagnostics for developing countries. CDRH also provides recommendations to many sponsors through the pre-submission consulting and an interactive review process.

Close cooperation with CDC has resulted in recently cleared diagnostic tests for dengue and Emergency Use Authorization for Middle East Respiratory Syndrome. Similar cooperation with the Department of Defense and manufacturers has resulted in breakthrough rapid diagnostics for malaria. Ongoing efforts to reclassify TB diagnostics will substantially reduce barriers to the development of rapid diagnostics for TB and multi-drug-resistant TB. FDA's Center for Biologics Evaluation and Research (CBER) has also been very active in performing research and helping provide needed standards, often as part of international collaborations, to improve diagnosis of tropical and neglected diseases; for example, TB, malaria, dengue, and Chagas disease, particularly in terms of ensuring safety of our blood supply. Ongoing cooperation with CDC, WHO, and others in developing diagnostic and blood-screening tests for emerging infectious diseases will help ensure their availability when needed.

#### Other FDA Efforts to Enhance Development and Review of Products to Treat Rare Diseases

In February 2010, FDA created a position of Associate Director for Rare Diseases in the Center for Drug Evaluation and Research (CDER), which has since expanded to become the Rare Diseases Program (RDP). The RDP's mission is to facilitate, support, and accelerate the development and approval of products to treat rare diseases. RDP responsibilities include,

among others, the development of rare-disease-specific guidance, policy, and procedures, education and training programs for the review and approval of treatments for rare diseases, and enhanced collaborations with external and internal rare disease stakeholders. FDASIA included provisions for the expansion of RDP and the establishment of a rare disease liaison in CBER. FDASIA also included additional provisions promoting rare disease efforts, including, but not limited to: enhanced opportunities for interaction between FDA and rare disease patient representatives, and the aforementioned Pediatric Rare Diseases Priority Review Voucher program and expanded profit provisions for HUDs approved under an HDE.

#### FDA Rare and Neglected Disease Review Groups

In March 2010, FDA established two expert working groups, the Rare Disease Review Group and the Neglected Disease Review Group, to make recommendations on appropriate preclinical, trial design, and regulatory paradigms as well as optimal solutions to prevent, diagnose, and treat: (1) rare diseases; and (2) neglected diseases of the developing world.<sup>2</sup> FDA held public meetings in 2010 and in 2011 to discuss these issues and submitted its recommendations to Congress. These recommendations included increasing the foundation of biomedical and regulatory science to support development of products for rare diseases, increasing collaboration within and outside FDA, analyzing the history of orphan drug approvals to identify effective development approaches, and issuing guidance documents on neglected-disease-related topics.

#### Collaboration with Stakeholders

FDA has participated in a number of stakeholder conferences, workshops, and meetings to foster education and to promote the development of products for rare and neglected diseases. FDA is enhancing collaborations to increase transparency, advance science, share advice, and establish

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<sup>2</sup> Section 740 of the 2010 Appropriations Act, Public Law 111-80, directed FDA to establish these review groups.

new programs with several pertinent organizations, such as the National Organization for Rare Disorders (NORD); the National Institutes of Health's (NIH) Office of Rare Diseases Research, Therapeutics for Rare and Neglected Diseases Program, and other NIH Institutes and Centers; the Critical Path to TB Drug Regimens Initiative, patient advocacy groups; academia; and the Institute of Medicine (IOM).

The following are a few examples:

1. On March 1, 2012, FDA hosted the first ever FDA Rare Disease Patient Advocacy Day to enhance the rare disease patient advocacy community's awareness of FDA's roles and responsibilities in the development of products for rare diseases.
2. FDA partnered with NIH to conduct two important scientific workshops: The first to discuss the role of natural history studies in the development of therapies for rare diseases and the second to focus on small clinical trial design and statistical issues.
3. In collaboration with NORD, NIH, the Drug Information Association, and Duke University Medical Center, FDA presents an annual regulatory education and training program for external stakeholders, the "United States Conference on Rare Diseases and Orphan Products."
4. FDA has hosted multiple orphan product designation workshops in the United States, Europe, and India to educate and collaborate with national and international stakeholders in furthering the development of medical products for rare diseases.

In addition, FDASIA includes a requirement for a public meeting to discuss ways to encourage and accelerate development of new therapies for pediatric rare diseases.

Global Collaboration

FDA recognizes the tremendous needs and opportunities to engage globally to solve the problems of rare and neglected diseases. FDA has traditionally worked closely and interactively with manufacturers to evaluate and approve vaccines intended for the U.S. population.

However, new paradigms of vaccine development supported by the Gates Foundation and other initiatives to prevent or treat diseases, often endemic outside the United States, have provided FDA an impetus for the development of new regulatory strategies and support for resolving key regulatory science issues. In 2008, FDA issued guidance on the development of vaccines to protect against global infectious diseases. The guidance helps facilitate the development and review of such vaccines and has been extremely well-received by the global health community. FDA scientists also played an important role, along with our colleagues at CDC and NIH, in developing the Global Vaccine Action Plan, which was recently adopted by the World Health Assembly and was particularly involved in its recommendations in support of vaccine research and development.

We are also actively involved in efforts to collaborate with and, where requested, assist foreign regulators, in assessing vaccines and in helping to ensure their quality and safety. A core component of FDA's efforts in this regard is its commitment to support and complement the efforts of WHO. FDA's contribution to the WHO vaccine quality and safety goals is longstanding and was formalized in 1998, with its designation as a Pan American Health Organization (PAHO)/WHO Collaborating Center for Biological Standardization. In recent years, FDA's support has grown beyond the routine collaboration of providing expert input to WHO consultations and laboratory collaborations for international reference standards. FDA now is an active key partner with WHO in its vaccine pre-qualification program and its efforts to build regulatory capacity in developing countries.

The vaccine pre-qualification program is a service provided by WHO to United Nations agencies that purchase vaccines, providing independent guidance and advice to the United Nations on the quality, safety, and efficacy of vaccines being considered for purchase. This assistance helps to ensure that each vaccine under consideration is suitable for target populations and complies with established standards of quality. In 2007, WHO designated FDA as a “reference” national regulatory authority (NRA) for WHO pre-qualified vaccines. In 2008, FDA and WHO signed confidentiality agreements specific to communications that would be undertaken in the context of the WHO vaccine pre-qualification process. Currently, FDA’s CBER is the reference NRA for a total of eight U.S.-licensed vaccines, attesting to their safety, efficacy, and quality and facilitating their worldwide use.<sup>3</sup>

CBER provides support to multiple WHO scientific working groups and to several WHO regional vaccine networks to enhance scientific and regulatory capacity needed to ensure the development of high-quality vaccines. Specifically, CBER actively engages with WHO’s Developing Country Vaccine Regulator Network (DCVRN), a WHO-funded network of NRAs from Brazil, China, Cuba, South Korea, India, Indonesia, the Russian Federation, South Africa, and Thailand. The DCVRN builds regulatory capacity among vaccine-producing developing countries through information sharing, training, and mentoring activities. Representatives from member DCVRN countries meet on a biannual basis to gain timely information from independent experts and developers on specific issues relating to vaccine trials occurring in

<sup>3</sup> Rotavirus Vaccine, Live, Oral, Pentavalent (Tradename: RotaTeq®); Prequalified Oct 7, 2008; Influenza Virus Vaccine (Tradename: Fluvirin®); Prequalified Dec 4, 2009; Influenza A (H1N1) 2009 Monovalent (No tradename; Manufacturer: Novartis Vaccines and Diagnostics Limited), Prequalified by WHO Dec 9, 2009; Pneumococcal 7-valent Conjugate Vaccine (Diphtheria CRM197 Protein)(Tradename: Prevnar®), Prequalified by WHO Dec 28, 2009; Influenza Virus Vaccine (Tradename: Fluzone®), Prequalified Jan 21, 2010; Influenza A (H1N1) 2009 Monovalent (No tradename; Manufacturer: Sanofi Pasteur, Inc.), Prequalified Jan 27, 2010; Influenza A (H1N1) 2009 monovalent (No tradename; Manufacturer: MedImmune LLC), Prequalified Feb 25, 2010; ; Meningococcal ACYW-135 Polysaccharide, ten dose vial (Tradename: Menomunc; Manufacturer: Sanofi Pasteur), Prequalified by WHO, May 22, 2013.

developing countries and to develop institutional plans and other activities that aim to strengthen regulatory capacity.

CBER provides expert input to the WHO African Vaccine Regulatory Forum (AVAREF). WHO coordinates this forum, in conjunction with the WHO African Regional Office, to assist in defining the role of NRAs of African nations in regulating clinical trials of vaccines, in interactions with national and local Institutional Review Boards (IRB) and ethical committees, and in strengthening the capacity of the NRAs to regulate new products. In this capacity, FDA participates as expert advisors, providing guidance on how to evaluate the safety and efficacy of investigative products.

In addition to rich global collaborations in the vaccine area, FDA is actively collaborating on global drug and diagnostic efforts and has joined the Executive Committee of the International Rare Diseases Research Consortium (IRDiRC), launched by the European Commission and NIH in 2011. IRDiRC's goals are to develop 200 new therapies for rare diseases, and to develop diagnostic tests for most rare diseases, by 2020.

It is not only critical to develop new drugs, vaccines and diagnostics, but also to make sure people in need have access to safe and effective currently approved products. Counterfeit and substandard medicines are serious problems that occur commonly in Asia and Africa and have been well-documented to lead to treatment failures and deaths and, potentially, to the exposure of already-sick people to contaminants and toxins often found in such medicines. Subpotent anti-infective drugs can also foster the development of antibiotic resistance, when infections are inadequately treated. For example, malaria kills more than 660,000 people globally each year, mostly children. Compromised anti-malarial medicines, often ranging in surveys from 10-50 percent or more of the available drug supply in some countries, typically have too little or none

of the labeled active ingredients, preventing adequate and timely treatment. Anti-malarial medicines made with subpotent dosages of active ingredients will not cure patients, and they can lead to resistant strains of the parasite, making it tougher to treat malaria, even with authentic medicines.

In a recent report<sup>4</sup> commissioned by FDA, IOM concluded that making counterfeit detection technology more accessible to low- and middle-income countries would be invaluable in controlling the trade in counterfeit, falsified, or substandard medicines. In April 2013, FDA announced a unique public-private partnership to help identify counterfeit or substandard anti-malarial medicines, including falsified products, with the deployment of the FDA-developed Counterfeit Detection Device, called CD-3. The partnership includes the Skoll Global Threats Fund, the U.S. Pharmacopeia (USP), NIH, CDC, and the multi-agency President's Malaria Initiative (PMI), which is led by the U.S. Agency for International Development (USAID). The partnership will focus on evaluating and optimizing the use of the handheld CD-3 to identify counterfeit or substandard anti-malarial medicines, including falsified products, in Africa and parts of Southeast Asia, where the rates of malaria infection are high and where counterfeit anti-malarial medicines are prevalent.

The effectiveness of the tool in detecting counterfeit or substandard versions of two common anti-malarial therapies will be tested in Ghana in 2013 and 2014. The USP's Promoting the Quality of Medicines Program (PQM), with funds from USAID and PMI, collaborates with the Ghanaian Food and Drug Authority to conduct drug surveillance programs at test sites in Ghana, and the new partnership will leverage this existing infrastructure. CDC and NIH will provide

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<sup>4</sup> <http://www.iom.edu/Reports/2013/Countering-the-Problem-of-Falsified-and-Substandard-Drugs.aspx>

technical support, and The Skoll Global Threats Fund will provide additional funding for the initial testing program in Ghana.

#### The Role of Regulatory Science

Researchers have now defined the genetic basis of more than 2,000 rare diseases and identified potential drug targets for many rare and neglected diseases. However, a large gap exists between advances in basic scientific research and needed applied product development and evaluation research, a gap that contributes to the lack of real products getting to patients for many such diseases. This gap can be filled in part through enhanced regulatory science, which is the development of tools, methods, assays, standards, and models that help speed and improve the development, review, and approval of innovative products. In particular, there is a need for better approaches to assess the effectiveness of candidate drugs and vaccines for neglected diseases, and to perform more efficient and simpler clinical trials, often under challenging field circumstances. Better models of disease and diagnostics are especially needed for rare diseases. In addition, better predictive biomarkers, that is, measurements that can help predict whether a treatment or vaccine will be safe and effective and potentially do so faster than waiting for what are often long-term clinical outcomes, can be extremely powerful and helpful in developing products for both rare and neglected diseases. Examples of applied regulatory science research at FDA in these areas include development of a new model to help develop drugs and vaccines against leishmaniasis (a disease that also can affect U.S. citizens who have lived or worked in the Middle East) and research to identify correlates of protection that could predict vaccine efficacy against TB. With respect to TB, FDA has also supported several researchers to develop better tools that can predict long-term cure of TB (or, conversely, identify hidden or latent TB) and the efficacy of drug combinations.

Also with respect to TB, which generally requires treatments with combinations of drugs and where drug resistance is an urgent problem, FDA issued science-based guidance that addresses the study in a more timely and less-costly manner of several new drugs in combination, rather than studying each one separately. FDA is partnering with the Critical Path to TB Regimens Initiative (CPTR), launched by the Gates Foundation, a collaboration of industry, civil society, government, and global regulatory officials. The collaboration is working to develop needed data standards that can allow researchers to combine and evaluate data from multiple studies. A remarkable example of how regulatory science can contribute to global health is in the recent development of a new vaccine to protect people against the Serogroup A meningitis, which causes devastating epidemics in parts of Africa. Working through a unique public-private partnership, the Meningitis Vaccine Project, FDA scientists developed and made available an innovation that allowed a safe and effective vaccine to be produced efficiently and at greatly reduced cost. To date, over 100 million people have been vaccinated, and this dreaded disease dramatically reduced in incidence across what had been called the “meningitis belt.”

Strong science, whether lab-based, clinical, or involving population and statistical sciences, is also critical in supporting the kind of interactive review processes that we know can improve the odds of success in product development. This is particularly true for diseases where experience is limited or to support product developers with more limited experience. FDA scientists can meet with sponsors early in product development, even before human studies are planned, to help identify and resolve critical issues and provide input on proposed development plans. Such meetings, and continued high-quality scientific interactions, while labor intensive, are particularly critical in identifying and resolving scientific issues with respect to products for rare and neglected diseases.

Selected Recently Approved Products to Treat Rare and Neglected Diseases

The approved products now on the market that qualified for orphan product designation are a testament to the important accomplishments and successes of FDA's programs and collaborations to facilitate the development and approval of products for rare diseases. Such success stories include:

- IXIARO (Japanese encephalitis vaccine, inactivated, adsorbed) was approved on May 17, 2013, for treatment of infants, children, and adolescents two months to less than 17 years of age for active immunization, for the prevention of disease caused by Japanese encephalitis virus. Japanese encephalitis is a viral infection of the brain that is endemic in several tropical and subtropical regions in Asia and affects over 50,000 people annually.
- Sirturo (bedaquiline) was approved in December 2012, and is indicated as part of combination therapy in adults with pulmonary multi-drug resistant TB (MDR-TB); Sirturo should be reserved for use when an effective treatment regimen cannot otherwise be provided. According to CDC, there were about 100 cases of MDR-TB in the United States in 2010, and WHO estimates there were more than 310,000 MDR-TB cases worldwide in 2011.
- Coartem (artemether and lumefantrine) was approved in 2009 for the treatment of acute, uncomplicated malaria infections due to *Plasmodium falciparum*. CDC states that in 2009, there were about 1,500 cases of malaria diagnosed in the United States, almost all occurring in persons who traveled to areas with ongoing malaria transmission. Worldwide, there are an estimated 300-500 million cases each year, and most deaths from malaria occur in children.
- Anascorp (Centruroides immune F(ab)<sub>2</sub>) was approved on August 4, 2011, for the treatment of clinical signs of scorpion envenomation. Poisonous scorpion stings present a problem worldwide, and the number of stings reported yearly in the United States averages around 12,000.
- Kalydeco (ivacaftor) was approved on January 31, 2012, for the treatment of cystic fibrosis (CF) in patients age six years and older who have a G551D mutation in the CF transmembrane conductance regulator (CFTR) gene. CF is a genetic disease that affects approximately 30,000 people in the United States, and Kalydeco was approved to treat a subset of CF patients with a specific genetic mutation (approximately 5 percent of the CF population). Kalydeco is the first FDA-approved treatment for CF that addressed the underlying genetic defect in CF, and not just the symptoms and clinical manifestations.

