DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

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

Testimony before the

House Democratic Steering and Policy Committee

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Leader Pelosi and Members of the Committee:

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

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

The overarching mission of NIAID is to conduct and support research to better understand, treat, and prevent infectious and immunologic diseases. This is accomplished through an array of research, from basic studies of the mechanisms of disease, to applied research focused on developing interventions such as diagnostics, therapeutics, and vaccines. NIAID has a dual mandate that encompasses both research on current biomedical challenges and the capability to respond rapidly to newly emerging and re-emerging infections such as Zika virus.

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

therapeutics are available to prevent or treat Zika virus disease. Improved diagnostic tests also are needed because Zika virus infection causes non-specific symptoms or no symptoms at all, and it can be difficult to distinguish clinically from other mosquito-borne infections, such as dengue, malaria, and chikungunya.

of new therapeutics to treat disease in people infected with Zika virus. This research is necessary to better understand this emerging infection and uncover optimal ways to diagnose, treat, and prevent Zika virus disease.

NIAID and other NIH Institutes are working to accelerate research on Zika and have issued several notices to researchers

DEVELOPING COUNTERMEASURES TO COMBAT ZIKA VIRUS

NIAID has responded to public health concerns about Zika virus by accelerating ongoing

flat Zika virus

acute phase of infection and up to seven days after the onset of symptoms using diagnostic tests for viral RNA (RT-PCR test). While prior infection can be detected by testing for the presence of antibodies against Zika virus, assays for Zika antibodies may also detect or cross-react with antibodies against other flaviviruses, particularly dengue virus. For this reason, a positive antibody test does not definitively confirm prior Zika virus infection in the setting of possible co-infection or prior infection with dengue and other related viruses, and separate confirmatory testing is required. This is a particular concern in South America where there is a high level of exposure to other flaviviruses, especially dengue virus.

Therefore, NIAID is facilitating the development of improved Zika virus diagnostic tests through support for NIAID investigators and grantees working to generate antibodies that can distinguish between Zika virus and dengue virus. Studies also are underway to create novel recombinant Zika virus proteins that are less cross-reactive to other flaviviruses. In addition, NIAID grantees are working to identify biosignatures unique to Zika infection that could form the basis of additional rapid diagnostic tests.

Vaccines

A safe and effective Zika vaccine would be an extremely 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 against 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 in people, the West Nile virus vaccine candidate was safe and generated a strong immune response, offering a model for Zika vaccine development. NIAID scientists also are designing live, attenuated vaccines, 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 February 2016, a large Phase 3 trial assessing the dengue vaccine candidate was launched in Brazil in collaboration with the Butantan Institute. In addition, NIAID is collaborating with BARDA and the Walter Reed Army Institute of Research (WRAIR) to make a whole-particle, inactivated virus vaccine. Preclinical testing of the vaccine candidate is underway, and human clinical studies, supported by NIAID and WRAIR, are expected to start in the fall of 2016. NIAID grantees also are in the early stages of developing a Zika virus vaccine based on a recombinant vesicular stomatitis virus – the same animal virus used successfully to create an investigational Ebola vaccine. Plans are underway to evaluate this potential vaccine construct in tissue culture and animal models.

While these approaches are promising, it is important to realize that the development of investigational vaccines and the clinical testing to establish their safety and effectiveness take time. Although

virus. Promising drug candidates identified by the assay are being further tested in a small animal model of Zika virus infection developed with NIAID support. For example, NIAID recently evaluated BCX4430, a broad-spectrum antiviral drug originally developed by Biocryst Pharmaceuticals as a candidate therapeutic for Ebola and Marburg viruses, and found the drug protected immune-deficient mice infected with Zika virus. The ultimate goal of NIAID-supported flavivirus therapeutic research is to develop a broad-spectrum antiviral drug that could be used against a variety of flaviviruses, including Zika.

Emergency Request for Vaccine Research and Diagnostic Development and Procurement

As I noted in the introduction to my testimony, the Administration has announced an emergency funding request of approximately $1.9 billion to combat the Zika virus both domestically and internationally. Included in the request are resources for Zika-related research, rapid advanced development, and commercialization of new vaccines and diagnostic tests for Zika virus. The funding will allow NIH to build on existing resources and work to develop a vaccine for Zika virus. Funding will allow this work to move forward on schedule and improve scientific understanding of the disease to inform the development of additional tools to combat it. We look forward to working with the Congress to implement this request.

COLLABORATIONS

Investigation of emerging and re-emerging infectious diseases requires expertise from a variety of fields. In the case of Zika virus, studies of virology, immunology, natural history, neurology, and neonatology will be required to fully understand the pathogenesis of this infection. As mentioned previously, NIAID is partnering with other NIH Institutes to better

understand the association between Zika virus infection and neonatal defects, particularly microcephaly. In addition, NIAID is working with CDC, DOD, and USDA to develop and advance promising vector control technologies and strategies.

NIAID also is employing partnerships with research institutions in South America to advance research on Zika virus infection. Additional collaborations with academic, industry, and government partners are underway or are being actively explored. NIAID held a joint meeting in December 2015 with the Brazilian research institute Fiocruz in which Zika was a key area of discussion. The meeting has helped to inform ongoing Zika research collaborations with Fiocruz, including the planned ZIP study. NIAID also is collaborating with other HHS agencies in responding to the Zika epidemic. For example, NIH, CDC, BARDA, ASPR, and FDA jointly convened a Zika virus workshop on March 28-29, 2016, where the latest information on Zika virus was discussed by experts from federal agencies, academia, and pharmaceutical and biotechnology companies. Topics addressed at the workshop included virology, epidemiology, links to microcephaly, and efforts to develop diagnostics, therapeutics, and vaccines. The information exchanged through this workshop continues to inform ongoing rem ongoingETBT1 0Tm[a)4(lso)]I

virus and employ this knowledge to develop needed tools to diagnose, treat, and prevent disease caused by this virus. In particular, NIAID will pursue the development of safe, effective vaccines to prevent disease caused by Zika, dengue, and chikungunya viruses. Such efforts also help to