

**DEPARTMENTS OF LABOR, HEALTH AND
HUMAN SERVICES, AND EDUCATION, AND
RELATED AGENCIES APPROPRIATIONS FOR
FISCAL YEAR 2017**

THURSDAY, FEBRUARY 11, 2016

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 10:02 a.m., in room SD-138, Dirksen Senate Office Building, Hon. Roy Blunt (chairman) presiding.

Present: Senators Blunt, Moran, Cochran, Alexander, Capito, Lankford, Murray, Durbin, Reed, Mikulski, Shaheen, Merkley, and Schatz.

**EMERGING HEALTH THREATS AND THE ZIKA SUPPLEMENTAL
REQUEST**

OPENING STATEMENT OF SENATOR ROY BLUNT

Senator BLUNT. The Appropriations Subcommittee on Labor, Health, and Human Services, and Education, and Related Agencies will come to order.

I am pleased that we have Dr. Tom Frieden from CDC, and Dr. Tony Fauci, who is the infectious diseases head at the National Institutes of Health, here with us today.

Obviously, this hearing is to discuss the outbreak of Zika and the administration's \$1.8 billion supplemental budget request. We look forward to hearing your testimony.

It doesn't seem that long ago that we were here having a similar hearing on Ebola. Maybe one of the things we can talk about some today is, as these problems face us, is there any way in the regular budget we could be better at anticipating and monitoring what happens around the world, so that we can prevent some emergencies and be even better positioned to respond to others.

But we are glad you are here. I think we will have a number of members come. I anticipate a vote at 10:30. If that happens, I'm assuming that we will have members here that will allow us to go back and forth, and continue the hearing. We will go individually and give our vote, and get back while we continue to have questions and your responses.

[The statement follows:]

PREPARED STATEMENT OF SENATOR ROY BLUNT

Good morning. Thank you, Dr. Frieden and Dr. Fauci, for appearing before the Subcommittee today to discuss the Zika outbreak and the Administration's \$1.8 billion supplemental funding request. We look forward to hearing your testimonies.

No sooner than the global health concerns over Ebola subsided, we are faced with another looming threat. The Zika virus has developed from an illness with mild, flu-like symptoms to one that may lead to severe birth defects or paralysis. There is no rapid test, specific treatment, or vaccine.

Little has been done in the United States to prepare for the threat of the Zika virus. While the National Institutes of Health and Centers for Disease Control and Prevention spend some funding on viruses like Zika that are transmitted by mosquitoes, neither agency currently spends any significant resources specifically on Zika.

After the Department of Health and Human Services received \$2.7 billion to spend on Ebola and other infectious diseases, more than half remains unspent, and none of the remaining funding thus far has been used for the current Zika outbreak.

This shows the fundamental problem in our public health system: it has a short attention span. We immediately forget about the outbreak that came before and do not adequately plan for the ones on the horizon. Today, we are asking about Zika. Last year, it was Ebola. What will it be next year?

As we examine the Administration's request for supplemental funding, we need to make certain that we are focusing resources not just on today's crisis, but on the infrastructure to prepare for tomorrow's as well. It is time to approach emerging health threats more proactively. We need to examine our capacity to respond to ever-changing threats, take precautions, and focus efforts on strategic planning.

Thank you.

Senator BLUNT. Certainly, I am pleased to recognize our ranking member, Senator Murray, for whatever comments she might have. Senator.

STATEMENT OF SENATOR PATTY MURRAY

Senator MURRAY. Thank you very much, Chairman Blunt.

Dr. Fauci, Dr. Frieden, thank you both for joining us this morning to talk about the Zika virus and other emerging health threats. I am sure we are all hearing from families in our home States who are concerned about this virus and its impacts. So I am glad we have the opportunity today to continue gathering the facts and discussing ways to fight the Zika virus at home and abroad.

I'm very hopeful that we can put politics aside and work across the aisle to protect our families and communities, and ensure that we are putting all the needed tools and resources into this effort.

Our understanding of the Zika virus and the public health community response is rapidly evolving. Last week, the World Health Organization declared Zika-linked birth defects a global health emergency. A day later, health officials in Dallas confirmed the first known case of sexual transmission of the disease.

In the current outbreak, it is a virus that most people had never heard of until recently, and it has quickly spread across the Americas, potentially threatening expectant mothers and their newborns wherever it develops.

There is still a lot we need to learn about this virus, but one thing that is clear is that we cannot wait to act. The scientific consensus at this stage is that four out of five of those who become infected show no symptoms. For the other 20 percent who do, the most common result is a week of flu-like symptoms.

However, in rare instances, there are indications that some people infected with the virus have developed Guillain-Barre syndrome, a potentially life-threatening neurological condition. And there is growing evidence that Zika can lead to microcephaly, a

birth defect that usually results in abnormal brain development with serious long-term consequences. In the past year, Brazil has experienced a 25-fold increase in the number of infants born with microcephaly, and scientists believe the Zika is the reason.

The same mosquitoes that carry the virus in South America can be found in many parts of the United States, including right outside our door here on Capitol Hill. Evidence now indicates the virus has spread to Puerto Rico, putting pregnant woman there at risk. And many are concerned that it will make its way to the mainland when the warm weather returns.

Speaking for moms and grandmothers across the country, this is really deeply concerning to all of us. So now is the time to prepare for that possibility and to develop strategies for controlling the mosquitoes that harbor the virus.

To make that possible, the administration has requested emergency funding to assist States and local communities with these efforts, including resources to expand mosquito-control efforts, as well as laboratory and diagnostic capabilities. Given the limitations of existing diagnostics and treatments, the request would provide additional funding to accelerate research and development of effective lab tests, antiviral drugs, and, of particular importance, a vaccine.

The request would also help fill in the gaps in our knowledge about the disease. Additionally, the administration's proposal would include funding to educate healthcare providers, pregnant women, and their partners about the virus, and would improve health services for low-income pregnant women in areas where Zika poses a risk.

I believe it is critical that, in Zika-affected countries, we do everything we can to ensure that women have access to a full range of reproductive healthcare. That is something that I will continue to be focused on.

We know other viruses that can cause pregnancy complications are often associated with a broad spectrum of possible conditions, so there may be other consequences for pregnant women who become infected. I'm glad this is a concern CDC is focused on answering.

While a mosquito bite is the most likely way to contract Zika, as the news from Dallas last week illustrated, we also need to understand other means of transmission, and whether there are any risks to our Nation's blood supply.

Time is of the essence, so I look forward to discussing the administration's proposal, and I hope that we will be able to work in a bipartisan manner to move legislation in the coming weeks, because when it comes to protecting our families from potentially serious threats like this, there shouldn't be, of course, any partisanship or politics. We should be able to work together to get this done.

Mr. Chairman, I am hopeful we will be able to do so.

Senator BLUNT. Thank you, Senator Murray.

Let's get the official titles on the record.

I want to welcome Dr. Frieden again, the director of Centers for Disease Control and Prevention, and Dr. Fauci, the director of the

National Institute of Allergy and Infectious Diseases. We are looking forward to your testimony.

Dr. Frieden, if you want to go first, followed by Dr. Fauci.

STATEMENT OF THOMAS R. FRIEDEN, M.D., DIRECTOR, CENTERS FOR DISEASE CONTROL AND PREVENTION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. FRIEDEN. Thank you very much, Chairman Blunt, Ranking Member Murray, Senator Mikulski, and others, for being here, and for inviting us to discuss Zika, which is, as you said, Mr. Chairman, the latest in a series of threats that we are dealing with.

At the outset, I want to make a few things really clear about where we are with Zika. First off, we are discovering more literally every day. This is a new phenomenon, and we are working around the clock to learn as much as we can as quickly as we can, and share that information with people, and take appropriate action.

Zika is new. New diseases can be scary, particularly when they affect the most vulnerable among us.

Right now, the most important thing for Americans to know is, if you are pregnant, it is better not to travel to a place where Zika is spreading. If you're pregnant in a place where Zika is spreading, do everything you can to protect yourself against mosquito bites.

The mosquito that spreads Zika is very difficult to control, and we are working 24/7 to try to figure out how we can best reduce the risks to pregnant women, which is the key goal at this time. This is the latest in a series of unpredicted and unpredictable health threats.

What is predictable, as you say exactly, is our need to improve systems to find, stop, and prevent health threats wherever they emerge, because we really are connected as a world, and it is very easy for disease to spread from one part of the world to another.

The virus was first identified in 1947. It wasn't until 2007 that the first outbreak was identified. CDC (Centers for Disease Control and Prevention) scientists investigated that outbreak on the island of Yap in Micronesia. Seventy-three percent of the adult population became infected. About four out of five people had no symptoms. It was generally considered a mild illness—rash, fever, sore joints, pinkeye.

But the mosquito that spreads it is the same mosquito that spreads the dengue and chikungunya. If I can just show you a couple slides of how that happens, this is the mosquito. It is very difficult to kill. It lives indoors. To really knock down the risk of dengue to a population, you may have to kill 90 percent or more of these mosquitoes.

This is the distribution of dengue around the world. It has spread rapidly over the past decade as people move more, and it is ideally suited to environments where there is standing water.

Chikungunya, also spread by the same mosquito, spread for more than 50 years in Africa and Asia, and only recently came to this hemisphere, but rapidly spread throughout the United States.

This is the current known transmission of these viruses, but I have to say "known" underlined, because there are areas where it is spreading, and we may not know because we don't have really good tracking systems. That is one of the things that we need to scale up in the longer term.

I want to share what happened just less than 2 years ago. The first known case of chikungunya spread by the same mosquito on the island of Puerto Rico occurred on May 5, 2014. I'm going to show you a series of slides that are a time-lapse of just 2 weeks. Two weeks later, it had begun to spread. Two weeks after that, it spread widely. Two weeks after that, even more widely. Two weeks, 2 weeks, 2 weeks, and then by October, it essentially was all over the island. So within 2 months, we had seen a really explosive spread.

This is because, in Puerto Rico, the particular mosquito is very abundant, and the environment is such that screens and air-conditioning are not as prominent as they are in some other places, so people are at a much higher risk.

The link to microcephaly is unprecedented. We have never before, that we know of, seen a mosquito-borne disease that could cause this kind of severe fetal malformation. Rubella was identified in 1941 as the cause of rubella syndrome, another virus in 1962, and then in more than 50 years, we haven't found something else that has done that.

Guillain-Barre would not be unusual. We do see paralysis after infection rarely in a number of conditions.

So I would like to just say right now what we are going to do going forward and what is likely to happen going forward.

First, we are going to learn more. We're going to do everything we can to understand the relationship with microcephaly, which increasingly looks like a causal association, though it is not completely proven yet. We are going to advance our ability to diagnose Zika. Currently, it is imperfect. And we are going to do better or try to do better at controlling this mosquito, which is very challenging to control.

We will undoubtedly see many travelers returning to the United States with Zika. There are about 40 million people who travel from the United States to Zika-affected areas each year. Many of those will come back with Zika. If it is like dengue and chikungunya in the past, we will see hundreds or thousands of travelers returning to the United States.

Unfortunately, some of those individuals will be pregnant women. We have already had one woman from Hawaii who was in Brazil in the spring, delivered late last year, and did have a child with microcephaly. So we think this may occur among travelers returning to the United States. That is one phenomenon that we are likely to see.

The second is, as I indicated, the likelihood of widespread transmission in parts of the United States such as Puerto Rico and the territories—the U.S. Virgin Islands, American Samoa, and others—where this mosquito is very prevalent and dengue can spread very rapidly. So we may see a very large number of cases there. That is the area that is most urgent for us in this response.

Third, we may see possible cases and clusters of other parts of the United States that have the same mosquito. Florida, Texas, Southern U.S., have the mosquito that spreads this very well. That is why we want to be able to support them to do a better job both diagnosing people that may have Zika and controlling mosquitoes that may spread Zika.

We may also see sporadic cases around the United States from another mosquito that doesn't spread it as efficiently or rare cases of sexual transmission.

And unfortunately, we are likely to continue to see some substantial spread around the world with a pace that sees lots of Zika and then, if it is associated with birth defects, 6, 5, 9 months later, lots of children born who may be affected.

As Senator Murray said, we are not sure whether the children who don't have apparent microcephaly are completely normal, or whether they may have other problems as well. We are looking at that, but it may take years to sort some of these things out. Some things we will learn in days or weeks. Some things may take much longer.

Zika requires an emergency response. Our request for the CDC component of that is \$828 million for Puerto Rico, for the rest of the United States, and for our international partners. That is an approach that looks at prevention, detection, response.

On prevention, we want to reduce the risk that pregnant women are bitten by an infected mosquito and prevent other rare forms of transmission.

On detection, we want to continue to scale up our ability to find the virus in people's blood. In the CDC laboratory, we have established the only tests in the United States that can identify Zika. One of these will do it accurately when someone is actively ill. That test was accelerated and produced in just 3 weeks, because of support Congress had given to the CDC before to do advanced molecular detection and genomic manipulation, to more rapidly do it.

The other tests are much more challenging to diagnose prior to Zika infection, because there is a lot of cross-reactivity between Zika and other viruses. So they may be falsely positive. But pregnant women who have been in such areas want to know, so we are scaling this test up and working with health departments all over the country to diagnose better.

We will also continue to look for and analyze microcephaly. Just yesterday, our weekly bulletin, Morbidity and Mortality Weekly Report, published the strongest evidence to date linking Zika with microcephaly. There was another report in the New England Journal also yesterday about a different situation. But here you see the actual Zika genome in the brain tissue of infants who tragically died within the first 24 hours of being born.

We also will respond as rapidly as responsible possible in controlling mosquitoes; providing clinical care; encouraging effective clinical care for mothers, infants, and people with Guillain-Barre syndrome.

We know that health threats will continue to emerge. We want to respond as an emergency to this situation, to protect pregnant women and reduce the risk to Americans and others of this disease. We want to understand it better, but also continue to strengthen systems around the world that can find threats when they first emerge, stop them as soon as possible, and prevent that wherever that's possible.

Thank you very much. I look forward to answering your questions.

[The statement follows:]

PREPARED STATEMENT OF THOMAS FRIEDEN, M.D., MPH

INTRODUCTION

Good morning Chairman Blunt, Ranking Member Murray, and members of the Subcommittee. Thank you for the opportunity to testify before you today with regard to the President's request for more than \$1.8 billion in emergency funding to respond to the Zika virus outbreak that threatens the United States and the world. The emergency funding requests a total of \$828,000,000, for CDC with no-year availability, in support of domestic and international response, with particular attention to emergency assistance to the U.S. Territory of Puerto Rico and the U.S. Territories and States with local transmission of Zika virus.

Vaccines and antibiotics have made many infectious diseases a thing of the past; we've come to expect that public health and modern science can conquer all microbes. But 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 mosquitoes and in birth defects. We must act urgently and swiftly to stop the spread of the Zika virus. There are many things we do not know yet about the Zika virus, including the following: the nature of maternal-to-child transmission, what cofactors may play a part in various consequences of the virus, relationship to microcephaly, Guillain-Barre and other sequelae, level of risk including symptomatic vs. asymptomatic transmission, duration of infectivity in semen. We are also doing work to accelerate optimal vector control strategies, better diagnostics, and vaccine discovery.

We are working to find information about these areas and will need the additional funding requested in the supplemental 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, veterinarians, and others at CDC are working around the clock to protect Americans from this and other health threats. We already have made significant progress identifying the virus in brain tissue of affected infants, developing and distributing new diagnostic tests, issuing guidance, conducting epidemiological investigations along with affected countries, and improving monitoring and surveillance in the United States including Puerto Rico and the territories. Much of what we know about Zika and similar viruses today is based on the work done by CDC scientists who have dedicated their lives to working in this area. But as hard as we work, there are still many things we cannot know now, and cannot do now. We will continue to use the best of modern science to protect the American people.

ZIKA AND ITS HISTORY

Zika is an emerging health threat; we face a rapidly changing situation involving numerous partners in this country and abroad. Zika virus causes understandable concern among people throughout the Americas, including those here in the United States. CDC is discovering better ways to prevent, detect, and respond to Zika and its complications. We are committed to ensuring that the American people have access to the most accurate, timely information about Zika virus and the current outbreak. Many areas of the United States have the type of mosquitoes that can become infected with and transmit Zika virus. Although we cannot predict with certainty the impact of Zika virus in the United States, we believe we will see additional cases in the U.S. based on experience with dengue and chikungunya, which have been spread locally in parts of the Southern United States, Hawaii, and the Territories and are spread by the same type of mosquito as dengue and chikungunya. Recent chikungunya and dengue outbreaks in the United States suggest that Zika outbreaks in the U.S. mainland may be relatively small and localized. Better housing construction, less crowding, regular use of air conditioning, use of window screens and door screens, and State and local mosquito-control efforts have helped to contain transmission of these mosquito-borne viruses. However, we understand that any local outbreaks will be of deep concern to the people living there. For the Commonwealth of Puerto Rico as well as the U.S. Virgin Islands and American Samoa, the outlook is different. There have been case reports of local transmission in all three territories. Furthermore, recent outbreaks of dengue and chikungunya suggest that Zika virus may spread widely in those areas. As we continue to learn more about Zika virus, including potential transmission risks, we are working 24/7 to incorporate our most accurate and up-to-date understanding of the virus. Given this, we need to be fully prepared, especially as the spring and summer months arrive. We are particularly concerned about Puerto Rico and the U.S. territories that may experience substantial spread of Zika. For comparison, more than

80 percent of adults in Puerto Rico have been infected with at least one strain of dengue, and about a quarter have been infected with the more recently introduced chikungunya virus. So, while only 9 cases of local transmission of Zika have been identified in Puerto Rico, it would be reasonable to expect that percentage to rise. Most people who may be exposed to Zika virus will have only mild symptoms. In fact, about four out of five people infected with Zika appear not to have symptoms at all. But increasing evidence that suggests that Zika virus infection may be associated with more serious health outcomes.

This emergency funding request is designed to support immediate response activities to reduce the Zika risk in the United States and around the world. CDC has unparalleled experience responding to emerging infectious disease threats. CDC's focus on Zika is consistent the core principles of public health:

- PREVENT or mitigate avoidable outbreaks and lessen the spread of disease.
- DETECT epidemics and new disease threats quickly.
- RESPOND effectively to public health emergencies, protecting lives abroad and in the U.S.

CDC is working in collaboration with other components of the Department of Health and Human Services (HHS), including the Office of the Assistant Secretary of Preparedness and Response (ASPR) and within that the Biomedical Advanced Research and Development Authority (BARDA), the Office of Global Affairs, the National Institutes of Health, and the Food and Drug Administration. We are working as well with partners across the U.S. Government to communicate with healthcare providers and the general public; issue travel alerts and clinical guidance; and step up our efforts on research to better understand the Zika virus, and on the development of tests, treatments, and vaccines, as well as improved mosquito-control methods.

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 an infected *Aedes* species mosquito. These mosquitos also spread dengue and chikungunya viruses. The mosquitoes become infected when they bite a person already infected with Zika virus. These infected mosquitoes 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 also can be passed from a mother to her developing baby during pregnancy.