**CONCLUSION**

FDA's multifaceted and collaborative approach to product development and evaluation for rare and neglected diseases, including regulatory science to address gaps in knowledge and speed product development, has resulted in many successes and real progress. Congressional engagement, innovation, and support of FDA programs, from ODA to FDASIA to GAIN, have made a real impact. We look forward to continuing to work with you and our colleagues in both the public health arena and private sector to address the challenges that we face. Thank you again for this opportunity to discuss rare and neglected diseases. We are proud that our nation and our Agency can make a difference, and we also know that these activities directly benefit and help ensure the health and security of the United States. I welcome your comments and questions.

Mr. SMITH. And Dr. Bera, I know, has to leave.

But thank you so much for both of you for your full statements, which will be made a part of the record. And I think it will provide some very useful guidance for this committee. And we look forward to collaborating with you going forward on how we might be helpful as a subcommittee on these issues.

Just a couple of questions. Again, I will submit many more, but because this committee was in recess for almost an hour, I won't keep you much longer.

But you mentioned the counterfeiting issue. We have heard a number of reports that artemisinin, that there are concerns that its efficacy, particularly in some parts of Southeast Asia, is becoming questionable because of wrongful use but also maybe because of some of the bogus medicines that are being proffered out there.

How big of a counterfeiting problem is it? Who are making the counterfeit drugs? Is it coming out of China? Is it coming from people in other countries, from the U.S.? Where are these drugs coming from?

Dr. GOODMAN. Well, you know, I would like to get back to you with more detailed data on issues like what we found in terms of sources of counterfeit drugs. It may, in fact, not always be apparent, but what I can tell you is it is a big problem.

As I mentioned, most of the studies were in Africa, but there are studies also in Southeast Asia that show substantial percentages of counterfeit or what are often substandard antimalarial medicines. They may contain lower amounts; they may contain other contaminants that are potentially harmful to health. Sometimes they are an antimalarial medicine but they are the wrong one, so that they may not work in an infection that would be resistant to the medicine the doctor doesn't know they are actually administering.

So this is a big problem. And our device is one approach. It can be used, you know, remotely in the field; it is a handheld device. It appears to be pretty effective, although it is undergoing field testing now.

You know, in addition, FDA has recently been working with INTERPOL and others to really crack down on Internet sales through fake Internet pharmacies and outfits. I suspect some of those fuel a lot of the bad product that is out there.

But we are really gratified that people have recognized the importance of this as a public health problem. As an infectious disease person, I will say misuse of antibiotics or use of antibiotics that are substandard or subpotent is very concerning, both because it hurts patients and it does contribute to this problem of increasing drug resistance that we are seeing.

Mr. SMITH. You note in your testimony the—or Dr. Hotez, I should say, notes in his testimony that, when you talk about stunting, that tropical diseases is also a major contributor to stunting.

And I know, you know, Congress and the administration is working very hard, as is the world, on that first 1,000 days, making sure that from conception to about the second year, children get the right kind of nutritional aid.

But how do you see tropical diseases as contributing to the stunting problem that we have seen all around the world, particularly in places like Africa and North Korea?

Dr. Hall?

Dr. HALL. Well, thank you. That is a very interesting question but a rather complex one.

I think the answer is that these tropical infectious diseases in many cases contribute to malnutrition in a variety of different ways. And, obviously, relieving or treating the infectious diseases or preventing them in the first place would be a great way to try to avoid this problem altogether. And that is really one of the things that we would want to focus on with the development of new interventions and other approaches to try to minimize the impact of these diseases.

Dr. GOODMAN. Dr. Hotez could probably shed even more light on it, but we know simple things like, you know, even improving anemia, which is common in young children who have parasites, can improve their performance in school and their learning.

There is both very obvious malnutrition and infection that occurs, but there are also much more subtle effects, you know, where, if these were our children, we would be deeply, deeply concerned, and we should be concerned more generally.

Mr. SMITH. You cite, Dr. Hall, in your testimony that the U.S. is the largest public funder of neglected tropical disease research. Who would be second? Third?

And what are we doing to try to—I mean, you mentioned, Dr. Goodman, you know, the importance of global collaboration. I will, for example, be in Istanbul on Saturday working as co-chairman of the Helsinki Commission with 300 parliamentarians from 57 countries. And while we usually work on issues related to human rights and democracy, rule of law, I have brought the autism issue there, have brought some other issues, you know, where we need to be working across—well, that is lawmakers; you obviously work with the experts.

Who are your best collaborators? And how can we be helpful, Members in the House and Senate, in promoting that?

Dr. HALL. So, again, it is very important, because of the multi-dimensional nature of this problem, to engage multiple stakeholders.

With respect to the actual rank ordering of who is first, second, and third, I would have to get back to you. I can tell you that, certainly, the U.S. Government is the largest funder for neglected tropical diseases. Certainly, other foundations, such as the Gates Foundation, have had a major role to play. And, certainly, USAID and other groups have also contributed in this area, as well as overseas agencies.

Mr. SMITH. It would be helpful if you could get back to us with that.

Dr. Zwane from Evidence Action points out that there are some 400 million children at risk, schoolchildren, without treatment for intestinal worms. How has that improved over the last—I mean, how do we reach those? I know the Carter Center works on, you know, certain parasites. Are we doing enough to rid the world of parasites and especially intestinal worms?

Dr. GOODMAN. Well, you know, I think they have, from reading the testimony, some very innovative programs and are delivering medicine and hopefully having a real impact on that.

You know, I think one of the things we are seeing increasingly in making a difference in global public health is also integrating these different efforts across multiple diseases. You know, it really becomes about people getting the care they need. I know WHO and others and Gates are really focusing on, you know, how do we deliver these interventions, of course, and how do you keep people from getting reinfected with some of these pathogens. So I think you need a holistic approach, but, as some of these efforts point out, you can make a tremendous amount of difference often with inexpensive medicines and interventions.

Mr. SMITH. Let me just ask a few final questions.

Are there gaps with USAID funding, funding that Congress has provided? You know, I know that OMB goes through everything, goes through your agencies to scrub and make final recommendations. But if you had a wish list, how much more do you think would need to be added in order to really even push the envelope even further?

And I would say parenthetically, 20 years ago I contacted WHO and asked their tropical disease side, what would it take, and actually got an amendment passed that tried to get us on a glide slope to meeting some of those figures.

What would it take? I mean, you know, we can work in a bipartisan way. I believe Dr. Bera and I have talked, you know, previously about filling in those gaps. How do we do it?

Dr. GOODMAN. Well, you know, I think for USAID and some—

Mr. SMITH. That is not to take anything away from the great work you are doing. Please don't—

Dr. GOODMAN. Right, right.

Mr. SMITH. I underscore that with exclamation points. It is a resourcing problem.

Dr. GOODMAN. You know, I was going to say, I think for the agencies, you know, delivering some of these medicines and care, they would be the best to answer, you know, how they feel they are doing. You know, I know the whole Federal budget is tight, and we all have a lot of obligations and responsibilities.

From the FDA point of view, there are certainly areas that, were there resources available, we could potentially build out. You know, those would include enriching our continuing collaborations with regulatory agencies around the world. It is sort of like, if you help people do something, then they can take that on themselves.

I think also in this applied science space, where we could develop better ways to develop and test these drugs more efficiently and work very interactively with industry, you know, those are things that are, to some extent, resource-dependent.

I will say we feel this is very important. And a lot of our staff work on these issues, you know, because it means a lot to them, even if they may not quite have the bandwidth.

Dr. HALL. So, again, this is a very important issue. And I think that having hearings like this that highlight this issue are important, because it is really crucial to try to engage multiple stakeholders because the solution is not going to come necessarily from one group or one agency. It is going to be a very collaborative process, working with a wide variety of groups. And there are many different aspects to this problem.

So it is very difficult to say in a short statement what would be required. I think that this is something that would require the engagement of many groups, and it would require a considerable amount of thought.

Mr. SMITH. If you could give it some thought.

Again, I will give you the example of the way we do business. When I was chairman of the Veterans' Affairs Committee, I became very, very aware that homeless veterans were not getting the kind of help they need, and it was a resourcing problem. I met with the VSOs, they gave some great ideas—American Legion, all the others.

But I sat down with the people at the VA who really do the homeless veterans programs, and I said, what works? Tell us what we can do. And I wrote a major landmark law called the Homeless Veterans Assistance Act of 2001, which, while it hasn't solved the problem, it has certainly made a major dent in it.

We would love to be helpful, you know, on this subcommittee if we just had a better roadmap as to how to proceed. So consider this an engraved invitation. I can't guarantee success, but we can build on your already very considerable success.

Dr. GOODMAN. I am sure, you know, we would be eager to work with you or comment on any ideas that you develop. You know, there are some roadmaps out there that may be of interest to you, like the Global Vaccine Action Plan we discussed in that area.

Mr. SMITH. Thank you.

One last question. You know, you mentioned new tools and incentives, and I think that is what we want to build on, as well.

You know, we have been admonished by the experts for some time now, you, of how important it is not to overuse antibiotic treatment, how resistance is growing. We have had hearings in our subcommittee on the tuberculosis extreme as well as multidrug-resistant.

Is there anything you might say about probiotic use and the lack of probiotics in people's gut, where the immunity is so important? Are we emphasizing that enough?

Dr. GOODMAN. Well, there has been incredibly exciting science in the last 5 years, I would say, particularly, as we have been able to now just take the contents of any environment or any part of the human and we find this entire world of microbes there. So we have realized that we are not at war with microbes. Some of the ones you discuss, you know, clearly they infect a person, it is a bad situation. But much of our health seems to depend on a normal balance of microbes.

For example, recently this has affected treatment of an antibiotic-associated diarrhea called clostridium difficile, which is a complication of antibiotic treatment. And it turns out that restoring the normal bacteria to the intestines can help in the majority of cases of severe disease.

So what we are learning is, many things humans do, including antibiotic treatment, which may have a very good purpose, may have other effects that are more complex. And so we are just getting the tools to study this. I think it is an area that we are going to find, as we understand better how to restore or nurture our nor-

mal microbiome, we may find innovations that really help in treatment of disease.

I think a lot of the reports and, to some degree, you know, products that are out there are not as well-substantiated yet, so we don't know yet what the role is. But I would be surprised if in some diseases, just like antibiotic-associated diarrhea, there isn't going to be a really important role for that.

Dr. HALL. Yes. And I would just add to what Dr. Goodman said, that we do have this large program at the NIH, the Human Microbiome Project, that is providing incredible insights into how the microbiome works and that, as we move forward with this, this will hopefully open up many new opportunities to not only better understand what is going on but to develop novel interventions that would allow us to better intervene in a number of these diseases and in some cases to do things—for example, convert vaccines that are delivered intramuscularly to perhaps an oral formulation, things like that—as we understand better how to capitalize on this new understanding.

Mr. SMITH. Thank you so much.

Mr. Weber?

Mr. WEBER. Thank you, Mr. Chairman. You actually asked one of the questions I was going to ask.

I think it is interesting—I will kind of back into my questioning, if I may. Dr. Goodman, you said the last 5 years we have discovered an entire world of microbes, I think you said. I guess it is kind of like what science fiction used to say, we are not alone in this world, and you all are discovering that.

You made a couple of statements early on, Dr. Hall. You said—or let me ask you a question from your testimony, actually. You talked about the rise of diseases. Is there any way to track or do we have guesstimates of how much of that disease is coming into our country through the immigration road? Is there any thought or discussion given to that?

Dr. HALL. That is something that I don't really feel I could comment on. It is really something that perhaps the CDC would be in a better position to comment on.

Mr. WEBER. Okay. Are you aware, do they track that in any form, do you know?

Dr. HALL. They do track—I don't know the extent to which they track this in particular. But they do have an interest in a variety of diseases, and they are tracking a variety of different ones.

Mr. WEBER. Okay.

Do you have knowledge of that, Dr. Goodman?

Dr. GOODMAN. For certain diseases, you know, which don't normally occur here, there is very good reporting—you know, for example, malaria. Typically, it is acquired in another country, and then a traveller comes here not knowing he has it and develops illness. For other diseases, you know, there is a focus on the health of people who may have moved here. And, certainly, when people come from other countries, they may have some of these infections.

Also, as Dr. Hotez may tell you, many of these infections can be acquired here, as I mentioned, even with dengue now. It is not really communicable from person to person, but now there are mos-

quitos in our southern climates carrying these diseases so that the diseases are coming to us, not even necessarily through people.

Mr. WEBER. Okay. And you mentioned that the dengue and the Chagas disease, I think is what you call it—I am a blood donor. I try to be. Like the Congress, I can't do it every 8 weeks for some reason. But I have AB-blood, which less than 1/2 of 1 percent of the American population has. Now you know what is wrong with me.

Dr. GOODMAN. That is what is right.

Mr. WEBER. You made the comment that dengue and Chagas disease is spreading to blood safety?

Dr. GOODMAN. Well, there is a potential. You know, actually, there has been very little documented spread for Chagas—

Mr. WEBER. Okay.

Dr. GOODMAN [continuing]. And virtually none for dengue. But we are aware that people—dengue, in certain ways, is like West Nile virus was, and so we want to be prepared. You know, so there may be a period where the virus is in the blood and could be transmitted, so we want to be prepared if that becomes a problem.

With respect to Chagas disease, people can be infected for years without being aware of it, and that is the reason for that concern.

But right now I don't think there is an active problem with the blood supply.

Mr. WEBER. Well, I get asked that that question every time I give blood, you know, have I ever been diagnosed with this and—

Dr. GOODMAN. That is why. So it is really in this stage of trying to be vigilant, do surveillance, and prevent there from being problems, develop tests in case they are needed.

Mr. WEBER. Okay. And then you also said the Orphan Drug Act—and, as a new Member of Congress, I am not really familiar with that—you said that neglected diseases almost always qualify. Elaborate on that.

Dr. GOODMAN. Well, the major cutoff point for the Orphan Drug Act, as I understand it, is that, to be eligible, a disease has to affect less than 200,000 people in the United States.

So when you think about things like Chagas disease or, certainly, rabies or many of the things on that list, while they may be extremely common if you were in Asia or Africa, they are rare here. So a sponsor developing a drug for one of those neglected diseases would usually be able to take advantage of the benefits of the Orphan Drug Act, which include, you know, grants for research, as I mentioned, additional exclusivity, which can be financially rewarding to companies.

Mr. WEBER. Right. And so if it is less than, say, 200,000—that was one of the questions I had.

How often—you track the number of infections to the best of our ability.

Dr. GOODMAN. Yeah.

Mr. WEBER. How often are those numbers updated? Is it every month? Every 6 months? Every quarter?

Dr. GOODMAN. It is a question that depends, to some degree, on the resources available to track them and how they are viewed in terms of as a public health threat in the United States. CDC has overall responsibility for that, and, you know, I am sure we could ask them to get back to you with some of that information.

But our country does have probably one of the strongest infectious disease surveillance systems in the world, and it really helps us know. But there is a balance between requiring reporting and not being too burdensome. So, for some diseases, we probably have extremely good idea of numbers, like tuberculosis. For others, we may have less certainty, particularly if they often have no symptoms, like Chagas disease, for example.

Mr. WEBER. Let's take that question and let's extrapolate it overseas to follow up on kind of what the chairman was saying, who is number two, who is number three. The United States has a great track record, and you mentioned the Gates Foundation helping, and you mentioned some others, USAID I think.

But when we are tracking in other countries and we see an outbreak, how often are those numbers updated?

Dr. GOODMAN. Well, I think a very positive thing that, you know, I have seen even in my time in the government and in the last 10 years as we faced various influenza threats, for example, is the world has become much more aware of the importance of surveillance of infectious disease, there is much more international collaboration—

Mr. WEBER. Okay. Is there an FDA counterpart in China or Japan or Russia?

Dr. GOODMAN. Well, in this case, it would be more, you know, the CDC counterpart for disease surveillance. But, yes, there are in many of these countries. And—

Mr. WEBER. They communicate back and forth?

