



U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE

May 19, 2017

TO: Members, Subcommittee on Oversight and Investigations

FROM: Committee Majority Staff

RE: Hearing entitled “U.S. Public Health Response to the Zika Virus: Continuing Challenges”

The Subcommittee on Oversight and Investigations will hold a hearing on Tuesday, May 23, 2017, at 10:00 a.m. in 2123 Rayburn House Office Building, entitled “U.S. Public Health Response to the Zika Virus: Continuing Challenges.” Last year, the Committee held a hearing on March 2, 2016, entitled “Examining the U.S. Public Health Response to the Zika Virus,”¹ where the Subcommittee examined the emergence of the virus across the Americas, the potential link between Zika and other illnesses, and the public health plan to respond to the virus. The Subcommittee held this hearing early relative to the initial outbreak of the virus and, as a result, the non-partisan Government Accountability Office (GAO) was only able to share preliminary observations in its testimony. On March 23, 2016, the Committee sent a letter to GAO requesting that they finish their work and issue a final report once their work is complete.²

At this Subcommittee hearing, the GAO will publicly release its final report entitled, “Emerging Infectious Diseases; Actions Needed to Address the Challenges of Responding to Zika Virus Disease Outbreaks.”³ This hearing will examine the findings and recommendations from the GAO report, as well as lessons learned from the federal government’s response to the initial spread of the Zika virus last year. These findings are critical to improving the federal government’s response to future outbreaks of the Zika virus and other emerging infectious diseases. The Subcommittee will also hear from federal officials about advancements made in the past year, including in vaccine and diagnostic test development.

¹ *Examining the U.S. Public Health Response to the Zika Virus, Hearing Before the H. Comm. on Energy & Commerce*, 114th Cong. (March 2, 2016), available at: <https://energycommerce.house.gov/hearings-and-votes/hearings/examining-us-public-health-response-zika-virus>.

² On file with the Committee.

³ U.S. Government Accountability Office, *Emerging Infectious Diseases: Actions Needed to Address the Challenges of Responding the Zika Virus Disease Outbreaks*, May 2017, [hereinafter GAO Report]. References to the GAO Report in this memorandum are references to the draft version, on file with the Committee. The final report was not available at the time of drafting. Any changes to final report are not expected to affect information referenced in this memorandum.

I. WITNESSES

- Timothy Persons, Ph.D., Chief Scientist, U.S. Government Accountability Office;
- Lyle R. Petersen, M.D., M.P.H., Director, Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention;
- Luciana Borio, M.D., Acting Chief Scientist, U.S. Food and Drug Administration;
- Anthony Fauci, M.D., Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health; and
- Rick A. Bright, Ph.D., Director, Biomedical Advanced Research and Development Authority; Deputy Assistant Secretary, Office of the Assistant Secretary for Preparedness and Response, U.S. Department of Health and Human Services.

II. BACKGROUND

a. History and Spread of the Virus

Despite medical and scientific advances in the last century, infectious diseases account for one out of every five deaths worldwide.⁴ Scientists first identified the Zika virus in 1947 among monkeys living in the Zika forest of Uganda. The first human cases of Zika were detected in Africa in 1952, with the first outbreaks reported on Yap Island in Micronesia in 2007 and French Polynesia in 2013.

The Zika virus spreads primarily through the bite of an infected mosquito. The virus is carried predominantly by the *Aedes aegypti* mosquito, and possibly by the *Aedes albopictus* mosquito, also known as the Asian tiger mosquito.⁵ These mosquitoes also carry yellow fever, dengue, and chikungunya. In addition to mosquito bites, the virus can spread through sexual transmission, blood transfusion, and from mother to child during pregnancy.

According to the Centers for Disease Control and Prevention (CDC), the most common symptoms of a Zika infection are fever, rash, headache, joint pain, conjunctivitis (red eyes), and muscle pain. The illness is usually mild with symptoms beginning two to seven days after infection and lasting for several days to a week. In past outbreaks, about four out of five people infected with Zika appeared not to have had any symptoms at all.⁶ The high rate of infected

⁴ GAO Report.

⁵ A recent study in a laboratory demonstrated that the *Aedes vexans* mosquito could also spread Zika. See https://www.researchgate.net/publication/315061412_American_Aedes_vexans_Mosquitoes_are_Compentent_Vectors_of_Zika_Virus.

