MEETING THE CHALLENGE OF DRUG-RESISTANT DISEASES IN DEVELOPING COUNTRIES

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

FIRST SESSION

APRIL 23, 2013

Serial No. 113–56

Printed for the use of the Committee on Foreign Affairs

Available via the World Wide Web: http://www.foreignaffairs.house.gov/ or http://www.gpo.gov/fdsys/

U.S. GOVERNMENT PRINTING OFFICE

80–545PDF WASHINGTON : 2013

For sale by the Superintendent of Documents, U.S. Government Printing Office
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MEETING THE CHALLENGE OF DRUG–RESISTANT DISEASES IN DEVELOPING COUNTRIES

TUESDAY, APRIL 23, 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 3:05 p.m., in room 2172, Rayburn House Office Building, Hon. Christopher H. Smith (chairman of the subcommittee) presiding.

Mr. SMITH. The subcommittee will come to order. And welcome, Dr. Frieden. Good afternoon. Today's hearing will examine a deadly phenomenon involving both natural and manmade elements: Diseases that are resistant to most or all available methods of treatment. While this is a growing problem of increasing concern throughout the world, the subcommittee will be focusing today on the impact of such diseases, known as superbugs, in developing countries and the challenge to preventing and treating these diseases in this part of the world.

There is a family of germs that occur normally in everyone's digestive system. They can cause infections when they get into the bladder, blood, or other areas where they don't belong. That is the natural part of this growing problem. Gut flora are absolutely essential for health and an effectively functioning immune response, and the increasing use of things like probiotics is testimony to the fact that more and more people are understanding that.

There are about 100 trillion microorganisms in our digestive systems, 10 times the number of cells in our bodies. Most of them help break down the foods that we eat, they help us with our immune systems. Those that are not helpful usually can be treated with existing medicines such as antibiotics.

The manmade part is that antibiotics have been increasingly used to treat naturally occurring germs, but many of them have become resistant to such treatment. These so-called superbugs pose a threat because of overuse or misuse of antibiotics, but they also pose a threat because of what some call a drug discovery void in which there has been insufficient research and development of new medicines to treat emerging mutating infections.

This situation recently has become much more serious. In the last 10 years, these drug-resistant diseases have been identified in patients in more than 200 hospitals in 42 States in this country. Over that period, there prevalence rate has increased from 1 per-

cent of patients to some 4 percent for those in short-term care, but for patients in long-term care facilities, the rate is as high as 18 percent.

Half of all patients who contract these diseases do not survive. MRSA, one of the better known of these superbugs, now kills as many as 19,000 Americans each year and a similar number in Europe. That is higher than the annual rate of deaths from HIV/AIDS.

Last year the World Health Organization identified strains of gonorrhea and tuberculosis that are currently completely untreatable, as well as a new wave of what might be called "super superbugs" with the mutation known as NDM–1. These frightening new strains were first seen in India, but they have now spread worldwide. The spread of the H7N9 birth flu in China is also causing considerable concern, with more than 100 confirmed cases and 22 deaths reported thus far. According to the AFP, the WHO said yesterday that there was still no evidence that H7N9 was spreading in a sustained way between people in China. I know Dr. Frieden will speak to that because we are working with the Chinese on that issue.

According to WHO, artemisinin, when used in combination with other drugs, is now considered the world's best treatment against malaria, but malarial parasites resistant to the drug have emerged in western Cambodia, along the border in Thailand, as well in parts of Burma and in Vietnam.

In the developed world, we pride ourselves on having top flight medical care widely available to patients. If we lose half of all patients who contract these drug-resistant diseases, what about patients in the developing world where statistics are often scarce and effective medical care can even be scarcer?

Using accepted protocols for treating these diseases, their rate of infection can be curbed. In Israel, infection rates in all 27 of its hospitals fell by more than 70 percent in 1 year with a coordinated prevention program. By following accepted protocols for handling these diseases, the Colorado Department of Public Health and Environment and the Florida Department of Health both have stopped outbreaks of these drug-resistant diseases in recent years. But then again, what about hospitals in developing countries?

For example, the brain drain has sent trained medical personnel in Africa in search of better working conditions and pay in the developed world. The lack of equipment and supplies that partly led to this brain drain would facilitate the rapid spread of drug-resistant diseases in these countries. What would be simple interventions, including removing temporary medical devices such as catheters or ventilators from patients as soon as possible, is less likely under current conditions in developing-world hospitals.

Adding to this problem is the presence of expired and counterfeit drugs. Patients whose lives could be saved may not be because of inadequate medical care. Unfortunately, because so many countries do not maintain and report statistics on medical issues, we have little idea how serious the situation is today in many developing countries in Africa and elsewhere around the world.

In our interconnected world, that means that infected people in the developing and developed countries pose a mutual threat. Last

month a Nepalese man was detained at the Texas border while trying to make an illegal crossing from Mexico. Officials found that he was infected with an extensively drug-resistant strain of tuberculosis and had carried this potentially deadly airborne disease through some 13 countries over 3 months, from his home of Nepal through South Asia, Brazil, Mexico, and finally into the United States. Who can say how many people he infected during this long journey.

Conversely, 6 years ago, an American infected with multidrug-resistant tuberculosis traveled from our country to France, Greece, and Italy, before returning through the Czech Republic and Canada. Upon his return to the United States, he became the first person subjected to a Centers for Disease Control and Prevention isolation order since 1963.

Clearly, both developed and developing nations must work together to prevent and treat these diseases and find a way to implement the new strategies in an era of constrained budgets and loosening control of authority in far too many countries. However, the administration's proposed budget for 2014 does call for a 19-percent cut in tuberculosis programming, and hopefully we might get some answers today and again on Thursday from Dr. Shah.

Today's witness, a very accomplished doctor, heads an agency that is charged with examining the elements of disease and helping to develop the strategies for addressing the threats they pose not just to Americans, but to all mankind. We look forward to hearing Dr. Frieden and exploring with him the means by which the U.S. Government is working with developing countries to counter global threats.

I would like to yield to Ms. Bass.

Ms. BASS. Thank you. And, Mr. Chairman, as always, I want to thank you for convening today's hearing on drug-resistant diseases in developing countries.

While we examine this very serious issue, I think it is worth noting that this is an issue with global dimensions that impacts all of us. While we sit in the halls of Congress, we are neither immune nor are we protected from what is a mere plane ride from this hearing room.

Globalization has done much for allowing us to be more interconnected. The challenge before us today, however, is how do we understand and move to effectively address the smallest of things, microscopic organisms that have the ability to rapidly adapt and either avoid detection or resist efforts that would eliminate something that often has mortal consequences if left unaddressed.

Dr. Frieden, I want to thank you for taking the time today to testify before the committee. I remember us talking about a very similar subject about a year ago, so I am very glad that you are here today. We all know that you have dedicated your life to addressing the great public health challenges of our day. You have been on the cutting edge of public health interventions and have undoubtedly saved millions of lives in the U.S. and around the world. For an extraordinary depth of work and experience, we owe you our thanks and look forward to your testimony.

Without objection, I would like to submit for the record a written statement by Ranking Member Engel. He has been a staunch

champion on a number of global health priorities and in particular the spread of tuberculosis, both multidrug-resistant and extensively drug-resistant TB.

It would be remiss for me not to acknowledge that in my hometown of Los Angeles there has been a recent outbreak of TB, and I understand it is close to 5,000 people that have been diagnosed, and there is a concern that there is not a sufficient supply of drug treatment to address this outbreak. Dr. Frieden, perhaps in your remarks you can update us all on the situation, how the CDC is working with local officials. I am sure Los Angeles is not the only city that is dealing with this.

But I will note that in the U.S. alone there are over 10,000 cases of TB infection annually. In a country like India, four times our population size, there are approximately 2.3 million cases each year and close to ½ million people can die from it. The Wall Street Journal reports that India has the largest number of people infected with drug-resistant strains.

In 2010, the Center for Global Development wrote a paper entitled "The Race Against Drug Resistance," and in that paper the authors address the health and economic consequences of global drug resistance, the drivers of drug resistance, and the current global response to the problem. They concluded with four recommendations that I would like to read for the committee's consideration but also to get your feedback on. Recommendation one, improve surveillance by collecting and sharing resistance information across network of laboratories. Two, secure the drug supply chain to ensure quality products and practices. Three, strengthen national drug regulatory authorities in developing countries. And four, catalyze research and innovation to speed the development of resistance-fighting technologies.

The challenge before us is multifaceted and will require a comprehensive approach. Understanding the drivers of drug resistance and addressing them is critical, including strengthening health systems to include well trained and equitably distributed health workers who can properly administer treatments, eliminating substandard and counterfeit drugs. And I would in particular like if you could comment about the role that counterfeit drugs might play in this.

We need to have well-structured surveillance and reporting systems that are in track to monitor outbreaks and infections and a strong focus on research development. I would add that public and private sectors must also play their part to ensure financial resources and regulatory standards are in place for the challenges of today. In Africa, for example, you don't have to look very far to find stories that report on totally drug-resistant TB or emerging concerns of increased drug-resistant strains of HIV and malaria. These are troubling trends as our Nation continues to fund programs that we hope will end these crisis in our lifetime. We have heard President Obama and former Secretary of State Clinton speak of an AIDS-free generation, while at the same time you read a BBC article with the headline, "Drug-Resistant HIV on Increase in Sub-Saharan Africa."

The World Health Organization reports that India, China, the Russian Federation, and South Africa are home to almost 60 per-

cent of the world's cases of multidrug-resistant TB. I would love to know your opinion, number one, if you agree with that or if you have a sense of why that is when we consider that, combined, India and China are home to over one-third of the global population of 2.6 billion people.

This problem won't go away on its own and we continue to see people becoming infected with any number of diseases, and as our world continues to become smaller as a result of globalization we will continue to be confronted with the challenges of how to adequately deal with drug resistance that may or may not be on our doorstep today, but might be tomorrow.

Thank you very much. I yield my time.

Mr. SMITH. Thank you, Ms. Bass.

Mr. Meadows.

Mr. MEADOWS. Thank you, Mr. Chairman.

This is a timely hearing on an important issue. And, Dr. Frieden, I appreciate your willingness to be here as well and I look forward to your testimony.

Obviously drug-resistant diseases are a serious problem everywhere. You know, our own healthcare providers are struggling to stay on top of this issue on a daily basis, and, you know, I firmly believe that to address this problem we must first determine the scale of the problem, and, you know, we need to make sure and ensure that we have the data necessary both here and in the developing world to properly define the problem.

These drug-resistant diseases, you know, they don't recognize a political boundary. You know, in a globalized world that we live in a threat anywhere is a threat here, and so, therefore, we are bound to work on this problem wherever it presents itself and that obviously creates challenges, as you know. We know that developing countries may struggle with sanitary practices, the use of nonprescribed antibiotics, limited access to care, you know, and so on. And so I look forward to hearing how we can address those challenges and improve our knowledge of these severe threats.

And with that, Mr. Chairman, I yield back.

Mr. SMITH. Dr. Bera.

Mr. BERA. Chairman Smith, thank you. And again thank you for calling this hearing. It is extremely timely. And today I will be a doctor as opposed to a Congressman because that is really how I look at this issue, from the perspective of being a doctor. You know, as the former chief medical officer for Sacramento County we dealt with issues of drug-resistant tuberculosis, but 5 or 6 years ago we had second and third line medications that we could use judiciously and still deal with these cases when we are called into consultation in the hospital.

What keeps me awake at night and what I worry about is the emergence of extremely drug-resistant cases of tuberculosis that we are starting to see pop up in Africa and other nations around the globe, and that is of critical concern not only to those countries abroad in Africa, but clearly to our hospitals and our patients here domestically. It is a real issue and it is one that we have to take very seriously.

You know, I have seen it firsthand, having travelled to South Africa a few years ago with a group of doctors to evaluate how they

were caring for the HIV epidemic there. You are seeing the devastating effects of these cases and the limited resources in the arsenal.

The other thing that keeps me awake at night, and I saw it firsthand this past weekend when I was back home and rounding with a group of doctors at Mercy San Juan Hospital, seeing what was happening there. If I am not mistaken, the nurse administrator who was rounding with us suggested that close to 50 percent of the patients that they are admitting now have a history of MRSA, or methicillin-resistant staph aureus. So there is a real concern of the efficacy of antibiotics that we are using and starting to run out of those tools in our arsenal as physicians.

That leads me to another body of literature that really is emerging. As we incent our pharmaceutical companies to come up with the fourth generation of antibiotics, we really have to extend the life of these medications. And I have been a doctor for over 20 years and for years we could use penicillin and so forth. But now, as we get into our first, second, third generation of cephalosporins and antibiotics, the lifespan of these drugs are increasingly shorter and shorter. And part of that is the ease of access of antibiotics in third world countries, the ability to just buy them over the counter, and there is no guarantee that they are being used in an appropriate manner.

So we have to work with industry to make sure, as we come up with the next generation of antibiotics, we are very judicious in how they are used, not only here domestically, but also abroad in other countries. And I would be interested in hearing your testimony on all of these issues, what we can do proactively here in Congress, as well as our medical community, to address that next generation of tuberculosis resistant, but then also how we work with industry as we develop the fourth generation of antibiotics and make sure we can extend the lives of these medications.

And with that, Mr. Chairman, again, thank you for this hearing, and I yield back.

Mr. SMITH. Thank you, Dr. Bera.

Mr. Weber.

Mr. WEBER. I will yield back.

Mr. SMITH. Okay. Thank you. Thank you.

I would like now to extend a very special welcome to Dr. Frieden. Tom Frieden, medical doctor, M.P.H., who has been the Director of the Centers for Disease Control and Prevention since June 2009, has controlled both infectious and chronic diseases in this country and globally. From 1992 to 1996, he led New York City's program that controlled tuberculosis and reduced multidrug-resistant cases by 80 percent. Dr. Frieden then worked in India for 5 years, helping to build a tuberculosis control program that has saved nearly 3 million lives.

As commissioner of the New York City Health Department from 2002 to 2009, Dr. Frieden led programs that reduced illness and death and increased life expectancy substantially, including programs that reduced adult and teen smoking dramatically and eliminated artificial transfats from restaurants, and the department eliminated racial/ethnic disparities in colon cancer screening

and began the country's largest community-based electronic health records project.