Zika is not a new virus. It was first recognized in 1947, and it was recognized to cause 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 9, 2016, more than 30 countries and territories, including the Commonwealth of Puerto Rico, a U.S. Territory, as well as the U.S. Virgin Islands and American Samoa have reported local transmission of the Zika virus. The World Health Organization Emergency Committee on Zika declared the recent cluster of microcephaly cases and other neurological disorders reported in Brazil, following a similar cluster in French Polynesia in 2014, a Public Health Emergency of International Concern. On February 1, the World Health Organization (WHO) declared the recent cluster of microcephaly cases and other neurological disorders reported in Brazil, following a similar cluster in French Polynesia in 2014, constitutes a Public Health Emergency of International Concern (PHEIC), a reflection of the seriousness of this unfolding epidemic.

SYMPTOMS AND ADVERSE OUTCOMES

Many people who may be exposed to Zika virus will have only mild symptoms. Those who do become ill usually have mild symptoms such as fever, rash, joint pain, and red eyes or conjunctivitis. The symptoms last a couple days to up to a week, and it is very rare for Zika to cause serious illness or death.

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 following Brazil's outbreak of Zika virus. Microcephaly, is a usually rare, serious condition among newborns where a baby's head is smaller than expected. 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 life threatening.

Laboratory tests at CDC strongly suggest a link between Zika virus infection during pregnancy and microcephaly. We do not know whether this link is causal, or, if so whether there are important cofactors such as other infections, nutritional factors, or environmental toxins. We also do not know what, if any, other outcomes might be associated with Zika infection during pregnancy. 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. Zika virus spread in the Americas and its effect on pregnancy are new developments that we are working with partners to better understand.

Our primary concern at this point is to protect pregnant women from Zika virus infection. That's why, during the same week we identified Zika in brain tissue specimens from affected infants, we issued a travel advisory warning to advise pregnant women not to travel to affected areas. And that's why we are working around the clock with Puerto Rico and other areas to get support to women who are or who may become pregnant and to do what we can to reduce the threat of Zika there.

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 many different infections with viruses similar to Zika. CDC is currently working with public health officials in Brazil to investigate whether there is any link between Zika infection and Guillain-Barré.

PREPAREDNESS AND RESPONSE

We know that there will be many more Zika virus cases in affected areas in Latin America and the Caribbean. That is why the President's Zika emergency funding request includes support for CDC's efforts to enhance international capacity for virus surveillance, and to expand the expertise in mosquito surveillance and control, laboratory testing, healthcare provider training, and epidemiological investigations in countries at highest risk of Zika virus outbreak.

While we have not yet seen transmission of the Zika virus by mosquitoes within the continental United States, we know that many returning travelers will have Zika infection—for comparison, there were 3,270 travelers in the United States diagnosed and reported with chikungunya infection in 2014 and 2015. So we expect that many travelers to the United States will be diagnosed with Zika infection, and the number of Zika cases among travelers visiting or returning to the United States will likely increase.

DOMESTIC ACTIVITIES

CDC has a long history of assisting county, State, tribal and territorial public health partners to detect, prevent, and control diseases spread by mosquitos. 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, Puerto Rico, and six large municipalities to conduct human case investigations, collect and test mosquitos, and perform laboratory analysis on arboviruses including Zika. State and local public health agencies are working with the CDC to maximize disease detection and reporting of Zika. CDC is also working with several States and 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 cooperative agreements to strengthen their capacity to prepare for and respond to emerging threats such as Zika virus. These resources may be used to help health departments expand their capacity to prepare for cases of local Zika virus transmission in their areas and to implement community education and prevention programs to reduce human-mosquito contact and therefore reduce the risk of Zika transmission. Resources may also be used to implement vector control strategies to prevent further spread of Zika virus in areas where local transmission has been found.

It also is critical that States and territories are able to receive specimens and test for Zika virus in order to diagnose and report travel-related and locally acquired cases of Zika. CDC, under the emergency request, will expand its efforts to assist public-health labs nationwide with the reagents necessary to test for Zika and the guidance on how to interpret test results. In addition, CDC is available to provide testing of any Zika samples upon request. Building on experience applying advanced molecular detection technology to address the emergence of chikungunya virus, CDC scientists have been working to develop and validate a Zika test that could detect emerging strains for use in laboratories throughout the Western Hemisphere. Significant progress has been made toward being able to detect the virus within three weeks of having received the first Zika virus sample. With older methods, this would have required three to 4 months. CDC also developed the IgM ELISA and Zika Virus Plaque reduction neutralization test in use at CDC to detect evidence of previous Zika infections. Currently, CDC scientists are also working to develop a faster, next-generation neutralization test that could detect prior Zika infection.

CDC experts are working intensively to learn more about the outbreak and provide people with the information they need to protect themselves. The same week the CDC laboratory identified Zika virus in samples from affected infants in Brazil, we issued a travel advisory indicating that pregnant women should consider postponing travel to Zika-affected areas. We issue travel alerts for the affected areas as confirmation of the virus is reported, and we'll keep you alert as the situation changes. CDC is also working with FDA to ensure the safety of the blood supply from Zika virus, particularly in regions experiencing local outbreaks. Finally, CDC also has provided guidance for doctors and other clinicians on the evaluation, treatment and follow-up care of pregnant women and infants with possible exposure to Zika virus.

Our guidance has and 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 on-going 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. We issued a health advisory to help clinicians in recognizing, managing, and reporting Zika and recently held a clinician outreach call that reached nearly 3,000 participants and more than 150 partner organizations. CDC will continue regular ongoing engagement of clinicians through direct outreach and partnerships with key medical societies.

CDC also wants to ensure that the general public knows what they can do to protect themselves. Pregnant women should consider postponing 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 by 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 to reduce exposure to daytime mosquitoes. For women living in areas with Zika virus outbreaks, CDC appreciates that the timing of pregnancy is a personal and complex decision for a woman to make in consultation with her doctor or other healthcare provider. Given the potential for Zika virus to be spread through sex, if male partners have or are at risk for Zika virus infection, pregnant women and their male partners should consider using condoms or abstaining from sex for the duration of the pregnancy. This is a rapidly-changing situation and our understanding of the risks concerning Zika virus infection, including those surrounding transmission from mother to fetus and those concerning transmission between sexual partners, is incomplete and evolving. As we get new information, we will update our recommendations.

GLOBAL ACTIVITIES

CDC is coordinating its response with the Pan-American Health Organization, the regional body of WHO, with 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 research partnerships. Specifically, one partnership will be studying the link between Zika virus infection and microcephaly, while another is examining the relationship between Zika virus and Guillain-Barré. Research teams from CDC are also in other countries to explore collaborations that

will shed light on the risk of microcephaly with maternal Zika virus infection during pregnancy.

In addition, CDC has offered to all countries to test samples from microcephaly cases for serologic evidence of Zika virus infection and to help these countries establish in-country diagnostic capacity. To that end, we are currently, in conjunction with the Pan American Health Organization of the World Health Organization, providing training to laboratorians in South and Central America on diagnostic tests, including two recent workshops in Brazil and Nicaragua.

CDC's Global Disease Detection (GDD) program rapidly detects, accurately identifies and promptly responds to emerging infectious diseases such as Zika virus. The GDD Operations Center has been monitoring the spread of the epidemic from Brazil to other countries in the Americas since Brazil first reported Zika transmission in May of 2015. CDC's Central American office has facilitated the verification of Zika cases in several countries throughout Latin America, including Colombia, Venezuela, and Nicaragua. The GDD program has also been working 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.

Investing in global health is not just the right thing to do to save lives, it is the right thing to do to protect Americans. The global health security agenda, with critical support from Congress, is collaborating with countries around the world so that we can prevent, detect, and respond to health threats when and where they first emerge. Zika has been present in Africa for decades, and it's possible that it causes 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.

RESEARCH ACTIVITIES

More research is critical to addressing several gaps in our ability to respond to Zika as outlined in the Zika Emergency Request. 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. Diagnosis of Zika is complicated by the fact that about 80 percent of infected people appear not to have symptoms. The virus can be reliably detected by current diagnostic methods only in the first 7 days of illness onset.

Currently, a Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test can provide a definitive diagnosis of Zika, but only if it is performed within about a week 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. Diagnosis is particularly challenging with Zika virus since most people will not experience symptoms and therefore will not go to their healthcare provider in time for PCR-testing to be utilized. We also need to determine the length of time a man who has been infected by a mosquito may continue to shed virus in semen.

Additional research is also needed to develop methods of mosquito control. Control of the particular mosquito that spreads Zika is very challenging. We need to both implement the best tools we have today, and conduct more work and research to develop better tools and strategies for mosquito control. Existing methods for mosquito control all have shortcomings, especially in areas where the population of *Aedes* vector mosquitoes is rampant. Vector control is particularly challenging with this specific type of mosquito because of its preference to live in and around houses, the fact that it bites during the day, the fact that it preferentially bites humans, and its ability to breed in very little water. Better mosquito surveillance is also vital to determine the location of mosquitoes 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 women of childbearing age. NIH, in collaboration with ASPR/BARDA, will address the possibility of developing such a vaccine based on vaccines for dengue and West Nile virus are under development as outlined in the Emergency Request. NIH also is exploring other vaccine development strategies. 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.

CONCLUSION

Nature is a formidable adversary. 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. Investment in both the practice and research on new means of mosquito control is particularly important, as is work on a vaccine. As the Nation's health protection agency, CDC is focused on responding quickly to new and emerging health threats such as the Zika virus.

In addition, of the more than \$1.8 billion in the President's emergency funding request to prepare for and respond to the Zika virus, \$828 million is for activities at CDC. This includes funding to support prevention and response strategies through:

- Supporting Zika virus readiness and response capacity in States and territories with mosquito populations that are known to transmit Zika virus, with a priority focus on areas with ongoing Zika transmission;
- Enhancing mosquito control programs through enhanced laboratory, epidemiology and surveillance capacity in at-risk areas to reduce the opportunities for Zika transmission;
- Establishing rapid response teams to limit potential clusters of Zika virus in the United States;
- Improving laboratory capacity and infrastructure to test for Zika virus and other infectious diseases;
- Implementing surveillance efforts to track Zika virus in communities and in mosquitoes;
- Deploying targeted prevention and education strategies with key populations, including pregnant women, their partners, and healthcare professionals;
- Expanding the CDC Pregnancy Risk Assessment Monitoring System, improve Guillain-Barré syndrome tracking, and ensure the ability of birth defect registries across the country to detect risks related to Zika;
- Increasing research into the link between Zika virus infections and the birth defect microcephaly and measure changes in incidence rates over time;
- Enhancing international capacity for virus surveillance, expand the Field Epidemiology Training program, laboratory testing, healthcare provider training, and vector surveillance and control in countries at highest risk of Zika virus outbreaks; and
- Improving diagnostics for Zika virus, including advanced methods to refine tests, and support advanced developments for vector control.

We look forward to working with the Congress on the implementation of the President's emergency funding request.

CDC's current response to the Zika outbreak in the Americas again demonstrates our commitment to global health security and why implementation of the Global Health Security Agenda (GHSA) is needed. Global health security is a shared responsibility that cannot be achieved by a single actor or sector of government. In partnership with other nations and international organizations, the CDC is committed to mounting a prompt, coordinated response to the emerging threat of Zika virus in order to protect the people both in the United States and around the world.

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.

Senator BLUNT. Thank you.

Dr. Fauci.

STATEMENT OF ANTHONY FAUCI, M.D., DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. FAUCI. Mr. Chairman, Ranking Member Murray, Senator Mikulski, and members of the committee, I want to first express my appreciation for your calling this very important hearing and giving me the opportunity to discuss with you the research that is conducted and supported by the National Institutes of Health in addressing all emerging and reemerging infections, including Zika.

I show this slide because it tells a little bit about the uniqueness of the mandate of the National Institute of Allergy and Infectious

Diseases. Like every other institute at the NIH (National Institutes of Health), we are responsible for maintaining a robust basic and clinical research portfolio in the disciplines of our mandate. In our case, it is infectious diseases and immune-mediated diseases.

However, unique among the institutes, we have the responsibility of responding rapidly to new and emerging diseases. This is really quite unique, because we can wake up in the morning the way we did 7 months ago and realize all of a sudden we have a new, very serious issue with Zika.

I show this slide, which is an empty map of the world, and I show it from a historical standpoint, because before this committee, probably in this room, 31 years ago, when I first presented the situation with HIV, I brought up the concept of new and reemerging infections, and I put this particular arrow of HIV on the map. And every year that I have testified before this committee, we always seem to add one, sometimes two, and maybe three, new diseases or reemerging diseases.

Some of them are only really curiosities. Others are very serious.

So if you take the sum of the 31 years that I have been doing this, this is what the map looks like now, which are all diseases that have cropped up, some of which have caused serious problems, others of which have been just curiosities.

Some of them are newly emerging infections. HIV/AIDS was one of the newly emerging infections. It was brand new. We hadn't seen it before. And it has had and still does have an extraordinary impact globally. There are others like MERS, SARS, and others.

As important as a newly emerging disease is a reemerging or resurging disease. Let me give you some examples, because it is relevant to what we are talking about today.

West Nile virus, which was never in the Western Hemisphere, for centuries was in Africa and the Middle East. All of a sudden, about a decade and half ago, it arrived in New York City and now is prevalent in the United States at a low level. Ebola virus disease, which was discovered in 1976, resurged in 2014 and 2015 in West Africa. We all know about that. Chikungunya, which was never in the Western Hemisphere, appeared there in 2013 and is now highly prevalent in the Caribbean and South America.

Now we are dealing with Zika virus, which essentially, since its discovery in 1947, was something that was under the radar. We didn't fully realize its impact until the explosion of cases that we have now seen.

In fact, in this article which I wrote just a few weeks ago in the *New England Journal of Medicine*, I underscored that Zika virus was yet again another arbovirus virus, or mosquito-borne virus, that has inflicted itself on our Western Hemisphere and the Americas. I mentioned the other ones, West Nile, dengue, now Zika, chikungunya.

What is NIH doing? What is our responsibility? As I told this committee many times in the past in previous hearings, we have the responsibility of conducting basic and clinical research, but also providing resources for researchers both in academia and industry to be able to do the kinds of research needed, be it in medical centers in Washington or New York or in California or where have you.

The endgame is ultimately to develop interventions in the form of diagnostics, therapeutics, and vaccines. Rather than go through all of the issues that we are going to address—and we will understand the virus better, work with the CDC in developing better diagnostics, understand better vector control—the issue that is of immediate importance right now is to be able to develop a safe and effective vaccine against Zika.

I want to remind you, and I think you all remember that in the United States decades ago, we had a similar problem in our country, and that was the congenital rubella syndrome. In the 1960s, there were 20,000 babies a year born in the United States with congenital rubella syndrome, which has varying degrees of severity of visual impairment leading to blindness, deafness, heart disease, and mental retardation.

When the rubella vaccine was developed, congenital rubella syndrome essentially disappeared. So although it was a vaccine that was targeted for all the population and is a required vaccine now, its real target was women of child-bearing age, because the concern is protecting pregnant women, as Dr. Frieden has emphasized in his presentation.

The advantage that we have is that Zika is a flavivirus. Fortunately, thanks to the support of this committee, we've had the opportunity to work for decades on other flaviviruses. We developed a successful vaccine for yellow fever, a successful vaccine for dengue, as well as another dengue vaccine, an improved vaccine, which is in a phase 3 clinical trial in Brazil, as well as a West Nile virus vaccine.

But unfortunately, we didn't have a pharmaceutical company to partner with us on the West Nile virus vaccine, because it wasn't felt to be something that would be profitable for them, because West Nile virus wasn't a major disease in the United States. I don't think we are going to have that problem now, because we have a number of companies that are very interested in developing Zika virus vaccines with us.

This is just an example of how you can use previous knowledge to make a vaccine that can go into clinical trial quickly.

So on the left-hand side, that little bit of DNA is called a plasmid. When we did the West Nile virus vaccine, we inserted the gene of the West Nile protein in that plasmid. We injected it into people and made virus-like particles. And it was a good vaccine. It was safe, and it induced a good immune response.

We have already taken that same plasmid, removed the West Nile gene, placed in the Zika gene, and now you have the beginning of a Zika vaccine.

It really is a testimony to having the experience of continued years of support in trying to respond to Zika.

We will likely go into phase 1 clinical trial with this vaccine sometime in late summer, and I hope, after several months, we will know if it is safe, and we will know if it induces a good immune response. If it does, then we will move to more advanced stages of testing. I can't guarantee when we will have the vaccine available, but I can tell you we have a very good head start because of years of prior work.

So I want to close on this last slide by, again, reiterating the mandate of what we do and why it is so important not only to do the fundamental basic research with established diseases, but also be able to respond rapidly to newly emerging and reemerging diseases.

I want to close by thanking the committee for the support you have given us, and telling you how important it is for us to get that supplement to our budget to be able to continue this degree of activity. Thank you.

[The statement follows:]

PREPARED STATEMENT OF ANTHONY S. FAUCI, M.D.

Mr. Chairman, Ranking Member Murray, and Members of the Subcommittee: Thank you for the opportunity to discuss the research response of the National Institutes of Health (NIH) to emerging infectious diseases threats to our Nation and the world. The current case in point is our response to the outbreak of Zika virus disease in the Americas. 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, on February 8 it announced a request to Congress for more than \$1.8 billion in emergency funding to enhance ongoing efforts to prepare for and respond to 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 NIAID mission 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 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 infectious diseases such as those caused by 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 that most often result from human activity. To address the challenges posed by emergent 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 vaccines and diagnostics for 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 maintains a program that provides preclinical research resources for use by scientists in academia and private industry worldwide to advance translational research against emerging and reemerging 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 development of effective countermeasures against these emerging infectious disease threats. NIAID also supports the Vaccine and Treatment Evaluation Units (VTEUs), a research network for conducting clinical trials to quickly investigate promising therapies 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 mosquitoes of the *Aedes* species. 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-Barre 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 microcephaly, as well as 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 nonspecific symptoms and can be difficult to distinguish from other mosquito-borne infections such as dengue, malaria, and chikungunya in antibody screening tests. 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 request 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 request would support basic research to understand the natural history and pathogenesis of the virus, 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, the notice indicates that NIH will pursue 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, the National Institute

of Neurological Disorders and Stroke, 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.

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. 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. In Phase 1 testing, the West Nile vaccine candidate was shown 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 candidate—that expresses the Zika E glycoprotein. 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 hope to begin early-stage clinical testing of one or more NIAID-supported vaccine candidates in 2016.

DEVELOPING VACCINES TO PREVENT CHIKUNGUNYA VIRUS

Chikungunya virus is transmitted to humans primarily via the bite of infected *Aedes* mosquitoes, the same mosquitoes that transmit Zika virus. Chikungunya virus causes a sometime-serious illness characterized by fever and severe joint pain, which can last for months and be disabling. Since 2013, chikungunya virus has spread rapidly in the Caribbean, as well as Central and South America. No licensed vaccines or therapeutics are available to prevent or treat chikungunya virus infections. NIAID has responded to the emergence of chikungunya virus by accelerating research on diagnostics, therapeutics, and vaccines to combat the disease.