⁶ *Examining the U.S. Public Health Response to the Zika Virus, Hearing Before the H. Comm. on Energy & Commerce*, 114th Cong. (Mar. 2, 2016) (statement of Dr. Thomas R. Frieden, Director, CDC), available at <https://energycommerce.house.gov/hearings-and-votes/hearings/examining-us-public-health-response-zika-virus>.

individuals who are asymptomatic, and therefore do not seek diagnostic testing or medical treatment, makes it difficult to have an accurate case count of Zika virus infections.

Further, a causal link has been established between Zika infection during pregnancy and congenital birth defects. Since the outbreak started last year, there have been numerous reports of microcephaly and other poor health outcomes in babies of mothers infected with Zika while pregnant. Microcephaly is a serious birth defect in which a baby is born with a head smaller than expected and exhibits improper brain development. On February 1, 2016, the World Health Organization (WHO) determined that the rapid spread of Zika infections and the suspected link to microcephaly constituted a “Public Health Emergency of International Concern” under the International Health Regulations.⁷ Further, the former Secretary of the U.S. Department of Health and Human Services (HHS), Sylvia Burwell, designated the Zika virus a public health emergency in Puerto Rico in August 2016.⁸

The outbreak in Latin America began in Brazil in February 2015, and was identified as Zika virus in May 2015.⁹ As of March 2017, the WHO reported that there are 84 countries, territories, or subnational areas with evidence of vector-borne Zika virus and 13 countries have reported evidence of person-to-person transmission of the virus.¹⁰ Further, there are 31 countries or territories that have reported microcephaly and other central nervous system malformations potentially associated with a Zika infection, or suggestive of congenital infection and there are 23 countries or territories that have reported an increase of incidence of Guillain-Barré syndrome (GBS) and/or laboratory confirmation of a Zika infection among GBS cases.¹¹

According to the recent report released by the Government Accountability Office (GAO), 94 percent of all cases in the United States are travel-associated cases, and most of these were associated with travel to the Caribbean, Central America, and South America.¹² Between January 1, 2015, and May 12, 2017, reported Zika virus cases numbered 5,273 in the United States and 36,581 in the United States Territories.¹³

Of the 5,273 cases reported in the continental United States:

- 5,001 cases are travelers returning from affected areas;

⁷ WHO statement on the first meeting of the International Health Regulations Emergency Committee on Zika virus and observed increase in neurological disorders and neonatal malformations, Feb. 1, 2016, <http://www.who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en/>.

⁸ U.S. Department of Health and Human Services, Public Health Emergency, Aug. 12, 2016, *available at* <https://www.phe.gov/emergency/news/healthactions/phe/Pages/zika-pr.aspx>.

⁹ World Health Organization, *Zika: Strategic Response Framework & Joint Operations Plan*, Feb. 2016 [hereinafter WHO Framework].

¹⁰ World Health Organization, *Zika Virus, Microcephaly, and Guillain-Barre Syndrome Situation Report*, Mar. 10, 2017, *available at* <http://apps.who.int/iris/bitstream/10665/254714/1/zikasitrept10Mar17-eng.pdf?ua=1>.

¹¹ *Id.*

¹² GAO Report.

¹³ Centers for Disease Control and Prevention, *Zika Virus*, *available at* <https://www.cdc.gov/zika/reporting/2017-case-counts.html>.

- 224 cases were acquired locally through mosquito-borne transmission in Florida (218) and Texas (6); and
- 48 cases were acquired through other routes, including sexual transmission.

Of the 36,581 cases reported in the United States Territories:

- 143 cases are travelers returning from affected areas; and
- 36,438 cases were acquired locally through mosquito-borne transmission.¹⁴

The first identified outbreak of mosquito-borne Zika infection in the continental United States occurred in Florida. To date, only two states in the continental United States—Florida and Texas—have documented cases of locally acquired mosquito-borne transmission of the Zika virus. While only two states have confirmed cases of locally acquired mosquito-borne transmission, except for Alaska, every state and three territories have reported cases of Zika.¹⁵

This month, Brazil announced the end to its Zika public health emergency declaring that from January to April 2017, there were 95 percent fewer Zika cases reported in comparison to the same time period in 2016.¹⁶ This dramatic decline in reported cases is attributable to both Brazil's aggressive mosquito eradication program and herd immunity among the population due to such a large portion of the population being infected by the virus.¹⁷ In the United States, there are no known current active transmission cases.

