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. Lyle R. Petersen, Director,
Division of Vector-Borne Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Center for Disease Control and Prevention

The Honorable Tim Murphy

1. How many facilities in the United States can perform the various Zika diagnostic tests?

There are three laboratory tests used for Zika: 1) a nucleic acid-based test (NAT), which are performed on acceptable specimens including human serum, plasma, blood, or urine collected during the first two weeks after symptom onset to detect Zika; 2) serological test (e.g., IgM), which detects Zika antibodies within 2 to 12 weeks of exposure; and 3) the PRNT test, which is used for the qualitative detection of Zika virus IgM antibodies to confirm the findings of the IgM test. Forty-nine states, Puerto Rico, and Guam are able to perform the NAT test developed by CDC (Trioplex Real-time RT-PCR Assay). Forty-six states and Puerto Rico are able to perform the IgM test developed by CDC (Zika Mac-ELISA). Two CDC laboratories and six state public health laboratories in California, Florida, Maryland, Massachusetts, Michigan, and New York can perform PRNT testing. Four of these state labs (Massachusetts, Michigan, California, and New York) have agreed to serve as reference labs for other states that do not have the capability to perform the PRNT test. Commercial testing for both NAT and IgM assays is also available in all 50 states.

a. What steps is the CDC taking to disseminate these tests, particularly the PRNT test, more widely?

For the PRNT test, individual laboratories are responsible for developing and validating their own PRNT protocols, and CDC does not distribute, oversee, or approve PRNT testing in non-CDC laboratories. CDC does provide technical assistance upon request to laboratories seeking to implement PRNT testing.

b. How many PRNT tests can the CDC process in one day?

CDC laboratories can perform up to approximately 600 PRNT tests per week. The PRNT test is a multi-day, multi-step test. The turn-around time for a test result may range from 14 to 22 days.

c. How do you plan to ramp up your capacity to process Zika diagnostic tests, in particular the PRNT test, in the coming months?

If additional testing capacity is needed, CDC has plans in place to increase the number of tests performed at its laboratories each week to 1,000. In addition, the four reference labs

mentioned above are available to conduct PRNT testing on behalf of other states, if the need exceeds CDC's testing capacity. These four PRNT reference laboratories have agreed to perform this service through September 2017 with current emergency response funding.

2. The PRNT test is considered the "gold standard" but is not scientifically proven. How can something be considered the "gold standard" when it has not been scientifically proven?

PRNT is a well-recognized, established, and standard laboratory technique that is used to confirm the IgM test by testing for the presence of Zika antibodies. Due to cross-reaction with other flaviviruses such as dengue or chikungunya, results from other testing methods may be difficult to interpret, therefore, presumed positive, equivocal, or inconclusive tests must be forwarded for confirmation by the PRNT. CDC will continue to invest in improving the test, in accordance with available resources.

3. How many pregnant women with Zika infections have been accounted for in the United States?

As of May 23, 2017, there were 1,883 pregnant women with laboratory evidence of possible Zika virus infection in the United States and the District of Columbia. In the U.S. Territories of Puerto Rico, American Samoa and the U.S. Virgin Islands, there have been 3,916 pregnant women with laboratory evidence of possible Zika virus infection, as of May 23, 2017.

a. How many of these women completed their pregnancy?

Of the 1,883 pregnant women with laboratory evidence of possible Zika virus infection in the United States and the District of Columbia, 1,579 women have reported completing their pregnancy, as of May 23, 2017. The number of completed pregnancies with or without birth defects include those that ended in a live birth as well as pregnancy losses.

The reported number of pregnant women with laboratory evidence of possible Zika virus infection is cumulative and includes not only women who have completed their pregnancies, but also ongoing pregnancies that have not been completed. There are some delays in reporting. For some jurisdictions, the latest total number of pregnant women with Zika are available on the individual websites for each jurisdiction. In addition, reported numbers may increase or decrease as preliminary information is clarified.

Between October 13, 2016, and May 23, 2017, CDC did not report the number of completed pregnancies or outcomes for all completed pregnancies with laboratory evidence of possible Zika virus infection in the US Territories.

b. How many of these fetuses or infants had congenital birth defects?

As of May 23, 2017, CDC was aware of 72 infants born with Zika associated birth defects and 8 women had pregnancy losses with birth defects in the United States and the District of Columbia.

The Honorable Michael Burgess, M.D.