The emergency funding request for NIH would support efforts to develop a safe and effective chikungunya vaccine to prevent this debilitating mosquito-borne disease. Additional funds would enable animal model and human clinical tests of promising vaccine candidates. This research will build upon efforts of scientists at the NIAID VRC, who have developed a candidate chikungunya vaccine based on a DNA vaccine that leads to the production of virus-like particles. The NIAID VRC vaccine candidate was safe and generated an immune response in a Phase 1 clinical trial. The vaccine is currently in Phase 2 clinical testing at six study sites in the Caribbean. NIAID also is planning a Phase 1 trial of a live, attenuated measles virus-vectored vaccine candidate to be conducted through the NIAID VTEUs. Several additional chikungunya vaccine candidates will be evaluated for safety, ability to generate immune responses, and efficacy in preclinical and animal model studies; if promising, these candidates will advance to clinical testing.

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 chikungunya and Zika viruses.

FUNDING FOR PUERTO RICO

Senator BLUNT. Thank you, Dr. Frieden and Dr. Fauci.

Dr. Frieden, of the \$1.8 billion request, based on the breakdown, that looks like about \$228 million would go specifically through CDC to efforts in Puerto Rico and other territories, and then CMS (Centers for Medicare & Medicaid Services) has \$250 million to supplement Medicaid in Puerto Rico. So about half a billion of that \$1.8 billion is focused largely on Puerto Rico.

Do you want to talk about that a little bit?

Dr. FRIEDEN. We are most concerned about Puerto Rico because it is an area, because of its natural environment and human environment, where viruses spread by this particular mosquito spread very widely.

Dengue first arrived in Puerto Rico about a decade ago. Our studies in Puerto Rico show that 80 percent to 90 percent of adults have been infected in the past with dengue. And chikungunya, which just arrived a year and half, less than 2 years ago, studies sometime back showed that about a quarter of all adults have already been infected by this virus spread by the same mosquito.

So we think there is a real possibility that, at some point in the coming months—and we can't predict with certainty when. It could happen very soon. It could happen months later. But at some point, we may well see tens or hundreds of thousands of Zika infections in Puerto Rico.

There are approximately 34,000 births per year in Puerto Rico, so we are concerned with 3,000 deliveries per month, roughly, with the risk of microcephaly there.

So our priority would be to reduce the risk to pregnant women. That can be done by two broad means. First, personal and household protection, where you provide to pregnant women mosquito repellent, clothing that repels mosquitoes; encourage use of long sleeves, long pants; encourage people to stay indoors if possible in air-conditioning, or at least in screened space; provide screens and possibly insecticide-treated screens, which are effective.

Those are personal measures that we can support through programs in Puerto Rico, and we are already moving as quickly as we can to try to do that, sometimes with support from foundations, and sometimes with support that we can find within our resources.

The second area is vector control. That means control of the mosquito. That is very challenging. That means getting rid of standing water everywhere, eliminating tires, puddles, anywhere that this mosquito can breed. It can breed in the top of a bottlecap, if there's some water in it. So there's a real challenge in reducing breeding sites.

We also apply larvicides—these are natural materials or chemicals that can reduce mosquito larvae—to any water surfaces, drains, or other areas where mosquitoes can breed. There may be a role for spraying of insecticides in some outdoor places, but even possibly in some indoor places.

TIMELINE FOR VECTOR CONTROL

Senator BLUNT. I'm going to run out of time so I will be brief. With the mosquito effort in Puerto Rico and the Virgin Islands and American Samoa, and then as you move into the Southern United States, including Texas and Florida, is that a 1-year effort? Is the Zika virus likely to spread beyond the lifecycle of the individual mosquito? How long does this effort need to be made?

Dr. FRIEDEN. We think this is something that we need to scale up as rapidly as possible and will likely be needed for the longer term. Zika is likely going to continue to spread, if it acts as dengue and chikungunya have for years. But sometimes it spreads explosively and then comes down to a more low level of transmission.

But we can't predict it. We will just have to see what happens with time and what we can prevent.

ZIKA TRANSMISSION

Senator BLUNT. And, Dr. Fauci, when it does spread, is there a possibility that you have it wherever you are, or you come back from Brazil or Puerto Rico and you have it and don't know it? Talk a little bit about the way this virus shows itself.

Dr. FAUCI. About 80 percent of people who get infected have no symptoms and would likely not realize they have been infected. Of the other 20 percent, it is a relatively mild illness, generally fever, some muscle and joint aches, a rash, and some conjunctivitis, or pinkeye.

We know that when you are infected, the virus stays in your blood for a week or so, 10 days. After that when you do test for the presence of the virus, it is not there.

The issue that we are following closely, and that the CDC is very heavily involved in, is that we know that it can be transmitted sexually, but we don't know how long it stays in the seminal fluid. Is it only during the acute phase of infection? Is it a week, a month, or what have you?

We have experience with Ebola, which taught us that we should be circumspect before we make any firm conclusions. In studies of survivors of Ebola, we find that a certain percentage have continued presence of Ebola virus in the semen for several months following infection. Now that may not be the case with Zika, but it's something we want to keep an eye on. That is why you do natural history follow-up studies.

With regard to the blood, Zika virus essentially leaves after a period of about 10 days.

Senator BLUNT. Okay. Thank you.

There will be time for multiple rounds of questions, but the order will be Senator Murray, Senator Cochran, Senator Mikulski, Senator Moran, Senator Schatz, Senator Capito, Senator Merkley, Senator Shaheen, and then others as they come in. We will go back and forth, based on order of arrival.

If these floor votes do start, I would just ask the members, if you have time to go vote and come back, we will just continue the hearing and let other people do their 5 minutes or so of questioning while others are going over to vote and coming back.

Senator Murray.

ZIKA DIAGNOSTICS

Senator MURRAY. Thank you very much.

Dr. Frieden, last week, the CDC updated its testing recommendations for pregnant women. They are now recommending that all pregnant women be offered Zika testing after they have traveled to an area where the virus is spreading, regardless of whether they have experienced symptoms or not. I think that is a really good recommendation, to include the asymptomatic women, because we do know that four out of five people don't know they have had the virus, because they don't have any reaction.

That means a lot of women will need to be screened. How readily available are these diagnostic tests?

Dr. FRIEDEN. There are, broadly speaking, two types of tests.

One is to find the virus when it is in your blood, when you're acutely ill. That test is amply available through or becoming available. We have produced enough materials for it, and we are shipping them out and training State laboratories and city laboratories through the public health systems. So that test for someone acutely ill, I think we won't have a supply problem.

The bigger challenge is diagnosing prior infection. First off, it is an imperfect science. The virus is very similar genetically to other flaviviruses, and, therefore, people who have had dengue or yellow fever vaccine or even West Nile virus may have a falsely positive test. So there are two different tests that are done for prior infection.

We are literally working around the clock to produce enough of those. We produced an initial batch of 32,000, a second batch of 30,000 this week. We hope to have a third batch of 30,000 by the end of the month. And we are working with four or five different companies to try to encourage them, on a nonexclusive licensing agreement, to produce more.

But we do think that, for a few weeks and potentially couple months, there could be people who want to be tested and the test is not available. It hasn't happened yet, but we will see spot shortages of some States that are ready and others aren't. If that initial test is positive, there is a much more complex secondary test, which is little more accurate but still can have false positive results. And that takes up to a week, and our scientists are now working over the next couple months to reduce the time from a week to 3 or 4 days by splicing the antigens into a faster growing virus, because that second test requires growth of the virus.

MICROCEPHALY AND OTHER BIRTH DEFECTS

Senator MURRAY. Okay. There have been about 4,000 cases of children with microcephaly at this point reported in Brazil. And we have all seen the heartbreaking pictures of the children born with that really devastating birth defect.

I understand that the link between Zika and microcephaly has not been determined conclusively. But regardless, that is a lot of children and families who have been dealing with this condition for a long time. What is long-term prognosis for those children and their families?

Dr. FRIEDEN. At CDC, one of the characteristics that we have to help protect Americans is a broad range of expertise, including what Congress has funded as the National Center for Birth Defects and Developmental Disabilities. So we have some of the world's leading experts in congenital abnormalities, and they are part of our emergency response.

They tell us that the lifetime additional cost of caring for a child with a severe birth defect may range from \$1 million to \$10 million per child in this country. There's going to be range of disabilities associated with microcephaly. We just won't know until more time has gone.

We've already seen cases that were so severe they resulted in early death. We have seen cases that resulted in blindness or deafness or severe problems with eyesight or hearing. We have seen other cases where infants appear to be normal, from a morphological standpoint.

So these are all things that we need to understand further so we can give information to people so they can decide what they want to do with their health.

FUNDING FOR VECTOR CONTROL

Senator MURRAY. Okay. There has been a rise of mosquito-borne illnesses—you both talked about it—affecting the United States at the same time CDC's budget for mosquito control has declined. There has been a 60 percent decrease from 2004 to 2015 in the epidemiology and laboratory capacity grant funding for vector-borne disease surveillance. According to a recent assessment, as a result of these funding decreases, human surveillance has become more passive, laboratory capacity has declined, and mosquito-surveillance activity has diminished now to the point where some State and key local health departments no longer even do it.

That is a trend that obviously needs to change. What do we know about the effectiveness of existing mosquito-control interventions?

Dr. FRIEDEN. To control mosquitoes, you first need to monitor them. So mosquito surveillance, as we call it, is quite important. Unfortunately, it is not done as well as we would like across the United States. It is done in a patchwork. Some areas do a superb job. Other areas don't do it at all. When we show you maps of where these two mosquito vectors are present, those are our best estimates of where those mosquitoes are. They may be partial, out of date, no longer correct.

So we need, first, to improve our tracking for where mosquitoes are, and then our means to control them. And we can do that through controlling outdoors baby mosquitoes, larvae, and adult mosquitoes.

But with this particular mosquito, because it is an indoor-biting mosquito, it's very difficult to control.

ZIKA SUPPLEMENTAL REQUEST

Senator MURRAY. Okay. The supplemental request from the President, how much did they ask for, for mosquito abatement strategies?

Dr. FRIEDEN. So the CDC component of that is \$828 million. Of that, all three of the components include mosquito control. The

three components meaning Puerto Rico and the territories, at-risk States, and our international work.

Senator MURRAY. Which is clearly important for Zika but for a number of the other mosquito-borne illnesses.

Dr. FRIEDEN. Yes. Anything that controls the Zika-spreading mosquitoes will also reduce the risk of both dengue and chikungunya.

Senator MURRAY. Okay. Thank you.

Senator BLUNT. Senator Cochran.

Senator COCHRAN. Thank you, Mr. Chair, for convening this hearing.

We appreciate the witnesses coming in and helping us understand the nature of the challenge that we face dealing with infectious diseases and other challenges in the public health arena. Thank you for the excellent job you are doing in helping target funds where they are needed most.

I understand that we have already received \$1.8 billion in funding to enhance Zika virus programs. Is this enough? Are we in need of an additional request for the Senate and House to approve?

Dr. FRIEDEN. Thank you very much.

For the Zika virus emergency supplemental request, we have provided our best estimate of what we think we need at this point. We think that will cover for the next 1 to 2 years.

But there is a lot that we don't know. We are literally learning more every day. But based on what we know now, I can say that the funding that CDC has asked for, we have a clear plan for. We don't know that we will be able to absolutely prevent every infection and every adverse health outcome, but it will allow us to flex up; to robustly respond in areas at risk; and, most importantly, to support the States, territories, and localities that are potentially at risk, as well as provide information to patients and doctors and those who need to know.

Senator COCHRAN. Dr. Fauci, is there any further appropriation needed beyond that which we have already approved by Congress?

Dr. FAUCI. Similar to what Dr. Frieden said for the CDC, when the NIH was asked for justification for what we would be able to do to respond to Zika, the money that is in the President's request, of the total \$1.8 billion, the portion for the NIH is adequate to do what we need to do right now. Thank you.

Senator COCHRAN. Thank you for your good efforts and your leadership, and cooperating with our committee in discharging our responsibilities, too. Thank you very much.

Senator BLUNT. Senator Mikulski.

EBOLA FUNDING FOR ZIKA

Senator MIKULSKI. Thank you very much, Mr. Chairman. In the interest of time, I ask that my entire statement be put in the record. And I want to thank you and Senator Murray for holding this hearing, and Senator Cochran for being here.

I am going to get right to my question, but I think what this shows is, once again, the defense of the Nation does not only rely in DOD (Department of Defense). We might be fighting ISIL (Islamic State of Iraq and the Levant) with airstrikes, but we could be protecting America with mosquito eradication. We need to be

able to be prepared, and we need a reliable infrastructure along the way.

Dr. Frieden, I am going to go right to you. The President is asking for an urgent supplemental. The numbers have been explained and so on. There are others who say, "Hey, Tom, you have the Ebola money. Why don't we just reprogram that? You helped the world contain that. America has acted once again." And yet when I spoke to you, you were on the edge of your chair about the possibility of reprogramming and also that we would be very dithering in the way we proceed, and you had a sense of urgency, particularly over the next couple weeks.

So could you say why you need a supplemental, according to the definition of urgent, sudden, and unforeseen? Or should we reprogram the money?

Dr. FRIEDEN. First, the situation is urgent, because we are learning more every day. We have already seen more than two dozen locally acquired cases in Puerto Rico. We may see rapid spread through the island, and we need to respond urgently.

It is, certainly, sudden. This is something which, until late last year, no one had any idea that a mosquito bite could result in a serious fetal malformation.

And it is unforeseen. We have actually never before had a mosquito-borne cause of malformations, as far as we know, on a major scale.

Our Ebola supplemental, we are deeply grateful that Congress provided that and allows us to continue to respond to the Ebola outbreak in West Africa. We continue to have about 100 CDC staff on the ground. Last month alone, we did 10,000 tests for Ebola, to identify a new case of Ebola and a new cluster. We then responded to that cluster of cases with intensive contact investigation of more than 100 high-risk contacts. It's a very challenging environment still. So first off, Ebola is not over.

Second, if you look at the dollars for Ebola, those dollars are fully committed. Within the United States, the budget was about \$600 million. By the end of this year, more than 95 percent of that will be gone.

In the three affected countries, we budgeted \$300 million. By the end of this year, we will spend at least \$300 million in those areas.

For the rest of the Ebola supplemental, it is about the Global Health Security work. And for Global Health Security, this is about finding things like Zika before they become problems like this. It is finding threats when they first emerge.

Senator MIKULSKI. Doctor, what you are saying is that the Ebola money is actually committed, that it is not a pot of money we can turn to and move around in a fungible way to deal with Zika, that we have to deal with Zika on its own—that is number one—to immediately be able to respond, because in Puerto Rico, as you said, 40 million people are traveling back and forth.

We do not know the full extent of the disease. Dr. Fauci has also spoken to that. We do not know about the impact on people over 65. We have talked about pregnant women, really quite an eye-popper in and of itself. We do not know about the impact on people with compromised immune systems. We do not know that. We do

not know a lot. And we do not know about the long-term consequences.

You mentioned chikungunya, a new thing to me. But the effects of this last 10 months simulate like arthritic conditions. It could leave long-lasting consequences.

So we need to get over that there are pots of money sitting around—am I right?—that you can move around. We have to deal with this now. Also the same for CDC and NIH, we need reliable infrastructure ongoing.

Am I right in this?

Dr. FRIEDEN. Absolutely.

Senator MIKULSKI. I don't want to put words in your mouth.

Dr. FRIEDEN. Yes, absolutely.

Senator MIKULSKI. You conveyed a pretty good sense of urgency to me.

Dr. FRIEDEN. Yes. Absolutely correct, Senator. Thank you very much for those remarks.

We do need urgently to not let down our guard against the threats we know and strengthen the system so we don't always have to address things that we might have been able to find earlier.

Senator MIKULSKI. Well, my time is up.

Dr. Fauci, I could ask you so many questions, but I remember 30 years ago, you and I kind of began together. We have been on a very long journey together. And when men began to die, particularly on the West Coast, and we didn't know what was going on, we turned to CDC because you are our bio-detectives. And then we turn to NIH.

The rest is history. It is a history we can be proud of. We need to be proud of that fact now. We need a reliable infrastructure that you are turning to do the basic research.

From our conversations, you will be looking at the institute that does research on the brain. You'll be looking at the institute that looks out for maternity and child health. You are going to be cutting across NIH, and you can't just keep moving it around.

Research dollars are committed for the long-term. Am I correct?

Dr. FAUCI. You are correct.

Senator MORAN [presiding]. Thank you very much, Senator.

In order to accommodate Senator Schatz's ability to vote, Senator Schatz is recognized.

DENGUE VIRUS

Senator SCHATZ. Thank you very much.

Dr. Frieden, I first of all want to say thank you on behalf of the people of the State of Hawaii for your aggressive response and your assistance with State and local government on Hawaii Island in terms of the dengue fever outbreak. As you know, this is a public health crisis in its own right, and we now have the emerging threat of a possible Zika crisis.

I don't think there is really any doubt that we ought to fund the supplemental as quickly as we can.

Like Zika, dengue is a virus that can be transmitted by mosquitoes, namely the yellow fever mosquito and the Asian tiger mos-

quito. Both of these mosquito types are in Hawaii and both could transmit Zika.

Our State has now had about 250 confirmed cases of dengue since September 2015, most on the west side of the Big Island. Your response has been robust and particularly helpful.

So my question for you is whether or not I can count on your continued commitment to address Zika and dengue. It seems to me some of this at this point ought to be simultaneous, where we both have a current crisis and a potential new crisis.

Dr. FRIEDEN. Thank you very much. You are absolutely correct that the measures that will protect against one of the viruses will also protect against the other. I have to be frank that the unit that deals with these viruses is relatively small at CDC and is now fully taken up with the Zika response. But we won't turn our back on any part of the country where this is a risk and spreading.

We are stretched because of that, and there aren't a large number of experts in control. So Dr. Lyle Petersen, who has traveled to Hawaii, is now the incident manager for the Zika response.

But if we have the supplemental dollars in hand, one of the key components will be providing funding, technical assistance, and materials to areas, including Hawaii and the Southern States that have the other mosquito *aegypti* presence, so they can strengthen mosquito-control activities.

TELEMEDICINE

Senator SCHATZ. In terms of public health education, obviously, a fair amount of the public health education has to happen in rural areas, which by definition are going to have difficulty getting the latest information on the best practices. I am wondering how much you've used or are considering using teleconferencing technology and other means to push out the information as efficiently as possible?

Dr. FRIEDEN. We use extensive teleconferencing, Internet, other actions. We had during the first week of the response a call with clinicians throughout the United States, with more than 3,000 groups or individuals calling in. We push out information very actively through Twitter, through our social media, and also through the clinical networks. We have been working really very closely with the American College of Obstetrics and Gynecologists to get information out as well.

VECTOR CONTROL

Senator SCHATZ. I want to talk a little bit about vector control. One of the problems that we have in the State of Hawaii is that in 2009, we decimated the vector-control branch within the Hawaii State Department of Health. I wouldn't be surprised if other States and local governments decimated their respective vector-control branches under budget pressure.