b. Status of Zika virus research

Research into the Zika virus, particularly into the impact of infection during pregnancy, is ongoing. The National Institutes of Health (NIH) recently implemented a cohort study with a goal of enrolling as many as 10,000 pregnant women at up to 15 sites internationally in order to study the outcome of women who test positive for the Zika virus as well as those who test negative and their infants.¹⁸ The goal of this study is to assess the different risk factors for congenital disease in pregnant women and evaluate the short- and long-term clinical outcomes of babies born to women infected with the Zika virus.¹⁹

In addition, the CDC established the U.S. Zika Pregnancy Registry, which is used to track and monitor pregnant women who contracted the Zika virus. In the United States, the registry publicly reports biweekly numbers of pregnant women with laboratory evidence of a possible

¹⁴ Sexually transmitted cases are not reported for the Territories because, with the local transmission of Zika, it is not possible to determine whether infection occurred due to mosquito-borne or sexual transmission.

¹⁵ GAO Report.

¹⁶ The Atlantic, *Brazil Declares an End to Its Zika Health Emergency*, May 12, 2017, available at <https://www.theatlantic.com/news/archive/2017/05/brazil-ends-zika-emergency/526509/>.

¹⁷ BBC News, *Zika Virus: Brazil Says Emergency is Over*, May 12, 2017, available at <http://www.bbc.com/news/world-latin-america-39892479>.

¹⁸ *Id.*

¹⁹ *Id.*

Zika virus infection.²⁰ According to the CDC, as of May 15, 2017, there have been 1,409 completed pregnancies with or without birth defects, 58 liveborn infants with birth defects, and eight pregnancy losses with birth defects.²¹

On April 4, 2017, CDC released a report that indicates roughly one in ten women in the United States with a confirmed Zika virus infection during pregnancy resulted in a fetus or infant with virus-related birth defects. The chances of birth defects were even higher among fetuses or infants whose mothers were infected with Zika during the first trimester of their pregnancies.²²

In addition to the concerns regarding microcephaly, as of March 10, 2017, the WHO has documented 23 countries and territories that have reported an increase in the incidence of GBS or laboratory confirmation of Zika virus infection among GBS cases.²³ GBS “is an uncommon sickness of the nervous system in which a person’s own immune system damages the nerve cells, causing muscle weakness, and sometimes, paralysis.”²⁴ “Current research suggests that GBS is strongly associated with Zika; 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.”²⁵

c. Current Status of Diagnostics, Vaccines, and Other Treatments for Zika

Though there are no commercially available diagnostic tests cleared by U.S. Food and Drug Administration (FDA) for the detection of Zika virus, the FDA has authorized two different types of diagnostic tests for the Zika virus—molecular and serologic.²⁶ Molecular tests are used to detect genetic material of the virus in samples of bodily fluid such as urine or serum. Serologic tests detect antibodies against the virus in blood. The FDA authorized 16 Zika virus diagnostic tests via Emergency Use Authorizations (EUA) during the outbreak—13 molecular tests and three serologic tests.²⁷ FDA officials later revoked one of the tests, leaving 15 diagnostic tests that are currently authorized.²⁸

²⁰ *Id.*

²¹ Centers for Disease Control and Prevention, *Zika Virus, Outcomes of Pregnancies with Laboratory Evidence of Possible Zika Virus Infection in the United States, as of April 25, 2017*, available at <https://www.cdc.gov/zika/geo/pregnancy-outcomes.html>.

²² Centers for Disease Control and Prevention, *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, Apr. 7, 2017*, available at https://www.cdc.gov/mmwr/volumes/66/wr/mm6613e1.htm?s_cid=mm6613e1_w.

²³ World Health Organization, *Zika Virus, Microcephaly, and Guillain-Barre Syndrome Situation Report*, Mar. 10, 2017, available at <http://apps.who.int/iris/bitstream/10665/254714/1/zikasitrep10Mar17-eng.pdf?ua=1>.

²⁴ Centers for Disease Control and Prevention, *Zika and Guillain-Barre Syndrome*, Last Updated Aug. 9, 2016, available at: <https://www.cdc.gov/zika/healtheffects/gbs-qa.html>.

²⁵ *Id.*

²⁶ GAO Report.

²⁷ *Id.*

²⁸ *Zika Virus Response Updates from FDA, Emergency Use Authorization (EUA)*, last updated May 17, 2017, available at <https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm#eua>.