As CDC Director, Dr. Frieden has intensified CDC's 24/7 work to save lives and protect people, including through more effective response to outbreaks and other health threats at the local, State, Federal, and global levels. New programs have prevented infections from food and healthcare, helped Americans quit smoking, reduce childhood obesity, and save lives of teens and others from car crashes, and extended lifesaving treatment and disease prevention in more than 50 countries.

A graduate of Columbia University's College of Physicians and Surgeons and School of Public Health, Dr. Frieden completed infectious disease training at Yale University and CDC's Epidemic Intelligence Service. The recipient of numerous awards and honors, Dr. Frieden speaks Spanish and has published more than 200 scientific articles, and we welcome him back.

And the floor is yours, Doctor.

STATEMENT OF TOM FRIEDEN, M.D., DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION

Dr. FRIEDEN. Thank you so very much, Chairman Smith, Ranging Member Bass, and the other members of the committee, both for your support for global health issues and for this opportunity to speak with you today about such important threats that we face and the important work that the CDC does in this country and around the world to protect Americans 24/7.

CDC's work is critical to addressing antimicrobial resistance and other global threats. What I would like to do here is briefly outline what the problem is, what we are doing about it, and what more needs to be done in three broad sections. Obviously, any one of those three could take a lot of time, so I will just give you some of the highlights. And I would really agree with all of what was said in the introductory comments from the chair, the ranking member, and the panel. This is a critical problem for us. If there is one basic concept, it is that we are inevitably interconnected as a world, and whether we like it or not, whether drugs are used correctly all over the world affects what happens to people in our communities.

I think we are facing essentially a perfect storm of vulnerability. There are four trends that are combining to make us in some ways at greater risk than we have ever been in the past. The first is the emergence and spread of new microbes, things like SARS and H7N9 influenza, which I can speak about later if you would like.

The second is globalization of travel, where people just a plane ride away can bring new organisms and resistant organisms from one part of the world to another, and also globalization of our food and medical supply. We are increasingly interconnected.

The third and the main topic of this hearing is the inexorable rise of drug resistance. We now face an increasing rate of resistance in many different types of organisms. To mention just three, we have tuberculosis strains—and tuberculosis is an area that I worked in for many years—that are resistant to virtually all antibiotics. We have strains of Gram-negative organisms, a group, a problem referred to as CRE, or carbapenem-resistant

enterobacteriaceae, basically very dangerous bacteria that are now resistant to most or even all antibiotics and are spreading in our country. And third, malaria. We are now beginning to see resistance to the last best drug we have treated on an outpatient basis, the artemisinin drugs and that class of drugs.

There are about 12 million Americans a year who go visit malarious areas, areas where they are at risk for getting malaria. If these resistant strains spread, the risk to people in this country will be substantial, in addition to the number of deaths and the amount of suffering and economic hardship that that will cause around the world.

The fourth risk is the potential of people, either intentionally or unintentionally, to create dangerous organisms and then to release those into the environment, either intentionally or unintentionally. Unfortunately, that has become easier as we have had technological advances.

Poor quality treatment, whether of tuberculosis or of pneumonia in the hospital, anywhere in the world, in Asia or Africa, can and in fact has become a nightmare in communities in the U.S. Today in many communities, most likely each of the communities that you represent in this country, there is someone in a nursing home or a hospital who is fighting for their life against an infection that doctors have limited or no tools to treat. And as we saw, for example, in Colorado, where there was an outbreak recently, the indexed patient had just come from Asia and undoubtedly had brought that organism with them through no fault of the individual and unavoidably.

Given the four big challenges that we face, I think there are two broad areas that give me a great deal of hope for being able to tackle them in the future. One is, frankly, political and one is technological. On the political side, I think we have more commitment to addressing this in more countries than we have ever had before. The SARS outbreak cost the world more that $30 billion. H7N9 Avian influenza in less than a month has cost China more than $2 billion. So I think countries get that, in addition to the human suffering, there are strong economic incentives to address health threats more effectively.

In addition, we have global commitments through things like the International Health Regulations which require countries of the world to find, report, and stop disease threats, and we are getting reporting from an increasing number of countries. We are nowhere near where we need to be, but we have the political framework to provide the support and assistance so that the world can be safer because each of the countries around us is safer and each of the countries in the world is safer.

And also, in terms of the commitment, we have success stories, and I will go into some of them, but we have seen that when we work with China or Thailand or Brazil or many, many other countries and help them see what needs to be done, they invest their own resources, their own substantial talent, their own capacities in doing that, so that we end up with a true partnership to reduce health risks both for their country and for the whole world.

The second broad reason for optimism is the advances in both laboratory work and informatics. They are breathtaking. We are

able to do things in the laboratory now that we could not have even dreamed of even just a few years ago. When I started at the CDC as an Epidemic Intelligence Service officer, we were just beginning to do genetic sequencing of tiny parts of the genome and to use that to figure out how tuberculosis and other organisms were spreading and to stop them sooner. It took a large room, months of work, a lot of very difficult comparison by hand sometimes of different patterns. Now much more information can be obtained in just 3 or 4 hours.

In the President's budget for fiscal 2014, there is an initiative called Advanced Molecular Detection. This initiative would allow us to go to this next generation of tools, find outbreaks that we are missing now, find them sooner, stop them more effectively, and figure out how they are spreading so we can prevent more of them. This is our single highest priority for the 2014 budget at CDC. And in addition, there are really exciting bioinformatics developments where we can look at huge amounts of data and begin to make sense of it. So I think we have real reasons for optimism.

In terms of what CDC is doing today, Ambassador Carson, the recently retired former Ambassador to Africa, said to me CDC is the 911 for the world, and we are happy to play that role, but we are even happier that we are now teaching countries to do that for themselves. And we are doing that in critical ways and with important platforms, and I want to thank the chairman, ranking member, and all members of the committee for your steadfast support for the PEPFAR program over the years. PEPFAR is really changing the world. There are more than 5.3 million people alive today who would be dead or dying otherwise. Last year alone a quarter of a million babies were born without HIV because of PEPFAR.

And in order to do what we have done with PEPFAR, with the leadership of the State Department and the Global AIDS coordinator, in order to have those results, we have also used PEPFAR as a platform. We have come in under budget and ahead of schedule, but we have also used PEPFAR as a platform to strengthen laboratories for HIV and for other conditions, to strengthen diagnosis, to strengthen maternal and child health. And what we have seen with that, for example, is strengthening through PEPFAR, and also through the Global Disease Detection Program, which is a CDC program that is a platform to find and stop outbreaks. We have seen strengthening of laboratories, which are crucial, of epidemiologists or disease detectives who are essential to finding and stopping problems and of prevention measures.

And just to mention a few of them, through the laboratory work, we now have created an African Society for Laboratory Medicine. Hundreds and soon thousands of laboratories throughout Africa will be certified so doctors and patients can rely on accurate results. Do they have an infection or not? Is it resistant or not? Is treatment working or not? Right now, without good laboratories, you can't answer those questions in far too much of the world.

We are also expanding influenza surveillance throughout Asia and Africa so that we can get a better handle on where it is emerging, how it is happening. We know that a risk anywhere can be a risk everywhere, and though we have worked with 50 countries on influenza surveillance, we were taken off-guard by H1N1 which

emerged in Mexico. We have expected new influenza strains to emerge in China and Southeast Asia, as H7 is now, but H1 took us by surprise. And that emphasizes a key point, which is that a blind spot anywhere is a risk to all of us. But our laboratory work at CDC has strengthened work throughout the world so that there is much more accurate diagnosis.

I will give you one example of this that CDC is doing with Uganda right now. Our CDC lab in Fort Collins, Colorado, came up with a new way to diagnose plague. Plague is often fatal, but with a simple $1 dipstick test, we are determining whether patients have plague.

CDC is working with local traditional healers. We are working with the medical care system, and CDC is also working to see what treatment is best for plague. As a result, in just the past few months, we have diagnosed people who would likely have died otherwise and treated them before they have spread plague to others, and we are transferring this technology to Uganda so that they don't need for us to do it in the future, as we have done with Ebola as an example. We have taught them how to control it, how to diagnose it, so instead of the large outbreaks that we saw a decade ago, we are seeing isolated cases or smaller outbreaks now.

The second key area is epidemiology, disease detectives, and this is so crucial to what we do, figuring out where disease is spreading, what the threats are, how to stop them, and whether our efforts are working. Our flagship program in epidemiology at the CDC is the Epidemic Intelligence Service. What we have done with more than 30 countries is help them start similar programs, called Field Epidemiology Training Programs. In the next year or 2, we will graduate the 3,000th disease detective. It is a 2-year, intensively mentored program. Eighty percent of the graduates stay in their home country, often in leadership positions, finding and stopping health threats. We also do epidemiologic investigations, and we start on average one of these a day in this country and on average, with our partners, one a day around the world to identify and stop a new threat.

And third is prevention, and we do this in important ways, including vaccination. After all, if you vaccinate and prevent an infection from happening, it won't be resistant, and we are seeing that with, for example, pneumococcal infections now, with vaccination resistances less of a concern in that one organism.

And of course we are closer than ever to the finish line in polio eradication, and the work of Rotary International and so many partners with CDC as the spearheading partner for this country has brought us to this point from 1988, when there were more than 350,000 children affected by polio in that year alone, to last year, when there were 222, the lowest number ever in the history of humanity as far as we know. We are also active in quarantine, identifying passengers who are ill and helping to reduce risks of people who come here from other countries.

That is some of what we at CDC are doing. In terms of what more is needed, I have to say, frankly, that we are not keeping pace with the threats. Microbes evolve and emerge rapidly, and we need to keep pace with that evolution. What we are faced with is a need to accelerate progress in three specific areas.

The first is detection. We need to fund and implement the Advanced Molecular Detection program. I brought for you a remarkable thing. This is a chip. It is one company. It fits very easily to carry. There are about five different companies that make something like this. But this chip in less than 4 hours can sequence the entire genome of not just one, but many different microbes, and with advanced supercomputing, we can then take—there are actually more than 10 million individual wells on this chip. We can take the fragments of DNA, and with a supercomputer put them back together like a jigsaw puzzle with tens of thousands of pieces to figure out where the connections are, whether it is resistant, how it is spreading, and whether it is becoming more virulent. We are using this technology now to track H7N9, and this is the kind of thing that we need to invest in more to make an even bigger difference going forward. We have too many blind spots.

Second, we need to improve our ability to respond to infectious disease and other threats. At CDC, we have an Emergency Operations Center, and if any of you are ever passing through Atlanta, please come by and spend an hour or 2 with us to see what we do there. We track what is happening around the world. We have an information system. We have a communication system. We respond rapidly. Ideally every country in the world should have some system like that. They will be safer and we will be safer.

And third, we need to increase our ability to prevent, through better vaccines, through antibiotic stewardship, through better supply chain control in terms of antibiotics.

So I will be happy to get into specific issues that you have raised. I don't want to take too much time with my introductory statement. But I do want to conclude with one simple thought, which is that a safer United States and a safer world is within reach if we invest in it, if we work with partners, if we take advantage of the unique opportunities that both the commitment of countries around the world has and this very exciting technology that we have to bring to bear on longstanding threats to our health. Thank you so much for your interest.

Mr. SMITH. Thank you so very much, Doctor.

[The prepared statement of Dr. Frieden follows:]

Testimony before the
Committee on Foreign Affairs
Subcommittee on Africa, Global Health, Human Rights, & International Organizations
United States House of Representatives

Meeting the Challenge of Drug-Resistant Diseases in Developing Countries

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U.S. Department of Health and Human Services

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For Release upon Delivery
Tuesday, April 19, 2013
Expected at 3:00 p.m.

Chairman Smith, Ranking Member Bass, Members of the Committee, thank you for the opportunity to testify today and for your ongoing support of the Centers for Disease Control and Prevention's (CDC) work in global health, which is critical to addressing antimicrobial resistance and the other global threats I will discuss today. I am Dr. Thomas Frieden, Director of CDC. CDC works 24-7 to save lives and protect people from harm. Today, I would like to specifically address how CDC works to protect Americans from threats that can cross our borders with ease. Four key trends have emerged in recent years. These trends are the rise of antimicrobial resistance, emerging global threats such as the Novel Influenza A (H7N9) virus, globalization of travel and trade, and the potential for deadly pathogens or products to inadvertently or intentionally be released. These trends demonstrate the need for public health action to identify serious health problems and to coordinate a targeted response that ensures the protection of our Nation.

Antimicrobial Resistance

Antimicrobial resistance is one of our most serious health threats. Infections from resistant bacteria are now too common, and some pathogens have even become resistant to multiple types or classes of antibiotics. The loss of effective antibiotics will undermine our ability to fight infectious diseases and manage the infectious complications common in vulnerable patients undergoing chemotherapy for cancer, dialysis for renal failure, and surgery, especially organ transplantation, for which the ability to treat secondary infections is crucial.

When first-line and then second-line antibiotic treatment options are limited by resistance or are unavailable, healthcare providers are forced to use antibiotics that may be more toxic to the patient and frequently more expensive and less effective. Even when alternative treatments exist, research has shown that patients with resistant infections are often much more likely to die, and survivors have significantly longer hospital stays, delayed recuperation, and long-term disability.

Resistance is not just a problem for the infected patient. When an infection is not effectively treated because of resistance, the microorganisms can persist and spread to others, further extending the resistance problem. The emergence of new forms of resistance that we have not previously encountered remains a risk. There are now at least 6 different deadly microbes that have strains resistant to all or virtually all antibiotics (e.g. Enterobacteriaceae, Acinetobacter spp., Pseudomonas aeruginosa, Enterococcus, Mycobacteria tuberculosis, and Neisseria gonorrhoeae), and healthcare providers are limited to providing supportive care rather than directly treating an infection. The costs of treating antimicrobial-resistant infections place a significant burden on society – a burden that will grow as drug-resistance spreads.

CDC combats antimicrobial-resistant infections here at home by collecting data on highly antibiotic-resistant infections and triggering the "Detect and Protect" strategy that identifies pathogens and transmission within and between facilities. CDC's work is critical to improve the capacity of healthcare facilities and states to detect drug resistant organisms and protect patients and communities. CDC regularly releases information on antimicrobial-resistant pathogens including our recent "Vital Signs" on carbapenem-resistant enterobacteriaceae (CRE), and issues guidance to healthcare providers on recognizing and treating resistant infections.