I'm wondering whether you would be in a position, not over the table, but over time, to work with the committee to provide recommendations to each State and county and local government on what you think the resource requirements would be. I think even if we are able to fund this supplemental, and I anticipate that we will be, the vector-control piece has to be at least partly funded by

State and local governments. And I anticipate that the experts in local areas are going to know what they need, but this going to be a political decision. This is going to be an appropriations decision. So what we need from CDC is for you to communicate through our U.S. Senators, our Members of Congress, our Governors, what it is that is required, because the reason a vector-control branch gets cut when the budget is tight is that it is such an abstract reason to spend taxpayer dollars. It is very difficult to justify to somebody who is walking down the street wondering why their taxes just went up.

Now we have an urgent public health crisis, and I would like for you to provide recommendations so that States and counties can actually resource this appropriately.

Dr. FRIEDEN. We can certainly do that. I would add that you are absolutely correct. This is quite variable around the United States and underinvested in many places.

There are really several areas to work on. The first is surveillance, so we understand where the mosquitoes are. That is not simple. It is a labor-intensive, year-round or much of the year-round process. The second is implementing what we know now to reduce mosquito populations. The third is optimizing our current intervention. And fourth is coming up with some new strategies; new chemicals; safer, more effective insecticides; new means of stopping mosquitoes.

We need to do all four of those things. We could get a good start on that with the emergency supplemental.

Senator SCHATZ. Thank you.

ZIKA OUTBREAK IN PUERTO RICO

Senator MORAN. Senator, thank you.

Dr. Fauci, Dr. Frieden, welcome. I heard your testimony. I didn't hear any of the questions or answers to questions, so I perhaps will be repeating. But in order to accommodate Senator Blunt's ability to vote, I was unable to be here to hear those things.

Let me first ask, is Puerto Rico different because the outbreak is occurring there as compared to one of the 50 States, something we ought to be aware of different in their public health capabilities or structure?

Dr. FRIEDEN. There are a series of differences in Puerto Rico. In order to get a big outbreak of a disease like Zika, you need the virus present, the mosquito present, and the human conditions present. In Puerto Rico, we have all three.

So these particular mosquitoes, the aegypti mosquitoes, are present in large numbers throughout the island. Second, the prevalence of air-conditioning and screens is less than it is in some other locations. Third, the ability to reduce mosquito populations is less than elsewhere, both for natural and for human reasons.

If we look at other parts of the United States, parts of Florida and Texas have had clusters of dengue infections. Wherever dengue goes, Zika can follow. So in those areas, we have a lower risk of widespread transmission.

We don't know what will happen. We don't have a crystal ball. But if it behaves as the other infections have behaved in the past, we don't expect to see a widespread transmission because of several

things. First, there tend to be lower numbers of mosquitoes. Second, people tend to be inside air-conditioning in a greater proportion of the day, and less crowded together. So crowding means that a mosquito can bite many people at once and result in an explosive spread.

Travelers are likely to come back throughout the United States from Zika-affected areas.

Senator MORAN. Is the public health infrastructure different from Puerto Rico to the 50 States?

Dr. FRIEDEN. I think it is safe to say that there are real challenges with the public health infrastructure. States and territories are variable in their capacities, and Puerto Rico is challenged in this, as it is in some other areas.

EBOLA FUNDING FOR ZIKA

Senator MORAN. I heard a bit of the questioning by the former chairman of the full committee, who was attempting not to elicit an answer from you different from the one she wanted, and I'm sure that didn't happen. But I want to make sure I understand the relationship between Ebola funding and the potential use of that funding to combat this or other incidents of outbreaks.

So tell me what has transpired since the supplemental Ebola funding occurred? And is there any opportunity for those funds to be used in fighting other outbreaks?

Dr. FRIEDEN. The bottom line for the Ebola supplemental funds that were provided to CDC is that they are all planned for and committed. If we were to reprogram those funds, we would be either risking letting down our guard in the fight against Ebola, which is not yet over, or risking letting down our partners in parts of the world where we have committed to doing a better job finding things like Zika when they first emerge, and doing a better job stopping them and preventing them.

LESSONS LEARNED FROM EBOLA RESPONSE

Senator MORAN. Ebola and Zika, I assume, are significantly different in their presentation to the world, their ability to do significant damage. But you are telling us we are better able to respond now as a result of things that have transpired from the response to Ebola?

Dr. FRIEDEN. Yes, that is correct. But we still have a lot of gaps around the world, where we are tracking new health threats when they first emerge.

The Ebola supplemental fundamentally did two broad things. One was give us the wherewithal to stop Ebola. That is a fight that we are still on. We still have around 100 people in West Africa fighting Ebola. We did 10,000 tests for Ebola last month from partners around the world. And we're making the world safer from future health threats through the Global Health Security Agenda.

Senator MORAN. In that regard, let me thank you, Doctor, and the folks at CDC for their tremendous response and effort, particularly in Africa and globally in regard to Ebola.

You are reminding me of something that shouldn't need to be reminded of: Crises still occur even when they are not on the front

pages or on the nightly news. So, just because we don't see or read doesn't mean that the problem doesn't continue to exist.

ROLE OF FDA IN ZIKA RESPONSE

Let me ask a final question. My responsibilities have shifted a bit, with a greater focus now on the FDA. Is there anything in particular that you would tell me on the role that FDA can, should, and will play in this regard? A significant portion of the money of the supplemental is intended for FDA. I would be delighted to hear, Dr. Fauci, if there's something that you would like me to know about that.

Dr. FAUCI. It's a very good question. I have to tell you that our experience, both with the Ebola situation and currently now as we are gearing up for the development of countermeasures for Zika, that our interactions with the FDA have really been as good or better than they have ever been.

We get them involved and they get us involved right from the beginning, when we are developing a clinical trial protocol. For example, the phase 1 study that we will hopefully get going by late summer for the first early look at a Zika vaccine involves very heavily the FDA right from the beginning. That is really much better than going ahead and doing it and then having the FDA figure out if you've done the right thing or not. They are with us right from the beginning.

So the FDA's part of the supplemental and the things they need to do to gear up to be able to meet this challenge with us is very well justified. You will see part of that request is for the FDA.

Senator MORAN. Thank you.

Thank you both.

FLAVIVIRUS

Senator BLUNT [presiding]. Mr. Merkley.

Senator MERKLEY. Thank you very much.

I wanted to express appreciation for both of your organizations and the great work that they do, and then turn to a couple pieces of this puzzle. One is that I think you both alluded to the similarity between West Nile, dengue fever, and the Zika virus. Do we have any initial sense of whether there is any immunity created by previous exposure to West Nile or dengue?

Dr. FRIEDEN. We think not. We have seen lots of this virus in people who have been exposed and been affected with both of those viruses before. But we are still learning a lot about this virus.

Senator MERKLEY. This may be another question that we will learn more about, but as we look at the DNA comparison, do we have a sense of whether the differences between these three viruses are recent in terms of hundreds or thousands of years, or ancient, distinct diseases?

Dr. FRIEDEN. The genome of Zika is about 30 percent different from the genome of dengue, according to what our science has shown. Of course, there are four different strains of dengue.

But I would have to get back to you with more details on the evolutionary history.

[The information follows:]

HISTORY OF ZIKA

Zika virus was first discovered in 1947 and is named after the Zika Forest in Uganda. In 1952, the first human cases of Zika were detected and since then, outbreaks of Zika have been reported in tropical Africa, Southeast Asia, and the Pacific Islands. Zika outbreaks have probably occurred in many locations. Before 2007, at least 14 cases of Zika had been documented, although other cases were likely to have occurred and were not reported. Because the symptoms of Zika are similar to those of many other diseases, many cases may not have been recognized.

Source: <https://www.cdc.gov/zika/about/overview.html>.

Senator MERKLEY. One you mentioned that it virtually disappears from the blood after 10 days. Does that mean that at that point of a mosquito biting you, after 10 days, it would be very unlikely to transmit the disease?

Dr. FRIEDEN. It would not be able to, correct.

Senator MERKLEY. And once I have had it, if I am 10 years old and I have had Zika, and now I am 18, would there be immunity from having had the disease previously?

Dr. FRIEDEN. We don't know, but we think and we hope that would be the case. That is one of the reasons we are so optimistic about NIH work with the vaccine.

Senator MERKLEY. So in that case, when you have an initial population with no immunity, you would expect the virus to run very rapidly through the population. But at that point, if there is immunity from previous illnesses, now you have a population that has been partly immunized by the spread of the disease previously, and the risk of infection might drop substantially in that type of situation. Is that an accurate picture of how it would work?

Dr. FRIEDEN. Yes.

DISEASE MODELING

Senator MERKLEY. In addition to the medical research teams, do we have a modeling team working on demographics of this to understand how the natural immunization of populations might slow the spread and reduce the risk?

Dr. FRIEDEN. Yes, although, given the large confidence intervals and the large number of unknowns, that type of exercise is perhaps less productive in this situation.

Senator MERKLEY. Do we believe, at this point—I realize we will learn a lot more—that women who have had Zika say in childhood would be very unlikely to have the virus at a level that would cause concern in their childbearing years?

Dr. FRIEDEN. If this behaves as other viruses, infection with Zika before pregnancy would not have an impact on subsequent pregnancies. But we have to caveat everything we say. This is a new, unexpected phenomenon, and we are still learning more. But if it behaves the way most viruses behave, we would be very surprised to see an effect on subsequent pregnancies.

CYTOMEGALOVIRUS

Senator MERKLEY. Can either of you say a little bit about CMV (Cytomegalovirus) and the type of birth defects that come from that?

Dr. FRIEDEN. CMV was identified as a cause of birth defects, including microcephaly, around 1962. It primarily affects in the first trimester of pregnancy, although it can have effects later in preg-

nancy. According to information provided by our scientists, it may affect only about 10 percent of the women who are infected. We are not really sure why that is the case.

Senator MERKLEY. Is that also a cousin to the Zika virus? Or is that something entirely different?

Dr. FRIEDEN. No, it is totally different.

Senator MERKLEY. Do we understand the disease mechanism by which it produces this impact on the brain as a result of exposure?

Dr. FRIEDEN. I would have to get back to you on that.

[The information follows:]

Both cytomegalovirus (CMV) and Zika are viral infections. There are no FDA-approved vaccines to prevent either Zika or CMV. It is not known whether there is a connection between the two viruses, or whether prior or co-infection with CMV increases the likelihood of infection with Zika.

The Zika virus is a flavivirus, a group of infections that also includes dengue, West Nile, and yellow fever. The Zika virus is neurotropic, meaning that it primarily affects the brain. Research is unclear at this point whether these effects are a direct result of the virus itself or due to an immunologic response to Zika infection. The Zika virus is transmitted by the *Aedes aegypti* mosquito, common in warmer climates; recent studies have also suggested that it can be transmitted sexually. In early March 2016, researchers showed that the Zika virus could infect nerve cells. Another new study of 88 pregnant women with rash in Brazil found that many who were infected with the Zika virus demonstrated a range of health concerns, including pregnancy loss, central nervous system abnormalities, growth restriction, low amniotic fluid, and abnormal blood flow to the baby, along with babies born with microcephaly.

CMV is one of the herpes viruses, from a group of infections that also include chickenpox. A common infection that is usually harmless or causes mild symptoms, it can be transmitted through contact with bodily fluids (such as saliva or blood), can be sexually transmitted, or, if a pregnant woman has an active infection, it can be transmitted to her fetus. CMV can cause serious disease in babies infected prior to birth (congenital CMV). According to the CDC, about 1 in 5 children born with congenital CMV infection will develop permanent problems, such as hearing loss or developmental disabilities, and a small number may die. At this time, there are no FDA-approved vaccines to prevent either Zika or CMV.

MICROCEPHALY AND OTHER BIRTH DEFECTS

Senator MERKLEY. Okay. Listen, thank you all very much.

Is there anything else you would like to add?

Dr. FRIEDEN. No, just that, as you indicate, this is a really unprecedented phenomenon. With each passing day, the evidence that Zika is causally related to microcephaly gets stronger, though it is not yet proven.

As I mentioned, just yesterday, we published data showing the Zika virus genome in the brain tissue of infants who had died from Zika infection, or with Zika infection with microcephaly. That is really the strongest direct evidence to date that this, at least in the course of the pregnancy, is a neurotropic virus. It grows in and only in the brain tissue for the infected infants.

Senator MERKLEY. I want to clarify a point. You said it grows only in the brain tissue?

Dr. FRIEDEN. In the situation where our scientists examined two infants who had died in the first 24 hours, they were able to identify the Zika virus only in the brain tissue.

Senator MERKLEY. Yes, okay. I was aware of that. When you said it grows in the brain tissue, do we have a sense that it inhabits cells in the brain and replicates itself within the brain?

Dr. FRIEDEN. We do not know the answer to that question yet.

Senator MERKLEY. Thank you all very much.

Senator BLUNT. Senator Capito.

ZIKA TRANSMISSION

Senator CAPITO. Thank you, Mr. Chairman.

I thank both of the gentlemen. This has been a very interesting hearing, and I think very timely, too.

I also would like to say that the further out front that both of you are on this issue I think will help alleviate some of the massive questions we are going to be getting.

One technical question, I guess. Can the mosquitoes be transmitted? Say you are traveling in an area where they are heavily populated and you come back to the United States. Can you transmit the mosquitoes with you? Is that a danger, bringing the actual transmitter of the virus into the country?

Dr. FRIEDEN. That generally is not how the disease is spread. It is generally spread within the body, where somebody is infected, they have it in their blood, and then the mosquito bites them and then bites someone else.

Senator CAPITO. Okay. So actually having the mosquitoes in the United States is not our biggest concern?

Dr. FRIEDEN. The parts of the United States that have the mosquitoes that can spread this are at risk of having some locally acquired cases.

Senator CAPITO. So if a person is infected, if that mosquito were to happen to bite that person, they could pick the virus up from the person and then transmit?

Dr. FRIEDEN. Exactly.

Senator CAPITO. That's pretty interesting.

PUBLIC OUTREACH AND EDUCATION

I would say, in looking at what happened with the Ebola virus and the news and a lot of reaction, and some might have said overreaction or underreaction, but in any way, anyway, in a public way, I'm thinking man on the street kind of thing, the best that we can do to avoid that kind of—it wasn't hysteria, but high, high alarm that maybe wasn't based on facts, in this case, I think the better.

So I guess what I would say to you is, you are dealing with the science, you are dealing with the vaccine, possible vaccine, mosquito eradication. What kind of outreach are you doing to public health departments and others to make sure that we tamp down any kind of stampeding kind of reaction, because it is frightening for young women thinking about having children?

Dr. FRIEDEN. We do extensive outreach to health departments, to doctors and other clinicians, and to the public. What we have done is to emphasize that there is something that everyone can do, because when people understand there is something they can do, I think that helps focus their attention.

The key here is to reduce the risk that pregnant women will be bitten by an infected mosquito. The way to do that is, first and foremost, advise pregnant women in the continental U.S. that it would be better not to travel to a place where Zika is spreading while they are pregnant. For women who are pregnant in an area like Puerto Rico where Zika is already present, the key is to reduce the risk of mosquito bites.

For communities, there are things that they can do to understand and control mosquito populations. For us in public health and at NIH, the goal is to learn more quickly and inform people what we are learning and take whatever steps we can to reduce the risk to pregnant women.

Dr. FAUCI. It's really important, too, and we are trying our best to do this, to gain as much knowledge as we can, and to communicate the knowledge. When we have something that is firmly evidence-based, we want to be able to say this is what you can expect or not. When we don't know the answer, we must not be afraid to say we don't know the answer, but we are trying to get it.

I think when the public gets confused is if you give half answers. If we don't know, we don't know. If we do know, we will tell you as often as we possibly can.

VACCINE DEVELOPMENT

Senator CAPITO. I think that is a good response, and, certainly, as I said, for the man on the street and the woman on the street, that is extremely important.

You mentioned a bit about a vaccine where the goal of the vaccine was to protect pregnant women. But it ended up being, and it is now, widely distributed to infants and children and even those of us who are over a certain period of years.

Do you envision that this could become something like that. You're trying to protect pregnant women—I guess you can't really tell, but—

Dr. FAUCI. That is the reason why when you develop the vaccine, you target it for everyone. Even though there may be a greater at-risk group, you target it for everyone.

Envisioning how it will be used is really going to depend on how the Zika outbreak evolves. Let me give you an example. If it turns out that the outbreak is still raging 2 years from now, 1.5 years from now, at a time when we actually have shown that a vaccine works and that it is safe and that it is effective, even if it is on an emergency basis, you would want to widely distribute that vaccine. If you are in a country where the risk is always there of an outbreak of Zika, you might want to make that part of the normal vaccination program. If you are in a country where you haven't had any outbreaks of Zika and it is unlikely that you would, I wouldn't foresee that the Zika vaccine would be part of a required vaccination schedule.

So you really have to take a look at where you are and what the risk is.

MICROCEPHALY AND OTHER BIRTH DEFECTS

Senator CAPITO. Okay, can I just ask one quick question? If a pregnant woman has Zika and has a child with no microcephaly, are there other issues associated with that? That is my question.

Dr. FRIEDEN. We don't know.

Senator CAPITO. We don't know. Thank you.

Dr. FAUCI. I totally agree with Dr. Frieden that we don't know. There are other things besides just classic microcephaly or small brain. Like recently, there has been a report, yesterday and the day before, about ocular issues, real problems with vision that don't

necessarily involve underdevelopment of the brain, but where the virus actually can attack the retina. There are some very striking pictures in a recent publication of the retina of some children who have been affected by Zika that are really quite concerning.

Senator BLUNT. Senator Shaheen.

INTER-AGENCY COORDINATION

Senator SHAHEEN. Thank you, Mr. Chairman.

And thank you both for being here and for all of the work that the CDC and NIH are doing to address this challenge.

I know that Senator Moran asked about the FDA, but obviously there are other Federal agencies—Homeland Security, the State Department, the Department of Agriculture, Customs and Border Protection—that have a role to play as we think about how to respond to this kind of outbreak.

Can you talk about how you are coordinating with other agencies within the Federal Government to address this?

Dr. FRIEDEN. HHS (Health and Human Services) is the lead dealing with this response and coordinates across many different components across HHS that have to respond. The State Department, for example, uses the CDC travel advice for their advice not only for travelers but also for our mission personnel under chief of mission authority at post, including the CDC staff who were there. And we work closely across the U.S. Government with coordination, wherever necessary, by the National Security Council.

INTERNATIONAL COOPERATION

Senator SHAHEEN. With respect to other countries around the world, the European Medicines Agency, for example, has established a task force of European experts with knowledge in vaccines and other infectious diseases.

How are we working with them? Are we part of what they are doing? What other international efforts are we involved in?

Dr. FRIEDEN. We work very closely with countries around the world. CDC has teams of our doctors and other epidemiologists today in both Brazil and Colombia. We also work very closely with the Pan-American Health Organization of the World Health Organization here and the World Health Organization in Geneva as a good way of having a ground where everyone can collaborate together.

CLIMATE CHANGE

Senator SHAHEEN. Now, New Hampshire, in the last 15 years or so, had cases of West Nile virus that never used to exist that far north. To what do we attribute the spreading of these kinds of mosquitoes? Is it just globalization? Is it also the warming of the climate that is affecting that? Do we have any analysis that tells us it is going to get worse? Is it going to retreat? What do we think the future is going to be?

