

EXAMINING THE U.S. PUBLIC HEALTH RESPONSE TO THE ZIKA VIRUS

HEARING BEFORE THE SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS OF THE COMMITTEE ON ENERGY AND COMMERCE HOUSE OF REPRESENTATIVES ONE HUNDRED FOURTEENTH CONGRESS SECOND SESSION

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¹ Mr. Person's testimony is available at: <http://docs.house.gov/meetings/if/if02/20160302/104594/hhrg-114-if02-wstate-personst-20160302.pdf>.

EXAMINING THE U.S. PUBLIC HEALTH RESPONSE TO THE ZIKA VIRUS

WEDNESDAY, MARCH 2, 2016

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:15 a.m., in room 2322 Rayburn House Office Building, Hon. Tim Murphy (chairman of the subcommittee) presiding.

Members present: Representatives Murphy, Burgess, Griffith, Brooks, Mullin, Hudson, Collins, Cramer, Castor, Tonko, Clarke, Kennedy, Welch, and Pallone (ex officio).

Also present: Representative Bilirakis.

Staff present: Brittany Havens, Oversight Associate, Oversight and Investigations; Charles Ingebretson, Chief Counsel, Oversight and Investigations; Tim Pataki, Professional Staff Member; Chris Santini, Policy Coordinator, Oversight and Investigations; Alan Slobodin, Deputy Chief Counsel, Oversight and Investigations; Sam Spector, Counsel, Oversight and Investigations; Dylan Vorbach, Deputy Press Secretary; Christine Brennan, Minority Press Secretary; Jeff Carroll, Minority Staff Director; Waverly Gordon, Minority Professional Staff Member; Ryan Gottschall, Minority GAO Detailee; Chris Knauer, Minority Oversight Staff Director; Una Lee, Minority Chief Oversight Counsel; Elizabeth Letter, Minority Professional Staff Member; Andrew Souvall, Minority Director of Communications, Outreach and Member Services; and Kimberlee Trzeciak, Minority Health Policy Advisor.

OPENING STATEMENT OF HON. TIM MURPHY, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Mr. MURPHY. Good morning. We are here for the subcommittee on Oversight and Investigations for the Committee on Energy and Commerce for a hearing called “Examining the U.S. Public Health Response to the Zika virus.”

This morning we’ll be examining this other public health crisis affecting the Western Hemisphere, that Zika virus. This virus of mosquito-borne pathogen is currently rampaging through South and Central America, and in total has spread to more than 48 countries and territories.

While as of late February there have been no known locally-acquired mosquito-borne cases reported in the Continental U.S., over 100 travel-associated Zika virus cases have been identified in over

20 states. Outside of the 50 states local mosquito-borne transmissions have been reported in Puerto Rico, the U.S. Virgin Islands, and American Samoa. Public health officials in the U.S. are bracing for the time when Zika passes from a traveler with Zika in his or her blood to a local mosquito, and then to another person.

Only about one and five people with Zika infection exhibit symptoms, most of which are mild and flu-like. Of greater concern is growing evidence of a link between Zika infection and microcephaly, a congenital birth defect in infants born to infected mothers, as well as Guillain-Barre Syndrome, an immune disorder that can result in temporary paralysis. On this basis, the World Health Organization recently declared Zika a public health emergency of international concern.

The virus may also be transmitted through blood transfusions and sex, leaving the Center for Disease Control to issue interim guidelines for prevention of sexual transmission, and the Food and Drug Administration to take steps to reduce the risk to the U.S. blood supply.

Thus far, there has been only one reported case in the U.S. of a child born with microcephaly to a mother with travel-associated Zika virus. However, other pregnant American women have become infected with Zika. Our understanding of how the virus may impact a developing child during pregnancy is nearly non-existent. We can, however, reasonably assume that a virus affecting development of the brain on a large scale leading to microcephaly in the first trimester will also impact significant developmental functions for infants, toddlers, and children exposed to the Zika virus. These include my concerns for developmental disorders of difficulty with learning, primary sensory and sensory integration, memory, attention, concentration, behavior, mood, language, motor, and others.

Given all of the unknowns the importance of acting now to protect pregnant women and women of reproductive age from exposure to Zika virus cannot be overstated. However, we must be equally concerned with protecting infants and children with developing brains and not wait 5 to 10 years for symptoms to appear before we take action to protect, to track, and to treat.

To help prepare for and respond to Zika, the Administration recently requested Congress provide over \$1.8 billion in emergency funding. The request includes support to states, U.S. territories, the International Community for Mosquito Control, virus testing, and expanding surveillance and response activities. It also supports efforts to build upon existing resources to develop a vaccine for Zika.

While the Administration's request has worthy aims, it's one-off emergency funding approach like the \$6 billion for Ebola emergency funding demonstrates a reactionary posture towards public health preparedness rather than a strategic one. We want a strategic posture.

On February 12th, this subcommittee held a hearing examining the federal government's preparedness for biological threats focused on the finding of the Blue Ribbon Study Panel on Biodefense. The panel concluded that the federal government is ill prepared to handle future biological threats, an alarming conclusion because since 2002 infectious disease outbreaks, epidemics, and pandemics

have emerged with increasing frequency, and Zika is just the latest example of this trend.

The Administration's response to Zika raises very serious questions. There are no commercially available diagnostic tests for Zika, nor has a vaccine been developed. In the absence of these measures, mosquito control is the nation's critical defense. However, mosquito control in the U.S. is a patchwork of 700 mosquito abatement districts depending on the state, county, and city funding and personnel with varying capabilities. This unorganized hodgepodge could leave the U.S. vulnerable to a rapid outbreak of Zika. The Administration has not explained how its emergency request will address issues with vector control. We want to work with the Administration to solve that problem.

Public Health Departments and the CDC are using two Zika diagnostic tests only available for U.S. labs. As the Government Accountability Office testimony makes clear, these tests have serious limitations, including the ability to either detect Zika or to be able to distinguish Zika from other viruses.

In addition, the confirmatory testing for Zika detection is used only by CDC and a few labs, is cumbersome and not suitable for screening a large number of individuals. This very limited capacity for confirmatory testing is very troubling when we consider the expected surge and the demand for Zika testing as we reach the warmer months. Again, the Administration must explain its plan to address this testing capacity issue.

Once again as with Ebola, we are assured that Zika will not be a significant problem in the U.S., and while Dr. Anthony Fauci of NIH has stated that it is unlikely the U.S. will have a major Zika outbreak, other experts differ. In his written testimony to this committee, Dr. Peter Hotez of Baylor School of Medicine notes the experience of Texas showed a Dengue outbreak occurred in the poorest areas of Houston and other Gulf Coast cities vulnerable to Zika.

This morning we'll be taking testimony from a panel of federal witnesses and experts, including the Assistant Secretary for Preparedness and Response at HHS, the Director of CDC, the Director of the National Institute of Allergy and Infectious Diseases at NIH, the Acting Chief Scientists of FDA, as well as the Chief Scientist of the GAO. Welcome. We will then hear from a second panel featuring specialists in tropical and maternal fetal medicine, mosquito control, and global health law.

I want to thank all our witnesses for joining us this morning and look forward to hearing your testimonies.

I now recognize, since Ms. DeGette is not here, we're promoting her to the Ranking Member Pro Tempe of the subcommittee, Ms. Castor of Florida, for 5 minutes.

[The statement of Mr. Murphy follows:]

PREPARED STATEMENT OF HON. TIM MURPHY

This morning, we will be examining a public health crisis afflicting the Western Hemisphere. The Zika virus, a mosquito-borne pathogen rampaging through South and Central America, advances menacingly toward the U.S. The Zika virus has spread to more than 48 countries and territories. While as of late February there had been no known locally acquired mosquito-borne cases reported in the continental U.S. states, over 100 travel-associated Zika virus disease cases have been identified in over 20 states. Outside of the 50 states, local mosquito-borne trans-

mission has been reported in Puerto Rico, the U.S. Virgin Islands, and American Samoa. Public health officials in the U.S. are bracing for the time when Zika passes from a traveler with Zika in his or her blood to a local mosquito, and then to another person.

Only about one in five people with Zika infection exhibit symptoms, most of which are mild and flu-like. Of greater concern is growing evidence of a link between Zika infection and microcephaly, a congenital birth defect in infants born to infected mothers, as well as Guillain-Barre AE1 Syndrome, an immune disorder that can result in temporary paralysis. On this basis, the World Health Organization recently declared Zika a “public health emergency of international concern.”

The virus may also be transmitted through blood transfusions and sex, leading the Centers for Disease Control (CDC) to issue interim guidelines for prevention of sexual transmission and the Food and Drug Administration (FDA) to take steps to reduce the risk to the U.S. blood supply. Thus far, there has been only one reported case in the U.S. of a child born with microcephaly to a mother with travel-associated Zika virus; however, other pregnant American women have become infected with Zika. Our understanding of how the virus may impact a developing child during pregnancy is nearly non-existent. Given all of the unknowns, the importance of acting now to protect pregnant women and women of reproductive age from exposure to Zika virus cannot be overstated.

To help prepare for and respond to Zika, the Administration recently requested Congress to provide over \$1.8 billion in emergency funding. The request includes support to states, U.S. territories, and the international community for mosquito control, virus testing, and expanding surveillance and response activities. It also supports efforts to build upon existing resources to develop a vaccine for Zika.

While the Administration’s request has worthy aims, its one-off emergency funding approach, like the \$6 billion for Ebola emergency funding, demonstrates a reactionary posture towards public health preparedness rather than a strategic one. On February 12th, this Subcommittee held a hearing examining the federal government’s preparedness for biological threats, focused on the findings of the Blue Ribbon Study Panel on Biodefense. The panel concluded that the federal government is ill-prepared to handle future biological threats—an alarming conclusion because, since 2002, infectious disease outbreaks, epidemics, and pandemics have emerged with increasing frequency. Zika is just the latest example of this trend.

The Administration’s response to Zika raises very serious questions. There are no commercially available diagnostic tests for Zika, nor has a vaccine been developed. In the absence of these measures, mosquito control is the nation’s critical defense. However, mosquito control in the U.S. is a patchwork of 700 mosquito-abatement districts dependent on state, county, or city funding and personnel, with varying capabilities. This unorganized hodgepodge could leave the U.S. vulnerable to a rapid outbreak of Zika. The Administration has not explained how its emergency request will address issues with vector control.

Public health departments and the CDC are using two Zika diagnostic tests only available for U.S. labs. As the Government Accountability Office’s testimony (GAO) makes clear, these tests have serious limitations, including the ability to either detect Zika or to be able to distinguish Zika from other viruses. In addition, the confirmatory testing for Zika detection is used only by CDC and a few labs, is cumbersome, and not suitable for screening a large number of individuals. This very limited capacity for confirmatory testing is very troubling when we consider the expected surge in the demand for Zika testing as we reach the warmer months. Again, the Administration must explain its plan is to address the testing capacity issue.

Once again, as with Ebola, we are assured that Zika will not be a significant problem in the U.S. While Dr. Anthony Fauci of the NIH has stated that it is unlikely that the U.S. will have a major Zika outbreak, another expert differs. In his written testimony to the committee, Dr. Peter Hotez, of Baylor School of Medicine, notes that the experiences of Texas showed dengue outbreaks occurred in the poorest areas of Houston and other Gulf Coast cities vulnerable to Zika.

This morning we will be taking testimony from a panel of federal witnesses, including the Assistant Secretary for Preparedness and Response at HHS, the Director of CDC, the Director of the National Institute of Allergy and Infectious Diseases at NIH, the Acting Chief Scientist of FDA, as well as the Chief Scientist of the GAO.

We will then hear from a second panel featuring specialists in tropical and maternal-fetal medicine, mosquito control, and global health law. I would like to thank all of our witnesses for joining us this morning.

I now recognize the Ranking Member of the Subcommittee, Ms. DeGette, for her opening statement.

OPENING STATEMENT OF HON. KATHY CASTOR, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

Ms. CASTOR. Well, thank you, Mr. Chairman, for calling this important hearing, and I want to thank all of our expert witnesses who are here today for everything that you do to keep American families healthy and safe.

So many of my neighbors across the State of Florida, and the Gulf Coast, and Puerto Rico are very concerned with the impacts of the Zika virus. We want our states and our communities to be well prepared and we want to better understand the impacts of the virus.

In Florida, CDC has confirmed the Zika case count is now up to 44 cases. All of these cases are travel-related, so there are no locally-acquired cases in Florida. Overwhelmingly, people who have traveled to Brazil and Latin America to visit family and friends, or travel on business or for pleasure have contracted the virus and have brought it back. Fortunately, the Zika symptoms are not severe but there is a great concern for emerging evidence to support the association between Zika and microcephaly in infants born to mothers who contracted the Zika virus during pregnancy.

I'm also especially concerned with the American citizens in Puerto Rico because we now have 117 confirmed cases. It is the most affected area in the United States, and the CDC predicts a sharp rise. Again, family and friends who travel back and forth from Puerto Rico to the U.S. want to know what the impacts are and how they can be better prepared, especially as spring and summer approach. That's going to bring larger and more active mosquito populations. The U.S. must be prepared to quickly address local transmission within Puerto Rico, the Gulf Coast, and the entire United States.

I'm also particularly concerned with the weakening of our public health infrastructure across the country. After the Great Recession, I saw very significant cuts in the State of Florida, but Florida is not alone. We have those cuts and weakenings to public health departments and public health infrastructure. And I think Ebola was something of a wake-up call, but the Zika virus and other viruses, diseases, we've got to be better prepared. I agree with Chairman Murphy, a much more robust prevention strategy would be in our best interest.

For the Zika virus, addressing the crisis requires a multidimensional response, including accelerating the research, development, and procurement of vaccines and diagnostics, providing emergency assistance to states. Thank you, CDC, for what you've done in responding quickly to the State of Florida's request, and we've got to enhance our surveillance capacity.

Thank you, again. I look forward to your testimony. I yield back.

Mr. MURPHY. Thank you. Now we'll take Mr. Upton's testimony, and for the record recognize Dr. Burgess for 5 minutes.

OPENING STATEMENT OF HON. MICHAEL C. BURGESS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. BURGESS. Thank you, Chairman, thank you for the recognition, thank you for having this hearing this morning, thanks to our

witnesses. We always learn so much when we have a panel like this in front of us, and today I'm sure will be no exception.

This virus continues to spread through the Americas and it really has become clear that this is a direct threat to our public health and our public safety. So I'm in contact with people back in my state, and my county health officials, and one of the things that they've expressed to me is concern over the flexibility and the scalability of federal aid at the state level, so I'm actually interested in hearing from our panel about that this morning. Obviously, I share that concern. It is important that state and local agencies, as well as the local docs on the ground have the ability to fight what they need to fight and not have barriers from us at the federal level.

You know, Ebola happened in our backyard in north Texas, and many ways we thought we were prepared, but in some ways we turned out not to be prepared. So I guess I'm interested this morning; yes, I want the reassurances that we're prepared, but I really also want to hear what were the Lessons Learned when we went through the Ebola crisis in September and October of 2014, and what is the applicability of those lessons to what's going on on the ground today. A variety of other questions concerning the testing and the development of tests for this illness. And, obviously, I'm terribly interested, Dr. Fauci, in the pathogenesis of the illness as it affects pregnancies, both miscarriages and infants who are born affected, and very interested in learning the status of the vaccine development.

Thank you, Mr. Chairman. I will yield back my time.

Mr. MURPHY. Anybody else on our side wish to take any time? If not, Mr. Pallone on his way but what we'll do is we will begin our testimony, or begin that process. When he comes in, we may interrupt after one of you speak.

Let me introduce the panel, start off with this. We have Dr. Nicole Lurie, Assistant Secretary for Preparedness and Response with the Department of Health and Human Services; Dr. Thomas Frieden, Director of the Centers for Disease Control and Prevention; Dr. Anthony Fauci, Director of the National Institute of Allergies and Infectious Diseases at NIH; Doctor, is it Luciano or Luciana?

Dr. BORIO. Luciana.

Mr. MURPHY. Luciana Borio, Acting Chief Scientist at FDA; and Dr. Timothy Persons, Chief Scientist at the U.S. Government Accountability Office. Welcome everyone for being here.

You're aware that the committee is holding an investigative hearing and when so doing has the practice of taking testimony under oath. Do any of you have any objections to taking testimony under oath? Seeing no objections, the Chair then advises you that under the rules of the House and the rules of the committee you're entitled to be advised by counsel. Do any of you desire to be advised by counsel during your testimony today?

Dr. BORIO. No.

Mr. MURPHY. No one wants that, so in that case would you all please rise, raise your right hand. I'll swear you in.

[Witnesses sworn.]

Mr. MURPHY. Thank you. You are now all under oath and subject to the penalties set forth in Title 18, Section 1001 of the United States Code. We'll have you give a 5-minute opening statement. Mr. Pallone, do you want to give yours now or do you want to wait until we do some of the panel? We can go right to your opening statement.

Mr. PALLONE. It's up to you.

Mr. MURPHY. Well, let's make a smooth transition. If you're ready, we'll do that now, and then I'll call on Dr. Lurie. We just did the swearing in so you're aware of what we did. So Mr. Pallone is recognized for 5 minutes.

Mr. PALLONE. Thank you, Mr. Chairman, and the witnesses today for joining us to discuss the Zika virus and what the federal government is doing to respond to the threat.

Zika represents a serious threat to global health and security and we must address that threat decisively both at home and abroad. It's suspected of causing a multitude of devastating birth defects, most notably microcephaly, a condition which babies are born with severe brain defects. In adults, the virus has been associated with Guillain-Barre AE1 Syndrome which can result in paralysis and even death. Although scientists are not able to say definitively that Zika is the cause, evidence is mounting each day to support a causal relationship between the virus and these serious health conditions.

The Zika virus is spreading explosively through the Americas with active local transmission in 31 countries and territories. The Pan American Health Organization predicts that the virus will eventually spread to every country in the Americas except perhaps Canada and Chile.

The crisis in Puerto Rico could become particularly severe as Zika is expected to infect one in five Puerto Ricans, and given the territory's debt crisis and inability to fund even the most basic health services robust assistance from the federal government will be absolutely crucial to contain the virus and protect as many pregnant women as possible.

As spring and summer approaches we must also be prepared to address local transmission of Zika within the Continental United States, particularly in southern states where the mosquitoes that carry the disease are common.

As Dr. Hotez on our second panel has previously noted, "Local transmission of Zika in the U.S. will likely disproportionately affect poor neighborhoods in the southern states where inadequate window screening, standing water, and imperfect waste disposal provide ideal mosquito breeding grounds, and addressing Zika will require a multidimensional public health response. It must include accelerating research, development, and procurement of vaccines and diagnostics, providing emergency assistance to states and the U.S. territories, and enhancing our surveillance capacity to track the Zika virus in people and in mosquitoes."

The Administration has requested emergency funding to address each of these components, and I look forward to hearing more about the details of this request today. Unfortunately, the Republican chairs of the House Appropriations Committee have declined to fund the Administration's request and have, instead, called upon

the agencies to divert unobligated Ebola funds. I believe this decision is shortsighted and would increase health risks both at home and abroad.

As our witnesses will make clear today, Ebola remains and will continue to remain a threat to human health for the foreseeable future. It could reemerge at any point, and as we've seen it can cause outbreaks that decimate economies, trigger widespread panic, and result in a tragic loss of human life.

NIH is using its Ebola funds to conduct essential ongoing research including the development of an Ebola vaccine, and CDC is continuing to conduct its global efforts to combat the Ebola Virus on the ground. Shortchanging these efforts would damage our ability to effectively respond to both Zika and Ebola, as well as to any future threats. The remaining Ebola funds are largely committed to the global health security agenda, a multi-year effort to keep Americans safe by strengthening the capacity of developing countries to prevent, detect, and respond to emerging epidemics.

Let's not forget how Ebola managed to spiral out of control. To build an effective global system for containing infectious disease we must make sure that the poorest and most vulnerable countries have the surveillance capacity to identify outbreaks and respond quickly, and fighting Zika will not be easy. Like Ebola, it thrives in impoverished communities and its heaviest burden falls on vulnerable populations least able to respond. The disease is difficult to track as most people infected with Zika experience no symptoms, and the research agenda is extensive given how little we know about the disease. But I'm confident that our federal agencies are up to the task as long as Congress does its part and provides the necessary resources. And I hope that all my colleagues on both sides of the aisle recognize the importance of these investments and that we'll be able to work together in a bipartisan manner to address the Zika threat in the coming weeks.

Thank you, Mr. Chairman. I yield back.

Mr. MURPHY. Thank you. Now we'll go and proceed with the testimony. We'll start with you, Dr. Lurie. You know how this works; watch your lights and try and keep it at 5 minutes.

Thank you very much. You may proceed.

STATEMENT OF NICOLE LURIE, M.D., ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; THOMAS FRIEDEN, M.D., DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION; ANTHONY FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH; LUCIANA BORIO, M.D., ASSISTANT COMMISSIONER, COUNTERTERRORISM POLICY, U.S. FOOD AND DRUG ADMINISTRATION; TIMOTHY PERSONS, Ph.D., CHIEF SCIENTIST, U.S. GOVERNMENT ACCOUNTABILITY OFFICE

STATEMENT OF NICOLE LURIE

Dr. LURIE. Thanks. Good morning, Chairman Murphy, Ms. Castor, and distinguished members of the subcommittee. I'm Dr. Nicole Lurie, the Assistant Secretary for Preparedness and Response, and

thank you for the opportunity to talk to you today about yet another emerging threat, the Zika virus.

While we don't yet know everything we need to know about Zika, as a primary care physician and as a mom, I know how deeply concerning what we're all learning is. As you know, ASPR was established almost a decade ago by the Pandemic and All Hazards Preparedness Act in part to overhaul the government's approach to emergencies that threatens the public's health, whether naturally occurring or manmade. Since that time and with the support of Congress including many of you, ASPR has done just that, developing a flexible set of capabilities to quickly adapt to challenging threats, including Ebola, MURS, and now Zika virus.

Since early reports of the potential link between Zika virus and microcephaly, HHS has taken proactive and as scientific evidence has mounted increasingly targeted actions to protect the American people. Today I'll highlight three areas in which ASPR's work is critical.

First, our central role is to coordinate across HHS and beyond ensuring that all components have the latest information and best scientific evidence to inform key decision making, and that all are driving toward the same goals.

Second, ASPR has a mandate to develop the most promising medical countermeasures through the Biomedical Advanced Research and Development Authority or BARDA. I know this committee is aware of how successful BARDA has been producing 22 licensed products and support nearly 200 countermeasure candidates over the years.

Third, ASPR is clearing longstanding obstacles to progress in this area, such as agreements on virus sample sharing and close collaboration with regional and international partners. You should know that well before the first case of Zika in the U.S. in early January, I convened the HHS Disaster Leadership Group to coordinate our preparedness efforts. This group is made up of leaders from across HHS including CDC, NIH, and FDA, and it ensures that the department's senior leaders have shared awareness and the ability to make timely, informed, and coordinated decisions during emergencies. We've convened this group for every emergency and it will continue to meet throughout this crisis.

Similarly, on December 2nd of last year I directed the Public Health and Medical Countermeasure Enterprise or PHEMCE to conduct a comprehensive review of its portfolio to identify candidate products with the potential to stop transmission of Zika.

This committee is well aware that the best ideas for medical countermeasures won't translate into the drugs, vaccines, diagnostics we need without investment. The BARDA component of ASPR is tasked with transitioning promising medical countermeasures through advanced development and across the so called valley of death toward FDA approval. In the case of Zika we've established three countermeasure priorities, vaccines, diagnostics that can detect both acute and previous infections, and insuring a blood supply that's safe by developing blood screening tests for Zika, and techniques for virus inactivation in blood.

Because access to virus samples is critical for developing diagnostics and vaccines, we've worked across government to suc-

cessfully establish sample sharing and vaccine development agreements, including with Panama and Brazil, respectively. We've also established a mechanism to address international requests for assistance because we recognize that health security knows no borders.

While we move forward aggressively to prepare for the threat of Zika, many of our efforts will depend on new resources. The Emergency Supplemental Request includes funds for CDC, which is responsible for the bulk of the public health response, for medical countermeasure development, and for contingencies that may arise over the course of the response.

For countermeasures we've been successful in moving from a reactive model of preparedness to a proactive one, building on strong day to day systems and a flexible set of capabilities to do this. The same goes for state and local health departments which is why preparedness for all hazards is so important.

A lesson from both H1N1 and Ebola was the need for flexible funding to insure that we can move quickly as other departments can so that something that starts as a crisis does not become a full-blown emergency. The contingency fund included in the President's supplemental request addresses this overarching need; enabling us, if needed, to make emergency procurements or quickly take other actions that become necessary but that we cannot currently anticipate.

In sum, HHS has mounted a proactive and coordinated response to the Zika virus, building on Lessons Learned from previous challenges, and the domestic preparedness infrastructure we've worked so hard to establish. Congressional approval of the Administration's funding request will provide critical resources to improve our ability to prevent, detect, respond, and rapidly adjust to Zika and other emerging vector-borne infectious diseases.

Thank you again for inviting me here. I look forward to your questions.

[The statement of Dr. Lurie follows:]



**“Examining the U.S. Public Health
Response to the Zika Virus”**

Statement of

Nicole Lurie MD, MSPH

*Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services*



For Release on Delivery
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Good morning Chairman Murphy, Ranking Member DeGette, and distinguished Members of the Subcommittee. I am Dr. Nicole Lurie and I am the Assistant Secretary for Preparedness and Response (ASPR) at the Department of Health and Human Services (HHS).

Thank you for the opportunity to testify before you again. ASPR was established by the Pandemic and All-Hazards Preparedness Act (PAHPA) to lead the country in preparing for, responding to, and recovering from the adverse health effects of emergencies and disasters. Over the past nine years, with the support of Congress and this committee, ASPR has built a comprehensive array of capabilities that enable us to ably and expeditiously fulfill this mission. ASPR works within HHS and with its Federal, state, tribal, and local partners to advance the public health preparedness of our nation by helping build communities that are more resilient to events that threaten the public's health, whether they are naturally occurring disasters, infectious disease outbreaks, or acts of terrorism. Our structure enables us to operate efficiently and simultaneously manage multiple responses including the recent Ebola epidemic, and the current Zika virus (Zika) outbreaks in the Americas.

The Administration is taking proactive and aggressive action to protect the American people and address the threat posed by Zika virus. As you know, the President recently announced a request to Congress for \$1.9 billion in emergency funding, including \$295 million for urgent and emerging threats to enhance ongoing efforts to prepare for and respond to outbreaks of the Zika virus or other vector borne or infectious diseases, both domestically and internationally. Within the \$1.9 billion funding request, there is support for the development and emerging manufacturing of new Zika-specific vaccines; development of vaccine platform technologies for multiple emerging infectious diseases; development of rapid serological diagnostics to determine whether someone has

been infected previously with the Zika virus such as pregnant women; and pathogen reduction technologies for blood supplies related to the recent Zika virus outbreak in the Western Hemisphere.

An important lesson learned from the Ebola epidemic is the need for a flexible funding stream that can adapt to whatever crisis comes our way. We learned how important it is to get ahead of a crisis, before it becomes an emergency. Ebola was not the first such crisis, and Zika will certainly not be the last. However, to be prepared for new or emerging, threatening diseases, we must maintain a readiness posture, and right now that means being prepared for and doing everything we can do to stop Zika and other potentially dangerous vector-borne diseases. The funds for Zika will support our efforts to direct the right resources at the right time as the Zika epidemic unfolds and we learn more about its impact and how it is transmitted. An effective, coordinated response, to this significant public health threat requires a comprehensive, immediate response with the ability to adapt to unanticipated needs. Regardless of the shape this crisis takes, it is clear that funding for work on the development of vaccines and diagnostics, including blood and tissue donor screening tests, and to rapidly improve scientific understanding of the disease is required. Furthermore, aggressive education and outreach is needed to ensure health care providers are prepared to counsel and treat patients with Zika virus or its complications.

The Zika virus is primarily a mosquito vector-borne viral disease currently threatening the United States and many other countries in the Americas, Pacific, and Africa. Named after the Zika Forest in Uganda, acute Zika infection can cause common symptoms such as skin rash, fever, joint pain, or conjunctivitis. Most Zika infections are associated with no symptoms at all; however, there has been a concerning association between women who become infected with

Zika during pregnancy and babies born with microcephaly and other complications. Zika infection has also been associated with Guillain-Barré Syndrome, in which the body's immune system attacks the nervous system and causes muscle weakness or paralysis. On February 1, the World Health Organization (WHO) declared the clusters of microcephaly and other neurological disorders that are possibly associated with Zika virus a public health emergency of international concern. The Brazilian Ministry of Health estimates that between 440,000 and 1.3 million suspected cases of Zika occurred in Brazil in 2015. As of February 25, 34 countries and three U.S. territories, including the Commonwealth of Puerto Rico, the U.S. Virgin Islands, and American Samoa have reported cases of local mosquito-borne transmission. Considering these recent outbreaks in the Pacific Islands, Mexico, Central America, South America, and the Caribbean, we anticipate that the number of Zika cases among travelers visiting or returning to the United States is likely to increase. We have already seen cases of travelers returning to the United States with confirmed Zika virus disease and are particularly concerned about limiting transmission of the virus in the Commonwealth of Puerto Rico, the U.S. Virgin Islands, American Samoa, and the Marshall Islands. Last week, CDC published the first information on pregnancy outcomes for women in the United States known to be infected with Zika virus. That information continues to add to the evidence base about the association between Zika virus and adverse pregnancy outcomes.

ASPR took some early steps to address Zika virus. On December 2, 2015, one of the first steps we took to address Zika virus was to call on the infrastructure of the Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) to assess what medical countermeasures were in the development pipeline. In addition, on January 3, 2016, we convened the HHS Disaster

Leadership Group (DLG) to coordinate Zika-related issues across HHS's Operational and Staff Divisions. Both of these structures were created to improve coordination within the Department and in the case of the PHEMCE, across U.S. Government stakeholders. Specifically, the DLG is comprised of leadership from several HHS components, such as the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the U.S. Food and Drug Administration (FDA), to facilitate coordinated policy decision making on critical preparedness matters, ongoing response activities, and mitigation efforts to limit the lasting effects of disasters. We also elevated the activation level of the Secretary's Operations Center (SOC), which, in coordination with the DLG, serves as the focal point to collect and share operational information on this new threat across other federal departments, state, local, and tribal governments and our external stakeholders, including nonprofits, the private sector, and the international community. In this way, the SOC leverages our combined capabilities to effectively prepare our nation and execute an organized response.

As was the case for H1N1 and for Ebola, ASPR is coordinating medical countermeasure activities in the Zika response by activating the PHEMCE infrastructure, which, on a daily basis, supports the development and acquisition of medical countermeasures to prepare for biological threats. ASPR convenes a weekly Senior Steering Group composed of senior leaders across the PHEMCE to discuss Zika-related medical countermeasure policy and operational issues and to coordinate activities. In addition, through guidance documents such as the PHEMCE Strategy and Implementation Plan and the National Health Security Strategy, ASPR leads the path forward for our partners and stakeholders.

The Biomedical Advanced Research Development Authority (BARDA), within ASPR, has a mandate from PAHPA to transition medical countermeasure candidates from early development into advanced research and development towards FDA approval. BARDA has established strategic goals to address medical countermeasure needs for the Zika response domestically and globally. These are: prevention of Zika virus infection through new vaccines; detection of acute and previous Zika virus infections through new rapid diagnostics; ensuring a blood supply safe from Zika virus through donor screening and virus inactivation in blood products, and activation of our National Medical Countermeasure Response Infrastructure to aid medical countermeasure developers. As we did for the Ebola response, we are assisting medical countermeasure developers through our National Medical Countermeasure Response Infrastructure comprised of six core service assistance programs that provide animal and human clinical testing, product development and manufacturing, and regulatory and modeling needs. This infrastructure could potentially be used to develop vector protection countermeasures such as mosquito repellants. We are also encouraging and receiving numerous inquiries from academic and industrial stakeholders for potential medical countermeasures through our TechWatch program.

Building on existing and new partnerships and lessons learned from the H1N1 and Ebola responses, we are implementing our Zika medical countermeasure strategy through the development and manufacturing of new Zika-specific vaccine candidates. In collaboration with NIH, FDA, and the Walter Reed Army Institute of Research, we are working on vaccine development, pre-clinical and clinical testing, and commercial scale production, including vaccine manufacturing through our Centers for Innovation in Advanced Development and Manufacturing. We are also providing technical assistance to our global partners in Brazil for

Zika vaccine development and commercial scale manufacturing. We are supporting industry partners to develop and utilize new innovative vaccine platform technologies for public health emergencies for multiple emerging infectious diseases to produce new Zika vaccine candidates.

In regards to diagnostics, we are working with CDC to expand the number of health departments that have the ability to perform testing, but will need to increase the existing capacity to meet the projected demand for Zika testing. We are collaborating with CDC, FDA, and NIH to facilitate the development of rapid point-of-care and laboratory-based serological assays for Zika to determine who has been infected previously, especially pregnant women. ASPR/BARDA is collaborating with CDC, FDA, and NIH to facilitate the development and availability of commercial assays to identify Zika virus and diagnose infection. Interagency efforts are underway to acquire and distribute virus and clinical samples needed for test development and evaluation. BARDA has released a solicitation to advance the development of assays that would expand capability to provide reliable, accurate testing beyond public health laboratories to doctors' and other health care providers' offices, hospitals, and commercial laboratories.

We are collaborating with FDA to support the development and implementation of rapid high-throughput molecular diagnostic screening and pathogen reduction technologies to ensure a safe blood supply. CDC is providing technical assistance to FDA to help prevent transfusion-related Zika transmission. ASPR is working with partners across HHS to ensure that the Commonwealth of Puerto Rico has adequate blood supply.

Realizing the lessons we learned from Ebola, informative, consistent, and widely distributed messaging to the U.S. population from HHS components is a primary focus. We have delineated a leadership structure, and identified primary spokespeople for the response. Adhering to the principles of risk communication, we are updating information as soon as possible through multiple sources including translated materials for non-English speaking communities and enhanced outreach to vulnerable populations. Clear, concise, and accurate information can reduce the level of concern among the general population and support appropriate action by health care providers.

ASPR has facilitated opportunities for coordination among state and local health systems through Hospital Preparedness Program (HPP) grants and Health Care Coalitions. HPP enhances the capability of health care coalitions in communities across the country to build resiliency by strengthening systems, improving surge capacity, and advancing science-based decision-making before, during, and after emergencies. In response to Zika, HPP is including Health Alert Network (HAN) advisories and links to other CDC-produced guidance in its weekly update and continues to remind coalition leaders and awardees of their key role in sharing information about Zika virus with their member facilities and organizations. Further, HPP is prompting coalitions with limited specialized resources (e.g., neurology, maternal-fetal medicine, etc.) to pre-identify these resources and share information with member facilities and organizations about how to access and utilize them as coalition resources for preparedness, communications, messaging, and consultative purposes.

Whether it is pandemic influenza, Ebola, or a vector-borne disease like Zika, viral epidemics do not respect borders. Recognizing the domestic impact of global public health emergencies, we have strengthened our international partnerships as cited above for vaccine development with Brazil. Through our standing ASPR capacity building programs in the region, we have obtained viral isolates and serum samples from Panama that are being distributed to CDC, NIH, FDA and others in the government to conduct research and expedite development of serological diagnostics and blood safety screening tests. In collaboration with the Department of State and the U.S. Agency for International Development, we are currently leveraging trusted networks and relationships with key international partners that we have forged over the years. We are closely collaborating with the World Health Organization (WHO); WHO's regional arm, the Pan American Health Organization; the United Nations; and countries around the world about best emergency preparedness practices and surveillance data on infectious diseases. We maintain regular communications and coordination with partners of the Global Health Security Initiative or GHSI, which includes the G7 countries, Mexico, the European Commission, and WHO as an advisor.

On behalf of the HHS Secretary, ASPR hosted the 16th GHSI Ministerial meeting in Washington, D.C. on February 26. Within GHSI, we are collaborating to mount coordinated responses to the Zika virus to enhance information sharing about a) public health practices and policies in our countries, and b) a list of scientific and public health studies done in our institutions, and in collaboration with Latin American and Caribbean countries, to unify our efforts to expedite knowledge about potential linkages between Zika and microcephaly and

between Zika and Guillain-Barré Syndrome, as well as on the development of medical countermeasures.

ASPR, in collaboration with the HHS Office of Global Affairs, is hosting teleconference calls with U.S. Government partners to coordinate activities in the Latin American and Caribbean region. Together with the Department of State, we have implemented a tracking system to receive and respond to international requests for information and assistance in a coordinated manner for the U.S. Government. These are just examples of the myriad of coordination efforts to outreach to our international partners to collaborate in the response to Zika.

In closing, our foremost concern is protecting public health from known or emerging threats. Zika is our newest threat, but not our last. Congressional funding for the Administration's approximately \$1.9 billion funding request will ensure an effective and rapid response to outbreaks that threaten the health of the American people and can accelerate our ability to prevent, detect, and respond to Zika and other emerging vector-borne and infectious diseases. Thanks to our combined efforts and with lessons learned from previous challenges, we are a better prepared and more resilient nation with the flexibility to successfully address a variety of public health threats. Thank you again and I look forward to your questions.

Mr. MURPHY. Thank you, Dr. Lurie.
Now, Dr. Frieden, you're recognized for 5 minutes.

STATEMENT OF TOM FRIEDEN

Dr. FRIEDEN. Thank you very much, Chairman Murphy, Representative Castor, and members of the subcommittee.

At the outset, I want to make a few key points. First, we're literally still discovering new things every day about Zika. CDC has about 600 staff currently working on this response. We're activated at Level 1, the highest level of our emergency operations center. We have staff in Brazil, Colombia, Puerto Rico, and other parts of the world looking at and learning from a developing situation.

Zika is new, and new diseases can be scary particularly when they affect the most vulnerable among us. And it's also particularly scary because in Puerto Rico today cases are doubling every week. By April we're likely to see widespread transmission in Puerto Rico, and by June, mosquito season is likely to start in parts of the U.S. where the mosquito that can spread Zika is present. There's a limited window of opportunity to take action. When we look at chikungunya which affected Puerto Rico, started in 2014, within 2 months it was all over the island, within 8 months one out of four adults were infected. If that pattern is followed with Zika we could see hundreds of thousands of infections by the end of the year.

CDC is working 24/7 to respond to this, learning more about the link with microcephaly, Guillain-Barre AE1 Syndrome, improving diagnostics, looking at ways to optimize vector control with current tools. This is the latest in a series of unpredicted and unpredictable health threats. What is predictable is that there will be more health threats, and that's why it's so important that we continue to improve the ability of countries around the world to find, stop, and prevent health threats.

Now, first, what do we know about Zika? You've outlined, Mr. Chairman, other members some of the key facts here. It's been around since 1947. We didn't know it could cause outbreaks until 2007. It was thought to cause mostly mild disease. It spread primarily by the *Aedes aegypti* mosquito. This is the cockroach of mosquitoes. It lives indoors, it lives in the shade, it is hard to kill, and it's very effective at spreading diseases. That's why Dengue and Chikungunya and other diseases spread by it can spread so explosively.

What is really new and unprecedented is the link to microcephaly. It's been more than 50 years since a pathogen causing microcephaly or other severe birth defects was identified that would do so on such a broad level. And as far as we know, never before has there been a mosquito-borne cause of a severe fetal malformation.

The link to Guillain-Barre AE1 Syndrome looks increasingly certain. Studies published this week, if replicated would basically prove that link, and it wouldn't be surprising. We've seen Guillain-Barre AE1 Syndrome after a wide variety of infections. But microcephaly, the complication of microcephaly is truly unanticipated, potentially catastrophic, and permanent, the very definition of the need for an emergency supplemental response.

Fundamentally, there are four different patterns of spread. First, among travelers, some of them pregnant. And we have 40 million people going to and from Zika-affected areas each year. Second, sexual partners. This is why we issued guidance to reduce the risk of sexual transmission. Third, possible cases and clusters in parts of the U.S. that have the mosquito vectors present. That's why we need to scale up our support for those entities. Fourth, areas likely to have widespread transmission around the world, and especially in parts of the U.S., including Puerto Rico, that have had large outbreaks of Dengue.

The supplemental is critically important for CDC to respond as part of a whole of government response. The request of CDC is for \$828 million in three categories: urgent support for Puerto Rico, a response in the Continental U.S., and international support, as well.