Globalization of Travel and Trade

Today, the high mobility and interconnectedness of global populations complicate the detection and prevention of both emerging organisms and antimicrobial resistant infections. The ease of international travel and trade, increasing population density, changes in animal husbandry practices, environmental changes, continuous pathogen evolution, and immune suppressive therapy have all increased the potential for the emergence and rapid dissemination of new microbes and new forms of known pathogens.

treatment of tuberculosis or of hospital-acquired pneumonia in Asia or Africa can become a challenge in United States hospitals within days.

The scope and complexity of today's antimicrobial threats underline the critical need for a public health response that is fully integrated domestically and globally to prevent not only antimicrobial resistant infections but also the broad range of other global health security threats that originate around the world and put our citizens at risk. Efforts to prevent such threats build on the foundation of proven public health strategies: immunization, infection control, protecting the food supply, antibiotic stewardship, and reducing person-to-person spread through screening, treatment and education. To mitigate global health threats we need better information about health threats anywhere in the world, better information to help guide the use of resources available to keep us safe, and ultimately a robust response to detect, prevent, and stop urgent and emerging global health threats. CDC, with its integration of laboratory and epidemiologic science and ongoing commitment to public health, both within the United States and abroad, is unique in its ability to leverage its expertise and respond aggressively to urgent and emerging global threats.

Current CDC Efforts to Strengthen Global Health Security

Throughout its history, CDC and its local, national, and international partners have addressed global health security threats by improving detection, response, and prevention. In the past decade alone, CDC has helped to detect, track, and respond to major public health threats in the United States and abroad including H1N1 influenza, H5N1 influenza (avian flu), Severe Acute Respiratory Syndrome (SARS), and West Nile Virus; numerous *Salmonella* and *E.coli* outbreaks; the cholera outbreak in Haiti and the earthquake and tsunami in Japan; and Hurricanes Irene, Katrina, and Sandy. In the past month, we have activated our Emergency Operations Center and been fully engaged in responding to a novel strain of influenza, H7N9.

CDC works with our partners around the globe to improve disease detection and response and help them develop capacity to respond to emerging threats. Our international influenza partners, including those in Africa and Asia, have made great strides in their ability to detect and respond to novel influenza viruses. For example, right now in China, authorities are moving quickly to limit the spread of Novel Influenza A (H7N9) virus. This type of flu has never before been detected in humans, and with the recent human cases and deaths, the government in China is working to monitor the illness and share information quickly. CDC's partnership with China over the past decade has allowed authorities there to move quickly to sequence the genome of this particular strain of Novel Influenza A (H7N9) virus, and post it in an internet database for others to see.

CDC strives to address these and other global health security threats in a comprehensive manner through programs that work on multiple, complementary levels, including:

- CDC's Global Disease Detection (GDD) Program develops and strengthens global capacity to detect, identify, and contain emerging infectious disease and bioterrorist threats through a network of 10 regional centers around the world.
- CDC supports the development of clinical laboratories in partner countries, improves labs to meet international quality standards, supports the creation of national laboratory strategic plans, and trains laboratorians to enable partner countries to detect and respond to a broad range of infectious diseases.
- CDC's Field Epidemiology Training Program (FETP) works with Ministries of Health to implement in-country programs to train disease detectives who lead detection and response efforts locally. Approximately 80 percent of FETP graduates continue to serve their home public health system. In China, we have helped train more than 100 disease control specialists who are now available to help contain H7N9 and other similar programs.

- The Global Foodborne Infections Network—founded by CDC, the World Health Organization (WHO), and other partners—it equips countries to better detect and control foodborne and other enteric infections, including antimicrobial resistant pathogens.
- CDC's Division of Global Migration and Quarantine (DGMQ) protects the health of United States communities by preventing the introduction, transmission, and spread of infectious diseases in mobile populations such as travelers, immigrants, and refugees.
- CDC, along with NIH, FDA, and others, developed the Public Health Action Plan to Combat Antimicrobial Resistance, a blueprint for specific, coordinated Federal actions to address antimicrobial resistance.

These and other CDC programs play a critical role in supporting the 194 WHO Member States that have committed to detect, assess, notify, and respond to public health emergencies of international concern (PHEICs). Under these commitments, Member States must report to WHO any cases within their borders of certain diseases, as well as notify WHO in a timely way of any threat that qualifies as a PHEIC—whether infectious, chemical, biological, or radiological.

Unfortunately, many countries lack the essential resources and sufficient health infrastructure to meet these commitments. CDC helps promote compliance and coordination for the United States and WHO member states, and supports countries with limited resources to develop the essential detection and control capacities for full and effective implementation. CDC's global health resources support at least one commitment in over 90 countries through our network of laboratories, surveillance systems, training programs in field epidemiology and laboratory science.

The Path Forward

CDC and our partners have made tremendous progress building the human resources, infrastructure and systems necessary to safeguard the health of the American people. My testimony reviews four key issues that we continue to focus on in this work: drug resistance, emerging organisms, globalization of travel, food, and medical supplies, and potential use of laboratories to engineer and inadvertently or intentionally release deadly pathogens or products.

While we are not able to predict with certainty which diseases will present epidemic threats to the United States and the world, or when they will threaten us, we do know that such potential threats will continue to be an important area of our focus. Globalization of travel and trade means that every day, people and goods that can transport disease are moving between and among nations as never before.

The following are just a few of the most dangerous emerging and urgent threats related to antimicrobial resistance and inappropriate antibiotic use that challenge us domestically and globally:

- carbapenem-resistant Enterobacteriaceae (CRE).
- drug-resistant gonorrhea: Strains of Neisseria gonorrhoeae circulating in the United States are showing evidence of declining susceptibility to cephalosporins, the only drugs left to treat this infection. Treatment failures were first detected in Asia several years ago and are now being observed around the world, raising concerns about the threat of untreatable gonorrhea in the United States.
- *Salmonella*: Antibiotic resistance is increasing among some strains of non-typhoidal Salmonella, a frequent cause of foodborne infection outbreaks. CDC focuses on judicious use of antibiotics in both healthcare and agriculture.
- multi-drug resistant (MDR) and extremely drug resistant (XDR) tuberculosis; : A significant and

international travel. United States cases are almost always imported or related to overseas exposure, where diagnostic capabilities for susceptibility testing are often limited and treatment is too often poorly organized and monitored.

- *C. difficile:* The rapid spread and burden of deadly *Clostridium difficile* infections is directly attributable to the accelerating use of broad-spectrum antibiotics; a significant proportion of these drugs are used unnecessarily research indicates that up to 50% of antibiotic use in healthcare is inappropriate.
- *Artemisinin*-resistant malaria. Since 2008, malaria infections in parts of Southeast Asia have been shown to be resistant to artemisinin drugs. This is the last remaining class of antimalarial drugs and forms the basis of malaria treatment around the world. If these resistant parasites were to spread to sub-Saharan Africa (which has occurred with other forms of drug resistant malaria), the results could be devastating.

Window of Opportunity

Despite these threats, we have an unprecedented opportunity to make progress. Given the scope of the threats that we face, we need to equip our scientists with the best available tools to identify these threats rapidly and accelerate our nation's response. That is why the FY 2014 President's Budget request proposes an Advanced Molecular Detection (AMD) initiative that would equip CDC's scientists with two powerful technologies -- molecular sequencing and bioinformatics -- to help solve complex disease mysteries. With new technology CDC can find outbreaks we're currently missing, find outbreaks sooner, stop them faster, and identify ways organisms are spread so we can better prevent them. With these new tools we will be able to take many important disease threats off the table, if we act now.

The basic tools of shoe leather epidemiology and spreadsheets that CDC's disease detectives rely on to

mysteries and solve them faster. Bioinformatics at CDC allows experts in the fields of molecular science, epidemiology and computer science to join forces as never before to prevent illness and save lives. AMD technology has already been used to investigate several outbreaks of drug-resistant infections. For example, researchers in the United Kingdom used whole-genome sequencing (WGS) to re-examine a Methicillin-resistant *Staphylococcus Aureus* (MRSA) outbreak that had occurred earlier in a neonatal unit, and were able to identify a cluster of associated infections as well as other cases not related to the outbreak. Although this investigation was performed retrospectively, it highlighted the potential use of WGS in providing timely and highly accurate information to better guide patient care and to improve infection control.

Genetic sequencing of infectious microbes, if funded, will revolutionize how CDC investigates and controls disease outbreaks, including those caused by antimicrobial resistant pathogens. CDC has attracted some of the brightest minds in science today. They need the right tools at the right time to protect Americans from infectious microbes.

A Safer United States and A Safer World

The United States must intensify our efforts to support countries in their development of systems to detect threats early, respond effectively, and prevent avoidable catastrophes. We must strengthen international laboratory systems and support the development of safe, secure national laboratory systems capable of conducting the full range of tests necessary to detect and characterize new threats. We must help our partner countries to develop real-time information platforms to manage and use critical disease data.

This is both a challenge and opportunity, and it is the shared responsibility of many actors: the United States Government, partner countries and governments, multilaterals including WHO, private sector, non-

respective strengths and identify critical needs that they can contribute to. Ultimately, three major components need to be addressed: Detection, Response, and Prevention.

Detecting Threats Early

To detect global health threats as soon as they emerge, all nations must develop epidemiologic and laboratory capacity that can detect and characterize any epidemic or threat in every part of every country. As our partner nations develop this core public health capacity, we must support them to ensure that their laboratory systems are safe and secure. We must help our partner nations develop effective surveillance systems that identify disease cases and outbreaks earlier. Effective laboratory systems are needed to characterize pathogens in order to inform appropriate responses. Developing nations face a critical shortage in trained disease detectives who can lead outbreak investigations and epidemic responses. Many nations lack basic infrastructure for surveillance and health information systems, and sufficient laboratories and other needed facilities. As I mentioned before, infectious diseases do not recognize national borders, which makes the need for effective international detection systems even more apparent.

Responding Effectively

When health threats are detected, nations must have rapid response capability and trained rapid response teams to respond to emerging information and contain disease outbreaks. All nations should develop interconnected, appropriately-scaled public health Emergency Operations Centers (EOCs). All nations should also develop and maintain real-time information systems able to securely store disease surveillance and other relevant data, present visualizations of outbreak data in real-time for actionable decision-making, and securely share health information with international health officials. Nations must also improve their border safety and ability to implement quarantine measures when necessary to control disease outbreaks and prevent the exportation of disease outside their borders through travel, migration, and trade.

There are excellent examples of detection and response capacity paying dividends—in Uganda, where CDC has supported the Uganda Virology Research Institute, the government has significantly reduced the amount of time between the first known case and the investigations, laboratory confirmations, and containment during Ebola virus outbreaks. Uganda no longer needs to send laboratory samples to Atlanta or other nations for confirmatory testing—they can do it in-country, cutting down their response time and saving lives. Due in part to this in-country capacity, recent outbreaks have been more effectively contained and have resulted in fewer cases and deaths. If disease outbreaks occur where detection and response capacity is poor, the impacts could be devastating.

Preventing Avoidable Catastrophes

To prevent these global health threats, we must ensure the global food, drug, and medical device supply is safe. We must improve infection control as well as the judicious use of antibiotics and other drugs, and intensify our efforts to develop new drugs and tools to reduce the impact of drug resistance. Nations must improve the safety and security of their laboratories and other facilities working with dangerous organisms to prevent the intentional or unintentional release of disease.

Conclusion

Epidemic threats to our security arise at unpredictable intervals and from unexpected sources, affecting Americans and others around the world. However, we have an unprecedented and unique opportunity to make progress in preventing these threats. We have the commitment and goodwill of partner governments, multilateral organizations and other critical stakeholders necessary to strengthen global health security. Now we must continue our work of adapting this commitment to global health security into action.

CDC is committed to work with our partners to leverage our current investments, and to support partner countries to detect, respond to, and prevent global health threats, including antimicrobial resistant threats. However, to reach the goal of a world safe from epidemic threats, the United States must redouble our efforts to generate commitment from partner countries and accelerate progress. The stakes are too high for the United States and international partners to delay.

Mr. SMITH. And without objection, your full written statement will be made a part of the record, as well as that of Ranking Member Eliot Engel.

Let me just ask you a couple of opening questions. Artemisinins, the power of these very important drugs to help cure people with malaria, may be thrown a huge curveball in, as I said earlier, in Cambodia, Burma, and particularly along the Thai border. And my question is, you know, there are 104 malaria-endemic countries. Obviously, and you know it, because you have been a part of this, we went from a $100 million in the year 2000 to $1.8 billion worldwide in 2012, certainly below what the target was if we wanted to really look to eradicate this horrible disease.

But how concerned are you and CDC about this problem? I know WHO talks about containment and trying to ensure that this does not spread to other places, particularly Africa, where it would be even more catastrophic. If you could spend some time on that, I would appreciate it.

Dr. FRIEDEN. Thank you. Thank you very much. And thank for your support for the President's Malaria Initiative. I have seen, as you have, this program in action in Africa and elsewhere and it is breathtaking. I have gone into communities that previously had extensive amounts of malaria. CDC has documented that in some of these communities, one out of every four medical visits of children was for malaria. One out of every two units of blood used for transfusion was for malaria. And in communities where they have implemented good control measures, we have seen essentially zero cases of malaria with good control and zero deaths. So we know that tremendous progress is possible.

We are quite concerned about artemisinin resistance. We have seen areas, as you say, in Cambodia and elsewhere where as many as 30 percent of patients have evidence that their particular strain of malaria is responding much less well to the artemisinins. This is our last hope for good malaria control. We have to preserve this drug.

I think you can think of drug resistance and prevention of drug resistance as something that we owe the world, we owe our children, that these antibiotics that we have been bequeathed by people who worked so hard to come up with them are preserved and can be used to protect lives for many years going forward.

What we think is possible is, first, to understand better what has happened and, second, to contain as well as possible, through a comprehensive approach to vector control, that is stopping the mosquito, treating effectively, diagnosing and treating well. And I think overall with malaria, we are quite reassured by the overall amount of progress that is happening.

The challenge with malaria is the challenge of persistence. We have seen big progress with malaria before, we let off our guard, and it came roaring back. That is exactly what we have to avoid. We have to intensify our work in Southeast Asia to understand and contain artemisinin resistance. At the same time we have to scale up the core malaria control interventions in Asia and Africa, especially so that we can reduce the number of deaths and the burden of illness.