Dr. FRIEDEN. As Dr. Fauci showed in his opening presentation, we do think the continued emergence and reemergence of health threats, including those spread by mosquitoes and ticks and other

vectors, is the new normal. It is going to continue for the foreseeable future.

For the mosquito population specifically, and these viruses specifically, our scientists tell us that the key drivers have been the movement of people from one part of the world to another, because the virus basically hitchhikes inside of someone's blood. And then a mosquito that can spread that virus spreads it elsewhere.

And urbanization, having lots of people close together makes it ideal for mosquitoes to be able to spread this quite explosively.

The mosquitoes that spread Zika, as far as we know, are not present as far north as New Hampshire. But as there are changes in the climate, it may change some of the environments in ways that are very difficult to predict the implications of.

HEALTH REGISTRY

Senator SHAHEEN. Can you talk about how important registries are, as we think about how we figure out where this is affecting populations?

Dr. FRIEDEN. Registries are a key tool to identify affected individuals and enable us to get population-based information and deeper information about individual cases and about the range of illness that can be present.

Senator SHAHEEN. Someone was explaining to me that one of the reasons this suddenly popped and got the world's attention was because there was a large enough population in Brazil, and enough babies born, to suddenly see a pattern. We had seen it in other islands and other places where we did not have enough of a population to really be able track what might be happening.

So you talked about the virus being identified in 1947—was that the year? So can we track back? And do we have any idea what may have happened in some of these other places before we saw a large enough population to be able to identify this as a problem?

Dr. FRIEDEN. Some of that work will be very difficult to do because the blood test cross-reacts with other viruses. There was a relatively large outbreak in French Polynesia. In retrospect, what we have heard from various reports is that they have identified children with microcephaly born following that outbreak. But we haven't yet seen definitive information on that.

Dr. FAUCI. The point you made is a very good point, Senator, because when you are dealing with a disease, even if it is difficult to track for the reasons that Dr. Frieden mentioned, when you are dealing with a disease that is smoldering at a low level, and there is a complication that is relatively uncommon, you may completely miss it.

Once you see a disease in which it explodes in a population, and then all of a sudden you have so many cases of what would be otherwise an unusual complication, then you start to see it. We saw that with Ebola when, prior to the outbreak of Ebola in 2014 and 2015, there were mini outbreaks, affecting as few as two, and as many as 100 people. When you get 28,000 cases, the way we did in West Africa, we started seeing things with Ebola that we didn't realize that were associated with Ebola.

I think the point that you made is a good one, and that is why we are keeping a close eye on what is happening with Zika, be-

cause literally every week or month, we learn something new and important about this.

Senator SHAHEEN. Thank you.

Thank you, Mr. Chairman.

Senator BLUNT. Senator Alexander.

PREGNANT WOMEN

Senator ALEXANDER. Thank you.

Thanks to both of you for your remarkable work and for being here.

You said, Dr. Frieden, that our focus should be on reminding pregnant women that they should try to avoid being bitten by a certain type of mosquito. That is really the focus of what we are talking about, right?

Dr. FRIEDEN. Well, first, to avoid going to a place that has Zika spreading. And for those who are—

Senator ALEXANDER. But the goal is, for pregnant women to avoid, a certain type of mosquito. If you are not a pregnant woman, and if there are none of those types of mosquitoes, this is not a concern. Is that correct or is that not correct?

Dr. FRIEDEN. That is generally correct. There might be a small exception for men who may be infected and whose partners may be pregnant.

TRAVEL ADVISORIES

Senator ALEXANDER. I go fishing in Minnesota and Canada. There are lots mosquitoes up there. But I gather those are not the mosquitoes likely to carry this virus. If you were about to travel, where would you go to get the best list today of the places where you could go where you are not likely to be infected by this type of mosquito?

Dr. FRIEDEN. The CDC Web site will have that information updated on a regular basis.

Senator ALEXANDER. If a pregnant woman's husband has traveled to an affected country, what precautions should that couple take?

Dr. FRIEDEN. We recommend, at this point, until we know more, that if they have sex, they use a condom.

Senator ALEXANDER. If a woman is planning on becoming pregnant, and if she has traveled to an affected country, how long should she wait before she becomes pregnant?

Dr. FRIEDEN. There is still a lot we don't know, and so we are giving information to the public and to the obstetricians about situations like that.

We believe that if someone has been infected on the last day that they were somewhere, they could get sick for about 2, maybe 3 weeks. After that, the virus would be out of their blood. If this behaves as other viruses behave, there would be no increased risk to the next pregnancy after some period of a month or so.

But we don't know that for sure.

Senator ALEXANDER. So while you don't know for sure, 4 to 6 weeks after returning from an affected area would probably mean the virus is gone?

Dr. FRIEDEN. I don't know what Dr. Fauci would say, but—

Dr. FAUCI. I think that would be a reasonable assumption. But then, just as I said in answer to one of the other questions, we really want to do a natural history study and study a lot of people and understand really how long it is until that virus is gone.

I would think 4 weeks would be reasonable, but before you say definitively, we really want to do the studies that we are now undertaking.

HEALTH EFFECTS ON CHILDREN

Senator ALEXANDER. Does this virus have an effect on a newborn or a toddler whose brain is not yet fully developed?

Dr. FRIEDEN. We don't know the answer to that. We have not seen reports of adverse effects.

ZIKA DIAGNOSTICS

Senator ALEXANDER. You may have answered this, but on diagnostic tests and vaccines, if I'm a pregnant woman and I want to know if I have the virus, who do I call?

Dr. FRIEDEN. Your doctor should get in touch with your local health department.

Senator ALEXANDER. And what will your local health department do?

Dr. FRIEDEN. If you are actively ill, they will use the CDC tests that accurately can say whether the virus is in your blood. If you weren't ill, or it has been a few months since you traveled, your local health department will do a CDC-developed test that may be able to determine whether you have been infected.

Senator ALEXANDER. But you are likely not to feel ill, did you not say?

Dr. FRIEDEN. That's correct.

Senator ALEXANDER. Eighty percent of the time, there are no symptoms.

Dr. FRIEDEN. That's correct.

Senator ALEXANDER. So you might return from an affected area. You may feel good. But you may worry that you might have contracted the virus. The chances are four out of five that you don't have any symptoms. So you still call your local health department. Do you have enough diagnostic tests to meet the need?

Dr. FRIEDEN. We are working around the clock to scale that up. We are already in the process of sending out 62,000 tests developed at the CDC lab, working with private companies to try to do more.

But there may be a period of weeks or a couple months where there aren't enough tests for the people who want to have them done.

ZIKA VACCINE DEVELOPMENT

Senator ALEXANDER. Dr. Fauci, it sounded yesterday in our discussions that you felt pretty confident that there would be a vaccine, and it sounded like the amount of time it could take might be as quickly as 12 or 15 months. Is there anything we should do to help you speed that up?

Dr. FAUCI. The answer is that I don't think we can speed it up, but I want to clarify for the committee exactly what I meant when I said 12 to 15 months.

If you look at the natural way that you would get a vaccine approved with all of the i's dotted and t's crossed through the FDA, in which you did a trial where you definitively showed that it worked, that generally would take, for a vaccine like this, anywhere from 3 to 5 years. The point that I made about an accelerated approach was that we know we can start early trials, probably by the end of the summer in phase 1 just to ask the questions, is it safe, and does it induce an immune response that you would predict would be protective?

Once we get finished with the phase 1 trials, which would likely be by the end of 2016, if the epidemic is still raging, let's say in Brazil, and you have enough people who are at risk for infection, you could go into an accelerated phase 2 trial there. And probably within a period of 6 to 8 months, you will be able to definitively say whether the vaccine works.

If that circumstance exists, then you could ask for an accelerated approval from the FDA or from whatever regulatory authority is involved, which would truncate that 3- to 5-year period to much shorter.

However, if there are no infections around, which is exactly what we saw when we got to that point with the Ebola vaccine, just as we were getting ready to do the definitive trial, because of the public health capabilities and what CDC and others had done in West Africa, there were no new cases of Ebola. So we were unable to definitively show the Ebola vaccine works.

Senator ALEXANDER. Mr. Chairman, my time is up. You have taken me toward the end of 2017, assuming there is a raging epidemic. Then you still have a period of time for manufacture. Or does that go pretty fast?

Dr. FAUCI. For the product that we are talking about, manufacturing goes pretty fast, Senator. That is the reason we are engaging the pharmaceutical companies right now, in anticipation of that.

Senator ALEXANDER. Thank you, Mr. Chairman.

Senator BLUNT. Senator Reed.

INTERAGENCY COORDINATION

Senator REED. Thank you very much, Mr. Chairman.

Thank you, gentlemen, for your service.

I know Senator Shaheen touched on the interagency coordination, but I was at Fort Dietrich on Monday at the NIH laboratory, the DHS laboratory, and the DOD laboratory, and there are many pictures of you there, Dr. Fauci, and deservedly so. Just a report from the front.

Anything you might want to add about coordination between departments? And one aspect that I particularly find intriguing is sort of identifying the problem at the earliest possible stage.

We know the Zika virus, mosquito-borne virus, is a current issue, but we can all sort of expect there will be another wave of mosquito-borne viruses. What are we doing in terms of coordination ef-

forts between departments to try to identify the next threat, as well as deal with this one?

Dr. FAUCI. I think, Senator, you picked up on something that is quite true. Our cooperation and collaboration with a number of agencies, particularly the Department of Defense and the interactions that we have had now for some time up in Frederick at Fort Detrick, has really been very important. I think it showed itself wonderfully during the Ebola outbreak when we had an extraordinary amount of interaction that hastened things.

With regard to the surveillance, Dr. Frieden and the CDC are very much involved as part of an international health security network to try to surveil and find outbreaks before they get out of hand. That is the goal of this global health security agenda that we have.

Senator REED. Dr. Frieden.

Dr. FRIEDEN. I just would reiterate what you have said and what Dr. Fauci said. The Department of Defense played an extremely important role in the Ebola response. We are already in conversations with them on diagnostics. We provided them with our kits and materials, and also on mosquito control, where they have a high degree of excellence and some significant capacity in mosquito control. So they are fully integrated into the response here.

And in a broader sense, the Global Health Security Agenda is our way of cross-governmental collaboration to find threats when they first emerge, stop them as quickly as possible, and prevent them wherever that is possible.

COORDINATION WITH STATE PUBLIC HEALTH DEPARTMENTS

Senator REED. Let me follow up on that question in terms of surveillance and preemption, if you will, in terms of the State and local level.

Are you coordinating with the State public health departments and other agencies for spraying mosquitoes? You mentioned how, in response to Senator Alexander, the State health departments are really the point of contact for particularly pregnant women who have concerns. Can you elaborate on your coordination with State and local?

Dr. FRIEDEN. We work very closely with State, tribal, territorial, and local health departments, and mosquito-control districts, which can sometimes be separate areas. In fact, one of the key components of the emergency supplemental request is to provide funding to do better at tracking and stopping the growth of mosquito populations.

VECTOR CONTROL

Senator REED. Do you anticipate that there will be widespread preemptive spraying beginning very soon when the weather changes? And how far north, essentially, will that go? Do you have an idea?

Dr. FRIEDEN. Well, as spring and summer approach, we will see an increase in mosquito populations, and we will see areas particularly. There are two types of mosquitoes that spread this virus. One of them, *Aedes aegypti*, spreads it in primarily the Southern

States. That is the mosquito that spreads this virus more effectively.

So those are the areas that are at the greatest risk of having clusters or local transmission of this virus. We have already seen some of those States scaling up their activities. We would like to have the resources to provide them to do that as rapidly and effectively as possible.

There is a secondary mosquito vector called albopictus, or the tiger mosquito, that is much more widely distributed, and that will somewhat depend on the local populations of mosquitoes and the capacities. But we have another component of the supplemental request, which would also strengthen activity there.

Senator REED. Thank you very much.

Thank you, Mr. Chairman.

Senator BLUNT. Senator Lankford.

Senator LANKFORD. Thank you.

I want to pick up on what Senator Reed was talking about there.

Walk me through the balance between a mosquito-borne virus and our aggressive pursuit of bringing down the population of that mosquito versus getting a vaccine ready, done, produced, and out. Walk me through the balance there of how you are trying to attack that.

Dr. FRIEDEN. It is all of the above. A vaccine is not going to be here for some time, and so right now we need to do as well as we can to reduce mosquito populations and reduce the risk to pregnant women.

If a vaccine that is safe and effective becomes available, that will greatly simplify our effort, and then it will be a different type of approach.

But the mosquito-control activities will benefit not just Zika but also dengue, chikungunya. And if we do them better, in areas where malaria is spreading, it will help our malaria-control activities as well.

Senator LANKFORD. So is the assumption, both domestically and internationally, step one of this is not only development of a vaccine, but aggressive population control of that mosquito?

Dr. FRIEDEN. Correct.

Dr. FAUCI. They really go hand-in-hand. We get asked this all the time. The thing that you could do immediately now is to accelerate vector control. It's not going to be easy, because this is a very wily mosquito, the *Aedes aegypti*. But that is the thing that could be immediately done now, as we are working our way toward developing a vaccine.

VACCINE DEVELOPMENT

Senator LANKFORD. Okay, then walk me through when we get the vaccine. Because it sounded like you anticipate having a vaccine at least done that works in the laboratory by the end of this year. Is that correct?

Dr. FAUCI. What I said is that, by the end of 2016, we will have a Zika vaccine trial that will have been completed that will ask, is it safe, and does it induce a response that you would predict would be protective?

There is a far leap from that to having an effective vaccine. But that first stage is one that we are accelerating, and we will likely have the trial finished by the end of 2016.

Senator LANKFORD. So at this point, as far as dealing with the virus that we have, is it harder or easier or about the same—talk me through the complications of this versus a flu vaccine.

Dr. FAUCI. Well, flu is entirely different, but I will try to be brief and explain.

We have made successful vaccines against other flaviviruses. Zika is a flavivirus. We have a successful vaccine against yellow fever. We have a successful vaccine—we can do a little better, but is reasonably successful—against dengue. And we would've had a successful vaccine against West Nile, but we couldn't advance it because companies did not want to partner with us.

Influenza is an entirely different situation because influenza changes from season to season. We have influenza vaccines, and sometimes they are not as effective as we would like them to be.

Senator LANKFORD. Last year, not so much.

Dr. FAUCI. Not so much, last year, correct. This year, better.

Senator LANKFORD. Okay, so then the hope is to have this and then try to distribute this internationally first? Domestically? Let's take this out 2 years from now. Let's say it is still moving at some point. Obviously, we have to deal with the source area in South America, but we are also dealing with Americans here.

Dr. FAUCI. Again, just to give you a potential scenario, you want to target the areas where you have an outbreak. In the United States, we don't anticipate—although we are ready for everything and we never say never, and never say always—we don't anticipate a massive outbreak like we are seeing in Brazil. We do anticipate that it is likely we will see a small number of local transmissions of Zika, just as we did see with dengue and that we did see with chikungunya in the Southeast part of the country.

Unless something radically changes, I don't see broad Zika vaccination of the entire U.S. population.

Senator LANKFORD. Would that include Puerto Rico?

Dr. FAUCI. Puerto Rico is a different story, as Dr. Frieden said very clearly. Puerto Rico is a much different story than the continental United States, because of the special conditions there. And to see how rapidly chikungunya spread throughout Puerto Rico, that is the thing that we are concerned about with regard to Zika in Puerto Rico.

TRAVEL RESTRICTIONS

Senator LANKFORD. Any talk about limiting movement of people or travel from South America or Puerto Rico into the continental United States where you are seeing outbreaks start? Is there conversation about that? Or is there a threshold where you would say, when it reaches this point, we may want to do more than just say, be aware there's a travel advisory, but to say no?

Dr. FRIEDEN. There are more than 40 million trips a year.

Senator LANKFORD. Correct. A lot.

Dr. FRIEDEN. So our focus now is to broaden the emphasis on reducing risk to pregnant women by advising them to defer travel, if possible.

PUBLIC HEALTH EMERGENCY FUND

Senator LANKFORD. Okay. Just a quick question on this. We are talking about emergency appropriations at this point, having a conversation about that. At what point do you think that you would make a request to say, "We are the United States of America. We deal with emergencies worldwide all the time. We should have a fund set aside that is appropriated dollars." We know we are going to have hurricanes and tornadoes and earthquakes. We also know that we are going to have global issues like this with health, and we would have a part of an appropriations request dealing with an emergency fund.

Dr. FRIEDEN. We would, certainly, be eager to follow up with you on that concept.

Dr. FAUCI. Agreed.

Senator BLUNT. Senator Durbin.

Senator DURBIN. Thanks, Mr. Chairman.

Thank you, both, for being here.

Let me say at the outset a special thanks to the chairman and ranking member, Senator Blunt and Senator Murray. I believe that our appropriation this year for both of your agencies reflects the importance of your work, and this hearing reminds us that we never know where the next challenge is going to come.

VACCINE DEVELOPMENT

Dr. Fauci, from the NIH perspective, if NIH did not engage in these clinical trials and this research to develop this vaccine, would the private sector do it?

Dr. FAUCI. The private sector would be less enthusiastic about going from A to Z on Zika vaccine development, because that is a major investment in a vaccine that likely would not have worldwide general use. So what we have done and continue to do at the NIH is try to de-risk it for the company. If you look at how much money it would cost in getting from the concept all the way through to a product, the numbers they give vary, but it is somewhere between \$750 million and \$1 billion.

What NIH does to de-risk is to develop the concept, do the pre-clinical testing, provide the research resources, and go at least into phase 1 trial. And then generally, we like to hand it off to a company that will then take it into advanced development.

If they don't do that, what we do then is we then push into phase 2. We have a part of HHS called BARDA, the Biomedical Advanced Research and Development Authority, which actually helps us in that advanced development and partners with industry. So if you look at a spectrum from the concept to the vaccine, the further we push it toward the product, the more enthusiastic the company is about getting involved, because we have taken away from them a lot of the risk and much of the expense.

So if NIH just backed out completely, I don't think that you are going to have the enthusiasm from companies for developing these types of vaccines.

Vaccines and products that everyone will use, you don't need an incentive for them. But when it is a public health issue that isn't

immediately profitable, not every company, but many, would not want to go near that.

SURVEILLANCE

Senator DURBIN. I have a whole line of questions about then pricing the product, but I'm going to save those for another day and perhaps another hearing. But I'm glad you made the point that you did about the necessity of your work when it comes to such public health challenges.

Dr. Frieden, it was an honor to visit your headquarters 10 days ago, or 11, in Atlanta and see the amazing array of talent that America has and you have, and to hear what was done there when Brazil was struggling with uncertainty about this challenge and went to the one place in the world that they could trust to help them find the answers, and that was the Centers for Disease Control in Atlanta, Georgia. And to meet the doctors and researchers there was a great day for me and a real eye-opener.