Dr. GOODMAN. Yeah. In many cases, there are scientific exchanges between our governments and theirs. There is also something called the Global Health Security Initiative, which involves some of the U.S.'s major allies, that shares information on these diseases.

So there is much, much more than there used to be. But there also is a concern, as you can imagine, in many countries of the world that are very resource-poor; they may not have either the resources or, in many cases, the expertise to devote to disease surveillance. So there is a lot of recognition of the importance of trying to, wherever we can, improve surveillance in those areas too.

Mr. WEBER. And that was one of my questions. Would you agree that developing countries that maybe don't have an infrastructure, maybe not as much clean water, maybe not as good health care, that part of helping to stabilize them, if you will, in some fashion, is going to be training and equipping them even at that basic level?

Dr. GOODMAN. Absolutely. Absolutely. You know, knowing what is going on—even in the United States, if you think about health of our communities, if you don't understand fully and you don't have good data about the diseases people have, you know, how do you track changes, how do you make people healthier?

So that disease surveillance is very important all over the world, and the same with the other kinds of expertise. You know, there are many countries throughout the world that have made tremendous progress, and there are a lot of exciting models for how to improve things in those areas.

Mr. WEBER. Well, I am just wondering how much of our focus—it is kind of like the old saying, you give a man a fish, you feed

him for a day, you teach him to fish—we can give them vaccines, but can we help with their infrastructure and their training so that the underlying—I won't say problem—the underlying situations that keeps them from being maybe as healthy and as knowledgeable as they could—might help.

Let me shift gears for just a minute. You made the comment you are trying to build regulatory capacity around the world and you are trying to get, I think, access to the products sooner. What is that time frame, when a product is begun and studied and put out? Is that typically 3 months? Three years?

Dr. GOODMAN. You mean for other countries?

Mr. WEBER. Well, for us to get a product—well, your comment was you were trying to build regulatory capacity around the world and get access to the products sooner.

Dr. GOODMAN. Well, so what I am thinking about, for example, is, what if there is a lifesaving intervention that could help people, you know, who are primarily in other places? You know, there are many factors in having access to that. There is cost; there is their ability to deliver it.

But one of them also is that, you know, really, FDA or the European medicines agencies, you know, which are relatively well-resourced and experienced, you know, in reviewing products, we don't approve products for use in other countries, rightly so. You know, countries have their autonomy and need to be sure that their assessment of a product for use in their country is science-based and satisfies their needs.

So one of the things we have tried to do through WHO is support both countries and regions who are trying to develop that regulatory capacity.

Mr. WEBER. Do you find generally that most of those countries—how do you say it—they rely on us, rely on the FDA's assessment? Or do they pretty much want to do their own testing?

Dr. GOODMAN. You know, as you can imagine, there is incredible diversity. A lot of countries look to FDA and also to our European colleagues, you know, as having expertise and really may not rely on but use our reviews as part of the basis for their decisions.

But many of them are coming together also in regions, for example, in Africa and in the pan-American region, to build their own regulatory capacity and to cooperate with us, you know, almost as partners and equals. We have had situations where we can learn from work they are doing—for example, in Latin America, the monitoring of the 2009 influenza outbreak. Studies of vaccine safety for other vaccines have been performed there.

So it is really a win-win solution when we build that capacity. You know, of course, people have to want that and invite us, and we have to provide it in a way that is useful to them, which may be different than what we do.

Mr. WEBER. Right.

Okay. That is all my questions. Thank you, Mr. Chairman.

Mr. SMITH. Thank you very much.

Just one final question. And, again, thank you for your patience.

Dr. Peter Hotez, as you know, the president of the Sabin Vaccine Institute, in his testimony will say that NTDs are the most impor-

tant diseases you have never heard of. He talks about how well over 1 billion people suffer from it.

But he has a very important part in his testimony where he talks about a problem that is coming to light with regards to female genital schistosomiasis that mal-affects some 100 million girls and women in sub-Saharan Africa, and makes a point that one thing very concretely that we might do—you might do, we might do collectively—is to establish a center of excellence for NTDs, that the time has come for such a center.

Again, I would note parenthetically, back in 1998, I am the author of the Combating Autism Act. It took me 3 years to get it passed. We put it as Title I of the Children's Health Act in 2000. And then, just most recently, I was the author of the reauthorization for 3 years.

And there was pushback initially from some within the agencies about a center of excellence for NIH and for CDC. I noted at the time that we were spending \$287,000 per year straight line for 5 years at CDC on autism, even though there was a huge seeming epidemic, developmental epidemic, arising.

And I am wondering if perhaps it might be time for a center of excellence for NTDs. What are your thoughts?

Dr. Hall?

Dr. HALL. Well, again, I think that product development is a very complex area. It requires a multidisciplinary approach. And it is really important to bring together groups that have a variety of different expertise. And that is one of the things that really makes for successful product development.

At the NIH, we have tried a variety of different methods, and what we have found works is that you have to have a spectrum of activities that run from basic research through to preclinical target validation, preclinical research, translational research, and then on to clinical and field evaluation, and that when these parts are working together well, then you really are able to accelerate the development of products.

Our current mechanisms are actually quite flexible, responsive, and timely. And just to give you an example, about a third of the global antimalarial drug pipeline came out of NIH-supported research and has been handed off to partners. We have supported multiple products for NTDs, including vaccines, drugs, and diagnostics. And we worked with a wide variety of different technologies, different companies, and different entities to try to accelerate that.

And just to build on this question about screening donated blood that came up earlier, in fact there are at least two blood tests for screening the blood bank, the blood supply, and at least one of those came out of NIAID-supported research.

So our feeling is that a strong multidisciplinary approach with a variety of mechanisms and technologies is really very helpful in terms of bringing these things forward.

Mr. SMITH. Thank you. I do have a lot of questions but, in the interest of time, will submit them.

Thank you for your tremendous leadership, and we look forward to working with you.

Dr. HALL. Thank you.

Dr. GOODMAN. Thank you very much.

Mr. SMITH. Now we would like to invite our second panel to the witness table, beginning with Dr. Peter Hotez, who is the president of the Sabin Vaccine Institute and leads the Texas Children's Hospital Center for Vaccine Development based at the Baylor College of Medicine in Houston, Texas. He is also the founding dean of the new National School of Tropical Medicine at Baylor College of Medicine.

His academic research focuses on vaccine development for a wide range of neglected tropical diseases around the globe as well as studies to increase awareness about the neglected tropical diseases in developing countries and in the United States. Dr. Hotez created the Sabin Vaccine Institute Product Development Partnership and was instrumental in creating the Global Network for Neglected Tropical Diseases.

We will then hear from Dr. Jay Siegel, who is the chief biotechnology officer and head of scientific policy at Johnson & Johnson. He is actively engaged in R&D leadership and in policy development at the national as well as international levels with regard to regulatory and scientific issues.

Dr. Siegel joined J&J in 2003, and prior to that he worked at the FDA's Center for Biologics Evaluation and Research, where he worked to regulate the biotechnology industry. He has authored numerous publications in the area of clinical trials, design, biotechnology, immunology, and drug development policy.

J&J submitted written testimony on April 20th at one of our hearings back on drug-resistant disease, and we are very grateful for that but also even more to have you here today.

We will then hear from Dr. Alix Zwane, who is executive director of Evidence Action, a new organization working to scale proven interventions to improve the lives of the poor in Africa and Asia, and the Deworm the World Initiative, which supports the scaleup of school-based deworming programs worldwide to improve children's health, education, and long-term development.

She previously worked for the Bill and Melinda Gates Foundation, where she led the Water, Sanitation, and Hygiene Initiative strategic planning process and their measurement and evaluation plan. Dr. Zwane worked at Google.org to develop and manage health and water issues, as well.

Dr. Hotez?

**STATEMENT OF PETER J. HOTEZ, M.D., PH.D., PRESIDENT,  
SABIN VACCINE INSTITUTE**

Dr. HOTEZ. Thank you very much, Chairman Smith. I appreciate the opportunity. Congressman Weber, thank you so much. It is a pleasure to come before you today to discuss the importance of U.S. Investments in neglected tropical diseases. But what I also want to do today is make you aware of a very troubling and disturbing problem of neglected tropical diseases in Texas and in the southern United States that we have not been aggressively addressing.

A copy of my written testimony has been submitted for the record.

As you pointed out, I serve as president of the Sabin Vaccine Institute, which has just celebrated its 20th anniversary, and also

founding dean of the new National School of Tropical Medicine at Baylor College of Medicine in Houston which was launched in 2011. I am a pediatrician and a scientist who has devoted my entire life to developing innovations to combat neglected tropical diseases (NTDs) including new vaccines and drug packages.

You are absolutely right; these are the most important diseases you have never heard of. Today, virtually every person on our planet who lives in extreme poverty, lives below the World Bank poverty figure of \$1.25 a day, the bottom billion, as they are sometimes called, and suffers from one or more of those neglected tropical diseases.

A couple of people brought up the problem of intestinal worms, such as hookworms, which feed on blood and actually rob children of nutrients. The problem with stunting is that instead of feeding the kid, you are feeding the worms. These are the leading causes of growth stunting on our planet.

What is even worse is intestinal worms like hookworms have been shown to reduce childhood intelligence and cognition. And now the economists have come in from the University of Chicago to show that chronic hookworm infection can reduce future wage earning by 40 percent.

So this is why these diseases are so devastating: Not necessarily because they are killers; they are trapping people in poverty. They actually thwart future wage earnings. So getting rid of hookworms, it turns out, may be one of the most cost-effective ways to lift the bottom billion out of poverty.

And it is not just children. More than a quarter of pregnant women in sub-Saharan Africa have hookworms and go into labor and delivery with profound anemia and risk for severe morbidity or even death. As my obstetrician colleagues point out, it is not that African women bleed more during childbirth, but it is that they begin the delivery process with two strikes against them because they start out with so little blood because they have hookworms. These are not rare diseases. One-quarter to one-third of pregnant African women have this condition.

But an even more or equally concerning problem that I also want to tell you about in Africa today before I move to the U.S. is what is coming to light is a manifestation of snail fever known as female genital schistosomiasis, a parasitic infection that produces bleeding ulcers on the cervix, the uterus, the lower genital tract. It causes bleeding, pain, terrible shame, terrible stigma.

This is not a rare disease—it impacts 100 million girls and women and this may be the most common gynecologic condition of girls and women on the African continent. Now, can you imagine if we had 100 million girls and women in the U.S. With female genital schistosomiasis? As a society, we would never tolerate it. But because it affects girls and women who live in abject poverty, most often in remote parts of rural Africa, they go untreated.

Now, what is very equally concerning is the fact that this female genital schistosomiasis is associated with a three- to four-fold increase in horizontal transmission of HIV/AIDS. It may be Africa's most important co-factor in the AIDS epidemic, and you have never heard of it. So we need to change that.

Just a couple of other final examples to wrap up the global situation is the stigmatizing effects of cutaneous leishmaniasis, also known as Aleppo ulcer or Aleppo evil. It is now affecting more than 100,000 people living in Syria who have fled to refugee camps. It has also been a problem among our U.S. troops in Iraq and Afghanistan. But in the Middle East, again, it is girls and women who are permanently scarred and rendered unmarriageable or not allowed to hold their children as a result of this neglected tropical disease.

And the point I keep wanting to emphasize is the magnitude. Everything I say is multiplied times 100,000 or, in some cases, 100 million—it is just an enormous amount of suffering.

So every year we are learning about these new tragedies from neglected tropical diseases, many of which are counterintuitive. Our recent study found that these diseases, for instance, hit Catholic-majority countries particularly hard, such as Chagas disease in Honduras or hookworm and schistosomiasis in Angola and the Philippines. It is no accident.

You know, these diseases are—you all know about emerging infections. This is what gets the newspapers' attention, right? Avian flu or H7N9. These diseases are just the opposite. These have been around forever. These have plagued humankind for centuries. I like to call them the biblical diseases, because you can find detailed descriptions of these diseases in the Bible, and also in the Talmud, the Vedas, the writings of Hippocrates, and Egyptian papyri. That is how long they have been around.

Now, the good news—and there is some good news to this story—is that we can do something about seven of the most common neglected tropical diseases for a ridiculously low cost, approximately 50 cents per person per year.

So what happened was, in 2005 and 2006, with colleagues from the United Kingdom, we put forward this concept of a rapid impact package in 2006, which is now being scaled up through the support of the United States Agency for International Development, USAID, and with advocacy from our Global Network for Neglected Tropical Diseases, which is a Sabin initiative. And thanks to generous drug donations from leading pharmaceutical companies like Johnson & Johnson, a unique and innovative public-private partnership has been created to efficiently and cost-effectively address neglected tropical disease control.

And the cost is, again, ridiculously modest, partly because we are leveraging more than \$4 billion worth of drugs that have been donated from the pharmaceutical industry. And more than 250 million people have been treated. This may be one of the world's largest public health interventions.

So, I don't want to leave today without saying that it is extremely important that you continue support for USAID's Neglected Tropical Disease Program. It is very low-cost. It is important that we at least match 2013 levels to deliver these medicines to people who need them the most so they can benefit from these treatments.

While these diseases are incredibly potent, the U.S. Government has actually been the lead in supporting these neglected tropical disease packages; the U.K. has now also provided support. We also think the private sector needs to step up, as well as some of the

other G-20 countries. We established the Global Network for Neglected Tropical Diseases and our END7 campaign to raise awareness about these diseases.

And, if I may, I would like to show a 1-minute video about these conditions.

[Video shown.]

Dr. HOTEZ. This is lymphatic filariasis, or elephantiasis. That is 120 million people with lymphatic filariasis, 800 million with roundworm, 700 million people with hookworm. Notice the numbers add up to more than 1 billion. People are polyparasitized. They have multiple diseases at the same time.

Now, given the recently revealed links between snail fever and female genital schistosomiasis and AIDS, as well as malaria and hookworm. You've asked, where do we go from here? Well, I think version 2.0 includes looking at better links between the USAID Neglected Tropical Disease Program and other U.S. global health investments, such as PEPFAR or the Global Fund. So, for instance, PEPFAR doesn't actively have a program to link it up with female genital schistosomiasis, even though it may be the most important co-factor in the AIDS epidemic. So we need to do a better job linking.

But all of them are extraordinary programs. The Global Fund to Fight AIDS, TB, and Malaria needs to do the same thing. And the few times they have done it, the results have been extraordinary. Because Global Fund supported lymphatic filariasis, one of those diseases in Togo, it has now been eliminated in Togo. So there is incredible power that could be brought to bear by bringing PEPFAR and the Global Fund into the equation.

We also need to encourage governments beyond the U.S. I think it is unfair that we put all of the burden on U.S. taxpayers. Our country has been more generous than any other, but we need to bring in some of the other G-20 countries. What is Indonesia doing about this? What is India doing about this? What is China doing about this? China is investing billions of dollars in sub-Saharan Africa, and, so far, not a penny is going to neglected tropical diseases.

So action item number two is we have an exciting new Office of Global Health Diplomacy in the State Department. What is going to be the role for them? Well, I think one of them would be putting diplomatic pressure on all the G-20 countries to step up support for NTD control and elimination.

So we are finding a lot of these NTDs among G-20 countries. One of the surprising findings that we have made in the last 2 years is that, while we think of these diseases exclusively as sub-Saharan African diseases, in fact, the lion's share of most neglected tropical diseases are in the G-20 countries, the 20 wealthiest economies. It is the extreme poor living in the wealthiest economies.

And that includes the United States. We have 20 million people now in the U.S. that live in what is called extreme poverty; that is a standard deviation below the poverty line. It also includes now—and this is an amazing fact—1.46 million families, with nearly 3 million children, who live on less than \$2 a day. So, for the first time to my knowledge, we are taking that same global bench-

mark for global poverty and applying it to the United States, especially in the southern United States.

At our National School of Tropical Medicine based in Houston, what we have done now is to take that global health lens and turn it inward. Beginning in 2008, I identified a group of neglected tropical diseases in the U.S., mostly in the southern U.S. and particularly in Texas, that is affecting 5 million Americans.