While this number appears high and promising, the GAO found that the tests varied in their performance and operational characteristics—most notable was the variation in the ability of the diagnostic tests to detect the virus and provide accurate results. Each of the existing 15 tests have varying strengths and limitations; therefore, multiple tests and sample types are often required to diagnose an individual with the Zika virus. Furthermore, CDC and FDA guidance are critical in assisting health care providers and laboratories in determining the most appropriate test(s) for each individual.

During the first two weeks after onset of symptoms, Zika can be diagnosed by performing a reverse transcriptase-polymerase chain reaction (RT-PCR) test on serum.²⁹ This test can accurately determine whether a person has been infected with Zika, but is only effective while the virus is still present in the blood or other fluid. After this initial period, tests to examine the presence of antibodies must be used. These antibodies can persist for several weeks after an infection—currently, an Enzyme-Linked Immunosorbent Assay (ELISA) test is used about four days to 12 weeks post onset of symptoms. However, the presence of similar antibodies from dengue, chikungunya, or even a yellow fever vaccine can cross-react and give a positive result. As a result, a plaque-reduction neutralization testing (PRNT) may be needed to measure virus-specific antibodies and discriminate between cross-reacting antibodies.³⁰ The PRNT test is described as a highly specialized and lengthy test. GAO found that the delays between getting initial antibody test results and the PRNT confirmatory results may have led some clinicians and patients to make family planning decisions without confirmation of Zika virus infection.³¹

Throughout the developmental stages of the diagnostic tests, manufacturers encountered obstacles including access to clinical samples and other diagnostic tests for comparison purposes. Users of the tests also faced challenges, including determining the most appropriate test to use, access to different tests, and obtaining the equipment needed to conduct the tests.³² Concerns remain regarding the accuracy of the diagnostic tests and CDC's guidance for testing procedures. A recent report notes that retests of a 2016 batch of samples from Washington, D.C. found that three patients tested positive for the virus, 26 were inconclusive, and 394 remained negative.³³ One of the three positive test results was for a pregnant woman. Since the retesting, CDC has sent updated testing procedures to public health labs throughout the United States.

Currently, there is not a specific therapy or vaccine approved for the Zika virus by the FDA. Several vaccines are in various stages of development, with one experimental vaccine currently in Phase II trials being tested in humans. More vaccine candidates are expected to enter Phase II trials this year. Last month, Dr. Anthony Fauci, the Director of the NIH National Institute of Allergy and Infectious Diseases (NIAID), stated that the DNA vaccine candidate

²⁹ Centers for Disease Control and Prevention, *Diagnostic Testing*, page last updated May 5, 2017, available at <http://www.cdc.gov/zika/hc-providers/diagnostic.html> (last accessed May 15, 2017).

³⁰ *Id.*

³¹ GAO Report.

³² *Id.*

³³ *3 Retest Positive for Zika in DC; CDC Updates Testing Procedures*, NBC Washington, May 8, 2017, available at: <http://www.nbcwashington.com/news/health/3-Retest-Positive-for-Zika-in-DC-CDC-Updates-Testing-Procedures-421656883.html>.

developed by scientists at NIAID's Vaccine Research Center had been a success in animal trials and in the first human trial of the vaccine.³⁴

d. Vector Control

There are four types of mosquito control methods that are available in the United States: physical control or nonchemical mosquito control, larval mosquito control, adult mosquito control, and using personal protection.³⁵ According to the CDC, the best way to prevent diseases spread by mosquitoes is to avoid mosquito bites. Official recommendations include using insect repellent, wearing long-sleeved shirts and long pants, protecting your baby or child, and taking steps to control mosquitoes inside and outside your home.³⁶ For pregnant women, special precautions include not traveling to areas with risk of Zika and using protection during sex during your entire pregnancy due to the risk of infection via sexual transmission.³⁷

Additional efforts to prevent the spread of Zika include surveillance of the mosquito population. GAO identified different mosquito control methods that target different stages of the mosquito lifecycle.³⁸ Therefore, surveillance of the mosquito population is a critical component of preventing the spread of vector-borne diseases such as Zika. The *Aedes aegypti* mosquito can breed in very small containers of fresh water, including in roadside trash, discarded tires, flower pots, and even bottle caps. The mosquito bites during the day and night—and favors biting humans over animals. This characteristic makes the use of pesticides challenging because daytime spraying would be required for the pesticides, or adulticides, to be most effective. Public resistance is a significant limitation to utilizing this method. Further, mosquitoes are becoming increasingly resistant to currently available pesticides. Reduction of the breeding sites is an effective means to control the mosquito population, but this method depends heavily on broad public participation and education. Other emerging technologies continue to be explored, including the release of genetically modified mosquitoes, biological control, and auto-dissemination traps.