There are many very concerning diseases out there whether it's Ebola, SARS, MURS, or the next HIV. We can't let down our guard. Supplemental funding is essential for us to do several things, including reducing the risk to pregnant women by finding out more and doing more especially in Puerto Rico and other areas where it may spread widely, by finding where mosquitoes are spreading in the U.S., and better controlling them, by establishing a registry for birth defects and improving the monitoring of pregnant women, by supporting states and territories directly to improve prevention and management of cases, diagnosis of patients, increased laboratory capacity, and implement key interventions. This is a critically important and urgent need, and I look forward to answering your questions. And thank you for the invitation to appear before you today.

[The statement of Dr. Frieden follows:]

March 2, 2016

Witness: Tom Frieden, MD, MPH, Director, Centers for Disease Control and Prevention

Testimony before the House Committee on Energy and Commerce Oversight and Investigations Subcommittee

Introduction

Good morning Chairman Murphy, Ranking Member DeGette, and members of the Subcommittee. Thank you for the opportunity to testify before you today on Centers for Disease Control and Prevention's (CDC's) efforts to prepare for and respond to the Zika virus outbreak, which threatens the United States and the rest of the Americas. The Administration has requested approximately \$1.9 billion in emergency funding to respond to the Zika virus outbreak, including \$828 million for CDC, in support of both the domestic and international response, with particular attention to emergency assistance to the Commonwealth of Puerto Rico and other U.S. Territories and States with local transmission of Zika virus.

CDC is the nation's health protection agency, working 24-7 to save lives and protect people against unpredictable threats such as the Zika virus. Nature is a formidable adversary, and Zika is our newest threat, particularly to pregnant women. CDC has some of the world's leading experts both in diseases spread by mosquitos and in birth defects. We must act swiftly to stop the spread of the Zika virus, both domestically and globally. While we are learning more about the Zika virus every day, there are many things we do not know yet about Zika. These include our understanding of the spectrum of effects of Zika infection during pregnancy, the risk the virus may play in microcephaly, Guillain-Barré syndrome and other possible complications, the duration of Zika infectivity in semen, and determining what other factors may play a part in the consequences associated with the virus. In addition to answering these questions, we are also working to accelerate optimal mosquito control strategies, improve testing and assure preparedness for rapid detection, control, and prevention within the United States and U.S. territories.

We are making advancements in these areas and will need the additional requested funding to do so. We are figuring out more about Zika literally every day, and will share information – and adjust our guidelines and recommendations – as we learn more. That is the nature of a scientific response to an emerging health threat. The doctors, scientists, entomologists, and others at CDC are working nonstop to protect Americans from this and other health threats. We have already made significant progress identifying the Zika virus in brain tissue of affected deceased infants, developing new diagnostic tests, issuing guidance, conducting epidemiological investigations along with affected countries, and improving monitoring and surveillance in the United States including in the Commonwealth of Puerto Rico and the other U.S. territories. Much of what we know about Zika and similar viruses today is based on the work that's been done by CDC scientists. But there are still many things we do not yet know. We will continue to use the best of modern science to protect the American people. I understand that Zika virus and the emergence of serious birth defects cause concern. We are committed to

providing the American people with the most accurate and timely information about Zika virus and the current outbreak.

CDC is working in collaboration with other components of the Department of Health and Human Services (HHS), including the Office of the Assistant Secretary for Preparedness and Response (ASPR) and its Biomedical Advanced Research and Development Authority (BARDA), the National Institutes of Health, and the Food and Drug Administration (FDA). We are also working with partners across the U.S. Government to communicate with travelers and health care providers, update travel alerts and clinical guidance, and develop improved mosquito-control methods.

Zika and its history

Zika is a flavivirus, which is closely related to dengue, yellow fever and West Nile viruses. Zika virus is primarily spread to people through the bite of infected *Aedes* species mosquitos, particularly *Aedes aegypti*. The *Aedes aegypti* mosquitos, which also transmit dengue and chikungunya viruses, are extremely difficult to control. They bite during the day, indoors and outdoors, and they preferentially feed on humans. And they need only the smallest bit of water to breed – just a bottle cap is enough. The mosquitos become infected when they bite a person with Zika virus. These infected mosquitos can then spread the virus to other people through bites. Case reports of other modes of transmission include spread through sexual transmission and blood transfusion. Of great concern, Zika virus infection in a pregnant woman has been linked to issues in fetal development, and the virus has been detected in association with fatal brain malformation in newborns as well as in miscarriages.

While its adverse effects were unforeseen, Zika is not a new virus. It was first recognized in 1947 and has caused occasional illness in Africa and Asia, but the first outbreak we know of occurred in 2007 in the small Pacific island of Yap. Last May, the first local transmission of Zika in the Americas was reported in Brazil, and by the end of 2015, Brazilian authorities estimated that the outbreak there involved perhaps a million suspected cases of Zika virus. In recent months, the virus has spread rapidly throughout Latin America and the Caribbean, as well as to parts of the Pacific. As of February 18, 2016, 32 countries and territories, including the Commonwealth of Puerto Rico, a United States Territory, the U.S. Virgin Islands, and American Samoa have reported local transmission of the Zika virus.

Symptoms and Adverse Outcomes

Many people exposed to Zika virus will have only mild symptoms - such as fever, rash, joint pain, and red eyes or conjunctivitis - that will last no more than a week. In past outbreaks, about four out of five people infected with Zika appear not to have had symptoms at all, although we do not know if that is the pattern in this outbreak.

Increasing evidence suggests that Zika virus infection may be associated with more serious health outcomes. In October 2015, Brazilian authorities recognized a concerning increase in microcephaly, which has occurred in

close sequence to Brazil's outbreak of Zika virus. Microcephaly is a usually rare, serious condition where a baby's head is smaller than expected based on age and sex. Microcephaly is not a diagnosis in and of itself, but a sign that the brain did not develop as it should in the womb. Babies with microcephaly can have a range of problems, including seizures, developmental delay, feeding problems and hearing loss. In some cases these problems can be fatal.

Laboratory tests at CDC strongly suggest a link between Zika virus infection during pregnancy and microcephaly. We do not fully understand the nature of this relationship, or if there are important cofactors. We also do not know what, if any, other outcomes might be associated with Zika infection during pregnancy among infants who do not have microcephaly. Microcephaly in infants can be devastating to the affected families, and this ongoing outbreak is concerning to everyone, especially for pregnant women, and their families who may travel to or live in the infected areas. The association between Zika virus and microcephaly is unexpected. A new infectious cause of fetal malformations has not been identified in decades. Zika virus spread in the Americas and its effect on pregnancy are developments that we are working with partners to better understand.

Our key priority at this point is to reduce the risk to pregnant women of Zika virus infection. Given the potential risks associated with maternal Zika infection, prevention is key for this response, with a parallel approach of acting based on what we know now and, at the same time, discovering more so that we can better prevent adverse health outcomes in the future. That's why, during the same week we identified Zika in brain tissue specimens from affected infants, we issued a warning to advise pregnant women not to travel to affected areas. That's why we are working intensively with the Commonwealth of Puerto Rico and other areas to get support to women who are or who may become pregnant and do what we can to reduce the threat of Zika there. And that's why we are engaging in studies with international partners so that we can more fully understand the magnitude of risk and the range of outcomes associated with Zika virus infection during pregnancy.

Health authorities in Brazil and elsewhere have also reported an increase in suspected cases of Guillain-Barré syndrome, a rare neurologic disorder in which a person's own immune system damages nerve cells, leading to nerve damage or paralysis that lasts for several weeks or several months. Most people fully recover, but it can take a few months or even years to do so. Some people with Guillain-Barré syndrome have permanent damage and, in rare cases, people have died. It is difficult to determine if any particular pathogen "caused" or "triggered" Guillain-Barré syndrome. Currently, we do not know if Zika virus infection causes Guillain-Barré syndrome. However, the development of Guillain-Barré syndrome is a recognized after-effect of a variety of different infections. CDC is currently collaborating with public health officials in Brazil to investigate whether there is any causal link between Zika infection and Guillain-Barré syndrome.

Domestic Activities

While we are working to better understand these health outcomes, transmission, diagnostics, and mosquito control, CDC is moving quickly to respond. We have moved our Emergency Operations Center to the highest

alert level for Zika virus to further enhance our response activities in areas with current local transmission and to accelerate preparedness efforts in anticipation of local transmission in the continental United States.

For the Commonwealth of Puerto Rico as well as the U.S. Virgin Islands and American Samoa, a surge in resources is urgently needed. The population of *Aedes aegypti* mosquitos is widespread on these islands, protective environmental factors such as window screens are not as prominent, and the density of people puts people there at high risk for transmission. All three areas have already reported local Zika transmission, with Puerto Rico alone reporting at least 30 cases. Furthermore, recent outbreaks of dengue and chikungunya suggest that Zika virus may spread extensively and rapidly in these areas. CDC has deployed staff to the U.S. Virgin Islands, American Samoa, and Puerto Rico to support response activities and provide technical assistance to health departments there. CDC and the CDC Foundation are also partnering to create Zika prevention kits. Containing educational materials, and initial supplies of prevention tools such as insect repellent, the purpose of these kits is to help pregnant women in areas with local Zika transmission protect themselves and their pregnancies. Five thousand of these kits have been dispatched to the Commonwealth of Puerto Rico, the U.S. Virgin Islands, and American Samoa; and CDC plans to distribute more than 45,000 kits to these areas in the future.

While we have not yet seen transmission of the Zika virus by mosquitos within the continental United States, we expect many returning travelers will have Zika infection. As a potential benchmark, we received reports of 3,270 travelers from 49 states with laboratory confirmed cases of chikungunya infection in 2014 and 2015. There are about 40 million people travelling between the continental U.S. and Zika-affected areas each year. Therefore, all U.S. jurisdictions must be prepared to evaluate, test, and manage patients with potential Zika virus infection, particularly pregnant women. Furthermore, *Aedes aegypti* is found in many areas of the United States, raising the risk of local transmission. The most recent data available suggest that *Aedes aegypti* are found in 13 states and *Aedes albopictus* are found in 31 states and the District of Columbia. Recent chikungunya and dengue clusters in the United States suggest that Zika outbreaks in the U.S. mainland may be relatively small and localized due to protective factors like window screens and less dense living conditions; however, any local outbreaks will be of deep concern to the people living there, and we must be prepared for different scenarios including more extensive transmission risk.

CDC is working with health departments across the country to ensure coordination and to expand capacity for detecting and responding to Zika virus. Surveillance is essential to monitor and quickly identify areas with local transmission. We conduct multi-faceted surveillance for arboviruses, including Zika, through ArboNET, an integrated network which funds, through our Epidemiology and Laboratory Capacity cooperative agreements, staff in 49 states, the Commonwealth of Puerto Rico, and six large municipalities to conduct human case investigations, collect and test mosquitos, and perform laboratory analysis on arboviruses including Zika. Zika virus is now a nationally notifiable disease, meaning states report the virus to CDC, which will aid Zika

surveillance efforts. CDC is also working with several states and the Commonwealth of Puerto Rico to determine a baseline prevalence of microcephaly so that any increase, should it occur, can be quickly and accurately identified.

With support from the President's emergency request, CDC will build on its current efforts to provide financial and technical resources to states and territories through its cooperative agreements to strengthen their capacity to prepare for and respond to emerging insect-borne threats such as Zika virus. These resources may be used to help health departments expand their capability to manage cases of local Zika virus transmission in their areas and to implement community education and prevention programs to reduce human-mosquito contact and subsequently, the risk of Zika transmission. Resources will also be used to implement mosquito control strategies, including mosquito surveillance. Current mosquito surveillance capacity is uneven across the country, which makes our knowledge about the locations of the two mosquito vectors that transmit Zika virus potentially incomplete. To effectively track the spread of the outbreak, it is critical that states and territories receive specimens and test for Zika virus to diagnose and report travel-related and locally acquired cases of Zika. Under the emergency request CDC will expand its efforts to assist public-health labs nationwide to test for Zika and to provide the guidance on how to interpret test results. In addition, CDC is available to provide testing of any Zika samples upon request. We are working to expand the number of health departments that have the ability to perform testing, but will need to increase the existing capacity to meet the projected demand for Zika testing. Given that, last year, it is estimated that approximately 500,000 travelers to areas of current Zika transmission were pregnant women and 36,000 pregnant women are currently living in the Commonwealth of Puerto Rico, the expansion of testing capacity in public health labs nationwide, included in the request, is urgently needed in order to ensure that every pregnant woman needing testing for Zika virus has access.

Recognizing the potential for Zika virus transmission through blood transfusions, CDC is collaborating with FDA to ensure the safety of the blood supply from Zika virus, particularly in regions experiencing local outbreaks. CDC has sent experts to the Commonwealth of Puerto Rico to assess the steps needed to assure both that Puerto Rico's blood supply needs are met and that transfusion-transmitted Zika is prevented.

CDC experts are working intensively to learn more about the outbreak and provide people with the information they need to protect themselves. We will continue to issue travel alerts for the affected areas as confirmation of the virus is reported, and we'll keep the American people informed as the situation changes. We recognize people are eager for information, and our website has exceeded half a million views in recent days.

CDC has also provided guidance for doctors and other clinicians on evaluation, treatment and follow-up care of pregnant women and infants with possible exposure to Zika virus, partnering with organizations from around the health care community to help distribute this information as widely as possible. Our guidance will continue to be updated as our knowledge increases. We have recently updated our guidance to provide recommendations for the

clinical care and management of pregnant women living in areas where Zika transmission is widespread, with special consideration to the ongoing risk of maternal Zika virus infection throughout pregnancy. These guidance documents were prepared in consultation with the American College of Obstetricians and Gynecologists, the Society for Maternal Fetal-Medicine, and the American Academy of Pediatrics.

CDC also wants to ensure that the general public knows what it can do to protect itself. Pregnant women should postpone travel to regions with ongoing Zika virus transmission. If they must travel, or if they live in affected areas, CDC recommends pregnant women talk to their doctors or other healthcare providers first and strictly follow steps to prevent mosquito bites. Reducing exposure to mosquitoes is important for anyone traveling to or residing in areas where the virus is circulating. Wearing long sleeves, long pants, using EPA-registered repellents such as DEET and permethrin-treated clothing (both of which are safe to use in pregnancy), and using other protections such as air-conditioning will reduce exposure to mosquito bites. Given the potential for Zika virus to be spread through sex, pregnant women and their male partners living in or who have been to Zika-affected areas should abstain from sex or use condoms for the duration of pregnancy. This is a rapidly changing situation and our understanding of the risks concerning Zika virus infection is incomplete and evolving. As we get new information, we will update our advice.

Global Activities

On February 1, the World Health Organization (WHO) declared the recent cluster of microcephaly cases and other neurological disorders (such as Guillain-Barré syndrome) and their possible association with Zika virus, a public health emergency of international concern, a reflection of the seriousness of this unfolding health threat. CDC is coordinating its response with the U.S. Agency for International Development, as well as the Pan American Health Organization (PAHO), the regional arm of the World Health Organization (WHO), and other parts of WHO, and is collaborating with many international partners to learn more about this outbreak. We are working with the Brazilian Ministry of Health on investigation and research partnerships. Specifically, one partnership involves studying the link between Zika virus infection and microcephaly, while another is examining the relationship between Zika virus and Guillain-Barré syndrome. Research teams from CDC are also in other countries, including Colombia, to explore collaborations that will shed light on the risk of microcephaly in relation to Zika virus infection during pregnancy.

In addition, CDC is offering support to all countries so that they can test samples from microcephaly cases for serologic evidence of Zika virus infection, and CDC is helping countries throughout the Americas establish in-country diagnostic capacity. To that end, we are currently, and in conjunction with PAHO, providing training to laboratorians in South and Central America on diagnostic tests, including two recent workshops in Brazil and Nicaragua.

CDC's Central American office has also facilitated the verification of Zika cases in several countries throughout Latin America, including Colombia, Venezuela, and Nicaragua. At the request of the Department of State's Bureau of Medical Services, staff from CDC's Global Disease Detection Center in Guatemala has been involved in communication efforts to ensure that new information regarding Zika virus and its possible link to birth defects is communicated to U.S. Mission Health Unit staff throughout the Americas.

The Global Health Security Agenda, with critical support from Congress, is collaborating with countries around the world so that we can find, stop, and prevent health threats when and where they first emerge. Zika has been present in Africa for decades, and it's possible that it could become linked to microcephaly there as well. The sooner we detect a problem, wherever it occurs, the more rapidly we can respond to it and prevent it from spreading. It is in all of our best interests to work with others to improve public health capacity around the world.

Improving the tools and information for responding to Zika

We need a better understanding of the epidemiology of Zika and potential Zika-associated birth defects and other adverse health outcomes. We need better diagnostic methods that can quickly and clearly differentiate between similar viruses to detect evidence of past Zika infection. Testing for current Zika infection is only reliable in the first week of illness. A Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test can provide a definitive diagnosis of Zika, but only if it is performed within about seven days of symptom onset. The tests we have available for Zika in persons who are no longer ill may have cross-reactivity with similar flaviviruses, particularly dengue, which can lead to false-positive or inconclusive results and confirmatory testing is required. Diagnosis is particularly challenging with Zika virus since most people will not experience symptoms. We also need to determine how long a man who has been infected with Zika may continue to be able to sexually transmit the virus to a partner, and we need better tools to screen the blood supply.

We also need to advance our ability to control the mosquito population. Existing methods for mosquito control all have shortcomings, especially in areas where the population of *Aedes* mosquitos is rampant. Furthermore, in some areas like the Commonwealth of Puerto Rico, mosquitos may have developed resistance to certain insecticides, which could reduce the range of substances that can be used to effectively decrease mosquito populations. We need to implement the best tools we have today, improve current vector control strategies, and identify better options. We also need better mosquito surveillance to determine the location of mosquitos and areas with mosquito resistance to insecticides, which would inform the implementation of new mosquito control techniques.

Finally, a vaccine is needed to protect people at risk of Zika virus infections, particularly preventing infection among women of childbearing age. At CDC, our scientists developed both a West Nile virus vaccine, which is currently in use for animal protection in the United States, and a dengue vaccine, which is currently in clinical trials. The President's request will increase Zika research, improve diagnostics and support advancements in vector control methods. Although availability of a licensed Zika vaccine is several years away, we do not know

how long Zika will be a problem in the Americas nor whether the mosquito control efforts that must be implemented will yield durable results.

Conclusion

Microbes continue to be formidable adversaries. To protect Americans, the Zika emergency request invests in the laboratories, disease detectives, disease tracking systems, mosquito control, and investigations needed to continue to improve these essential tools.

The emergence and reemergence of health threats, including those spread by mosquitos and other vectors is not a unique event but something we expect to continue to see in the future. These outbreaks cannot be expected to occur in isolation of one another. The Commonwealth of Puerto Rico and Hawaii were already responding to outbreaks of dengue when Zika virus arose as an urgent health threat. We need to address the threat of mosquito-borne diseases systematically, rather than episodically. Thank you again for the opportunity to appear before you today. I appreciate your attention to this concerning outbreak and I look forward to answering your questions.

Mr. MURPHY. Thank you, Dr. Frieden.
Dr. Fauci, you're recognized for five minutes.

STATEMENT OF ANTHONY FAUCI

Dr. FAUCI. Mr. Chairman, Ms. Castor, members of the committee, first I want to thank you for giving me the opportunity to discuss with you today the role of the National Institute of Allergy and Infectious Diseases and the NIH in general in the research endeavor to address this. As you know, the NIH is part of a multi-component aspect of the Department of Health and Human Services, and we're responsible primarily for the research for the development of countermeasures.

As I have told this committee in past hearings, the dual mandate of the Institute is somewhat unique among NIH institutes because although we, like others, have the responsibility of developing a robust basic and clinical protocol and agenda in all of the areas for which we're responsible, for us it happens to be infectious diseases, microbiology, and immunology. However, we also have the unique dual mandate of being able to respond very rapidly to emerging threats. And as a matter of fact, that's exactly what we're doing right now.

I had the opportunity and the privilege to write this perspective in the New England Journal of Medicine in January in which I said exactly what Mr. Chairman said in his opening statements, that this is yet again another threat, another arbovirus threat. If you historically over the last couple of decades we had West Nile, we have chikungunya, we have dengue, and now we have Zika. And as Tom said just a few moments ago, we're going to have others, so it's very important for us to have as part of the overall effort a research component to be able to develop the response. And as shown on this slide it's multifaceted. We do everything from basic research to fundamental clinical research and clinical trials. We do provide, not very well appreciated, the research resources for pharmaceutical companies, as well as for academics who want to get into the field of studying this disease, and we're already negotiating with a number of them.

The bottom line of it all, and the end game is to develop diagnostics, therapeutics, and vaccines. I just want to spend a minute or so going through some of the things that we are now addressing.

First, natural history. We were discussing just a couple of moments ago, it's very important to understand the true natural history, not only of the disease, symptomatic versus asymptomatic. Can an asymptomatic person who's infected and pregnant actually have a baby who is a microcephalic baby, or a baby that has a congenital defect? We need to study that. We also need to have cohort studies to understand how this has evolved. What we call pathogenesis of disease is trying to understand how this disease evolves. We did this with Ebola, we did this with HIV, and we're planning to do that with Zika.

Another is the fundamental basic research. We know an awful lot about viruses like HIV, like chikungunya, like dengue. We need to know a lot more about Zika. Luckily, it's related to some of those diseases.

Also, the immune response. We don't understand a lot about the immune response. The immune response is generally helpful. We know with dengue that immune response can actually enhance disease. We need to know the protection against Zika, and whether or not there are any deleterious effects. And also, we need to establish animal models.

You mentioned vector control. We do have basic research collaborations with pharmaceutical companies and individual investigators looking at novel ways to have vector control. You've heard of several of these such as Wolbachia infection of mosquitoes or genetic modification of mosquitoes.

Also in diagnostics, the CDC has taken the role in developing and now distributing widely some of the diagnostics that are available, but we still need high specific, easy to perform diagnostics that can tell an important question. To tell if someone is infected is relatively easy. We do a PCR, it's highly specific. The question that is really on everyone's mind is, have I been infected and if so, how long ago? And that is something that needs specificity because the current available antibody tests tend to cross-react with diseases that are prevalent in these societies, particularly dengue.

Now the issue that we're really concentrating much of our effort on is the issue of vaccines, and we now do have a couple of candidates that we're looking at putting into a Phase 1 trial, hopefully by the end of this summer and early fall, which will take a couple of months to determine if, in fact, they're safe and do they induce an immune response that will allow us to go to the next phase of the response, which is an efficacy phase. And we have a number of candidates that I'll be happy to talk to the group about during the question period.

One I want to bring up in particular, and that is why we have what we call vaccine platforms, things that we have experience with. An example is, we developed a vaccine for West Nile virus several years ago. It was safe, and it induced a good immune response. Unfortunately, there was no company that was particularly interested in partnering with us. I don't think we're going to have that problem now because we have a number of companies that are interested. But what we've done is we've taken that DNA platform and done a very simple thing; we've pulled out the gene of West Nile and we stuck in the gene of Zika, and we're going to be starting a Phase 1 trial, as I mentioned, hopefully. And then finally, we have our screening assays for the development of therapeutics we're going to be looking at because, obviously, therapeutics are a very important part.

So I'll close with this last slide, reiterating what Dr. Frieden, and Dr. Lurie, and I said, that these threats will continue to confront us. And I want to thank the committee for your interest and support of us during these periods. Thank you.

[The statement of Dr. Fauci follows:]

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Research Conducted and Supported by the National Institutes of Health (NIH) in Addressing
Zika Virus Disease

Testimony before the
House Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

Anthony S. Fauci, M.D.

Director

National Institute of Allergy and Infectious Diseases
National Institutes of Health

March 2, 2016

Mr. Chairman, Ranking Member DeGette, and Members of the Subcommittee:

Thank you for the opportunity to discuss the National Institutes of Health (NIH) research response to Zika virus, an emerging public health threat of international concern. I direct the National Institute of Allergy and Infectious Diseases (NIAID), the lead NIH institute for conducting and supporting research on emerging and re-emerging infectious diseases, including those caused by flaviviruses such as Zika virus.

The Administration is taking appropriate action to protect the American people and, as you know, it announced a request to Congress for approximately \$1.9 billion in emergency funding to enhance ongoing efforts to prepare for and respond to outbreaks of the Zika virus, both domestically and internationally. This includes funding for work on the development of vaccines and diagnostics and to improve scientific understanding of the disease.

The overarching mission of NIAID is to conduct and support research to better understand, treat, and prevent infectious and immunologic diseases. This is accomplished through a spectrum of research, from basic studies of the mechanisms of disease to applied research focused on developing interventions such as diagnostics, therapeutics, and vaccines. As part of this mission, NIAID has a dual mandate encompassing both research on ongoing public health issues and the capability to respond rapidly to newly emerging and re-emerging infections such as Zika virus.

These emerging and re-emerging disease threats, whether man-made or naturally occurring, are perpetual challenges, in part due to the capacity of microbial pathogens to evolve rapidly and adapt to new ecological niches. To address the challenges posed by emerging infectious diseases, NIAID employs both targeted, disease-specific research as well as broad-spectrum approaches. NIAID maximizes its efforts by prioritizing the development of drugs

effective against multiple bacteria or viruses, and “platform” technologies to facilitate rapid development of vaccines and diagnostics applicable to multiple infections.

NIAID is well-positioned to rapidly respond to infectious disease threats as they emerge by leveraging fundamental, basic research efforts; domestic and international research infrastructure that can be quickly mobilized; and productive partnerships with industry. NIAID provides preclinical research resources to scientists in academia and private industry worldwide to advance translational research against emerging and re-emerging infectious diseases. These resources are designed to bridge gaps in the product development pipeline and lower the scientific, technical, and financial risks incurred by industry in order to incentivize them to partner with us in the advanced development of effective countermeasures. NIAID also supports our Vaccine and Treatment Evaluation Units (VTEUs), a research network that conducts clinical trials to quickly investigate promising therapeutic and vaccine candidates when public health needs arise. NIAID collaborations with other federal agencies, including those undertaken within the Department of Health and Human Services (HHS) Public Health Emergency Medical Countermeasures Enterprise (PHEMCE), help advance progress against newly emerging public health threats. In addition, partnerships with academia, the biotechnology and pharmaceutical industries, and international researchers and organizations such as the World Health Organization (WHO) and WHO’s regional office, the Pan American Health Organization (PAHO), are integral to these efforts.

OVERVIEW OF ZIKA VIRUS

Zika virus is a flavivirus. These viruses typically are transmitted by mosquitoes and often have the ability to spread quickly to new geographic locations because of the widespread

prevalence of these vectors. Other well-known flaviviruses include dengue virus and yellow fever virus; like Zika virus they are transmitted by *Aedes* mosquitoes. Zika virus was discovered in monkeys in Uganda in 1947 and is now endemic to Africa and Southeast Asia. During the past decade it has emerged in other areas of the world, including Oceania, the Caribbean, and Central and South America, where countries, notably Brazil, are currently experiencing unprecedented Zika transmission.

Infections caused by Zika virus are usually asymptomatic. About 20 percent of infected individuals experience clinical symptoms such as fever, rash, joint pain, and conjunctivitis (red eyes). Symptoms of Zika virus infection in humans are typically mild and brief, with very low hospitalization and fatality rates. The recent outbreak of Zika virus disease in Brazil has coincided with a reported increase in the number of infants born with microcephaly, a birth defect characterized by an abnormally small head resulting from an underdeveloped and/or damaged brain. In addition, increases in suspected cases of Guillain-Barré syndrome (GBS), a rare, acute, immune-mediated peripheral nerve disease that leads to weakness, sometimes paralysis, and infrequently, respiratory failure and death, have been noted in Brazil and other countries in the Americas.

Further research is needed to better understand the effect of Zika virus infection on the body, particularly during pregnancy; to investigate the potential relationship between Zika infection and congenital abnormalities including microcephaly, as well as to explore the potential relationship between Zika infection and GBS; and to develop better diagnostics, vaccines and treatments, and new methods of vector control. Currently, no vaccines or specific therapeutics are available to prevent or treat Zika virus disease. Improved diagnostic tests also are needed because Zika virus infection causes non-specific symptoms or no symptoms at all and can be

difficult to distinguish by antibody screening tests from other mosquito-borne infections such as dengue, malaria, and chikungunya. Moreover, current antibody screening tests can be falsely positive or inconclusive if the individual was previously infected with related viruses such as dengue, which is prevalent in South America and the Caribbean. Therefore, a positive result with the antibody screening test requires an additional test to confirm the diagnosis.

NIH RESEARCH ON ZIKA VIRUS

NIAID has a longstanding commitment to flavivirus research, including extensive efforts to combat diseases such as dengue, West Nile virus, and yellow fever. This research has informed our understanding of the viral genetics, vector biology, and pathogenesis of flaviviruses and provides a strong foundation for our efforts to learn more about Zika virus. NIAID has responded to the newly emerging Zika virus disease outbreak by expanding our portfolio of basic research on Zika virus and other flaviviruses. NIAID also is accelerating efforts to develop improved diagnostics and candidate therapies for Zika virus as well as prioritizing the development of Zika virus vaccines. In addition, screening tests and pathogen reduction technologies are critically important to assure safety of the U.S. blood supply.

The emergency funding for NIH would support development of vaccines to prevent Zika virus infection, from the discovery phase through preclinical and eventually clinical testing. In addition, the funds would support basic research to understand the natural history, viral biology and pathogenesis, including potential links to microcephaly; establishment of animal models to test candidate countermeasures; development of rapid, sensitive, and specific diagnostic tests; and discovery and preclinical development of new therapeutics to treat disease caused by Zika virus. This research is necessary to better understand this emerging infection and uncover the best ways to diagnose, treat, and prevent Zika virus disease.

In January 2016, NIAID issued a notice to researchers highlighting NIH's interest in supporting research and product development to combat Zika virus. Areas of high priority include basic research to understand viral replication, pathogenesis, and transmission, as well as the biology of the mosquito vectors; potential interactions with co-infections such as dengue and yellow fever viruses; animal models of Zika virus infection; and novel vector control methods. In addition, NIH is soliciting Zika virus research to develop sensitive, specific, and rapid clinical diagnostic tests; drugs against Zika virus as well as broad spectrum therapeutics against multiple flaviviruses; and effective vaccines and vaccination strategies.

NIAID also is partnering with other NIH institutes, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Institute of Dental and Craniofacial Research, to accelerate Zika virus research as it relates to the mother-infant pair. The Institutes issued a notice that indicates NIH's interest in supporting research to understand transmission, optimal screening and management in pregnancy, and the mechanisms by which Zika virus affects the developing nervous system, including potential links to microcephaly and other congenital abnormalities.

DEVELOPING TOOLS TO COMBAT ZIKA VIRUS

In response to public health concerns about Zika virus, NIAID has accelerated ongoing flavivirus research efforts to speed the development of tools that could help control current and future outbreaks of Zika virus.

Vector Control

For many years, NIAID has supported extensive research to understand the biology of mosquitoes to help develop tools to limit the spread of deadly mosquito-borne diseases such as dengue and malaria. This research aids in vector control strategies to reduce mosquito bites or limit mosquito populations. In the Americas, Zika virus is transmitted primarily by *Aedes aegypti* mosquitoes, and vector control or other methods to prevent exposure to these mosquitoes are currently the only ways to prevent Zika infection. NIAID plans to support vector competence studies to test various mosquito species for their ability to carry and transmit Zika virus and for insecticide resistance. Understanding the specific mosquito species involved in Zika outbreaks and which insecticides may be effective against them will aid current vector control efforts and may inform novel mosquito control strategies in the future.

Diagnostics

Accurate diagnostic tests for Zika virus infection are needed to distinguish it from other flavivirus infections and to identify women who have been infected with Zika virus during pregnancy and may be at risk for developing fetal complications. Blood, organ, and tissue donor screening tests are also needed to assure the safety of transfusion and transplantation in areas of active mosquito-borne virus transmission. Currently, Zika virus itself can often be detected during the acute phase of infection and up to seven days after the onset of symptoms using diagnostic tests for viral RNA (RT-PCR test). While prior infection can be detected by testing for the presence of antibodies against Zika virus, assays for Zika antibodies may also detect or cross-react with antibodies against other flaviviruses, particularly dengue virus. For this reason, a positive antibody test does not definitively confirm prior Zika virus infection in the setting of possible co-infection or prior infection with dengue and other related viruses, and separate

confirmatory testing is required. This is a particular concern in South America where there is a high level of exposure to other flaviviruses, particularly dengue virus.

To facilitate the development of improved Zika virus diagnostic tests, NIAID grantees are working to generate antibodies that can distinguish between Zika virus and dengue virus. They also are working to identify biosignatures unique to Zika infection that could form the basis of additional rapid, specific, and sensitive diagnostic tests. In addition, NIAID is pursuing the development of a mouse model of Zika virus infection that could be used to test new diagnostic and therapeutic tools.

Vaccines

A safe and effective Zika vaccine would be a very valuable tool to help stop the spread of infection and prevent future outbreaks. NIAID is investigating multiple Zika virus vaccine candidates, including vaccines based on technologies that have shown promise in targeting other flaviviruses. The NIAID Vaccine Research Center (VRC) is pursuing a DNA-based vaccine for Zika virus that is similar to a West Nile virus vaccine previously developed by NIAID. The West Nile vaccine candidate was shown in Phase 1 testing to be safe and generated a strong immune response in humans, offering a model for Zika vaccine development. NIAID scientists also are designing a live, attenuated vaccine, using an approach similar to that used for making a vaccine against the closely related dengue virus. The dengue vaccine candidate showed an excellent safety profile and generated strong immune responses in early-phase clinical trials. In January, a large Phase 3 trial assessing the dengue vaccine candidate was launched in Brazil in collaboration with the Butantan Institute. In addition, NIAID grantees are in the early stages of developing a Zika virus vaccine based on a recombinant vesicular stomatitis virus – the same

animal virus used successfully to create an investigational Ebola vaccine. Plans are underway to evaluate this potential vaccine construct in tissue culture and animal models.

While these approaches are promising, it is important to realize that the development of investigational vaccines and the clinical testing to establish whether they are safe and effective takes time. Although a safe and effective, fully licensed Zika vaccine will likely not be available for a few years, we plan to begin early-stage clinical testing of one or more NIAID-supported vaccine candidates in 2016.

Therapeutics

NIAID has an active program to screen for antiviral drugs active against viruses in the flavivirus family, including dengue, West Nile, yellow fever, and Japanese encephalitis viruses, as well as the closely related hepatitis C virus. NIAID has enhanced these efforts with the recent development of an assay to test compounds for antiviral activity against Zika virus. NIAID will make this test available to the research community and will soon test 10 antiviral compounds with activity against other flaviviruses to determine if they are effective against Zika virus. Promising drug candidates identified by the assay could be further tested in a small animal model of Zika virus infection developed with NIAID support. The ultimate goal of NIAID-supported flavivirus therapeutic research is to develop a broad-spectrum antiviral drug that could be used against a variety of flaviviruses, including Zika.

Emergency Request for Vaccine Research and Diagnostic Development and Procurement

As I noted in the introduction to my testimony, the Administration has announced an emergency funding request of approximately \$1.9 billion to combat the Zika virus both domestically and internationally. Included in the request are resources for Zika-related vaccine research, rapid advanced development, and commercialization of new vaccines and diagnostic

tests for Zika virus. The funding will allow NIH to build upon existing resources and work to develop a vaccine for Zika virus and the chikungunya virus, which is spread by the same type of mosquito. Funding will accelerate this work and improve scientific understanding of the disease to inform the development of additional tools to combat it. The request also includes resources for FDA to support Zika virus medical product development, including the next-generation diagnostic devices. We look forward to working with the Congress to implement this request.

COLLABORATIONS

Investigation of emerging and re-emerging infectious diseases requires expertise from a variety of fields. In the case of Zika virus, studies of virology, immunology, natural history, neurology, and neonatology will be required to fully understand the pathogenesis of this infection. As mentioned previously, NIAID is partnering with other NIH institutes including NICHD and NINDS to better understand the potential association between Zika virus infection and neonatal defects, particularly microcephaly.

NIAID also is employing partnerships with research institutions in South America to advance research on Zika virus infection; additional collaborations with academic, industry, and government partners are under active exploration. NIAID held a joint meeting in December 2015 with Brazilian research institute Fiocruz in which Zika was a key area of concentration. In addition, NIAID is collaborating with other HHS agencies in responding to the Zika epidemic. For example, NIAID, CDC, BARDA, ASPR, and FDA are jointly convening a Zika virus workshop on March 28-29, 2016, where the latest information on Zika virus will be discussed by experts from Federal Agencies, academia, and pharmaceutical and biotechnology

companies. Topics to be addressed at the workshop include virology, epidemiology, possible links to microcephaly, and efforts to develop diagnostics, therapeutics, and vaccines.

CONCLUSION

NIH is committed to continued collaboration with HHS agencies and other partners across the U.S. government in advancing research to address Zika virus infection, and we look forward to working with the Congress to implement the President's emergency funding request. As part of its mission to respond rapidly to emerging and re-emerging infectious diseases throughout the world, NIAID is expanding our efforts to elucidate the biology of Zika virus and employ this knowledge to develop needed tools to diagnose, treat, and prevent disease caused by this virus. In particular, NIAID will pursue the development of safe, effective vaccines to prevent disease caused by Zika and chikungunya viruses.

Mr. MURPHY. Thank you, Dr. Fauci.
Dr. Borio, you're recognized for 5 minutes.

STATEMENT OF LUCIANA BORIO

Dr. BORIO. Good morning, Chairman Murphy, Representative Castor, and members of the subcommittee. Thank you for the opportunity to discuss the FDA's actions to respond to the Zika virus outbreak.

FDA is working closely with our partners to help minimize the impact of yet another tragic outbreak. Last month I had the privilege of traveling to Brazil, my country of birth, with a small HHS delegation to meet with the Brazilian Minister of Health and several of his senior officials. The engagement was extremely productive. In particular, FDA and ANVISA, Brazilian's National Regulatory Agency, committed to working very closely and reach convergence in the areas of vaccine development and diagnostic tests.

FDA is working to help protect the safety of our nation's blood supply, to facilitate the development and availability of blood donor screening and clinical diagnostic tests, to support the development and investigation of vaccines and therapies, to review a proposal for the use of innovative strategy involving genetically engineered mosquitoes to enhance vector control, and to protect the public from fraudulent products. To help mitigate the risk of Zika transmission from blood transfusions, FDA issued guidance recommending important measures to keep our nation's blood supply safe. And just yesterday, FDA issued new guidance with recommendations to reduce a risk of transmission of Zika by human cellular and tissue-based products are used in medical procedures.

I'm happy to report that last week we issued the first emergency use authorization for a test developed by the CDC. We continue to work very interactively with the CDC and several diagnostic companies, several diagnostic companies to support development of additional tests.

The association between Zika, microcephaly, and other pro-pregnancy outcomes results in a very serious and challenging situation for pregnant women who test positive for Zika virus infection. Just last week, CDC reported that among nine pregnant travelers with laboratory confirmed Zika virus infection there were two early pregnancy losses, two elective terminations, and one infant with severe microcephaly at birth. It is not difficult to imagine the fear, uncertainty, and anguish these women and their families likely experienced; therefore, it is essential that diagnostic tests for Zika virus provide accurate results.

In recent weeks we have seen an increased interest by clinical laboratories to develop their own tests for Zika. We share the goal of expanding the availability of good tests, and to support these efforts FDA developed simple templates that developers can use to submit data to the FDA for expedited review, but FDA is urging developers to work with us to insure that their tests meet the standards for accuracy and precision. And I need to make clear that FDA will not hesitate to take appropriate action to prevent the use of tests that did not meet our standards.

FDA is actively engaged with NIH and BARDA to help accelerate the development of vaccines, and as we did during the Ebola epi-

demic we will do all we can to facilitate access to investigation of vaccines through appropriate clinical trials as quickly and safely as possible.

Finally, we are reviewing a proposal for a field trial to determine whether the release of a genetically engineered line of *Aedes aegypti* mosquitoes will suppress the local *Aedes aegypti* mosquito population in the release area of Key Haven, Florida. We are preparing to very soon release for public comment a Draft Environmental Assessment regarding the potential impacts of this proposed field trial.

In closing, FDA is deeply engaged and fully committed to sustaining our aggressive response activities to mitigate the impact of Zika. Thank you.