So 5 million Americans have one or more neglected tropical diseases. It includes 2.8 million African-Americans with toxocariasis, a larval worm infection of the lungs and the brain that has been now linked to pulmonary dysfunction and asthma, developmental delays, and seizures; millions of African-American women with trichomoniasis that has been linked with HIV/AIDS; hundreds of thousand of Hispanics with Chagas disease, a debilitating heart condition.

To get to your question, Congressman, we have found now in Texas that 1 in 3,500 blood donors are seropositive for *trypanosoma cruzi*, or have Chagas disease.

Now, for the most part, extremely poor people and people who live under extreme conditions don't give blood. So this is an extreme underestimate of the number of true cases of Chagas disease. Some estimates say 200,000 people with Chagas disease are in the State of Texas. That is probably a little high. We are finding it now possibly among the homeless in Houston. We are finding it widespread.

Another key point to mention is, one, they are not rare diseases; two, everyone thinks this is a problem of immigration. Immigration may be a part of it, but we believe there is actual transmission of these diseases going on in the U.S.

The link is poverty. There is something about people living in extreme poverty, whether it is in the Third or Fifth Ward of Houston, whether it is in south Texas. This is what seems to be predisposing it.

We have a dengue problem in Texas. We know it is widespread in south Texas. We believe now that it might have emerged in Houston, as well. We have had the *Aedes aegypti* mosquito here for a long time. It is occurring primarily in the poorest parts of Houston.

Why the link to poverty? Why is dengue linked to poverty? We don't really know. You know, when you drive through some of these areas, you see people without window screens, without air conditioning, or they will have those box-like air conditioners that are very porous. Maybe that has something to do with it.

Our scientists at the National School of Tropical Medicine have identified a new syndrome linked with West Nile virus. Everyone knows about the very rare condition of neurologic involvement. We are finding maybe 10, 20 percent of people with West Nile are getting chronic renal disease, something that we didn't know about before.

So this is a problem that we really need to take on. What do we do about it? We are not doing programs of active surveillance looking for these diseases. These problems are being largely ignored. We are not really doing anything to investigate how these diseases are transmitted. Partly because the CDC has been terribly under-

funded, they haven't had the resources to really take this on. So we are trying to fill in the gaps and are doing this at the National School of Tropical Medicine.

And, this gets to this whole idea of creating a "Center of Excellence." I think the Center of Excellence concept has to take on neglected tropical diseases abroad among the bottom billion, taking on the biblical diseases, but we also need to have that "Center of Excellence," address the at least 5 million Americans living in extreme poverty in the United States with these NTDs.

A fair amount of effort is going to be needed for research and development. That is one of the things that we are doing at our Sabin Vaccine Institute, which is a nonprofit product development partnership, a PDP, that will make the products that the drug companies can't make or won't make. Not that the drug companies are bad guys. They have been amazing, incredibly generous in donating medicines. But it is another leap of faith to ask them to go back to their shareholders and ask them to invest tens of millions of dollars for R&D.

That is what we are doing at Sabin Vaccine Institute and our National School of Tropical Medicine. We have a low-cost hookworm vaccine that is in phase one trials; a schistosomiasis vaccine that is moving into phase one trials through support from Dr. Lee Hall, through the National Institute of Allergy and Infectious Diseases.

And now we are developing new vaccines for Chagas disease and leishmaniasis through support from the Carlos Slim Health Institute and a man named Len Benckenstein, through the Southwest Electric Energy Medical Research Institute. So we are very excited about being able to advance these products into clinical development.

So we do urge you to vigorously support private-public partnerships, product development partnerships, that will develop not only the developing world but will ultimately lift people out of poverty.

Mr. Chairman, Congressman Weber, Congressman Stockman, this concludes my testimony. Again, I thank you for your interest in furthering U.S. engagement in neglected diseases and the opportunity to address you this afternoon. And, of course, I am always happy to answer questions. Thank you.

[The prepared statement of Dr. Hotez follows:]

**TESTIMONY**

**Peter J. Hotez MD PhD  
President, Sabin Vaccine Institute  
Dean, National School of Tropical Medicine at Baylor College of Medicine**

**“Addressing the Neglected Diseases Treatment Gap”**

**Subcommittee on Africa, Global Health, Global Human Rights, and International  
Organizations  
Committee on Foreign Affairs  
United States House of Representatives**

**June 27, 2013**

Chairman Smith, Ranking Member Bass, and Members of the Subcommittee, it is my pleasure to come before you today to discuss the importance of U.S. investments in neglected tropical diseases (NTDs), the work of the Sabin Vaccine Institute (Sabin) and its academic partner, the new National School of Tropical Medicine at Baylor College of Medicine, and suggested ways the U.S. government could refine its strategy to more effectively help those who suffer most from these devastating diseases.

My name is Peter Hotez and I serve as both the President of the Sabin Vaccine Institute, which this year celebrates its 20<sup>th</sup> anniversary, and the founding Dean of the National School of Tropical Medicine at Baylor College of Medicine that was launched in 2011. After obtaining my MD and PhD degrees from the Rockefeller University and Weil Cornell Medical College, I have devoted the last 25 years my life to developing innovations to combat the NTDs, including new vaccines and drug packages. Together with colleagues in the United Kingdom we first put forward the concept of NTDs in the biomedical literature in 2005 and shaped the science and the policy leading to deployment of rapid impact packages of donated medicines for NTDs for more than 364 million people in 25 countries across the developing world through the support of the U.S. government and the U.S. Agency for International Development (USAID).

I like to call the NTDs “the most important diseases you have never heard of.” Today virtually every person on the planet who lives below the World Bank poverty figure – approximately 1.3 billion people, as well as most people who live on less than \$2 per day suffers from one or more NTD. For instance almost all of the children who live in extreme poverty have intestinal worms such as hookworms, which feed on blood and rob children of nutrients. Hookworms have actually been shown to reduce childhood intelligence and cognition – and as a result, reduce future wage earning by 40% or more. In this way, NTDs not only occur in the

setting of poverty, but they actually cause poverty. Moreover more than one-quarter of pregnant women in sub-Saharan Africa have hookworms and go into labor and delivery profoundly anemic infants. As my obstetrician colleagues point out, it's not that African women bleed more in childbirth, but that they begin the delivery process with two strikes against them because they start out with so little blood because of their hookworms. In this way, hookworm is a leading contributor to maternal morbidity in Africa.

Indeed the NTDs have a particularly horrific impact on girls and women. One of the worst problems just coming to light is female genital schistosomiasis – a parasitic infection that produces bleeding ulcers on the cervix, uterus and lower genital tract of as many as 100 million girls and women in sub-Saharan Africa. It's a cause of bleeding, pain, and terrible shame and grounds for spousal abandonment, as well as depression. I believe it is the most common gynecological condition of girls and women on the African continent. Can you imagine if 100 million girls and women in the U.S. had female genital schistosomiasis (FGS)? As a society we would never tolerate it, but because it affects girls and women who live in abject poverty, mostly in remote parts of Africa, they go untreated. Additional information indicates that FGS is also associated with a 3-4 increase in acquiring HIV/AIDS and may be Africa's most important co-factor in its HIV/AIDS epidemic you have never heard of, but I will come back to that in a minute.

One final example of the NTDs is the disfiguring and stigmatizing effects of cutaneous leishmaniasis – also known as “Aleppo Ulcer” or “Aleppo Evil” now affecting more than 100,000 people living in Syria and who have fled to refugee camps. In the Middle East, again its girls and women are permanently scarred and rendered unmarriageable or not allowed to hold their children as a result of this NTD.

These are the reasons that NTDs are so devastating. More often than not, nobody dies, but they are disfigured, stigmatized, stunted in their growth and mentally disabled. As a result, we now have an increasing body of evidence that the reason the poorest of the poor are trapped in poverty is because the NTDs block their ability to achieve their full mental and physical capacity and live a normal life.

The good news is that we can do something about seven of the most common NTDs, including hookworm and schistosomiasis (also known as snail fever), but also lymphatic filariasis (elephantiasis), trachoma, river blindness, ascariasis (roundworm) and trichuriasis (whipworm) for an extraordinary low cost – on average 50 cents per year or even less to prevent and in some cases eliminate these diseases. In 2005 and 2006 with colleagues from the UK and WHO and elsewhere we put forth in the Public Library of Science (PLOS) the concept of a rapid impact package, and now since 2006 this approach has been scaled up through support of USAID and with advocacy from our Global Network for Neglected Tropical Diseases, a Sabin initiative.

Thanks to the generous drug donations from leading pharmaceutical companies, including Merck & Co. Inc., GlaxoSmithKline, Eisai, Johnson & Johnson, Merck Serono, and Pfizer, and the efforts of the USAID a unique and innovative public/private partnership was formed to efficiently and cost effectively address NTD control and elimination. To date, USAID's NTD Program has improved the lives more than 364 million people, delivered nearly 820 million NTD treatments, and trained over 500,000 community workers. It has exceeded expectations in its ability to deliver treatments for the seven most common NTDs, leveraging more than \$4 billions of donated drugs, and operated in 25 countries such as Cambodia, Haiti, Indonesia, Nigeria, and Senegal.

We applaud USAID's NTD Program and the U.S. government's steadfast and vital dedication to this fight, which has been instrumental in inspiring similar efforts by partner countries to initiate control programs and allocate funding. It is important to note that, if funding for USAID's NTD Program does not at least match FY 2013 levels, the capacity to deliver these medicines to those who need them most will be significantly reduced and we may see a resurgence of many of these NTDs. Furthermore, the momentum generated over the past few years could well stall if the United States steps back from its global leadership role in NTD control and elimination efforts.

In fact, the time is right for the U.S. government, through USAID and NIH/NIAID, to establish one or more Centers of Excellence for Neglected Tropical Diseases. The Centers of Excellence concept -- investing in multi-faceted research and development and the scientific infrastructure needed to support it -- is very effective in many different areas of therapeutic, vaccine and diagnostic research. For instance, NIAID currently supports 11 Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases (RCEs), focused on countering threats from bioterror agents and emerging infectious diseases. I hope we can find the resources, even in this difficult fiscal climate, to fund at least one Center of Excellence for NTDs.

However, while the USG commitment to NTDs must remain strong, we must also increase support from other sources, including the private sector. The Global Network for Neglected Tropical Diseases and our END7 campaign are hard at work raising awareness and support to address these diseases.

I would like to play for you a short promotional video that brings in the celebrity community and explains the urgency for supporting the NTDs.

## PLAY VIDEO

Given the recently revealed links between snail fever and female genital schistosomiasis and HIV/AIDS, as well as malaria and hookworm, I think we now need to look to Version 2.0 of NTD control and elimination which better links the USAID NTD Program to other USG global health initiatives such as PEPFAR as well as the Global Fund to Fight AIDS, TB, and Malaria. A recent victory published in PLOS found that when Global Fund support is used for NTDs it can actually lead to the elimination of an NTD in Africa, with the example being lymphatic filariasis – elephantiasis in Togo.

We also need to encourage other government support beyond the U.S. We are grateful to the UK Government, which has also been a stalwart supporter of NTD control, while other European governments have supported R&D efforts, but the other G20 countries have been underachievers when it comes to global NTD control and elimination support. This finding is ironic given my new analysis published a few weeks ago in *Foreign Policy* that more than half of serious NTDs actually occur among the poor living in G20 countries, especially India, Indonesia, and China. I believe that a potentially important role of the new State Department Office of Global Health Diplomacy could include stepping up diplomatic pressure on the G20 to support NTD control and elimination.

Along the theme of NTDs among the poor in wealthy countries is new information coming to light from the U.S. census that 20 million Americans live in extreme poverty and University of Michigan Center for Poverty finding that 1.46 million families with almost 3 million children live on less than \$2 per day. Although we call them neglected *tropical* diseases – the truth is that poverty (more than climate) is the overwhelming determinant of these unique

infections. At our National School of Tropical Medicine, we have turned the global health lens inward to find a previously hidden burden of NTDs among the poor in the U.S. In a paper published in PLOS in 2008, I identified a group of NTDs now afflicting at least five million Americans living in poverty, mostly in the American South. They include:

- Millions of African Americans with toxocariasis a larval worm infection of the lungs and the brain linked to pulmonary dysfunction and asthma and developmental delays and seizures, respectively;
- Millions of African Americans with trichomoniasis linked with HIV/AIDS
- Hundreds of thousands of Hispanics with Chagas disease, a debilitating heart condition
- Tens of thousands of Hispanic Americans with cysticercosis a parasitic worm infection of the brain.
- Widespread arbovirus infections including dengue fever in Texas and Florida.

It's important to emphasize that these are not rare diseases. Scientists at our National School of Tropical Medicine are finding that these diseases are widespread in Texas and elsewhere in the American South, and we are now investigating the basis for their links to being extremely poor. Of interest is our finding that we have actual transmission of many of these NTDs within U.S. borders. This is not a primarily a problem of immigration – it is a problem of extreme poverty, extraordinary magnitude and simultaneous neglect. We urgently need to expand our local and national surveillance efforts for these diseases and to investigate how they are transmitted, as well as to conduct R&D for new tools, i.e., drugs, diagnostics, and vaccines.

Indeed, greater investment in NTD-related R&D for NTDs both globally and here in the U.S. is needed to support the introduction of new technologies (e.g., drugs, vaccines and

diagnostics); to ensure the achievement of the goals of disease control and elimination, as noted earlier, and address the urgent needs of particularly neglected patient populations.

Our work in R&D includes the development of novel, low-cost vaccines for NTDs – ironically for both developing countries and the U.S. Vaccines against NTDs are considered to be cost-efficient if not cost-saving with the potential to avert the suffering of millions and hundreds of thousands of deaths annually. Although the pharmaceutical sector has the knowledge base and resources to create therapies or possible vaccine candidates, there is little potential market for these new technologies and we are forced to use alternative market mechanisms to spur research and development. Sabin Vaccine Institute’s non-profit product development partnership (PDP) based at the National School of Tropical Medicine at Baylor College of Medicine is helping to fill this gap. The Sabin’s PDP focuses on creating safe, effective, and low-cost vaccines for human hookworm, schistosomiasis, Chagas disease and leishmaniasis – among the NTDs that are ravaging communities in developing countries and in the U.S. in the case of Chagas disease and leishmaniasis. Drawing on over a decade of experience, the Sabin PDP has created a comprehensive, relatively low-cost model that serves as a blueprint for vaccine development and ongoing efforts to fight public health threats that adversely impact more than one billion people worldwide. Three of Sabin’s vaccine candidates are either currently undergoing clinical testing or moving into clinical testing this year.

Over the last two decades there has been a growing recognition that the existing system for stimulating research and development has failed to deliver needed health technologies, particularly for diseases that disproportionately affect the world’s poor. Currently the vaccine pipeline is largely concentrated on the pre-clinical through phase II stages of clinical development. Projections suggest that up to a handful of new neglected disease vaccines will be

approved in the coming years because of the impressive work coming out of the PDPs. As later stage clinical trials are much more costly than earlier stage development, increased costs remain an important obstacle. While strong support has come from the Bill & Melinda Gates Foundation during the last decade, the Foundation does not have sufficient resources available to cover the needs that lie ahead. Consequently, other sources of funding will be necessary to support product development for the world's poor. Sustained investments in NTD R&D are critical to ensure the progress made is not squandered and to keep the momentum needed to ensure these new products reach those in need. The U.S. government has a significant role to play in this, as both a world leader with influence over other country investments and as a strong investor in neglected diseases R&D that help create a new generation of tools to eliminate NTDs, support U.S. foreign policy, and spur the U.S. economy both through job creation, but also to cure and prevent NTDs that now trap at least five million Americans living in extreme poverty. While the U.S. government invests in early stage neglected disease research and development through the National Institutes of Health and several other agencies, new and sustained funding is needed to enable continued progress.

We urge you, therefore, to vigorously support public/private partnerships that will benefit not only the developing world, but will ultimately benefit the economic prosperity and national security of the United States by helping to lift millions across the globe out of a vicious cycle of poverty and disease.

We, at Sabin and the National School, appreciate that global health issues have been a bipartisan priority for the United States for more than 50 years. Relatively modest financial investments have not only saved lives, but also improved the economic growth and regional stability of developing nations, and bolstered public perceptions of the United States. Since

national borders do not stop the spread of diseases and indeed many of the NTDs are widespread in the United States, addressing global health issues is vital for the protection of America's health and security. And, we certainly believe that U.S. investments must continue to support efforts to develop, implement, and adapt health tools that are culturally, financially, and technologically suited for impoverished communities.