We went into your, for lack of a better word, war room, and you showed me the charts with Zika. I looked up and saw that one of the key areas of concern was in the Caribbean, Puerto Rico and the Virgin Islands, if I recall. And then I think you gave us numbers, or I have heard numbers subsequently, that they have identified some 20 indigenous cases in Puerto Rico and some 30 in the United States that were likely people who traveled to areas where the Zika virus could be borne by mosquitoes. Have those numbers changed since I visited?

Dr. FRIEDEN. We have continued to see the advancement of two things—first, travelers returning to the U.S. We are now at more than 50 who have come back to the U.S. We expect that there could be hundreds or thousands in the months to come. And Puerto Rico, we continue to identify new cases of Zika spread locally.

Senator DURBIN. You are America's first line of defense when it comes to public health attacks. And I thank you and the people who work at CDC.

PUERTO RICO

I want to zero in, again, as others have, on Puerto Rico, because, as you described to me before the arrival of a vaccine, which we pray will be soon, if needed, but before that, it sounded to me like the way we address this challenge and danger from a public health perspective is pretty basic, in terms of standing water, bug repellents, screened homes, air-conditioning, and gathering in crowds.

So it seems like it is a basic public health issue. I came away from there concerned, because you and I both know the status of the economy in Puerto Rico. They are flat on their back. They are bankrupt. They don't have local resources to deal with customary public health challenges, let alone this new challenge.

How do we resolve that? Will the President's \$1.8 million request take into consideration the need to supplement what would otherwise be available if this were the continental United States fighting this challenge?

Dr. FRIEDEN. Yes, we would surge in, and we are now doing what we can in Puerto Rico to reduce the risk to pregnant women by en-

couraging personal, household, and community activities to reduce the risk of mosquito bites.

What you outlined is exactly what we need to do, and what we are moving forward to do. There are some other measures of controlling mosquitoes that we are going to try to implement there, working with the communities in Puerto Rico that are affected.

EVOLUTION OF ZIKA VIRUS

Senator REED. How long has the Zika virus been around?

Dr. FRIEDEN. It was first discovered in 1947, but not until the past few months has there been this association with microcephaly recognized.

Senator REED. And the carrier in this case, the aegypti mosquito, it also carries dengue and chikungunya?

Dr. FRIEDEN. Yes.

Senator REED. So this is an aberration of the original Zika virus, or an evolution of it that is causing this challenge today?

Dr. FRIEDEN. We don't know if this Zika virus changed. What has changed is the population it is affecting. It is affecting large numbers of people that had not been recognized previously.

It is possible that Zika was causing something like this in Africa for decades, but because we didn't have the monitoring systems, we didn't know. We just don't know that at this point.

Senator REED. Thanks for your good work.

Thank you, Doctor.

VACCINE FUNDING

Senator BLUNT. Senator Durbin, Senator Alexander, I mentioned before you got here, we would have time for more questions. I think both Senator Murray and I have a couple. If you would like to ask anything else, that would be good.

Dr. Fauci, you mentioned in your testimony, and it's possible while I went to vote maybe some of these topics may have been discussed, but you mentioned that we want to continue the studies that we are doing right now on Zika. How are you funding those studies right now?

Dr. FAUCI. Right now, in the absence of the implementation of the supplemental funding, we are using money that was allocated to other flaviviruses. So I am moving money out of certain areas to pay for the things that we are doing right now.

So we have some time-limited flexibility to move money from one area to another to, for example, get the early production of that vaccine candidate, so we can start this trial by the end of the summer.

We have essentially taken several millions of dollars from one area to another. It is almost all by providing funds to our grantees that have existing grants for other flaviviruses, both in the United States and to our Brazilian collaborators. These are scientists who have been working on dengue, who have been working on West Nile, people who are, essentially, ready to hit the ground running. Those are the ones that we are funding right now.

We are trying to get new people involved, because we can't get to where we want to go just with the people who are, essentially, dividing their time between two goals.

PUERTO RICO ACTIVITIES

Senator BLUNT. Dr. Frieden, you just said, regarding actions in Puerto Rico, we would surge in and we are doing so now. The same question, how are you funding that effort?

Dr. FRIEDEN. So our division of vector-borne disease control usually deals with dengue outbreaks of yellow fever around the world, as well as West Nile disease in this country, and new viruses such as two that we have identified in the past year that are tick-borne, Heartland and Bourbon viruses, in the past few years.

We have taken the staff off those programs and put them into the response to Zika. We currently have about 300 people working in this response.

Our dengue branch is in Puerto Rico and has been there for many decades, so basically, we rededicated the staff to do that.

And we have activated our emergency operations center, which allows us to coordinate more effectively and ask for people from throughout the agency, in the case of Puerto Rico, who speak Spanish to go and help with the response there.

Senator BLUNT. I am reassured by both of those answers. It creates a sense for us that this is, in your view, an emergency that has to be dealt with like an emergency, and appreciates the fact that Congress, even in an emergency often, the House and Senate working together is not going to happen in the next couple days or the next couple weeks, in all likelihood. That is reassuring to me.

EBOLA SUPPLEMENTAL FUNDING

I think, Dr. Frieden, you said that you don't want to use Ebola funds to meet this crisis. Does that mean that you wouldn't even be using Ebola funds that aren't scheduled to be spent yet in the infectious disease area, if we need to in the next 3 weeks? Or is there plenty of money for the next 3 weeks?

Dr. FRIEDEN. So for our part of the emergency supplemental request, to me it would make a big difference to understand whether we are talking about reprogramming dollars. That would be a big concern, because the Ebola dollars that are not spent are all planned for activities that we believe are critical of the dollars that are allocated to CDC.

We are looking throughout our entire agency to see how we can scrape together funds to function effectively in the next few weeks. The challenge are mechanisms like sending money out to States for strengthening vector control, sending more diagnostic kits out, enhancing our ability to protect pregnant women, improving vector-control activities in different places, and doing more extensive surveillance for microcephaly.

But we will do whatever we can to respond as effectively as we can, because it is an emergency.

Senator BLUNT. So your big concern there, if I understood that answer right, would be if we actually reprogrammed dollars in a way that could become permanent as opposed to access to dollars that arguably could be used in the short term, with the definition that you are pursuing.

Dr. FRIEDEN. Yes.

ZIKA DIAGNOSTICS

Senator BLUNT. When you mentioned vaccine—you weren't talking about vaccine. That was actually a note I made, just to be clear. When you talk about the testing material not available yet, but possible, you are not talking about the long-term vaccine challenge that Dr. Fauci is talking about. You are talking about a test that you believe adequately works?

Dr. FRIEDEN. We have two different tests. The test for early infection works not as well as we would like, but it can rule out infection. And we are scaling up production of that and working with the private sector to try to have them share some of the burden of getting those tests out.

Senator BLUNT. And the fact that you said you were scaling up production on that would indicate you are actually spending money and creating effort to do that right now.

Dr. FRIEDEN. Yes, absolutely.

Senator BLUNT. I don't want to be difficult about this, but actually, for me as a member of this committee, knowing that you are changing other priorities to meet this one helps us make the case that, clearly, this is something that is an immediate priority, as opposed to some long-term thing that would be wonderful to do, but doesn't have the same immediacy.

Senator Murray.

U.S. BLOOD SUPPLY

Senator MURRAY. Thank you, Mr. Chairman.

I don't think anybody touched on this, but can you talk a little bit about what the implications of Zika are for our blood supply? And should people who have returned from traveling overseas give blood?

Dr. FRIEDEN. Yes, as of February 1, the American Association of Blood Banks has advised that individuals who have traveled to Zika-affected areas not donate blood for 28 days. We think that is reasonable. The FDA will follow up on that, which is already in effect, with more formal guidance.

The more challenging situation is in Puerto Rico, and we are in active discussions now. There are logistic and financial implications of not collecting blood from Puerto Rico, so that is something that needs to be worked through.

Over the next 6 to 12 months, we hope that FDA, CDC, and NIH will be able to develop a screening test for Zika in blood and/or a way of inactivating Zika in blood.

Senator MURRAY. How long will that take?

Dr. FRIEDEN. Six to 12 months, if things go well. So we don't currently have that type of test, and that is one of the things that the FDA ask in this supplemental request would help to cover.

PUBLIC HEALTH EMERGENCY FUND

Senator MURRAY. Okay. Finally, we spent a lot of time talking about Zika today. We talked about Ebola before. Mother Nature has a way of providing us with surprises. There will be more in the future.

Do you have gaps in your funding that concern you in your preparation for whatever future hearing we're going to have on a name of something that we never said before?

Dr. FRIEDEN. To me, the biggest concern is, both within the United States and globally, our ability to find, stop, and prevent health threats. And for the global work, that is what the Global Health Security Agenda addresses. We have been able to get good commitments from other countries, so we don't have to go it alone.

But our commitment is very important there. That is a multiyear effort to close those gaps in our knowledge, because the weakest link, the blind spot anywhere in the world, is really a risk to all of us.

Also, within the United States, our core public health capacity is not as strong as it needs to be for detect and response. In this case, we are seeing the weaknesses in mosquito control around the United States. But there are other weaknesses as well in our ability to find threats rapidly and stop them.

And I just want to take a moment to thank the members of the committee for their support in the 2016 budget. Our highest priority program to protect Americans better on combating antibiotic resistance was funded at a significant increase, and we are moving that out quickly. That is an example of an area where we weren't doing enough testing; we weren't doing enough tracking; we aren't stopping outbreaks that are happening. That is the kind of threat that we need to continue to scale up our response to.

Senator MURRAY. That is the basic public health, right?

Dr. FRIEDEN. Absolutely.

Senator MURRAY. Okay.

Dr. Fauci, from your end?

Dr. FAUCI. I agree. The kind of support we got in the 2016 budget was really very much appreciated. I want to thank you very much for that. It was very important.

Senator MURRAY. Okay.

Thank you, Mr. Chairman.

Senator BLUNT. Senator Cochran.

Senator COCHRAN. Thank you very much for being here today and helping us understand the challenges that you are facing in carrying out your responsibilities. We appreciate the determined effort that obviously exists to do the best job we possibly can to protect the public health of citizens of the United States.

I know, as taxpayers, people are going to be willing to share in the burden of spending and finding the money that we need to have to devote to these very important research projects and programs to help protect the public health of our citizens.

I don't know of any higher calling than that engaged in by capable and creative scientists, doctors, researchers. So thank you for what you do. We appreciate it.

MICROCEPHALY AND OTHER BIRTH DEFECTS

Senator BLUNT. I have three more quick things, one on microcephaly.

Do you have a sense of how long it will be before you have a firmer determination of absolute connection?

Dr. FRIEDEN. I will comment first, and Dr. Fauci can say more.

I think, with each passing day, we have an increasing level of suspicion or confidence that it is a causal relationship. Some of the time we will wait for two studies that are currently getting underway.

One is in Brazil that is called a case-control study where we look retrospectively at women whose infants were infected and those whose infants weren't, to understand the differences with infection rates and other risk factors.

And the second is a cohort study, which is the more definitive type of study, which we are getting underway in Colombia now with our team that is down there now. That will follow hundreds of women who were infected in different stages of pregnancy and do meticulous examination of them and their infants to see what the rates are.

So those are two things where we will learn more. But I will say, even in this week, the data that has come out through the scientific publications makes it look very much like this is a virus that is what we call neurotrophic. It targets the nerve cells, the central nervous system, and it is looking increasingly certain, although not yet proven, that it is causal.

Senator BLUNT. Dr. Fauci.

Dr. FAUCI. I totally agree. The definitive report when it gets out in the literature is the case control cohort study. We are really getting much more evidence now. Just yesterday, the publication came out reporting four cases that the CDC looked at, in two babies that were stillborn and two babies that died within 20 days of birth. The presence of Zika virus in the neural tissue of those babies make it really quite convincing.

It is starting to look, as Dr. Frieden said correctly, literally every week that goes by, there is more compelling evidence.

Senator BLUNT. And is there any more evidence of association with short-term or long-term paralysis?

Dr. FRIEDEN. So the Guillain-Barre syndrome, there is, I would say, fairly strong evidence and suspicion of correlation. We see Guillain-Barre following a range of infections. A diarrheal disease caused by a bacteria, *Campylobacter influenza*, can cause Guillain-Barre as a post-infectious complication. It is a system where the body's immune system attacks our nerves, and it can be quite severe, although it usually does resolve in a period of weeks to months.

We have done two types of studies on this. One is to look at the epidemiology with a pattern of the disease in the population. That really does look suggestive, because Zika comes and then you see a bump in Guillain-Barre after that.

The second kind of study, which we have already completed the field work on, was a case-control study in Brazil. I will say the Brazilians have been very collegial, very open, very transparent about this. So we did a case-control study of people with Guillain-Barre and controls. We have done the initial work on that. The field work is complete. The laboratory work we hope to finish in the next couple of weeks. That will give us some more definitive information as well.

GLOBAL HEALTH SECURITY FUND

Senator BLUNT. My last question, on the Global Health Security fund, I believe, to this point, there have been no agreements made with South American countries. Am I correct on that?

Dr. FRIEDEN. So the Global Health Security Agenda in the first phase of it, phase 1, there were 17 countries. In phase 2, there were 13 countries. In addition, that included Peru and Haiti, as well as partnering with the Caribbean community, an organization called CARICOM. But in phase 2, we have not yet identified funds for the phase 2 countries.

Senator BLUNT. So there are identified countries but no funds for those countries in South America yet?

Dr. FRIEDEN. At this point, that is correct.

Senator BLUNT. Anything else either of you would like to add? Senator Murray.

Senator MURRAY. No, thank you very much, both of you.

Dr. FRIEDEN. Just to thank you for holding this hearing and for your interest and support for public health.

Dr. FAUCI. Thank you very much.

Senator BLUNT. Thank you, both, for being here.

ADDITIONAL COMMITTEE QUESTIONS

The record will stay open for 1 week for any additional questions. [The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED BY SENATOR ROY BLUNT

Question. It appears that much of the supplemental request is for activities that CDC's annual budget already supports or to programs that were further increased through the Ebola Supplemental. Why is our foundational public health system not able to deal with infectious disease outbreaks?

And if the public health system is not prepared, why does CDC's annual budget request not reflect an increase for preparedness programs?

Should we be concerned that CDC needs an influx of money every time there is an epidemic?

\$666 million was provided in the Ebola supplemental for domestic preparedness activities. Now, you are asking for \$453 million more, on top of the discretionary dollars already provided to these same preparedness programs in the fiscal year 2016 Labor/HHS bill. If hospitals are prepared to respond to Ebola, why aren't they prepared to respond to Zika? And if the public health system cannot respond to Zika, can it adequately respond to any infectious disease?

Answer. The Nation has significantly enhanced its preparedness in the years following the September 11th attacks, when funds were provided for enhancing public health preparedness. State and local health departments have greatly increased their capacity to respond to an array of hazards, which is evidenced through States' proven success in responding to critical events without requesting direct Federal support (such as the 2011 Joplin, Missouri tornado and the 2013 explosions in West, Texas). Zika virus response requires additional equipment, facilities, and specialized training beyond what is typically required for all-hazards preparedness. The unique nature of this disease requires additional steps to enhance our response measures to ensure whole community preparedness. Fundamentally, Ebola prevention in the United States is about hospital infection control and tracking of returning travelers, and Zika prevention and control is about mosquito surveillance and control and rapid response to cases through mosquito control and other interventions. These are largely unrelated activities, except for the common denominator of the need for a strong public health system.

Mosquito-borne disease prevention and control requires specialized activities not typically included in all-hazards preparedness, such as entomology, mosquito surveillance, and specialized laboratory capacity. While all-hazard preparedness has

improved, critical funding for response to mosquito-borne illness has waned in recent years. According to an analysis by the Council of State and Territorial Epidemiologists, Epidemiology and Laboratory Capacity grant funding decreased by 61 percent between 2004 and 2012:

- Only 62 percent of jurisdictions had a formal plan for killing adult mosquitos in the event of an outbreak.
- 67 percent of jurisdictions decreased mosquito trap sites.
- 70 percent of jurisdictions decreased testing of mosquito pools.
- 45 percent of jurisdictions decreased tests on human, mostly the result of inadequate laboratory staffing.

In addition to the unique needs for mosquito-borne disease response, the association between Zika virus and microcephaly is unexpected and unprecedented. A new infectious cause of fetal malformations has not been identified in decades and never has a mosquito-borne virus been connected with birth defects. Specialized prevention and response activities also are needed to prevent birth defects, support families affected by them, monitor the outcomes of potentially affected infants, and better identify risks.

Question. The Department of Health and Human Services has confirmed with my staff that they have the legal flexibility to use all but \$35.2 million of the remaining \$1.5 billion Ebola supplemental for other infectious disease outbreaks. Have you asked Secretary Burwell to use this funding for Zika response and preparedness?

When HHS briefed Senators on February 9, 2016 with Secretary Burwell and Drs. Fauci and Frieden, both Directors stated this was an “emergency” and that both the CDC and NIH could begin obligating funding “today.” If this is a true emergency, why are you not trying to use any funds currently available to you?

Answer. CDC is using funds currently available for immediate Zika response needs. However, current funding will not support all efforts needed to respond to Zika, and we are drawing funds from activities directed by Congress. The \$50 million in reprogrammed CDC funds used in the initial stages of the Zika emergency response were taken from the preparedness account, including the Strategic National Stockpile (SNS) and the Public Health Emergency Preparedness (PHEP) Cooperative Agreements. Without reimbursement, the \$5.75 million reduction of SNS will result in decreased acquisition of 20,000 vials of anthrax vaccine that would be used to treat and/or prophylax 67,000 individuals exposed to anthrax. Reimbursement will allow for purchase later in the fiscal year. The \$44.25 million reduction of PHEP will result in reduced preparedness awards to States and cities. Reimbursement by June will allow for full planned awards to each State in fiscal year 2016.

While Zika is an emergency, Ebola and emerging health threats continue to endanger the health of Americans here and around the globe. CDC is still working to ensure prevention and control of Ebola in West Africa. CDC still has 100 staff on the ground, and has continued to test more than 10,000 samples per month in Liberia, Sierra Leone, and Guinea. There is a possibility that small clusters of Ebola could emerge in the future, or other diseases could emerge that will test the public health infrastructure we are strengthening. In January, 68 days after the WHO declared the end of Ebola transmission in Sierra Leone, a new case was found, sparking the need for rapid response. As we continue to learn about Ebola and how it can be transmitted, it is essential that Ebola funding remain in place to rapidly address needs, such as:

- Deploying new countermeasures and diagnostics for Ebola; and
- Accelerating development of Ebola therapeutics and vaccines to more rapidly and effectively respond to the next outbreak.

In addition to Ebola, other infectious disease outbreaks like Lassa fever continue to pose threats to Americans health and safety. For example, CDC has been actively consulting on a suspected case of Lassa fever in an American healthcare worker. Transmitted by rats, Lassa virus causes large, seasonal outbreaks in West Africa. An outbreak is currently ongoing in Benin, which neighbors Togo. CDC is sending a team to Benin and a staff member to Togo to assist in responding to Lassa fever. Human-to-human transmission is possible through contact with blood, tissue, or excretions of a person who has Lassa fever. This case reminds us that our Global Health Security work is critically important to protecting Americans abroad and here at home. And it shows us the importance of continuing to use our remaining Ebola funds not just to address the possibility of small Ebola clusters but to strengthen the public health infrastructure of countries so they are prepared for other existing and emerging diseases.