There is still a lot we know that we are not doing and we need to scale up that net use and high quality diagnosis and treatment. There is still certain things that we don't know that we need to understand better about the malaria parasite, about the best tools to control it.

Mr. SMITH. And isn't it true that about half of those who should have bed nets have it, but we are running into the problem of the bed nets now losing their efficacy to keep the mosquitos out? So we need a replacement effort as well.

Dr. FRIEDEN. CDC scientists have looked at this carefully. The life of a bed net is not an easy one. They get embers put on them from the stove, they are worn out. And so having the first set of nets out was great and knocked down child mortality enormously. We have documented at CDC overall reductions, not malaria specific, but overall reductions in child deaths of 25 percent just from the malaria control program. But exactly as you say, Mr. Chairman, the nets now need to be replaced, and that requires resources.

Mr. SMITH. You know, in terms of drugs that are actually in the pipeline, you know, we know that newer orders of new types of antibiotics are few and in between. On tuberculosis, without objection, we are including testimony from Dr. Adrian Thomas from Johnson & Johnson. And he points out that Janssen is bringing forward a new medicine specifically indicated to treat a drug-resistant form of tuberculosis. It is called Sirturo. It seems to have gone to the next stage, although it is not used yet.

My question on that drug specifically and other drugs that are or not in the pipeline, particularly as it relates to malaria and multiresistant tuberculosis.

Dr. FRIEDEN. I think a key concept is that the development of new antimicrobials, new antibiotics is a necessary but not a sufficient condition. Now, for those two conditions particularly, we are very encouraged. It is the first new anti-tuberculosis drugs in decades. We think at this point it should be reserved for people for whom other drugs are not available. The CDC has convened national experts to look at what is the optimal way of using this new drug. We will need to have some clinical trials and the FDA moved very quickly to approve it so that patients could get it and their lives could be saved. There are some other drugs for tuberculosis that are in the pipeline that are somewhat encouraging, but what we know is, unless we improve our treatment system, we will lose those drugs as well.

In terms of malaria, the situation is perhaps a little less encouraging because virtually everything in the pipeline is either an artemisinin-related product, a synthetic artemisinin, or something that has the same resistance mechanisms as the artemisinins appear to have. So if we lose the artemisinins, we may lose the new drugs before we even get them.

I think this comes back to one of the core concepts of antimicrobial resistance. Resistance develops because of poor quality programs. It is very straightforward. If you have a good quality program, you will not get lots of drug resistance. And in tuberculosis, which I worked in for many years, one of the core concepts is that a poor quality program can create multidrug resistance faster than a good program can treat it, no matter how many resources

you have. And it is critically important to stop resistance from emerging and then to stop it from spreading.

We documented in New York City in the early 1990s that as many as half of all of the multidrug-resistant tuberculosis patients had actually caught it in the hospital. So hospitals can become an amplification point for drug resistance. That is why in our work in this country and our recommendations to other countries we have advocated a program called Detect and Protect. Detect and Protect. It is a simple concept: Find the patients that have the resistant organisms, protect them from harm with it, and protect other patients from getting it from them. And one of the things that we are encouraged by is the amount of progress in things like methicillin-resistant staph aureus where since 2005 we have documented a more than 50 percent reduction in the serious infections with that highly resistant organism.

This is not a problem for which we have no solution. We know what to do. It is a question of doing it. We also need some new knowledge, but what we can do now is a much better job at reducing the risk of detecting it, so we find the patients who have it and are protecting others from them and protecting them from the organism.

Mr. SMITH. Dr. Frieden, you made a very strong appeal to Congress to include in its budget what is in the Fiscal Year 2014 President's budget for the Advanced Molecular Detection initiative. As you point out, it combines two powerful technologies, molecular sequencing and bioinformatics. Could you perhaps elaborate on exactly how that works, and if you could also—and then I yield to my colleagues for their questions—speak to the area of labs, which you made reference to. How much connectivity is there with CDC and those labs? Are they at a basic level?

When I travel, I always ask about the labs myself. As a matter of fact, we had hearing in the last Congress with CURE International and the magnificent work they are doing with the infection-based hydrocephalic condition. And they have cured over 5,000 children in Uganda alone with a simple intervention that does not require any stents, it doesn't require, you know, the kind of follow-up that we often would need here. But it is infection based, they believe, and I watched one of the operations myself. The lab you mentioned in Uganda, I am not sure if that lends itself to the kind of detection that they need to do on this, but the labs. Where are they? Particularly in Africa, but elsewhere in the world, how do we grow those labs, as well as their sophistication and their connectivity to you?

Dr. FRIEDEN. Thank you very much. The Advanced Molecular Detection initiative would give our top-quality disease detectives the cutting-edge tools to find problems and stop them sooner. We have terrific scientists at CDC. We have a mandate within this country and abroad to detect and stop problems. But our hands are in some ways tied because we can't look into the microbe's genome in the way that technology actually allows us to today.

To give you just one example of that. With H7N9 influenza, which we can talk about more a bit later, we are very concerned to see will it develop the capacity to spread easily from person to

person. So far we are confident it hasn't. If it does, it has major implications for all of us and for every country.

We think we could learn more if we could go into clinical specimens and sequence the entire genetic material in those specimens. What happens when you grow an organism is that one particular strain grows very well and you can analyze that in a laboratory, but that is not exactly what is happening in the patient's body. What is happening in the patient's body is that there are many different—an assortment of different sub-strains or what are sometimes called quasi-species of that organism, and by sequencing from there you can figure out what is going to happen. You can skate to where the puck is going, not where the puck is.

AMD (advanced molecular detection) would allow us to do that, not just for influenza but for other organisms as well. It is a critical tool in helping us not only avoid problems, but prevent them in the future.

The laboratories, we are very encouraged by the progress around the world. I think there are two broad areas where we are going to see more progress. The one is what are called point-of-care tests, things that a doctor or nurse or other health worker can do at the patient's bedside or at the patient's hut side. Things that use a dipstick, as we are using in Uganda with plague now. So these are great technologies because they take not much time, they are highly accurate. It is how we are diagnosing HIV and malaria now in the field.

The other are the high-tech things where we can go in and look at a specimen, and there are now technologies which can look at two dozen different organisms to say in this one specimen of blood or sputum, which of these organisms are present. We have already use this on an experimental basis, for example, to look at an outbreak that we couldn't figure out what was causing it, and to our surprise it was a yellow fever outbreak, and because of that, we were able to do control measures. So there is the ability to bring these new technologies to bear on laboratories throughout the world.

The African Society of Laboratory Medicine, which PEPFAR helped to start, has made really progress by leaps and bounds. In fact, the Ethiopian Government has given them, the African Union has given them free space. Countries all over Africa are doing more with that. In Africa they are being very willing to do regionalization so that not every country needs to create everything. It is not efficient. They can work regionally very effectively. Our polio labs, our measles labs, our influenza labs, our foodborne labs are a global network where all of us are safer if every country can do a better job finding and tracking it.

Mr. SMITH. Before I yield to Ms. Bass, is there an inventory of all of those labs that could be made a part of the record and give us a better sense of—and also would be a place that when we do travel, we will visit.

Dr. FRIEDEN. We will certainly get you what we have in terms of an inventory. I will also mention that Congress requested that CDC do summaries of CDC's laboratory work last year and this year, so we have two reports on laboratory work that CDC does in

this country and around the world, and we would be delighted to share those as well, as the global laboratory network information.

Mr. SMITH. Thank you so much.

Ms. Bass.

Ms. BASS. Thank you.

Once again, thank you for your testimony. And I do look forward to, I was saying to the chairman, I would love to go to Atlanta and to see the CDC. So I hope to do that in the future.

You know, I wanted to ask you to address two areas, and one is, especially, you know, you said that internationally you thought there were good news on the political framework, so a couple of international issues I would like for you to address as to how countries are dealing with the unregulated sale of antibiotics, I mean, you know, you can get them over the counter in a lot of different countries, and how you are relating to countries and trying to get them to stop that practice.

The other thing is on counterfeit drugs and how prevalent do you think that is. You know, I have heard it is only anecdotal, though, but I have certainly heard that there is a lot of countries, countries in Africa and also many other countries around the world that are buying medications that they think are legitimate and they are not.

Dr. FRIEDEN. Both of those problems are big problems, and I don't think we have great news in terms of what is happening today to address them, but we do have a pretty clear pathway to get there.

On the unregulated sale of antibiotics, fundamentally this is a question of strengthening governmental public sector capacity to do core things that we take for granted in this country. We take for granted in this country that you can't go to the local pharmacy and pick up the latest antibiotic because you think maybe you need it. There is control over the use of antibiotics.

I think many countries are not in that world yet, and one of the things that we do at CDC and the FDA does as well is to work with partner governments, both the public sector and the private sector, to strengthen their capacity to do those core governmental capacities that they need to have and it will protect them and us. As an example, the Government of India has recently passed rules outlawing an inaccurate test for tuberculosis that was being used very widely in India and very misleadingly. So people were being told they didn't have TB when they did and that they did have TB when they didn't. They have also ruled that you can't get TB over the market.

Well, it is wonderful that they have taken those steps to have those rules so that people would need a prescription and you would have an accurate test. The next step is get them implemented effectively, and that is something that with any country we are willing to partner to help them get it right because that helps them and it helps us.

In terms——

Ms. BASS. Could I ask you a little bit, just one question about that? How about Mexico? You know, living in Los Angeles, I am just 2 hours from the border and a lot of times people do go across the border to get antibiotics and bring them back. We also had a problem in Los Angeles, frankly, with people selling them over the

counter at swap meets and different places. What is our relationship with Mexico?

Dr. FRIEDEN. We have a longstanding relationship with Mexico. We have, at CDC, binational programs, especially for some of the border areas. Mexico has a very robust public health system. In terms of antibiotic availability, I would have to find out and get back to you.

Ms. BASS. Okay.

Dr. FRIEDEN. In terms of counterfeit drugs, I don't think we have a good sense of the scope of the problem. We know it is a risk. We are very concerned about counterfeit artemisinins which we have seen and we are very concerned about the continued sale of monotherapy with artemisinin. One of the great ways to protect antibiotics is to the give them in pairs or groups of three or four. This makes a huge difference because it reduces the risk that if you develop resistance it will spread. This is one of the key lessons from tuberculosis and from HIV, that by using multiple drugs together you can cure patients more effectively and prevent the emergence of drug resistance.

So the sale of monotherapy artemisinin alone is just a terrible thing. It should never happen. And one of the things that we need to do more of is work with WHO, work with other international organizations, work with individual countries on reducing both counterfeit and irrational drug formulations on the market.

Ms. BASS. So then do you think the counterfeiting of drugs is not that big of a problem? I mean, it is talked about huge, and I don't know if it is playing that big of a role in drug resistance.

Dr. FRIEDEN. I think what I was trying to say is I don't think we know how big of a problem it is.

Ms. BASS. Oh, okay.

Dr. FRIEDEN. We know that there are many problems of which that is one, and the FDA has some new technologies that they are looking at which may help countries to identify counterfeit drugs more easily. A lot of this involves strengthening national regulatory authorities in other countries. That may sound like something, why would we want to do that? But we want to do that because we don't want people anywhere getting drugs that they shouldn't be getting or drugs that are ineffective when their resistance will soon be just a plane ride away from us in the U.S. We have already seen this happen with patients from Asia coming here and creating outbreaks of disease.

The answer to this isn't to try to say we are going to keep all microbes out. We are a globalized world, whether it is in our food supply, whether it is in our medications, whether it is in the travelers from the U.S. who go abroad and come back or people who come here, and in the case of tuberculosis, may have been here for decades and then develop an infection or an active infection with tuberculosis.

Ms. BASS. Thank you.

Mr. SMITH. Mr. Weber?

Mr. WEBER. Wow, where do I start?

I think you might have answered it, Doctor. You held up the chip, and you said the chip was instrumental, I think, in the detection of H7N9? And then you mentioned it had, oh, I don't know

how many pieces of information on it. Would you go back through that again, please?

Dr. FRIEDEN. Sure. And if you would like, I will also talk some about H7N9 at some point.

Mr. WEBER. Okay.

Dr. FRIEDEN. But this chip allows you to take either a culture that you have in a laboratory or a patient's specimen, blood or urine, and then to isolate the DNA and put it in these wells and then, through testing, figure out what DNA is in it, so what organism it is, whether the DNA encodes for resistance genes, whether, when we learn more, whether it is related to other organisms. So two people may have the same species infection, but they may be totally unrelated or they may have gotten it one from the other.

That kind of information can come from this kind of technology, but we need to learn more about it, we need to invest in it, we need to study the genome of many of the organisms that are causing human illness.

Mr. WEBER. Does that give us the ability to look at that DNA and say some strings of DNA are more resistant to drugs than others?

Dr. FRIEDEN. Yes, it would allow you to say which of the strains are more dangerous. I should give the caveat that this is only effective if it is done along with a lot of our traditional tools of laboratory work and what we call shoe-leather epidemiology, going out, asking people questions, figuring out who is sick, figuring out who is resistant, and who had contact where with who.

Mr. WEBER. Okay. So this gives the ability to predict, for lack of a better term, I think the phrase you used was to skate not to where the puck is, but is going to be.

Dr. FRIEDEN. That is what we hope it will do.

Mr. WEBER. Yeah. Wayne Gretzky he said over here.

Dr. FRIEDEN. That is right.

Mr. WEBER. Okay. I didn't know he was a doctor.

So what does that look like? I mean, are you anticipating strains evolving? What do you mean by that?

Dr. FRIEDEN. So we could see within an individual patient with influenza, in our current way of doing it, we can only see one dominant strain. With the new technology, we would actually see many strains that are in their body and making them sick.

Some of those strains may be drug-resistant. Some of them, in the case of H7, may have picked up the ability to spread person to person. We don't know that yet. That is something we will be tracking very, very closely as H7 progresses and as we learn more about it.

Mr. WEBER. And then you do what? You skate to where the medicine that he or she needs?

Dr. FRIEDEN. We might, for example, use a different drug to treat that patient. We might change the way we create the vaccine so that the parts of the vaccine that are active are active against a different strain of the virus or a different type of the virus. So it would help us to both find it and stop it and prevent it.