In May 2013, the World Health Assembly passed its first comprehensive NTD resolution recognizing the progress made in combating NTDs, noting the diversity of these 17 diseases—from leishmaniasis, dengue, and Chagas disease to leprosy and schistosomiasis—advocating for predictable long-term, international financing, urging stronger commitments to research, and calling on nations to expand and implement, as appropriate, interventions against NTDs. The U.S. has clearly shown extraordinary leadership on NTDs, but the U.S. investment needs to continue if the WHA hopes to meet its goals and targets.

Mr. Chairman and Members of the Subcommittee, this concludes my testimony. I thank you, again, for your interest in furthering U.S. engagement in neglected diseases and global health and the opportunity to address you this afternoon. I am now happy to answer any questions you may have.

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Mr. SMITH. We have been joined by Congressman Stockman.

Mr. STOCKMAN. I have a question for Dr. Hotez.

Congress Weber and myself are both in the area in which they spray for dengue fever. And I know in our neighborhood in the evenings as the sun is setting they are spraying. I think it is for dengue fever.

Dr. HOTEZ. Actually, you are spraying more for culex mosquitos that transmit West Nile virus. So the spraying could be extended to daytime spraying to get the *Aedes aegypti* mosquitos, as well.

Mr. STOCKMAN. So those are the ones that carry the dengue, the daytime mosquitos?

Dr. HOTEZ. That is right.

Mr. STOCKMAN. I understand, too, it is mostly the female mosquitos, right?

Dr. HOTEZ. Yeah.

Mr. STOCKMAN. Do you know Edward Rensimer? He is a travel doctor in Houston. Do you know him too?

Dr. HOTEZ. I don't.

At our National School of Tropical Medicine now, we have actually created what we think is the first tropical medicine clinic in the United States at Baylor College of Medicine with Ben Taub General Hospital—it is a partnership—where we now see patients with all of these diseases coming in every Friday.

Mr. STOCKMAN. So you are at the medical center?

Dr. HOTEZ. I am at the medical center, right, Baylor College of Medicine at the Texas Medical Center.

Mr. STOCKMAN. Yeah.

Dr. HOTEZ. So it is amazing, every Friday we have patients coming in with Chagas disease, with cysticercosis, a brain parasitic infection. And we are seeing amazing stories of cutaneous leishmaniasis coming in. So it is pretty impressive.

Mr. STOCKMAN. But there was a prominent scholar—and correct me if I am wrong, but is some of this or a lot of it, can it be delegated or attributed to immigration?

Dr. HOTEZ. So, I am not sure when you walked in. I think immigration may be a part of it, but I don't think it is a major part of it.

My point is it is linked with poverty, so that we have transmission of these diseases right now going on within the borders of Texas, more south Texas, in Houston. It is also along the Gulf Coast. It is in Florida.

There is something about this pernicious combination of extreme poverty and warm, moist climate, just like it is elsewhere. I mean, after all, Houston is on the 30th parallel, right?

Mr. STOCKMAN. Yeah.

Dr. HOTEZ. It is on the same parallel as New Delhi and Cairo and—

Mr. STOCKMAN. And in reference to our own city, I think the mosquitos bite anybody. I don't think they just bite poor people.

Dr. HOTEZ. Yeah, so, as I said, we are trying to get our arms around what is it about poverty that seems to make people particularly susceptible.

Mr. STOCKMAN. I mean, they are pretty smart mosquitos if they know the difference.

Dr. HOTEZ. No, I will tell you what it is. Here is what I think it is. I think it is, people living in extreme poverty have more exposure because they don't have the adequate housing, hence they are getting exposed more to mosquitos. We are seeing very high rates of West Nile virus among the homeless. One of our faculty members has found the same with Chagas disease.

So I think—and we haven't proven it; this is only a hypothesis—that the link between poverty and these diseases is levels of exposure to the vectors.

Mr. STOCKMAN. I was in DRC, and I was telling the chairman about how I experienced firsthand some of the tropical diseases. And their inability to deal with it is pretty sad, actually. I think the basic stuff they didn't have in their—in fact, it was supposed to be their advanced hospital. I was in Kinshasa, and it was horrible.

Dr. HOTEZ. Yeah.

Mr. STOCKMAN. It was absolutely horrible. So I appreciate what you are doing and the research you are doing. It is really needed. And for someone that got sick, pretty sick there, I very much appreciate what you are doing.

Dr. HOTEZ. We actually have a paper coming out at the end of July on the Democratic Republic of the Congo (DRC), and NTDs. And I call them "Neglected Tropical Diseases in the Heart of Darkness," referring to Joseph Conrad's book. So you are absolutely right, the DRC is a brutal place for these diseases.

Mr. STOCKMAN. Yeah. And I know some of our people from WHO are over there dressed up in the suits, and they thought they were ghosts, and they murdered them, which—

Dr. HOTEZ. Oh, my God, that is terrible.

Mr. STOCKMAN [continuing]. Was not good. They were there for, what is it, the bleeding of the pores—

Mr. SMITH. Ebola.

Dr. HOTEZ. The Ebola virus, right, right.

Mr. STOCKMAN. So we have to do something to educate them before we put people in that kind of situation.

Dr. HOTEZ. Yes, we have this epidemic now of healthcare workers getting killed while doing noble pursuits. We see this now in the delivery of polio vaccines with healthcare workers in Pakistan—

Mr. STOCKMAN. Yeah, they spread the rumor that it was—

Dr. HOTEZ. Yeah. It is just so profoundly sad, yeah.

Mr. STOCKMAN. Well, Mr. Chairman, I would just—go ahead.

Mr. SMITH. Oh, I was going to go to Dr. Siegel.

Mr. STOCKMAN. Oh, okay.

Mr. SMITH. Unless you want to—

Mr. STOCKMAN. No, I would just yield back. And thank you. I appreciate it.

Mr. SMITH. Dr. Siegel, please proceed.

**STATEMENT OF JAY SIEGEL, M.D., CHIEF BIOTECHNOLOGY OFFICER AND HEAD OF SCIENTIFIC STRATEGY AND POLICY, JOHNSON & JOHNSON**

Dr. SIEGEL. Thank you.

Chairman Smith, members of this esteemed committee, thank you for inviting me to testify. My name is Jay Siegel. I am chief biotechnology officer and head of scientific strategy and policy at Johnson & Johnson.

On behalf of the Johnson & Johnson family of companies, I applaud you for organizing this hearing on the important subject of treatments for neglected diseases. As an infectious disease physician, a retired United States Public Health Service officer, and a former senior FDA official, as well as a pharmaceutical R&D executive, I greatly appreciate both the importance and challenge of this issue.

There is a deep and lasting commitment at Johnson & Johnson to global public health. In 2012, we extended that commitment as we signed the London Declaration on Neglected Tropical Diseases. And, earlier this week, we created Johnson Global Public Health, an internal organization to coordinate and advance our efforts in developing and providing access to therapies with important global public health impact.

Johnson & Johnson has several active efforts in this area. We are collaborating on development of a new bioavailable formulation of flubendazole with potential to eradicate the parasites that cause lymphatic filariasis and onchocerciasis, debilitating diseases affecting millions of people in tropical countries.

We donate more than 200 million doses of mebendazole yearly through the Children Without Worms partnership as part of a comprehensive strategy to reduce the burden of intestinal parasites. And we are now developing a chewable formulation of mebendazole to enable its use in younger children.

We discovered and developed Sirturo, the first new medicine for tuberculosis, or the first medicine with a new mechanism of action, in more than 40 years. Recently approved for use in treatment of adults with pulmonary multidrug-resistant tuberculosis, Sirturo will help address this important and growing public health challenge. Our 10 years' investment in Sirturo discovery and development will continue and grow to address product introduction, to ensure appropriate use and access, and to continue clinical research. Cost recovery from sales of Sirturo is expected to be relatively small, elusive, and incomplete.

Of course, our investments in these projects are not motivated by the potential profits, but rather by the opportunity to make a contribution to global public health. Notwithstanding our efforts and the laudable efforts of many other public- and private-sector organizations, as you have been hearing, much, much more remains to be done.

In the U.S., we ought to address these issues with a sense of urgency. Given the realities of climate change and increasing international travel, it may be more prudent for us to conceive of several diseases that occur predominately in developing countries but rarely in the U.S. not as orphan diseases but rather as morphing diseases—morphing in terms of size and extent of their reach. Americans at home are at increasing risk, as you have heard from several before me, for example, with regard to dengue fever.

Even diseases that are more tightly constrained to resource-limited settings often take their toll not only in terms of tremendous

human suffering but also in terms of social and economic impact that can reverberate across our increasingly interconnected world.

We greatly need new and improved therapies, and Congress can accelerate progress toward that goal. U.S. Government agencies and departments, including FDA, NIH, CDC, and the DoD, play important roles in addressing neglected diseases and can be and have been valuable partners.

These efforts and partnerships can be facilitated. A reworking of R&D models, regulatory models, incentive models, and partnership models could enable greater investments and greater progress. In my written testimony, I describe several existing models that might stimulate more investment and more progress in this area.

Drawing on our experiences, we encourage Congress to reflect upon three considerations in the design of policies to stimulate investment and accelerate progress in this area.

First, such policies should take into consideration a holistic view of the costs and risks across all stages of developing and supporting treatments.

Second, the menu of options available to stimulate investment should be varied and extensive. This approach would help spark the level of investment needed, would address all stages of development, and would expedite assessment of which options work best.

Third, policies should encourage partnerships that bring broad expertise to bear and help to diffuse the risk of drug development and delivery across multiple actors.

In conclusion, the challenge of addressing neglected diseases is large and complex, but the U.S. Congress has opportunities to facilitate, coordinate, and incentivize the needed efforts of many interested and capable parties, thereby accelerating important advances against these devastating diseases.

Thank you, Chairman Smith and members of this committee, for your leadership on this issue. I look forward to answering any questions you may have.

Mr. SMITH. Dr. Siegel, thank you very much for your testimony and for your very concrete recommendations.

[The prepared statement of Dr. Siegel follows:]



**Written Statement of Jay Siegel, MD  
Chief Biotechnology Officer and  
Head of Scientific Strategy and Policy  
Johnson & Johnson**

**Before the  
Subcommittee on Africa, Global Health, Global Human Rights, and  
International Organizations  
United States House of Representatives**

**“Addressing the Neglected Diseases Treatment Gap”  
June 27, 2013**

Chairman Smith, Ranking Member Bass, members of this esteemed committee: Thank you for inviting me to testify today. It is an honor to be here. My name is Jay Siegel, and I am Chief Biotechnology Officer and Head of Scientific Strategy and Policy at Johnson & Johnson.

On behalf of the Johnson & Johnson family of companies, I applaud you for organizing this hearing today on the important subject of neglected diseases of the developing world.

It is my privilege to be able to view this topic through many different lenses of experience. Early in my career, I was trained in Infectious Diseases Medicine at the Stanford University School of Medicine. That training instilled in me a lasting awareness of the devastating impact of many infectious diseases in the developing world.

During two decades in the U. S. Public Health Service and at the FDA, I gained a deep appreciation for the complexities of drug development. Also, I witnessed the rise of the AIDS epidemic and its crushing impact, and experienced first-hand the importance of building broad-based collaborations across the public and private sectors in accelerating the development of and patient access to life-saving therapies.

Ten years ago, I became president of what was then Centocor Research & Development, a biotechnology company within Johnson & Johnson. There, and in subsequent posts, I came to know firsthand the staggering costs, risks, and challenges of global drug development.

Additionally, as an FDA negotiator and signatory for 16 international harmonized guidances on drug development, and in my current role overseeing Global Regulatory Affairs operations in more than 100 countries, I have gained many insights into how differences in the practice of medicine, the regulation of drugs, culture, and economic circumstances can have major impact for global drug development.

Together, all of these experiences have deepened my personal commitment to addressing unmet medical needs, particularly needs most pronounced in developing countries. That same depth of commitment is reflected on a broad scale at Johnson & Johnson.

Last year, Johnson & Johnson was a proud signatory to the London Declaration on Neglected Tropical Diseases, or “NTDs.” Standing alongside the U.S. and UK governments, the Bill and Melinda Gates Foundation, our counterparts in industry and leading NGOs, we pledged a “new level of collaboration” in the global effort to conquer NTDs. Since that signing, we have followed through on our pledge, building collaborations and expanding our efforts to address NTDs.

As part of our NTD efforts, Johnson & Johnson is collaborating with the Drugs for Neglected Diseases Initiative, with funding from the Gates Foundation, on pre-clinical development of flubendazole, a potential new treatment against parasites that cause lymphatic filariasis (elephantiasis) and onchocerciasis (river blindness), two debilitating diseases affecting millions of people in Southeast Asia, sub-Saharan Africa, Central and South American and other tropical countries. Currently available treatments are unable to kill the adult worms associated with these diseases—worms that live in the body and lay millions of larvae in the lymphatic system, blood and tissues, perpetuating a cycle of infection and suffering. If our pre-clinical efforts are successful, in collaboration with the Gates Foundation, J&J will launch a full clinical development program with the intention to register and distribute flubendazole to all countries where these diseases are endemic.

Our company is also a leader in efforts to expand distribution of existing treatments for intestinal worms. Through Children Without Worms, a partnership between Johnson & Johnson, GlaxoSmithKline and the Task Force for Global Health, our company donates more than 200 million doses of mebendazole every year to almost 40 countries where children are disproportionately afflicted with intestinal worms. Our commitment to innovation in this area continues as we explore the development of a new chewable formulation of mebendazole which, if successful, will one day enable treatment of younger children.

In addition to flubendazole and mebendazole, we have a sizeable and growing portfolio of products with high potential public health impact. This portfolio includes a newly approved medicine known by its trade name as SIRTURO™. SIRTURO™ is an antimycobacterial drug indicated as part of combination therapy in adults with pulmonary multi-drug resistant tuberculosis, or MDR-TB. It is the first new medicine for TB with a new mechanism of action to be developed *in more than 40 years*, and is the first new drug specifically indicated to treat a drug-resistant form of tuberculosis. Our experiences with SIRTURO™—today and since its discovery in our labs more than a decade ago—illustrate some of the challenges associated with the development and introduction of a new therapy for a neglected disease.

MDR-TB can be transmitted by a simple cough. As MDR-TB is resistant to the two drugs most effective in the routine therapy of TB, it is associated with frequent treatment failures and a high mortality rate. The World Health Organization estimates that with existing treatment options, fewer than 50 percent of patients treated for MDR-TB will be cured. And although Margaret Chan, the WHO Director General, aptly described MDR-TB as “a time bomb” in 2009, alarmingly little has been done to control this global public health threat.

Against this backdrop, SIRTURO™ received accelerated approval from FDA in December 2012. Product introduction responsibilities for SIRTURO™ are daunting: they include patient registries aimed at bolstering the safety and efficacy data, global medical education to ensure appropriate use and sustained longevity of this drug, and lending support to strengthen pharmacovigilance efforts in developing countries.

And our work doesn't end there. Our post-marketing commitments for SIRTURO™ are substantial. They include a lengthy Phase 3 research program; a pediatric formulation and first-ever randomized, open label, controlled clinical study in a pediatric MDR-TB population; and a 5-year prospective study to characterize the acquisition of resistance to this new drug.

Our experience with SIRTURO™ highlights the breadth of post-approval responsibilities and the magnitude of sustained investments required to appropriately ensure its safe and effective use worldwide. We estimate that approximately half of all investments required to develop and support Sirturo™ will be realized *after* regulatory approval.

These are investments for which we expect no “return” as the term is traditionally defined. Normal cost recovery and profit-deriving sources for the pharmaceutical industry are well

characterized and continue to rely on advanced-economy markets with more equitable and advanced healthcare systems. However, MDR-TB case numbers in the U.S. and EU amount to fewer than 2,000 patients per year. In the United States, fewer than 150 cases are reported annually. As is the case for most neglected diseases, cost recovery and profits associated with eventual sales of SIRTURO™ will prove to be relatively small, elusive and incomplete.