1. What has CDC done to support the limited capacity of local public health departments through technical assistance and grants, and where has the agency found challenges in supporting local responses to the Zika epidemic? Furthermore, how does HHS plan to further support capacity building efforts in the coming months, particularly as we get into the months where we could see local transmission of Zika in the United States?

   CDC is coordinating closely with state and local partners to ensure local public health departments are equipped to prevent, respond to, and eliminate the threat of Zika virus. These actions range from regular communications to direct personnel support. Examples include:

   - Developed the Zika Interim Response Plan for use by state, territorial, local and tribal jurisdictions[1], including posting online with resources such as an epidemiologic investigation toolkit, and a communication planning guide
   - Created Zika virus testing kits, which state public health laboratories receive free of charge
   - Conducted additional testing for states that lacked sufficient capacity
   - Provided guidance on mosquito control and evaluation of mosquito control district plans and interventions, as requested
   - Created the U.S. Zika Pregnancy and Infant Registries to collect health data about pregnant women with laboratory evidence of Zika virus infection and their babies through the first year of life and created rapid Zika Birth Defects Surveillance system to identify babies born with birth defects associated with Zika regardless if their mother's Zika infection was detected during pregnancy.
   - Established Zika Care Connect [2], a network of specialty healthcare providers that connects pregnant women, parents, and caregivers of infants and families affected by Zika to specialized care
   - Placed field assignees on-site at 26 local health departments in communities with pregnant women with laboratory evidence of possible Zika virus infection through the Local Health Department Initiative
   - Deployed CDC Emergency Response Teams (CERT) to 14 different cities to support local communities in responding to Zika

   As of May 15, 2017, CDC has provided $251 million directly to state, local, and territorial health departments through grants from redirected and supplemental funding. CDC also provided $44 million in Public Health Emergency Preparedness (PHEP) reimbursement funding to states and territories in October 2016. CDC directed emergency funding to areas with the greatest need and continues to provide ongoing, in-depth support to Florida, Texas, and U.S. territories where public health officials are battling local transmission of mosquito-borne Zika.

   In addition to direct funding, CDC has awarded funding that supports state, local, and territorial efforts, including support to partner organizations, vector-borne disease regional Centers of Excellence, and the Puerto Rico Vector Control Unit. These financial resources have been

[1] Zika Interim Response Plan https://www.cdc.gov/zika/pdfs/zika-draft-interim-conus-plan.pdf

[2] Zika Care Connect - https://www.zikacareconnect.org/

coupled with technical support to states and territories through rapid response teams, as well as laboratory, epidemiologic, entomologic, field investigation, and data management support.

CDC has plans for all remaining supplemental funds, including needs that may arise with the 2017 mosquito season. The majority of remaining funds will be provided directly to state, local, and territorial health departments through the Epidemiology and Laboratory Capacity cooperative agreement for Zika activities, including epidemiology and laboratory capacity, vector surveillance and control, and the U.S. Zika Pregnancy and Infant Registries. Remaining funds will also support CDC operations, including staff, travel, rapid response teams (if needed), and laboratory supplies and equipment.

2. Last year as we began to discuss appropriating funds to support our efforts in addressing the Zika epidemic, there were discussions around the potential establishment of a new, flexible emergency preparedness fund for addressing future, emerging threats like Zika and Ebola. There are two existing revenue streams that the CDC receives that I would like to examine as potential infrastructure for developing such a fund: the Public Health Emergency Preparedness Cooperative Agreement and the Public Health Emergency Fund. Current appropriations levels aside, what flexibility has the CDC been able to wield in utilizing either of these funds, and what barriers would prevent the CDC from utilizing either of these funds in the future?

The distribution of Public Health Emergency Preparedness (PHEP) cooperative agreement funds is calculated using a formula established under section 319C-1(h) of the Public Health Service Act. Once a PHEP award is provided to an eligible entity, an awardee may not redirect the cooperative agreement funding to a public health emergency unless the awardee requests and HHS grants approval to use PHEP funds for emergency activities that fall within the existing PHEP cooperative agreement scope of work. The majority of CDC's Zika response activities were funded through the Public Health Preparedness and Response (PHPR) Zika cooperative agreement (see: https://www.cdc.gov/phpr/readiness/funding-zika.htm).