Mr. WEBER. So when you do that, when you have this data—and I forget how many pieces you said was on there, hundreds of millions, I am sure—are you able to get that into a database that says,

okay, we can share this and we know—at some point, somebody named the H7N9. And so at what point do you determine that a particular strain is wide and it gets a name? Who determines that, and when does that happen?

Dr. FRIEDEN. So, for influenza, we have really a wonderful global partnership. We work with more than 50 countries, we work with the World Health Organization. And after the SARS epidemic in China, the Chinese got very interested in improving their system. So we have worked very closely with them to set up systems to track influenza, to help them develop their laboratory abilities to be able to detect it and to do the genetic sequence of influenza.

And, in fact, we helped them become a World Health Organization collaborating center on influenza. And that is important, because, as a collaborating center, they are required to post on the Internet the entire gene sequence of every new influenza organism that they sequence, and they are happy to do so.

So, within days of receiving the first sample, the China CDC, which is the collaborating center there, had sequenced the genome in ways that we had helped them to do and then posted that on the Internet. We brought that sequence down and used the sequence to create a test to see if someone has this organism.

We have already had about two dozen people in this country coming back from China with severe illness who we have tested in our laboratories. None of them have had this. We don't think any have had it yet, of the ones that are still pending. But, in addition, we have already begun through what is called reverse engineering to make a vaccine against H7 based on this information from the Internet.

That is all great, but there is actually a next generation of genetic work that can be even more powerful and allow us to see in advance—we only saw this once it had made a bunch of people sick. It has now made over 100 people sick in China——

Mr. WEBER. Well, and that is my question. How do know over here in this country? How do you get that word out? At what point do you know that these people—do they have a common theme? They have been overseas, I guess.

Dr. FRIEDEN. So for the H7N9, if I can just address that for a moment, influenza is, of all of the infectious diseases, the one that can kill the most people. During the 1918 pandemic, more than 50 million people around the world died. The death rate among people who got the virus in 1918 was around 1.7 percent.

Now, in an average flu year in the U.S., average seasonal flu year, about 20 percent of people, 60 million Americans, get the flu. So if a virus could be that severe and infect that many people, it would be of enormous risk.

Mr. WEBER. Knock out 6,000 people, basically, if you went—and more than that at 1.7 percent of 60 million.

Dr. FRIEDEN. So that is why flu we take so very seriously and we track it all around the world. In fact, the Southern Hemisphere tends to get flu before we do, and we use the pattern there to decide which strains of flu to put into the virus for the coming year, and they use for the next year what happens here. So it is really a global collaboration on influenza.

H7N9 is a new scenario. We have never seen anything quite like this before in China. And there are aspects of it that are reassuring, there are aspects that are not reassuring, and there are things that we are specifically doing.

I will tell you the most reassuring thing about the bird flu in China now, the H7, is that it is not spreading from one person to another efficiently. And we are quite confident in that. The Chinese Government has checked more than 2,000 contacts of people with flu, and they have found only a very small handful of secondary cases, whereas with a usual flu we might expect to see as many as 20 or 30 percent of those people sick. So we are not seeing spread. And we are seeing most of the cases had contact with birds—ducks, pigeons, quail, or chickens.

So what is reassuring is we are not seeing person-to-person spread. We are also seeing very good collaboration with the Chinese authorities. In fact, the head of our flu program is there now on a World Health Organization delegation and getting great collaboration. The Chinese Government has asked us to send them three of our top experts in flu to work with them for weeks and months to come so that they can do everything possible to get ahead of it. And for 10 years we have been increasing our preparedness for threats and working better across the U.S. Government. That is the good news.

The not-so-reassuring news is that this particular strain of bird flu, H7, is severe. So, of the 100 people or so who have gotten it, about 20 have died, and many of the remaining are quite sick. We also don't see birds getting sick from it. Now, you might say that is a good thing, but it is not, because with H5N1, another bird flu that we have been tracking for 10 years, with H5, the birds get sick and the country culls the flock and it stops spreading. Here the birds aren't sick, so you can't cull the flock. You don't have that marker.

And H5, the other bird flu, spread all over the world in years. So it started in Asia and soon was all over the Middle East and Africa. And for H5, it took about 18 months between the time the first case came and we had 100 cases. H1 was recognized on April 1st of this year, and we already have 100 cases.

So there are things that we are very concerned about in what the genome looks like, and creating a vaccine is particularly challenging for these types of virus. But our plan for addressing the flu basically uses four pillars that the Department of Health and Human Services coordinates. The first is tracking so we know what is happening. The second is mitigation, figuring out how we can reduce damage if it comes by treating people and helping them survive flu, by good care in hospitals. Third is vaccine development. Vaccine development in influenza takes at least 6 months, and for H7 it is likely to require probably two doses and maybe an adjuvant because the human body doesn't respond well to this. And communication. We are very up front. We have a fundamental rule: Tell them what you know when you know it; tell them what you don't know and how you are trying to find out. And that is our approach to this.

The bottom line with H7 is that, currently, it is not spreading person to person. If it does not gain that capacity, it will not cause

a pandemic. But I cannot predict if it will and, if it does, if it is going to be tomorrow or in 10 years.

Mr. WEBER. Sure.

Let me ask one final question, if I may, Mr. Chairman.

In your remarks, you said there were four trends, and your fourth trend was the potential for folks to intentionally or unintentionally create dangerous organisms and release them, which got my attention, because in all this talk about, you know, biological warfare, for example, with all of these databases up on the Web you talked about, where they identify a strain, they are supposed to post it as a member of the WHO, do you guys, for national security reasons, work with the branch of government that would track something like that?

And I don't know if you can really go into it. How do you identify that strain, if you will? And how do you know who is working on it?

Dr. FRIEDEN. So within this country, within the United States, CDC operates something that looks at what are called select agents, things that could be used for terrorist purposes or could be dangerous if they got out of the laboratory. There are currently about 354 laboratories in this country that work with one or another toxin or select agent.

We are generally not a regulatory agency, unless you want to import or work with plague or something like it in your laboratory, in which case we will do the regulation. And for each of these laboratories, we do on-site visits and we oversee them. And we ensure that both the workers there don't get infected, because if they got infected, they could bring it outside and they could be very sick, and we do everything possible to minimize the risk of spread.

Mr. WEBER. Well, I am not too concerned about the laboratories that are here. I was concerned about your example or, for example, other foreign countries posted their stuff online. If they find something that is so bad that there is really hardly a cure for it, what would keep them from just sending it over to our country? That is really my question.

Dr. FRIEDEN. Yep. The risk of biological warfare is real.

Mr. WEBER. Do you all track that?

Dr. FRIEDEN. We do. And we also retain under our jurisdiction the strategic national stockpile. It is countermeasures for a natural or manmade disaster that we can deploy to anywhere in the U.S. within 12 hours.

Mr. WEBER. So if you see a country that is hostile to America—of course, they probably aren't going to post that on the Web. That is the catch-22. If they come up with something like that, there is no good way for us to have a preventative vaccine in place without foreknowledge.

Dr. FRIEDEN. Well, we look at all the potential risks. So we have scientists at CDC who are essentially the world's experts in just about all of the threats that could be faced.

We know, for example, that smallpox is something that we have been very concerned about someone reintroducing in the world. CDC, working with World Health Organization, eradicated smallpox from the world, but we have been concerned that someone might bring it back as a terrorist agent. We have in the stockpile

enough vaccine to vaccinate the country. So we have essentially taken that risk off the table.

Mr. WEBER. Okay.

Dr. FRIEDEN. Not all risks are that amenable to our intervention, but we both track and think of how to prepare.

And I would mention that the advanced molecular detection allows us to do very specific fingerprinting of strains which would help us in identifying the source of it. So that it is something that has additional benefits, as well.

Mr. WEBER. Okay. Thank you.

Thank you, Mr. Chairman. I yield back.

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

Mr. Bera?

Mr. BERA. Thank you, Mr. Chairman.

And my apologies, Dr. Frieden, if you have been asked this question. But in my opening statement, I talked a little bit about how we come up with the next generation of antibiotics and certainly extend the life of those antibiotics.

Part of the challenge that we face is, as our domestic pharmaceutical companies and global pharmaceutical companies look at making those investments and the amount of research that goes into developing that next generation and then the return on that investment, many of these companies are making those cost-benefit analyses and realizing, you know, the costs of prohibitive. So, clearly, the Federal Government has a role in making sure we are providing adequate resources and funding, creating that partnership between industry and academia to do this research and develop the next generation.

But the critical question here is, as we are making those investments, we certainly want to extend the life of these therapeutics. And we are seeing—I was reading my home medical journal, the Annals of Internal Medicine, in this latest issue, and they were touching on the increasing incidents of CRE and the impact that is having and potentially will have in the future.

What are some thoughts that you might have as we come up with this next generation to both protect and extend the life of these discoveries here domestically? But then also, we talk about the ease of obtaining antibiotics overseas in third world countries. What are some creative things that we can do here in Congress, working with industry, to, again, extend the life?

Dr. FRIEDEN. I think everything you say is a critical issue. We need to figure out how to preserve the antibiotics we have now and ensure that, as new antibiotics come on line, which we anticipate and hope they will, we don't lose them as quickly as we have lost some of the current ones.

The amount of antibiotic usage in the U.S. is actually astonishing. CDC just published data on this within the past week, I believe. There are more than a quarter of a billion, "B," quarter of a billion courses of antibiotics prescribed in this country each year, about 8 courses of antibiotics for every 10 people in the country. And in some parts of the country, it is 12 for every 10 people.

So I think we really have to work on antibiotic stewardship, making sure that when people need antibiotics, they get them, and when they don't need them, they don't get them. And CDC has

sponsored some antibiotic stewardship programs which have been shown to save money for facilities. They require an investment; you have to have staff doing them. But they pay off. And this is something that is really quite important.

In terms of the pipeline of how to get new antibiotics, the NIH is critical in that regard, and the FDA as well. It is figuring out ways to help companies bring products to the market sooner and at lower cost so that we can address this gap, because we don't have a lot of great antibiotics in the pipeline.

In terms of preserving antibiotics, I talked briefly before about the new antibiotic for tuberculosis, which we are trying to do just that with, saying, let's just reserve this for the patients for whom there are no other options while we figure out the best mechanism for it.

As you know as a doctor, Dr. Bera, if you use antibiotics correctly, you won't get drug resistance. A lot of the things that we need to do are fairly simple and straightforward: Getting healthcare workers to wash their hands, removing urinary catheters and intravenous lines very promptly and only using them when essential, getting patients off ventilators as rapidly as possible, reducing healthcare-associated infection.

And CDC's healthcare-associated infection program does that in this country. Other countries, particularly low- and middle-income countries, are not doing much in that area. And that is an area we would like to expand work on, but we are unable to for lack of resources.

Mr. BERA. You have touched on a couple areas. I am astonished at the number of courses of antibiotics. I realized there was a lot being prescribed; I didn't realize it was that high.

Are there best practices that we can make sure physicians around the country are utilizing that have been shown to be effective? So for years we have been talking about appropriate antibiotic prescriptions and prescribing habits. Are there best practices that you have seen and effective models?

Dr. FRIEDEN. Yes, we have seen antibiotic stewardship models that really make a difference. We have a program at CDC called Get Smart About Antibiotics. And we think it is important to involve both the clinicians and the community. Because the clinicians will say to us, you know, the patient came in and they demanded antibiotics, and they said if I don't give them to them, they are going to go to the guy down the street.

Mr. BERA. Right.

Dr. FRIEDEN. So I think it is important to get more awareness that antibiotics—no medicine is without risk. So things should absolutely be taken when they are needed but not be taken when they are not needed. And I think that is the essence of the best practice.

We have often seen that getting nondoctors involved in the system—pharmacists, nurses, allied health workers—can be very important.

And the other thing that has been very effective is to track the prescribing trends of different doctors, not as a way of criticizing someone, but providing feedback, and if there are outliers, pro-

viding them that information and education so that they can do a better job.

When I worked in tuberculosis control, we were able to standardize treatment for tuberculosis across an entire city, an entire country, using outreach workers to reach out to doctors, private doctors, in case the prescription wasn't appropriate or rational, and just provide them with education and information so we could improve the quality of care.

Mr. BERA. Great.

You know, just one last question. My colleague, Mr. Weber, touched on the threat of biological agents and so forth and the imminent threat here locally, or domestically. You know, in the full committee, we have certainly had a few hearings on Syria, a country that increasingly looks like it is going to fall and a country that we know possesses some of these biological agents.

You know, as we prepare ourselves for, you know, all threats and so forth, is there anything that you would like to see from this body in terms of helping the CDC make sure that we are fully prepared for——

Dr. FRIEDEN. Well, at CDC we work 24/7 protecting Americans from threats, whether they are natural or manmade, whether they are infectious or environmental, whether they are from this country or abroad.

What we do, frankly, is dependent on the resources we are provided. So when we have fewer resources, that means the resources that we provide to State and local entities to detect and respond to problems are less, that means the resources we have to work globally are less.

Sequestration has had broad and serious impacts on CDC's ability to detect and respond to a wide variety of problems. We understand that we are in fiscally constrained times. We have done a lot to be more efficient, to make sure that as much of our money that we are entrusted goes out for direct program services. But we are concerned that our ability to respond is really at the breaking point in some of our programs.

Mr. BERA. Right. Thank you.

Mr. SMITH. Thank you.

Mr. Meadows?

Mr. MEADOWS. Thank you, Mr. Chairman.

And thank you for your illuminating testimony.

And one of the areas that I want to broach is, Dr. Bera and I actually have had a lead letter together where we had Dr. Collins come in with NIH, National Institutes of Health. And he was sharing some of the groundbreaking, exciting research that they have been doing, particularly in influenza.

And so what kind of correlation or partnership has there been with that group? And what can be learned from that partnership?

Because as he was sharing, you know, right now we treat, and he described it, it is kind of like a mushroom. And, you know, every year you get a flu shot, and, you know, it is a different strain, and we are coming up with that, and that there is a hope that one day we will be able to, in the not-too-distant future, just have one shot for that stem that, from a DNA perspective, helps us address that.

And so are you working with them, and in what ways?

Dr. FRIEDEN. We work very closely with NIH, with FDA, with other parts of HHS. In fact, in the H7N9 response, we are having twice-weekly coordination calls to make sure we are perfectly aligned.