While efforts such as those described are complex and costly, we are proud of what we have done and are increasing our efforts to address Global Public Health issues. Indeed, this week, we announced the establishment of a new Global Public Health organization within our company – a group dedicated to developing and creating access to medicines that can improve the health of those who live in some of the most economically challenged areas of the world.

We applaud the many other organizations that have undertaken similar goals in this area— including government agencies such as FDA and NIH, WHO, the Gates Foundation, public-private partnerships, other private organizations and alliances, and other companies; they have yielded substantial benefit. Still, however, the challenge remains large and complex, and much more remains to be done. We believe that a re-working of current models—R&D models, regulatory models, incentive models, partnership models and otherwise—could enable greater investments and greater progress. Public policy can play an essential role in bringing these new models to life.

As we approach this exercise in the U.S., we ought to do so with a sense of urgency.

We might wish to be able to comfortably and permanently classify many diseases as “diseases of the developing world” and, at most, “orphan diseases” here in the U.S. However, given the realities of climate change and international travel, it may be most prudent for us to conceive of these not as “orphan diseases,” but rather as “*morphing* diseases” —morphing in terms of the size and extent of their reach. Not only are American travelers, military personnel and diplomats potentially exposed, but with climate change and with exposure to returning travelers, Americans at home are also at increased risk. For example, Dengue fever acquired in the U.S. has re-emerged as a public health threat as warmer temperatures enable carrier mosquitos to flourish and expand their range.

Even for those diseases that appear to be more tightly constrained to resource-limited settings, the absence of therapeutic and other means for managing those diseases can have devastating and reverberating impacts. The ravages of Chagas disease, Trachoma, rabies and other afflictions

stretch far beyond the physiological, relegating those affected to the margins of their societies and economies. Such diseases have *root-cause* roles in perpetuating poverty and deprivation. Thus, they take their toll not only in terms of tremendous human suffering but also in social and economic impacts that can ripple across our increasingly interconnected world.

For these diseases, we need new therapies where none exists and better therapies where those that are available are suboptimal. Congress can help to create the conditions that accelerate progress toward these aims.

The complexity and enormity of the challenge demands that we be thoughtful in analyzing what has been done and that we learn as we go. Drawing from our own experiences in neglected-disease R&D and drug delivery, we encourage Congress to reflect upon three considerations in the design of policies to accelerate progress:

1. First, such policies should take into consideration a *holistic view of the costs and risks required to develop, introduce and support these products worldwide*. The development of innovative therapies is recognized for its cost, risk, complexity and lengthy duration. Less than one in every 10 drug candidates entering Phase I clinical trials ever makes it to market.<sup>i</sup> Extensive and expensive clinical testing is necessary and for those that do succeed to the point of market approval. The list of *post-market* commitments can be extensive. Policies intended to incent R&D investments for neglected diseases should be structured in ways that appreciate innovators' pre- and post-market costs and risks.
2. Second, to spark the types and level of investment needed to close research gaps for neglected diseases, incentives should be ample in number and capable of being accessed in combination. A menu of incentives should include both so-called "push" and "pull" mechanisms: "Push" incentives that encourage research inputs—such as preclinical studies—and "pull" mechanisms that reward successful research outputs, such as a fully developed drug.<sup>ii</sup> Well-designed incentive structures include both these methods.
3. Third, and finally, policies should encourage partnerships including public-sector and non-industry entities as well as industry. Such partnerships can serve both to bring a variety of critical capabilities and perspectives together and also to help to *diffuse the risks* of drug development and delivery across multiple actors. Where funding is sufficient, public-private co-funding models supporting early- to late-stage drug

development can themselves serve as incentives for companies to participate in neglected disease R&D.

On this point, a number of federal agencies and departments, including FDA, NIH, CDC, USAID and DoD, play important roles in addressing neglected diseases and can be valuable partners. We applaud this committee's work to facilitate partnerships between and among these agencies, and also with partners from other sectors.

We also note that through various actions including, for example, the Orphan Drug Act of 1983, Congress has already demonstrated the favorable impact it can have in this area.

Regulatory approaches and requirements can have a major impact on drug development challenges, risks, and costs. Providing access to a new medicine for patients in developing countries generally requires obtaining approval from FDA and/or European regulatory authorities. But approval requirements based upon potential use in the U.S. may be challenging to address for drugs primarily intended to treat diseases in the developing world since factors influencing need and use including, for example, stage and severity of disease, disease prevalence, underlying conditions, supportive or alternative therapies available, distribution channels and availability of cold chain, in the U.S. may differ substantially from those in the developing world.

The Neglected Diseases Priority Review Voucher program at FDA, established by Congress in the Food and Drug Administration Amendments Act of 2007, is a significant step in providing innovator firms with tangible incentives to enter the neglected disease space. Our company received a Priority Review Voucher with the accelerated approval of SIRTURO™ in December of last year. However, the voucher program provides limited incentive to invest in high risk early research into innovative therapies because, in considering such investments, the voucher value is discounted both by the high risk of program failure and the substantial delay (typically over a decade) before the voucher would be received. We believe the Priority Review Voucher would be most effective as an incentive for firms to pursue R&D for neglected diseases if it were part of a more complete, diverse and integrated set of incentives that Congress can help to make available.

**Examples of Incentive Models and Complementing Programs to Support Increased R&D for Neglected Diseases of the Developing World (presented in alphabetical order)**

There are many different types of incentive models and complementing programs available for policymakers' consideration. With few exceptions, most remain in concept form only, yet to be implemented or tested. Until such testing occurs and programs are assessed and refined, the key questions of *what will work?* and *how, when and where will it work best?* will be difficult or impossible to answer. A multi-tiered or "package" approach to incentives and programs—allowing innovator firms and their partners to access an assortment of incentives—offers potential to address various issues facing different organizations and programs at different stages of development. Such an approach could also allow for efficient testing and refining of incentive models; indeed, finding what "works" within an acceptable period of time will almost certainly require the testing several options simultaneously.

While by no means comprehensive, the list that follows is designed to illustrate for the committee the variety and types of options available for its consideration. While Johnson & Johnson does not endorse any one model at this time, we would welcome the opportunity for further dialogue with Congress on any of these or other options.

#### **Advanced Market Commitments**

An Advance Market Commitment (AMC) guarantees a market in return for reduced pricing. This can reduce the market risks, thereby providing incentives for potential providers of needed therapies to make necessary investments, such as expanding manufacturing capacity. A promising AMC for pneumococcal vaccines was implemented by the GAVI Alliance in 2009 with the support of a number of developed countries. In this program, funders have guaranteed \$1.5 billion for a specific annual supply of pneumococcal vaccines. Companies are then compensated with a share of this fund directly proportional to the percentage of the vaccine order which they fulfill. By the end of this year, 43 developing countries are expected to be participating in this program.<sup>iii</sup>

An AMC program structured to encourage the development and distribution of therapies for neglected diseases could function in a similar fashion.

#### **Cures Acceleration Network**

Often, insufficient funding and support leads to stagnation in development of new cures and therapies. The NIH is attempting to break that stagnation with its Cures Acceleration Network (CAN). This new model provides direct R&D funding for promising medical advances that

might otherwise not be carried through the more expensive and difficult stages of clinical development.

Interestingly, the structure of the CAN program is based on the research and development branch of the Department of Defense—DARPA—whose innovative format for R&D has yielded substantial returns since its implementation over 50 years ago.<sup>iv</sup> CAN involves a vetting process and grant structure very similar to this Department of Defense program.<sup>v</sup>

If CAN is able to emulate the success of DARPA, it could open a pathway to the successful and expeditious manufacture of new treatments and cures for a wide variety of diseases, including neglected diseases. A specific focus within the CAN program on NTDs could drive considerable progress in the future.

#### **Export-Import Bank Model for Market Creation and Strengthening**

Experts in global health have long maintained that when it comes to explaining the historical dearth of drug-development for neglected diseases, “The heart of the problem is the lack of market demand sufficient to induce the private sector to commit resources to R&D...the people who suffer from neglected diseases do not have substantive purchasing power, and cannot constitute a profitable market.”<sup>vi</sup> As we consider sustainable solutions to advance the development and delivery of needed treatments, it behooves us to examine options for addressing this market challenge in particular.

Thankfully, there are models in place that have helped to address similar challenges for other industries in the U.S. Several federal agencies use financing programs to help provide important products to developing countries. Loan guarantee, loan subsidy, and grant programs help to promote the sale of U.S.-made products to developing countries. Title I of the Department of Agriculture’s “Food for Peace” program, for example, allows for the provision of government-to-government sales of agricultural commodities to developing countries under long-term credit arrangements.

Likewise, the Export-Import Bank of the United States (or “Ex-Im Bank”) is one of the most prominent models for market creation and bolstering. As this committee is well aware, the Ex-Im Bank was founded to sustain and maintain American jobs by supporting the export of U.S. goods and services to foreign buyers. The Ex-Im Bank is dedicated to creating trade finance programs that help both American exporters and emerging countries that otherwise would not be

able to purchase U.S. products. The Bank accomplishes this through a range of Special Initiatives in Agribusiness, Aircraft, Renewable Energy, and Construction Equipment, to name a few.

The Ex-Im Bank also has Special Initiatives in the area of Medical Equipment & Services. On this front, the Bank has noted, “It is a priority for good business and international citizenship to support the creation of American jobs and of facilities that deliver humanitarian benefits.”<sup>vii</sup> Building on this priority, and in line with shared humanitarian and economic objectives, there may be an opportunity for Congress to facilitate a partnership among the U.S. Department of Health & Human Services, the U.S. State Department, and the Ex-Im Bank to expand the Bank’s Special Initiatives in Medical Equipment & Services to include financing for U.S.-made medicines, diagnostics, and other medical technologies capable of countering the incidence and spread of serious diseases of the developing world. The potential for positive synergies via this kind of partnership could be substantial.

#### **The Global Health Investment Fund Model**

The Global Health Investment Fund (GHIF) is a novel initiative designed to raise low-cost capital to develop drugs and vaccines for neglected diseases. The GHIF, established by JP Morgan in collaboration with the Bill & Melinda Gates Foundation and Lion’s Head Global Partners, is currently in its first phases of implementation. For its initial investments in neglected-disease R&D, the GHIF will leverage at least \$100 million USD, provided as seed money from the government of Canada through its “Grand Challenges Canada” program.

Unique to the GHIF’s equity model is the Gates Foundation’s commitment to bear 60 percent of potential losses—a critical de-risking strategy to gain and secure valuable investors for future health ventures. The project, launched at the end of last year, is expected to have a return on investment of four to six percent in five years.<sup>viii</sup>

The U.S. government can play a role in supporting GHIF and similar social impact investment models, whether through direct funding or through less direct but still meaningful approaches to encouraging the creation and success of such funds.

#### **Milestone Based Prizes (push + pull)**

Milestone prizes are simple cash prizes awarded at various stages along a new therapy's development. For example, an innovator of a new neglected disease therapy might receive a prize payment upon presenting a well-developed treatment proposal, another upon completing pre-clinical research for the drug, another upon finishing clinical trials, and another upon the therapy's approval by the FDA, and another for successful conduct of post marketing studies and pharmacovigilance. This approach could be relatively simple to implement, and potentially could encourage all phases of a new drug's development.<sup>ix</sup>

Milestone rewards programs are widely recognized as a straightforward way to goad the sustained development of new medications, and have been endorsed by the WHO as a promising way to "maximize public health returns in the developing world."<sup>x</sup> This simple mechanism may be well suited to a coupling or integration with other incentive models for neglected disease R&D.

#### **Project BioShield Model**

The Project BioShield Act of 2004 was designed to incent the pharmaceutical industry to develop medical countermeasures (MCMs) against chemical, biological, radiological and nuclear (CBRN) attacks by providing a large, guaranteed market. The Act mandated a Strategic Reserve Fund for the purchase of MCM agents and authorized purchase of such agents prior to extensive testing in humans. Since its inception nine years ago, eight MCMs against CBRNs are in the government's hands in case of an attack, and eighty more MCMs are undergoing advanced development investments to commercialize countermeasures that are not yet mature enough for a guaranteed market contract.<sup>xi</sup>

Some elements of the Project BioShield model may be suited for adaptation to the context of R&D for neglected diseases.

#### **Public-Private Partnerships Designed to Diffuse Risks in R&D for Neglected Diseases**

R&D partnerships between the public and private sectors can be useful models for leveraging the strengths and resources of both. Public-Private Partnerships, or "P3s," are a "push" strategy being tested now in a broad range of R&D contexts around the world. P3s are co-managed and funded by both public and private sector entities. To date, P3 models have been used effectively to raise billions of dollars in both public and private funds to increase access to existing vaccines and accelerate R&D for NTDs.<sup>xii</sup> Current examples of P3 models with co-management and

funding from the U.S. government include USAID’s Malaria Vaccine Development Program and the Medicines for Malaria Venture. A significant benefit of the P3 model is its inherent diffusion of R&D costs and risks across a broader pool of actors.

### **Social Impact Bonds Model**

Social Impact Bonds (SIBs) are a relatively new method for financing programs of potential social value, built on a distinct “pay by success” design. The model leverages private investments to cover the upfront costs of an innovative social program, with the promise of public payment, contingent upon demonstrated fulfillment of pre-defined objectives.

While SIBs have yet to be tested in pharmaceutical R&D or healthcare delivery contexts, the model may lend itself to either or both. Under the leadership of the Center for Global Development, a non-profit international development think tank, and Social Finance, a UK-based non-profit and originator of the social impact bonds concept, efforts are currently underway to explore the application and adaptation of the SIBs model to address unmet needs in developing countries.

### **Transferable Market Exclusivity Periods**

One potentially effective “pull” incentives for innovators might be the reward of *transferable* market exclusivity periods (MEPs), granted in exchange for developing and obtaining market approval on a “socially desirable but unprofitable medicine” that can address unmet medical needs in poor countries.<sup>xiii</sup> Transferable MEPs could be an effective way to compensate for and incentivize investment in otherwise low-grossing drugs (like drugs for neglected disease) by increasing the amount of time full revenues can be collected from higher profitability products.<sup>xiv</sup> Transferable MEPs might be quite attractive to drug developers even if relatively brief in duration.

### **Conclusion**

In conclusion, there are many synergies in this area yet to be created or maximized—synergies among stakeholder institutions, and also synergies among the array of incentive models not yet available. The U.S. Congress is well positioned to bring together these key components, to create a new wave of momentum to address current challenges, and to make progress against the devastating set of illnesses for which no sufficient treatments exist today.

Thank you, Chairman Smith, Ranking Member Bass, members of this committee, for your leadership on this issue and many others in global public health.

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- <sup>x</sup> *Ibid.*
- <sup>xi</sup> Gottron, Frank. *The Project BioShield Act: Issues for the 112<sup>th</sup> Congress*. (March 2013) [[http://www.idsociety.org/uploadedFiles/IDSA/Policy\\_and\\_Advocacy/Current\\_Topics\\_and\\_Issues/Emerging\\_Infections\\_and\\_Biothreats/Background/The%20Project%20BioShield%20Act%20Issues%20for%20the%20112th%20Congress.pdf](http://www.idsociety.org/uploadedFiles/IDSA/Policy_and_Advocacy/Current_Topics_and_Issues/Emerging_Infections_and_Biothreats/Background/The%20Project%20BioShield%20Act%20Issues%20for%20the%20112th%20Congress.pdf)]
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Mr. SMITH. Dr. Zwane?

**STATEMENT OF ALIX ZWANE, PH.D., EXECUTIVE DIRECTOR,  
EVIDENCE ACTION**

Ms. ZWANE. Thank you. Thank you very much.

Mr. Chairman and members of the committee, thanks for the opportunity to speak with you today.

My name is Alix Zwane, and I am the executive director of the Deworm the World Initiative. That is a consortium of organizations which actively supports the scaleup of national or, in the case of India, state-level school-based deworming programs.

I come to my leadership role in the Deworm the World Initiative because my full-time job is the executive director of Evidence Action, a new nongovernment organization working to scale proven interventions to improve the lives of the poor in Africa and Asia. We are the leaders of the Deworm the World consortium.

School-based deworming is now recognized as one of the smartest and most cost-effective global health investments by leading academic centers, including our partner, Innovations for Poverty Action. This year, Deworm the World has helped our Government partners provide deworming treatment to over 35 million children in Kenya and in India.