The Public Health Emergency Fund has not received any appropriations for a number of years. The Public Health and Social Services Emergency Fund has received appropriations, but is managed by the Department of Health and Human Services.

The Honorable Frank Pallone

1. HHS recently reported that CDC has obligated $332.2 million of its fiscal year 2017 Zika funds. How much funding does CDC have remaining for 2017 Zika preparation and response? Does CDC have sufficient funds remaining to support these efforts for the remainder of fiscal year 2017?

   As of May 15, 2017, CDC has obligated a total of $338 million of the $394 million appropriated in the Zika Response and Preparedness Act (division B of Public Law 114-223).

   CDC has plans for all remaining supplemental funds, including needs that may arise during the 2017 mosquito season. The majority of remaining funds will be provided directly to state, local, and territorial health departments through the Epidemiology and Laboratory Capacity cooperative agreement for Zika activities, including epidemiology and laboratory capacity, vector surveillance and control, and the U.S. Zika Pregnancy and Infant Registries. The rest of

the remaining funds will support CDC operations, including staff, travel, rapid response teams (if needed), and laboratory supplies and equipment.

The Honorable Kathy Castor

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

   This question is best addressed by the National Institute of Health (NIH) and Biomedical Advanced Research and Development Authority (BARDA).

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

   Questions related to the licensing agreement between the U.S. Army and Sanofi are best addressed by the Department of Defense (DoD), Department of the Army.

3. With many members of Congress, states and public health advocates worried that the Zika vaccine being developed by 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 consumers?

   This question is best addressed by the DoD, Department of the Army.

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?

   Prior to 2015, there was limited knowledge about Zika virus and no awareness of the potential effects of Zika on infants exposed to the virus during pregnancy. Zika was a newly emerging infectious disease in the Western Hemisphere and had only been seen previously in outbreaks among small populations. We have since learned that pregnant women and infants are the most vulnerable to adverse outcomes associated with Zika virus infection, including:

   - In April 2016, CDC [3] published the evidence to confirm that Zika virus is the first known mosquito-borne virus to cause birth defects in humans.
   - A CDC study [4], issued in March 2017, has demonstrated that Zika virus directly attacks the developing infant's brain, causing microcephaly and other birth defects. A distinct pattern of birth defects, called congenital Zika syndrome [5], has emerged among fetuses and infants of some women infected with Zika during pregnancy. Congenital Zika syndrome likely represents the most severe impact of congenital infection (infection acquired during pregnancy) that can be seen at birth. This syndrome includes severe microcephaly (small

[3] *The New England Journal of Medicine.* "Zika Virus and Birth Defects — Reviewing the Evidence for Causality." http://www.nejm.org/doi/full/10.1056/NEJMsr1604338?query=featured_zika

[4] *Emerging Infectious Diseases.* "Zika Virus RNA Replication and Persistence in Brain and Placental Tissue." https://wwwnc.cdc.gov/eid/article/23/3/16-1499_article

[5] *JAMA.* "Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians." http://jamanetwork.com/journals/jamapediatrics/fullarticle/2579543

head size) resulting in a partially collapsed skull; decreased brain tissue with brain damage; damage to the eye; limited range of joint motion, such as clubfoot, and too much muscle tone restricting body movement. However, the full spectrum of poor birth outcomes caused by Zika virus infection during pregnancy remains unknown. With other congenital infections, some babies are born apparently healthy but have later onset problems such as deafness. In order to understand the full range of disabilities that might occur, it is essential to follow up with infants and children who were exposed to Zika during pregnancy until they are at least 2-3 years of age, and longer will be needed to understand the full impact of congenital Zika virus infection.

CDC has also discovered a link between Zika virus and Guillian-Barré syndrome (GBS). Current CDC research suggests that GBS is strongly associated with Zika infections; however, only a small proportion of people with recent Zika virus infection get GBS. CDC is continuing to investigate the link between GBS and Zika to learn more.