What we are finding—really, what NIH is working on we really hope will work out.

Mr. MEADOWS. Right.

Dr. FRIEDEN. They are doing the basic research to try to come up with a universal, long-lasting flu vaccine.

Mr. MEADOWS. Right.

Dr. FRIEDEN. This would be phenomenal. Right now, our flu vaccine works okay. It doesn't work as well as most of our vaccines. You have to take it every year. Sometimes we have a mismatch, and it doesn't——

Mr. MEADOWS. Right.

Dr. FRIEDEN [continuing]. Meet the strains. If you look at something like H7, it doesn't work particularly well. You have to give two doses and maybe an adjuvant.

Mr. MEADOWS. Right.

Dr. FRIEDEN. So we have real challenges, and we ardently hope that they will succeed.

But our job really is to take what is existing knowledge and turn it into practice. That is the CDC space——

Mr. MEADOWS. Okay.

Dr. FRIEDEN [continuing]. Take what we know how to do and get it happening as broadly as possible to protect as many people as possible.

And we are able through our laboratory, for example, to accelerate and improve some of the current vaccine development techniques. We are able through our laboratory to cut a month off vaccine production time through a new technology that we have developed.

So it really is a partnership across the system.

Mr. MEADOWS. All right. So you mentioned the FDA. And, obviously, there is this, where you are analyzing and seeing the issue and identifying the problem, so to speak. And then we have to figure out a way, how do we deal with the problem. And so there are a number of components there. One would be the FDA; the other would be pharmaceutical companies.

What are the barriers that you face right now with either sharing that information or speeding up the process? You know, if you are identifying the issue, how do we make sure that as quickly as possible that we see the enemy and that we know how to fight it, with drugs or whatever? What are the barriers that you are seeing there?

Dr. FRIEDEN. I think within the Federal system, we are very well-aligned. I honestly might not have said that a few years ago, but that——

Mr. MEADOWS. So that is part of the government that is working well, is what you are saying?

Dr. FRIEDEN. Yeah.

Mr. MEADOWS. Okay.

Dr. FRIEDEN. Just to take food safety as an example, we have weekly reviews with both USDA and FDA on every potential cluster and investigate those that make sense.

On influenza development, we are really very tightly aligned between FDA, USDA, NIH, and ourselves. So, for example, if we go forward to make vaccine for H7, even trial vaccine——

Mr. MEADOWS. Right.

Dr. FRIEDEN [continuing]. It would be part of HHS that contracts for that, it would be NIH that does the clinical trials, it would be FDA that licenses it. So I think that is going well.

There are at least two areas where we face real challenges. One of them is, as I have mentioned, our limitation in being able to do some of the advanced molecular work that would open doors and make things visible that are currently invisible to us.

Mr. MEADOWS. Right.

Dr. FRIEDEN. The second are sometimes some of the incentives. The private sector is a crucial partner in this work, but for some of the work they don't have the incentive to do what might do the most good, either because a product wouldn't pay or because the market isn't necessarily there. If we don't have an H7 pandemic, there will be no market for the vaccine. So there are areas where the government needs to step in because there is no natural incentive for it.

New antibiotics are an area where we are trying to get the incentives right, because it does cost so much money to develop a new antibiotic. How do we make sure that, if they do get one to market, it is preserved and they can get a return on their substantial investment to bring it to market?

So I think those are two of the issues that we are looking at more.

Mr. MEADOWS. All right. And so let's look at that prioritization, because I think you have come up and you have said, okay, you know, we have fiscal constraints, we have, you know, a priority on where we are in terms of our investment on these.

How would you look at those areas and prioritize them? I mean, I have a number of friends that have worked for the CDC. I mean, they come up to the mountains of North Carolina to get away, and so I get to see them on a regular basis. And all of them are very dedicated, capable individuals.

I still at times, though, see the CDC, what I believe, may have mission creep in terms of getting into areas that tangentially maybe have to do with disease. For example, I mean, I was real surprised to see some of the advertising done by the CDC with regards to gun control. You know, there was an issue there that came up, and I was just blown away that there would even be anything there.

And so, how can you—or who is the best person to prioritize those things for us?

Dr. FRIEDEN. Well, first, I am not aware of any advertising CDC has done on gun violence. So if there is any example of that, I would like to see it.

Mr. MEADOWS. I will get you a copy of it.

Dr. FRIEDEN. I think the bottom line for us is a return on investment, return on investment both in terms of health and in terms of dollars.

So with influenza as an example, we are looking at what will be the return on investment from a better vaccine. Now, we hope we will come up with a universal vaccine. It might or might not happen. But we know that if we can increase——

Mr. MEADOWS. Right.

Dr. FRIEDEN [continuing]. The use of existing tools, we can tamp down the impact of influenza.

For many of the vaccines, we know that if we got to higher vaccination rates, we would have less disease in the future. In fact, vaccines are a great example of that. For every $1 we spend on vaccines, we get $3 back in healthcare savings and $10 back in societal savings.

So I think, for me, the key concept is the return on investment. It is not something we do because it makes us feel good or we think——

Mr. MEADOWS. Oh, no, no. And I realize that. And I guess my question becomes, how do we share the issue of how concerning these issues are without creating panic and yet, at the same time—because, you know, funding becomes—you know, you only go to the doctor when you know you are sick. And a lot of these issues are here, that are out there, that, quite frankly, the average person on Main Street has no idea that the threat exists.

So how do we share that information where we build, you know, public consensus and yet, at the same time, not create a fear, you know, where everybody is running around on Main Street with masks on their face?

Dr. FRIEDEN. So, right now, for H7 as an example, there is nothing for people to do differently. As a family member, as a parent, there is nothing that I am advising my family to do differently.

Mr. MEADOWS. Because of the contagious nature that you talked about earlier.

Dr. FRIEDEN. That is right.

Mr. MEADOWS. Okay.

Dr. FRIEDEN. For 10 years, we have told people, if you visit China, don't go to live markets. That was to protect you against SARS and avian influenza and other things. And that remains our advice, and that is——

Mr. MEADOWS. Sure.

Dr. FRIEDEN [continuing]. Essentially the only thing different.

For us at CDC, it is different. We have activated our emergency operations center. We are tracking it 24/7. We are sending teams out to look at it. We are working with State and local governments. We are working with neighboring countries. So there is a lot that we are doing.

I think the issue of building consensus is a challenging one, and it really gets to the heart of this hearing, I think, which is, how do we ensure that there is a widespread recognition that in terms of global health threats we are inevitably interconnected, that a risk anywhere is a risk everywhere, that a blind spot anywhere puts us all at risk? And that is something that I think all of us can think together on, how to convey that most effectively.

Mr. MEADOWS. So you think the Federal answer—and this is my last question, Mr. Chairman—you think the Federal answer to that would be to prioritize those, identify those areas, as we did with smallpox when there was a potential risk with smallpox after 9/11, and identify those areas that may not have a pharmaceutical payback, so to speak, and say that is where the Federal Government needs to get involved, and on the others leave it to the private sector?

Dr. FRIEDEN. Yes, in general. I would say that it is not an either/or. There are very important public-private partnerships where, say, take the example of the cell-based flu manufacturing capacity that the public sector invested in but Novartis also invested in.

Mr. MEADOWS. Right.

Dr. FRIEDEN. So I think there are partnerships possible there.

In terms of the gaps, we have talked about the advanced molecular detection. We have also talked about the global health security and the need to have that network around the world, because if any country is weak, we are all at higher risk. And, ultimately, things like vaccines can take diseases off the table but require more investment or, where we have the vaccine, investment to get it into people.

Mr. MEADOWS. Okay.

I thank you, Mr. Chairman, and I yield back.

Mr. SMITH. Thank you very much.

Dr. Frieden, you have been very generous with your time. If I could just ask you a couple of final questions, and perhaps any other colleagues who would like to ask a final question as well.

You mentioned drug-resistant gonorrhea. If you perhaps could speak to how prevalent that is, that we saw strains, "we" being the government, detected in Asia, and now it has been observed around the world, including the United States.

On MRSA, is that something that is multiplying globally, and at what rate, perhaps?

I, on one trip to Korea, met with a number of people, but one of them was a priest who was doing work in Pyongyang to help multi-resistant TB and XDR TB-affected patients, who are unbelievably sick, and yet he was allowed in. In that case, Kim Jong Il welcomed him because he was doing such a great humanitarian initiative.

When you have a country like North Korea, or perhaps Iran or Eritrea, or some other country where human rights abusers are in power, like China and even Vietnam, they welcome, thankfully, the collaboration to try to mitigate and stop disease spread, but in a country like North Korea, that is not happening. Do you have any recommendations on what could be done, you know, to build that bridge? Because, obviously, I am sure CDC would love to be there helping to eradicate something like—or help people with drug-resistant tuberculosis.

Let me also just ask you briefly if you can comment on the, maybe you might not want to, but the $236 million in last year's budget for Fiscal Year 2012 will be cut by $45 million in the President's budget for TB to $191 million. I mean, yes, these are hard times, but it seems to me that that money, minimally straight-lining it, if not increasing it, is—every dollar well-spent.

And, finally, back in the early 1980s, during the child survival revolution, Jim Grant and all the others at UNICEF, and of course our Government was pushing hard for it, David Stockman came along as OMB Director and zeroed out in its second year the child survival emphasis on vaccines or rehydration therapy and the like. I offered the amendment to double it, to double down and say not only should we not end that money, we need to increase it.

And I travelled to El Salvador and many other places when vaccination days were called. And pertussis, diptheria, and other killers of children, kids were vaccinated against it. Now, this is obviously several decades later, and I am wondering, are we hitting all the diseases? Are any of those diseases, like pertussis or diptheria, morphing into something that becomes drug-resistant?

We thought we were on our way to eradication and universal immunization, but obviously they keep rearing their ugly heads. I mean, we need to redouble our efforts on the child survival effort as well.

If you could speak to that.

Dr. FRIEDEN. Thank you so much.

On drug-resistant gonorrhea, we have seen an increasing proportion of strains in this country and around the world that are resistant to cephalosporins. So, earlier, just a few months ago, we issued new treatment guidelines to use two drugs for patients, not one, because, again, using two will reduce that emergence.

We know that it is a problem globally and we will have to address it globally. There is a lot of global transmission. And what we have seen is the need to have that kind of action. We have worked very actively with the World Health Organization to track it.

In terms of MRSA, I think there is very limited evidence or knowledge about where it is globally. So that is one of the things that we would like to work with other countries on to further develop. But we do know that in this country we have been able to substantially reduce invasive MRSA through some commonsense, low-cost ways of reducing infections in hospitals.

I agree with you completely that health is often a great way to foster collaboration. I mean, look at the partnership, steadfast partnership, over the past 10 years with China on influenza and other infectious diseases, regardless of what else may be happening. Or if you look at smallpox eradication, that was done when the Soviet Union still existed. There was a partnership between the CDC, the U.S., and the Soviet Union for smallpox eradication.

So health can be a safe space. And the days of tranquility that you mentioned of James Grant and UNICEF were a very inspiring example of that, where people actually stopped the war to vaccinate kids.

I can't comment on the budget on TB. I believe that is the USAID budget that you are referring to.

In terms of the child survival revolution and what is happening now, vaccinations remain one of the great accomplishments of all time in humanity. Take measles alone. There are about 10 million children who would be dead who are alive today because of measles vaccinations. Low cost, it is highly effective.

We know that there are limits to vaccines. For example, our pertussis vaccine doesn't work as well as we would like. Many countries are not using the vaccines that we know work. So rubella vaccines have to be used at a high rate or you actually can do more harm than good. So the vaccine work is very important.

One thing that has been very encouraging is GAVI, the Global Alliance for Vaccines and Immunizations, which is funding and creating an incentive for companies to sell at a reasonable price vaccines around the world. And the vaccine manufacturers have been wonderful partners in this. The result of that is that new vaccines against rotavirus, something that CDC helped develop; against pneumococcal disease, which killed lots of kids last year; and against haemophilus are being introduced around the world.

We still have much further to go to make sure that every child in the world can have the potential of receiving those vaccines. And there are some new vaccines that we are hoping to see developed in the coming years. But right now we have kind of a full plate getting these scaled up.

We have worked in Haiti, for example, to help that country implement new vaccination programs at a higher rates for three of leading killers that they were never vaccinating against before post-earthquake, so rotavirus, pneumococcal, and haemophilus. Major killers, at least probably 10,000 deaths per year per pathogen. And those are getting introduced last year, this year, and next year in Haiti.

So I think it is a great example of how much can be accomplished in global health. And I really thank the committee, the chairman for how much you have done in this area.

At CDC, we also have searing memories of the zeroing out of the child survival revolution, because we were expanding vaccination. And lot of children could have had a fuller, longer life if that program hadn't been stopped.

Mr. SMITH. Doctor, is there anything you would like to say in conclusion?

Dr. FRIEDEN. Only to thank you again for your attention to these issues and to emphasize that, despite all the problems, despite all the threats, despite all of the risks, I remain fundamentally optimistic. We have commitment and we have tools, we have great people, we have will in this country and around the world. There is a broad consensus in this country and around the world of what needs to be done. And I am confident that we will make even more progress in the future.

Mr. SMITH. Thank you so very much for your great testimony but, more importantly, your leadership. It is making a huge difference and deeply appreciated by this committee. Thank you.

Dr. FRIEDEN. Thank you very much.

Mr. SMITH. The hearing is adjourned.

[Whereupon, at 4:44 p.m., the subcommittee was adjourned.]

APPENDIX

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

April 16, 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 2172 of the Rayburn House Office Building (and available live on the Committee website at www.foreignaffairs.house.gov):

DATE: Tuesday, April 23, 2013

TIME: 3:00 p.m.