My testimony today offers some practical recommendations on how to bridge the treatment gap in mass drug administration for the treatment of soil-transmitted helminths, schistosomiasis, and other intestinal parasites.

I am not going to focus primarily on a plea for a large infusion of donor resources. Thanks to generous drug donation programs by our pharmaceutical company partners like Johnson & Johnson, the quantity of available drugs currently outstrips programmatic demand. Our experience suggests that targeted, catalytic investments can be hugely beneficial.

I also do not focus on calling for additional political will from developing-country governments. We recognize that our partner governments have many competing priorities and limited budgets. They have to make hard choices, even with the very best of intentions.

In this summary of my submitted testimony, I highlight instead how the gap between service need and service delivery can be bridged by bringing useful but nonintuitive information and evidence to the attention of policymakers; how sharing targeted and practical lessons about best practices and implementation can leverage and unlock developing-country government money; and reducing the NTD knowledge gap. I will discuss each of these very briefly in turn.

First, on the question of evidence, as has been discussed earlier in this session, the magnitude of the benefits from deworming primary-school-age children is truly striking. A 2007 study that measured the impact of an early 20th-century hookworm eradication effort in the southern United States found treatment to increase school enrollment, school attendance, and literacy. A randomized control trial in Kenya of a school-based deworming program found similar results.

And by tracking those children over time, it has been shown that the benefits translate into more hours worked and higher wages for adults when they enter the formal labor market. This suggests a clear and identifiable link between global health interventions that reduce the suffering of children now and economic growth over the longer run.

Sharing these kinds of results with policymakers as part of a larger package of services or a structured engagement on doing more evidence-based policymaking more generally can help the decision-makers prioritize investments so that their scarce resources stretch further.

Increasing the capacity of governments to implement school-based deworming can make a path to sustainable, scalable services less daunting and more politically palatable. It is a challenge to convince a ministry of health official to take on a new national program, but by demonstrating how this can be done, by showing what kind of support can be provided that is targeted and straightforward, it can make it easier to take on a new program.

The kind of support needed includes mapping which areas of the country have the highest level of worm infection, creating plans and budgets that actually target those areas carefully, designing program processes and materials for training teachers and coordinating implementation logistics, and developing monitoring and evaluation systems to reliably assess program performance.

Joint ownership across ministries of education and health is crucial to school-based deworming. At Deworm the World, we help to cultivate that partnership. We also identify opportunities to integrate with other synergistic programs, such as micronutrient initiatives or vitamin A programs that also target schoolchildren. By leveraging other programs and piecing together budgets from different pots, we can unlock government resources and point the way to success.

Donor support for technical assistance in school-based deworming can be a highly leveraged form of support for child health. For example, we estimate that for every dollar of donor resources that we bring to bear for our work in India, we leverage something like \$17 of Indian Government money. That has helped us to treat some 30 million Indian children across several states in the past year.

Finally, reducing the knowledge gap. Thanks to investments by USAID and The Gates Foundation and others, we understand increasingly well the benefits of deworming and how to achieve scale with quality. However, we continue to face uncertainty about the necessary duration of mass treatment.

As an implementing organization, I can tell you it is difficult to work with a government counterpart to bring a new program on board when you can't tell them with certainty if they are making a 5-year commitment or a 10-year commitment. Those are very different things from a budget perspective and a political perspective.

But right now there is a lot of uncertainty just from a science perspective about how long to do mass treatments. This uncertainty makes risk-averse officials hesitant to act. Increased effort to understand how treatment strategies should change over time

would be enormously beneficial to achieving our collective goals around coverage.

In summary, our experience in the Deworm the World Initiative suggests that supporting the activities I have discussed here can address the political, technical, and managerial challenges to expanding deworming programs at a cost that is less than 50 cents per child per year. This is one of the most cost-effective means of improving educational outcomes for children in developing countries that we know, and expanding its reach is well within our grasp.

Thank you for your attention and the opportunity.

Mr. SMITH. Dr. Zwane, thank you very much for your testimony and for your leadership.

[The prepared statement of Ms. Zwane follows:]

**Bridging the treatment gap: Mass school-based deworming**

Alix Peterson Zwane  
Executive Director, Deworm the World Initiative/Evidence Action

COMMITTEE ON FOREIGN AFFAIRS  
U.S. HOUSE OF REPRESENTATIVES  
Subcommittee on Africa, Global Health, Global Human Rights, and International Organizations  
“Addressing the Neglected Diseases Treatment Gap”  
June 20, 2013

Mr. Chairman, members of the committee:

My name is Alix Zwane. I am executive director of the Deworm the World Initiative, a consortium of organizations which actively support the scale-up of school-based deworming programs worldwide to improve children’s health, education, and long-term development. I come to my leadership role with the initiative because I am the executive director of Evidence Action, a non-governmental organization working to scale proven interventions to improve the lives of the poor in Africa and Asia, that is the lead member of the consortium.

The Deworm the World Initiative (DtW) was launched at the 2007 World Economic Forum in Davos, Switzerland to expand school-based deworming programs. School-based deworming is now recognized as one of the smartest and most cost-effective investments by leading academic centers, including our partner Innovations for Poverty Action, the Copenhagen Consensus Center, and the Jameel Poverty Action Lab at MIT. This year, DtW has helped our government partners provide deworming treatment to over 35 million children in Kenya and India.

DtW expands school-based deworming by strategically supporting governments and development partners to launch, strengthen and sustain large-scale programs. This support includes:

- Increasing capacity of governments and other partners to implement national or state level school-based deworming by providing tailored technical assistance for all programmatic phases, from planning through to monitoring and evaluation.
- Facilitating resources and partnerships to provide the financial, technical and in-kind inputs to scale up and sustain school-based deworming programs.
- Generating commitment to high quality, large-scale school-based deworming programs by advocating with policymakers, donors and other stakeholders.

My testimony offers recommendations on means to bridge the treatment gap in mass drug administration for the treatment of soil transmitted helminths, Schistosomiasis and other intestinal parasites. I do not focus primarily on a plea for a large infusion of donor resources.

Thanks to generous drug donation programs by our pharmaceutical company partners, including Johnson&Johnson, the quantity of available drugs currently outstrips programmatic demand. Our experience suggests that targeted, catalytic investments can be hugely beneficial. Nor do I focus on calling for additional “political will” from developing country governments. We recognize that our partner governments have many competing priorities and limited budgets; they must make hard choices even with the very best of intentions. I highlight instead how the gap between service need and service delivery can be bridged by:

- Bringing useful, but non-intuitive, knowledge to the attention of policymakers;
- Sharing practical and targeted lessons about best practices in implementation via technical assistance that leverages and unlocks government funds;
- Reducing the knowledge gap. If our government partners, and our donor partners, understood better how long a commitment to mass treatment is warranted, it would be easier to dedicate resources for a discrete period of time.

*A strategic approach to expand school-based deworming and bridge the treatment gap*

Over 400 million at-risk school-age children remain without treatment for intestinal worms due to the challenges in scaling deworming programs. There are several reasons for which current efforts fall short of global deworming targets, including why new programs aren’t being established fast enough or existing programs have yet to achieve their full potential.

School-based deworming programs, which are often designed to reach preschool-age populations as well, target the segments of the population that typically carry the highest worm burden. These programs leverage the existing and extensive infrastructure of schools, employing teachers to safely administer treatment with support from the local health system and efficiently reaching large numbers of children.

DtW works to overcome the specific challenges to expanding school-based deworming programs through the provision of strategically identified support to government implementers. Support is tailored to the needs of each program, and the barriers to expanding high quality treatment identified above.

*Sharing evidence* The magnitude of the benefits from deworming are striking. Rigorous evidence demonstrates that school-based deworming can transform the lives of children over the short and long term. A 2007 study that measured the impact of an early 20th century hookworm eradication effort by the Rockefeller Foundation in the southern United States found treatment to increase school enrollment, school attendance, and literacy. A randomized trial in Kenya in the early 2000s found school-based deworming reduces school absenteeism by 25%. By tracking these children over the long-term, this study revealed that adults who had received 2.5 additional years of deworming as children worked 12% more hours and earned 20% more when in wage-employment as adults.

Sharing these results as part of a larger package of services, or a structured engagement on evidence-based policymaking more generally, can help decisionmakers prioritize investments so that their scarce resources stretch further.

Increasing capacity of governments to implement school-based deworming by providing tailored technical assistance for all programmatic phases, from planning through to monitoring and evaluation, can make a path to sustainable, scalable services less daunting and more politically palatable. The kind of support needed includes:

- Conducting national surveys to map which areas of the country have high levels of worm infection.
- Creating operational plans and budgets that target high burden areas.
- Designing program processes and materials for training teachers, distributing deworming medicine, generating public / community awareness, and collecting program data.
- Coordinating implementation logistics and systems for effective program coverage at scale.
- Developing monitoring and evaluation systems to reliably assess and capture program performance, and analyzing information to continuously refine programs for improved quality, cost and coverage.

Joint ownership across ministries of education and health is crucial to school-based deworming, and DtW helps to cultivate this partnership through facilitating the set-up of joint steering committees and working with ministry teams to outline respective roles and responsibilities. DtW also identifies opportunities to partner with other synergistic organizations or programs, such as hand-washing campaigns or micronutrient initiatives. By leveraging other programs and unlocking government resources by pointing the way to success, donor support for technical assistance in school-based deworming can be a highly leveraged form of support for child health.

**Reducing the knowledge gap** Thanks to investments by USAID, the Bill & Melinda Gates Foundation, the Children's Investment Fund Foundation, and others, we understand increasingly well the benefits from deworming and the means by which cost-effective treatment can be achieved. However, we continue to face uncertainty about the necessary duration of mass treatment, especially as sanitation coverage changes and incomes rise. Do governments sign on to a mass treatment campaign for five years or ten years when they begin? Our experience tells us that uncertainty about this question makes risk averse officials hesitant to act. Of course, it is precisely a lack of experience with sustained mass treatment that is partly responsible for our uncertainty about its long run effectiveness as part of a control strategy. The knowledge gap and treatment gap reinforce each other. Increased effort to understand how treatment strategies should change over time would be enormously beneficial to organizations dedicated to treatment and our collective goals around scale.

*Summary and conclusion*

Our experience in the Deworm the World Initiative suggests that supporting the activities I have discussed here can specifically address the political, technical, and managerial challenges to expanding deworming programs. The result of these efforts is programs that quickly, efficiently, and reliably deliver deworming medicine to millions of children each year at a cost that is less than \$0.50 per child per year. This is one of the most cost-effective means of improving educational outcomes for children in developing countries that we know and expanding its reach is well within our grasp.

Thank you for your attention and the opportunity to be here today.

Mr. SMITH. And I can say, I am practically in awe with the information conveyed to this committee. I have followed this, but, as you said, Dr. Hotez, this is the disease that you never heard of, most people have not heard of, and yet it is having such a debilitating impact on countries, including our own.

Dr. Zwane, you mentioned the 1-to-17 ratio in India. Are the occurrences of worms, the prevalence, is it mostly with the Dalits? Is it, like Dr. Hotez talked about, disproportionately poor people who suffer from it?

And when you mentioned the Kenya study, that also comports with what you were saying, Dr. Hotez, about the hookworms have actually been shown to reduce childhood intelligence and cognition and earnings by 40 percent or more. If we want to see economic growth, people reaching their objectives and maximizing their potential, it seems to me that getting rid of the worms has to be a very significant priority for us here and people all over the world.

Dr. HOTEZ. As they say, it is the worm, stupid. Right?

Mr. SMITH. You said, Dr. Hotez, that more than one-quarter of pregnant women in sub-Saharan Africa have hookworms, go into labor, and deliver profoundly anemic infants. If you could speak to the impact it is having on the women themselves in terms of morbidity and mortality for those women.

You did say—and the number is astonishing—schistosomiasis mal affects 100 million girls in sub-Saharan Africa and young women.

And you also mentioned, I think all of you perhaps referenced it, but you did especially, the Global Fund. We had Mark Dybul, the executive director, the former AIDS czar for George W. Bush, before us. I wish we had this hearing first because I would have asked him, but we will follow up with him. What is the Global Fund doing on this?

You know, you mentioned the 3–4 percent increase in acquiring HIV/AIDS. It may be Africa's most important co-factor in the HIV/AIDS epidemic. How many times have we had PEPFAR hearings, and we don't hear that, but you have brought it to this committee.

Dr. HOTEZ. Yes, indeed. I mean, there are a couple of issues.

So, first of all, these are the most common diseases of girls and women on the planet. And, I think we often don't think about neglected tropical diseases as a girls' and women's issue; everyone talks about how we can address the plight of girls and women living in poverty and how we are going to do it. This is how you do it. This is the cheapest way to do it and have the greatest bang for your buck, point number one.

Point number two, Mark Dybul is a wonderful man. When we worked with the Bush administration on getting those funds appropriated through USAID, it was Mark Dybul who was providing a lot of the conduits. So he gets it, he understands the importance of neglected tropical diseases.

That is not the issue. The problem is these big organizations, whether it is PEPFAR or whether it is the Global Fund to Fight AIDS, TB, and Malaria, tend to get very siloed because it is everything we can do to keep up with their current agreements. So, when you go to them and you say, guys, you have to take on neglected tropical diseases, they just look and sigh and say, "We

know, Peter, but, I mean, we are so buried right now, how we going do it?”

And, so I don't know how we enable PEPFAR and the Global Fund to take it on. You know, they are exhausted, amazing public servants and really smart people. We have good people that work in PEPFAR, good people that work in USAID, good people that work in the Global Fund to Fight AIDS, TB, and Malaria. And I think this could be an important role for Congress, is to help that, help facilitate that process. But it has to be done.

Mr. SMITH. Dr. Siegel, you mentioned three very specific recommendations. Is that something that would lend itself to putting into a bill, or could it just be done by admonishing the current administration and other governments and NGOs do more?

Dr. SIEGEL. I think a lot of what can be done and needs to be done would not require legislation, although I won't say that I have a lot of expertise in this area.

So one of the areas, of course, in my testimony, particularly the written testimony goes into significant length about, is establishment of different mechanisms, systems, partnerships that would create either incentives or facilitate investment from not just industry but private foundations, other parties, private investors, to help address this problem.

A lot of that work, I think, does not require legislation. I think congressional support, exhortation, increased involvement, and perhaps increased funding for involvement from public health agencies and the Department of Defense can all play an important role in making that happen. And I think Congress can really, you know, stimulate those sorts of actions. There might be some areas and some types of investment scenarios that would require legislation, though.

Mr. SMITH. Yes, Dr. Hotez? And, Dr. Hotez, do you think that a centerpiece of a neglected diseases bill, tropical diseases, would be these “Centers for Excellence”?

Dr. HOTEZ. So the “Centers of Excellence” would be a key component, you know, both to focus on neglected tropical diseases abroad as well as here.

So what we are seeing is a blurring; it is wherever poverty exists. In fact, I have this new provocative map that was just published in Foreign Policy about where the neglected tropical diseases are, and it is those pockets of intense poverty in G-20 countries—northeastern Brazil, southern Mexico. And right there is the southern United States, with Texas and elsewhere and the Gulf Coast. So that is point one.

I think point two is—and I have written about this—we need to set aside a portion of the President's Global Health Initiative, it could be just 1–2 percent, for new product R&D. I think that would be a real game-changer. That would put a lot of support into the system and to make that happen. So that is a key component.

And I think, lastly, we need to really look at these diseases as girls' and women's issues and think about, when we talk of addressing women's health, ask, what are we doing about the neglected tropical diseases? I think that is extremely important.

And, finally, I will just say, NIH, you know, the leadership of NIH, including Roger Glass at Fogarty, Tony Fauci at NIAID, have

really bent over backwards to keep NTDs on the radar screen, oftentimes against political pressure. We really have to congratulate them for their leadership.

The other thing we are not doing, though, is we are not supporting our military. We are not supporting the Walter Reed Army Institute of Research. We are not supporting the Navy equivalent.

We often forget, many of these products that everyone talks about for scaling up were actually invented by the U.S. military. One of the reasons why we initially set up in Washington, DC, is, how do you learn how to make a vaccine in a nonprofit sector? Well, we do it through learning from—people from Walter Reed Army Institute of Research have been our teachers.