CDC has collected and communicated information to assist men, women and families in understanding 1) the risks of Zika, 2) ways to prevent Zika, 3) diagnostic methods for Zika, and 4) clinical services that may assist with the long-term consequences of Zika during pregnancy. Guidance from CDC as part of its public health response to Zika has been directly informed by several major findings gleaned from surveillance data:

1) CDC issued guidance to the American population in early 2016 to advise pregnant women and couples planning pregnancy not to travel to areas with Zika. This guidance was issued as a precautionary measure even before Zika was a proven cause of adverse outcomes, and we will never know how many families were protected from Zika as a result of this rapid action.
2) Data captured through the Zika Pregnancy and Infant Registries, newly established public health surveillance systems, provide rough estimates of the potential risk of fetal/infant birth defects associated with a maternal Zika virus infection at different timeframes during pregnancy. These data are used by healthcare providers counseling patients and are the first population-based risk estimates available.
    - In April 2017, CDC reported on data from the Zika Pregnancy and Infant Registries [6] indicating that among 1,000 pregnant women with evidence of Zika with completed pregnancies in 2016, 10 percent of those with confirmed Zika infection had babies with Zika-associated birth defects.
3) Surveillance data have shown that the risk for birth defects among infants exposed during pregnancy is the same regardless of whether an infected pregnant woman had symptoms of Zika virus. This was the first time it was determined that women without symptoms were at risk, which strengthened the current recommendations to avoid travel and to screen pregnant women for Zika virus infection.
4) In July 2016, CDC confirmed [7] that Zika virus can be sexually transmitted from person to person. This has the most profound impact on young men and women who become pregnant or are planning a pregnancy because of the risks of simultaneous sexual transmission of Zika and conception.

[6] *Morbidity and Mortality Weekly Report.* "Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016." https://www.cdc.gov/mmwr/volumes/66/wr/mm6613e1.htm

[7] *Morbidity and Mortality Weekly Report. "*Update: Interim Guidance for Prevention of Sexual Transmission of Zika Virus — United States, July 2016." https://www.cdc.gov/mmwr/volumes/65/wr/mm6529e2.htm?s_cid=mm6529e2_w

5) Surveillance data indicates that Zika virus may persist in the body longer than expected. This directly impacts recommendations for couples planning a pregnancy.
   - Current research indicates that Zika virus RNA can remain in semen up to 6 months, longer than in other body fluids, including vaginal fluids, urine, and blood.
   - Emerging data from case reports [8] of some pregnant women published in October 2016 indicates that Zika virus RNA persists in some pregnant women longer than the 1-2 weeks previously reported and may provide a window into the way the virus crosses the placenta.

Many questions remain. Among the most urgent are:

What is the full spectrum of adverse outcomes caused by Zika virus infection during pregnancy?

- CDC established the Zika Pregnancy and Infant Registries to monitor pregnancy and infant outcomes to learn more about the timing, absolute risk, and spectrum of outcomes associated with Zika virus infection during pregnancy. The surveillance effort is dependent on the collaboration of clinicians and state, tribal, local, and territorial health departments and sustained resources.

What is the best way to detect and diagnose congenital Zika virus infection?

- Much of the data about the detection and persistence of Zika virus is limited. It is unclear what the best testing paradigm is that provides a timely diagnosis and correlates with risks. In addition, the findings of Zika virus persistence requires further exploration to determine how this can help men, women and families plan for pregnancy.

What are the long-term medical and developmental outcomes for infants and children affected by congenital Zika syndrome?

- Many infants enrolled in the Zika Pregnancy and Infant Registries are now approaching one year of age, which limits the ability to study long-term effects of the disease. Information is needed by families, healthcare providers, communities, governmental organizations and others to identify needs and plan for necessary services.

- Recognizing that coordinated surveillance systems are the only way to obtain accurate information about the scope and nature of impacts of the Zika virus infection, CDC awarded funds to 45 jurisdictions to collect information about birth defects thought to be related to Zika virus infection. The surveillance system closes the gap in reporting by including infants with birth defects and congenital Zika virus exposure who may have been missed by pregnancy and infant registries if the mother's Zika infection was not detected prenatally.

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?

   All remaining supplemental funds will be obligated by September 30, 2017. The majority of remaining funds will be provided directly to state, local, and territorial health departments through the Epidemiology Laboratory Capacity cooperative agreement for Zika activities, including

[8] *Obstetrics & Gynecology.* "Prolonged Detection of Zika Virus RNA in Pregnant Women." http://journals.lww.com/greenjournal/Pages/articleviewer.aspx?year=2016&issue=10000&article=00007&type=Fulltext

epidemiology and laboratory capacity, vector surveillance and control, and the U.S. Zika Pregnancy and Infant Registries. The rest of the remaining funds will support CDC operations, including staff, travel, rapid response teams (if needed), and laboratory supplies and equipment.