[The statement of Dr. Borio follows:]



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

STATEMENT
OF
LUCIANA BORIO, M.D.
CHIEF SCIENTIST (ACTING)

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
HOUSE ENERGY AND COMMERCE COMMITTEE

U.S. HOUSE OF REPRESENTATIVES

EXAMINING THE U.S. PUBLIC HEALTH RESPONSE TO THE ZIKA VIRUS

MARCH 2, 2016

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Good morning Chairman Murphy, Ranking Member DeGette, and members of the Subcommittee. I am Dr. Luciana Borio, Acting Chief Scientist at the Food and Drug Administration (FDA or the Agency). Thank you for the opportunity to appear today to discuss FDA's actions in response to the Zika virus outbreak.

As you know, Zika virus was first identified in 1947 in Uganda. Since then, sporadic cases and a few outbreaks have been recognized in a number of locations, including parts of Africa, Asia, and the Pacific. However, the situation has changed dramatically since May 2015, when the first local transmission of Zika virus in the Americas was confirmed in Brazil. By December 2015, Brazil had reported more than 56,000 suspected cases of Zika virus and has since stopped counting cases due to the magnitude of the outbreak, which Brazilian national authorities estimate to encompass from approximately 500,000 to 1.5 million cases.

Zika virus is now spreading throughout Latin America and the Caribbean, as well as in parts of the Pacific and Africa. As of February 25, 2016, 34 countries and territories, including the Commonwealth of Puerto Rico, the U.S. Virgin Islands, and American Samoa, have active, local transmission of Zika virus.

Potential links between Zika virus infection and neurological complications (e.g., Guillain-Barré Syndrome), as well as microcephaly and other poor pregnancy outcomes in babies of mothers who were infected with Zika virus during their pregnancy have dramatically increased concerns about the risks associated with Zika virus. On February 1, 2016, the World Health Organization

(WHO) declared the recent clusters of microcephaly and other neurological disorders a public health emergency of international concern.

No locally transmitted mosquito-borne Zika virus disease cases have been reported in the continental United States to date. There have, however, been travel-associated cases, as well as local cases of sexual transmission to women whose only known risk factor was sexual contact with an infected male partner who traveled to an area with active transmission. These imported cases have the potential to result in local spread of Zika virus in areas of the United States where *Aedes* mosquitoes that transmit Zika virus are found. CDC and state, local, and territorial health departments are monitoring for any such events.

FDA RESPONSE TO THE ZIKA VIRUS OUTBREAK

FDA is working in collaboration with other components of the Department of Health and Human Services (HHS), including the Office of the Assistant Secretary for Preparedness and Response (ASPR) and its Biomedical Advanced Research and Development Authority (BARDA), the National Institutes of Health (NIH), and the Centers for Disease Control and Prevention (CDC), as well as with partners across the U.S. Government and with international partners to respond to the Zika virus outbreak. FDA's primary areas of activity include: (1) protecting the safety of the nation's blood supply and tissues for transplantation; (2) facilitating the development of donor screening and medical diagnostic tests that may be useful for identifying the presence of, or prior exposure to, Zika virus; (3) supporting the development of investigational vaccines and therapies; (4) reviewing proposals for the use of innovative strategies to help suppress the population of virus-carrying mosquitoes; and (5) protecting the public from fraudulent products that claim to prevent, diagnose, treat, or cure Zika virus disease.

Blood Supply and Tissue Safety

In the absence of an available donor screening assay, the risk of transmission of Zika virus by blood transfusion is considered likely, based on the most current scientific evidence of how Zika virus and other flaviviruses (including West Nile and dengue) are spread, as well as recent reports of transfusion-associated infection outside of the United States. Realizing this risk, and to better protect the U.S. blood supply, FDA issued new Zika-related blood donor guidance. In areas with active Zika virus transmission, FDA recommends that whole blood and blood components for transfusion be obtained from areas of the United States without active transmission. Blood establishments may continue collecting and preparing platelets and plasma if an FDA-approved, pathogen-reduction device is used. FDA also recommends deferral from donating blood for four weeks for individuals in areas without active Zika transmission if they a) have been to areas with active Zika virus transmission; b) have recovered from an illness with symptoms suggestive of Zika virus infection that developed within two weeks of exposure in an affected area; or c) have had sexual contact with a man who has traveled to, or resided in, an area with active Zika virus transmission during the prior three months. The guidance also recommends that blood establishments update donor education materials with information about Zika virus signs and symptoms, ask potentially affected donors to refrain from giving blood, and update the donor history questionnaire to elicit information on recent exposure to an affected area. FDA is working with public health authorities in territories with confirmed Zika virus to take rapid and appropriate steps to ensure that safe blood is available.

In addition, to advance blood safety against Zika virus, FDA is facilitating the development of screening tests for identifying the presence of the virus in donated blood and pathogen-reduction

technologies to kill viruses in blood components through establishment of reference materials, clarification of regulatory pathways, and interactive review of sponsor-submitted data.

Furthermore, FDA is developing guidance that will address appropriate donor deferral measures for human cells, tissues, and cellular and tissue-based products. This guidance is particularly important given evidence of sexual transmission of Zika virus.

Diagnostic Tests

Unfortunately, there are no commercially available diagnostic tests cleared by FDA for the detection of Zika virus. Two types of diagnostic tests are needed for Zika virus: (1) a test to diagnose acute infection; and (2) a test to assess whether individuals, especially pregnant women, who were potentially exposed to Zika virus were actually infected. In keeping with FDA's practice for responding to emerging infectious disease outbreaks, FDA has been reaching out to potential diagnostic manufacturers to encourage them to develop needed diagnostic tests for Zika virus. In addition, FDA is working interactively with diagnostic manufacturers interested in developing diagnostic tests for Zika virus to help accelerate development programs, including clarifying data requirements for the authorization of the use of Zika diagnostic tests under FDA's Emergency Use Authorization authority (EUA). FDA has authorized the use of a Zika virus diagnostic test developed by CDC under EUA for the qualitative detection of Zika virus-specific immunoglobulin M (IgM) antibodies by qualified laboratories. This diagnostic test can help expand domestic readiness for Zika virus by enabling the identification of patients recently infected with Zika virus in support of response efforts. The authorized test has already been made available to 19 states and territories. FDA is ready to authorize the use of additional

Zika virus diagnostic tests under our EUA authority as soon as we receive data regarding the accuracy and precision of the test from a diagnostic manufacturer to enable such authorization.

Vaccines and Therapies

There are no vaccines or treatments in advanced development for Zika virus at this time. Development programs for investigational vaccines and therapies are in the very early stages and FDA is actively engaged with NIH and BARDA to help accelerate development programs. FDA stands ready to work with medical product developers to provide technical support and clarify regulatory and data requirements necessary to move products forward in development as quickly as possible.

Vector Control

In the United States, mosquito control is typically achieved by a multi-faceted approach that includes a range of tools, including surveillance of mosquito activity, reduction in breeding sites, and the use of chemical and biological control methods. There has been public discussion of a new method to potentially help control mosquito populations through the use of a genetically engineered (GE) line of the mosquito *Aedes aegypti* (OX513A) developed by Oxitec, Ltd. The release of male Oxitec GE mosquitoes is intended to cause suppression of the mosquito population in a release area over time because the offspring resulting from the mating of male GE mosquitoes with wild type females do not develop to adulthood. The Brazilian National Biosafety Commission found the Oxitec GE mosquito safe for use in Brazil in 2014 after extensive field testing, and open field trials of these GE mosquitoes have also been conducted in the Cayman Islands, Panama, and Malaysia. Although multiple pilot studies have been

authorized in Brazil, the country's national regulatory authority, the Agência Nacional de Vigilância Sanitária (ANVISA), is currently reviewing Oxitec's request to approve its product for commercial sale.

FDA is reviewing information in an Investigational New Animal Drug (INAD) file from Oxitec regarding the potential use of the company's GE mosquito with the intent of suppressing the population of *Aedes aegypti* mosquitoes at the release site(s). FDA ordinarily cannot acknowledge or discuss INAD files due to confidentiality concerns; however, FDA is able to do so in this case because Oxitec has publicly announced that they have opened an INAD file.

Oxitec is seeking to conduct a field trial to determine whether the release of its GE mosquito will suppress the local *Aedes aegypti* mosquito population in the release area at Key Haven, Florida. As with similar applications, FDA plans to release for public comment a draft environmental assessment submitted by Oxitec that assesses the potential environmental impacts of conducting a field trial in Key Haven with the GE mosquitoes. A field trial of the GE mosquito may only be authorized if—after a draft environmental assessment has been released for public comment and the Agency has had the opportunity to review those comments—FDA issues a final environmental assessment and Finding of No Significant Impact on the environment, or FDA prepares an Environmental Impact Statement. If such a trial is authorized and conducted, Oxitec could use the results from a field trial in an application for approval if the company decides to pursue one in the future.

Fraudulent Product Claims

Unfortunately, during emerging infectious disease outbreaks such as this, fraudulent products that claim to prevent, treat, or cure a disease rapidly appear on the market. FDA is actively monitoring for fraudulent products and false product claims related to Zika virus and will implement enforcement actions, as warranted, to protect the public health.

CONCLUSION

FDA is fully committed to remaining highly responsive and adaptive to the complex range of issues the Zika virus outbreak has presented and will continue to present. Developing the medical products necessary to help bring this outbreak under control is highly complex and will, unfortunately, take time. Close cooperation and collaboration within FDA, within the U.S. Government, with our international partners, and with product developers, is essential to help facilitate the development and availability of medical products to respond to Zika virus. There is an urgent need to accelerate medical product development programs, and FDA anticipates that—similar to the Ebola epidemic in West Africa—there will be a strong desire for access to investigational medical products as soon as they become available.

While the Ebola and Zika viruses have important differences, the response to the Ebola epidemic demonstrated that the typical, phased approach to medical product development can be accelerated and streamlined as appropriate, for the particular health circumstance; it may be appropriate in certain emergency circumstances to accept a greater than usual degree of uncertainty and risk in order to move rapidly to clinical trials, with the goal of getting safe, effective therapies or vaccine products to patients sooner. However, while greater risks may be acceptable during a public health emergency or when there is the potential for a public health emergency, the responsibility to protect patient welfare never ceases. The Ebola epidemic

highlighted the importance of determining whether investigational products may help patients, do nothing, or cause unintentional harm. Thus, it is essential that clinical trials be designed to provide interpretable data— with respect to both safety and efficacy—that will enable the global community to learn whether investigational products are safe and effective for broader use.

FDA is fully prepared to leverage its authorities to the fullest extent practicable to help accelerate the development and availability of safe and effective products with the potential to help mitigate the Zika virus outbreak as quickly as the science will allow.

Thank you. I am happy to answer your questions.

Mr. MURPHY. Thank you, Dr. Borio.
Now, Dr. Persons is recognized for 5 minutes.

STATEMENT OF TIMOTHY PERSONS

Mr. PERSONS. Thank you, Mr. Chairman, Ms. Castor, and members of the subcommittee. I'm pleased to be here today to discuss GAO's preliminary observations on Zika virus disease. I'll summarize our findings of the four topics you asked us to examine; specifically, one, the epidemiology and transmission of Zika including what's known about its link to microcephaly and neurological diseases. Two, the current diagnostic and testing methods for Zika. Three, the methods for mosquito control. And, four, the proposed federal research agenda as it relates to Zika virus and disease.

With regard to epidemiology and transmission, while several countries noted over here on this graphic have reported outbreaks of Zika virus disease, unanswered questions remain regarding the epidemiology and transmission of the disease. Accurate information on the incidents of Zika is lacking. Five primary reasons for this are first, about 80 percent of persons who are infected do not show clinical symptoms resulting in potentially significant underestimation of the true incidence of infection. Second, since many of the remaining 20 percent of those who manifest clinical symptoms may not go to a physician because the symptoms are mild, the true incidence of disease is potentially significantly under-reported. Third, an accurate count of the number of cases of Zika virus disease requires a consistent standardized international case definition; however, at the moment different countries have different definitions, thus complicating epidemiological analysis and research. Fourth, on February 1st of this year the World Health Organization acknowledged that there was no international standard surveillance case definition for microcephaly. Problems with changing case definitions, lack of sufficient information on underlying causes of brain pathology, and lack of baseline data make it difficult to accurately determine the increase of microcephaly in Brazil, and how much stems from the Zika virus. And fifth, the lack of approved diagnostic tests complicates our understanding of the virus and may hinder our response to the current outbreak.

With regard to detection and testing, currently no commercially available test exists for Zika, as the Chairman pointed out. The FDA recently issued an emergency use authorization for an antibody-based test for the Zika virus; however, the main limitation is the inability to differentiate between infection with Zika and infection with other closely related flaviviruses such as dengue. Since closely related flaviviruses such as dengue may also be present in regions where Zika has broken out, the use of this test could incorrectly identify non-Zika virus associated infections, thus risking extra burden on laboratory and health care systems, and distorting epidemiological analyses.

With regard to mosquito control, because Zika virus disease cannot yet be prevented by drugs or vaccines, controlling the vector remains a critical factor in mitigating the spread of the virus, and hence disease. GAO identified three categories of mosquito control. First, standing water treatment. Second, insecticides. And third, emerging technologies.

The WHO determined that maintaining vector control after a disease subsides is complicated by dwindling resources. In the United States, vector control methods are under state and local jurisdictions which determine the method to use by local needs and factors. Emerging control technologies include the use of biologicals, genetically modified mosquitoes, and auto dissemination traps. According to the scientific literature these technologies show some promise in studies and field trials but would need to be part of an overarching integrated mosquito control strategy.

With regard to the federal research agenda, the NIH and CDC have identified several high priority areas for research; for example, linkages between Zika and microcephaly, improving diagnostic tests and vaccine development. Efforts in these areas are necessarily ambitious but agencies may face challenges in implementing this agenda. For example, given the number of known cases in the U.S. is so few, NIH and CDC may have to rely on the cooperation of other countries to account for a sufficient number of cases to carry on the proposed research. However, data from other countries may differ because of differing definitions of Zika virus disease and microcephaly.

Turning to vaccine development, NIH officials told us that given their experience with the development of a vaccine for dengue fever, a vaccine for Zika could be ready in 3 to 4 years. Zika virus disease poses new challenge to vaccine development testing especially on pregnant women for whom several barriers to developing and testing vaccines exist. Overcoming these barriers may extend the time for vaccine testing and approval, and the information we have from NIH in our prior work suggests that developing a Zika virus vaccine may take longer than currently anticipated.

In conclusion, GAO's past work including, for example, our recent analysis on Swine Enteric Coronavirus Disease outbreaks in pigs has shown some similarities such as a lack of validated diagnostic tests, immature mechanisms for reporting the disease and no approved vaccine. These preliminary observations on the Zika virus point to a persistent and urgent need for a proactive, agile, integrated, and coordinated set of programs in research and development including epidemiological studies, mosquito control, testing capabilities, modeling and simulation, and vaccine development, especially in light of other emerging diseases such as chikungunya and dengue which spread via the same mosquito vectors as Zika, and which also pose a risk to human health.

Mr. Chairman, Ms. Castor, members of the subcommittee, this concludes my prepared remarks. I'd be happy to respond to any questions that you or other members may have at this time. Thank you.

[Mr. Person's written statement has been retained in committee files and can be found at: <http://docs.house.gov/meetings/if/if02/20160302/104594/hhrg-114-if02-wstate-personst-20160302.pdf>.]

Mr. MURPHY. Thank you. I thank all the panel for your information. Now we'll begin questioning. I'll begin with 5 minutes myself.

Dr. Lurie, under the Pandemics and All Hazards Preparedness Act and its reauthorization, the Assistant Secretary for Preparedness response was create a lead federal official for coordinating these health emergencies. My understanding, Secretary Burwell

designated you as Lead Federal Official for coordinating the response with Flint and Ebola. Am I correct?

[No response.]

Mr. MURPHY. Has she named you the Lead Federal Official for the Zika response?

Dr. LURIE. So in terms of the Zika response, ASPR's role as it usually is, is to coordinate for her and on her behalf policy issues and other issues related to the Zika response. ASPR is very actively fulfilling that role, as you heard in my testimony. As part of that role, the CDC has primary responsibility for the operational public health response, and Dr. Frieden has the lead for that.

Mr. MURPHY. So is that how it's going to break down, the Lead Federal Official will be Dr. Frieden, and not you, or do we—

Dr. LURIE. ASPR has coordinating responsibility on behalf of the Secretary for this. The primary response is an operational public health response and that's what CDC does day in and day out.

Mr. MURPHY. We just want to make sure we have some sense of how this is working out.

Dr. LURIE. Yes, absolutely.

Mr. MURPHY. Dr. Persons, what are the concerns associated with the assay recently authorized by the FDA for emergency use?

Mr. PERSONS. Yes, thanks, Mr. Chairman. The test is called the MAC-ELISA test. Its main concern is just its cross-reactivity with other flaviviruses, as other witnesses have pointed out. So you can tell that you have a related flavivirus but you cannot have the specificity to say you have Zika with assurance, unless or until you have the RT PCR basis to back you up and do that.

Mr. MURPHY. But is all this going to put an extra burden on the labs and health care systems, and will that distort some of our analysis then if we can't fully do that?

Mr. PERSONS. That is, indeed, a risk to the system.

Mr. MURPHY. Dr. Frieden, do you want to comment on that, too?

Dr. FRIEDEN. Just to clarify, the IGM that was FBUA approved by FDA in wonderful excellent time with good collaboration, that test we believe is accurate, particularly in people less likely to have been exposed to dengue. There is a second test that we do which is a neutralization assay, a PRNT on the IGM positive, so we would in some cases, depending on the combination of the IGM and the PRNT be able to say we believe it is definitively Zika. In other cases we can say only that it's a flavivirus that may or may not—

Mr. MURPHY. So we can get a false positive if they've been exposed to dengue. Is that what happens, Dr. Borio?

Dr. BORIO. Well, just for clarity, is that the emergency authorization is not just for the ELISA test, the one that causes the cross-activity. The authorization is for the ELISA test and a confirmatory test done at CDC. We will have very high standards for the UA.

Mr. MURPHY. I'm aware of that, and you had elaborated this point, too. I just want to find out if we have enough capacity in our public health labs and health care system to handle what the GAO is concerned about with this emergency response. If we don't, we need to know that as Congress.

Dr. FRIEDEN. So we are concerned about the capacity in terms of the number of tests. Our laboratories have been working around

the clock for the PCR. We've produced more than 370,000 of them. We think that's ample for the MAC-ELISA. We're up around 100,000 level. It could be that in some places, in some areas individuals who want to be tested will not be able to be tested until we further scale up production and roll out validation of the state labs.

Mr. MURPHY. Let me make sure I understand this. So if we're also currently trying to develop a vaccine and some people who have been exposed to Zika virus will be immune to it. And is that the avenue? I guess, Dr. Fauci, this is your area. Is that the avenue by which will help us determine a vaccine, if some people have developed their own immunity? Does that give us some other ideas of where to go with this? Am I down the right road there?

Dr. FAUCI. Yes. I think in a vaccine trial it depends on what stage of the trial. When you're in a Phase 1 trial those are people who are completely normal. That's the thing I was mentioning that would start at the end of the summer. When you get into a trial in the field in Brazil, obviously you're going to want to know people who were pre-exposed, as well as people who were not exposed as a subgroup of the study. The fundamental study will be to determine the extended safety and some degree of efficacy in a Phase 2A2B. As a subset of that group, you'd want to know what the response would be in those who were previously exposed, perhaps asymptotically, versus those who were never exposed.

Mr. MURPHY. And so where we are now, we don't have the capacity and you're asking Congress for help because we just don't have the capacity to handle this. Right, Dr. Frieden?

Dr. FRIEDEN. There are many things that we will not be able to do or do at scale without the emergency supplemental.

Mr. MURPHY. And this will delay our responsiveness and detection in developing a vaccine until we get this level higher? We all agree with that?

Dr. FAUCI. Agreed.

Mr. MURPHY. Thank you. Ms. Castor, recognize you for 5 minutes.

Ms. CASTOR. Thank you. The Zika outbreak began in Brazil nearly a year ago, and it's rapidly spread across the Americas. I'm very concerned by the virus' recent arrival in Puerto Rico and its rapid spread there. News reports earlier this week said there are well over 100 confirmed cases of Zika in Puerto Rico, and that the number is almost sure to rise over the next few weeks.

Dr. Frieden, can you give us an update on the situation in Puerto Rico? What should we expect to see there in the coming weeks? And then could you go into greater detail on the current diagnostic tools in Puerto Rico, and whether or not they differ in Brazil and across the Americas?

Dr. FRIEDEN. Thank you very much. In Puerto Rico we have basically the 1-2 punch of Zika and similar viruses. We have the mosquito that can spread the virus, and we have a human environment without screens and air conditioning widely available that lead to explosive spread of viruses spread by this mosquito. So as I mentioned earlier, we have chikungunya which spreads by the same mosquito. One out of four adults became infected with it within 8 months of the introduction of that virus to the island.

In terms of the diagnostic tests, the tests are the same but they perform differently in different places depending on what the individuals there have been exposed to. So first off, as Dr. Fauci mentioned, the test for active infection, that's straightforward and accurate, so if someone is sick, they have fever, then between the onset of symptoms or maybe a day or two before until about four to seven days after symptom onset, that test will be positive and it's definitive. But past that period it's much more challenging to determine whether someone was previously infected with Zika. That requires looking at antibodies, and the EUA that the FDA approved on Friday allows us to do that in a way that looks at the IGM or short-term antibody response which may become positive within the first week, and stay positive for some as yet undetermined period of time, it could be months. And then to confirm that with a test that actually grows the virus and sees if it is inhibited by the patient's own serum, the neutralization assay. So it's an algorithm-based testing. CDC has a dengue branch in Puerto Rico. We currently have all 50 of our people from that branch plus another 25 from the rest of CDC on the island now working hard on every aspect of the response.

Ms. CASTOR. Dr. Fauci, Dr. Borio, do you want to add anything on the diagnostics?

Dr. FAUCI. No, but we will do better. As Dr. Frieden said, this is what we have right now, but we are all of us trying very hard to develop a much more specific test that would answer the question directly that everyone is concerned with. But for what we have now, that's what we're talking about.

Dr. LURIE. I would only add that we've been really approached by a whole array of companies who are now actively working to develop their own diagnostic tests. We're in a position to provide them support and to work closely in collaboration with FDA to make a smooth, easy path if those diagnostics are effective.

Ms. CASTOR. Thank you. And, Dr. Frieden, Puerto Rico has seen recent outbreaks of other related infectious diseases in Puerto Rico. What have those outbreaks taught us about Puerto Rico's public health infrastructure and its capacity to respond?

Dr. FRIEDEN. Well, I think it's fair to say that mosquito control, the capacity is very limited. In addition, the challenges of controlling this mosquito are very great so even though there have been efforts to reduce spread of dengue and chikungunya, they have had very little, if any, impact on the actual disease spread.

Ms. CASTOR. I understand that the FDA has issued guidance on blood donation calling on blood banks in areas where Zika is locally transmitted to import blood from regions without an outbreak, instead of using local donations. Dr. Borio, what does that mean for Puerto Rico? Does it affect their ability to provide medical care to their residents?

Dr. BORIO. So FDA's guidance meets an important public health need, which is to keep the nation's blood supply safe. In areas with active transmission, the guidance does require whole blood and blood components to be imported from areas without active virus transmission until a diagnostic test that can be used to screen the blood supply is available. So there is a potential that our guidance

could impact in theory the supply of blood to areas of active transmission.

That being said, that should not be the case in Puerto Rico because we have been working very closely with our partners, Puerto Rico health officials, CDC, and Dr. Lurie's office to mitigate the impact of our guidance. And Dr. Lurie may have more to add on that.

Ms. CASTOR. Well, I note that the President's emergency budget request includes \$225 million for grants in technical assistance for Puerto Rico and other U.S. territories facing Zika outbreaks. Is that going to get to the heart of the matter?

Dr. FRIEDEN. That is crucially important for us to be able to mount a robust response, and the sooner the better.

Ms. CASTOR. Thank you very much. Thank you, Mr. Chairman.

Mr. MURPHY. Yes, just a follow-up. Would you say that Florida and Texas are probably some of our highest risk states?

Dr. FRIEDEN. Yes, we've seen clusters of dengue and chikungunya in Florida or Texas, and because of the presence of the vector we anticipate that these could be areas where we might see clusters of local transmission.

Mr. MURPHY. OK.

Ms. CASTOR. In fact, Mr. Chairman, there was recently a map published in the national newspaper and it had Florida in bright red, so it's definitely gotten everyone's attention, so this is very timely. Thank you.

Mr. MURPHY. I will then recognize the doctor from Texas to follow up there. Dr. Burgess, you're recognized for 5 minutes.

Mr. BURGESS. Thank you. And again, thanks to our panel for being here today, and we always do learn so much when you come in to talk with us.

So, Dr. Frieden, let me just ask you, after talking to my folks on the ground back in Denton County yesterday, what constraints has the CDC placed on states when it comes to the expenditure of preparedness Ebola dollars to combat Zika?

Dr. FRIEDEN. We have several different funding streams available that includes the Public Health Emergency Preparedness dollars. Those I believe but would have to confirm, we have indicated to states that they can use for the Zika response.

Mr. BURGESS. Those dollars should be able to travel freely between missions?

Dr. FRIEDEN. That's the PHEP, the Public Health Emergency Preparedness grants. For the Ebola dollars, I would have to get back to you.

Mr. BURGESS. And please do, because that is important. And we're hearing stuff about funding. I get that. It always come up in this subcommittee, and I'm not immune to that. But, Dr. Frieden, let me just ask you, the travel restrictions, Tier 2 travel advisory right now for countries in the Caribbean and Central America, and South America. Is that correct?

Dr. FRIEDEN. Yes.

Mr. BURGESS. What is the reluctance to go to Tier 3 restrictions?

Dr. FRIEDEN. There's not really a reluctance. It's a question of what's appropriate to the circumstances. We're not saying that nobody should go; we're saying that women who are pregnant should consider not going. And similarly in other situations.

Mr. BURGESS. You're asking us for more money. OK, I get that, and you're saying it's an emergency. I might believe you more that it's an emergency if you would be willing to say and we really don't want you to go down there. The State Department, when I talk to them they say oh, we rely entirely on the CDC, but they're also not assigning women of reproductive age to those outposts. So there's kind of a disconnect there.

Dr. FRIEDEN. What we feel is we need to give people information and allow them to make the choices. We've heard of situations where someone is going back for a funeral or a very important personal event, and so we say you shouldn't go, but we also say we understand there are some circumstances in which women will go. And in those circumstances we provide the information on how they can best protect themselves with mosquito repellent and other means.

Mr. BURGESS. Again, it just seems logical that nonessential travel really should be circumspect right now.

Dr. FAUCI, let me just ask you a question, because going back several years to what was called the Swine Flu outbreak, and we talked on several occasions during that. I remember the conference call that occurred during March Madness of 2009, and I remember talking to you during the August recess about the availability for the vaccine was a few weeks away. It wasn't quite going to be there for the start of school, but it would be a week or two after, so the middle of September. So that's a 6-month time frame if I'm doing my math correctly that you were able to identify the genetic sequence of the virus, reverse engineer a vaccine, test it, assure its safety and efficacy, and get it to school teachers on the second week of school. That's pretty impressive.

Dr. FAUCI. Right.

Mr. BURGESS. And why are we different with this? Is this just because it's a different virus?

Dr. FAUCI. Yes. Well, what you have with influenza was a strain change and a production to have over 150 million doses available over that period of time. What we're talking about right now, as I mentioned, and if I may, let me just clarify—

Mr. BURGESS. Sure.

Dr. FAUCI [continuing]. What is a feasible time frame within the context of there are always vicissitudes when you're dealing. So we have this couple of candidates, two or three that are likely going to go into a Phase 1 trial in 2016. The one I mentioned as a prototype because it seems to be temporally ahead of the others, is one that we think by the end of the summer we'll have enough, and we have our own pilot plant where we're making doses. We're working very closely with the FDA colleagues on trying to make sure we get that same smooth transition that they helped us with when we went into the Phase 1 trial with Ebola. So let's say we start at the end of the summer/the beginning of the fall, it's likely it will take a few months, similar to the Ebola Phase 1 where you know if it's safe and it can induce an immune response.

In 2017, likely in the first couple of months, if the epidemic is still raging in South America, that's very important for a vaccine trial.

Mr. BURGESS. Sure.

Dr. FAUCI. Because we're now in a trial, not a distribution. We'll likely get an answer of its efficacy very quickly. When I say quickly, I say 8 to 10 months, at which point then you make a decision, you look at the data and you decide what kind of regulatory decision or not you're going to make.

Remember with Ebola, by the time we were ready to go with the vaccine the cases due to the CDC and other efforts had gone all the way down, and there were very few cases to be able to prove efficacy. I don't think we're going to see that because nobody anticipates that this outbreak is going to just disappear in Brazil.

Mr. BURGESS. Correct.

Mr. MURPHY. Thank you.

Mr. BURGESS. Well, I do appreciate that, and I've got a number of questions. And certainly after communicating with my folks back home, this is going to be an ongoing evolving difficulty, and I really would appreciate the ability to interact with all of you as things develop. Thank you, Mr. Chairman.

Mr. MURPHY. Thank you. The gentleman's time has expired. Recognize Mr. Pallone for 5 minutes.

Mr. PALLONE. Thank you, Mr. Chairman.

I'm going to talk about the money, too. The President submitted the \$1.9 billion request for Zika that directs funds to areas that the agencies have identified as priorities. But, of course, the House Republicans have thus far declined to fund the Administration's request; instead, calling upon the agencies to divert unobligated Ebola funds to finance the Zika response. And I believe this decision is ill-advised, and it will force federal agencies to either compromise the critical work that they're doing in other areas, or shortchange the federal response to Zika and Ebola. So let me ask questions in this regard.

Dr. Frieden, can you explain to us what you plan to do with the agency's remaining Ebola funds?

Dr. FRIEDEN. Ebola is not over. As of today, 84 CDC top staff are in West Africa responding to the Ebola outbreak. Last month labs in West Africa tested approximately 10,000 samples for Ebola. It was only in January that we had the most recent Ebola case in Sierra Leone, so we're still actively responding and tracking. And as you noted in your remarks, the Ebola supplemental funds also directed CDC to work over a 5-year period to strengthen the systems around the world that could find, stop, and prevent other health threats such as Zika before they spread widely so that we can learn more rapidly about them and protect Americans more effectively.

Mr. PALLONE. All right. Let me go to Dr. Fauci, same questions. What do you expect to do with the Agency's remaining Ebola funds, and why is it important that the Agency complete this work?

Dr. FAUCI. Well, the NIH was given \$238 million from the Ebola supplement. We only have less than \$10 million left. We have about \$9 million left, and we have ongoing studies, both the survivor study, as well as the next phase of the vaccine study, so quite frankly, Mr. Pallone, we don't have any Ebola money to switch over. Right now what I'm doing in anticipation of hopefully the approval of the supplement, is I'm moving money from other areas right now to get a start on the things that I just mentioned to Dr. Burgess; namely, the vaccine and other components. So we're using

money that we have to shift around from other places. We don't have any really substantial money that's left on Ebola.

Mr. PALLONE. So let me ask both of you, Dr. Frieden or Dr. Fauci, if Congress does not move quickly to fund the Zika supplemental the way the President has requested, how will the agencies meet the demands of fighting the Zika epidemic? How will this affect the other work that you do?

Dr. FRIEDEN. Well, first off we're already drastically scaling back the work we're doing on other diseases, such as dengue and tick-borne disease because we're devoting those staff to the Zika response, even the area of birth defects which usually considered to be an area that would respond to an emergency. We've been pulling staff to work on this who would otherwise be working on a series of other challenges in that field.

And without the supplemental we won't be able to most effectively reduce the threat against pregnant women by learning more and doing more to protect them. We won't be able to rapidly improve our awareness of where the mosquito populations are in the U.S., and to control them before mosquito season. We won't be able to establish a robust birth defects registry to further understand this, or initiate and follow-up on critical studies to understand key unknowns, such as for babies born to mothers with infection who don't have microcephaly, do they have other severe problems? That's going to be a many month and many year undertaking that has to be started now or we'll lose the opportunity to do it most effectively. And we won't be able to support states and territories in their ability to rapidly increase their effectiveness here to the extent that we would like to.

Mr. PALLONE. Dr. Fauci, do you want to add to that?

Dr. FAUCI. Yes, Mr. Pallone. Ditto what Dr. Frieden said about not being able to do several of the things that I showed on the slide of our research agenda. But one of the additional things that also worries me about not getting the supplement is that we are now starting to forge partnerships with the pharmaceutical companies that are getting quite interested in, and they're linked to BARDA, and we're all working together to try and push to develop products.

If it turns out we don't get the supplement, we will be viewed as an unreliable partner, and we don't want that because we had that, you might remember, when we were doing the biodefense issues years and years ago where we would start partnering with the pharmaceutical companies, and when it looked like we weren't going to get a particular amount of partnership money, they pulled back. And that would be the worst thing in the world for us, is to have the pharmaceutical companies think we're not a reliable partner.

Mr. PALLONE. Thank you, gentlemen.

Mr. MURPHY. Thank you. Now recognize Mr. Griffith for 5 minutes.

Mr. GRIFFITH. Thank you, Mr. Chairman.

Dr. Borio, as you mentioned in your opening the FDA is currently considering an application for a field trial with genetically engineered mosquitoes that would take place in the Florida Keys. Can you update us on where it stands today with your agency, and when you expect the Florida field trial to start? And I'm going to

leap forward in an attempt to save a little bit of time because you know we're limited. Does the FDA have sufficient legal authority to expedite the review process for this product given the current Zika emergency? And if not, what additional authorities are needed?

Dr. BORIO. We do have the authorities, and we are expediting the review of this. And like I said, very soon we hope to release for public comment the Environmental Assessment and associated findings.

Mr. GRIFFITH. Do you have the ability since there's an emergency to truncate or eliminate the public comment before you do the field trials, particularly in light of the fact that the particular modification of the mosquito has been tested in a number of countries in tropical environments?

Dr. BORIO. Mr. Griffith, it's very important for us to go through the process and include the period of public comment. We need to give the public an opportunity to comment on the Environmental Assessment given the significant attention that this novel technology has generated, especially in the communities for the proposed sites. So it is true that there have been many field releases done, especially in Brazil. I learned more about them when I was there last week. The data seems to be promising in terms of reducing the mosquito populations in those small field trials, but we need to go through our process. And we are greatly expediting the process.

Mr. GRIFFITH. In light of the concerns in the Commonwealth of Puerto Rico, is it possible to expand, do you have the authority to expand and maybe look at a field site not only in Florida, but also in Puerto Rico? And since you have not yet opened the public comment you're going to go through that process, have public comment there, as well?

Dr. BORIO. So if the company and public health authorities in Puerto Rico are interested in that, we would be very supportive of the process. So the geography might be a little bit different from the field trial that is being proposed, so the company would have to submit the assessment for that—anything that may be different for the new field trial. But we will look to create efficiencies as much as possible.

Mr. GRIFFITH. As I understand it, it's been a multiple year, I want to say 4 but don't hold me to that, years in getting to this point. Would they have to go through that same process in Puerto Rico, or is there some way that we could shorten that time period up extensively so the tests could be going simultaneously?

Dr. BORIO. I understand that's the case, and what I can tell you is that this is being greatly expedited now. And I believe that where we are today in the process, that it would not be a protracted process to be able to rapidly assess the request for a field trial elsewhere.

Mr. GRIFFITH. All right, I do appreciate that.

Dr. Fauci and Dr. Frieden, you all have been involved somewhat in this with the genetically engineered mosquito. How is your agency assisting the company that's developed this novel technology? It looks like it's trials of 5,000 people, lots of mosquitoes. Looks like

it's been about 90 percent effective in some of the areas it's been tried in.

Dr. FRIEDEN. We have a number of vector control experts who have consulted with the company and others, listened to them as well as provided our input. I think one of the challenges is the issue of scalability. These particular mosquitoes don't fly very far, so you may have to release millions upon millions of them every short distance in order to get the knockdown.

The other thing that's very important to understand is, this mosquito is so tricky that even when we've seen very large knockdowns in mosquito populations, we haven't necessarily seen commensurate reductions in human infections, so it'll be important to look at both of those factors.

Mr. GRIFFITH. And while it could just be other factors. I do know in one situation some of the disease that they carry was knocked down substantially, but there may have been some other factor involved. It's hard to eliminate all the other factors, as well. I do appreciate that, as well.

I do think it's something we ought to look at. It's pretty exciting stuff, and it's got to be a whole lot easier to release millions of mosquitoes than it is to go door to door with pesticides. Did you have something you want to say, doctor?

Dr. FAUCI. Yes. Actually, we've been negotiating and discussing with Oxytech, the company that involved with that.

Mr. GRIFFITH. Yes.

Dr. FAUCI. And looking at trying to make sure we correlate what Dr. Frieden was saying, the decrease in mosquitoes with actually a decrease in disease because it may be that that we don't really have that exact correlate. You really want to prove that before you start doing a massive thing, because scalability is really going to be a major problem. And you don't want to scale up unless you know it works.

Mr. GRIFFITH. And I have a follow-up question for you that's off subject, but U.S. Pharmacopeia is looking at allergy injections for folks and trying to change some of those rules, and they may have some right. But have they consulted with you about that?

Dr. FAUCI. Nothing to do with Zika.

Mr. GRIFFITH. Nothing to do with Zika. But since you're involved with the Institute of Allergy and Infectious Diseases, I thought I'd ask.

Dr. FAUCI. I'm sorry. I was taken by surprise with that.

Mr. GRIFFITH. But they have not consulted—

Dr. FAUCI. Not to my knowledge. They may have consulted with my staff, but not directly with me.

Mr. MURPHY. If you need to think about that, you can get back to him on a time. Thank you. Now recognize Ms. Clarke for 5 minutes.

Ms. CLARKE. Thank you very much, Mr. Chairman. I thank our panelists today. It's good to see you again, Dr. Frieden.

This question is for Dr. Frieden, Dr. Lurie, and Dr. Fauci. Just as a bit of background, it's my understanding that the majority of people infected with the Zika virus will remain asymptomatic. However, 20 percent of those infected will experience symptoms which range from fever to GBS, which can leave persons paralyzed.

Though so far there have been no local transmission of the virus in the Continental U.S., does CDC expect to see local transmission in the U.S. as the mosquito population increases this summer? While the mosquitoes that carry Zika are common in southern states, they can range as far north as my home district of Brooklyn, New York. Your location, as well as lack of access to air conditioning increases one's chance of coming in contact with the virus, as was pointed out by Dr. Frieden in discussing the situation in Puerto Rico.

Many of my constituents living in the Brownsville section of my district in Brooklyn are very low income, and likewise the low income communities of the south has some of the highest concentrations of poverty in the United States, and tend to lack access to air conditioning. In the south not only do these communities lack access to air conditioning, but they also lack access to health insurance as many southern governors have chosen not to expand Medicaid coverage under the ACA. If they do get sick with the Zika virus, having access to care may become problematic. The bottom line is that economically distressed Americans will likely be the ones most impacted by the spread of Zika were that to manifest.

With that in mind here's my question. What are we going to do to assist low income and disadvantaged communities to prevent being infected in the first place, as well as spread the word of the virus in their communities especially since Zika can be sexually transmitted?

Dr. FRIEDEN. Thank you very much. Our primary concern or most urgent concern is places like Puerto Rico which are likely to see widespread transmission. In addition, we're advising pregnant women and their sexual partners to use condoms if the sexual partner has come from an area where there has been Zika transmission.

Furthermore, there are parts of the U.S. that have a secondary vector, the albopictus mosquito, the tiger mosquito is much more widely distributed, but it appears to be much less effective at spreading Zika. So unlike aegypti, which bites multiple people, bites only humans, lives indoors, albopictus is less of a threat. It appears that it can spread Zika, and dengue, and other viruses but much less efficiently than the other virus. So our goal with the supplemental funding would be to provide resources for states and local communities to both reduce the risk of mosquito-borne transmission where that is at higher risk, and also to respond to cases so that people who come back with Zika minimize their chances of being bitten by a mosquito, and thereby initiating a chain of transmission.

Ms. CLARKE. And my hope is that there will be a lot of public information, education, particularly as the summer hits, especially in a place like New York where you have that international mix and blend of individuals.

Dr. Fauci and Dr. Frieden, the CDC expects to see local transmissions of the Zika virus at some point in the Continental U.S. Currently, the south has the highest number of people living with HIV in the United States, over 40 percent of those living in the south are HIV positive. I'd like to know how the Zika virus impacts with those living with HIV? Do we expect to see some more serious

symptoms in HIV positive individuals who are infected with Zika? Do we have a sense of that yet?