SUBJECT: Meeting the Challenge of Drug-Resistant Diseases in Developing Countries

WITNESS: Tom Frieden, M.D.
Director
Centers for Disease Control and Prevention

By Direction of the Chairman

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

COMMITTEE ON FOREIGN AFFAIRS

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

Day *Tuesday* Date *April 23, 2013* Room *2172 Rayburn HOB*

Starting Time *3:00 p.m.* Ending Time *4:44 p.m.*

Recesses [*0*] (____to ____) (____to ____) (____to ____) (____to ____) (____to ____) (____to ____)

Presiding Member(s)

Rep. Chris Smith

Check all of the following that apply:

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

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

TITLE OF HEARING:

Meeting the Challenge of Drug-Resistant Diseases in Developing Countries

SUBCOMMITTEE MEMBERS PRESENT:

Rep. Randy Weber, Rep. Karen Bass, Rep. Mark Meadows, Rep. Ami Bera

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.)*

Prepared statement from Rep. Engel
Prepared statement from Dr. Adrian Thomas of Johnson & Johnson
Materials submitted by Dr. Frieden of the Centers for Disease Control

TIME SCHEDULED TO RECONVENE _____
or
TIME ADJOURNED *4:44 p.m.*

Subcommittee Staff Director

Ranking Member Eliot L. Engel
Statement for the Record
Hearing on "Meeting the Challenge of Drug-Resistant Diseases in Developing Countries"
April 23, 2013

Chairman Smith and Ranking Member Bass, thank you for holding today's hearing on drug-resistant diseases in developing countries.

One of my proudest accomplishments as a member of this Committee was the enactment of the Tom Lantos and Henry J. Hyde United States Global Leadership Against HIV/AIDS, Tuberculosis, and Malaria Reauthorization Act of 2008. This legislation incorporated provisions of my bill, the Stop Tuberculosis (TB) Now Act, and represents a historic United States commitment to the global eradication of TB. As a result of this law, 4.5 million individuals are projected to have been successfully treated for TB by the end of the year.

Unfortunately, in 2011, there were still an estimated 8.7 million new cases of TB and 1.4 million individuals lost their lives as a result of TB. Furthermore, the prevalence of multi-drug resistant TB (MDR-TB) continues to rise, as does that of extensively drug resistant TB (XDR-TB). India, China, Russia, and South Africa are believed to be home to 60% of the world's MDR-TB cases and the WHO estimates between 2009 and 2011, the number of MDR-TB cases reported in high-burden countries nearly doubled. In 2011 alone, there were approximately 310,000 MDR-TB cases reported, of 9% of which were XDR-TB. Totally drug resistant TB has already been found in India, Iran, Italy and South Africa.

The United States is also feeling the impact of drug-resistant TB. One need look no further than the recent discovery of a Nepalese man in Texas, who, after traveling through 13 different countries in the last three months, was diagnosed with XDR-TB. This individual exposed thousands of people to this dangerous strain of TB, and his treatment alone will likely cost between $100,000 - $300,000. Unfortunately, he is not alone -- it is estimated the United States has had more than 28 cases of XDR-TB over the last decade.

Worldwide, the World Health Organization (WHO) estimates that 3.7% of new cases and 20% of previously treated cases of TB are thought to be multi-drug resistant. As we look at the drivers of the epidemic of drug resistance, it is critical that our bilateral and multilateral TB programs are well-funded to ensure those who have TB get and maintain adequate treatment for this devastating disease.

I am disappointed to see that the Administration's FY 2014 budget calls for a significant cut in bilateral TB program funding, down to $199 million from the FY2012 funding level of $256 million. It is my hope this Congress will recognize the significant public health threat posed worldwide by drug resistant TB and provide adequate funding for these programs as part of the Fiscal Year 2014 State and Foreign Operations appropriations bill.

Chairman Smith and Ranking Member Bass, I commend you for holding today's hearing and thank our witness, Dr. Thomas Freiden, for his time and expertise in the fight against drug-resistant diseases both in the United States and worldwide.

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

Written Testimony of
Adrian Thomas, MD, FRACP
Vice President, Global Market Access & Commercial Strategy Operations and
Head, Global Public Health at Janssen, the pharmaceutical companies of
Johnson & Johnson

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

United States House of Representatives
April 2013

Meeting the Challenge of Drug-Resistant Diseases in Developing Countries: Perspectives from an Innovator Pharmaceutical Company

Remarks as prepared for delivery.

Chairman Smith, Ranking Member Bass, members of this important Subcommittee: Thank you for inviting me to testify today. I am Dr. Adrian Thomas, vice president of Global Market Access and head of Global Public Health at Janssen, the pharmaceutical companies of Johnson & Johnson.

On behalf of Johnson & Johnson, I applaud you for your leadership in bringing to light one of the most critical global issues of our time: drug-resistant diseases in developing countries.

And before we delve into the frightening array of problems that drug-resistance presents, I am pleased to be able to bring to the Subcommittee some very good news.

This year, Janssen is bringing forward the first new medicine specifically indicated to treat a *drug-resistant* form of a tuberculosis mycobacteria. The medicine is known as Sirturo™, or bedaquiline. Sirturo™ is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in adults with pulmonary multi-drug resistant tuberculosis, or MDR-TB. Sirturo™ received conditional approval from FDA in late December of last year, based on Phase II data. While Phase III and other research on Sirturo™ moves forward, patients in need of the drug in the U.S. have begun to receive it. Throughout the next several years, pending regulatory approvals in other countries, patients around the world who suffer from multi-drug resistant TB will likewise begin to access this new medicine.

There is great cause for celebration here. And there is cause for caution.

Sirturo™ must be used appropriately to preserve its efficacy. The challenge of ensuring its appropriate use is a massive one, especially within weak, overburdened and fragmented health systems. As our teams have met with government leaders in countries with disproportionately high burdens of MDR-TB, this much we've learned: Even where there is a *will* to ensure appropriate use of first- and second-line TB drugs, there is not always a clear *way*.

Globally, MDR-TB is on the rise. The World Health Organization estimates that more than 500,000 new cases of MDR-TB are added each year, even as rates of drug-sensitive TB are declining.[i] Although an estimated 60 percent of the total MDR-TB burden is currently clustered in three countries—India, China, and the Russian Federation[ii]—this is a disease that knows no boundaries. Nearly every country in the world has reported one or more cases of MDR-TB in recent years.[iii] In Eastern Europe, MDR-TB accounts for at least 20 percent of all new TB cases.[iv] In some countries, that rate exceeds 30 percent,[v] and continues to climb.

The threat of drug-resistant disease anywhere poses a threat to all of us, everywhere.

And so the challenge is great, as you know. In the short time that I have with you today, I'll outline, at a high level, several recommendations for the Subcommittee's consideration—all of which point toward a way forward in meeting the challenge of drug-resistant disease in developing countries.

1. Encourage the establishment of National Drug-Resistance Prevention Strategies in Developing Countries, Especially in Current and Prospective High-Burden Countries

First, we must encourage the development and implementation of National MDR-TB Strategies—and Drug-Resistance Prevention Strategies generally—in high-burden countries around the world.

The drivers of drug resistance are many, and multi-layered. In tuberculosis, drug resistance can arise from a patient's inability or failure to complete a full course of treatment as prescribed. We all know this – but it's not the end of the story. Medicines of substandard quality also contribute to drug resistance. So, too, does an erratic drug supply—too often the case for fragile, conflict-affected states. Other drivers of resistance include the inaccurate diagnosis of illness, or no diagnosis of illness, and incorrect or cavalier prescribing practices.[vi] And this is to say nothing of the deeper social drivers of drug-resistant disease, chief among them the health and living conditions attendant to extreme poverty.

Once a drug-resistant strain emerges in a tuberculosis patient, that strain becomes transmissible. Today, direct transmission is the leading cause of MDR-TB's spread.[vii]

As nations battle against this spread, they must account for the factors which contribute to resistance, and work systematically to mitigate them. Every country where MDR-TB is present must have a National MDR-TB Strategy in place. Clear prioritization and dedicated funding will be necessary to make such Strategies meaningful and actionable.

At minimum, these Strategies should include investments in diagnostic tools and laboratory infrastructures for better detection and monitoring of drug-resistant disease. These Strategies can also incorporate the dissemination of new mobile technologies to improve patient adherence to treatment. Ultimately, all tactics pursued must fit within the broader goal of ensuring tightly controlled and tightly enforced protocols for the appropriate use of drug therapies.

Indeed, we cannot allow any new medicine in our public health arsenal—Sirturo™ or otherwise— to be rendered less effective by improper, inadequate, or incomplete treatment regimens.

2. ***Leverage the United States' Diplomatic Strength and its Relationships with Supranational Organizations to Rally a Global Response to the Spread of Drug-Resistant Disease, Including MDR-TB***

Through the force of its diplomatic strength and its relationships with supranational organizations, the United States is uniquely positioned to rally a global response to drug-resistant diseases like MDR-TB.

The U.S. has proven its leadership in the fight against drug-resistant disease, both through its past efforts to combat the threat of MDR-TB in its major cities, for example, and through a sustained vigilance that is evident in hearings like this one today.

As MDR-TB experts Salmaan Keshavjee and Paul Farmer have observed: "The U.S. response to the outbreaks of MDR tuberculosis in New York City and elsewhere was bold and comprehensive; it was designed to halt the epidemic. A similar response has not yet been attempted in low- and middle-income countries."[viii] This Subcommittee, in partnership with U.S. agencies, can help to light a way forward for these low- and middle-income countries—to help them put into place the kind of bold and comprehensive investments required to halt the epidemics of drug-resistance within their borders.

3. ***Encourage and Invest in the Research & Development of New Therapies to Treat Drug-Resistant Disease.***

Ultimately, to conquer the upsurge in drug-resistant disease, we will need new medicines. On this front, the story of Sirturo™ can be instructive.

I hope to be able to share that full story with each of you at some point in the near future. For now, suffice it to say that the R&D process behind Sirturo was—and remains—lengthy[, risky,] and very expensive.

Going forward, novel approaches and policies will be needed to invigorate research for drug-resistant diseases. The U.S. government has begun to chart this path with promising new programs, including two newer programs at NIH: The Therapeutics for Rare and Neglected Diseases program and the Cures Acceleration Network. Likewise, the Priority Review Voucher, created by Congress in 2007, marked a positive step forward in encouraging R&D for neglected diseases.

But for drug-resistant diseases especially, the need for more R&D remains stark. To address this need, we must explore, together, a broader array of options for the *de-risking* of drug development. These options include, potentially, public-private co-funding models to support early- to late-stage drug development. Advance Market Commitments; social-impact-bond financing; prize models and other innovative mechanisms can all help to propel this field forward.

As proud as we are to have been a pioneer in drug development for drug-resistant disease, we will be prouder when our industry counterparts join this effort en masse. We look forward to working with you to bring this larger effort to fruition, saving lives in the process.

Thank you, Chairman Smith, Ranking Member Bass, and members of this Subcommittee, for your leadership on this issue and many others. I look forward to answering any questions you may have.

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[i] World Health Organization. (2013, March). *Multidrug-resistant tuberculosis (MDR-TB) 2013 update*. Retrieved from http://www.who.int/tb/challenges/mdr/MDR_TB_FactSheet.pdf

[ii] World Health Organization. (2013, February). *Tuberculosis fact sheet n°104*. Retrieved from http://www.who.int/mediacentre/factsheets/fs104/en/

[iii] World Health Organization. (n.d.). *Notified MDR-TB cases (absolute numbers), 2011*. Retrieved from https://extranet.who.int/sree/Reports?op=vs&path=/WHO_HQ_Reports/G2/PROD/EXT/MDRTB_Indicators_map

[iv] Shah, Wright, Bai Et al. (2007, March). *Worldwide emergence of extensively drug-resistant tuberculosis*. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2725916/

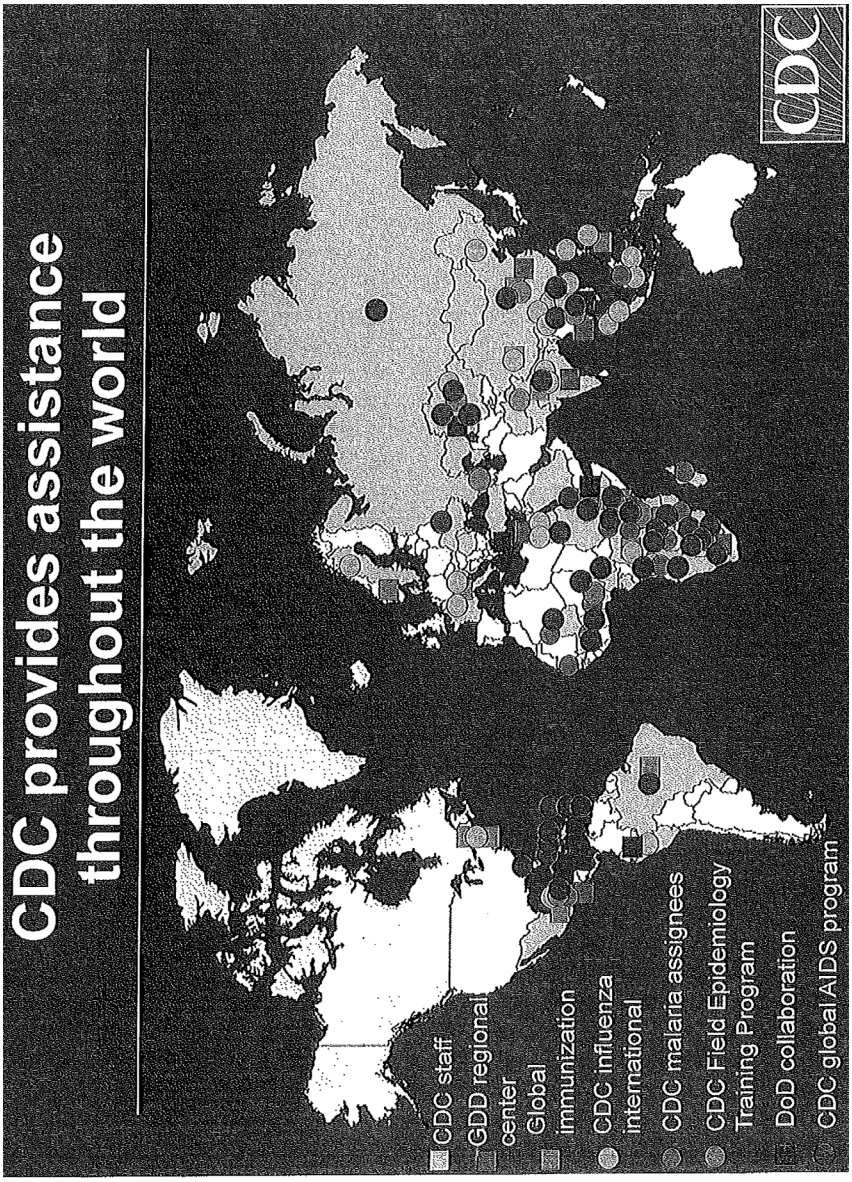
[v] Global Alliance for TB Drug Development (n.d.). *MDR-TB / XDR-TB*. Retrieved from http://www.tballiance.org/why/mdr-xdr.php

[vi] World Health Organization. (2013, February 04). *Support for monitoring MDR-TB treatment in Belarus.* Retrieved from http://www.euro.who.int/en/where-we-work/member-states/belarus/news/news/2013/04/support-for-monitoring-mdr-tb-treatment-in-Belarus

[vii] Keshavjee, S. and Farmer, P. (2012, September 06). *Tuberculosis, drug resistance, and the history of modern medicine.* Retrieved from http://www.nejm.org/doi/pdf/10.1056/NEJMra1205429

[viii]Keshavjee, S. and Farmer, P. (2012, September 06). *Tuberculosis, drug resistance, and the history of modern medicine.* Retrieved from http://www.nejm.org/doi/pdf/10.1056/NEJMra1205429

MATERIAL SUBMITTED FOR THE RECORD BY TOM FRIEDEN, M.D., DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION



U.S. Department of Health and Human Services

Centers for Disease Control and Prevention (CDC)

Report to Congress on Internal Laboratory Activities of CDC and Associated Funding Levels

[Signed]

Thomas R. Frieden, M.D., M.P.H.

