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

before the

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

March 2, 2016

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

Executive Summary

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

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

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

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

Poverty and the US Gulf Coast

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

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

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

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

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

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

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

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

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

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

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

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

Therefore, we need to consider the following:

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

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

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

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

Vaccines

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

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

Let's briefly review what happened – the fundamental science for developing the adenovirus-vectored Ebola vaccine was published in 2003 http://www.ncbi.nlm.nih.gov/pubmed/12904795; the VSV-Ebola vaccine a few years after that. But the technology waited a decade until the African situation became dire, and the US Government put up close to US$100 million through its Biomedical Advanced Research Development Authority (BARDA) http://www.phe.gov/about/BARDA/Pages/default.aspx . The funds incentivized three major pharmaceutical companies to license these technologies in order to produce vaccines for large-scale clinical testing. By the time clinical trials commenced in West Africa the Ebola epidemic was mostly halted, but not before 11,000 people perished.

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

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

- NTDs emerging in the Middle East and North Africa, including the ISIS-occupied conflict zones of Syria, Iraq, and Libya, as well as Yemen http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003852. Among them are MERS coronavirus, leishmaniasis, malaria, TB, and schistosomiasis. In some cases these diseases are also now threatening Southern Europe https://www.washingtonpost.com/opinions/preventing-the-next-disease-outbreaks/2015/10/23/c4564ec0-7817-11e5-a958-d889faf561dc_story.html

- Arbovirus infections, such as dengue fever, Rift Valley fever, chikungunya, and West Nile and Zika virus infections.

- Chronic and debilitating NTDs, such as helminth infections (e.g., schistosomiasis and hookworm), Chagas disease, leishmaniasis, Buruli ulcer, and mycetoma. These diseases have not shown gains under the current USAID NTD Program.

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

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

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

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

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