Dr. FRIEDEN. I'll let Dr. Fauci continue, but I would say the primary issue we see at this point is to pregnant women regardless of HIV status with the risk of birth defects.

Dr. FAUCI. Yes. If you look at the historical analogies with other flaviviruses, we have not seen a serious difference at all in an HIV infected versus non-HIV infected person with that kind of—however, I'm glad you brought that point up, Ms. Clarke, because that's part of natural history studies. When you do natural history studies of cohorts you will be able to get subgroups of that who are HIV positive or not, and actually definitively answer your question, as opposed to saying our impression is that there really is not. But just to reiterate what Dr. Frieden said, we really focus on the pregnant women. That's the real target issue here.

Ms. CLARKE. Very well. Mr. Chairman, I yield back.

Mr. MURPHY. The gentlewoman yields back. Now recognize Mr. Hudson for 5 minutes.

Mr. HUDSON. Thank you, Mr. Chairman, and thank you to the panel for this very informative discussion.

It was mentioned that there are clusters of dengue in Florida and Texas. It got me thinking, just in terms of folks coming across our southern border. There's been a lot of discussion about different diseases and other public health concerns.

Dr. Frieden, is this also a concern that folks coming across the border could be bringing Zika with them? Is that something we're looking at?

Dr. FRIEDEN. Well, on the one hand we know that Zika and other diseases do spread largely because of human migration. But, in fact, there are 40 million Americans or 40 million people from the U.S. who travel to Zika-affected areas each year and then travel back, and so the number on the border crossing will be a very minute proportion of that.

What we have seen is in some communities that are essentially across the border, for example, Brownsville and Matamoros in Texas, when dengue spread it spread in both parts, but it spread eight times more in Matamoros because it was more crowded and had less access to air conditioning.

Mr. HUDSON. I understand. Dr. Lurie, what role will mosquito or vector control play in our response to Zika?

Dr. LURIE. Well a we talk about this paradigm of prevent, detect, respond, prevention is key, so mosquito vector control has got to underpin our efforts for the foreseeable future for Zika, and also for other vector-borne diseases.

Mr. HUDSON. Well, there are currently 700 mosquito control districts across the United States at the state and local level. What role should the federal government play in mosquito control?

Dr. FRIEDEN. One of the areas that we would like to enhance and for which we need supplemental funding is to better understand the capacity of mosquito control districts, and to support improvement of that capacity, and better linkage of the mosquito control districts with the health departments and environmental departments, whatever is most effective within that state or county. They often bridge multiple counties and they may not always be well in-

tegrated, but in effective vector control programs for vector-borne disease you may need an integration of the public health staff and the mosquito control staff to identify the places or even the houses to target. And that's really important, and one of the areas that we want to urgently improve.

Mr. HUDSON. When you talk about houses to target are you talking about spraying insecticide?

Dr. FRIEDEN. Yes.

Mr. HUDSON. Is that the effective way to—

Dr. FRIEDEN. Both insecticide and what's called larvicide that kills the developing mosquito.

Mr. HUDSON. OK. Well, because the mosquito that carries Zika breeds in small pools of water often indoors near houses, aggressive trash cleanup and removal is something that's been talked about as one of the most effective ways. Do you envision a federal role in terms of trash cleanup and those sort of things, or is it more information—

Dr. FRIEDEN. No. I mean, we really want to support state and local entities with technical guidance. We also recognize that reduction in breeding sites, cleanups is important, it's high profile, but it's very difficult, as you pointed out with mosquitoes that can breed in the amount of water of a bottle cap. It can be extremely difficult to be effective, so it is a component of integrated vector control strategies. We do think that is a state and local responsibility, but we have, I believe, a responsibility to provide technical guidance, best practices, and catalytic funding to try to improve that, especially when something as unanticipated and potentially devastating as Zika is upon us.

Mr. HUDSON. So the funding request doesn't cover any of those type activities. It's more just the coordination and information?

Dr. FRIEDEN. We would have some support for local vector control, mostly along the lines of rapidly surging in if there's an area that's not able to do it, and for a particular cluster by establishing rapid response teams, sharing best practices, identifying resources that can be shared among jurisdictions.

At CDC more than 60 percent of our funding or thereabouts goes out to state and local entities. We exist to support the front lines at the state and local government, but what we do at CDC is to develop the tools, the science, the things like the test kits for Zika that we then distribute to and support local entities to use.

Mr. HUDSON. Makes sense. Is it possible to predict or anticipate using surveillance or other means what the next emerging infectious disease would be?

Dr. FRIEDEN. There are many people who would tell you yes. My own belief is probably not, because there are so many possibilities. Just to give you a sense, I just returned from a trip to Africa looking at some of our programs there. I've recently spoken with our teams in India. They've identified two tick-borne viral hemorrhagic fevers, this is Congo Crimean Hemorrhagic Fever and Kyasanur Forest Disease that are much more widely distributed than anyone knew before. So whether we're going to have now a tick that could bite you and you could have a bleeding disease that kills you, I don't know if that's going to come next. But no one, I think, would have predicted that H1N1 would have come from Mexico, or MURS

from the Middle East, or Ebola widely distributed in West Africa, or Zika causing birth defects.

Mr. HUDSON. Thank you. Mr. Chairman, I'm out of time. I yield back.

Mr. MURPHY. Thank you. Now recognize Mr. Tonko for 5 minutes.

Mr. TONKO. Thank you, Mr. Chairman. Thank you to our witnesses for providing very valuable information.

I'm encouraged by our government's rapid response to the Zika virus, and the assistance we have provided and are continuing to provide in the areas most affected by the outbreak. This in my opinion underscores one of the most important messages we hear every time we have a hearing on disease outbreak, and that is that we have to be prepared for what we can't predict.

So with that in mind, Dr. Frieden, how is our response on Zika, and our continued response on Ebola preparing us for the next emerging threats?

Dr. FRIEDEN. We use the framework of prevention, detection, response. Those are three core areas of what we need to do both in this country and around the world. Prevention may be things like better vaccines or reduced risk of spread of Ebola and other diseases in hospitals. Detection is about laboratory networks, as well as disease detectives or epidemiologists, and tracking systems so we know how common certain conditions are and can quickly detect an increase, whether it's in microcephaly or other conditions. And response, the ability to have rapid response teams that can be on the ground within hours or days and have the tools needed to assess the situation and mitigate to the greatest extent science allows.

Mr. TONKO. Thank you. And how are we assisting our state and local health departments in their preparedness, and certainly their response efforts? What can we do to coordinate the response across all levels of government?

Dr. FRIEDEN. There are many aspects of the response which are critically important to be coordinated. For example, we provide diagnostic tests, we work with health care providers, we inform of the latest scientific evidence about it. And with the supplemental request we would be able to be much more robust and involving many parts of state government around the U.S., and within states strengthening the hands of state and local health departments in their ability to provide services, education, information, and interventions to address the spread of Zika, and to reduce the risk.

Dr. LURIE. If I might—

Mr. TONKO. Sure, Dr. Lurie.

Dr. LURIE [continuing]. Add that one of the most important components of this is being sure that our day-to-day public health system is strong so that it can do this detection. If you start from a low level each time and we build and then let it decay it doesn't really make any sense. Our country has a pretty good history of national attention deficit disorder when it comes to preparedness and maintaining a strong public health infrastructure, and a strong preparedness system is going to be key both for this outbreak and for all the questions about how we are going to deal with the next outbreak. Those day to day systems are critical.

Mr. TONKO. Thank you. And it seems as though keeping each one of those independent bodies strong and functioning then provides for a better sense of coordination. And infectious diseases that are threats out there need to be addressed in a way that addresses individual states and individual nations. No one can escape some of those impacts, so I think coordination is important. And the key to containing those infectious diseases is to contain them at their source, I would think. So the coordination here, I agree, is very important.

Dr. LURIE. Yes. No, thank you for that, and that's the job of my office, to do that coordination.

One of the things that we also do is think about Lessons Learned from other outbreaks. And as I said earlier, one of the things that has characterized challenges in our response whether it was to H1 or to Ebola is that Congress was very generous in providing supplemental funds, but we can't move out quickly and prevent a crisis before it becomes an emergency unless we have some kind of a contingency fund to be able to get going at the beginning.

We've shortened the time dramatically between when Congress is able to approve funding and when we can get it out the door, but each one of those things still creates a lag. I work with FEMA all the time, and you know that when a Presidential emergency is declared and the Stafford Act is activated, money moves right away. At HHS, we don't have that kind of a response fund to respond to public health emergencies, and that's something that I think we're very focused on.

Mr. TONKO. OK. That's good information to have. And finally, Dr. Frieden, how does our assistance in Latin American countries as they grapple with Zika help keep America safer, Americans safer?

Dr. FRIEDEN. The more quickly we can understand Zika from our work in Latin America and the Caribbean the better for those countries and the better for Americans. This is where it's spreading now, this is where the evidence is. That's why we have teams on the ground in Brazil and Colombia, and we're working side by side in partnership with those countries and others. We disseminated our diagnostic test to countries around the world, and we learn together so we're safer together.

Mr. TONKO. Thank you very much. Mr. Chair, I yield back.

Mr. MURPHY. Thank you. Now recognize Mr. Collins for 5 minutes.

Mr. COLLINS. Thank you, Mr. Chairman. I want to thank the panel.

I've just got a couple of questions. Certainly, in the past, whether it was dengue fever or West Nile, the threat was there, but nothing like what we potentially have here with Zika and the link to the microcephaly. So if a woman is tested and she tests positive, I'm trying to—is there a treatment today? There isn't, so for a pregnant woman to be diagnosed with Zika is a very bad, stunningly bad day for her, her family, and the potential of which—

Dr. FRIEDEN. That's why we've worked very closely with the American College of Obstetricians and Gynecologists. We've provided detailed guidance in conjunction with ACOG. They've sent that out to their members as well, and we provided information so

that as soon as we know more information we provide that to clinicians, as well as women.

Mr. COLLINS. So here's a question. We do know, there's been some studies done that there's some women that have a history of breast cancer in their families, and some women will decide to forego the test for fear of what the test will show, especially if there may not be a treatment. So if you're a pregnant woman and there is no treatment if you test positive, there are women who just for their own sanity would opt to not be tested.

Dr. FRIEDEN. We leave that up to the pregnant woman and her—

Mr. COLLINS. Well, I know, but—

Dr. FRIEDEN [continuing]. Clinician, but we do find that there's a great desire on the part of pregnant women to be tested. And it's not that there's nothing that can be done. For example, we would want to insure that that infant were delivered in a facility that has advanced care capacity to provide the intensive support that it might need. Dr. Fauci?

Dr. FAUCI. Actually, just to confirm that what we're seeing, the anxiety associated with people who are traveling there, there is a great need to know. We're not seeing denial. There are people who really want to know as much information as we can give them. And as Dr. Frieden said, we leave the individual response to that information up to the individual and their physician, but they are really very much in desire of information, which is what we're trying to get them. This relates to the answer to the question about ultimately getting a highly specific and sensitive test to tell you if, in fact, you were infected.

Mr. COLLINS. So to lead to that, now I'm assuming the rapid tests that people are looking at are all antibody tests pretty much.

Dr. FAUCI. Well, as we said you have to ask are you infected now? That's not an antibody test, that's a molecular PCR test. The test that people are more in desire of, they go and come back and say I know that 80 percent are likely asymptomatic, so I don't know if I were infected or not.

Mr. COLLINS. What was your—

Dr. FAUCI. They want to know an antibody test. Right?

Mr. COLLINS. That's correct. So I'm assuming the industry is looking at the rapid tests, are in fact antibody tests. They're not going to pick it up pre-antibody but—

Dr. FAUCI. Right.

Mr. COLLINS. I'm assuming that's what's being done.

Dr. FAUCI. A lot of activity is trying to develop an antibody test that's highly specific for Zika and doesn't cross-react with other similar viruses.

Mr. COLLINS. All right. So like in HIV where you've got some false positives, there's the Western Blot that will look for P24 protein or something like that.

Dr. FAUCI. Right.

Mr. COLLINS. Is there such a protein in Zika?

Dr. FAUCI. You could actually—in fact, Dr. Frieden will just explain it, so why don't you go ahead about the—

Dr. FRIEDEN. There are several proteins in Zika that are specific to Zika. However, they're not that dissimilar from similar proteins

with dengue and Yellow Fever, so there can be cross-reactivity. But we can give as of today a definitive diagnostic result to a person with prior infection in some circumstances. In other circumstances where there's more cross-reactivity in the serum it's more difficult.

Mr. COLLINS. But I was hearing from GAO or others that some of these confirmatory tests, they are not widely available.

Dr. FRIEDEN. Right.

Dr. FAUCI. What you can do to make it specific is that you can actually—and this is what our grantees are working on right now, is that if you look at the molecule for dengue, which is the most likely bad actor of cross-reactivity, and you look at the molecule of Zika, you could mutate out of Zika those components that are common between Zika and dengue and still have a protein that's left that the only thing it has is things that are highly specific to Zika. That's what we're working on right now. We don't have that, but that's—

Mr. COLLINS. So now one last question in the last few seconds. If somebody has antibody, they progress to that state, they do a PCR test. Wouldn't the PCR test still identify the—

Dr. LURIE. No.

Dr. FAUCI. No. The virus is gone within days of infection, within 7 to 10 days it's gone. So once the virus is cleared you could do PCR all you want, you won't get anything.

Mr. COLLINS. Interesting. All right. Well, thank you for that update, especially on what we ultimately need is—I mean, if there's possibly some treatment if someone tests positive. Appreciate the information.

Mr. MURPHY. Thank you. The gentleman's time has expired. Now recognize Mrs. Brooks of Indiana for 5 minutes.

Mrs. BROOKS. Thank you, Mr. Chairman, and thank you so much for holding this important hearing.

I think what you were just talking about, Dr. Fauci and Dr. Lurie, I'm curious about what is BARDA, and HHS, and NIH doing to support and facilitate these platform-based technologies that you're referring to against the known and emerging threats? You've kind of talked about it a little bit, but what are you actually doing to support platform technologies? Dr. Lurie, you want to start?

Dr. LURIE. Sure, great question. So, back in 2010 when we took a look at the countermeasure industry and decided to pivot, we decided to move away from one bug/one drug to these platform technologies, so we are actually now engaged with a host of vaccine development companies, we have open solicitations to work with them. We are providing technical assistance on the use of platforms specifically. The same thing with diagnostics and tests in that regard. We built these Centers for Advanced Development and Manufacturing. One of them is in your home state, and they also are positioned to use various platform technologies to make vaccines so that when a candidate is ready they would be the kind of place that you could actually do the scale up, development, the pilot lot manufacturing, and potentially even with technology transfer be able to, when they're ready, manufacture large volumes of vaccines. So Dr. Fauci's group and mine are working extremely actively, talk every day to be sure these hand-offs are ready and the platforms are ready.

Mrs. BROOKS. Thank you. Dr. Fauci, anything else you want to add to that?

Dr. FAUCI. Yes. Actually some examples, just for your information. You have the DNA platform which we've worked with BARDA on. We have the vector platform, the VSV vector where you insert the gene of a particular virus. We did it with Ebola, we're doing it right now with Zika. You have nanoparticles, ferrite nanoparticles so there are all things that can be transferred across all infections, and that's what we mean by a platform, something that you could say this is the way we're going to go, and we're going to stick in the appropriate infection. Once you have those and you have a good solid group of platforms you're going to cut down very, very significantly the amount of time it takes to go after a particular infection.

Mrs. BROOKS. And is there anything we need to be doing to encourage this so it does go faster?

Dr. FAUCI. Yes. I think that we need some money.

Mrs. BROOKS. Let me ask Dr. Lurie about money. Speaking of money.

Dr. LURIE. Yes.

Mrs. BROOKS. I'm confused because the President requested just \$350 million for the special reserve fund for FY 2017, and the language that was included in the President's request would expand the allowable use for the SRF. This was a reduction in funds, if I'm not mistaken. It was a reduction in funds for the SRF, and so how is it that the President can put that in his budget, reduce those funds, and yet we're still needing to do all of these things we need to do with respect to other threats like anthrax or smallpox?

Dr. LURIE. So there's no question at all that the funding is critically important. You know, BARDA gets—

Mrs. BROOKS. But, Dr. Lurie, why did the President request a reduced amount of funding?

Dr. LURIE. Because it provided additional flexibility for advanced research and development funds so that we could move forward with those platforms. Right now the Special Reserve Funds are limited to being able to purchase things that are material threats on the material threat determination, and our pretty profound need right now is in the advanced research and development area.

Mrs. BROOKS. And so you're not concerned about the level of funding with respect to material threats.

Dr. LURIE. Oh, we—

Mrs. BROOKS. You believe it's sufficient?

Dr. LURIE. No, we are always concerned that we can do the job we need to do for the American people and having enough money to be able to procure for bio threats. As you know, in the multi-year budget we've got a 5-year projection of what it is that we need. We believe that for Fiscal Year '16 or '17, sorry, that we have sufficient funds to procure the countermeasures that will be ready.

Mrs. BROOKS. Thank you. Dr. Frieden, I'm very concerned about the stockpiling, the strategic national stockpile, and could you talk to me about things that BARDA, CDC can do to improve the effectiveness, the coordination of the strategic national stockpile because I don't think we're ready.

Dr. FRIEDEN. Well, we've been optimizing the stockpile for some time. We're able to deliver——

Mrs. BROOKS. What does that mean?

Dr. FRIEDEN. We're able to now deliver products to more places more quickly. We're also looking at how to get as much protection for our dollar as possible in terms of the mix of products in the stockpile. And we're also looking at the different threats that we may face to make sure that we have a balanced portfolio to be able to address those that might be the greatest risk to Americans.

Mrs. BROOKS. Based on the hospitals and the folks I talked to back home we seem to lurch from crisis to crisis and I'm very concerned that we are still not ready. Thank you, I yield back.

Mr. MURPHY. Gentlewoman yields back. Now recognize Mr. Bilirakis of Florida for five minutes.

Mr. BILIRAKIS. Thank you very much, Mr. Chairman. Thanks for allowing me to participate in this subcommittee. Appreciate it and thanks for holding the hearing.

The Zika outbreak like global issues especially pressing in Florida and other Gulf States given that these locations are vulnerable to the spread of Zika. In Florida we already have two cases in Hillsborough County, one of the counties that I represent.

A question for Dr. Borio. You mentioned innovation strategies being proposed to help suppress virus-carrying mosquitoes. It is my understanding that FDA is currently considering an application for a field trial with genetically engineered mosquitoes in Florida. The question is, could you update us on where the field trial application stands today, and when the earliest starting date could be?

Dr. BORIO. Thank you. So we are working to soon release for public comment the Draft Environmental Assessment that the company developed. We work closely with EPA and CDC in reviewing the materials, so hopefully very soon it will be released. Once we have an opportunity to review the comments we receive from the public, then we'll make a final decision regarding the application. We're expediting the process. It's part of our Emerging Infectious Disease Task Force in response to Zika, so our—the reviewers involved in this technology are part of our Emergency Response Task Force, so we're doing everything we can to move this as expeditiously as we can.

Mr. BILIRAKIS. Well, give me an estimate.

Dr. BORIO. Yes. I'm unable to give an estimate at this time because it really will depend a little bit on the volume and interest from the public. We are working those——

Mr. BILIRAKIS. Well, I'm sure there's a great deal of interest based on what my constituents tell me.

Dr. BORIO. Yes, it has been an area of tremendous interest, and including some opposition. I think, you know, what we don't right now is where the public stands in the setting of Zika and the new developments associated with Zika. So we're doing everything we can to move this very quickly. We're collaborating across government with CDC and EPA. We'll learn a great deal about this technology also during my visit to Brazil last week, last month, so what I can tell you right now is that we are prepared to move very quickly on this.

Mr. BILIRAKIS. Thank you. Next question. You mention FDA's emergency use of authorization referencing diagnostic tests. Would FDA be able to use an emergency use authorization to advance the use of this technology should the Secretary declare a public health emergency? So if you can answer that question.

Dr. BORIO. Our EUA authority is currently limited to human products, not to animal products. And this technology is regulated under our animal drug regulations, so it's separate, so we do not have currently authorities on emergency authorization for animal drugs.

Mr. BILIRAKIS. OK, next question. Are there other innovative products or strategies being proposed that you're aware of, and able to discuss at this time?

Dr. BORIO. I would like to defer those answers to my colleagues from CDC.

Mr. BILIRAKIS. Please, please, please.

Dr. FRIEDEN. There are a variety of other mosquito control approaches that are being considered. One is simply to optimize our currently available products. And we think there's considerable progress that we could make by doing that, different ways of applying different combinations of products, different ways of assessing mosquito populations after the application of these products. That's very important and needs to be done.

In addition, there are new tools that are exciting. One of them is the genetically modified mosquitoes that you mentioned. Another is Wolbachia, a bacteria that infects mosquitoes and then can reduce their life expectancy and their ability to spread disease. This has been done on a pilot basis. But, again, the question about all of them are are they scalable, will they reduce human disease, are they practically implemented? And NIH is doing work in this area, as well.

Mr. BILIRAKIS. Anyone else wish to comment on this? Thank you.

Right now there are three tests I understand for detecting Zika during different stages of infection. It is my understanding that Florida and a few other jurisdictions are able to utilize the RT PCR test to detect infection. However, given that those who are infected often don't show symptoms, it seems crucial that we are able to disseminate diagnostic capabilities such as the antibody testing to state and local authorities. So what hurdles do we face in increasing access to these diagnostic tests nationwide?

Dr. FRIEDEN. We're working around the clock to do that.

Mr. BILIRAKIS. Yes, go ahead.

Dr. FRIEDEN. Excuse me. We've already produced 375,000 of the realtime PCR. We've got roughly 15 to 20 states already approved for use of that. Now with the IGM EUA just last Friday, we expect to have another 15 or 20 states approved for that. That's where most of the returning travelers live and we'll continue to produce them. We've been able to accelerate our production capacity at CDC so that we can increase the proportion of the need that's met, but we recognize that there may be a period of weeks or a month or two where people who want the test can't get it. We're in active discussions as is BARDA and other parts to encourage the private sector to do more in this area. But right now, the CDC developed a test which scientists at CDC spent years working on, is the best

thing out there in terms of what's available. And we're working around the clock to make it more widely available.

Mr. BILIRAKIS. All right. Well, thank you very much, Mr. Chairman. I appreciate it. I yield back.

Mr. MURPHY. I know we're done with this. I know Ms. Clarke has 1 minute. She'd like to ask one more question for 1 minute.

Ms. CLARKE. Thank you, Mr. Chairman. Thank you for your indulgence.

Clearly, there's still a lot more to learn about the Zika virus. No doubt the public health response to Zika virus will be complex and require coordination at the global, regional, and national level. While the response to Zika may evolve, one thing is clear; governments and international organizations must commit to funding and providing access to comprehensive reproductive health services to meet the needs of communities during this public health emergency and far beyond.

Preventing pregnancy and the spread of the disease is desired by women in their childbearing age as has been suggested already in Brazil during this outbreak. As a follow-up to Congressman Collins' line of questioning, what more can the CDC be doing, or what else can Congress do to support the CDC to help women prevent unintended pregnancies, if so desired, and prevent continued spread of this disease through possible sexual transmission?

Dr. FRIEDEN. Thank you. As you noted, about half of the pregnancies in the U.S., and about two-thirds of pregnancies in Puerto Rico are unintended. We do not issue advice to women on whether or not to get pregnant. We don't think that's our role. We do provide information so that women, their families, and their providers can make a decision about whether to use effective contraception. We provide guidelines for which methods of contraception are most effective, and how those might be used. This is basically the approach that we're taking, is providing information.

Mr. MURPHY. Thank you. Dr. Burgess would like 1 minute.

Mr. BURGESS. And, Dr. Frieden, if we can just talk one second about the spraying issue. You and I have talked about this a lot in the past, straight spraying, aerial spraying. Obviously for this mosquito it is a little bit different, and as I understand it, it's backpacks and going into yards and gardens. So is the CDC developing any guidance for our local public health offices as to what they can and cannot do, or can and cannot expect? As far as local spraying, is it always going to require consent to go on property? Do people need to identify when they have an ill person at home so that those areas can be perhaps on heightened surveillance?

Dr. FRIEDEN. We've looked at all of these issues and compared experiences across jurisdictions. We have a public health law project which provides information and advice to jurisdictions on models and what's possible in different places. I do think that there are ways to optimize current mosquito control practices, and that's one of the things that we need to rapidly accelerate, and for which the supplemental request would be used.

Mr. BURGESS. Do people have the ability to actually get the insecticide themselves and use it in their homes if they don't want the CDC coming in with backpacks?

Dr. FRIEDEN. The CDC wouldn't go in with backpacks, but this is a thing that we're looking at quite actively. It depends on mosquito resistance. We're currently doing studies in Puerto Rico to see which products the mosquitos are resistant to, and we found that for some there's 100 percent resistance, for others they're largely susceptible. And it'll depend on what those results are for whether that could be done in exactly what you mentioned, showing people here's where you need to spray. Here are the products that work, is one approach that we're considering.

Mr. BURGESS. Thank you. Thank you, Chairman.

Mr. MURPHY. I want to thank this panel for your work. We have a second panel coming up here. As you know, other members may have questions for you, so I ask members to submit the questions and then please respond in a prompt manner. I'm sure we'll be following up with all of you by phone, by visits, by other hearings. This is critically important for our nation's health, so thank you so much for attending today.

And while this panel is stepping away and we're preparing the next panel to come to the table, I'll begin the introductions of Panel Two.

We have with us today Dr. Peter Hotez, the Dean of the National School of Tropical Medicine at Baylor. He's also President of the Sabin Vaccine Institute and Endowed Chair in Tropical Pediatrics at Texas Children's Hospital. Second, we have Lawrence Gostin, Linda D. and Timothy J. O'Neill Professor of Global Health Law at Georgetown University Law Center. Next we have Joseph Conlon, Technical Advisor to the American Mosquito Control Association, and Dr. Jeanne Sheffield, Director of the Division of Maternal-Fetal Medicine at the Johns Hopkins School of Medicine. And as soon as we have our panel seated; again, it'll be Dr. Hotez, Lawrence Gostin, Joseph Conlon, and Dr. Jeanne Sheffield, I'll begin with some of the parts here.

Let me just say to the panelists, you are aware that the committee is holding an investigative hearing. When doing so it has the practice of taking testimony under oath, so if you could all please be seated, I'll swear you in. Do any of you have any objections to testifying under oath? Seeing no objections, the Chair then advises you that under the rules of the House and the rules of the committee you are entitled to be advised by counsel. Do any of you desire to be advised by counsel during testimony today? No, say no then.

In that case if you would please rise and raise your right hand, I'll swear you in.[Panel sworn.]

Mr. MURPHY. Thank you. All the panelists have affirmed that, so now you're under oath and subject to the penalties set forth in Title 18, Section 1001 of the United States Code.

We will now ask each of you to give a 5-minute summary of your opening statement. Dr. Hotez, you are recognized first. Please make sure you're turned on, bring the mic close to you, and watch for the red light. Thank you.

STATEMENT OF PETER HOTEZ, M.D., Ph.D., DEAN, NATIONAL SCHOOL OF TROPICAL MEDICINE, BAYLOR COLLEGE OF MEDICINE, PRESIDENT, SABIN VACCINE INSTITUTE, AND TEXAS CHILDREN'S HOSPITAL ENDOWED CHAIR IN TROPICAL PEDIATRICS; LAWRENCE O. GOSTIN, J.D., LINDA D. AND TIMOTHY J. O'NEILL PROFESSOR OF GLOBAL HEALTH LAW, GEORGETOWN UNIVERSITY LAW CENTER; JOSEPH CONLON, M.S., TECHNICAL ADVISOR, AMERICAN MOSQUITO CONTROL ASSOCIATION; JEANNE SHEFFIELD, M.D., DIRECTOR, DIVISION OF MATERNAL-FETAL MEDICINE, JOHNS HOPKINS SCHOOL OF MEDICINE

STATEMENT OF PETER HOTEZ

Dr. HOTEZ. Mr. Chairman, Representative Castor, and members of the subcommittee, I thank you for giving me the opportunity to speak today. I'm Dean of the National School of Tropical Medicine at Baylor College of Medicine. I also head a product development partnership that makes neglected tropical disease vaccines that the big pharmaceutical companies won't make because they're vaccines for the diseases of the poorest people.

For my remarks about Zika today, I want to focus on my perspective living and working in the Gulf Coast of the United States, and our unique vulnerability to Zika epidemics, and why I believe that this spring or summer Zika could begin affecting pregnant women living in economically distressed areas of Texas, Louisiana, Mississippi, Alabama, and Florida. And why I worry that by the end of this year we could see microcephaly cases appearing on the Gulf Coast. I also want to talk a little bit about some of the hurdles in vaccine development if there's time.

The reason I'm concerned particularly about the Gulf Coast is because the Gulf Coast is unique in that it's the only part of the United States with the possible exception of Tucson, Arizona that has the *Aedes aegypti* mosquito. That's the mosquito that's now mostly responsible for transmission all over Latin America and the Caribbean, so it's *Aedes aegypti* that we mostly have to be concerned about. But my other reason I'm concerned about the Gulf Coast, and one not really being talked about enough is extreme poverty. I mean, the reason why we're seeing Zika in Pernambuco State and Recife in Brazil is because that's the poorest area, one of the poorest areas of Brazil. It is the epicenter, not just of Zika, but all of Brazil's neglected tropical diseases. It's where we see lymphatic filariasis, that's where we see schistosomiasis. And the reason there's so much Zika there is when you—and it doesn't take much to understand it. You can just view one of the poor communities, you see no window screens, holes in the window screens, but it's also the environmental degradation around the area. You see discarded tires, you see plastic containers filled with water, and all of those factors combine to make the perfect storm, and why Pernambuco is such a deadly place in terms of microcephaly cases and Zika.

It's the same reason why I'm very worried about Haiti. I know we're mostly focusing on the United States, but I'd just like to make the point that I think Haiti is going to be decimated by Zika. UNICEF estimates there's 264,000 pregnant women every year in

Haiti, so we could be looking at more than 100,000, maybe 200,000 pregnant women with Zika in their first or second trimester. We could be looking at tens of thousands of cases of microcephaly in Haiti, in a country that basically has no health system. So this is a humanitarian catastrophe that's unfolding in front of our eyes, and I really don't see any significant global action right now happening in Haiti.

And the reason I'm particularly worried about the U.S. Gulf Coast, dengue actually caused outbreaks in Houston in 2003, 2004, and 2005. That was worked on by our National School of Tropical Medicine. The reasons are clear, we have *Aedes aegypti*, but where this is most happening are in the poor areas of Houston, so the historic African American wards like the Fifth Ward in Houston where I can take you there just a minute off the highway. This is not hard to find, and what I'll show you are dilapidated housings with no window screens, holes in the window screens. You'll see discarded tires all along the side of the road filled with organic debris and water, and the *Aedes aegypti* mosquito likes nothing more than discarded tires along the side of the road.

Right now our Harris County Mosquito Control Division is finding *Aedes aegypti* mosquitoes. Those numbers are going to start to climb beginning April and into May, and I'm quite worried that we won't learn that there's going to be a Zika outbreak until we start seeing microcephaly cases towards the end of the year. So what do we need to do about this?

First of all, I think the U.S. Government needs a more active role in coordinating what's going on in Haiti, or what's not going on in Haiti, working with the Organization of American States and WHO. Remember this is a disease we can fight. Between 1947 and 1962 we eradicated the *Aedes aegypti* mosquito from the Western Hemisphere for most of Latin America. We did it by old-fashioned mosquito control programs and being aggressive by draining water sources. The *Aedes aegypti* mosquito was eradicated in 18 Latin American countries and resulted in dramatic reductions in dengue and yellow fever.

Equally important, we need a coordinated response to combat the threat of Zika on the Gulf Coast. This means surveillance of mosquitos and Zika detection. Beyond mosquito control we need to collect the garbage, we need to get rid of the discarded tires and standing water in poor neighborhoods, provide pregnant women living in poverty with adequate screens for their homes. This approach goes beyond the health sector and beyond the remits of the CDC. It could require involvement of Housing and Urban Development, EPA, even Homeland Security. Remember, even if a few babies are born with microcephaly on the Gulf Coast it will be talked about in the same context as Katrina, it will be talked about in the same context as the BP Oil spills; so, therefore, I urge this committee to aggressively pursue policies to protect that region. Thank you.

[The statement of Dr. Hotez follows:]

**Testimony of Peter Hotez, M.D., Ph.D.
Dean, National School of Tropical Medicine, Baylor College of Medicine
President, Sabin Vaccine Institute
Endowed Chair in Tropical Pediatrics, Texas Children's Hospital**

before the

**Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
United States House of Representatives**

March 2, 2016

Examining the U.S. Public Health Response to the Zika Virus

Executive Summary

- Beginning this spring or summer, Zika could begin affecting pregnant women who live in or have travelled to the Gulf Coast of the United States
- We are susceptible to Zika due to the prevalence of *Aedes aegypti* mosquitoes and areas of extreme poverty in the Gulf Coast, including major urban centers such as Houston.
- To fight Zika, the US Government needs to coordinate with our global health partners on a two-pronged approach towards controlling the spread of Zika: aggressive mosquito control with insecticides, and source reduction to remove standing water that breeds mosquitoes.
- HHS is not the only federal department that can and should play a role in fighting Zika. In addition to coordination on mosquito control and source reduction within the federal government, there needs to be similar coordination between the federal, state, and local governments.

- We urgently need to move vaccines for neglected tropical diseases from research laboratories into clinical development, and we should not rely exclusively on the pharmaceutical industry to do so.

Mr. Chairman and Members of the Subcommittee, thank you for the opportunity to speak with you today. I am Peter Hotez, a biomedical scientist and pediatrician, the dean of the National School of Tropical Medicine at Baylor College of Medicine and also the Texas Children's Hospital Endowed Chair in Tropical Pediatrics based at the Texas Medical Center in Houston. I am also past president of the American Society of Tropical Medicine and Hygiene, and currently serve as President of the Sabin Vaccine Institute, a non-profit which develops vaccines for neglected tropical diseases (NTDs) through a product development partnership (PDP) model. This year I am also serving as US Science Envoy for the State Department and White House Office of Science and Technology Policy focusing on the urgency to develop vaccines for neglected and emerging diseases.

For my remarks about Zika virus infection today I want to focus first on my perspective living and working on the United States Gulf Coast and our unique vulnerability to Zika epidemics. Second, as a vaccine developer for neglected diseases I also want to call attention to the gaps in our US biomedical R&D efforts that hinder timely vaccine development Zika and why we did not have an Ebola vaccine in time to prevent 11,000 deaths in West Africa, and why we won't have a Zika vaccine in time for this outbreak.

Poverty and the US Gulf Coast

First the Gulf Coast – I believe that beginning this spring or summer Zika could begin affecting pregnant women living in Texas, Louisiana, Mississippi, Alabama, and Florida. The reason I am especially concerned about these states is because they represent the perfect storm of the two major factors needed to ensure both dengue and Zika transmission.

The first is that the Gulf Coast is practically unique in the US in that it has *Aedes aegypti* mosquitoes, the species that is responsible for most of the Zika transmission now occurring in Latin America and the Caribbean. It also has a second species – *Aedes albopictus*, which is also found in the Eastern United States.

My second concern is the extreme poverty found on the US Gulf Coast.

To explain the role of poverty I need to highlight that Zika belongs to a unique category of diseases known as neglected tropical diseases or 'NTDs'. The term NTDs was one that we coined shortly after the launch of the 2000 Millennium Development Goals. At that time MDG 6 "to combat AIDS, malaria, and other diseases" galvanized global action against AIDS and malaria through PEPFAR, PMI and the Global Fund but it did not address the most common afflictions of the poor such as schistosomiasis, hookworm, trachoma, leishmaniasis, and dengue. We invoked the term NTD to describe how these diseases are neglected because mostly affect the poorest people living in the poorest countries. They are forgotten diseases of forgotten people. In addition to their adverse health effects NTDs also reinforce poverty through their long-term and debilitating effects on maternal and child health. A good example is Zika virus infection estimated to soon affect 4 million people in the Americas and cause

thousands of cases of congenital birth defects and still births. A key is the link between Zika and poverty.

A more recent observation about NTDs is that currently most of these diseases are paradoxically found in the G20 countries, the 20 largest economies as well as Nigeria. We're finding that most of the world's parasitic infections including worm infections, leishmaniasis, and Chagas disease, as well as arbovirus infections such as dengue and Zika are mostly found among the poorest people living in these countries – thus the old concept of developing versus developed countries is giving way to a new global health paradigm in which all national economies are rising but leaving behind a bottom segment of society now suffering from widespread NTDs. It's a concept that I call blue marble health and I have a book forthcoming in a few weeks that details this concept.

For instance, let's look at Pernambuco State in northeastern Brazil, and its largest city, Recife. Brazil has the largest economy in Latin America and it is an important G20 country. Yet the level of poverty is profound in Pernambuco and indeed it is where we can find most of Brazil's NTDs such as schistosomiasis, elephantiasis, leishmaniasis, and others. It's where we also find Zika, because women living in extreme poverty in Recife are exposed daily to the bites of *Aedes aegypti* mosquitoes that carry the virus. These women live without window screens or broken window screens, certainly without air conditioning. Moreover, garbage and plastic bottles and discarded tires go uncollected outside the home and breed mosquito larvae. In the setting of such urban poverty *Aedes aegypti* mosquito are widespread and transmit Zika, dengue, and sometimes yellow fever.

In the Western Hemisphere this type of extreme urban poverty is not unique to Recife or Pernambuco, Brazil - we'll soon see Zika affecting all of the poor cities of Central America, Guatemala City, Tegucigalpa, San Salvador, and Managua. It's why Haiti will be decimated by Zika. According to UNICEF there are 264,000 births annually in Haiti, more or less 200,000 pregnant women living in the same type of extreme poverty that affected Recife. We could be looking a human catastrophe of epic proportions as thousands of women in Haiti give birth to babies with horrific microcephaly and brain damage or have stillbirths in the most depleted health system in the Western Hemisphere.

For all the same reasons, I fear for the Gulf Coast. For the last few weeks the narrative we have been mostly hearing from the US Government is that the continental United States is a wealthy country where people live in air conditioning, so that while the arbovirus infections, such as dengue and chikungunya are widespread in Latin America and the Caribbean, we are largely protected. I disagree, for example scientists at our National School of Tropical Medicine and Texas Children's Hospital found that dengue caused outbreaks in Houston in 2003, 2004, and 2005, and the poorest areas of Houston Texas and other Gulf Coast cities are vulnerable to Zika. The reasons are clear – *Aedes aegypti* mosquitoes are highly prevalent along the US Gulf Coast, including major urban centers such as Houston, and we have a level of extreme poverty that can be found anywhere in the Americas. I can take you to areas such as the historical African American wards of Houston such as the fifth ward, or other areas and show you conditions of extreme poverty that closely resemble Recife – dilapidated housing, no window screens, discarded tires filled with water and organic debris – it looks like the global health movie we might show to first year medical students, but it's Houston. In 2014, I published estimates that

12 million Americans live in extreme poverty with an NTD such as Chagas disease, toxocariasis, and others.

In discussions with our Harris County mosquito control division I learned that *Aedes aegypti* mosquitoes are already out but they are being collected in small numbers. Those numbers can be expected to increase significantly as we move into the warmer spring and summer months. They will begin testing them for Zika and I think the likelihood is high that we might see evidence for Zika transmission in Houston and elsewhere on the Gulf Coast, especially in poor urban areas of New Orleans, Mobile, Tampa, and Miami.

It's not going to be easy to track outbreaks of Zika. If the observation holds that most people with Zika show mild or no symptoms, without actively looking for the disease in mosquitoes we might not learn of a Zika outbreak on the Gulf Coast until babies with microcephaly appear next fall or winter on our obstetrical wards and labor and delivery suites. This is what happened in Brazil.

Therefore, we need to consider the following:

1. Zika is affecting Haiti now and infecting pregnant women. Haiti and other poor areas of the Caribbean and Central America are experiencing only now the rapid acceleration in Zika cases similar to the ones Recife experienced last year. The US Government needs to coordinate with the Organization of American States (OAS) and the Pan American Health Organization (PAHO) of the World Health Organization (WHO) to take a two-fisted approach towards preventing Zika, namely aggressive mosquito control with insecticides and source reduction to remove standing water that breeds mosquitoes.

Between 1947 and 1962 this approach successfully eradicated the *Aedes aegypti* mosquito in 18 Latin American and several Caribbean countries, and resulted in dramatic reductions in dengue and yellow fever during the 1950s and 60s.