They are dying on the vine right now because they are not being provided any funding, even though they have one of the greatest track records in leadership. We have an article talking about the role of military leadership in tropical disease coming out in the fall.

Mr. SMITH. We had a representative from Walter Reed testify on malaria just a few weeks. But true to form, because, you know, he is a good—he knows the border—

Dr. HOTEZ. Yeah, they can't say it. That is why I have to say it.

Mr. SMITH. I asked him, what do you need? How can we be helpful? And he was very creative in how he answered; well, we are doing the best we can with what we have.

Dr. HOTEZ. You know, Walter Reed is one of our greatest national treasures. And we are not doing either the military or our U.S. citizens a service by cutting them short.

Dr. SIEGEL. Chairman Smith?

Mr. SMITH. Yes?

Dr. SIEGEL. I just want to get back to your earlier question and say that I would like to take the opportunity to consult with a broader range of experts, because there is a lot that can be done without further legislation, but there is also a lot, potentially, where legislation would be helpful. And we would be pleased to—

Mr. SMITH. If you could help us craft a bill. I find sometimes when you get a bill passed in the House, even if it doesn't pass the Senate, it does have an impact.

Some years ago, I introduced a bill to deal with obstetric fistula. And I visited a hospital which many people have visited in Ethiopia that has worked miracles on women who suffer from that horrible, disfiguring, and debilitating outcome from obstructed delivery and other reasons.

And we got the bill passed in the House. The Senate never took it up. I asked USAID if they would just follow the parameters. They had the authority to do what the bill had recommended. And Kent Hill, who was then the USAID health official, the top guy, he did it. And 20,000 obstetric fistula surgeries so far have been performed via USAID dollars, augmenting what the Africans are doing, what everyone else is doing, including that great hospital in Ethiopia.

So, you know, any ideas you have, we will work hard to get it enacted into law when we get a, you know, tropical disease—

Dr. HOTEZ. That is so reassuring. And we are not talking billions. We are not even talking hundreds of millions. We are talking very modest amounts that can be transformational.

Mr. SMITH. Please give us your best ideas on what it should look like. And we work very collaboratively, obviously, with our folks over at the State Department, USAID, NIH, and CDC. But best ideas, please, fork them over.

Dr. Zwane, did you want to comment, particularly on the Dalits issue? Are they mostly—

Ms. ZWANE. Oh, yes. On the issue of who has worms in India, the first thing I would say is there is a lot we don't know about that. Unlike in Africa, where quite a bit of mapping has been done to understand where the worms are, we know relatively less about that in South Asia.

A highly catalytic investment would be to systematically map India for the likelihood of soil-transmitted helminth infections, which would cost something on the order of \$8 million to \$10 million and wouldn't be, you know, from the—maybe I am an ex-Gates Foundation person, but that is not a lot of money in the grand scheme of things.

But what we do know even without that systematic map of India is that the worms are a problem of rural poverty. So there are fewer worms even amongst the poor in urban settings. And where there is lack of sanitation is where there are a lot of worms. So, you know, without saying I have the perfect maps that would satisfy Dr. Hotez or CDC, the primary maps are concentrated amongst the poor in the Hindi Belt, so Bihar, Rajasthan, that area of India.

Mr. SMITH. The two Millennium Development Goals, one dealing with reducing maternal mortality and also infant mortality—again, getting back to your statement, Dr. Hotez, about the anemic infants, is there any number of how many of those children, because they are born prematurely and anemic, actually die or suffer from other diseases that would reduce their quality of life?

Dr. HOTEZ. Well, again, this is one of the reasons why neglected tropical diseases have been neglected. With some exceptions, most of these are not killer diseases. So none of the children are dying from the diseases that Dr. Zwane talked about or I talked about. But they are no longer wage-earning, productive individuals.

And, so what needs to be done is to aggressively scale up things like deworming, but we are going to need new interventions. So you talk about the fact that you don't know how long we are going to have to treat for; it depends. So for that horrific limb-disfiguring disease, four or five yearly treatments can actually eliminate the disease as a public health problem. We are talking pennies a year. So incredible.

For some of the intestinal worms, like hookworm, they keep coming back. So what we are doing at Sabin Vaccine Institute through Texas Children's and Baylor is we are making a hookworm vaccine. The idea is that you fold this in, so after you vaccinate, they don't come back.

Now, the key is, it has to be a cheap vaccine, right? So our economists tell us that we have to make these vaccines under \$2 a dose. So it is a very fascinating process of how we make vaccines. We use the cheapest inexpensive expression vectors, column resins that have been off-patent for years. Because we know we can make a vaccine for hundreds of dollars; the trick is doing it for \$2. And I think we are succeeding in that, and now it is in clinical trials.

Mr. SMITH. Do they require a cold chain?

Dr. HOTEZ. Well, right now our vaccines require a cold chain. It would be nice if we can factor that out, as well. But for version 1.0 of our vaccines, we still need a cold chain.

Ms. ZWANE. Just to follow up on that with respect to very young children, the drug donation program and the program—please correct me if I say anything incorrect—as overseen by WHO focuses on primary-school-age children. But we know that, in fact, children who are 1 year old or certainly 2 years old also may very well often have worms. But the drug donation program does not provide drugs for those children.

So if we want to work with a country government to expand treatment down, getting into that 1,000-days period, then they themselves have to purchase the drugs, which changes the cost, the calculus of the program and the complexity of the program significantly. Expanding our conversation around how to handle children under primary-school age could also be something quite valuable.

Dr. SIEGEL. That is true, and that is one of the—we are actually investing some number millions of the dollars in the development of chewable, as I mention in my testimony, a chewable version of mebendazole. And one of the main reasons is in order to be able to bring that down and make it more accessible to younger children.

Dr. HOTEZ. Yes, one of the things that has been found now which is very curious is that we are seeing high rates of hookworm infection in young neonates, as well. There is some suggestion that the neonates are acquiring it vertically through breast milk, that the women are infected, the larvae get into breast milk, and it is being transmitted vertically from mother to child.

So we are finding all these new mother-to-child NTDs. So, for instance, maternal-child Chagas disease, we are finding it is transmitted from mother to baby. And it is, we estimate, 300,000 pregnant women in Latin America with Chagas disease. Researchers at Tulane have estimated 40,000 pregnant women in North America alone with Chagas disease, transmitting it from mother to baby around 5–10 percent of the time.

We have nothing to offer those pregnant women, because the medicines that are used to treat Chagas disease, like many of the NTDs, they are basically poisons. And you hope you can poison the parasite before you poison the person who is getting the medicine. These medicines were developed in the Pleistocene era, right? They were developed a long time ago, and we need to do better.

So organizations like ours, Sabin Vaccine Institute, and Texas Children's and Baylor College of Medicine, their National School of Tropical Medicine, are making vaccines. And then you have very exciting drug product development partnerships like DNDI, the Drugs for Neglected Disease Initiative, Institute for OneWorld Health working on the small molecule. And then, together, we think we want to create a whole portfolio of these products that can be made.

Mr. SMITH. Real quick, two final questions. How many total people are malaffected by worms, you know, hookworm, every other worm?

And, secondly, in treating that one-quarter of pregnant women in sub-Saharan Africa who have hookworms, is the treatment injurious to the mother and baby?

Dr. HOTEZ. So what we do is we treat—we now recommend treating in the second or third trimester. Nobody likes to give the medicine in the first trimester of pregnancy. And it has been shown to be extremely beneficial, both to mother and the baby in terms of infant survival downstream.

Total number of people infected, well, wherever you find poverty, you find a worm. So we know they are ubiquitous among the 1.3 billion people who live on less than \$1.25 a day. A significant percentage of people live on less than \$2 a day. So it would not be an exaggeration to say 2 billion people on our planet with worms.

Mr. SMITH. Do the worms go through the placenta, or is it at birth?

Dr. HOTEZ. Worms, generally speaking, do not go through the placenta, but the Chagas disease parasite can go through the placenta. The malaria parasite can go through the placenta. These are single-celled organisms that have the ability to do that.

Mr. SMITH. We are joined by Congressman Meadows, who I know had a meeting with the Ambassador from Turkmenistan that prevented him from being here.

But thank you for joining us.

Mr. MEADOWS. Thank you, Mr. Chairman.

And thank each of you. And I came back to show the importance of it. Actually, I have a meeting in a few minutes with a head of the cabinet from Japan. So I am going to run out.

Dr. HOTEZ. You can congratulate the Ambassador to Japan if you like. They just stepped up and provided the first major contribution for neglected disease product—

Mr. MEADOWS. I spoke to him—

Dr. HOTEZ. It is a partnership with Japanese industry.

Mr. MEADOWS [continuing]. And it is a wonderful partnership, and we have a great relationship. So I will pass that on to him.

But I want to just say thank you for highlighting this. And the chairman is correct; when we highlight things, it may not pass in legislation, but we do see a difference, truly, in terms of other programs that are discretionary in terms of where those dollars go. And so your testimony today is very key and very apparent in terms of making real changes.

I would ask each of you, but specifically Dr. Siegel, if you will get back to us in terms of legislative tweaks or legislative initiatives that we can look at. And I will work with the chairman in terms of putting forth and working hard to make that a reality.

The other thing that I would ask, not necessarily for you to comment, unless you have strong comments on that today, is with regards to this 40 percent, where we are talking about a 40 percent reduction in terms of mental capacity or economic benefit, that is huge because there are those that will sign on to a piece of legislation based on the humanitarian aspect of it, but there is another group that will sign on based on the economic benefit.

And what we are seeing is we are having to spend major economic dollars to go into these countries in Africa and Central Asia

and other places, that we could hopefully reduce our long-term economic support if we increase that ability.

And so I would really like, if you would, to focus on that, where we can put together a model that—

Dr. HOTEZ. We can pull together all the numbers from the different counties—India loses \$1 billion a year in economic losses from lymphatic filariasis. We have now collected all those numbers in one repository. We can provide that. When we provide information on the legislation, we will be happy to provide this data—and it is the same in the U.S. These diseases are trapping people in poverty in the U.S.

Mr. MEADOWS. Well, and it is not the whole story. I mean—

Dr. HOTEZ. The humanitarian piece is important, but you are absolutely right, this is enlightened self-interest.

Mr. MEADOWS. Well, I appreciate it. And I am going to have to run, but I wanted to come and say thank each of you.

Thank you, Mr. Chairman, for once again being a great voice. I yield back.

Mr. SMITH. Thank you, Mr. Meadows.

Is there anything you would like to add before we conclude?

Dr. HOTEZ. Just to thank you for your leadership. And, you know, as we often say, we need leaders in Congress to take the “N” out of “NTD.” And I am profoundly appreciative.

Dr. SIEGEL. Again, I also want to thank you.

And, you know, it was interesting that we heard earlier from perhaps some younger members, but I lived through seeing the impact the Orphan Drug Act had, and so you don’t need to sell me on the importance that legislation but also—and the reason for my comment earlier was, just congressional attention to an issue can make a big difference, as well.

So thank you very much, and we will get back with further thoughts.

Ms. ZWANE. Thank you very much.

Mr. SMITH. Thank you.

We will use this hearing and your tremendous contributions to combating these horrible diseases to launch what I hope will be a significant bill. We will look to make it totally bipartisan and look for some friends over on the Senate side to do likewise, but we need your input.

And I would say, Dr. Hotez, in the early 1980s, I traveled with Dr. Sabin to El Salvador when they had a “day of tranquility.” The FMLN and President Napoleon Duarte’s government, at the behest of Jim Grant from UNICEF, actually had a day or days of tranquility. They vaccinated about 200,000 kids. Nobody knows the exact number, but it was incredible. And everywhere we went to the vaccination sites, kids got the vaccinations for pertussis, diphtheria, and other diseases, but they also got the drops for polio. And it was amazing to see.

I was back there at a conference on trafficking, combating human trafficking, about 4 years ago. And I looked around, and everybody in the audience seemed to be the age that they were little tikes, little children when I was there before. And I said, I bet you I met some of you 25 years ago, in a different setting of course.

Dr. HOTEZ. And we shouldn't underestimate American technology and its role as Ambassadors. And how do we project power? Well, I think a lot of it has to do with what we are doing for these infectious and neglected diseases.

Mr. SMITH. I couldn't agree more.

Thank you so much.

The hearing is adjourned.

[Whereupon, at 5:10 p.m., the subcommittee was adjourned.]

# A P P E N D I X



MATERIAL SUBMITTED FOR THE HEARING 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**

June 26, 2013

**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 2200 of the Rayburn House Office Building (and available live on the Committee website at [www.foreignaffairs.house.gov](http://www.foreignaffairs.house.gov)):

**DATE:** Thursday, June 27, 2013  
**TIME:** 2:00 p.m.  
**SUBJECT:** Addressing the Neglected Diseases Treatment Gap

**WITNESSES:** Panel I  
Lee Hall, M.D., Ph.D.  
Chief  
Parasitology and International Programs Branch  
Division of Microbiology and Infectious Diseases  
National Institute of Allergy and Infectious Diseases  
National Institutes of Health  
U.S. Department of Health and Human Services

Jesse Goodman, M.D.  
Chief Scientist  
Food and Drug Administration  
U.S. Department of Health and Human Services

Panel II  
Peter J. Hotez, M.D., Ph.D.  
President  
Sabin Vaccine Institute

Jay Siegel, M.D.  
Chief Biotechnology Officer, and  
Head of Scientific Strategy and Policy  
Johnson & Johnson

Alix Zwane, Ph.D.  
Executive Director  
Evidence Action

**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 202/225-5101 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 June 27, 2013 Room 2172 Rayburn HOB

Starting Time 2:06 p.m. Ending Time 5:06 p.m.

Recesses 1 (2:19 to 3:20) (\_\_\_\_ to \_\_\_\_) (\_\_\_\_ to \_\_\_\_) (\_\_\_\_ to \_\_\_\_) (\_\_\_\_ to \_\_\_\_)

Presiding Member(s)

Rep. Chris Smith

Check all of the following that apply:

Open Session

Electronically Recorded (taped)

Executive (closed) Session

Stenographic Record

Televised

TITLE OF HEARING:

*Addressing the Neglected Diseases Treatment Gap*

SUBCOMMITTEE MEMBERS PRESENT:

Rep. Bera, Rep. Stockman, Rep. Weber, Rep. Meadows

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.)

*Question for the Record from Rep. Smith for Dr. Hall*

TIME SCHEDULED TO RECONVENE \_\_\_\_\_

or

TIME ADJOURNED 5:06 p.m.

*Gregory B. Simpson*  
Subcommittee Staff Director

**QUESTION FOR THE RECORD OF THE HONORABLE CHRIS SMITH****U.S. HOUSE OF REPRESENTATIVES, COMMITTEE ON FOREIGN AFFAIRS,  
SUBCOMMITTEE ON AFRICA, GLOBAL HEALTH, GLOBAL HUMAN RIGHTS, AND  
INTERNATIONAL ORGANIZATIONS**

“Addressing the Neglected Diseases Treatment Gap”

June 27, 2013

Can you list the top three public funders of neglected tropical disease research?

**NIAID:** The G-FINDER Survey Report is a source of information on global research funding for various diseases. The 5<sup>th</sup> Annual G-FINDER Survey Report (2012) provides data for the following diseases on the World Health Organization’s list of neglected tropical diseases (NTDs) ([http://www.who.int/neglected\\_diseases/diseases/en/](http://www.who.int/neglected_diseases/diseases/en/)): dengue, kinetoplastids (including Chagas’ disease, African sleeping sickness, and leishmaniasis), helminth infections (including lymphatic filariasis, onchocerciasis, schistosomiasis, and soil-transmitted helminthiasis), Hansen’s disease (also known as leprosy), trachoma, and Buruli ulcer.

NIAID used funding data for 2011, the most recent year available, for the NTDs listed above in the 5<sup>th</sup> Annual G-FINDER Survey Report (2012) to calculate the top three public funders of NTD research. The top three funders are listed below.

1. U.S. National Institutes of Health (NIH)
2. European Commission
3. U.K. Department for International Development (DFID)

The full 5<sup>th</sup> Annual G-FINDER Survey Report (2012) is available at this link:  
<http://policycures.org/g-finder2012.html>.

