Committee on Energy and Commerce
Subcommittee on Oversight and Investigations
Hearing: "U.S. Public Health Response to the Zika Virus: Continuing the Challenge"
May 23, 2017

Questions for the Record for Dr. Anthony Fauci, Director,
National Institute of Allergy and Infectious Diseases, National Institutes of Health

The Honorable Tim Murphy

1. What is the expected production volume for the vaccine once it is approved?

The National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), facilitates research and development of vaccine candidates, which typically includes the support of early stage clinical trials to investigate vaccine safety and efficacy. The production volume of an FDA-approved Zika vaccine would be determined by the vaccine manufacturer, and will depend in part on the licensed indications and approved usage of the vaccine in the U.S. and elsewhere.

   a. Which population will be prioritized for the vaccine and why?

   The initial target population for an approved Zika vaccine will likely be adults and adolescents of reproductive age, excluding pregnant women. This is the same target population as for the Phase II/IIb clinical trial testing of the NIAID Vaccine Research Center (VRC) investigational DNA vaccine.

   NIAID also is supporting research on other vaccine candidates, including live-attenuated approaches that could potentially induce longer-lasting protection, possibly for decades. These vaccines might be evaluated in children, anticipating that vaccination in childhood could protect individuals through childbearing years. A strategy of childhood vaccination may be particularly effective in areas where Zika virus is endemic and there is greatest risk of congenital Zika syndrome. In the future, Zika vaccine candidates that have been found to be safe in non-pregnant populations may be investigated to determine if they are safe and effective in pregnant women.

2. Why does Zika cause microcephaly, yet other flaviviruses such as dengue, chikungunya, and yellow fever are not known to cause microcephaly?

NIAID is actively engaged in efforts to better understand the Zika virus, including any differences between Zika virus and other related flaviviruses that may help explain why Zika can cause microcephaly. For example, NIAID-supported investigators have developed animal models of Zika virus infection during pregnancy to better understand congenital Zika syndrome, which is a pattern of birth defects that includes severe microcephaly. These NIAID-funded animal studies have shown that Zika virus is capable of crossing the placental barrier and impairing fetal brain development in pregnant animals.

In addition, NIH-supported investigators have discovered that neural precursor cells, which give rise to new cells in the developing brain, have receptors that make these cells particularly vulnerable to infection by Zika virus. NIH-supported researchers are now investigating how Zika virus exploits the cellular, molecular, and biochemical pathways within these cells to propagate the virus and cause these cells to die. They also are investigating how the immune system interacts with Zika virus within the central nervous system to better understand which aspects might be enhanced to help control the virus and whether the brain's immune response to the virus might also cause collateral damage that contributes to cell death.

NIAID also is supporting research to address concerning reports of infants born to Zika virus-infected mothers that appear healthy at birth but later experience slowed head growth during the first year followed by postnatal microcephaly. NIAID is partnering with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institute of Environmental Health Sciences, and the Brazilian research institute, Fiocruz, to better understand these observations. This study, Zika in Infants and Pregnancy (ZIP), is a multi-center, international, prospective cohort study of 10,000 women in Zika-affected regions. Enrollment of women early in their pregnancy is ongoing, and their children will be followed for at least one year after birth. The information gained from this study will help improve our understanding of congenital Zika syndrome, enhance care for pregnant women and their infants, and guide interventions for affected children.

The Honorable Frank Pallone

1. HHS recently reported that NIH has obligated $68.8 million of its fiscal year 2017 Zika funds. How much funding does NIH have remaining in 2017 for Zika preparation or response? Does NIH have sufficient funds remaining to support these efforts for the remainder of fiscal year 2017?

As of May 15, 2017, the National Institute of Health (NIH) has obligated $71.36 million of the $152 million in NIH supplemental funds provided by the Zika Response and Preparedness Act 2016 (division B of Public Law 114-223). The remaining $80.64 million will be obligated by the end of FY 2017. We anticipate these funds will be sufficient to support Zika-related activities currently planned through FY 2017.

The Honorable Kathy Castor

1. Please provide an update on vaccine development and clinical trials.

A safe and effective Zika vaccine would be an invaluable tool to help stop the spread of infection and prevent future outbreaks. NIAID is developing and investigating multiple Zika vaccine candidates.