2. We need a coordinated response to combat the threat of Zika on the US Gulf Coast.

This means surveillance of mosquitoes and Zika detection in the major urban areas, but especially in the poor neighborhoods such as those I described in Houston. Beyond mosquito control we need to collect garbage, discarded tires and standing water in poor neighborhoods, and provide pregnant women living in poverty with adequate screens for their homes. This approach goes beyond the health sector and remits of CDC. It could require involvement of Housing and Urban Development, the Environmental Protection Agency, and even Homeland Security and the office of Emergency Preparedness at DHHS.

It should be noted that if even a single baby is born with microcephaly due to Zika or if Zika results in a stillbirth on the US Gulf Coast, it could create widespread concerns. Zika on the Gulf Coast will be placed in the same context as our previous national responses to Hurricane Katrina and the BP oil spills. Therefore I urge this committee to aggressively pursue policies to protect the Gulf Coast from Zika.

Vaccines

As I recently wrote in briefings for the UK Parliament and in testimony for the House Foreign Affairs Committee, we learned several difficult lessons during the 2014-15 Ebola epidemics in Guinea, Liberia, and Sierra Leone, and we are learning even more lessons about Zika. For me a

critical realization is that we also have a broken system for developing, manufacturing, and testing countermeasures to combat NTDs like Ebola and Zika.

Let's briefly review what happened – the fundamental science for developing the adenovirus-vectored Ebola vaccine was published in 2003

<http://www.ncbi.nlm.nih.gov/pubmed/12904795>; the VSV-Ebola vaccine a few years after that.

But the technology waited a decade until the African situation became dire, and the US Government put up close to US\$100 million through its Biomedical Advanced Research Development Authority (BARDA) <http://www.phe.gov/about/BARDA/Pages/default.aspx>. The funds incentivized three major pharmaceutical companies to license these technologies in order to produce vaccines for large-scale clinical testing. By the time clinical trials commenced in West Africa the Ebola epidemic was mostly halted, but not before 11,000 people perished.

Ebola was a debacle in terms of how we advance urgently needed NTD vaccines beyond research laboratory and into advanced process development, manufacture, regulatory filing, and clinical development. Our technical capacity has outpaced our financial and social instruments required to make vaccines for the poor.

The scary piece of this dilemma is that Ebola virus infection will not be the last catastrophic NTD that we will face. The same forces that promoted the emergence of Ebola in West Africa – poverty, conflict and post-conflict decimation of health systems, climate change, internal displacements and human migrations – remain in play. There are at least a dozen new serious NTDs that require vaccines <http://www.ncbi.nlm.nih.gov/pubmed/26356803>. They include vaccines for:

- NTDs emerging in the Middle East and North Africa, including the ISIS-occupied conflict zones of Syria, Iraq, and Libya, as well as Yemen
<http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003852>. Among them are MERS coronavirus, leishmaniasis, malaria, TB, and schistosomiasis. In some cases these diseases are also now threatening Southern Europe
https://www.washingtonpost.com/opinions/preventing-the-next-disease-outbreaks/2015/10/23/c4564ec0-7817-11e5-a958-d889faf561dc_story.html
- Arbovirus infections, such as dengue fever, Rift Valley fever, chikungunya, and West Nile and Zika virus infections.
- Chronic and debilitating NTDs, such as helminth infections (e.g., schistosomiasis and hookworm), Chagas disease, leishmaniasis, Buruli ulcer, and mycetoma. These diseases have not shown gains under the current USAID NTD Program.

How then do we best close the technology gap in order to develop these NTD vaccines? There is no one-size-fits-all answer, but there are several opportunities and options. First, we need to recognize that the major pharmaceutical companies have an outstanding track record of developing new drugs and vaccines, including a few that target NTDs, as well as malaria and tuberculosis. But the failures in Guinea, Liberia, and Sierra Leone have taught us that we should not rely exclusively on big pharma. We urgently need additional actors, including those with track records for advancing NTD technologies.

Product development partnerships (PDPs) are non-profit organizations that were established to develop and test products for NTDs, TB, malaria, and other neglected diseases. There are

approximately 20 PDPs globally, including a half-dozen that are developing vaccines. Our Sabin Vaccine Institute PDP in Houston, Texas, for example has a pipeline of six vaccines for NTDs <http://www.sabin.org/programs/vaccine-development>.

Unlike the EU, and governments of Japan and several individual European countries, the USG does not specifically fund initiatives that support the PDPs. The SBIR mechanism for instance fosters innovations among small businesses but because PDPs are non-profit organizations they are not eligible for SBIR support. Similarly the priority review voucher (PRV) system does not allow vaccine PDPs to obtain PRV funds until they license a vaccine, which is a very high and lengthy threshold. One idea would be to allow vaccine PDPs to be eligible for PRVs by reaching milestones just short of licensure such as completing phase 1 or 2 clinical trials. In a Public Library of Science article I estimated that setting aside just 1-2% of the USG budget for global health initiatives for PDPs could provide sufficient finances for the PDPs to develop a new generation of antipoverty drugs, diagnostics, and vaccines <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0001133>. We urgently need to open windows that allow PDPs to gain financial support.

Together the G20 nations and lead UN agencies have enormous capacity to expand the pipeline of urgently needed neglected disease vaccines. Last year's Ebola epidemic highlighted the fact that NTDs are a global security issue that is every bit as important as wars, terrorism, and climate change. We desperately need innovation in our global response to produce NTD countermeasures. Thank you again.

Mr. MURPHY. Thank you, doctor. Your time has expired. We'll come back to you.

Professor Gostin, you're recognized next for five minutes.

STATEMENT OF LAWRENCE GOSTIN

Mr. GOSTIN. Thank you, Mr. Chairman Murphy, Representative Castor, and the House subcommittee. I'm going to discuss four is very briefly. First is the President's supplemental appropriation. Secondly, how we continually under-invest and the financing of these kinds of ongoing threats. Third, our public health measures like travel isolation, quarantine. And fourth is child, maternal, and reproductive services.

First in terms of the President's appropriation which I strongly support. So why act now? Well first, as you've heard from the first panel, there's a clear and present danger to the United States and our hemisphere. The United States is the global health leader, humanitarian leader, and we are the major leader in our own hemisphere in the Americas and the Caribbean. We also have our own domestic homeland to protect.

We remember when Ebola arose here in Dallas and other places, how ill-prepared we were, and the public would not accept that. Ebola taught us a vital lesson to act quickly, act decisively, mobilize funding, and attack the hazard as its source. There have been four global commissions since Ebola. I was a member of two of them, and they have strongly urged us to act and act now.

I remember during the Ebola appropriations and when the President sent military forces and the Department of Defense into West Africa. I was on PBS News Hour and they asked me what I thought, and I said I was very proud of America, and I think we need to be proud of America now in our response to Zika.

Should we take Ebola funding for Zika? I think we should not. We would be robbing Peter to pay Paul. This is still a major threat in West Africa. We promised to rebuild and strengthen the decimated health system in West Africa, and America's word is its bond, and its leadership should never be placed in doubt. And that should be on a bipartisan basis, in my opinion.

Zika, moreover, has a deep moral as well as a health dimension. I'm a public health ethicist, and if you had a hearing, for example, nine months from now and there was a mother with a microcephalic child here and we failed to act decisively now, I think the American public would find that unacceptable.

From financing, we have continually underestimated our financing needs. I was a member of the National Academy of Science's Global Health Risk Framework Commission. They said that an Ebola epidemic, a SARS epidemic, an influenza epidemic, and now Zika could affect up to 10 percent of global GDP in the affected areas, and the commission suggested that there was an estimated \$60 billion loss to GDP every year expected with \$6 trillion in the 20th century, in the 21st century. With that, the President's \$1.8 billion supplemental appropriation to me looks modest and would reap great benefits. I would also support a contingency fund so that we don't have to mobilize funds in the midst of an epidemic.

Third are public health measures. I believe that the CDC was absolutely right in its travel advisory for pregnant women. In fact,

the CDC went further than the World Health Organization. I think it was right to do that. I think any of us if we had a daughter who asked us if she were pregnant should she go to a Zika-affected country, we would tell her what the CDC is telling her, that she should consider postponing that travel. But I would not go further and have travel restrictions or bars, isolations, quarantines, or border controls, some of which were used during Ebola, some successfully, but many not. I think there would also be Constitutional challenges appropriately to many of those measures.

And then, finally, I believe that we need to be very attentive to child, maternal, and reproductive services. Pope Francis supported the use of contraception particularly in relation to Zika. We have women in the United States and in Puerto Rico that need reproductive services and health care services for them and their children, and we shouldn't let them down if they're under-insured or uninsured.

So I thank you, Mr. Chairman and the committee for your clear recognition of this health threat facing the United States and the Americas, and for your leadership in this regard.

[The statement of Mr. Gostin follows:]

ZIKA VIRUS: THE GLOBAL AND UNITED STATES DOMESTIC RESPONSE

*Prepared for the
Subcommittee on Oversight and Investigations
U.S. House of Representatives*

Representative Tim Murphy, Pennsylvania
Chairman

March 2nd, 2016

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Executive Summary

Following the 2014/15 Ebola epidemic, the World Health Organization (WHO) was widely criticized for its delay in taking decisive action and leadership to protect global health. Four international panels found that the WHO unreasonably delayed declaring Ebola a Public Health Emergency of International Concern (PHEIC) to call the international community to action in providing financial and technical resources for the global health humanitarian and security threat posed by Ebola.

The WHO appeared to learn from the Ebola experience. On February 1st, 2016, the Director-General, Margaret Chan, declared the clusters of microcephaly and neurological syndromes (including Guillain-Barré Syndrome) associated with Zika virus infection a PHEIC. The link

between Zika virus infection and microcephaly and Guillain-Barré Syndrome is not yet proven, although suspected. Now the international community, including the United States, must answer the call to action to ensure global health security and equity against the risk posed by the spread of Zika virus.

As the only developed country in the Americas with the *Aedes aegypti* mosquito, the United States bears not only a unique responsibility to take leadership for global health in our region, but also to protect the health of United States residents. The Zika virus is already embedded in Puerto Rico, and it is likely that by the summer time there will be local transmissions in Florida and the Gulf Coast. During the summer, the *Aedes aegypti* mosquito has been observed as far north as Washington, DC,¹ and the *Aedes albopictus* mosquito, believed to also transmit the Zika virus, is found in at least 32 states in the United States.²

As Ebola demonstrated, the health security of the United States is intrinsically tied to ensuring strong health systems and a coordinated international response at the source of the outbreak. Furthermore, as a global leader for humanitarian action, the United States can provide the financial and technical resources necessary to address the Zika epidemic and protect global health. The work of the United States military and the Centers for Disease Control and Prevention (CDC) during Ebola proved to be transformative. The Ebola response was made possible by a special appropriation during the height of the epidemic, as requested by the President and allocated by Congress.

¹ Andrew Lima et al., "Evidence for an Overwintering Population of *Aedes Aegypti* in Capitol Hill Neighborhood, Washington, DC," *The American Journal of Tropical Medicine and Hygiene* 94, no. 1 (January 6, 2016): 231–35, doi:10.4269/ajtmh.15-0351.

² Anthony S. Fauci and David M. Morens, "Zika Virus in the Americas — Yet Another Arbovirus Threat," *New England Journal of Medicine* 374, no. 7 (February 18, 2016): 601–4, doi:10.1056/NEJMp1600297.

I fully support President Obama's FY2016 emergency supplemental appropriations request of \$1.86 billion to respond to the Zika virus domestically and internationally. This must be in addition to existing global health security funding – including unobligated Ebola funding – to ensure flexibility to respond to the United States' needs as we progress towards Summer and the threat of domestic mosquito-borne transmission.

The Global Response to the Zika Epidemic

I have served on several high-level panels reviewing the WHO and international community's response to the 2014/15 Ebola outbreak including on the Harvard-London Hygiene and Tropical Medicine Independent Panel on the Global Response to Ebola and the National Academy of Sciences Global Health Risk Framework Commission. I also closely advised the United Nations Secretary General's High Level Panel on Global Health Crises. The WHO's failure to act quickly and decisively cost thousands of lives.³ Of particular concern was the unreasonable delay in the convening of an Emergency Committee to advise to the WHO Director-General whether she should declare the Ebola outbreak a Public Health Emergency of International Concern (PHEIC) under the International Health Regulations (2005). The Director-General was also late in mobilizing the international financing needed to prevent international spread of the Ebola Virus.

Despite these critiques from numerous independent panels as well as implementing internal reforms, the WHO delayed taking its leadership role in response to Zika. The CDC and Pan American Health Organization had been working actively on Zika, in collaboration with the Brazilian government for months prior to the WHO's active engagement. Given the broad,

³ Suerie Moon et al., "Will Ebola Change the Game? Ten Essential Reforms before the next Pandemic. The Report of the Harvard-LSTM Independent Panel on the Global Response to Ebola," *The Lancet* 386, no. 10009 (November 2015): 2204–21, doi:10.1016/S0140-6736(15)00946-0.

global distribution of the mosquitoes that transmit Zika virus, and in the absence of rapid diagnostic tests or a vaccine, on January 27, 2016, my colleague Daniel Lucey MD and I called for the WHO to not repeat its mistakes from Ebola, and for the WHO Director-General to immediately convene an Emergency Committee on Zika virus to assess whether a PHEIC should be declared.⁴ On January 28, 2016, the WHO announced that the Director-General would convene an Emergency Committee on Zika virus and the observed increase in neurological disorders and neonatal malformations.⁵

Following this announcement, the WHO acted decisively and with leadership. On February 1st, 2016, the WHO Director-General Margaret Chan declared the clusters of microcephaly and neurological syndromes including Guillain-Barré Syndrome a PHEIC.⁶ This was the fourth PHEIC the WHO Director-General has declared since the International Health Regulations (2005) came into effect in June 2007, including for Influenza A (H1N1), polio, and Ebola.⁷ While a causal relationship between these clusters and Zika virus is strongly suspected, it is not yet scientifically proven. Nonetheless, the declaration of a PHEIC reflects the pressing need for the coordination and resourcing of international efforts to address the Zika epidemic.

Accompanying the PHEIC, the Director-General issued temporary recommendations to countries on handling the Zika epidemic. While not legally binding, these temporary recommendations

⁴ Lucey DR and Gostin LO, "The Emerging Zika Pandemic: Enhancing Preparedness," *JAMA*, January 27, 2016, doi:10.1001/jama.2016.0904.

⁵ WHO, "Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformation" (January 28, 2016), available at: <http://www.who.int/mediacentre/news/statements/2016/emergency-committee-zika/en/> (accessed: February 24, 2016).

⁶ WHO, "WHO statement on the first meeting of the International Health Regulations (2005) (IHR 2005) Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations" (February 1, 2016) available at: <http://www.who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en/> (accessed: February 24, 2016).

⁷ The previous declarations were the Influenza A H1N1 pandemic in April 2009, Polio resurgence in May 2014, and the Ebola outbreak in West Africa in August 2014.

have significant normative weight and are issued in accordance with the legally binding International Health Regulations (2005). The recommendations advise countries to enhance surveillance for Zika virus infections, develop diagnostic tools, communicate the risks of Zika virus infection, aggressively implement vector control and personal protective measures, and ensure reproductive health services, including access to contraception (including emergency contraception) and maternal health care.

On February 16th, 2016, the WHO released its “Zika Strategic Response Framework & Joint Operations Plan”.⁸ This plan is a critically important step towards an effective response to the Zika epidemic. It is also a critical step towards re-establishing the WHO’s global health credibility which was significantly undermined during Ebola. The plan estimates that \$56 million will be required for the Zika epidemic response.⁹ The majority of the funding is for risk communication and community engagement (\$15.5 million) and care for those affected (\$14.2 million). Given the vital role that the Pan American Health Organization (PAHO) plays in leading the global health response in the Americas, a large amount of the funding under this plan is appropriately earmarked for PAHO (\$8.1m), including \$1.5 million for surveillance and \$2.25 million for vector control measures. Yet, despite this estimate of the needs, the WHO has yet to mobilize the required funding. That is still another reason to support the President’s proposed emergency Zika appropriation.

While the WHO’s commitment to raising funds needed for the global response is positive, the estimate of \$56 million is far less than that required to stem the Zika epidemic in the Americas.

⁸ WHO, “Zika Strategic Response Framework & Joint Operations Plan” (February 16, 2016), available at: <http://who.int/emergencies/zika-virus/strategic-response-framework.pdf?ua=1>

⁹ Specifically, \$55,743,651: See, WHO, “Zika Strategic Response Framework & Joint Operations Plan” (February 16, 2016), available at: <http://who.int/emergencies/zika-virus/strategic-response-framework.pdf?ua=1>, Part III: Annexes.

Major global funding is needed for aggressive mosquito control, surveillance, and research. Under the WHO's plan, the overall estimates for these strategies are \$6.4 million, \$7.1 million, and \$6.4 million respectively. The Zika epidemic is likely to spread to many regions of the world beyond the Americas, which will require considerably greater funding. During the Ebola outbreak, the WHO released financing estimates that were far from adequate, requiring repeated increased cost estimates as the Ebola outbreak unfolded. Overly conservative estimates for the Zika epidemic response could result in the same mistakes seen with Ebola: waiting until a global emergency to mobilize funding will always be too little, too late. The WHO must have access to a much larger emergency contingency fund. The trigger for use of this fund would be the declaration of a PHEIC.

The Global Health Risk Framework Commission (on which I served) estimated that it would cost \$4.5 billion annually to truly reduce pandemic risks.¹⁰ While this may appear to be a great deal of money, it pales in comparison to the global costs of a pandemic. Previous epidemics have demonstrated that states with major emerging disease outbreaks experience a loss in GDP of up to 10%. Brazil is may experience a similar economic impact with the upcoming 2016 Olympics and Paralympics in Rio de Janeiro. The World Bank has advised that while initial estimates of the short-term economic impact of the Zika epidemic in the Latin American and Caribbean region is 0.06% of GDP, such estimates are based on a swift, coordinated international response. The World Bank however advises such estimates could be significantly larger given the high dependence on tourism in the region if the virus is not promptly contained, if a causal association

¹⁰ Commission on a Global Health Risk Framework for the Future and National Academy of Medicine, Secretariat, *The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises* (Washington, D.C.: National Academies Press, 2016), <http://www.nap.edu/catalog/21891>.

between Zika virus and clusters of microcephaly and Guillain-Barré Syndrome is established, and if public perceptions of the risks of Zika change.¹¹

In addition to the financial and technical resources dedicated by the WHO, it is vital that the WHO use its normative power for global public health. The WHO was criticized for prioritizing politics over public health during the Ebola outbreak. It must not let the same happen with the Zika epidemic, which disproportionately burdens women and the poor. In particular, calls by governments that women avoid getting pregnant – including Brazil, Honduras, Colombia, and El Salvador – without providing access to reproductive health and rights services, are not only ineffective but also unfair to women. In Central and South America, there is limited access to contraception – especially in poorer communities most at risk of Zika virus infection and cultural and religious norms still restrict the availability and use of contraception. Nearly all countries in the Americas currently experiencing or likely to experience Zika virus cases have laws preventing women from accessing reproductive health services such as emergency contraception and abortion. In addition, the quality, accessibility, and affordability of maternal health care systems vary greatly between and within countries, with varying degrees of post-partum support services for children born with disabilities. Pope Francis recently supported the expanded use of contraception in the face of potential harms to pregnant women from Zika virus infection.

Both the WHO and the international community's response to the Zika epidemic must therefore be comprehensive, equitable, and substantial.

The United States' Domestic Response

¹¹ World Bank, "The short-term economic costs of Zika in Latin America and the Caribbean (LCR)", (February 18, 2016), available at: <http://pubdocs.worldbank.org/pubdocs/publicdoc/2016/2/410321455758564708/The-short-term-economic-costs-of-Zika-in-LCR-final-doc-autores-feb-18.pdf> (accessed February 24, 2016).

The Risk to the United States

The mosquitoes that transmit Zika virus – *Aedes aegypti* (primary vector) and *Aedes albopictus* – is present in the United States and its territories.¹² One recent study modeling possible Zika spread estimates that more than 60% of the US population lives in areas conducive to seasonal Zika virus transmission,¹³ with Florida and Southern Texas at risk of year round transmission. The United States is the only high-income country in the Americas at risk of local Zika virus transmission.¹⁴ As a result, the United States domestic response must cover not only returning travelers who may be infected and local transmission of Zika virus from sexual intercourse, but also local transmission of Zika virus due to infected mosquitoes.

On February 3, 2016, the CDC's Emergency Operations Center (EOC) moved into Level 1 activation to accelerate domestic preparedness in anticipation of local Zika virus transmission by mosquitoes in the Continental United States.¹⁵ Level 1 is the EOC's highest level of activation, reserved for critical emergencies. This involves assignment of the largest number of staff possible to work on a response. There have been three previous EOC Level 1 responses: the Ebola outbreak, Influenza A H1N1 outbreak, and Hurricane Katrina. Moving to this level of response demonstrates the importance of preparedness for the Zika outbreak and supports the

¹² CDC, "Surveillance and Control of *Aedes aegypti* and *Aedes albopictus* in the United States", available at: <http://www.cdc.gov/chikungunya/resources/vector-control.html> (accessed: February 24, 2016).

¹³ Moritz U. G. Kraemer et al., "The Global Distribution of the Arbovirus Vectors *Aedes Aegypti* and *Ae. Albopictus*," *eLife* 4 (2015): e08347, doi:10.7554/eLife.08347 as cited in: Isaac I Bogoch et al., "Anticipating the International Spread of Zika Virus from Brazil," *The Lancet* 387, no. 10016 (January 29, 2016): 335–36, doi:10.1016/S0140-6736(16)00080-5.

¹⁴ Canada does not have the *Aedes aegypti* mosquito. Developmental status taken from: UN, *World Economic Situation and Prospects Report 2014*, available at: http://www.un.org/en/development/desa/policy/wesp/wesp_current/2014wesp_country_classification.pdf (accessed February 24, 2016)

¹⁵ CDC, "CDC Emergency Operations Center moves to highest level of activation for Zika response" (February 3, 2016), available at: <http://www.cdc.gov/media/releases/2016/s0208-zika-eoca-activation.html> (accessed February 24, 2016)

development of laboratory tests to diagnose Zika infection, studies to investigate the association between Zika virus and microcephaly and Guillain Barré syndrome, surveillance in the United States and its territories, and support of efforts in Puerto Rico, Brazil, and Colombia.

Travel advisories and restrictions

The CDC has issued Level 2 (Alert: Practice enhanced precautions) general travel advisories for Zika virus in areas with local transmission such as South America, Central America, Mexico, Pacific Islands, and the Caribbean.¹⁶ In addition, these Level 2 travel alerts include specific interim recommendations that pregnant women should consider postponing any travel to affected regions. The CDC has not issued any Level 3 (Warning: Avoid all non-essential travel) travel advisories which would indicate danger to all travelers, not only travelers with specific risk factors, such as pregnancy.

Travel advisories are important for ensuring that individuals traveling to Zika virus affected countries have adequate information to decide whether to travel and what steps they should take to prevent Zika infection while in affected countries and upon return to the United States. Given the typically mild symptoms of Zika virus in healthy, non-pregnant individuals, Level 3 travel warnings are not currently warranted. Priority should be given to continuing the current information sharing process to travelers on how to prevent mosquito bites, such as through the use of EPA-registered insect repellents, the covering of exposed skin, and sleeping in screened or air-conditioned rooms, and how to prevent possible infection of pregnant partners through sexual intercourse upon return to the United States.

¹⁶ CDC, “Zika Travel Information”, available at: <http://wwwnc.cdc.gov/travel/page/zika-information> (accessed February 23, 2016).

Notably, the CDC and WHO have different advice to pregnant women traveling to Zika affected countries. The CDC's response is more proactive and one that I strongly support.

Travel bans are not warranted, including specific bans for pregnant women at any stage during pregnancy, which would be unnecessarily discriminatory and intrusive. It is important that the CDC is supported in its efforts to set, continually review, and update travel advisories as the public health circumstances change. The WHO Director-General's temporary recommendations issued with the PHEIC declaration specifically advise against travel or trade restrictions to prevent the spread of Zika virus.

Quarantine & Isolation

As a vector-borne disease, Zika virus is predominately transmitted through the bite of an infected female *Aedes aegypti* mosquito. In addition, most individuals infected with Zika do not show symptoms, making identification of individuals for isolation very difficult. The quarantine of persons suspected of Zika virus infection, or isolation of persons with Zika virus infection, is therefore not an effective or warranted public health strategy. While there is evidence of sexual transmission of Zika, this mode of transmission would also not be favorable to quarantine or isolation measures. As a result, the use of quarantine and isolation in response to Zika is unfounded and therefore likely to be considered an unreasonable and unnecessary burden on individuals' liberty that does not have justification in public health. In the temporary recommendations issued with the PHEIC, the WHO Director-General has advised against restrictions such as quarantine and isolation to prevent the spread of Zika virus. Control efforts should therefore focus on mosquito eradication, education about the measures individuals can take to protect themselves from infection, and funding the development of a vaccine.

Vector-Control

It is a public health priority that the main source of Zika virus transmission – principally the *Aedes aegypti* mosquito – is subject to aggressive vector control efforts. In addition to the physical removal of stagnant water that serves as mosquito breeding sites, the use of safe, effective and approved insecticides is necessary. However, insecticide resistance is growing and the WHO is investigating novel mosquito control strategies, such as the use of transgenic mosquitoes to reduce local mosquito populations.¹⁷

Given the public health impact of the *Aedes aegypti* mosquito, I support the watchful use of transgenic mosquitoes through a carefully controlled release that monitors the effects on mosquito-borne diseases – including Zika, Dengue, and Chikungunya viruses –as well as any potential ecological harms. Trials so far have demonstrated promising results in drastically reducing local mosquito populations that carry these diseases without causing other harms. There is also little evidence that transgenic mosquitos cause ecological harms, although potential harms need to be closely watched and controlled for.

Ensuring Equity and Justice in the United States' Health System

Given the disproportionate impact of the Zika epidemic on women, it is essential that women in the United States are guaranteed access to reproductive health services including contraception, emergency contraception, and maternal healthcare. Where it is lawful, pregnant women with a fetus known to have microcephaly should be offered the opportunity to abort the pregnancy.

¹⁷ WHO, "Mosquito control: can it stop Zika at source?" (February 17, 2016) available at: <http://www.who.int/emergencies/zika-virus/articles/mosquito-control/en/> (accessed: February 24, 2016).

Given the possible sexual transmission of Zika virus, condoms must be readily available and accessible to both men and women in the United States. In addition, concerns about fetal health cannot stop at birth: infant, child, and ongoing healthcare and support services for babies that may be affected by the Zika epidemic must be guaranteed. The Federal and States Governments must act to protect the health of US citizens, and meet their obligations under international health and human rights law.

Ensuring Financing for Response Efforts: President Obama's Supplementary Funding Request

On February 22nd, 2016, President Obama submitted a FY 2016 emergency supplemental appropriations request of \$1.86 billion to respond to the Zika virus domestically and internationally.¹⁸ The vast majority of this funding request is directed to the Department of Health and Human Services – \$1.48 billion, \$828 million of which is directed to the CDC. This funding includes \$200 million to support the development of a vaccine through to commercialization with the National Institutes of Health and product development and approvals with the Food and Drug Administration. The United States Agency for International Development (USAID) would receive \$335 million for targeted activities in South America, Central America, and the Caribbean. Finally, \$41 million would be directed to the Department of State to *inter alia* support WHO, PAHO, and UNICEF public health efforts to address the Zika virus in affected countries while ensuring United States health security. Given the unknowns of the health humanitarian and security risk posed by Zika – especially as we transition to Summer – this funding is essential to ensure flexibility to respond to the United States' needs, including beyond that already identified.

¹⁸ Letter from President Barack Obama to Speaker Paul Ryan (February 22, 2016), available at: https://www.whitehouse.gov/sites/default/files/omb/assets/budget_amendments/emergency_supplemental_2-22-16_zika.pdf (accessed February 24, 2016)

Use of unobligated Ebola emergency funds for the Zika response

While it may seem appealing to use money previously allocated to the Ebola outbreak, such a move risks making the United States more vulnerable to infectious disease threats. Failure to develop and secure health systems in developing countries – whether in West Africa or South America – risks the health, safety, and security of the United States.

Ensuring global public health is not simply about a rapid response, but a sustainable response. Reallocating money from one infectious disease outbreak to another undermines efforts to ensure surveillance, detection, response, and control strategies are not only operational but sustainable in countries at risk of outbreaks. While infectious diseases may appear quickly, the efforts to prevent and respond to them cannot simply be about extinguishing fires, but rather preventing them from flaring up and occurring again in the future. Given the economic impact of outbreaks, sustainable and systems-wide technical and financial resources are essential to ensure taxpayers' money is utilized effectively. Furthermore, reallocating money from one infectious disease outbreak to another infectious disease outbreak risks the long-term health, safety, and security of the United States. It is important to note that the USAID funding request in President Obama's FY2016 emergency supplemental appropriations request would provide flexibility in the use of remaining USAID Ebola funds.¹⁹

Global health security and public health is grossly underfunded. I strongly advise that the Zika supplementary budget request is funded independently from unobligated past emergency funds.

¹⁹ White House, Office of the Press Secretary, "Fact Sheet: Preparing for and Responding to the Zika Virus at Home and Abroad" (February 8, 2016), available at: <https://www.whitehouse.gov/the-press-office/2016/02/08/fact-sheet-preparing-and-responding-zika-virus-home-and-abroad> (accessed February 24, 2016).

Mr. MURPHY. Thank you, Professor.

Now we're going to turn to Mr. Conlon, who I also understand was an entomologist in the United States Navy for a couple of decades.

Mr. CONLON. Indeed.

Mr. MURPHY. So thank you.

STATEMENT OF JOSEPH CONLON

Mr. CONLON. Thank you. Good morning, Mr. Chairman and members of the subcommittee, Representative Castor. My name is Joseph Conlon. I'm a retired U.S. Navy Medical Entomologist and I serve as the Technical Advisor for the American Mosquito Control Association, and I welcome this opportunity to provide a mosquito control perspective to the deliberations of this committee.

The recent introduction and spread of Zika virus in the Western Hemisphere has reawakened in the United States an appreciation of mosquitoes as not just nuisances, but transmitters of devastating diseases. And I use the term "reawakened" advisedly for mosquito-borne diseases such as malaria, dengue, yellow fever were once quite common in the United States and, indeed, played a major part in shaping our nation's destiny. These diseases no longer claim victims in the United States as a matter of course largely due to the exemplary efforts of organized mosquito control agencies in conjunction with an enlightened and effective public health infrastructure. But even more mosquito-borne diseases are a mere 7-hour flight from our shores, and our public health agencies must be prepared to meet these challenges that they will eventually present.

Zika virus is thought to be primarily transmitted from human to human by the bite of an infected *Aedes aegypti* and possibly *Aedes albopictus* species of mosquitoes. Of these, *Aedes aegypti* has been primarily responsible for transmitting the disease due, in part, to its preference by humans both day and night and its predilection for biting the lower extremities out of sight. Moreover, females frequently take multiple partial blood meals often from different individual humans, not only increasing the likelihood of feeding on an infectious human, but also leading to single infectious females potentially feeding on and infecting multiple humans within a relatively short time period. This is unique.

Both *Aedes aegypti* and *Aedes albopictus*, the Asian Tiger mosquito are notoriously difficult to kill and/or prevent. They live inside our houses under furniture, beds, in closets. Their eggs can withstand months of drying and their young can develop in water containers as small as a discarded soda bottle cap. Virtually any collection of stagnant water in containers, tree holes, leaf axles, et cetera can serve as an egg-laying habitat for these species. Thus, draining wet areas does not prevent their development around our homes and yards.

Aedes aegypti has been found in isolated areas of California and along the southern tier of states up into Georgia and South Carolina. *Aedes albopictus* is a bit more cold-hardy and its range includes those states but extends northward to Illinois and New York. States within this range have excellent integrated mosquito control programs in some areas, but mosquito control outside of

their jurisdictions is spotty. Indeed, many potential ports of entry throughout the United States have limited or no mosquito control available and there is a pressing need for funding to establish sustainable mosquito control programs in these areas if outbreaks are to be contained.

Successful mosquito control is based first and foremost on a comprehensive knowledge of the vector in order to exploit its vulnerabilities. All prevention and control strategies are based on this knowledge; however, the cryptic nature of *Aedes aegypti* makes normal surveillance and control strategies problematic. This demands that mosquito control in the 734 established districts and over 1,100 municipal programs be improved in the following seven areas: improved mosquito surveillance tools for adult *Aedes aegypti*; availability of pesticide resistance testing kits and accurate rapid diagnostic tests for arboviral agents and trapped mosquitoes; faster communications about protocols between public health laboratories and mosquito control programs; funding to underwrite new data call-ins that might influence a pesticide registrant's decision to keep proven products on the market; funding for field validation of new control modalities such as lethal overtraps; intracellular controls using Wolbachia; genetically modified mosquitoes; new active ingredients such as dopamine receptor agonists to name a few. We also need a national strategy to elicit sustained public participation in removing and draining containers used by *Aedes aegypti* as position sites. Also identifying areas at risk of Zika transmission, assisting to the extent possible any federal programs, underwriting the startup of new vector control programs in impoverished areas at risk.

The federal government has several mechanisms available to help these needs if funds already authorized were to be appropriated. Three in particular come to mind. First, the expanded laboratory capacity program of CDC for funding increases in arboviral testing capacities. Second, the Mosquito Abatement for Safety and Health Act by which local governments could receive matching federal funds up to \$100,000 for the establishment and/or enhancement of mosquito abatement programs, and \$100 million total for building sustainable programs where they do not exist. The funding for this was authorized but never appropriated. Third, the Food Quality Protection Act which authorizes the use of federal funds when the cost of new data for public health pesticides was more than their producers could afford putting their registration at risk.

The national capacity to control mosquito-borne disease at present and in the future will largely depend on the extent to which these support programs or their functional equivalent in the President's February 22nd Emergency Supplemental Fund Request are implemented. Increased tourism, travel, and trade make continual introductions of exotic diseases carried by mosquitoes virtually inevitable. Resources for prevention and control programs must be made available and employed so that future cases of exotic diseases can be contained and eliminated before their establishment and spread.

The President's recent request for emergency supplemental funding for Zika prevention and control tangibly addresses our acknowledgment of current shortfalls in mosquito-borne disease control ca-

pability and seeks avenues to remedy them towards our shared goal of protecting the American people from exotic diseases. The American Mosquito Control Association agrees. Our citizenry deserves no less. Thank you.

[The statement of Mr. Conlon follows:]

Examining the U.S. Public Health Response to the Zika Virus

HEARING BEFORE THE
U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

TESTIMONY
OF
JOSEPH M. CONLON
TECHNICAL ADVISOR

ON BEHALF OF
THE AMERICAN MOSQUITO CONTROL ASSOCIATION
1120 RTE 73, SUITE 200
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March 2, 2016

Good morning, Mr. Chairman and Members of the Subcommittee. My name is Joseph Conlon and I am a retired U.S. Navy medical entomologist serving as Technical Advisor for the American Mosquito Control Association (AMCA), a nonprofit organization of 1600 members dedicated to enhancing health and quality of life through the suppression of mosquitoes and other vectors of public health importance. I welcome this opportunity to provide a mosquito control perspective to the deliberations of this committee concerning Zika Virus and will limit my testimony to mosquito management methodologies that contribute to its control.

The introduction and spread of Zika Virus in Central and South America and the Caribbean in 2014 reawakened in the United States an appreciation of mosquitoes as vectors of diseases. I use the term “reawakened” advisedly, for mosquito-borne diseases such as malaria and yellow fever were once quite prevalent in the United States and, indeed, played a major part in shaping our nation’s destiny. These diseases no longer claim victims in the United States as a matter of course largely due to the exemplary efforts of organized mosquito control agencies, in conjunction with an enlightened and effective public health infrastructure. But other mosquito-borne diseases are on the horizon and public health agencies need to be prepared to meet the challenges they present.

Progress continues in defining the transmission dynamics of Zika Virus so as to allow for its prevention and control. However, considering that it is a comparatively recent epidemiological phenomenon, there remains much to learn in order to establish and verify

baseline data. The virus is thought to be primarily transmitted from human to human by the bite of infected *Aedes aegypti* and (possibly) *Aedes albopictus* species of mosquitoes. Of these, *Aedes aegypti* has been primarily responsible for transmitting the disease due to its preference to bite humans both day and night and its predilection for biting the lower extremities. Moreover, females frequently take multiple partial bloodmeals, often from different individual humans, not only increasing the likelihood of feeding on an infectious human but also leading to single infectious females potentially feeding on and infecting multiple humans within a relatively short time period.

Aedes aegypti and *Aedes albopictus* are notoriously difficult to prevent or kill. They live inside our houses under furniture, beds and in closets; their eggs can withstand months of drying, and their young can develop in water containers as small as a bottle cap. Virtually any collection of stagnant water in containers, treeholes, leaf axils, etc. can serve as egg-laying habitat for these species. Thus, draining wet areas doesn't prevent their development around our homes and yards; predators do not consume enough to provide effective control; and repellents, while protecting individuals, just redirect the adult mosquitoes to bite somebody else.

Aedes aegypti has been found in isolated areas of California, and from Arizona, New Mexico, Texas, Louisiana, Mississippi, Alabama, Florida, Georgia and South Carolina. *Aedes albopictus* is a more cold-hardy species and its range includes those states but extends northward to Illinois and New York. Its range is thought to be defined by an average winter temperature of 50 degrees Fahrenheit.

Mosquito Control as currently practiced in the United States

The first mosquito control districts were established in NJ in 1912. California and Florida followed suit in 1915 and 1925, respectively. In the ensuing years, mosquito control districts and state agencies were established nationwide so that there are now more than 700 recognized districts within the United States along with over 1000 control entities within municipal service programs.

The integrated mosquito management methods currently employed by these organized control agencies and endorsed by the CDC and EPA are comprehensive and specifically tailored to safely counter each stage of the mosquito life cycle.

Larval control through water management and source reduction, where compatible with other land management uses, is a prudent pest management alternative - as is use of the environmentally friendly EPA-approved larvicides currently available.

When source elimination or larval control measures are clearly inadequate, or in the case of imminent disease, the EPA and CDC have emphasized in a published joint statement the need for considered application of adulticides by certified applicators trained in the special handling characteristics of these products.

In 2009 the AMCA published its “Best Management Practices for Integrated Mosquito Management” and promulgated it to its membership as a set of guidelines for safe, effective and efficient vector control programs. The AMCA is currently in the process of developing guidelines specifically geared toward control of *Aedes aegypti* and *Aedes albopictus*. This will emphasize urban mosquito control and the paradigm shift in control

practices from floodwater/salt marsh mosquitoes (predictable habitats) to container-inhabiting mosquitoes (unpredictable and ubiquitous in the peridomestic environment). In addition, the unique man-power, resources, and funding needed for proactive urban control will be covered. AMCA hopes to have a finalized version available as early as possible in 2016/2017 timeframe.

States thought to be particularly susceptible to Zika introduction, such as Florida, California, and Texas, have excellent integrated mosquito control programs in many areas, but emergency funds to respond to a Zika outbreak are needed if timely interventions to contain outbreaks in these districts and elsewhere are to be realized. Critically, many potential ports of entry throughout the U.S. have limited or no mosquito control available and there is a pressing need for funding to establish sustainable mosquito control programs in these areas.

Components of successful mosquito-borne disease control programs as currently practiced in the United States include, but are not limited, to the following:

Prevention

Surveillance - A sustained, consistent surveillance program targets the particular vector species, mapping their larval habitats by season, and documents the need for control through larval and adult trapping regimens. It thus also monitors the effectiveness of the control program. Appropriate and timely response to surveillance data is the key to preventing human disease associated with Zika. Control activity should then be intensified in response to evidence of virus in imported cases, as deemed necessary by the local statutory authority.

Public Information and Outreach – Studies have shown that information programs, while crucial to the overall prevention/control strategy, only exert a moderate effect on modifying population behaviors related to personal protective measures. Effective programs include development of a community task force, interventions to improve access to window screening materials or repellents, and social marketing to reinforce preventive behaviors. These are critical components of any mosquito control program, but cannot, in and of themselves, replace established prevention/control methodologies.

Source Reduction - Removing breeding habitat is the most effective long-term mosquito preventative/control and includes activities as simple as the proper disposal

of used tires, paint cans and trash, in addition to the cleaning of rain gutters and bird baths, by individual property owners.