Rebuilding the infrastructure that was lost and strengthening it for the future is essential. These investments are crucial to keeping Americans safe from emerging threats, here and abroad. Congress appropriated Global Health Security funds with

the expectation that they would be spent over 5 years, and we have plans in place to spend the unobligated funds through fiscal year 2019 as intended by Congress. The Global Health Security agenda (GHSA) is a multi-year effort between the Federal Government, other nations, international organizations, and public and private stakeholders, to accelerate progress toward a world safe and secure from infectious disease threats and to promote global health security as an international security priority to:

- Prevent and reduce the likelihood of outbreaks—natural, accidental, or intentional;
- Detect threats early to save lives; and
- Respond rapidly and effectively using multi-sectorial, international coordination and communication.

In July 2015, the United States and 17 partner countries announced 5-year plans to meet GHSA goals. Many of these plans have been published online and are part of the Presidential- or Prime Minister-level commitments with recipient countries. The countries are already using GHSA funds to respond to ongoing public health emergencies within their borders. At least 8 of these 17 countries are responding to disease outbreaks right now, and are applying the GHSA tools and approaches to respond more effectively. Building these systems and even more importantly using these systems to respond takes some time, but we know that these investments pay off. GHSA pilot projects delivered tangible results in just over 1 year, but sustained investment over 5 years will have a transformative effect to the entire health system.

GHSA is a synergistic effort to our current response to Zika and our ongoing response to Ebola. The need to respond to the Zika virus urgently does not diminish our need to continue to implement GHSA, which is a long-term effort to keep Americans safe from emerging threats, here and abroad. Building this capacity takes planning and implementation over time, and we have 5-year plans in place to spend these funds and build the capacity of countries to prevent, detect and respond to emerging threats.

Ebola supplemental funding provided to the National Institute for Allergy and Infectious Diseases (NIAID) has already been committed to ongoing activities as part of NIAID's research response to Ebola virus disease. NIAID-supported Ebola research has and will continue to provide important information about the disease. The ongoing NIAID-funded study of Ebola survivors has revealed eye, musculoskeletal, and neurological complications of the disease. It also detailed the risk of sexual transmission, demonstrating that viral material could persist in semen up to 18 months after experiencing Ebola symptoms, and that individuals could have intermittent detection of virus (after testing negative). In addition, NIAID conducted a randomized controlled trial that found two Ebola vaccine candidates were safe and immunogenic. Finally, NIAID conducted a randomized controlled trial of the monoclonal antibody cocktail ZMapp in the midst of the West African outbreak.

With respect to the Zika virus, NIAID has realigned some available funds from its fiscal year 2016 appropriation to respond rapidly to the current Zika outbreak. NIAID is accelerating research to understand the Zika virus and develop diagnostics, vaccines, and therapeutics against the virus, and the Administration has requested emergency funding to enhance and expand our ongoing efforts to prepare for and respond to the Zika virus.

Question. According to a recent article, the Zika virus might cause permanent blindness for babies born with microcephaly. Can you discuss this latest finding?

Answer. Findings show that infants with possible Zika virus infection have had abnormal eye development. It is not known if Zika virus infection caused any of these abnormalities. In a recent study of 29 infants in Brazil born with microcephaly (abnormally small head), presumed to be caused by Zika virus infection, approximately one third demonstrated eye abnormalities. Most of those affected (70 percent) had abnormalities in both eyes. Changes affected different tissues in the eye including the light-sensitive retina, iris, lens, and the optic nerve, which transmits signals from the eye to the brain. In the retina, the abnormalities involved disruption of the pigmented layer of cells that help keep the neurons alive. In the optic nerve, affected infants had fewer neurons, and the nerve exhibited incomplete development or malformation. The more severe cases could result in permanent vision loss or blindness.

For infants with possible congenital Zika virus infection, CDC recommends that an ophthalmologic evaluation be conducted either before discharge from the hospital or within 1 month after birth. Infants with abnormal initial eye evaluation should be referred to a pediatric ophthalmologist for further evaluation. CDC will continue to work with our partners to conduct studies to more fully understand the mag-

nititude of risk and the range of outcomes associated with Zika virus infection during pregnancy.

Question. The CDC and our States' public health systems have been successful in limiting the effects of other mosquito-borne diseases such as dengue fever and West Nile virus. If we are able to control those diseases and limit the affected areas to Southern States, why do you think Zika is different?

Answer. While we have had some success in responding to dengue and West Nile outbreaks in the past, mosquito-borne threats remain an issue, as evidenced by the 2015 dengue outbreak in Hawaii. In addition, while there is some overlap with mosquito control measures for dengue, West Nile Virus, and Zika virus, different prevention and control strategies are required. West Nile Virus is primarily spread by Culex mosquitoes. These mosquitoes are found throughout the continental United States while Aedes aegypti, the principal vector for Zika and dengue, has been identified across the southern half of the United States, primarily in the Southeast. Culex mosquitoes have been historically easier to control than aedes aegypti, in part because they bite at night. The other important difference that would impact mosquito control approaches is that West Nile Virus is maintained in nature through a cycle involving transmission between birds and mosquitoes. Zika virus, on the other hand, is believed to circulate in humans and mosquitoes and does not have a non-primate reservoir.

Unlike the West Nile virus and dengue fever, we are seeing unexpected and unprecedented clinical outcomes with Zika virus. Evidence suggests that the Zika virus is linked to adverse pregnancy and newborn health outcomes. However, there are a number of unknowns with Zika. We do not know the full spectrum of possible health affects to pregnant women and the fetus. Additionally, the Zika virus also can be spread by a man to his sex partners. We do not know how long the virus is present in semen in men who have had Zika or if infected men who never develop symptoms can have the Zika virus in their semen.

While we have not yet seen transmission of the Zika virus by mosquitoes within the continental United States, we expect many returning travelers will have Zika infection. There are about 40 million people travelling between the continental United States 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.

Question. What lessons were learned from the Ebola outbreak and how have those lessons influenced the response so far?

Answer. CDC is using the tried and true methods to manage emergencies within the Department, and interagency coordination has been a focus from the beginning. Through our response to Ebola we've learned several lessons that we are employing now:

- First, communication with the public is critical, and we plan to be aggressive in sharing information as we have it.
- Second, we want to be up front with the public that this is an evolving situation and we are learning new things as we go. We will update the public as new information becomes available, and our guidance will change as we learn more.
- Third, our core mechanisms for getting information out to clinicians, public health officials, and the public at large—like health alerts and clinician outreach calls—have been strengthened.
- Fourth, as it was for Ebola, the entire countermeasure enterprise is engaged in developing tests for early diagnosis and vaccines.
- And finally, just like with Ebola, our core strategies are to prevent, detect and respond.

While CDC and our State and local partners are building upon the lessons learned and the collaborations established during the Ebola response, many of the particular precautions and considerations relevant to the current Zika response will require different strategies and techniques.

The Zika request builds on the Ebola investments and provides for technical expertise at the State and local level to prevent, diagnose, and track Zika virus infections in all populations, but specifically focusing on pregnant women, the most vulnerable population. Arboviral disease expertise comprises a unique knowledge base that combines laboratory, human, and mosquito surveillance. Currently, this expertise does not exist in all State health departments. In order to adequately track the anticipated volume of travel-associated cases and possible local transmission cases, laboratory and surveillance expertise is urgently needed at the State/local level. We are learning more about Zika every day, and we are sharing information—and adjusting our guidelines and recommendations—as we learn more.

When new public health threats emerge, the specialized epidemiology, laboratory, and public health response surge capacity needs are not met within Federal, State,

and local public health budgets. This is clearly true with Zika response, which requires extensive entomology, mosquito surveillance and control, tailored risk communications and prevention efforts, and pregnancy and birth outcomes monitoring. We know that such threats will emerge each year, and we do extensive surveillance to predict those threats and detect them early, but we do not know in advance when and where these threats will ultimately appear. CDC's budget does not include resources for these surges. As the urgent and emerging Zika virus progresses during summer months, it is necessary to have maximum flexibility to respond in a manner that is most appropriate. As the Zika response and the Ebola response have demonstrated, CDC needs the ability to respond quickly at the beginning of an outbreak, even before Congress has time to provide additional resources. The Administration's supplemental request provides resources to support emerging needs related to Zika and other infectious diseases. The transfer authority associated with the funds for emerging needs allows transfers of resources within the Department of Health and Human Services, which could support CDC's response to Zika and future infectious disease threats.

Based on our Ebola response experience, the Zika supplemental includes several authorities for CDC to aid in flexible, timely response:

- Adding to Strategic National Stockpile: The proposed funding specifically authorizes that “products purchased with these Zika funds may... be deposited in the Strategic National Stockpile.”
- Overseas auto purchase and insurance authority was added to allow supplemental funds to be used overseas for car purchase and usage (global health funding already has this authority).
- Flexibility on Sec. 317S of the PHS Act was added to avoid burdensome matching requirements on grantees related to mosquito control.
- Construction authority for grantees was added to allow State and local health departments and other grantees to use funds for facilities that may be necessary to Zika response and prevention, for example, laboratory facilities.
- Acquisition and construction authority for CDC was added to allow CDC to use funds to expand vector-borne disease laboratory capacity in San Juan, Puerto Rico and Ft. Collins, Colorado.
- Funding transfer authority: Transfer authority would allow CDC to move these funds across CDC accounts to be able to more quickly respond to health security issues.

In addition, several General Provisions also support CDC's response:

- Expanded overseas facilities authority: This proposal would allow CDC to “acquire, lease, construct, alter, renovate, equip, furnish, or manage facilities” overseas without having to send payments through the Department of State.
- Hiring authorities:
 - Personal service contracts: This authority would authorize CDC to use personal service contracts for response staffing. Although this authority has already existed globally, it does not currently exist domestically. People working under personal service contracts would NOT be Federal Government workers.
 - Direct hire authority: This authority would allow expedited hiring authority for emergency positions.
- Reimbursement authority: This authority will allow CDC to use emergency funds to backfill transfers and reprogramming used before supplemental funds were available.

In responding to the Zika virus outbreak, NIAID draws on past experience and lessons learned from other emerging infectious diseases such as the HIV/AIDS pandemic and the recent Ebola outbreak. These prior public health emergencies have outlined a core set of clinical research principles that can help ensure studies conducted during such emergencies meet the highest scientific standards and mitigate any potential harm to participants. The core clinical research principles include collaborating with local partners, prioritizing candidate treatments and vaccines with plausible benefit, employing scientifically sound clinical trial designs, and promoting transparency through prompt dissemination of results. As research on potential medical countermeasures progresses to the point of clinical evaluation, NIAID intends to employ these principles in addressing the current Zika virus outbreak.

Question. Zika is the second significant infectious disease outbreak threatening the United States in recent years. Given that we live in a global society where diseases are only a plane ride away, should we change the way we react to disease outbreaks? Specifically, how does the research community pivot research efforts to address the outbreaks?

In recent years, why does it seem that the U.S. response is reactive rather than proactive?

Answer. The Zika outbreak is validating the Global Health Security Agenda's (GHSA's) core concepts, priorities and necessity—investments in the public health workforce, surveillance, laboratory and public health emergency management that help us respond better to public health crises, from MERS to Ebola to Zika and more. On any given day, there are disease outbreaks around that world that have the potential to impact the United States.

GHSA outlines the way forward toward a world more secure from infectious disease threats. Every country around the world needs to be able to prevent, detect and effectively respond to infectious disease threats, including emerging zoonotic diseases, such as Zika virus. Preventing the emergence and spread of health threats will help reduce the number and magnitude of disease outbreaks. The Zika outbreak shows that threats can come from anywhere in the world, and we are all connected by the air we breathe, the water we drink, and the planes we ride on.

The research community can pivot its efforts to address outbreaks by supporting, when applicable, the twelve identified GHSA activities, called "Action Packages" in the areas of prevent, detect, and respond. These activities facilitate regional and global collaboration toward specific GHSA objectives and targets that fall under Prevent, Detect, and Respond goals. More information on these action packages can be found at: <https://ghsagenda.org/packages.html>.

NIAID and its Federal partners can respond rapidly when infectious diseases emerge because we are able to build upon our broad and flexible research foundation and efforts of the Public Health Emergency Medical Countermeasures Enterprise. In the case of Ebola, NIAID investments in biodefense research provided basic knowledge and research capacity to address this urgent public health threat. Similarly with Zika virus, NIAID is utilizing its long-term research portfolio in related flaviviruses to accelerate research on Zika virus. NIAID maximizes its research resources by pursuing development of medical countermeasures with wide impact, such as broad-spectrum antibiotics and antiviral drugs effective against multiple bacteria or viruses. NIAID also seeks to establish and validate efficient platform technologies to more rapidly develop vaccines and diagnostics for a variety of threat agents. NIAID's migration from a "one bug, one drug" approach toward a broader, more flexible research paradigm is yielding scientific advances that will facilitate our ability to respond to emerging public health threats. In the case of Zika virus, antivirals developed for other flaviviruses, along with broad-spectrum antivirals with activity against a range of pathogens, are being tested for activity against Zika, potentially expediting identification of effective therapies. For example, NIAID supported mouse model testing of the broad-spectrum antiviral drug BCX4430 that found that the drug has activity against Zika virus. NIAID had previously supported the initial development of BCX4430 as a drug for filoviruses including Ebola. In addition, vaccine platforms developed for other viruses are being rapidly adapted for Zika, allowing NIAID to accelerate preclinical work.

Question. The National Institutes of Health is requesting \$80 million in the supplemental request. This is one-third the amount of NIH's funding request during the Ebola outbreak. How was this funding level developed and what research efforts will it be focused on?

It is my understanding that while NIH has spent money researching similar diseases, currently the NIH spends \$0 on the Zika virus. Why did the fiscal year 2017 budget request not include funding for Zika research?

Answer. The breadth, scope, method of transmission, pathogenesis, disease complications, and lethality of the Ebola and Zika virus outbreaks are very different. Additionally, the pipeline of countermeasures, such as vaccines, and the stage of their development are also dissimilar. For example, while the NIH funding request for Zika includes funds for early-stage (Phase I) clinical trials of Zika vaccine candidates, the NIH funding request for Ebola included funds for larger, advanced (Phase II and III) clinical trials of Ebola vaccine candidates that had already completed Phase I clinical trials.

Similar to the rapid response to Ebola, NIAID has and continues to rapidly respond to the current Zika outbreak by accelerating research on Zika and related flaviviruses. It is important to note that prior to the large-scale emergence of Zika virus in the Americas, Zika virus disease was thought to be a relatively benign illness. As we have learned more about its potential ramifications, we are now focused on rapid early-stage discovery and development of candidate vaccines, diagnostics, and therapeutics, and the Administration has requested emergency funding to enhance and expand our ongoing efforts to prepare for and respond to the Zika virus.

Within the Administration's Zika emergency funding request, \$130 million would support NIH research to immediately address the outbreak in fiscal year 2016. We did not include costs that would be incurred in fiscal years 2017–2019 to fund pivotal Phase IIb and Phase III vaccine clinical trials in endemic areas, nor the funds

required to continue ongoing research initiated in fiscal year 2016. This fiscal year 2016 request was based on the scientific assessments of NIH program staff who are familiar with the size and scope of the current Zika outbreak, the current state of the Zika research field, and the capabilities of extramural and intramural scientists to pivot to focus their research on this public health issue. The requested funding would support research to gain fundamental knowledge about Zika virus and the disease it causes, including potential links to microcephaly and Guillain-Barré syndrome. The emergency funding for NIH also would support the development of rapid, point-of-care diagnostics; therapeutics effective against Zika and other flaviviruses; and vaccines for Zika.

As of March 1, 2016, NIAID has stretched to commit \$10 million of its existing resources to combat the Zika health emergency. NIAID's fiscal year 2017 budget proposal provides some limited flexibility to fund research on Zika virus and other emerging and re-emerging infectious diseases.

Question. Is any of the fiscal year 2016 increase (\$212.4 million) for the National Institute of Allergy and Infectious Diseases being used for Zika research?

Answer. NIAID appreciates the Committee's support in the fiscal year 2016 budget, which provided an increase to NIAID's budget, including \$100 million dedicated to research to address the urgent challenge of combating antibiotic-resistant bacteria.

Question. The supplemental requests \$190 million for research and development efforts for a vaccine. Is this a one-time funding request or will NIH and BARDA need continued investments related to a vaccine for the Zika virus?

Answer. NIAID plans to obligate in fiscal year 2016 all of its proposed \$130 million funding, which, as described earlier, would support research to gain fundamental knowledge about Zika virus as well as the development of rapid, point-of-care diagnostics; therapeutics effective against Zika and other flaviviruses; and vaccines for Zika. The funding would support several leading Zika vaccine candidates in preclinical evaluation, and promising candidates would be taken through Phase I clinical trials in endemic areas. The proposed \$130 million would not fund advanced clinical evaluation such as Phase IIb trials.

Question. How have research efforts related to other mosquito-borne viruses such as dengue fever or West Nile virus helped us towards developing a treatment for the Zika virus?

Answer. NIAID is utilizing its existing flavivirus research program to help develop needed countermeasures for Zika virus. For example, NIAID has developed resources to screen for antiviral drugs active against viruses in the flavivirus family, including dengue, West Nile, and yellow fever viruses. Building on these efforts, NIAID has developed a specific assay to test drug candidates for activity against Zika virus. NIAID is making this assay available to the research community and is currently testing drug candidates that have activity against other flaviviruses (including broad-spectrum antivirals) to determine if they are effective against Zika virus. Successful candidates would be evaluated for further development as Zika virus treatments. In addition, NIAID research on vaccines for other flaviviruses has accelerated the development of candidate Zika virus vaccines. NIAID scientists are modifying candidate vaccines they developed for West Nile virus and for dengue virus to quickly generate candidate Zika virus vaccines for further evaluation.

Question. The Zika virus does not have a rapid diagnostic test, effective treatment, or a vaccine. How do you prioritize the development of these three necessary components to stopping the epidemic?

Answer. CDC recognizes the expertise and authorities that exist across the Federal Government and is collaborating with many agencies in order to effectively detect, prevent, and respond to Zika virus. CDC has prioritized access to diagnostic tests in its Zika efforts and continues to work with FDA to obtain Emergency Use Authorization (EUA) for Zika diagnostic assays. These assays will have the potential to diagnose Zika virus disease during the first week of illness, and can be used on serum samples from people with a history of symptoms associated with Zika and/or people who have recently traveled to an area during a time of active Zika transmission. CDC is also partnering with the Biomedical Advanced Research and Development Authority (BARDA) to expand lab diagnostics manufacturing in the short-term and in the long-term, to encourage commercial production of diagnostic assays. CDC and NIH work collaboratively to facilitate the transfer of research efforts into products and services that will effectively combat Zika virus and other mosquito borne diseases.