DNA-based Zika vaccine candidate: NIAID recently launched a multi-site Phase II/IIb clinical trial of the NIAID VRC's DNA-based vaccine candidate in March 2017 following positive

results in Phase I testing. This trial aims to enroll at least 2,490 healthy participants in various sites in the Americas, including the continental United States, U.S. territories, and countries in Central and South America. This Phase II/IIb study will further evaluate whether the experimental vaccine is safe and able to stimulate an adequate immune response, and importantly whether it can prevent disease in areas with ongoing mosquito-borne Zika virus transmission. The clinical trial will enroll adults and adolescents of reproductive age. Part A of the study will enroll 90 healthy men and non-pregnant women ages 18-35 years at Baylor College of Medicine (Houston, Texas) and University of Puerto Rico Medical Sciences Campus (San Juan, Puerto Rico). Part B will enroll 2,400 healthy men and non-pregnant women ages 15-35 years in these Part A sites and Brazil, Peru, Costa Rica, Panama, and Mexico. The effects of the vaccine on a developing fetus are unknown, and therefore women who are pregnant or plan to become pregnant will not be eligible for the trial. The study is expected to conclude in 2019, although the exact timing of the trial will depend on the intensity of Zika virus transmission and the efficacy of the vaccine candidate.

Zika purified inactivated vaccine (ZPIV) candidate: NIAID is collaborating with the Biomedical Advanced Research and Development Authority (BARDA) and the Walter Reed Army Institute of Research (WRAIR) to evaluate a ZPIV candidate developed by WRAIR. ZPIV is based on an approach used to develop vaccines against the related dengue and Japanese encephalitis viruses. NIAID is co-funding the Phase I clinical trials program with WRAIR. Trials testing ZPIV began in November 2016 at the WRAIR Clinical Trial Center in Silver Spring, Maryland; the Center for Virology and Vaccine Research, part of Beth Israel Deaconess Medical Center and Harvard Medical School in Boston; the Center for Vaccine Development at the Saint Louis University School of Medicine; and the clinical research center CAIMED, part of Ponce Health Sciences University in Puerto Rico. The Saint Louis University School of Medicine site is an NIAID-funded Vaccine Evaluation and Treatment Unit (VTEU) that is able to enroll large numbers of volunteers and vaccinate them in a rapid, safe, and effective manner. Having the rapid-response capability of the NIAID VTEUs in place ahead of an outbreak allows for accelerated testing of vaccines designed to address Zika virus and other emerging public health threats.

Live-attenuated Zika vaccine candidates: NIAID scientists are developing live-attenuated Zika vaccine candidates using an approach similar to that taken with an experimental vaccine against the closely related dengue virus. This vaccine candidate will enter an NIAID Phase I clinical trial in late 2017. Thereafter, this Zika-only candidate will be combined with the tetravalent dengue vaccine candidate designed to protect against all four circulating strains of dengue virus. A Phase I trial of this new pentavalent combination Zika/dengue candidate vaccine is scheduled to enter clinical testing by 2018. NIAID is working with development partners in Brazil to plan later-stage trials of this combination vaccine.

Early-stage Zika vaccine candidates: NIAID-supported researchers are evaluating investigational mRNA vaccines, which are broadly similar to DNA vaccines. The NIAID VRC and other NIAID intramural researchers are working with academic and industry partners to evaluate various mRNA vaccine technologies to identify potential candidates for further development. These include an investigational vaccine under development by the NIAID VRC and the pharmaceutical company GSK that may enter clinical trials in late 2017.

2. Please provide the latest information on the Zika vaccine licensing agreement between the U.S. Army and Sanofi and any relevant details.

The ZPIV candidate was developed by WRAIR, and NIAID is supporting Phase I clinical testing of this vaccine as described above. NIAID is not involved in the development of the Zika vaccine licensing agreement between the U.S. Army and Sanofi. You may wish to contact the Department of Defense to address any specific questions on the vaccine licensing agreement for the ZPIV candidate between the U.S. Army and Sanofi.

3. With many members of Congress, states and public health advocates worried that the Zika vaccine being developed at the Walter Reed Army Institute of Research with taxpayer dollars will be priced too high, how is the federal government working to ensure Sanofi, when/if a licensing agreement is made, will sell this taxpayer funded vaccine at an affordable price to federal and state governments and to consumers?

NIAID is not involved in the development of the Zika vaccine licensing agreement between the U.S. Army and Sanofi. You may wish to contact the Department of Defense to address any specific questions on the vaccine licensing agreement for the ZPIV candidate between the U.S. Army and Sanofi.

4. How has public health advice regarding Zika evolved over the past few years for young men and women? What do we know now that we did not before and what new information could be on the horizon?

NIAID defers to the Centers for Disease Control and Prevention to respond to this question about public health advice regarding Zika.

5. When does each federal agency believe they will run out of money to respond properly to Zika, including vector control, surveillance, vaccine and diagnostics development/ improvement and research?

The remaining NIH funds provided by the Zika Response and Preparedness Act 2016 (division B of Public Law 114-223) will be obligated by the end of FY 2017. We anticipate these funds will be sufficient to support Zika-related activities currently planned through FY 2017.