Control

Reducing the contact between the vector mosquito and humans - This is accomplished through removing, modifying or treating larval habitats; modification or removal of adult mosquito resting areas, adulticide treatments when indicated, and use of repellents. All of these interventions can be problematic regarding control of *Aedes aegypti*.

Best Management Practices (BMP) - Most larger mosquito control districts in states having potential ports of entry, such as California, Texas and Florida, usually employ a phased response based upon mosquito trapping data. Such programs consist of public education emphasizing personal protection and residential source reduction; municipal larval control to prevent repopulation of the area with competent vectors; adult mosquito control to decrease the density of infected, adult mosquitoes in the area; and continued surveillance to monitor virus activity and efficacy of control measures.

How mosquito control can be improved

- Mosquito surveillance tools for adult *Aedes aegypti* are ineffective for small populations and need to be improved and made more widely available to marginally funded programs.
- Training in the use and interpretation of survey results should be made available to both program managers and public health officials as continuing education adjuncts.
- Additional training resources and comprehensive participation in workshops and professional mosquito control conferences are key components of program upgrades.
- Faster and more efficient communications between public health laboratories and vector control programs need to be explored and implemented. The speed with which the public health sector can respond to either imported or locally-acquired cases will ultimately depend on the turnaround time between testing of suspect cases, laboratory confirmation and promulgation of surveillance results. In addition, variable interpretations of the Health Insurance Portability and Accountability Act (HIPAA) may delay release of results, further restricting timely interventions by vector control agencies. Mechanisms need to be developed that require health departments at all levels to disclose to local vector

control agencies the location of suspect cases of Zika while not violating HIPAA provisions. This will ensure more timely and targeted initiation of intervention measures that will prevent or rapidly contain outbreaks.

- Materials and training regarding pesticide resistance testing should be implemented nationwide.
- Funds should be made available to underwrite new data call-ins that might influence a pesticide registrant's decision to keep products on the market
- New chemical, genetic, and biological control methodologies and means of dispersal should be developed and field validated.
- Conventional pesticides are losing ground to resistance. New tools are in development (spatial repellents, ATSB, lethal ovitraps, intracellular biological control (*Wolbachia*), RNAi, GMO mosquitoes, and new pesticide chemical classes require more field validation prior to widespread use.
- Rapid diagnostic tests for Zika and other arboviral agents need development and deployment to mosquito control entities to provide timely notification of infected mosquitoes prior to human cases.

The Role of Federal Government

The federal government has a crucial role to play in how vector control is accomplished. Several agencies either conduct (e.g., USDA and to a lesser degree CDC) research on applied vector control topics, or fund (NIH) projects (e.g., *Wolbachia*) into novel technologies, FEMA supports large-scale vector control in declared disasters (under Stafford Act stipulations).

In addition, the Centers for Disease Control and Prevention (CDC) Division of Vector-borne Disease provides national expertise in mosquito-borne disease prevention and control in concert with members of the AMCA. They have also served as an effective conduit via the Expanded Laboratory Capacity (ELC) program for funding that can increase arboviral testing capacities at both state and local levels. To this end, we encourage Congress to authorize supplemental funding for 2016 and increased funding in FY 2017 to support vector-borne disease surveillance. Funding should be allocated through the Centers for Disease Control and Prevention's (CDC's) Division of Vector-Borne Diseases for dispersal to localities most vulnerable to disease introduction while lacking the capabilities.

The Mosquito Abatement for Public Health Act (MASH), Public Law 108-75, was passed during the first session of the 108th Congress but has not received appropriations for its implementation. This Act is a mechanism by which local governments could receive matching federal funds up to \$100,000 for the establishment and/or enhancement of a mosquito abatement program through the CDC. The MASH Act authorized \$100,000,000 in funds for FY 2003, but, as of this hearing, Congress has still not appropriated any funds to cover its provisions. In addition, it requires NIEHS to conduct or support research into methods to control the population of insects and vermin that transmit dangerous diseases to humans. The AMCA fully supports the MASH Act and requests action to

appropriate the funds for its full implementation to bolster long-term vector surveillance and control.

The critical challenge for the nation's public health system will be modifying the behavior of the US population to eliminate oviposition sites for these species. Vector control agencies do not possess the resources to provide the sustained service for each resident in their jurisdiction that is required to successfully control invasive *Aedes*. To accomplish that end via source reduction will entail a national effort, along the lines of the "buckle up" seat belt, Smoky the Bear, and "don't be a litterbug" campaigns of the 1960s. A sustained national program will required continued funding into the foreseeable future if the benefits from reduced introduction and spread of exotic mosquito-borne diseases are to be realized.

We further see a federal government role in maintaining our present, proven chemical tools at risk of losing their registration. In 1996 Congress unanimously approved the Food Quality Protection Act (FQPA) (PL 104-170) to modernize the regulation of pesticides and expand data requirements to demonstrate their safety to people and the environment. A key element was authorization to use federal funds when the cost of new data for public health pesticides was more than their producers could afford, putting registration at risk. Unfortunately, these essential funds have never been appropriated, and we are now losing critical public health tools because the cost to prove their safety is higher than return on investment.

Conclusion

Vector-borne diseases, whether ancient like malaria or relatively new like Zika, are an unfortunate reality, and Zika won't be the last to challenge our vector-borne disease control capabilities. There are many factors that contribute to the emergence of novel vector-borne diseases, including poverty, climate change, and global trade. They will require long-term solutions.

Mosquito control capabilities in the United States are the finest in the world, but in many cases, fall short of providing the level of protection needed to prevent outbreaks of mosquito-borne disease in all potential ports of entry. Increased tourism and trade make continual introductions of exotic diseases inevitable and resources for sustainable prevention and control programs must be made available so that future imported cases of exotic diseases beyond Zika can be contained and eliminated before their establishment and spread. Our citizenry deserves no less.

Summary

- Capacities to address mosquito-borne diseases in the U.S. are better than in the past, but require significant improvement to successfully meet the mosquito-borne disease threats such as Zika Virus surely to come our way in the future.
- Increased capacity must include capabilities to address survey control strategies applicable to the widest possible variety of vector-borne disease transmission cycles.
- The unique bionomics of *Aedes aegypti* require better surveillance and prevention/control tools and strategies over the long-term.
- The Federal role should consist of exploring and implementing funding mechanisms devoted to increasing sustainable integrated vector surveillance and control capabilities in areas with organized mosquito control and to develop startup programs in areas of potential risk.
 - The MASH act proposes just that sort of thing – providing support for developing new vector control where lacking, and enhancing capacities where they exist but are inadequate.
 - Fully fund the Food Quality Protection Act provisions to use federal funds when the cost of new data for existing public health pesticides is more than their producers can afford, putting their registration at risk.

- Increase the CDC/DVBD annual budget to levels that allow funds to be allocated directly for testing of mosquito pools conducted at the local mosquito control program level or intrastate testing collaborative below the state level.

Mr. MURPHY. Thank you, Mr. Conlon.
 Dr. Sheffield, you're recognized for 5 minutes.

STATEMENT OF JEANNE SHEFFIELD

Dr. SHEFFIELD. Thank you. Chairman Murphy, Ms. Castor and representatives, I'd like to thank you for the opportunity today to testify before you on the effects of Zika virus in pregnant women and how clinicians are responding to this virus threatening the United States and the rest of the Americas.

The Zika virus epidemic is a unique situation. It is a mild disease in adults in most cases, of little consequence to date other than the uncommon but potentially devastating complication of Guillain-Barre AE1 Syndrome. However, maternal Zika infection during pregnancy can have enormous consequences to the developing fetus. Zika has received international attention predominantly because of its effect on the developing fetus, specifically the association with microcephaly, significant effects on brain growth and development, and ocular abnormalities. Thus, much of the focus so far of current efforts has been on the management of the at-risk patients.

You've heard extensive testimony about the origin of this virus and its spread over the last six decades, so I won't repeat myself or repeat that information for the sake of time. While the Continental United States has not identified a case of local transmission of Zika, there is a growing number of confirmed travel-related cases, several of these in pregnant women as we've heard about. While transmission of Zika virus is primarily through the infected mosquito, transmission may also rarely occur through infected blood in laboratory accidents, vertical transmission from a pregnant mother to the fetus has been confirmed, and finally cases of sexual transmission of Zika from an infected person to an uninfected sexual partner is increasingly being documented.

Data regarding Zika virus infection in pregnancy are limited, and it is imperative that resources are directed to elucidating the pathophysiology of the infection on pregnancy, rate of fetal transmission, influence of timing in infection and relation to pregnancy on fetal manifestations of the disease, and long-term consequences of fetal infection. While it is unknown at this time if pregnant women are more susceptible to Zika virus, the disease itself does not appear any worse in pregnant women compared to non-pregnant women. Zika infects pregnant women in any trimester, and the virus has been found in multiple different tissues from fetal losses, amniotic fluid, the placenta, and the brain of infected neonates.

The Brazilian outbreak of virus was associated with a significant rise in microcephaly. Microcephaly itself is diagnosed when the head is significantly smaller than what would be expected for the sex and gestational age of the infant. There are many causes of microcephaly, average rate is about 2 to 12 per 10,000 live births in the United States. There are multiple etiologies or multiple causes, chromosomal abnormalities, genetic abnormalities, toxin exposures such as mercury, alcohol exposure during pregnancy, and in the case of Zika, also other infections such as cytomegalovirus and rubella.

The reason microcephaly develops in association with Zika is currently under investigation. Infants with microcephaly can have multiple long-term complications depending on the severity of the microcephaly and the associated abnormalities: seizures, developmental delay, including speech and motor abnormalities are just a few of these complications. There is no known cure, and treatments are very limited depending on what the etiology is of the microcephaly. Significant resources are going to have to be focused on the long-term care of these affected infants.

Since the microcephaly association was first noted several months ago, we now know that there's multiple other abnormalities, and I've detailed these in my written testimony. Soon after the association of Zika virus infection and fetal microcephaly was identified, the Centers for Disease Control and Prevention set up a health alert and brought together subject matter experts including arbovirus virologists, public health personnel, and obstetrics and gynecologists with expertise in infectious disease and pregnancy. While data were very limited at that time, interim guidelines were rapidly developed to inform physicians caring for pregnant women, management strategies were disseminated, and educational materials describing preventative measures were made widely available not just to physicians but to the general public. These guidelines have been updated several times as new information has been elucidated. As was mentioned, the American College of OB/GYN and also the Society for Maternal-Fetal Medicine have played a very integral part in the development and dissemination of this information, and I will be glad to answer any questions related to the management of these patients.

Zika virus infection is now a notifiable disease allowing for better surveillance of disease burden. The CDC has developed a pregnancy registry with confirmed Zika infection in the United States. They actually released a report on Friday that was briefly mentioned earlier detailing the initial results of 257 Zika tests performed for pregnant women in the report, 3 percent were positive. The nine women that were positive, two electively terminated, two had a miscarriage or first trimester loss, one delivered an infant with severe microcephaly, and two pregnancies are ongoing, two pregnancies have delivered and so far there are no known effects to the infant. One woman was infected in a third trimester and delivered a healthy infant. So while this initial report is an important first step, much more is needed for the physician to be able to effectively counsel pregnant women at risk for infection. Support for both national and international research targeting key populations such as pregnant women is imperative. Until effective treatments and/or a vaccine are developed, prevention of maternal infection is necessary to prevent the devastating consequences of fetal infection. Thank you.

[The statement of Dr. Sheffield follows:]

Good morning Chairman Murphy, Ranking Member DeGette, and members of the Subcommittee. Thank you for the opportunity to testify before you today on the effects of Zika virus in pregnant women and how clinicians are responding to this virus threatening the United States and the rest of the Americas. This virus has received international attention predominantly because of its effects on the developing fetus, specifically the association with microcephaly and abnormal intracranial findings.

The Zika virus is a mosquito-borne flavivirus closely related to yellow fever, West Nile and dengue viruses. It was first identified in 1947 in rhesus monkeys and subsequently noted to cause mild disease in humans throughout Africa and Asia. The first significant outbreak occurred in 2007 in the Yap Islands of Micronesia. French Polynesia in 2013-2014 reported that 10% of its population was infected - several cases of Guillain-Barre syndrome and 2 cases of vertical transmission were identified. It was not until May 2015 that local transmission of the virus in the Americas was reported in Brazil. This virus has now spread throughout South and Central America and the Caribbean following the global distribution of the *Aedes aegypti* mosquito. While the continental United States has not identified a case of local transmission of Zika, there are now greater than 100 confirmed travel-related cases, several of these pregnant women.

Transmission of Zika virus is primarily through infected *Aedes aegypti* mosquitos and, less common *Aedes albopictus* mosquitos. These mosquitos are found in the United States and are daytime biters. Once a person is infected, the incubation period is up to 2

weeks. Transmission may also rarely occur through infected blood and laboratory accidents. Vertical transmission from a pregnant mother to her fetus has been confirmed and transmission at the time of delivery may also occur. Viral RNA has been found in breast milk though no virus has been isolated and no case of transmission from breastfeeding has been reported. Finally cases of sexual transmission of Zika from an infected person to an uninfected sexual partner are increasingly being identified, currently all from an infected male to an uninfected female. All infected males were symptomatic within 2 weeks of travel to Zika affected areas.

The majority of persons infected with Zika virus are asymptomatic – only 20% develop symptoms and these symptoms are usually mild. Acute onset of fever, maculopapular rash, arthralgias and conjunctivitis are the predominant symptoms though myalgias, headache, retro-orbital pain, pruritis and vomiting have also been reported. Symptoms last up to a week and infection rarely results in serious illness or death. The primary concern of Zika virus infection is to the pregnant woman and her developing fetus.

Zika virus effects on pregnancy women and the developing fetus

Data regarding Zika virus infection and pregnancy are limited and it is imperative that resources are directed to elucidating the pathophysiology of infection in pregnancy, rate of fetal transmission, influence of timing of infection in relation to pregnancy on fetal manifestations of disease, and long term consequences of fetal infection. While it is

unknown at this time if pregnant women are more susceptible to Zika virus, the disease does not appear to be any worse in pregnant women compared to non-pregnant individuals. Zika infects pregnant women in any trimester and the virus has been found in tissues from fetal losses, amniotic fluid, placenta, and in the brain of infected neonates.

The Brazilian outbreak of Zika virus was associated with a significant rise in microcephaly cases, first recognized in September 2015. The Brazil Ministry of Health established a microcephaly registry and task force and on November 17, 2015 they reported a possible association of Zika virus infection during pregnancy and microcephaly. By December, Zika virus RNA was reported in the amniotic fluid of two pregnancies in the third trimester in which fetal microcephaly was diagnosed. The virus was also found in tissues from an infant with microcephaly who died soon after birth. January 22, 2016 Brazil reported 35 cases of Zika-virus related microcephaly; 74% of the mothers reported a rash during pregnancy and all women lived in Zika affected areas.

Microcephaly is diagnosed when the head is significantly smaller than would be expected at a specific gestational age and sex. There are many causes of microcephaly and in the United States, microcephaly is reported in 2 to 12 infants per 10,000 live births. Microcephaly has been associated with genetic abnormalities e.g. chromosome and single-gene disorders, environmental factors such as exposure to toxic substances during pregnancy e.g. mercury, severe malnutrition, maternal alcohol use in pregnancy

and infections such as rubella and cytomegalovirus (CMV). It can also occur when there is an insult to the fetus during development and the brain stops growing normally. In the case of infection, it takes weeks to months after the infection for microcephaly to develop. The reason microcephaly develops in association with Zika infection is currently under investigation.

Infants with microcephaly can have a wide range of long-term complications depending on the severity of the microcephaly and the associated abnormalities. Seizures, developmental delay including speech and motor abnormalities, cerebral palsy, intellectual disability, feeding problems and vision and hearing loss are not uncommon in these infants. There is no known cure or standard treatment for microcephaly. Because microcephaly can range from mild to severe, treatment options vary. Significant resources will need to be available for the long-term care of these affected infants.

Since the microcephaly association was first noted several months ago, a number of other fetal abnormalities have been identified. Fetal growth restriction, intracranial calcifications, abnormal brainstem and cerebellum development, almost complete agyria with brain atrophy, absence of the corpus callosum and thalami have all been documented. The majority of the infants with microcephaly have at least one of these other abnormalities. Eye abnormalities have been identified in 35% of the Brazilian cohort. The Zika virus is neurotropic, targeting the brain. The complications identified to

date reflect this. Autopsy specimens have identified the virus in the brain of affected fetuses and infants. It is unknown whether infants infected late in pregnancy that have not had time to develop microcephaly and other abnormalities prior to delivery will have long term sequelae.

Recommendations for pregnant and reproductive age women

Soon after the association between Zika virus infection and fetal microcephaly was identified, the Centers for Disease Control and Prevention (CDC) sent out a Health Alert and brought together subject matter experts including virologists with arbovirus expertise, public health personnel and Obstetricians/Gynecologists who specialize in infectious diseases in pregnancy. While data were limited, interim guidelines were rapidly developed to inform physicians caring for pregnant women. Management strategies addressing pregnant women who had traveled to Zika affected areas were disseminated and educational materials describing preventative measures were made widely available to physicians and the general public. These guidelines have been updated several times as new information has been elucidated. The CDC also maintains a hotline available to clinicians 24/7 for Zika related questions.

There is no vaccine or medication to prevent the acquisition of Zika virus. The CDC recommends that all pregnant women or women considering pregnancy postpone travel to areas of ongoing Zika virus transmission

(<http://wwwnc.cdc.gov/travel/notices>). If they have to travel to affected areas, avoid mosquito bites by wearing protective clothing, using U.S. EPA-registered insect repellent and stay in screened in or air-conditioned areas. DEET and permethrin can be used throughout pregnancy.

Pregnant women that do travel to areas of ongoing Zika virus transmission should be evaluated regardless of symptomatology. The CDC algorithms detail the laboratory evaluation that should be performed. While this initially could only be done at a central CDC laboratory, they have rapidly made the testing available to a number of state health departments and are rapidly expanding the laboratories able to perform the tests. Ultrasound guidance to evaluate the fetus for evidence of Zika infection has been developed in conjunction with the Society of Maternal-Fetal Medicine (SMFM) and the American College of Obstetricians and Gynecologists (ACOG). The CDC has also developed guidance for pregnant women living in endemic areas and to evaluate neonates born to mothers infected by Zika.

There have now been several confirmed and suspected cases of sexual transmission in the United States, all from men who traveled to areas of ongoing Zika virus transmission to female non-travelers. The concern now is that this is a more common mode of transmission than was previously suspected. Men who have a pregnant partner should either not travel to affected areas or if they do travel, abstain from sexual activity or use condoms “consistently and correctly” for the duration of the pregnancy. Pregnant

women who do engage in unprotected sexual activity with a partner who traveled to an affected area and who had symptoms of Zika infection during travel or within 2 weeks of return should be offered evaluation.

Zika virus infection is a notifiable disease in the United States, allowing for better surveillance of the disease burden. The CDC has developed a registry of U.S. pregnant women with confirmed Zika infection. They released a report February 26, 2016 detailing the initial results of the testing in pregnant women travelers. Of 257 Zika tests performed for pregnant women, 3% tested positive. The nine pregnant women with confirmed infection all reported symptoms (100% had a rash). Six women were infected in the first trimester: two had an early pregnancy loss, two elected to terminate their pregnancy, one delivered an infant with microcephaly and one is ongoing. Two women were infected in their second trimester: one woman delivered a healthy infant and one pregnancy is ongoing. One woman was infected in the third trimester and delivered a healthy infant.

While this initial report is an important first step, much more is needed for the physician to be able to effectively counsel a pregnant woman at risk for infection. Support for both national and international research targeting key populations e.g. pregnant women is imperative. Until effective treatments and/or a vaccine are developed, prevention of maternal infection is necessary to prevent the devastating consequences of fetal infection.

Conclusion

The Zika virus epidemic is a unique situation: it is a mild disease in adults of little consequence to date except for the uncommon complication of Guillain-Barre. However, maternal Zika infection during pregnancy can have enormous consequences to a developing fetus. As such, the Centers for Disease Control and Prevention has moved quickly to respond to this global threat. As we move into the warmer months in the United States and the mosquito population increases, we expect to see locally transmitted infections. Mobilizing resources to better characterize this disease is imperative.

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Mr. MURPHY. Thank you, doctor. I'll now recognize myself for 5 minutes of questions.

First, Dr. Sheffield, has any of the medical academies or the AMA come out with any recommendations with regard to asking mothers and keep ing the record if they have traveled to any areas where Zika virus is known?

Dr. SHEFFIELD. I think that's actually a superb question, and we talked about it quite extensively. My hospital, Johns Hopkins, we have developed a very comprehensive screening tool with a list of the countries and territories that are currently affected, and we are trying to spread this information out to multiple other centers. When I talk to other colleagues from around the country they are doing the same thing. So very similar to Ebola, we're working on a screening questionnaire.

Mr. MURPHY. So would you say at this point, should it be a standard that OBGYNs and pediatricians ask that question of mothers, if they have traveled to during pregnancy?

Dr. SHEFFIELD. Absolutely.

Mr. MURPHY. And with regard to that, and this is whether or not they had symptoms, just if they traveled there or nearby.

Dr. SHEFFIELD. Whether they traveled. The pregnant women regardless of symptoms require testing.

Mr. MURPHY. Even if in second or third trimester, of travel.

Dr. SHEFFIELD. Yes, sir.

Mr. MURPHY. I mean, I know myself as a psychologist, worked for many years with developmentally delayed children that there's a lot of long-term intellectual motor and sensory complications. I must admit, I'm also concerned that regardless, because we don't know yet all the route of what happened to this virus with the developing brain, that I wonder even if an infant or a young child is also infected with the Zika virus, the outcome on the brain, we simply don't know that. Am I correct?

Dr. SHEFFIELD. I think that is actually one of the big concerns, is that even if you're infected in the third trimester, have no evidence at delivery of microcephaly or neurologic abnormalities, the long-term follow-up of these babies is imperative because we don't know what the long-term consequences are going to be.

Mr. MURPHY. That's correct. I agree with you there.

Dr. Hotez, you've been critical what you call the narrative. We've been mostly hearing from the U.S. Government that the Continental U.S. is a wealthy place with few of the risk factors contributing to the rapid spread of the arbovirus infection such as Zika, dengue, and chikungunya in Latin America and the Caribbean. But as a specialist in tropical disease based in a major Gulf Coast urban center, why do you disagree with that narrative that we shouldn't worry as much?

Dr. HOTEZ. Thank you for that question. The reason is we have poor people in this country, we have 20 million Americans that live at half the U.S. poverty level. We now have 1.65 million families that live on less than \$2 a day according to the University of Michigan Center for Poverty. And what we're finding is something very interesting about the world's neglected diseases, that currently most of the world's neglected diseases, which include Zika, are actually found in wealthy G20 countries, but it's the poor living

among the wealthy that account to it for this. So the G20 countries account for most of the world's worm infections, and dengue, and chagas disease, and leishmaniasis. We have 12 million Americans now living with a neglected tropical disease in the United States, most of them in the American south, most living along the Gulf Coast. For all the reasons that I mentioned in my previous testimony that we know that poor areas are particularly vulnerable. I have pictures.

Mr. MURPHY. But even with that, I only have a minute, 50 seconds. I want to ask, and then we can look at those later. But even so, I don't know how far these mosquitoes may travel in their lifetime, get a wind. Do we have any idea? Mr. Conlon, is it miles?

Mr. CONLON. Not in the case of *Aedes aegypti* and *Aedes albopictus*. Their ranges are about 100 to 200 meters from where they actually breed.

Mr. MURPHY. I see. And along these lines, too, does anyone know if the virus can live in the water in which they breed, and can the virus be transmitted for an adult to offspring? Just to help the American public understand this. Does anybody know?

Mr. CONLON. To my knowledge, it can't reside in water. However, it is vertically transmitted from the mosquito, the adult mosquito to their offspring, so they're born with it.

Mr. MURPHY. That's disturbing, too. In your testimony, Mr. Conlon, you also observed that malaria and yellow fever, both mosquito-borne diseases were once quite prevalent, but that today they no longer claim victims due to the efforts of the Organized Mosquito Control Agencies. How is this accomplished? And the infrastructure given is pretty disjointed. How can we improve that?

Mr. CONLON. Well, as Dr. Hotez mentioned, there are many places in the United States that do have socioeconomic conditions that are conducive to the spread of these types of diseases. Those conditions were quite evident back in the past in places like Norfolk, places like Louisiana, all throughout Louisiana. There were a number of different areas that these got transmitted. Dengue fever was first discovered in Philadelphia, Pennsylvania, so we should not rely upon the south to be the potential breeding ground for these things, but anywhere that poverty occurs where you've got difficulties in trash removal, you've got certain socioeconomic conditions conducive to keeping water containers inside. Those can really hurt.

I want to emphasize, though, that mosquito control is conducted on an integrated basis and we should not think that there is any silver bullet for this. We've got to utilize all the tools that are at our disposal in order to keep these diseases from establishing. We need a number of different modalities.

Mr. MURPHY. Thank you. I'm out of time. Now turn to Ms. Castor for 5 minutes.

Ms. CASTOR. Thank you. Well, thank you all very much. In addition to the previous panel, you all have really given everyone a wake-up call about what has to be done. And I'm more convinced than ever that we've got to move this supplemental appropriation, and it can't get bogged down in the typical congressional budget battles. We need to move it as quickly as possible.

And, Dr. Gostin, I wanted to thank you for emphasizing the moral imperative for the Congress to act quickly. And Dr. Hotez, I think you're absolutely right to raise the issue of Haiti right now and the consequences because there hasn't been much discussion about Haiti. And I think they are particularly at risk. I think we can do better in mobilizing the international aid community and religious community that have so many initiatives there.

I want to focus back on pregnant women because it appears that the impact and the connection to microcephaly came as something of an unwelcomed surprise. Dr. Sheffield, you've been very involved in drafting the guidelines for the CDC, the Society of Maternal-Fetal Medicine, and ACOG. Can you go into greater detail on the science and what we know?

Dr. SHEFFIELD. So when the guidelines were first drafted—very soon after the reports initially came out about the microcephaly, they called a group of people together, and we freely admitted—I was not a Zika expert at the time. I knew very little actually about the Zika virus infection. However, the group of us had done a lot of work over the years with other infections and how it affects pregnancy, such as cytomegalovirus, and so the group of us that came together at the request of the CDC kind of looked at what data was available to us with the understanding of what happens with other viruses, and drafted just the original, the initial guidelines, which have subsequently been updated every time new data comes out. But the guidelines initially, if you look back a couple of months ago when they first came out, they were essentially screen everybody that traveled, and we talked a little bit about how to screen, the diagnostic tools that we've already talked about earlier today, and then ultrasound looking for actual fetal abnormalities, particularly in the head.

Ms. CASTOR. What's going on here? With other infectious diseases in maternal health, what—are there any other diseases where we've seen similar impacts to the fetus or child that would develop microcephaly?

Dr. SHEFFIELD. This virus is fascinating because this virus is very neurotropic. It likes the brain, it likes the fetal brain and nervous tissue obviously in adults since we're talking about Guillain-Barre AE1 Syndrome, but it is very neurotropic. There aren't a lot of other viruses that affect the developing fetus that is so specific to the nervous system, or to the brain. There are other viruses such as rubella, one of the most devastating viruses out there that cause multiple fetal abnormalities, but it causes abnormalities in multiple different systems. Same with some of the other viruses and parasites that will affect a pregnant woman. This one so far has been very, very focused on brain and neurologic abnormalities.

Ms. CASTOR. OK. So we're going to need extensive research on all that, and that is just starting. Is that right?

Dr. SHEFFIELD. Absolutely.

Ms. CASTOR. Is that how you would characterize it? So let's drill down on the recommendations for maternal health. Because in the Western Hemisphere, as Dr. Hotez says, we are so interconnected, Florida to Brazil, and Latin America and Colombia, and Puerto Rico, to Mexico, to Haiti. It's just millions and millions of families,

travelers where you're just not going to be able to talk about travel bans of things like that, so you've got to give folks the most constructive recommendations. So talk about citizens of the U.S. and Puerto Rico, what you're advising them right now if they are of childbearing age and intend to get pregnant?

Dr. SHEFFIELD. So right now myself as I'm sitting across the table from one of my pregnant women that is considering traveling and my colleagues across the country are all pretty much following the ACOG, SMFM, and CDC guidelines, which is if you have a pregnant woman that is interested in traveling to a Zika affected area currently we, one, recommend against it. If they do have to travel there is excellent education out there about prevention of mosquito bites because if they do travel, it all becomes prevention because, again, there is no treatment, and there's no vaccine currently available. So for right now it is prevention. So we spend a lot of time if they do have to travel talking about preventative measures, and there again is a lot of information on the CDC Web site for that.

We also, if they come back from travel, and this is where a lot of my patients are coming in, as two months ago they never heard of Zika virus. They've all traveled down to an affected area and they're coming back suddenly in a panic after seeing everything that's happened. And those are the ones where we have testing available. Again, not perfect as we've heard, but it's what we have available, and then ultrasound or evaluation.

Ms. CASTOR. Could you name those specific areas so that we have that?

Dr. SHEFFIELD. The specific areas for the evaluation?

Ms. CASTOR. The travel to.

Dr. SHEFFIELD. Oh, travel to. So the CDC has a linked Web site of travel notice, and they keep updating it. Every time a new country or a new territory comes up, they update that list. Last I saw it was about 30 or so countries and territories, and it's online. It's very easily accessible, and actually we update it for our clinicians. We have the link right there in clinic. They click on it, they pull it up, and they're able to say OK, where did you travel? All right, you're on the list.

Ms. CASTOR. But Brazil.

Dr. SHEFFIELD. Brazil, Colombia, Puerto Rico, though Cuba is not on it, we actually have tested one patient that's traveled from Cuba, so we're talking about the Caribbean.

Ms. CASTOR. And it's not going to be a static list. That list is going to change.

Dr. SHEFFIELD. No, it is frequently. It's actually frequently updated as new countries are reporting.

Ms. CASTOR. Thank you.

Mr. MURPHY. Thank you. Yes, that list is available on CDC's Web site. It's quite extensive, throughout the Caribbean, Central America, South America, Mexico. Other issues coming up, too, for the summer Olympics, as well.

Mr. Collins, you're recognized for 5 minutes.

Mr. COLLINS. Thank you, Mr. Chairman. I want to thank the panel as well. Maybe following up on Ms. Castor's comments.

I think what a lot of us are worried about is there is no vaccine, and if somebody does test positive there's no treatment, and it's somewhat disturbing but Dr. Sheffield, that some women would even choose to terminate the pregnancy. But picking up on that, education to me, because we're not going to have a vaccine tomorrow or next week, and we'll have better diagnostics before we're going to have vaccines and treatments. So I'm thinking education, guidelines, pamphlet, with a sense of urgency into the physicians' offices. I don't know how many typical doctors right now have this information in their waiting room, but a lot of times we think we're invincible, from what I'm hearing. So a couple of questions: do we have even an idea, a 25-year old woman who—she's got 15 years or longer to be in her childbearing years. How long if she's infected, so she gets the Zika virus, she's not pregnant. She waits X period of time. Is that 1 year, 2 years, 10 years, never? Do we have any idea?

Dr. SHEFFIELD. So right now the guidance is if you travel to an area you're not pregnant, we're recommending people wait at least 4 weeks. The reason for that is the incubation period is about up to 2 weeks. The viremic time period where the virus can cross to the placenta and then to the fetus is somewhere around 7 to 10 days.

Mr. COLLINS. Yes, but what I'm getting at is, OK, she's tested positive. She's not pregnant. How long would a woman who knows she's had the Zika virus, she was infected. Should she wait to consider having children? Is it never, or is it 1 or 2 years? Do we have any guidelines in that area?

Dr. SHEFFIELD. We don't. Right now we're saying about four weeks, but that is based on, again, very, very limited data. That's where we desperately need information coming out of Brazil, and Colombia, and some of the U.S. studies that are—

Dr. HOTEZ. It'll be important to determine if Zika is going by the same play book as something like dengue where the virus is in your system for a couple of weeks, and then it's gone. And that's probably the likely scenario. There is evidence that, for instance, West Nile virus can sometimes persist in the kidneys for periods of months or years, but that appears to be an exception—

Mr. COLLINS. So even though someone may be antibody positive, the virus, like you're saying with dengue, has cleared the bloodstream. You're saying then at that point it's to the best of your knowledge they would no longer be infecting a fetus?

Dr. SHEFFIELD. To the best of our knowledge, yes.

Dr. HOTEZ. Right.

Mr. COLLINS. That's very good news, actually, if there's such a thing as good news here.

Dr. HOTEZ. It's about the only good news about this virus.

Mr. COLLINS. Yes. But if it clears, which is the difference in HIV and some others, because it doesn't clear. Yes, sir?

Mr. GOSTIN. The other thing to consider is for women who are considering getting pregnant but are not pregnant now, what we tell them, because they won't necessarily go to their physician's office. That's why, in addition to education in the doctor's office, I think we need to do public health information campaigns to advise young women about what their risks are so that they can make

well-informed decisions. And this is particularly important with the Rio Olympics that are looming, because although it will be the Southern Hemisphere's winter, there still will be active transmission. And they'll be coming then to the northern height of the summer where we could then see local transmissions here. So those are all kinds of things to consider in addition to the fact that, as you've all said, you have so much interchange between Puerto Rico, other U.S. territories.

Mr. COLLINS. So if there is one absolute, I'm assuming the one absolute is a pregnant woman should not travel to those areas, because you're saying they could be third trimester and we don't know. So would that at least be a fair absolute; you're pregnant. You just stay away?

Dr. SHEFFIELD. I'm a physician. We never deal in absolute—

Mr. COLLINS. Well, sometimes you need absolutes.

Dr. SHEFFIELD. But we do strongly recommend they not travel.

Dr. HOTEZ. The problem will come and what happens in the summer when the Gulf Coast of Texas or Florida becomes an area included in the travel ban zone, and then we're going to—

Mr. COLLINS. That would be a nightmare.

Dr. HOTEZ. That would be a nightmare.

Mr. COLLINS. Total nightmare.

Dr. HOTEZ. That's a real—

Mr. COLLINS. But thank you for your testimony. This education is absolutely critical for us, as well as the public. And I want to thank the Chairman for holding this hearing, and thank the witnesses for your testimony. I yield back.

Mr. MURPHY. Thank you. Ms. Castor, going to recognize you for an additional couple of minutes here, 5 minutes.

Ms. CASTOR. Thank you very much.

In some of the countries experiencing outbreaks many do not have access to primary health services; that means limited access to family planning, as well. Dr. Hotez, it's fairly plain but would you explain to everyone why it is in the best interest of Americans and American families that we tackle the disease in Brazil, and in Puerto Rico, and other places in the Western Hemisphere?

Dr. HOTEZ. Well, thank you for that question. I think what's becoming clear is the Gulf Coast of the United States is part of the same eco-zone that the Caribbean and Central America is. There's a homogeneity there, especially in our impoverished areas. I can take you through parts of the Fifth Ward of Houston and you might think you're in Port Au Prince or Tegucigalpa, and so we have to realize that what is happening in Haiti and in Central America is the same vulnerability as the Gulf Coast, and take that accordingly.

Ms. CASTOR. Dr. Gostin.

Mr. GOSTIN. Yes. It's a very good, actually, because one of the things we've learned with SARS, with Ebola, with so many novel infectious diseases, and it's more true, or at least as much true with Zika is that we can't just be defensive in the United States. You actually have to go to the source of the infection; that, in other words, to protect ourselves we also need to protect the people and the ecosystem, and the mosquito population.

Ms. CASTOR. So what should we be doing, what should the U.S. be doing to insure that women in these countries have access to family planning services during this crisis?

Mr. GOSTIN. Well, I believe that for health reasons and for moral reasons we should encourage it. There are particular countries that have told women not to become pregnant for a year, 2 years, and more. And as Pope Francis said, we need to give them the tools to be able to achieve that goal. And, of course, if they do have infants, then we need to give the mother maternal health care, we need to give the child services. I think it's very important. And, of course, it's important in Puerto Rico because Puerto Rico is going through a major financial crisis, bankruptcies. Its Medicaid system is in shambles. And part of the President's appropriation request is to support that and it seems to me that as a territory of the United States it's very important. But also because of the interchange of travel between people in Puerto Rico and the United States.

Ms. CASTOR. Dr. Sheffield, give us the practical advice of doctor to patient you would give on family planning in the impacted areas.

Dr. SHEFFIELD. So practically speaking, I am an advocate of providing effective contraception in order to, as you mentioned, provide a tool to prevent pregnancy if the woman so desires, if she does have to travel to Zika-affected areas. So if I have a woman that is not pregnant and is not interested in becoming pregnant in the near future, we do talk contraception, particularly if she is traveling down to Zika-affected areas.

Ms. CASTOR. And then there's also been the discovery that Zika also poses a risk through sexual transmission, so it's not just women. We must also target communications and resources to men who may carry and spread the Zika virus. Dr. Sheffield, what guidance would you offer to men traveling to areas with active Zika transmission?

Dr. SHEFFIELD. So this has kind of thrown a wrench in it in our discussions over the last month or so. Now that sexual transmission has been confirmed and we are discovering more and more cases of sexual transmission, again all of them so far have been male to female transmission as was mentioned earlier. Our counseling right now is if you are a male who has a pregnant female partner, when you come back from travel from a Zika-affected area use condoms or actually abstain from sexual practice; however, if you don't abstain, use condoms. And we're using the word, consistently and correctly use the condoms, and trying to prevent transmission. It may not be 100 percent unless it's true abstinence, but it at least provides some protection.

Ms. CASTOR. It's a very important message for the millions, and millions, and millions of our neighbors who travel across the Americas and in the Western Hemisphere, so thank you all very much for your testimony today.

Mr. MURPHY. Thank you. I want to follow up with a couple of questions, as well. First of all, with regard to this you're recommending, obviously, abstain from travel, abstain from other contact here. Does anyone know if airlines, and cruise ships, and travel agents are spreading that word, as well? Professor Gostin?

Mr. GOSTIN. They have not yet, but what we saw with Ebola was that even before governments were implementing policies, the airline industry was doing that. This is a major financial issue for the industry, as well, particularly again because of the large travel to the Olympics and others, people canceling their flights, so I think it's very important for the United States Government and other governments to work with the airline industry to make sure that they follow the best public health advice.

Mr. MURPHY. Certainly advise that. Mr. Conlon, with regard to this, many times people travel to areas and then go to a resort area. One would assume that there would be some different sort of vector control there versus another part of the community. Do you have any advice on that?

Mr. CONLON. In places in the Caribbean that do have vector control capabilities in the resort areas, it tends to be rather problematic, even more so than in the United States. I would recommend that people, and particularly males that are going into this area, utilize EPA registered repellants. They do work against all these mosquitoes, and they just need to follow label recommendations. But I would caution everyone to make sure they're EPA registered. There's a lot of mosquito repellant products out there that have rather iffy data sets supporting them, so EPA has taken into consideration that they're safe to use and they're effective at least four hours when utilized properly. What you do is you reduce human mosquito contact, no problem with the disease.

Mr. MURPHY. So it isn't just the matter of looking at what islands and countries to avoid, but it doesn't necessarily give me confidence that even if it is a four or five star resort that they necessarily have full vector control. And if you still go there, to use some sort of mosquito repellant, so there's multiple levels.

Mr. CONLON. Absolutely. And I would also say that if you're going to a resort that's got an 18-story hotel you can find *Aedes aegypti* at 18 stories. They go up through the elevator shafts.

Mr. MURPHY. OK. In your testimony you also noted the American Mosquito Control Association is currently developing guidelines specifically geared towards *aegypti* and *albopictus*. What will these guidelines focus on, and when will they be ready, and how do you see them being put to use?

Mr. CONLON. Well, hopefully, we're going to get them ready by about April, but one can never know when you're talking about dealing with volunteers. We're specifically going to try to shift our control paradigms and our recommendations from reactive, which is oftentimes larvicide. Larvicide are not going to be the answer with this mosquito, primarily because we generally use larvicide because the larvae are contained in a small area, they're easy to get at, they're easy to kill, and then they spread out as adults, and make it difficult for us to deal with them with regard to adulticides. In the case of this mosquito, though, larvicide are not going to be the answer because they're occurring in the same area where the adults are, so you might as well kill the adults in addition to. So we're going to focus more on the adulticide issues, we're going to focus more on trying to get community support, elicit community support to get rid of the habitat. This is a human problem. This not necessarily an *Aedes aegypti* problem. We're creating the

problem, and we need to be conversant in creating the solution, as well.