> "CDC's laboratory scientists are at the heart of our work to protect America on a 24/7 basis. CDC could not succeed without them. State and local public health departments, health care professionals, and many others rely on our laboratory scientists for specialized testing, consultation, and new technologies to address a wide and growing spectrum of health threats. CDC is the de facto reference laboratory for the United States and for the entire world, an invaluable and indispensable resource."
>
> — Thomas R. Frieden, MD, MPH
> Director, Centers for Disease Control and Prevention

In Senate Report 112-84, which accompanied the Fiscal Year (FY) 2012 appropriations bill for the U.S. Departments of Health and Human Services, Labor, Education, and related agencies, the Senate Committee on Appropriations stated,

> "The Committee requests a report to Congress no later than 120 days after the enactment of this act that details CDC's various internal laboratory activities and associated funding levels."

The Centers for Disease Control and Prevention (CDC) has prepared this report in response to the committee's request. The body of the report is organized into 21 sections that correspond with the standard format of the CDC budget documents with which the Committee is familiar. Each section addresses a specific CDC budget activity and its associated internal laboratory activities. The report encompasses the majority of CDC's laboratory activities. Relevant definitions and descriptions of laboratory activities not addressed appear in the Explanation and Definition of CDC's Laboratory Activities section that follows.

Overview of CDC Laboratories

CDC is committed to keeping America safe from threats to its health, safety, and security, whether foreign or domestic. CDC promotes health and quality of life domestically and globally by preventing and controlling disease, injury, and disability. Achieving excellence in laboratory science and in delivering laboratory services is key to fulfilling CDC's mission.

CDC's laboratories are integral elements of its prevention and control programs that address infectious and chronic diseases, birth defects and developmental disabilities, and environmental and occupational health. These programs cannot succeed without the actionable information and knowledge generated by CDC's laboratory scientists, many of whom are nationally or internationally recognized as preeminent experts in their fields.

Thanks in part to the laboratories it operates, CDC has been able to

- identify and take action to address new disease threats (e.g., the influenza strain that erupted into the 2009 pandemic influenza A [H1N1] and the novel virus that triggered severe acute respiratory syndrome [SARS] in 2003);

- track the emergence of drug-resistant infections and develop new ways to counter these threats;
- confirm the sources of foodborne disease outbreaks (e.g., those associated with cantaloupes in 2011 and eggs in 2010), and advise industry, the Food and Drug Administration (FDA), and states on corrective actions;
- serve as World Health Organization (WHO) Collaborating Centers (e.g., for influenza, malaria, tularemia, rotavirus, rabies, poxviruses, and viral hemorrhagic fevers) and participate in global health networks;
- address priorities in human immunodeficiency virus (HIV) diagnosis, prevention, and treatment to reduce HIV-related illness and death in the United States and internationally;
- determine and address the causes of flare-ups of vaccine-preventable diseases (e.g., the spike in U.S. measles cases that appeared in early 2011 after 15 years of low incidence);
- examine suspicious substances to determine if they pose any threats and report findings so that appropriate actions to protect the public can be taken (e.g., the 2001 anthrax attacks);
- test for potential health dangers stemming from toxic releases (e.g., the Deepwater Horizon oil spill in 2010) and provide scientifically based information on their health implications to the public and to decision makers;
- collect objective data for use in designing interventions to prevent and control disease and disability (e.g., through the National Health and Nutrition Examination Survey [NHANES], the only U.S. collection of biologic samples related to nutrition and health on a populationwide basis);
- ensure accuracy of the tests state public health laboratories use to screen newborns in the United States for medical conditions that can lead to lifelong disability or death if not detected; and
- develop and disseminate authoritative public health guidelines (e.g., for the respirators that protect millions of health care professionals, first responders, and industrial workers from airborne viruses and pollutants).

CDC's laboratories are distinct from the many commercial, hospital, and physician-office laboratories that perform tests related to individual patients. CDC has the unique ability to develop and perform highly sophisticated, cutting-edge tests important for monitoring population health and to serve as the last-resort reference laboratory, able to confirm or rule out a new virus or other pathogens. Some of this work is performed in high-containment laboratories where scientists work with especially dangerous infectious and chemical agents. CDC is also uniquely capable of establishing definitive standards for laboratory testing, including tests used in both public health and clinical settings. In addition, CDC's laboratory scientists focus multiple,

complementary disciplines on solving complex public health problems. A recent example is the effort to develop and validate new mass spectrometry test methods for detecting human exposure to botulinum toxin — a result of collaboration between CDC's Environmental Health Laboratory, which specializes in assessing chemical exposures, and Foodborne Disease Laboratory, which specializes in biologic testing. The new test methods will support responses to biologic or chemical terrorist attacks and foodborne illness outbreaks, as well as investigations of potentially contaminated cosmetic products.

CDC laboratory scientists work closely with their programmatic partners within CDC, including epidemiologists and other colleagues across a wide spectrum of disciplines. In turn, CDC relies on the work its laboratory scientists conduct across multiple domains that are crucial to the agency's priorities and to its vital contribution to national security. Examples include the following:

- **Surveillance** — Testing to track trends in diseases and other health threats, monitor national health status, and evaluate the effectiveness of vaccines, treatments, infection control programs, and other public health and medical strategies.

- **Emergency Response** — Testing for rapid identification of the causes of disease outbreaks from natural or human-made biologic threats (BT), chemical threats (CT), or radiologic threats (RT) to ensure rational treatment decisions are made.

- **Standards Setting** — Establishing technical and scientific standards for public health and clinical laboratory tests (e.g., for the millions of cholesterol tests performed annually in our nation's hospitals and clinical laboratories, and for antimicrobial susceptibility testing).

- **Quality Assurance** — Developing, promoting, and evaluating standards and guidelines for public health and clinical laboratories, and providing technical assistance and reliable reference materials to support test validation, quality control, and proficiency testing.

- **New Product Development** — Applying research findings to develop new types of tests, new vaccines, and other products, many of which are licensed to private companies to manufacture and make available through the commercial marketplace.

- **Health System Support** — Providing scientific, technical, and financial assistance to help state and local public health agencies, health care providers, nonprofit groups, federal agencies, and other partners improve their laboratory practices and strengthen their laboratory systems.

Partnerships

CDC relies heavily on collaboration with other federal agencies, state and local public health departments, health care organizations, and other domestic and international partners to accomplish its mission. The agency's laboratory scientists partner closely with public health

laboratory professionals and scientists in other U.S. Department of Health and Human Services operating divisions, the U.S. Department of Homeland Security, the U.S. Department of Defense, the Federal Bureau of Investigation, the U.S. Agency for International Development (USAID), and the U.S. Department of Agriculture (USDA), among other federal agencies; WHO and ministries of health worldwide; and industry and nongovernmental organizations (e.g., the Association of Public Health Laboratories).

State and local public health laboratories protect health in their jurisdictions and partner closely with CDC as critical parts of the nation's public health laboratory safety net. Among other services, state and local public health laboratories perform many public health reference tests, confirming or ruling out patient diagnoses, advising providers on the significance of patient test results, and simultaneously using test results to monitor community health trends. Of special note are the critical roles they play in detecting the onset of threats at the front line and in providing surge capacity, helping to manage the high number of tests required during public health emergencies (e.g., the 2009 influenza A H1N1 pandemic).

CDC provides critical support to state and local public health laboratories by designing, developing, and transferring high-quality testing practices to them and by providing technical consultation, training, financial assistance, and high-priority supplies not available from other sources. In addition, CDC has sponsored creation and operation of national networks for disease cluster detection and investigation, rapid communication, and test result validation during foodborne disease outbreaks (e.g., PulseNet) and in response to BTs or CTs or other public health emergencies (i.e., the Laboratory Response Network [LRN]). PulseNet enables state and local public health agencies to detect clusters of illnesses in one or many states rapidly by comparing DNA fingerprints of bacteria from ill patients through the use of an online pattern database maintained by CDC. These disease clusters often represent silently developing foodborne disease outbreaks that can be controlled if detected early. More importantly, PulseNet-detected outbreaks provide industry and regulators the information they need to fix problems in our food supply that would otherwise go unnoticed. LRN — comprising 162 laboratories, most of which can confirm the detection of BT agents and a subset of which have additional capacity to do CT testing — expands and leverages the capacity of the public health laboratory system to respond to public health threats and emergencies. An estimated 85% of the U.S. population lives within 100 miles of an LRN member laboratory, ensuring broad access to testing during public health emergencies. Other federal agencies (e.g., the U.S. Department of Defense, the Federal Bureau of Investigation, FDA, USDA, the U.S. Department of Energy, and the U.S. Environmental Protection Agency), collaborate with the network and coordinate response activities through the Integrated Consortium of Laboratory Networks. Public health laboratories in Australia, Canada, Mexico, and the United Kingdom also participate in LRN.

University- and industry-based scientists and members of scientific and professional associations also are valuable partners for CDC's laboratory scientists. They bring important viewpoints from relevant disciplines and contribute new knowledge from research and front-line industry and clinical experience. In turn, CDC's laboratory scientists use multiple channels to disseminate information to these partners about the new tests, improved testing methods, and laboratory best practices CDC develops. These channels include the electronic Health Alert Network and

Laboratory Outreach Communication System and CDC's *Morbidity and Mortality Weekly Report*, among others. In addition, CDC maintains and continually expands its invaluable collections of unique biologic specimens that CDC scientists and colleagues in universities and other settings use for research into the causes of disease and for development of new medical and public health interventions.

Explanation and Definition of CDC's Laboratory Activities

For the purposes of this report, *internal laboratory activities* are defined as laboratory-related activities that CDC employees and contractors conducted during FY 2011 in the United States, primarily at CDC facilities, and which were funded by the budget activities that appear in the accompanying table. Those facilities are located in the Atlanta, Georgia, metropolitan area and in Anchorage, Alaska; Ft. Collins, Colorado; Cincinnati, Ohio; Pittsburgh, Pennsylvania; San Juan, Puerto Rico; Spokane, Washington; and Morgantown, West Virginia.

This report addresses testing and applied research activities, as well as selected scientific, technical, and laboratory support services. In general, support services include activities such as oversight and implementation of CDC's policy on dual-use research of concern; management of CDC's central collection of more than 6 million biologic specimens for use by CDC and extramural researchers; laboratory security and worker safety protection services; provision of bioinformatics and information technology services; and provision and maintenance of physical facilities. They also include assistance in complying with federal regulatory mandates (e.g., the Clinical Laboratory Improvement Amendments, diagnostic device regulations, and the Select Agents and Toxins regulations). The Emerging Infectious Diseases, Public Health Scientific Services, and Public Health Preparedness and Response sections of this report include information regarding laboratory support services funded from these three appropriations.

This report also addresses domestically based CDC laboratory activities that support external partners, including laboratories operated by ministries of health in other countries. Support for external partners includes provision of laboratory technical support and training, program administration, and cooperative agreement management. Many of these activities advance CDC's global health priorities. Several sections of this report (e.g., the Global Health sections) include descriptions of domestic CDC laboratory activities that support overseas activities.

Exclusions

Two types of laboratory-related activities that receive funds appropriated to CDC do not appear in this report, explained as follows:

Domestic Laboratory-Related Activities Conducted by Grantees — This report does not provide information on laboratory-related activities that state and local public health departments or extramural researchers conduct with funding they receive from CDC through cooperative agreements or other mechanisms. However, activities that CDC employees and contractors conduct in support of those grantees (i.e., managing cooperative agreements) are referenced where appropriate and as noted previously.

Global Laboratory Activities — CDC supports multiple laboratories located in other countries and also helps to build and operate global laboratory networks (e.g., the Global Polio Laboratory Network, which supports worldwide poliovirus surveillance). This report does not address these overseas activities or those of other CDC global laboratory networks. However, where appropriate, it provides information about CDC's domestically based support for such activities, as noted previously.

FY 2011 Funding for CDC Internal Laboratory Activities

The accompanying table indicates that CDC obligated $412,029,029 to its internal laboratory activities during FY 2011. These funds derived from three sources, as follows:

- CDC direct budget authority ($336,602,298 total);
- the U.S. Public Health Service Evaluation Fund ($39,648,974 total); and
- the Public Health and Social Services Emergency Fund ($35,777,757 total).

The table (next page) is organized according to the format of CDC's FY 2011 operating plan.

Certain internal CDC laboratory activities are supported by funds that other federal agencies transfer to CDC. Such activities are not included in this report, with the exception of those supported by the U.S. Public Health Service Evaluation Fund and the Public Health and Social Services Emergency Fund. Also excluded are laboratory activities supported by no-year funds appropriated to CDC in fiscal years before FY 2011 but obligated to laboratory activities during FY 2011.

The complete version of this report can be accessed at
http://www.cdc.gov/osels/lspppo/pdf/LSPPPO_Report_Signed_V2 (clear version).pdf

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