NIAID is working to develop all three of these needed countermeasures for Zika virus by building on existing scientific knowledge about flaviviruses. It is critical to have rapid, sensitive, and specific diagnostic tests for Zika virus to identify currently and previously infected individuals, particularly pregnant women who may

be concerned about potential congenital defects. In addition, drugs to treat Zika virus infection would be important tools to address the ongoing Zika outbreak. The top priority of NIAID is the development of a Zika virus vaccine that could prevent infection and thereby avert congenital defects potentially linked to Zika virus infection, including microcephaly.

To stimulate other Zika-related research, several NIH ICs have issued notices to alert the research community about NIH's interest in supporting Zika-related research and product development. High-priority research areas include assessing the impact of infection during pregnancy, developing rapid, specific, and sensitive clinical diagnostic tests; and broad-spectrum therapeutics effective against a range of flaviviruses, such as Zika. NIH also is encouraging research applications aimed at understanding how Zika is transmitted, as well as how the immune system responds when people are infected by Zika and other flaviviruses. These notices may be accessed by going to: <https://grants.nih.gov/grants/guide/notice-files/NOT-AI-16-026.html>, <http://grants.nih.gov/grants/guide/notice-files/NOT-HD-16-004.html>, and <http://grants.nih.gov/grants/guide/notice-files/NOT-HL-16-307.html>.

Question. How much concern should there be that Zika will become wide-spread in the United States with an infected mosquito biting multiple people?

Answer. While we have not yet seen local mosquito-borne transmission of the Zika virus within the continental United States, we expect that the number of cases of Zika infection among returning travelers will increase. Zika virus is transmitted to people primarily through the bite of an infected *Aedes* species mosquito (*A. aegypti* and *A. albopictus*). These are the same mosquitos that spread dengue and chikungunya viruses. In addition, CDC and State health departments are now investigating reports of sexual transmission of Zika virus, several involving pregnant women. These reports suggest sexual transmission may be a more likely means of transmission for Zika virus than previously considered.

Recent chikungunya and dengue clusters in the United States suggest that Zika outbreaks in the U.S. mainland may be relatively small and localized. Better housing construction, less crowding, regular use of air conditioning, use of window screens and door screens, and State and local mosquito-control efforts have helped to contain transmission of these mosquito-borne viruses. For the Commonwealth of Puerto Rico as well as the U.S. Virgin Islands and American Samoa, the situation is different; all three areas have already reported local Zika transmission.

Chikungunya provides a basis for estimating spread of Zika in the United States and territories. Chikungunya and Zika viruses have similar transmission cycles during outbreaks, using the same mosquito species to infect humans who amplify and typically spread the virus from one location to another. The number of cases of Zika transmission in Puerto Rico is doubling every week, and based on our experience with dengue and chikungunya, we believe this number will continue to rise. As a point of comparison, a quarter of the population in Puerto Rico has been infected with chikungunya, which arrived on the island less than 2 years ago, which would indicate that at least 600,000 infections of Zika are likely to occur there.

Question. In an attempt to end the spread of the Zika virus, Brazil is conducting trials releasing genetically modified male mosquitoes that do not produce offspring into the wild. Are you familiar with this project and what are your thoughts on this approach?

Answer. 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*-borne infectious agents. NIAID is in contact with Oxitec and other investigators pursuing a variety of novel approaches to mosquito control.

While a promising technique, mass release of genetically modified males is not suitable for emergency use. Reduction in *Aedes aegypti* populations was observed in small scale field trials in areas of Brazil, but these observed populations may or may not reduce transmission of Zika or dengue viruses. To be effective, massive numbers of genetically modified male mosquitos would need to be mass reared on an industrial scale, with excellent quality control. Furthermore, multiple release points would be needed, as *Aedes aegypti* has a short flight range. Releases would need to be sustained, due to high reproductive rate of *Aedes aegypti*. Finally, to date, the largest trial is a 4.5 hectare area in suburban Rio de Janeiro; covering the island of Puerto Rico (which is over 900,000 hectares) is not feasible in near term. Release of genetically modified male mosquitos may hold potential for use in concert with current mosquito control methods to suppress mosquito populations and to reduce the spread of diseases like Zika virus.

Question. Can you discuss the guidance that has gone out to State and local health departments about how to test for and treat Zika?

Is there a requirement that a local lab inform the State before sending samples to CDC?

Answer. Zika virus is a nationally notifiable condition. Healthcare providers are encouraged to report suspected Zika cases to their State or local health department to facilitate diagnosis and mitigate the risk of local transmission. Local laboratories should make sure the State or local health department and CDC have been notified and have approved of the receipt of all specimens before they are collected and shipped. Working closely with the State or local health departments ensure that the appropriate test is ordered and results are interpreted correctly. CDC provides State and local health departments with instructions on collection and submission of body fluids for Zika virus testing. This can be found at: <http://www.cdc.gov/zika/hc-providers/body-fluids-collection-submission.html>. CDC has developed interim guidelines for pregnant women and women of reproductive age with possible Zika virus exposure (http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm?s_cid=mm6505e2er.htm_w). Because there are limited data and experience with Zika virus in pregnancy, CDC continually evaluates any new or emerging data that may inform future recommendations. As more information becomes available, we will update the CDC Zika website (<http://www.cdc.gov/zika/>). CDC also has developed guidance and recommendations on Zika for travelers, healthcare workers, and other groups. As new guidance and recommendations are developed and updated, they are posted on CDC's Zika website (<http://www.cdc.gov/zika/>). CDC also has developed interim guidelines for healthcare providers caring for infants and children with possible Zika virus exposure (http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1er.htm?s_cid=mm6507e1er.htm_w). Q&As on these guidelines also are available (<http://www.cdc.gov/zika/hc-providers/qa-pediatrician.html>). Information on CDC's interim Zika guidelines can be found on CDC's Zika website at: <http://www.cdc.gov/zika>.

Question. Do you know how many States have labs that have the capacity to test for Zika?

If tests have to be sent to the CDC for testing, what is the lag-time before a physician will receive testing confirmation?

Answer. Testing capacity varies from State to State. As of February 11th, nine jurisdictions have the capacity to perform reverse transcription polymerase chain reaction (RT-PCR) testing for Zika. CDC has prioritized access to diagnostic tests in its Zika efforts and continues to work with FDA to obtain Emergency Use Authorization (EUA) for Zika diagnostic assays. These assays will have the potential to diagnose Zika virus disease during the first week of illness, and can be used on serum samples from people with a history of symptoms associated with Zika and/or people who have recently traveled to an area during a time of active Zika transmission.

Question. I was contacted by a constituent in Missouri who has a son that was born with congenital cytomegalovirus (CMV) which can also cause microcephaly in babies.

Is there any connection between CMV and Zika?

Answer. Both cytomegalovirus (CMV) and Zika are viral infections. There are no FDA-approved vaccines to prevent either Zika or CMV. It is not known whether there is a connection between the two viruses, or whether prior or co-infection with CMV increases the likelihood of infection with Zika.

The Zika virus is a flavivirus, a group of infections that also includes dengue, West Nile, and yellow fever. The Zika virus is neurotropic, meaning that it primarily affects the brain. Research is unclear at this point whether these effects are a direct result of the virus itself or due to an immunologic response to Zika infection. The Zika virus is transmitted by the *Aedes aegypti* mosquito, common in warmer climates; recent studies have also suggested that it can be transmitted sexually. In early March 2016, researchers showed that the Zika virus could infect nerve cells. Another new study of 88 pregnant women with rash in Brazil found that many who were infected with the Zika virus demonstrated a range of health concerns, including pregnancy loss, central nervous system abnormalities, growth restriction, low amniotic fluid, and abnormal blood flow to the baby, along with babies born with microcephaly.

CMV is one of the herpes viruses, from a group of infections that also include chickenpox. A common infection that is usually harmless or causes mild symptoms, it can be transmitted through contact with bodily fluids (such as saliva or blood), can be sexually transmitted, or, if a pregnant woman has an active infection, it can be transmitted to her fetus. CMV can cause serious disease in babies infected prior to birth (congenital CMV). According to the CDC, about 1 in 5 children born with congenital CMV infection will develop permanent problems, such as hearing loss or developmental disabilities, and a small number may die. At this time, there are no FDA-approved vaccines to prevent either Zika or CMV.

There are many unanswered questions about the Zika virus and its effects on health. Specifically, we need to establish whether Zika virus causes fetal abnormalities and/or other pregnancy complications, such as fetal loss, stillbirth, or ocular abnormalities, and if any other factors may be contributing to these effects (e.g., prior CMV or dengue exposure in the pregnant woman). Case-control studies will help to generate hypotheses for potential co-factors, and longer term prospective studies will provide more definitive evidence. To stimulate research on Zika, NIH issued notices for the research community to highlight the interest in supporting Zika-related research and product development. High-priority research areas include assessing the impact of infection during pregnancy, developing rapid, specific, and sensitive clinical diagnostic tests; broad-spectrum therapeutics effective against a range of flaviviruses, such as Zika; and vaccines. NIH also is encouraging research applications aimed at understanding how Zika is transmitted, as well as how the immune system responds when people are infected by Zika and other flaviviruses.

Question. What are the NIH and CDC doing related to research, generally, on microcephaly and how does this intersect with research related to CMV?

Answer. The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) has ongoing studies on CMV infection. NICHD is funding a large study of CMV transmission in pregnancy in Brazil (R01HD061959). This is a prospective study of congenital CMV of 10,000 women enrolling during pregnancy with a 2-year follow-up. In addition, the NICHD's Maternal Fetal Medicine Network is conducting a Phase III clinical trial on treatment for prevention of congenital CMV (<https://clinicaltrials.gov/ct2/show/NCT01376778>). NICHD is supporting other CMV studies to evaluate treatments to improve neonatal outcomes and on CMV vaccines. These studies may be able to incorporate Zika-related research, and the new funding opportunities (<http://grants.nih.gov/grants/guide/pa-files/PA-16-106.html>) should stimulate further research on Zika and its impact on children's health.

CDC is conducting research to:

- Examine long-term health problems that infants born with CMV infection may suffer. These health problems include microcephaly, mental disabilities, and hearing loss;
- Improve laboratory and newborn screening tests to identify infants with congenital CMV infection, about 1 percent of whom may be born with microcephaly; and
- Identify the burden of congenital CMV infection and CMV-related birth defects, such as microcephaly, among infants in populations where a large proportion of mothers are already infected with CMV.

QUESTIONS SUBMITTED BY SENATOR THAD COCHRAN

Question. Dr. Frieden, much of the funding requested for the Centers for Disease Control and Prevention is for domestic response activities like mosquito control programs. Such programs have long been a staple in Southern states like Mississippi with warmer climates. How would any new funding be used differently by State and local agencies that already conduct important mosquito control activities?

Answer. CDC's supplemental request includes direct funding for States and territories, prioritized based on risk of Zika transmission, primarily through two of CDC's existing cooperative agreements. CDC's Public Health Preparedness Emergency (PHEP) and Epidemiology and Laboratory Capacity for Infectious Diseases (ELC) cooperative agreements provide support to public health departments across the nation to enhance their ability to effectively respond to emerging public health threats, such as the Zika virus disease. These funds will provide critically needed flexible and adaptable funds to enable select health departments to effectively respond to this emergent need. Funding for jurisdictions through the ELC cooperative agreement supports prevention and control activities including maintenance and expansion of arboviral disease diagnostic capacity, human and environmental surveillance activities, and prevention and communication activities to prevent mosquito-borne disease.

In addition, much of the funding requested to support the CDC response will provide scientific, technical and logistical support to State and local efforts to respond to Zika virus. CDC staff continue to provide direct technical assistance, working with public health partners and State health departments to alert healthcare providers and the public about Zika, post travel notices and other travel-related guidance, provide State health laboratories with diagnostic tests, detect and report cases, publish and disseminate guidelines to inform testing and treatment of people with suspected or confirmed Zika, and study what might be responsible for the re-

ported rise in microcephaly and Guillain-Barré Syndrome, as well as studying the dynamics of sexual transmission.

Other key CDC work that supports State and local response includes:

- Providing reference and surge laboratory capacity for the Nation. CDC is building laboratory capacity and infrastructure to test for Zika virus and other infectious diseases across the United States by providing critical laboratory supplies, reagents, equipment, and training for diagnostic testing and surveillance activities in States and territories. CDC resources are supporting diagnostic test manufacturing and CDC laboratory surge capacity, both of which help meet State testing needs, especially in Puerto Rico. In addition, CDC continues to work on improving diagnostics for Zika.
- Providing a framework for tracking Zika-affected pregnancies and births. CDC-supported expansion of systems for maternal and child and birth defect surveillance improves the ability of State-run registries across the country to detect risks related to Zika.
- Helping States deploy and target effective mosquito control. CDC-supported investments in mosquito control will help States and cities identify and address areas where mosquitoes breed to drive down mosquito populations. Continued CDC work on development of innovative mosquito control tools, such as promising new products that may be safer and more effective than today's methods, will eventually help States reduce the population of mosquitoes that can spread Zika and other diseases.
- Supporting timely, accurate and effective communications to the public and healthcare providers. CDC development of targeted prevention and education strategies and supporting materials for key populations (including pregnant women, their partners, and healthcare professionals) are widely disseminated for use by State health departments and partners.

Question. Dr. Frieden, in my home State of Mississippi, we have more mosquitoes than people. For years, people have been concerned about the possibility of an outbreak of a mosquito-transmitted disease like West Nile virus. Why do you think Zika is more likely to develop into an outbreak than some other dangerous mosquito-transmitted disease?

Answer. Mosquito-borne diseases are among the most complex of all infectious diseases to prevent and control. Of particular concern, States throughout the southern United States are home to *Aedes aegypti* mosquitos that spread Zika virus most efficiently. 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 use screens and less dense living conditions; however, any local outbreaks will be of deep concern to the people living there. Furthermore, unlike other mosquito-borne diseases, evidence suggests that Zika is linked to fetal malformations such as microcephaly. The potential harm Zika has on the developing baby makes even small outbreaks particularly concerning. Furthermore, in territories, particularly Puerto Rico, *Aedes* mosquitos are abundant and local transmission has already been reported. The speed at which the outbreak is spreading in Puerto Rico is particularly concerning. As a point of comparison, a quarter of the population in Puerto Rico has been infected with chikungunya, which arrived on the island less than 2 years ago, which would indicate that at least 600,000 infections of Zika are likely to occur there.

QUESTION SUBMITTED BY SENATOR BRIAN SCHATZ

Question. The Vector Control Branch at the Hawaii State Department of Health was decimated in 2009 due to budget cuts. Can you provide specific recommendations on vector control resource requirements for State and local governments? We would like to be able to get back to each member, governor, and State with these recommendations.

Answer. Vector-borne diseases are among the most complex of all infectious diseases to prevent and control and requires unique capabilities of State and local public health departments. Public health departments need the laboratory surveillance, and epidemiological ability to track disease prevalence in people and mosquitos. States and localities also must be able to conduct sentinel surveillance and to implement scalable pesticide and non-pesticide based vector control to respond to emerging arboviral threats like Zika. Some areas have these capacities already in place but many State and local health departments do not have the laboratory, mosquito surveillance or human surveillance capacity to respond to a mosquito-borne outbreak as complex as Zika virus.

QUESTIONS SUBMITTED BY SENATOR TAMMY BALDWIN

Question. I am encouraged that both the NIH and the CDC have joined the more than two dozen government organizations, medical journals, and global health organizations in pledging to share scientific and research data related to Zika to speed the fight against the spread of this virus. This is an important step to help ensure that our global response to this and other outbreaks is coordinated and that impacted areas can benefit from the most up-to-date scientific advances.

But, what challenges remain in this area to improve sharing with our partners—such as physical sample sharing—and what have NIH and CDC learned from the recent Ebola crisis to improve scientific exchange?

Answer. HHS is coordinating a single process to obtain samples from endemic countries, including Brazil, and direct them to highest priority research needs (inside and outside of the government). To help in this effort, NIAID is supporting two biorepositories which make virus and other clinical specimens (e.g., plasma from infected individuals) available to researchers and commercial developers.

NIH has a longstanding commitment to make scientific data publicly available in a timely manner. Publicly-released data, including datasets generated and released by NIAID, serve as critical resources for scientists around the world, and are essential to enable the advancement of research and surveillance of infectious diseases. For example, in the recent Ebola outbreak in West Africa, NIAID genome sequencing efforts and resources provided additional information about the circulating Ebola virus strain. This genomic information, shared in real-time in publicly accessible international data repositories at the NIH's GenBank, helped researchers to understand how the virus is transmitted and causes disease, as well as guide strategies for developing new therapeutics, vaccines, and diagnostics. Similar activities are already underway for Zika virus. Rapid data sharing is an increasingly important aspect of collaborative research, and NIH is committed to sharing research results in the current Zika outbreak in order to facilitate better understanding of disease caused by the virus and to help develop safe and effective countermeasures.

Within the Global Health Sample Sharing Initiative (GHSSI), CDC is 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 the link between Zika, microcephaly and Guillain-Barré syndrome, as well as on the development of medical countermeasures. CDC is also sharing samples among GHSSI countries to rapidly to expedite research and development of diagnostics and life-saving vaccines and therapeutics by implementing a GHSSI Operational Framework for the Rapid Sharing of Biological Materials.

Question. Is there a centralized resource or list of CDC and NIH-funded studies related to Zika virus that researchers can use to avoid designing duplicate studies and to help facilitate partnerships with existing studies?

Answer. CDC has a centralized repository of currently funded studies related to Zika virus in its IMPAC (Information for Management, Planning, Analysis and Coordination) II system. This system allows staff to track and manage research grants and contracts, making information to the public more accessible.

Centralized information regarding CDC funded Zika activities can also be found through the Tracking Accountability in Government Grants System (TAGGS). The department-wide TAGGS database is a central repository for grants awarded by the eleven HHS Operating Divisions (OPDIVs). TAGGS tracks obligated grant funds at the transaction level. TAGGS data can be searched by the public at: <https://taggs.hhs.gov/>.

Grants.gov provides a centralized location for grant seekers to find and apply Federal funding opportunities, including those related to Zika supported by CDC. Grants.gov data can be searched by the public at: <http://www.grants.gov/>.

NIH's Research Portfolio Online Reporting Tools (RePORT) website (<https://report.nih.gov/index.aspx>) provides access to reports, data, and analyses of NIH research activities, including information on NIH expenditures and the results of NIH-supported research. This includes the Report Expenditures and Results (REPORTER; <https://projectreporter.nih.gov/>) tool, which allows users to search a repository of NIH-funded research projects. Information about NIH-funded studies related to Zika virus can be found using this tool, as well as on the NIAID website at: <http://www.niaid.nih.gov/topics/Zika/Pages/default.aspx>. Scientists interested in pursuing research on Zika virus can contact their NIH program official or search the NIH Guide for Grants and Contracts (<http://grants.nih.gov/grants/guide/index.html>) for NIH Funding Opportunities and Notices related to Zika virus.

SUBCOMMITTEE RECESS

Senator BLUNT. The subcommittee will stand in recess until 10 a.m. on Thursday, March 3.

The hearing is adjourned.

[Whereupon, at 11:54 a.m., Thursday, February 11, the subcommittee was recessed, to reconvene at 10 a.m., Thursday, March 3.]