Mr. MURPHY. All right, thank you. Dr. Sheffield, what do we know currently about the risk of a Zika infection passing from an asymptomatic mother to a child during pregnancy? It can still happen?

Dr. SHEFFIELD. We think it can. There haven't been excellent documented cases yet of an asymptomatic mother passing to an infant, or passing to her fetus. That being said, we are assuming that it could happen, and so the recommendations are the same whether you're symptomatic or asymptomatic.

Mr. MURPHY. And, again, that's something the OB and the pediatricians should always in screening questions, where have you been? So how frequently should pregnant women who could have had an asymptomatic Zika infection be tested for the virus?

Dr. SHEFFIELD. So right now when a pregnant woman comes back from a Zika-affected area, we're doing the initial test. We're doing the PCR, RT-PCR if she is symptomatic. If she is asymptomatic, we are doing the IGM and the plaque-reducing neutralizing antibody test. If that is negative, we still are following up the fetus with serial ultrasounds. If the ultrasound becomes abnormal, we will retest a mother that initially tested negative, and we will offer amniocentesis to test the fetus, also.

Mr. MURPHY. And do we have the capacity to handle all those tests?

Dr. SHEFFIELD. Right now we have not been turned down on a test. Maryland actually is able to do the test. It's the one of the states that's able to do the test. However, when we start rolling this out to all 50 states, I think that is a large question, is if every pregnant woman who travels needs to be tested at least once, do we have the capacity? And then you start looking at the asymptomatic, or the symptomatic men and testing. I think that is a concern.

Mr. MURPHY. Is it possible also for the Zika virus to be transmitted through a breast-feeding mother to her infant?

Dr. SHEFFIELD. So that's an excellent question. For breast-feeding mothers, so far they have found Zika RNA in the breast milk, so we know that at some point the virus has made it to the breast milk. That being said, there have been no cases of transmission from breast milk. There also have not been active virus identified from the breast milk, so we know that there's parts of virus there. That's why the PCR comes back positive. But as of right now we haven't found active virus in breast milk.

Mr. MURPHY. Well, I want to thank this panel and the previous panel. This is very sobering and, quite frankly, very frightening stories we have heard today about a very real nightmare of the spread of Zika virus. And we don't have the answers yet, we don't have the tests yet, we don't have the solutions, and I don't even think we know all the consequences yet of what this does to adults, to infants, and what we'll see in the future with children, whether it is those who have been affected in utero with the virus, or those who may have been affected during early childhood, because we don't know what that could do to the developing brain, as well. So we'll monitor this very closely.

We thank you and the other panelists for your information on this. So I'd like to thank the witnesses and the members who have attended today. Thank you, Ms. Castor, for stepping in here.

I remind all members they have 10 business days to submit questions for the record. I ask that the witnesses all agree to respond promptly to the questions. And with that, this hearing is adjourned. Thank you.

[Whereupon, at 12:56 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

PREPARED STATEMENT OF HON. FRED UPTON

Mr. Chairman, thank you for holding this hearing on the U.S. public health response to the Zika virus.

Since January, bipartisan committee staff has been examining our public health preparedness for Zika through meetings with federal agencies, state health departments, public laboratories, international organizations, experts in tropical diseases and mosquito control, as well as other key stakeholders.

While there has yet to be a confirmed case of mosquito-to-human Zika transmission across the 50 states, this may only be a matter of time. Meanwhile, we must confront the tragic incidence of microcephaly in babies born to women that acquired the infection from travel abroad. We must work diligently to reduce the chance of sexual transmission as well as contamination of the national blood supply.

Our understanding of the virus is growing by the day. However, there are still many questions that remain to be answered before we can be assured that we are doing our utmost to protect the American people from this and future pandemics. Of particular concern is the disorganization of mosquito control systems and the limited capacity for lab testing to diagnose Zika.

Zika is another example demonstrating the need for greater preparedness. Zika is one of the emerging biological threats that formed an important part of the inquiry of the Blue Ribbon Study Panel on Biodefense, discussed at a hearing before this Committee several weeks ago. The panel's findings should serve as an urgent reminder of the need to build capacity—and improve coordination—at all levels of government to address present and future public health crises, whether of manmade or natural origin.

The federal witnesses testifying before us this morning are uniquely positioned to discuss how the federal response to Zika has been formulated, expand upon the \$1.9 billion requested of Congress on February 22 under the emergency supplemental appropriation, and address how it builds upon the lessons learned from responses to past outbreaks, such as Ebola. Our GAO witness will add his preliminary observations on the contours of a successful domestic, regional, and global response, and our second panel will feature non-government perspectives that will assist us in identifying crucial questions for further study.

FRED UPTON, MICHIGAN
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

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April 4, 2016

Dr. Nicole Lurie
Assistant Secretary for Preparedness and Response
U.S. Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201

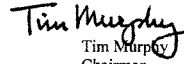
Dear Dr. Lurie:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Wednesday, March 2, 2016, to testify at the hearing entitled "Examining the U.S. Public Health Response to the Zika Virus."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Monday, April 18, 2016. Your responses should be mailed to Giulia Giannangeli, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to Giulia.Giannangeli@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary

Assistant Secretary for
Preparedness & Response
Washington, D.C. 20201

JUN 28 2018

The Honorable Tim Murphy
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
United States House of Representatives
Washington, D.C. 20515

Dear Chairman Murphy:

Thank you for the opportunity to testify before the Subcommittee on Oversight and Investigations on March 2, 2016. The Department of Health and Human Services (HHS) is committed to ensuring a resilient nation that is prepared for, can respond to, and recover from emerging threats, such as the Zika virus.

Since the early reports of the potential link between Zika virus and severe birth defects, the Administration and HHS have taken proactive and increasingly targeted action to protect the American people. I can assure you that my team, the Department, and our partners will continue our work to ensure that the United States is prepared for Zika. This includes delivering the latest guidance across the health care system through the Hospital Preparedness Program, coordinating medical countermeasures activities through the Public Health Emergency Medical Countermeasure Enterprise, and working with our federal partners to develop new Zika-specific vaccines.

I thank you again for the opportunity to address your questions. The safety and well-being of the American people is of the utmost importance and I look forward to continuing our work with you and the Committee towards this important goal.

With that in mind, I have enclosed a detailed response to the question presented for the record after the hearing concluded. If you have any additional questions, please do not hesitate to contact me at (202) 260-1158.

Sincerely,

Nicole Lurie, MD, MSPH

Enclosure

- **Is the Office of Refugee Resettlement screening unaccompanied alien children for Zika virus? If so, what are the procedures, including those for treatment and reporting, when a child tests positive for Zika virus? If not, why? Are there plans to develop a procedure?**

The Office of Refugee Resettlement (ORR) is committed to providing for the safety and well-being of unaccompanied children, as well as maintaining the health and safety of the communities in which these children live. ORR follows the Centers for Disease Control and Prevention (CDC) guidelines for prevention and control of communicable diseases, including Zika virus disease. Upon their arrival at ORR shelters, unaccompanied children receive a complete medical screening and vaccinations, if necessary, within 48 hours.

About one out of five persons infected with Zika virus become sick from it. The symptoms may include fever, a rash, joint pain, or conjunctivitis (red eyes), which the unaccompanied child would be examined for in the initial medical screening. Under ORR policy, and consistent with CDC guidelines, unaccompanied children exhibiting two or more Zika symptoms and who are from, or have traveled through, Central America, South America, the Caribbean, or Mexico in the past two weeks are examined by a health care professional and may be referred for Zika testing, in consultation with the health care provider.

ORR care providers also follow CDC guidance for the testing and care of women who might have been exposed to Zika virus during pregnancy. Testing is recommended for all pregnant unaccompanied children without symptoms, but who are from or traveled through areas with ongoing Zika virus transmission and are within 12 weeks of arrival in the United States. If a pregnant unaccompanied child tests positive for Zika exposure, additional prenatal care is provided consistent with CDC's guidelines.

There is no specific treatment for Zika virus. Supportive care, like rest, fluids, and use of medication to relieve pain and fever, may be used. Aspirin and other non-steroidal anti-inflammatory drugs should be avoided until Zika can be ruled out to reduce the risk of hemorrhage.

ORR requires care providers to protect any unaccompanied child who tests positive for Zika from further mosquito bites during his or her illness (~three weeks) to prevent local transmission. Protective measures are provided in accordance with CDC guidelines. Unaccompanied children who have been diagnosed with Zika virus will not be released from ORR care until their illness resolves. All ORR shelters have been directed to maintain active and aggressive mosquito control efforts consistent with the recommendations of their local vector control offices and in accordance with CDC guidance.

ORR is providing technical assistance on testing consistent with CDC guidelines; enforcing mosquito control activities at unaccompanied children shelters; providing direction to programs

regarding prevention of mosquito bites for all children and staff; developing a process to track pregnant UC and program compliance with Zika testing guidance for pregnant UC; developing an educational packet on how Zika is spread, including sexual transmission, and how to prevent it to provide to UC and their sponsors when they are released; and coordinating ORR's Zika efforts with the Assistant Secretary for Preparedness and Response (ASPR)-led HHS Zika response effort.

Zika is a nationally notifiable condition. Health care providers should report Zika virus disease cases to their state or local health department. State health departments then report cases to CDC following the standard reporting structure for nationally notifiable diseases. As an added layer of reporting, ORR shelters are required to alert ORR if a child has suspected or confirmed Zika virus disease; ORR will then notify the appropriate state health officials of cases diagnosed in their jurisdiction. ORR tracks diseases of public health significance diagnosed in unaccompanied children in ORR care, including Zika, and provides a monthly summary to federal and state public health partners.

FRED UPTON, MICHIGAN
CHAIRMAN

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House of Representatives
COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515-6115
Majority (202) 225-2927
Minority (202) 225-3641

April 4, 2016

Dr. Thomas R. Frieden
Director
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30333

Dear Dr. Frieden:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Wednesday, March 2, 2016, to testify at the hearing entitled "Examining the U.S. Public Health Response to the Zika Virus."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Monday, April 18, 2016. Your responses should be mailed to Giulia Giannangeli, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to Giulia.Giannangeli@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Tim Murphy

Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

Committee on Energy and Commerce – Subcommittee on Oversight and Investigations

CDC responses to QFR's asked following Dr. Thomas Frieden's testimony on March 2, 2016, "Examining the U.S. Public Health Response to the Zika Virus"

1. Please describe the process by which state and local public health departments can access funds from the Public Health Emergency Response grant for their Zika virus preparedness and response efforts.

CDC provides financial and technical resources to states and territories through our Public Health Emergency Preparedness (PHEP) cooperative agreements to strengthen their capacity to prepare for and respond to emerging threats like Zika virus. The PHEP cooperative agreement provides funding to public health departments across the nation to upgrade their ability to effectively respond to a range of public health threats, including infectious diseases, natural disasters, and biological, chemical, nuclear, and radiological events. The PHEP resources may be used to help health departments expand their capacity to prepare for cases of local Zika virus transmission in their areas. This includes Zika response planning, program management, and support activities including but not limited to emergency response coordination, community outreach, risk communications, coordinating response operations such as supporting the infrastructure needed to implement vector control, and outreach and training which target clinicians and other healthcare providers. CDC guidance allows PHEP awardees to use PHEP funds to provide public health emergency management and response support for potential Zika virus outbreaks in their jurisdictions.

2. Some preliminary analyses of previous Zika virus outbreaks are being cited as showing a positive correlation between Zika and microcephaly. Since dengue and chikungunya are arboviruses closely related to Zika, share similar symptoms and are co-circulating in South America, is it possible that dengue or chikungunya have similar effects during pregnancy? Is CDC undertaking similar analyses of historic dengue and chikungunya outbreaks and corresponding rates of microcephaly?

On April 13, 2016, CDC concluded that Zika virus is a cause of microcephaly and other severe fetal brain defects. To date, no studies of congenital dengue or chikungunya have shown a causal link between infection with these viruses and microcephaly or other severe fetal brain defects.

While chikungunya has some similarities to Zika virus, such as the same mosquito vectors and similar clinical features, the two viruses are not closely related genetically. However, Zika virus and dengue virus are more closely related genetically and also cross-react on diagnostic testing (e.g., serologic testing using blood serum),

making it very difficult to interpret test results in areas where both viruses have circulated. There have been prior investigations looking at congenital dengue and chikungunya infections, respectively, and their outcomes. Although some cases of severe infections, pregnancy losses, and neurocognitive defects have been noted in descriptive studies of groups with similar diagnosis published from areas with local transmission, findings have not been clinically similar or as frequent as those currently associated with the Zika virus outbreak.

3. The CDC has reported that the Zika virus can be transmitted through mosquito bites, from mother to child, through sexual contact, and through blood transfusion. How many cases of sexual transmission is the CDC aware of? Is Zika being treated like other blood-borne pathogens?

CDC has documented sexual transmission of Zika virus from males to their sexual partners. As of March 1, 2016, there were four confirmed cases of Zika acquired through sexual transmission in the continental U.S. Numbers are updated on [CDC's Zika webpage weekly](#).

CDC is currently working with partners including the American Association of Blood Banks, the American Red Cross, the U.S. Food and Drug Administration (FDA), state and territorial health departments, and blood collection centers to learn more about Zika and blood safety. On February 16, 2016, the FDA released [recommendations for donor screening and product management to reduce the risk of Zika transmission in the blood supply](#). FDA recommendations include information for areas with and without active Zika transmission, both for blood donors and blood donation centers.

4. It is estimated that the viremic period for Zika is 7 to 10 days – is this the only time that a human can transmit the virus? For those who test positive for Zika, what procedures are in place to prohibit further transmission? Are they placed in quarantine?

Based on current data, an infected individual can only transmit Zika virus to a mosquito during their viremic period (when the virus is circulated in the blood), as stated. However, sexual transmission has been documented and it is not clear how long an infected male would shed infectious virus in his semen. To prevent further Zika virus transmission:

- Symptomatic individuals with confirmed Zika virus infection, are advised to avoid mosquito bites for three weeks by adhering to prevention recommendations such as wearing long-sleeved shirts and long pants, using insect repellent, and using door and window screens to keep mosquitoes outside.
- Travelers returning to the United States from an area with Zika, are advised to avoid mosquito bites for three weeks by adhering to prevention recommendations such as wearing long-sleeved shirts and long pants, using insect repellent, and using door and window screens to keep mosquitoes outside.

- Persons with Zika virus infection and pregnant sexual partners should correctly and consistently use condoms during sex or abstain from it for the duration of the pregnancy.
- Returning travelers from areas with Zika should correctly and consistently use condoms during sex or abstain from it for at least 8 weeks if they never had symptoms of Zika infection, but for 6 months if they had any symptoms or laboratory evidence of infection.

The Zika virus is not transmitted by casual contact with infected people, therefore patients are not placed in quarantine.

5. **The 2016 Olympics are being hosted in Rio de Janeiro, Brazil this August. Brazil has seen the largest number of Zika cases during this outbreak. What plans are being put in place to protect the half-a-million athletes and spectators who will travel to Rio for the Olympics?**

Based on the scientific evidence available, CDC issued an Olympic Travel Notice Level 2 Alert in line with current guidance for pregnant women and their male partners to practice enhanced precautions to avoid Zika virus while traveling. CDC recognizes the importance of planning travel, and the Olympics represent a once-in-a-lifetime opportunity for most athletes, their families, guests, and attendees. CDC recommends that all travelers familiarize themselves with, and adhere to [CDC issued 2016 Summer Olympics guidance](#).

6. **You have previously stated that genetically modified mosquitos have been shown to successfully reduce the *Aedes aegypti* mosquito population by 90% in trials of up to 5,000 people. The technology has been tested in southern Brazil, Panama, the Cayman Islands, and Malaysia and has suppressed the *Aedes aegypti* mosquito population more than 90 percent. How is your agency assisting the company that developed this novel technology?**

CDC experts have talked with representatives of the company that developed this technology; however, CDC is not directly assisting them. The technology is awaiting approval by the FDA for use in a limited release in the Florida Keys. CDC and EPA have been working with FDA by providing subject matter expertise as they evaluate the application and environmental impact statements produced by the company. CDC provides assistance to companies through information sharing as a standard public health practice.

7. **In previous hearings, vector control has been described as “expensive and complicated.” From what I understand, that is not the case with regard to genetically engineered mosquitoes. Releasing mosquitoes out the window of a van seems easier than spraying insecticides door to door throughout a city. Have you reviewed the details of both the implementation and cost of genetically engineered mosquitoes? What are you doing to make this technology more affordable and accessible in the way that you are working to make vaccines and diagnostics more affordable and accessible? I ask this question because you have**

stated that in addition to the creation of diagnostics, the U.S. Public Health response will include both vaccine development and vector control.

An integrated approach using all vector control tools available today is needed. These tools may include immature and adult mosquito monitoring, as well as larval and adult mosquito control activities. In general, prevention or reduction of transmission of mosquito-borne viruses like dengue, Zika, and chikungunya is dependent on the control of mosquito vectors and limiting person-mosquito contact. Reduction of overall mosquito populations does not always translate into reduction of disease, however. While it is often used as a measure of success from an entomological standpoint we do not know if it reduction of mosquito population size is enough to suppress transmission of Zika virus. Studies in countries that have tested these strategies have yet to show that the technology has prevented or reduced cases, which is why the research community is continuing to pursue field trials to test which approaches can best prevent or reduce cases. Scaling up of facilities to mass rear mosquitoes will take several more months before there are enough mosquitos available to reduce populations, which will not protect pregnant women and the general public in the short term.

- 8. The President's emergency supplemental for the U.S. response to the Zika virus includes \$8 million in funding to the International Atomic Energy Agency in order to "implement sterile insect projects that help suppress mosquito populations." Why wouldn't the U.S. government want to direct all or part of this funding or even additional funding to a technology that is available today and that has already proven capable of suppressing the mosquito that carries viruses such as Zika and dengue?**

Currently, no single intervention has been shown to be effective for vector control. Research into these new technologies should include not just demonstrations that they reduce mosquito populations, but how they fit into integrated vector control strategies.

- 9. You stated that the issue of scalability, with regard to genetically modified mosquitoes, could be a challenge because the *Aedes aegypti* mosquitoes don't fly very far, therefore millions upon millions of GM mosquitoes may need to be released every short distance in order to reduce the *Aedes aegypti* mosquito population. You also said that this species of mosquito is tricky and that even when we've seen very large "knock downs" in mosquito population, CDC hasn't necessarily seen commensurate reductions in human infections. Could you elaborate on this? Have you talked directly to the company manufacturing the GM mosquitoes regarding these concerns and if not, would you be willing to do so in the near future?**

The metric usually used to measure reductions in mosquito populations, knock downs, has not been tied to reductions in human infections in part because the starting population density may vary greatly. Even at the peak of mosquito season, a reduction of 80% would still allow for there to be enough mosquitos in the

environment to sustain arbovirus transmission. Currently we do not know what level of suppression of a mosquito population is required for Zika virus transmission to be interrupted. Yes, CDC experts have talked with representatives of a company manufacturing the GM mosquitos and is open to the possibility of collaboration, especially if the technology is given FDA approval and further developed.

- 10. We know that abroad, some governments have instructed women to delay pregnancy, which is unacceptable without expanded reproductive health services. As the Zika outbreak continues to evolve, we are learning that the disease may be sexually transmitted as well. What specific education and prevention efforts, such as comprehensive sex education and access to contraception, are in place to ensure that Americans are aware of possible sexual transmission of the Zika virus and have access to information and services to make reproductive health choices?**

During this outbreak, information about Zika virus infection, its modes of transmission, and its effects on pregnancy and birth outcomes has rapidly evolved. Given the risks associated with maternal Zika infection, prevention is key for this response.

CDC has developed a suite of communication materials to increase awareness about sexual transmission of Zika virus and educate the public on prevention strategies, including web content and 1-pagers on [Zika and sexual transmission](#), [men with pregnant partners](#), and [information for pregnant women living in areas with Zika](#).

CDC has also developed a [preconception counseling tool](#), including a sample script and questions that healthcare providers can use when talking about pregnancy intentions to patients living in areas where Zika transmission is ongoing.

In addition, CDC developed [women's health profiles](#), which provide an overview of health services available in each state. Profiles include state specific women's health statistics, information on services available to women in each state for contraceptives and maternal health, and information on contraception and women's health partnerships and initiatives.

The expansive suite of Zika virus communication materials are available on [CDC's website](#) for individuals, healthcare providers, and state and local health departments to use and share amongst their friends, family members, and communities. Many of the documents are available in English and Spanish, in addition, a select number of documents have been translated into other languages such as Portuguese and Danish.

Zika virus infection in pregnancy is a cause of microcephaly and other severe fetal brain defects. A primary strategy to reduce Zika-related pregnancy complications and birth outcomes is to prevent unwanted pregnancy in women who want to delay or avoid pregnancy. Among pregnant women, prevention of Zika infection should

include avoidance of mosquito bites in areas of active transmission and precautions to prevent sexual transmission, including condom use or no sex during pregnancy with male partners who return from travel or have confirmed Zika infection.

CDC recognizes it is challenging for state and local health officials as well as individual health care providers to counsel the public about the risks of Zika virus and pregnancy. This is a rapidly changing situation and our understanding of the risks concerning Zika virus infection is incomplete and evolving. As the response evolves, and if localized transmission occurs, specific education and prevention initiatives that include comprehensive sex education or access to contraception would be addressed based on the scientific evidence.

FRED UPTON, MICHIGAN
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

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April 4, 2016

Dr. Anthony Fauci
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20892

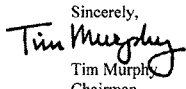
Dear Dr. Fauci:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Wednesday, March 2, 2016, to testify at the hearing entitled "Examining the U.S. Public Health Response to the Zika Virus."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

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Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

House Energy and Commerce Committee, Subcommittee on Oversight and Investigations
March 2, 2016 Hearing
Examining the U.S. Public Health Response to the Zika Virus
Questions for the Record

The Honorable Gus Bilirakis and The Honorable Morgan Griffith

1. You have previously stated that genetically modified mosquitoes have been shown to successfully reduce the *Aedes aegypti* mosquito population by 90% in trials of up to 5,000 people. The technology has been tested in southern Brazil, Panama, the Cayman Islands, and Malaysia and has suppressed the *Aedes aegypti* mosquito population more than 90 percent.
 - a. How is your agency assisting the company that developed this novel technology?

NIAID Response:

Oxitec, the company developing this technology, has briefed NIAID on the use of its self-limiting mosquito technology and the status of the controlled release studies in Brazil. This is one of several approaches currently under investigation for control of *Aedes aegypti*—a species of mosquito known to transmit human diseases such as Zika and dengue. NIAID is in discussions with Oxitec and other investigators pursuing a variety of novel approaches to vector control.

The Honorable Gus Bilirakis and The Honorable Morgan Griffith

2. In previous hearings, vector control has been described as "expensive and complicated." From what I understand, that is not the case with regard to genetically engineered mosquitoes. Releasing mosquitoes out the window of a van seems easier than spraying insecticides door to door throughout a city.
 - a. Have you reviewed the details of both the implementation and cost of genetically engineered mosquitoes? What are you doing to make this technology more affordable and accessible in the way that you are working to make vaccines and diagnostics more affordable and accessible? I ask this question because you have stated that in addition to the creation of diagnostics, the U.S. Public Health response will include both vaccine development and vector control.

NIAID Response:

NIAID is supporting the development of effective vector control strategies and has been in contact with a number of investigators pursuing this research. NIAID welcomes research applications related to vector control and will support meritorious projects as funding constraints allow. For information about implementation of vector control in State and local jurisdictions, you may wish to contact the Centers for Disease Control and Prevention. In addition, the Oxitec genetically engineered (GE) mosquito is subject to FDA regulation.

The Honorable Gus Bilirakis and The Honorable Morgan Griffith

3. The President's emergency supplemental for the U.S. response to the Zika virus includes \$8 million in funding to the International Atomic Energy Agency in order to "implement sterile insect projects that help suppress mosquito populations." Why wouldn't the U.S. government want to direct all or part of this funding or even additional funding to a technology that is available today and that has already

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Questions for the Record
proven capable of suppressing the mosquito that carries viruses such as Zika and dengue?

NIAID Response:

The U.S. Government (USG) is assisting States and local jurisdictions in implementing established vector control methods. In addition, the USG is pursuing the development of improved and/or novel vector control strategies. Supporting the development of multiple vector control strategies provides flexibility should an individual technology not prove as successful when moving from a small scale field study to wider application. As part of this effort, NIAID is in contact with investigators pursuing a variety of novel approaches to vector control and will support meritorious vector control research as funding constraints allow. Some of this research may be subject to FDA regulation.

The Honorable Gus Bilirakis and The Honorable Morgan Griffith

- 4. In your testimony, you state that you and your staff are already talking to Oxitec, the company that produces genetically modified mosquitoes. That is good news. Please walk me through what are the next steps as far as those conversations are concerned.**

NIAID Response:

As noted in response to question number one, NIAID is discussing possible opportunities with Oxitec regarding their GE mosquitoes. Should Oxitec decide to submit a research application for NIAID funding, it would be considered through the NIH peer review process, which evaluates and rates the scientific and technical merit of applications. Peer review of applications submitted to the NIH takes place in multiple steps. The initial step of the peer review process takes place in Scientific Review Groups. The second level of peer review is carried out by the NIH National Advisory Councils, which are composed of scientists from the extramural research community and public representatives. More detailed information on the NIH peer review process can be found at http://grants.nih.gov/grants/peer_review_process.htm. In addition, NIAID is in contact with and welcomes research applications from other investigators pursuing novel vector control strategies. NIAID will support meritorious vector control research as funding constraints allow, subject to regulatory requirements of other agencies.

The Honorable Gus Bilirakis and The Honorable Morgan Griffith

- 5. What type of follow up are you having with Oxitec to address your questions and concerns regarding the scalability of a project that would launch genetically modified mosquitoes? Why do you believe that scalability is going to be a "major problem?" You also said that "you don't want to scale up unless you know it works." Have you had discussions with Oxitec regarding its data on projects taking place outside of the US which indicate very positive outcomes in decreasing the *Aedes aegypti* mosquito population?**

NIAID Response:

Oxitec has briefed NIAID on the use of its self-limiting mosquito technology and the status of the controlled release studies in Brazil. It is important to note that to be effective, scale up of the

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release of GE mosquitoes is essential to cover the large areas needed to control the current epidemic. Since each release of Oxitec's GE mosquitoes only covers small areas and lasts a limited period of time, scale up is an important consideration due to the requirement for repeated releases at multiple time points and in multiple geographic areas. Furthermore, the speed with which GE mosquitoes would result in mosquito control over large areas may not be fast enough to stop the current Zika virus epidemic. The FDA's Center for Veterinary Medicine is currently reviewing information in an investigational new animal drug (INAD) file from Oxitec, Ltd. The company is seeking to conduct an open release field trial of their GE mosquitoes in Key Haven, Florida.

Successful control of mosquitoes will require a multi-pronged approach suitable to the particulars of each geographic area. Moreover, GE mosquitoes, or any other novel vector intervention, should be used in concurrence with established vector control approaches (e.g., insecticides, repellents, and destruction of breeding sites). In addition to the discussions with Oxitec, NIAID has been in contact with other investigators pursuing a variety of novel approaches to vector control.

FRED UPTON, MICHIGAN
CHAIRMAN

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RANKING MEMBER

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April 4, 2016

Dr. Luciana Borio
Assistant Commissioner for Counterterrorism Policy
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Borio:

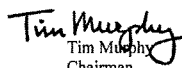
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Sincerely,


Tim Murphy

Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

AUG 26 2016

The Honorable Tim Murphy
Chairman
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

Dear Mr. Chairman:

Thank you for providing the opportunity for Dr. Luciana Borio, M.D., to testify at the March 2, 2016, hearing to discuss the U.S. Food and Drug Administration's response to the Zika virus. This letter provides responses for the record to questions posed by Members of the Committee.

If you have further questions, please let us know.

Sincerely,

A handwritten signature in cursive script, appearing to read "Dayle M. Cristinzio".

for Dayle Cristinzio
Acting Associate Commissioner
for Legislation

cc: The Honorable Diana DeGette
Ranking Member
Subcommittee on Oversight and Investigations
Committee on Energy & Commerce

Page 2 – The Honorable Tim Murphy

We have restated your questions below in bold, followed by our responses.

The Honorable Michael C. Burgess, M.D.

1. **On March 2, 2016, FDA warned two Texas hospitals, Texas Children's and Houston Methodist that their lab-developed tests to detect the Zika virus were being offered without premarket clearance, approval, or Emergency Use Authorization. What factors led FDA to take this step? What specific legal authority does FDA have to regulate laboratory-developed tests offered within a laboratory?**

Laboratory developed tests (LDTs) are a subset of in vitro diagnostic (IVD) devices that are intended for clinical use and are designed, manufactured, and used within a single laboratory. Patients, as well as their physicians, depend on the Food and Drug Administration (FDA or the Agency) to assure that the tests they use to make medical decisions are accurate, reliable, and clinically meaningful. FDA has had the authority to regulate in vitro diagnostics, including laboratory developed tests, since the Medical Device Amendments of 1976 were signed into law.

In public health emergencies, accurate and reliable tests are needed for the appropriate management of patients and for the public health community to take appropriate actions to prevent the spread of disease, mitigate its impact, and optimally allocate resources. Inaccurate and unreliable tests not only have the potential to result in harm to the patient tested, but may also have an impact on public health decisions and allocation of resources. Access to accurate and reliable tests is especially critical in the case of the Zika virus because, although most infected people experience either no or mild clinical symptoms, there have been reports of possible links between Zika virus infection and neurological complications (e.g., Guillain-Barré Syndrome). Moreover, the Centers for Disease Control and Prevention (CDC) recently established that Zika virus infection in pregnant women may lead to fetal brain damage, microcephaly, and other poor pregnancy outcomes. Thus, Zika tests may be used to guide the clinical management of pregnant women, and false results may present significant risks or even lead pregnant women to consider terminating an otherwise healthy pregnancy. It is essential, then, that IVDs for Zika virus provide accurate and reliable results.

Given the serious public health impact of the Zika virus, the Secretary of Health and Human Services (HHS) has declared that circumstances exist to justify authorization of emergency use of in vitro diagnostics for Zika virus, allowing FDA to use the Emergency Use Authorization (EUA) process for expedited authorization of in vitro diagnostics. EUA authority allows FDA to authorize the emergency use of certain unapproved medical products (or certain unapproved uses of an FDA-approved medical product) for certain emergency circumstances. FDA works interactively with developers to expedite the completion of their EUA submission. In past emergencies, such as the 2009 H1N1 influenza pandemic and 2014 Ebola epidemic, FDA demonstrated that it can quickly assess and authorize accurate in vitro diagnostic tests within as little as one to two days of receiving a complete EUA application.

FDA has authorized the use of two Zika virus diagnostic tests developed by CDC under its EUA authority. One of the tests (for which the EUA was issued on March 17, 2016) can diagnose acute infection, and the other test (for which the EUA was issued on February 26, 2016) can assess whether individuals, including pregnant women, who were potentially exposed to Zika

Page 3 – The Honorable Tim Murphy

virus were actually infected.

Since issuing the EUAs for the CDC tests, FDA has authorized the emergency use of seven commercial tests to diagnose active Zika virus infection. For more information on diagnostic tests for Zika virus available under EUA, see <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496>.

Recently, several developers announced they would be making their LDTs for Zika virus available to patients. In response, FDA requested that the developers submit information about their tests to help the agency better understand their design, validation, and performance characteristics. As expected, some developers encountered significant challenges to validate their tests. As discussed above, in public health emergencies, accurate and reliable tests are crucial not only for the appropriate management of patients but also for the public health community to take appropriate actions to prevent the spread of disease, mitigate its impact, and decide what resources need to be used. FDA recognizes the need for expanding laboratory testing capacity for Zika, and encourages laboratories to develop Zika IVDs and submit EUA requests for those IVDs to FDA.

The Honorable Frank Pallone, Jr.

The FDA is responsible for the review and approval of the medical products needed to diagnose, treat, and combat the spread of Zika. Access to diagnostic tests will be critical to helping to identify patients with Zika virus infections. Recently, FDA issued an Emergency Use Authorization for the use of a diagnostic test developed by CDC to detect Zika virus antibodies in individuals; however, a commercial diagnostic test is still not available.

1. How is FDA working with the public and private sectors to encourage and support diagnostic development as a part of the Zika response?

Developers of infectious disease tests, CDC, and FDA have a successful history of working together to ensure that diagnostic needs are met in public health emergencies, and are continuing to do so during the current Zika emergency. To date, FDA has authorized the emergency use of two Zika virus diagnostic tests developed by CDC as well as seven diagnostic tests for Zika virus developed by commercial developers under its Emergency Use Authorization (EUA) authority.

Early on, FDA began reaching out to manufacturers that were in a position to develop Zika diagnostic tests to determine interest, and to begin to assess barriers to development. As was the case in past emergencies, access to samples appears to be the main barrier to proper test development and validation by sponsors. The Office of the Assistant Secretary for Preparedness and Response (ASPR) is leading the HHS Sample Sharing Working Group, engaging FDA and others across HHS and other federal agencies to identify domestic and international sources of Zika-positive clinical specimens (serum and plasma) to support development and validation of commercial serological and molecular diagnostics. FDA has also communicated with CDC, the Biomedical Advanced Research and Development Authority (BARDA), and the World Health Organization (WHO), among others, to determine which tests need to be developed, which developers are in the best position to develop them, and what are likely to be the unmet needs in this area. Early interactions during an emergency are meant to make sure communications and

expectations are clear and allow everyone to proceed as efficiently as possible. To facilitate an expedited premarket review of Zika virus diagnostic devices for EUA, FDA developed draft interactive review templates that outline the minimum recommendations for analytical and clinical validation studies needed to support an EUA request. Currently, FDA has templates that outline the validation studies required to support molecular-based assays and IgM serological assays for Zika diagnostic devices. Any developer interested in pursuing a Zika diagnostic device can request these FDA templates via email to CDRH-ZIKA-Templates@fda.hhs.gov. These templates, and the review expectations, have also been shared with WHO as it certifies what tests are properly validated for use outside the U.S. FDA works interactively with developers to expedite the completion of their EUA submission. Additionally, to help Zika diagnostic manufacturers assess traceability¹ of their tests (a requirement for an EUA), FDA has created a bank of nucleic acid Zika virus reference materials for validating IVDs, the FDA Zika Virus Reference Materials² for nucleic acid test (NAT)-based IVD devices, available upon request to Zika device developers who have a pre-EUA submission with the agency and have established the analytical and clinical performance of their assay.

2. The President's emergency funding request for Zika includes \$10 million for FDA to support diagnostic development and review, as well as post-market surveillance. How will the agency use this funding to support diagnostics?

The \$10 million request for FDA will be used to: (1) support highly targeted regulatory science research required for the efficient development and regulatory review of medical products and blood screening assays for Zika virus disease (\$3.6 million); (2) support collaboration with, and provide technical support to, international partners (\$0.1 million); and (3) sustain additional staff and capacity to support the development, review, regulation, and surveillance of medical products to address emerging infectious diseases (\$6.3 million).

With respect to diagnostic tests, this funding will enable FDA to facilitate the development of safe and effective medical devices necessary to support Zika virus response, including blood donor screening tests and clinical diagnostic tests that may be useful for identifying the presence of, or prior exposure to, Zika virus. This support includes working interactively with diagnostic manufacturers interested in developing diagnostic tests for Zika virus to help accelerate development programs, including clarifying data requirements for the authorization of the use of Zika diagnostic tests under FDA's EUA authority.

In addition, the funding will support highly-targeted regulatory science research that is necessary to support the development of diagnostic tests, including:

- Expanding the FDA-Database for Regulatory Grade Microbial Sequences (ARGOS) database of regulatory-grade sequence information. The database will be expanded to include Zika viruses from the current outbreak, along with viruses that may be confused with Zika, to support NAT-based diagnostic assay development.

¹ Traceability refers to tracing analytical sensitivity/reactivity back to a FDA recommended reference material.

² <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm494615.htm# panel>

- Production of a reference serology panel. The panel could be used by vaccine, therapeutic, and device manufacturers to qualify and validate their assays. Identifying unique Zika peptide sequences improves the specificity of serological assays. This can be used to reduce the incidence of 'false positive' results and reduce testing burden on public health diagnostic laboratories.
- Development of assays to identify Zika virus neutralizing antibodies. These assays would be useful for measuring the potency and efficacy of Zika vaccine candidates and immune globulin products in clinical trials.

Developing a vaccine is only part of the equation. We have to make sure that we have pharmaceutical companies interested in manufacturing and distributing the vaccine.

1. What preclinical and clinical data will be necessary to approve a vaccine, and in particular, what preclinical and clinical data will be necessary for a Zika vaccine to be used in pregnant women?

The availability of a vaccine against Zika virus is first dependent on preclinical data demonstrating that it is safe to proceed with clinical development. Clinical development of the product will need to include studies demonstrating that the vaccine is safe and effective in the anticipated target populations. Although data are extremely limited for Zika virus, the risk to the fetus of microcephaly (a birth defect that may be associated with Zika virus infection), and other anomalies in other viral illnesses appears greatest if a woman is infected during the first trimester of pregnancy. Therefore, a vaccine administered to women before pregnancy and to their sexual partners could be most helpful in preventing fetal complications potentially associated with Zika virus infection.

FDA anticipates testing of investigational vaccines for prevention of Zika infection will be conducted first on both men and women of reproductive age who are not pregnant. However, should there be a need to conduct clinical research in pregnant women, FDA will consider the best available science and make decisions that protect the welfare of research participants, including pregnant women and their fetuses. FDA stands ready to work with researchers, industry and our Federal partners to address this important need as quickly as possible, and is committed to helping expedite the development of vaccines and other medical countermeasures that may help mitigate this outbreak.

Vector control is one effective way to helping reduce the transmission of Zika. This may include insecticides or repellents, among other techniques. Genetically engineered mosquitoes have emerged as a new tool that may hold some promise in reducing the population of mosquitoes that carry Zika or dengue for example.

The World Health Organization has recommended that further field trials and risk assessments should be used to evaluate how GE mosquitoes may help to reduce disease transmission. FDA is the responsible agency in the United States in determining whether a field trial of GE mosquitoes could proceed.

1. What role does FDA see the GE mosquito playing in protecting the public health from

further spread of Zika?

Limiting the population of mosquitoes that are a vector of disease, including Zika, is one potential approach to controlling these types of human disease, and mosquito population control is a component of integrated vector management strategies currently in use in the United States.

FDA has completed its environmental review of a proposed field trial of the Oxitec, Ltd. genetically engineered (GE) mosquito in Key Haven, Florida. After considering thousands of public comments, FDA published a final environmental assessment and finding of no significant impact, which concludes that the proposed field trial will not have significant impacts on the environment. While FDA's actions do not mean that Oxitec's GE mosquitoes are approved for commercial use, they do enable the proposed field trial to proceed in Key Haven, Florida. It is now Oxitec's decision—together with its local partner, the Florida Keys Mosquito Control District—to determine whether and when to begin the proposed field trial.

The Brazilian National Biosafety Commission found this mosquito safe for use in Brazil in 2014 and in April, 2016, Oxitec received a special temporary registration from the National Health Surveillance Agency of Brazil (ANVISA). Open field trials have been conducted in several countries including Brazil, the Cayman Islands, Panama, and Malaysia.

To date, Oxitec, Ltd. has made entomological (mosquito population suppression) claims for its GE *Aedes aegypti* mosquito, and FDA's review was limited to those claims. Oxitec, Ltd. has not made epidemiological claims that are directly related to the suppression of diseases transmitted by *Aedes aegypti*, including Zika virus. Therefore, it is premature for FDA to comment as to whether the Oxitec, Ltd. mosquito could be used as part of a Zika response strategy.

There has been much discussion around the use of genetically engineered mosquitoes as one potential tool in combatting the spread of Zika. Genetically engineered animals are regulated under the new animal drug provisions of the Federal Food, Drug, and Cosmetic Act and the applicable new animal drug regulations issued by the agency. In the context of Zika, this would mean GE mosquitoes would be subject to the new animal drug provisions and regulations.

1. Why are GE animals regulated under the new animal drug provisions? How will the regulation of new animal drugs differ from the regulation of drugs and devices?

The Oxitec GE mosquito contains a new animal drug subject to FDA regulation because the inserted recombinant DNA construct is intended to "alter the structure or any function of . . . an animal" and, therefore, meets the definition of a "drug" in the Federal Food, Drug, and Cosmetic Act (FD&C Act).

Regulation of new animal drugs is similar to regulation of human drugs. In both cases, the Agency looks at safety and effectiveness of the product. For a GE animal this would include issues such as whether the inserted construct is capable of encoding the claimed functions, is stable in successive generations of the animal, and whether the construct in the genome of the animal achieves the claim that the sponsor is making (i.e. population suppression).

- 2. There has been interest in testing the use of GE mosquitoes as a way to prevent the spread of Zika. The company that has developed the GE mosquito, Oxitec, Ltd., has publicly stated that they have been in conversations with FDA about field tests and have submitted an Investigational New Animal Drug file to FDA. Can you provide the Committee with a general update regarding the status of the company's file?**

On August 5, 2016, FDA completed its environmental review of a proposed field trial of the Oxitec, Ltd. genetically engineered (GE) mosquito in Key Haven, Florida. After considering thousands of public comments, FDA published a final environmental assessment and finding of no significant impact, which concludes that the proposed field trial will not have significant impacts on the environment. While FDA's actions do not mean that Oxitec's GE mosquitoes are approved for commercial use, they do enable the proposed field trial to proceed in Key Haven, Florida. It is now Oxitec's decision—together with its local partner, the Florida Keys Mosquito Control District—to determine whether and when to begin the proposed field trial.

To date, Oxitec, Ltd. has made entomological (mosquito population suppression) claims for its GE *Aedes aegypti* mosquito, and FDA's review was limited to those claims. Oxitec, Ltd. has not made epidemiological claims that are directly related to the suppression of diseases transmitted by *Aedes aegypti*, including the Zika virus. Therefore, it is premature for FDA to comment as to whether the Oxitec, Ltd. mosquito could be used as part of a Zika response strategy. However, mosquito population control is a component of integrated vector management strategies currently in use in the United States. Limiting the population of mosquitoes that are a vector of disease, including Zika, is one potential approach to controlling these types of human disease.

FRED UPTON, MICHIGAN
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FOURTEENTH CONGRESS
Congress of the United States
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Minority (202) 225-3941

April 4, 2016

Dr. Peter J. Hotez
Dean
National School of Tropical Medicine
Texas Children's Hospital
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Houston, TX 77030

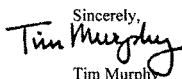
Dear Dr. Hotez:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Wednesday, March 2, 2016, to testify at the hearing entitled "Examining the U.S. Public Health Response to the Zika Virus."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Monday, April 18, 2016. Your responses should be mailed to Giulia Giannangeli, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to Giulia.Giannangeli@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment

**Responses by Peter Hotez, MD, PhD
to Questions for the Record of the March 2, 2016 Hearing
of the Subcommittee on Oversight and Investigations
of the House Committee on Energy and Commerce:
“Examining the U.S. Public Health Response to the Zika Virus”**

The Honorable Tim Murphy

Q: Now that the Zika Action Plan Summit on April 1, 2016 in Atlanta, GA has passed, do you have any additional concerns or issues that you would like to raise – and that you believe have not been adequately covered thus far – to improve the federal response to mosquito-borne illnesses?

A: Thank you Congressman Murphy for the question on the April 1 Zika Summit. I was not invited to attend the Summit but my understanding is that it represented an initial attempt to bring together state, county, and city public health agencies in order to begin a dialogue about Zika control. This is an important and necessary first step.

But for me, it's only the beginning. To my knowledge neither DHHS nor the US Public Health Service has developed a comprehensive plan for *Aedes aegypti* control in the affected/infested areas of the southern states, especially the Gulf Coast. Indeed, the track record of DHHS and USPHS is that they have not addressed *Ae aegypti* control for many decades, and in the past they have resisted efforts to move in that direction. A history of the absence of *Ae aegypti* efforts by the US Government was discussed in a sobering 1986 article (Slosek J. *Aedes aegypti* mosquitoes in the Americas: a review of their interactions with the human population. *Soc Sci Med.* 1986; 23(3):249-57). As a result the Gulf Coast has faced dengue and other arbovirus epidemics for decades, including a reported dengue outbreak in Houston in 2003 (Murray KO et al. Identification of dengue fever cases in Houston, Texas, with evidence of autochthonous transmission between 2003 and 2005. *Vector Borne Zoonotic Dis.* 2013 13(12):835-45).

Due to this inactivity, the CDC is essentially starting from scratch in addressing the Zika virus. Because the Gulf Coast and Florida are threatened by Zika virus infection (for reasons articulated in my February testimony), I would recommend immediate focus on the following:

- establishing an interagency initiative at the Federal level that includes CDC, EPA, and HUD, and possibly others, to comprehensively address the environmental clean-up and housing repair that will be required in impoverished neighborhoods on the Gulf Coast, in addition to focused insecticidal spraying and traditional public health efforts – the point here is that effective *Aedes* mosquito control may extend beyond the remit of the CDC/DHHS to involve other branches of government;
- developing a plan to coordinate and harmonize the state-county-city mosquito control authorities in the at-risk areas of the Gulf Coast together with waste-disposal and housing; and
- ensuring that federal activities are linked with state and county initiatives.

I have also testified before Congress previously on the need to establish centers of excellence for neglected tropical diseases (NTDs) to accelerate research and development of diagnostics, treatments and vaccines. This isn't a new concept: the National Institutes of Health has successfully created and

supported centers of excellence for rare diseases, for instance. Unfortunately, Zika and other tropical diseases are not rare, but like rare diseases they have historically struggled for attention and resources. The End Neglected Tropical Diseases Act (H.R. 1797) would authorize funding for NTD centers of excellence. This provision and others are awaiting action by the Energy & Commerce Committee, and I hope the Committee intends to approve the provisions in its jurisdiction as soon as possible.

The Honorable Joe Barton and the Honorable Michael C. Burgess, MD

Q: Dr. Hotez, an article that appeared in the *Houston Chronicle* on February 23, 2016, highlights the development of a hospital-based rapid test for the Zika virus by doctors at Texas Children's Hospital and Houston Methodist Hospital. Could you please tell the Committee more about how this test was developed and the benefits this test will have on diagnosing, tracking, and treating the Zika virus, as well as ensuring the public has relevant and timely information about the virus on an ongoing basis as we enter the warmer months? As a follow up, can the process you employed to quickly respond to this public health emergency be replicated to meet future threats in the same manner?

A: In responding to your question, I have consulted with James Versalovic, MD, PhD, the Pathologist-in-Chief at Texas Children's Hospital and Director of Texas Children's Microbiome Center. Dr. Versalovic also is the Vice Chair of Pathology & Immunology at Baylor College of Medicine.

The Department of Pathology at Texas Children's Hospital (TCH) and the Department of Pathology and Genomic Medicine at Houston Methodist Hospital collaborated on the initial development of the first hospital-based molecular tests for Zika virus. The collaborative science was then used by each institution's laboratory to design and make a test for use within each respective laboratory's hospital system. The new laboratory developed tests directly detect virus in blood, amniotic fluid and urine and provide results the same day testing is initiated. Results from these rapid tests (interpreted by a licensed professional) provide information to a pregnant woman who is at risk for the infection and consequently inform obstetrical management. The tests may also rapidly detect acute infection in adults or children with symptoms, thereby providing a firm diagnosis and avoiding unnecessary additional testing.

TCH, along with organizations like the Centers for Disease Control and Prevention, recognizes the need for a rapid detection test generally as a matter of preparation and to foster scientific understanding of the virus and its transmission. More rapid detection may facilitate real-time collection of information regarding transmission in regions of the United States infested with *Aedes* mosquitos and may prevent sexual transmission from an infected adult to an uninfected partner. In addition to efforts by individual institutions or companies, promoting meaningful scientific collaboration among leading research hospitals that leverage cutting-edge technologies within CLIA-certified laboratories staffed by highly trained laboratory personnel, can lead to efficient rapid test development as well as a roadmap for working together in acute circumstances that can be deployed to meet future threats.

The Honorable Marsha Blackburn

Q: In light of the Olympics later this summer, should Brazil be more aggressively deploying innovative solutions, such as genetically modified mosquitoes, to slow the spread of Zika virus?

A: This summer should present cooler and drier months in Brazil, and therefore a reduced risk of Zika transmission from *Ae aegypti* mosquitoes. I believe that if the Brazilians aggressively conduct traditional

Ae aegypti control methods, they could dramatically reduce the risk of Zika transmission. After all, through these approaches the Brazilians actually eradicated *Ae aegypti* and dengue/yellow fever during the 1950s and 1960s. Newer and innovative solutions such as genetically modified mosquitoes appear promising at small scales but they have not yet been proven to be effective at larger scales. Therefore, I suggest aggressively pursuing traditional methods while continuing to conduct tests on new methods at increasingly larger scales.

FRED UPTON, MICHIGAN
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FOURTEENTH CONGRESS
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Minority (202) 225-3641

April 4, 2016

Mr. Lawrence O. Gostin
Faculty Director, O'Neill Institute for National and Global Health Law
Georgetown University Law Center
600 New Jersey Avenue, N.W.
Washington, DC 20001

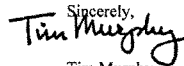
Dear Mr. Gostin:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Wednesday, March 2, 2016, to testify at the hearing entitled "Examining the U.S. Public Health Response to the Zika Virus."

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Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment



GEORGETOWN LAW

Lawrence O. Gostin

University Professor &
Professor of Global Health Law
Faculty Director, O'Neill Institute
for National and Global Health Law
Gostin@law.georgetown.edu

Attn: Giulia Giannangeli
Legislative Clerk, Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515
Giulia.Giannangeli@mail.house.gov

By post and email.

April 11th, 2016

Dear Ms Giannangeli,

Please find enclosed my responses to the additional questions for the record in relation to my oral testimony before the Subcommittee on Oversight and Investigations on Wednesday March 2nd, 2016 for the hearing "Examining the U.S. Public Health Response to the Zika Virus".

If you have any queries, please do not hesitate to contact me. On Wednesday, *JAMA* will publish on line a short article on United States Preparedness for Zika.¹ I will send you the PDF of that article on Wednesday to supplement my testimony and these answers to additional questions. The *JAMA* article can go on the record and be made public, as it is open access.

Sincerely

Lawrence O. Gostin

¹ Lawrence O. Gostin & James G. Hodge, Jr., Is the United States Prepared for a Major Zika Virus Outbreak? *Journal of the American Medical Association*, published on line April 13, 2016.

RESPONSES TO ADDITIONAL QUESTIONS FOR THE RECORD
RELATING TO TESTIMONY: “ZIKA VIRUS: THE GLOBAL AND UNITED STATES
DOMESTIC RESPONSE” (MARCH 2ND, 2016)

*Prepared for the
Subcommittee on Oversight and Investigations
U.S. House of Representatives*

Representative Tim Murphy, Pennsylvania
Chairman

April 11th, 2016

Lawrence O. Gostin, JD, LL.D (Hon.), Witness
University Professor and Faculty Director,
O'Neill Institute for National and Global Health Law

Alexandra L. Phelan, BBiomedSc/LL.B, LL.M
Adjunct Professor
O'Neill Institute for National and Global Health Law

The Honorable Tim Murphy

1. Now that the Zika Action Plan Summit on April 1, 2016 in Atlanta, GA has passed, do you have any additional concerns or issues that you would like to raise – and that you believe have not been adequately covered thus far – to improve the federal response to Zika?

There are worrying signs that the United States is unprepared to face the Zika response as a result of insufficient resourcing and variable legal authorities.¹ Scientific authorities now confirm a scientific consensus that the Zika virus causes neurological deficits including microcephaly and Guillain-Barré Syndrome. There is also a scientific consensus that it is highly likely that Zika outbreaks will occur this summer in the continental United States. Pregnant women, particularly those in lower socioeconomic status groups in the southern US are at heightened risk. Given that we know that Zika will affect the US population and that it has the potential to do harm to individuals and newborns, it would seem unacceptable not to fully fund preparedness efforts.

Insufficient Resourcing

The delay in approving President Obama's supplemental \$1.86 billion funding request is a serious public health and political mistake. Without this funding, United States health agencies will not have sufficient capacity for the necessary surveillance, vector abatement, and healthcare services needed immediately to prepare for the start of warmer weather and greater mosquito activity in the continental United States. Vaccine development may also be delayed, as the failure to pass the supplemental request may have economic implications with funding uncertainties threatening industry confidence in the viability of public-private partnerships vital to the development of Zika vaccines and diagnostic tests. Congress' hesitancy to act will have political repercussions if clusters of Zika infections this Summer are followed by avoidable cases of microcephaly nine months later. These delays have significant ethical, moral, political, and economic implications that Congress must not ignore.

The seriousness and immediacy of the situation was highlighted in the White House's temporary redirection of \$589 million from already allocated Ebola funds. These funds will

¹ Lawrence O. Gostin & James G. Hodge, Jr., Is the United States Prepared for a Major Zika Virus Outbreak? *Journal of the American Medical Association*, published online April 13, 2016.

go to critical Zika prevention measures including mosquito control, building lab capacity, and developing vaccines and diagnostic tests. However, this money is insufficient to adequately protect the United States from the Zika virus. Large funding gaps exist, with the CDC unable to fully fund state emergency preparedness grants, impeding the capacity of states' health officials to fully implement Zika preparedness and response plans. Without the supplementary Zika funding, the CDC has reportedly been forced to reprogram \$44.25 million for Zika preparedness and response that was previously allocated under the Public Health Emergency Preparedness Cooperative Agreement for states, territories and directly funded cities. This amounts to a 1-10% cut in the amount annually given to states under the preparedness agreement from July 1, 2016. These redirected funds are necessary to provide the direct technical and financial assistance to Puerto Rico and US Associated Pacific Islands now experiencing locally acquired Zika virus, as well as for the increased CDC internal operations necessary for a full United States response.

As outlined in my written testimony, while it may seem appealing to use money previously allocated to the Ebola outbreak, such a move risks making the United States more vulnerable to infectious disease threats. Failure to develop and secure health systems in developing countries – whether in West Africa or South America – risks the health, safety, and security of the United States. This is especially so with Ebola cases continuing to be reported in both Guinea and Liberia.²

Variable legal authorities

Mosquito vector control in the United States is primarily the legal authority of states and local governments, resulting in a considerable degree of variability in the resourcing, expertise, and power for vector control. While the federal government is not in a position to

² WHO, "New positive case of Ebola virus disease confirmed in Liberia" (April 1, 2016). Available at: <http://apps.who.int/ebola/current-situation/ebola-situation-report-30-march-2016>, Accessed: April 11, 2016. The latest Ebola Situation Reports can be accessed at: <http://apps.who.int/ebola/ebola-situation-reports>.

assert legal authority over states or local governments to conduct the necessary vector control programs, equipping federal health authorities with the funding necessary to offer financial and technical support to states is essential to promote the consistency needed for United States health security.

The Honorable Marsha Blackburn

- 1. In previous hearings, vector control has been described as “expensive and complicated.” Is vector control more complicated and more expensive than vaccine development?**

Preventing and responding to the Zika outbreak will require a multifaceted approach: one that includes strong vector control measures, as well as research and development into a vaccine. With sufficient funding, vector control measures can be implemented immediately, and while complexities exist, it is one of our primary methods of preventing the spread of Zika within the United States. It is true that the *Aedes* mosquito species most linked to Zika virus transmission is exceedingly difficult to control, however successful control efforts have been accomplished in the past, and we could significantly reduce the mosquito population today given sufficient resources and legal authorities. The development of a vaccine must be done in parallel however the outcomes are much less certain. Existing research into other vaccines may be able to be modified, reducing the time and cost for development of a Zika vaccine. However, none of the current candidate vaccines have reached the stage of testing in human subjects. As a result, vaccine development is a longer term – but also critical – measure, that may vary greatly in cost depending on how research proceeds and the involvement of industry partners.

2. **In your opinion, if a vaccine were tested on 5,000 people and proved to be safe and 90 percent effective would that warrant further development? The genetically engineered mosquito has achieved such success in suppressing the *Aedes aegypti* mosquito.**

If demonstrated to be effective and safe to humans in the clinical environment, I would support the watchful use of genetically engineered mosquitoes through a carefully controlled release that monitors the *in situ* effects on mosquito-borne diseases such as Zika, as well as any potential ecological or unanticipated harms. Thus far, the Food and Drug Administration and other scientific authorities have not found ecological or other harms from the release of transgenic mosquitos.

3. **How high of a priority should vector control in Puerto Rico be for the federal government? Should the federal government focus more resources on the development and deployment of innovative vector control solutions?**

Puerto Rico is already experiencing local transmission of the Zika virus.³ In the absence of a vaccine, vector control – especially in impoverished areas of Puerto Rico – is critical. Vector control and other preparedness measures are vital in Puerto Rico to safeguard the island's population and also to safeguard the US mainland. Given the high travel between Puerto Rico and mainland US (and given the right of free travel), there is every reason to stem the spread in Puerto Rico for all of our national interests. Innovative vector control solutions that are safe and effective should form part of a multifaceted strategy – including existing vector control measures, personal insect repellants, and vaccine development – to stop the spread of the Zika virus.

³ CDC, "Zika Virus in Puerto Rico", Available at: <http://wwwnc.cdc.gov/travel/notices/alert/zika-virus-puerto-rico>
Accessed: April 10, 2016.

The current delay in Congressional approval the President's supplemental Zika funding request means that health agencies are unlikely to have the capacity to focus on the development of innovative solutions, with funding for existing safe and proven strategies already disastrously insufficient.

4. In light of the Olympics later this summer, should Brazil be more aggressively deploying innovative solutions, such as genetically modified mosquitoes, to slow the spread of Zika virus?

The World Health Organization has noted that Brazil faces many challenges with traditional insecticide control measures for Dengue, which may be similar for stopping the spread of Zika virus. Innovative strategies for mosquito control – which may include genetically modified mosquitoes or mosquitoes infected with bacteria that inhibit virus development – may therefore be necessary to slow the domestic transmission of Zika virus in Brazil. However, these innovative strategies will require carefully monitored pilot program deployments or further initial research.⁴ It will also require significant funding and technical support to Brazilian authorities. This should be well in advance of the Rio Olympics, which will have an amplifying impact on the spread of Zika virus.

⁴ WHO, "Zika virus: mosquito control works if implemented well; new control tools in the pipeline" (March 18, 2016), Available at: <http://www.who.int/emergencies/zika-virus/articles/mosquito-control-tools/en/> Accessed: April 10, 2016.

VIEWPOINT

Is the United States Prepared for a Major Zika Virus Outbreak?

Lawrence O. Gostin, JD
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JAMA Patient Page

From its initial discovery in Ugandan forests nearly 70 years ago, Zika virus has emerged as a worldwide public health crisis, with active transmission in more than 40 countries in the Americas and Caribbean. On February 1, 2016, the World Health Organization (WHO) declared a Public Health Emergency of International Concern (PHEIC), concerned about clusters of microcephaly and Guillain-Barré syndrome (GBS). A week later, the Centers for Disease Control and Prevention (CDC) triggered the highest "level 1" activation of its emergency operations center, and President Obama requested \$1.86 billion in emergency funding.¹ On April 7, the WHO reported there is scientific consensus that Zika is a cause of microcephaly and GBS.

Although none of the continental states has reported local mosquito-borne transmission, Health Secretary Sylvia Burwell warned that Zika has a "significant potential to affect national security or the health of Americans."² The virus severely threatens Puerto Rico, with one-quarter of its 3.5 million inhabitants projected to be infected.³ The Olympics in Brazil will have an amplifying affect because the competition will be during the Northern summer. Travelers visiting or returning to the United States could likely escalate the spread of Zika. Epidemiologists estimate that Zika could affect a majority of US states including large cities where *Aedes* species mosquitoes are active.

Epidemiologists estimate that Zika could affect a majority of US states including large cities where *Aedes* species mosquitoes are active.

Is the United States prepared for major clusters of Zika? Certainly, a highly functioning health system will help protect the domestic population. Yet there are signs of unpreparedness with insufficient resources and variable legal authorities.

Zika Funding

WHO Director-General Margaret Chan characterized Zika as a "severe public health crisis."⁴ Despite the exigencies, Dr Chan sought only \$56 million for 2016, and governments have thus far pledged about \$27 million. As with Ebola, global financing has not been commensurate with critical health needs.

President Obama's supplemental \$1.86 billion request is more robust, aimed at surveillance, mosquito control, research, and health services especially for low-income pregnant women. Importantly, funding would support Zika control in the region, including Puerto Rico. Yet Congress has not acted, in part due to concerns about

whether federal resources would be used to fund contraception or abortions abroad.⁵ Legislators urged reallocating preapproved Ebola resources for Zika, even as new cases of Ebola emerge in West Africa. Concerned that Congress will not appropriate new funding, President Obama recently authorized reallocation of \$589 million of Ebola and other public health funds toward Zika preparedness, research, and the creation of response teams.

Failure to fund Zika preparedness would be a serious public health and political mistake. Health agencies will have insufficient capacity for surveillance, vector abatement, and health care services. Vaccine development could be delayed. Congress's inaction is also likely cost-inefficient. Each preventable case of Zika-related morbidity, especially among newborns, saves health care resources. Beyond cost, Zika has deep moral dimensions, with impoverished women and their newborns at greatest risk. Reluctance to act will have political repercussions if clusters of Zika this summer are followed by avoidable cases of microcephaly 9 months later.

Knowledge Gaps

Funding for Zika is essential to fill major gaps in knowledge and medical technologies. Despite the US Food and Drug Administration's (FDA's) issuance of emergency use authorizations, diagnostic tests are slow, expensive, and of variable accuracy. With 80% of Zika infections asymptomatic, individuals may not take precautions to avoid transmission through sex or the blood supply. It is also unknown how long the body harbors the virus, the duration that patients remain immune, or when it becomes safe for women to become pregnant (the CDC currently recommends waiting at least 8 weeks after initial infection).⁶ Importantly, the risk factors, frequency, and severity of neurological deficits in patients (GBS, myelitis, meningoencephalitis) and infants (microcephaly) are unknown.

Mosquito Abatement

Aedes aegypti, the "cockroach of mosquitoes," lives in close proximity to humans, is an aggressive daytime biter, and hides inside households. These and other Zika-carrying mosquitoes breed in minute water sources (flowerpots, bottle caps, tires), and their desiccated eggs can survive for months. Abatement is arduous and legally complex. Sterilizing male mosquitoes with radiation or through genetic engineering is controversial due to novelty and unforeseen ecological harms. Removing trash and water sources from family homes and gardens is intrusive. Spraying of habitats in homes or neighborhoods may be injurious to health or the environment.

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The exigencies of mosquito control, however, have driven action. The WHO is considering recommendations concerning transgenic mosquitos⁷ and mosquito-killing bacteria.⁸ The FDA invited public comment on the release of genetically engineered mosquitos in the Florida Keys. The Environmental Protection Agency has given several states experimental permits to introduce *Wolbachia* bacteria to inhibit mosquito reproduction.

States and localities are repurposing regulations crafted during West Nile virus outbreaks for Zika, including public education, environmental clean-ups, and relaxing legal requirements for pesticide applications (waivers for permits or notice and comment). Hawaii's "Fight the Bite" campaign educates the public about *Aedes* breeding grounds in homes, schools, and businesses. Puerto Rico is mobilizing the community to collect a million discarded tires and trash.³ South Carolina coastal officials are going door-to-door to share abatement information and conduct consensual property inspections. Local governments can classify private property as a public nuisance, requiring owners to eliminate breeding habitats.

Nevertheless, legal doctrine protecting personal property and privacy can impede abatement—for example, restrictions on entering homes and lots while owners are absent thwarted Puerto Rico's policy to treat the premises of every pregnant woman.³

Reproductive Services

Brazil, Columbia, Ecuador, and Puerto Rico, among others, have advised women to temporarily postpone pregnancy. El Salvador urged delays until 2018. These recommendations stand in tension with existing policies impeding access to contraceptives, safe abortions, or maternal-child health services. Latin America is among the world's most restrictive regions in terms of reproductive services. Similar problems arise in the United States, especially for poor women who lack affordable access to reproductive services. Some states have restrictive abortion laws, have withdrawn funding for Planned Parenthood, or have refused to expand Medicaid under the Affordable Care Act. Moral and health concerns arise if a poor woman chooses to avoid pregnancy, but government impedes her access to affordable reproductive services.

Legal Authorities

Legal authority for mosquito or nuisance abatement rests principally with states and localities, with considerable variability in resources, expertise, and powers. There exists a patchwork quilt of more than 700 mosquito control districts—some within local health agencies and others within departments of agriculture, transportation, or parks. Most US localities do not even fall within existing mosquito control districts, leading to highly divergent practices. Large cities such as Houston, Los Angeles, and New Orleans are planning major mosquito abatement campaigns, but Miami-Dade County reports significant underfunding for its abatement efforts. Other smaller jurisdictions can do little more than advise inhabitants to use over-the-counter insect repellents.

Federal agencies often have few direct legal powers to implement control measures, but can exert influence through scientific guidelines and funding. Florida, Hawaii, and Puerto Rico have declared states of emergency, authorizing rapid response and infusing new resources. Puerto Rico plans to fix the price of condoms, repellents, and screens to discourage retailer gouging of consumers.³

Recalling unwarranted quarantines and travel impediments during Ebola, it is essential not to overreact to Zika. New Jersey Governor Chris Christie, for example, said he would quarantine Zika-infected individuals despite no public health justification.⁹ Although the CDC advised pregnant women to postpone travel to Zika-affected countries, more restrictive policies would likely waste limited resources and lack public health justification. The Department of Homeland Security resisted political requests to screen travelers, noting its futility.

The Nation's State of Preparedness

Ebola demonstrated that even advanced health systems can fail to eliminate the risks of novel infections. As the CDC noted at its national summit on April 1, local Zika virus transmission will likely occur in the continental United States this summer; the question is whether we are ready. The nation's state of preparedness is compromised by Congress's inaction on supplemental funding, epidemiologic uncertainties, and the weak capacities and powers of states and localities. If preventable cases of Zika-related infant abnormalities emerge, there will be a high political price for the failure to act decisively.

ARTICLE INFORMATION

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Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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April 4, 2016

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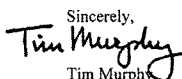
Dear Dr. Conlon:

Thank you for appearing before the Subcommittee on Oversight and Investigations on Wednesday, March 2, 2016, to testify at the hearing entitled "Examining the U.S. Public Health Response to the Zika Virus."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on Monday, April 18, 2016. Your responses should be mailed to Giulia Giannangeli, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to Giulia.Giannangeli@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,


Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

Attachment



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April 15, 2016

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Dear Members of the Subcommittee on Oversight and Investigations:

Pursuant to your request to provide answers to member's questions generated by my testimony before the Subcommittee, the following are provided for the record:

The Honorable Tim Murphy

1. Now that the Zika Action Plan Summit on April 1, 2016 in Atlanta, GA has passed, do you have any additional concerns or issues that you would like to raise – and that you believe have not been adequately covered thus far – to improve the federal response to mosquito-borne illness?

Clinicians and epidemiologists were the featured parties at the Plenary Session. There was no entomologist as a speaker for any of the plenary sessions, so basic bionomic and control issues related to *Aedes aegypti* and *Aedes albopictus* were presented by Lyle Peterson, a physician and Director of the CDC Division of Vector-borne Disease in Fort Collins, Colorado. CDC has a number of superb medical entomologists on staff that could have made valuable contributions towards educating the public health officials sorely in need of their input to facilitate making informed decisions on preparedness and control response. In addition, mosquito control specialists from the American Mosquito Control Association were invited to attend, but were not given the opportunity to speak at the Plenary Sessions.

The breakout workshop sessions in the afternoon included two identical vector control sessions of 1.5 hours, which addressed questions from participants at three separate tables, but which was of insufficient length to allow each table to share its discussion topics with the others. In all, vector control received short shrift throughout the one-day conference. Future summits should allow for adequate time for vector control issues to be discussed before the entire assemblage so that decision-makers are aware of the complexities involved that could profoundly influence prevention/control strategies.

The focus on Zika virus as a neonatal problem is understandable, but more time should have been taken to outline priorities with regard to how we intend to contain

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the virus should it begin to appear in force during the summer, when mosquito populations are expected to surge. It was also quite evident that the public health officials present were in need of considerable education of the idiosyncrasies attendant *Aedes aegypti* and *Aedes albopictus* which might profoundly influence planning. It should be remembered that, while Zika is the current threat, it may fail to emerge and spread to the extent of our fears in the U.S. as in the case of chikungunya last year. We will have thus wasted much time and energy that could have been better spent bringing more comprehensive and universally applicable control options to the table in terms of new active ingredients, control strategies, vector control capabilities and the like that could be used to prevent/counter a variety of mosquito-borne disease challenges. Regardless, Zika certainly provides the springboard for us to begin to address gaps in knowledge of vector distribution and control preparedness (resources available/needed, nature of their deployment), but we shouldn't lose sight of the long-term picture beyond Zika.

I fear that the lions share of resources will ultimately be allocated to public health officials epidemiologists tracking the occurrence and (potential) spread of Zika in the U.S. (as happened with West Nile virus), while funds involving actual intervention strategies for training increased numbers of vector control personnel, comprehensive public education campaigns, development of memoranda of agreement, etc. will remain an afterthought.

To be sure, Zika is the latest in a series of mosquito-borne viruses to challenge our control capacity. More (Mayaro virus and Oropouche virus come to mind) are most certainly on their way in the future. Preventing their introduction and/or controlling their spread will entail eliminating their vectors or at least keeping their numbers below transmission threshold. To the extent we can prepare our public health infrastructure to control *Aedes aegypti* and *Aedes albopictus*, we will have saved considerable time in playing our usual game of catch-up after the fact.

The Honorable Marsha Blackburn

- 1. In light of the Olympics later this summer, should Brazil be more aggressively deploying innovative solutions, such as genetically modified mosquitoes, to slow the spread of Zika virus?**

The risk of infection by Zika virus attendant to the Olympics is difficult to quantify. The vast preponderance of infections, to date, have been in areas of depressed socioeconomic conditions involving overcrowding, lack of screening, inconsistent trash removal, non-functional potable water distribution systems, problematic sewerage, among others.

Olympic athletes will be exposed to mosquito bites to varying degrees while staying in the hotels in Olympic Village or in resort areas. Whether this presents a true risk of acquiring the disease is open to question. Dining out in cafes or bars is definitely a potential risk. Effective EPA-registered repellents should be made available to the athletes and they should be encouraged to use them, providing the ingredients in the

repellents do not compromise them in drug testing. I'm unaware of any conflicts in this regard, but the potential is there and should be thoroughly investigated with the manufacturers prior to use by the athletes.

Public education programs are in effect countrywide. Many private enterprises are supporting governmental public education campaigns. Billboards, bus flyers, flyers in elevators, airports, etc. are very evident everywhere according to sources in country. In a survey where participants were asked about their knowledge of dengue and Zika vectors, 91% were knowledgeable, which is a very high percentage of the population. An identical survey here in the United States involving Zika or West Nile, would, in all likelihood, not approach that percentage. The problem remains, though, that even though 91% know what to do, less than 55% actually do it, according to the survey.

Should the Brazilian government be deploying more innovative strategies? It's a more complex question than it might seem at first. We must remember that ongoing outbreaks of mosquito-borne disease require intervention measures that kill infective adult mosquitoes in the here and now. This is provided by the proper use of approved pesticides to which the mosquitoes are susceptible. On the other hand, GMO/*Wolbachia*/etc are rather slow to take effect compared to pesticides, which provide immediate reduction of infective mosquitoes on the wing. The vector population suppression that GM technologies provide, while critical in the long term, are clearly not effective in reducing ongoing transmission.

In my opinion, they should be both investigating and judiciously employing GM mosquitoes, while emphasizing tactics with a proven history of efficacy such as source removal and effective interior sprays/exterior barrier treatments. It appears they are doing this, but whether this will be sufficient to prevent any and all transmission remains to be seen. In particular, they should be testing for insecticide resistance and adjusting their chemical use to ensure the products they use are actually working. This is problematic at present. According to public health sources in-country, governmental approval is required for product use and deployment. This can impede timely delivery of control interventions. Many mosquito control/public health agencies (Secretarias Municipais de Saude) are trying to use both innovative and tested approaches, but are hindered by regulations issued from other federal government agencies. Furthermore, the availability of only one or two approved insecticide products makes rotation of chemistries for resistance prevention extremely difficult. In effect, at times they are forced to utilize certain pesticides that they already know are ineffectual due to resistance by the mosquitoes, because of a lack of approved alternatives. This is not a public health agency problem, but a regulatory agency bureaucracy issue.

Genetically modified mosquitoes using the Release of Insects with a Dominant Lethal gene (RIDL) are only one facet of a program that should include public education focusing on comprehensive removal or modification of container breeding habitat around residences and businesses, space sprays indoors, provision of bednets and repellents in addition to training on their proper use. The developers of the RIDL technology recognize that it's most effective in isolated, widely dispersed small outbreaks. Thus,

they too, recommend it be part of a more comprehensive program integrating source removal and adulticide sprays where appropriate.

RIDL shows promise and the Brazilians are using it already in some areas. Use of *Wolbachia* bacteria, CRISPR gene drivers and the like, while certainly innovative, are in their nascency and shouldn't be relied upon in lieu of established technologies – but they should be actively investigated and employed in due time – particularly in light of pesticide resistance issues. If employment of these technologies is not in the offing, at least immediate approval of a greater range of pesticides per WHO recommendations is warranted.

The Honorable Gus Bilirakis

1. What role does the federal government play, or should it play, in mosquito control given that most programs are designed and implemented at a local level?

The federal government is most adept at appropriating and distributing funds during emergencies to the states, which are in the best position to determine how they should be allocated at a local level. This is best done through the CDC, which is keenly aware of shortfalls in local mosquito control capacity that could be successfully addressed by funds duly allocated by state agencies according to identified needs. This could take the form of augmenting local vector control staff through federal volunteer organizations in locating breeding habitat, for example. It could also take the form of reimbursements to local districts loaning personnel/chemical/equipment to other jurisdictions within the state needing assistance. The federal government could also assist by funding contracts let by local jurisdictions to commercial companies specializing in comprehensive mosquito control services already on the books as part of contingency plans.

The CDC Division of Vector-Borne Disease is in a prime position to offer consultation and resistance testing and/or training to local districts to assess efficacy of various product chemistries both before and during control operations. This would be invaluable to the local agencies and would reap substantial benefits in all future control scenarios.

The federal government is uniquely positioned to engage in a national effort to educate the public about their role in control of the particular mosquito species that transmit Zika and a number of other viruses. A national public relations campaign along the lines of those against smoking, the “Buckle Up” program promoting seatbelt use, the “Don’t be a litterbug” and the “Smoky the Bear” campaigns to prevent forest fires were exceptionally effective and have become iconic in their influence on public behavior. A similar national program whose aim is to make harboring mosquito habitat on one’s property socially unacceptable would be a critical component of a Zika control campaign having salutary effects with respect to future mosquito-borne disease challenges long after the current issue with Zika fades from the public’s memory.

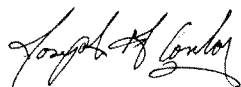
2. **My home state of Florida has one of the best mosquito control programs in the country. However, you mention that ports of entry throughout the U.S. have little to no mosquito control. Can you specify where in the country you are referring to? Does this include ports in those states that have more advanced and integrated mosquito control programs?**

By ports of entry I mean those transportation venues/hubs in the United States where passengers from international travel ultimately end up, as in their residences or businesses – not merely a seaport or international airport with immigration/customs jurisdiction. As a resident of Florida, myself, I'm fully aware of the extraordinary nuisance mosquito and vector control capabilities of the mosquito control entities within the state. Potential initial ports of entry in major metropolitan areas via international air travel in Florida and elsewhere have robust vector control capability, to be sure.

However, control of *Aedes aegypti/albopictus* is exceedingly manpower-intensive and will entail significant upgrades in numbers of field mosquito control personnel beyond cadre should an outbreak due to virus imported through international air travel or cruise line occur. Furthermore, incubating cases coming through those large ports of entry can easily be transported afield to any of a number of communities within the geographic range of both vectors via connecting flights or automobile/train while the victims are still infective to the mosquitoes. This is most likely to occur in poorer rural communities along the Gulf coast of Texas, Louisiana, Mississippi, Alabama and Florida in addition to economically-challenged rural communities along the Atlantic seaboard up to Virginia, but, in fact, may potentially occur anywhere within the geographical range of the two vector species.

The wide range of potential final ports of entry make it impractical to maintain functioning vector control programs in each to contain an outbreak, however limited. Local tax bases are insufficient to support sustained programs in these areas. Thus, rapid response teams deployed and coordinated through the state agency having jurisdiction over public health mosquito control programs would be the most effective, efficient and timely rapid response vehicles. Any federal funding for these interventions would need to be earmarked for vector control to prevent redirection to other public health programs, whether Zika-related or not. All states within the range of the two putative vectors should be drafting action plans for rapid response teams to cover these minor ports of entry.

Highest regards,



Joseph M. Conlon
Technical Advisor
American Mosquito Control Association

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April 4, 2016

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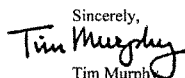
Dear Dr. Sheffield:

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Sincerely,


Tim Murphy
Chairman
Subcommittee on Oversight and Investigations

cc: Diana DeGette, Ranking Member, Subcommittee on Oversight and Investigations

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To The Subcommittee on Oversight and Investigation:

I have reviewed the additional questions by the esteemed members of the Subcommittee on Oversight and Investigations and will address each one in the following paragraph. I would like to thank you again for the opportunity to testify regarding Zika virus infection and the medical, economic and social effects on reproductive age women.

The Honorable Tim Murphy: Following our testimony on March 2nd, many things have changed regarding Zika virus infection, as you would expect with an evolving epidemic. Many of these concerns were raised at the Zika Action Plan Summit in Atlanta and are available in the meeting summary. Specific areas affecting reproductive age women that need to be mentioned are as follows and the federal response for these mainly focuses on making monies available to complete the needed research.

1. The causal link of Zika infection and the abnormal fetal findings reported in the last several months is now established. The confirmation of the strong association should provide legislators with enough evidence to move forward with funding to further investigate Zika infection in pregnant women with regards to modifying factors such as gestational age of the pregnancy at infection. Prevention strategies including vaccination development is also vital to the global management of this disease. Finally, as we understand better the pathophysiology of fetal Zika infection, therapeutic measures can be developed and tested to try and prevent or at least attenuate the fetal response.
2. Sexual transmission is also now established so focus should be on improving not just the current tests but the availability of the tests to allow for screening of males that have traveled, regardless of symptoms. Many women interested in becoming pregnant or who are already pregnant are now not traveling – their male partners however are traveling and better ascertainment of the risks of transmission to their partners is needed to help control the spread of this disease. This is particularly true in developed nations such as the U.S. where mosquito control is better and we will have a higher proportion of infections occurring from the sexual transmission route.
3. Reproductive endocrinologists focusing on Assisted Reproductive Techniques for infertility management are expressing concerns regarding the safety of egg and sperm donation – guidelines are now in place regarding screening and donation exclusion criteria but there is a paucity of research to inform these guidelines.

The Honorable Marsha Blackburn: There is significant concern among the reproductive age population regarding travel to Brazil, both for and outside the 2016 summer Olympics. Brazil is working with several international organizations to control the mosquito population, including assuring a safe living facility for the athletes and aggressive mosquito spraying. It is a daunting task to significantly improve mosquito

control secondary to the poverty and overcrowding in many of the areas in the large cities. As to genetically modified mosquitos, I will defer to my colleagues as I am not current on the literature.

The Honorable Gus Bilirakis: I share your concern about ZIKV and fetal anomalies and the CDC has now come out confirming the link as discussed above. I address subpoint (a) above but subpoint (b) concerns everyone working on the front line, seeing patients and counseling those women regarding risks. We just do not know the long term consequences regarding the infection. We have good data about microcephaly and long term care and have been using that as a springboard for counseling. That being said, fetal Zika infection is not just microcephaly but a whole range of neural abnormalities and that makes counseling more difficult. The other huge gap in our knowledge relates to those infants born to infected mothers who do not have obvious abnormalities. "Will these infants develop intellectual disabilities or developmental delay secondary to viral effects that did not result in microcephaly or another obvious abnormality?" is a question that we cannot yet answer. The infants born to Zika affected mothers are being followed-up so hopefully in a few years we will have an answer to that question.

Sincerely,



Jeanne S. Sheffield, M.D.
Director, Division of Maternal-Fetal Medicine
Professor, Gynecology and Obstetrics