In the United States, vector control is handled at the state and local level. The federal government has a very limited role in implementing mosquito control. Many states create mosquito control districts funded by the state, locality, or both. The level of services varies greatly—some local jurisdictions provide services directly, others contract for services with private companies.

While the federal government does not appear to specifically provide funds for mosquito abatement, grants provided by the CDC to states through Epidemiology and Laboratory Capacity (ELC) grants allow for funds to be used to detect, monitor, and control mosquito- and tick-borne

³⁴ CNN, Promising Zika vaccine moves to next stage, April 10, 2017, *available at* <http://www.cnn.com/2017/03/31/health/zika-vaccine-nih-trial/>

³⁵ GAO Report.

³⁶ Centers for Disease Control and Prevention, *Zika Virus: Prevent Mosquito Bites*, *available at* <https://www.cdc.gov/zika/prevention/prevent-mosquito-bites.html> (last updated Jan. 17, 2017).

³⁷ Centers for Disease Control and Prevention, *Zika Virus: Pregnant Women*, *available at* <https://www.cdc.gov/zika/pregnancy/protect-yourself.html> (last updated May 3, 2017).

³⁸ GAO Report.

diseases in the United States.³⁹ However, not all localities are served by vector control. Further, grant funds awarded for mosquito control may not make it to some local mosquito control districts. The GAO found that the federal government faced challenges in supporting mosquito control efforts, including sustaining staff expertise in mosquito control during periods when there are no outbreaks, and effectively communicating information about the geographical distribution of mosquitoes that transmit the Zika virus.

e. Unknowns and Challenges Remain

While the scientific and public health communities have learned much about the Zika virus over the past year, the GAO report identifies many areas where unknowns remain, including:⁴⁰

- The total number of infections in the United States;
- The biological mechanisms, risks, reasons for geographic differences, and full spectrum of outcomes associated with mother-to-child transmission;
- The risk of transmission from different bodily fluids and routes, including maternal-fetal transmission;
- The role of prior Zika virus infections or exposure to other related arboviruses; and
- The full spectrum of short-term and long-term outcomes of Zika virus infection, with or without clinical symptoms.

Based on the totality of evidence from epidemiological studies, scientific consensus is now that Zika virus causes microcephaly, brain abnormalities, and other birth defects. The CDC has also reported that its own research suggested a strong association between GBS and Zika virus. At this point in time, we do not know the complete risk of Zika to an individual pregnancy, nor do we know the definitive risk of Zika in causing additional disorders such as GBS. Some researchers have speculated that, in the future, we may see cases where a child presents as normal, but has mental or physical disabilities after becoming infected with Zika in utero.⁴¹ Further, recent research done by the NIH shows that the virus may also have a negative—and possibly long-lasting—impact on male fertility.⁴² The research results come from

³⁹ Centers for Disease Control and Prevention, *Epidemiology and Laboratory Capacity for Infectious Diseases*, available at http://www.cdc.gov/ncezid/dpei/epidemiology-laboratory-capacity.html#_blank (last updated Dec. 21, 2016); American Mosquito Control Association, *Funding for National Disease Surveillance Network through Epidemiology and Laboratory Capacity (ELC) Grants from the Centers for Disease Control*, available at <http://www.mosquito.org/cdc-funding-position-paper>.

⁴⁰ GAO Report.

⁴¹ Centers for Disease Control and Prevention, *Morbidity and Mortality Weekly Report, Description of 13 Infants Born During October 2015-January 2016 with Congenital Zika Virus Infection Without Microcephaly at Birth—Brazil*, Dec. 2, 2016, available at <https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6547e2.pdf>.

⁴² National Institutes of Health, NIH Director's Blog, *Could Zika Virus Have Lasting Impact on Male Fertility?* Nov. 8, 2016, available at <https://directorsblog.nih.gov/2016/11/08/could-zika-virus-have-lasting-impact-on-male-fertility/>.

a mouse study, which found that the Zika virus can persist for weeks in the reproductive systems of male mice. As a result of the infection, levels of testosterone and other hormones drop, sperm counts fall, and in some cases, the testicles shrink, possibly irreversibly.⁴³ In addition, we do not know whether individuals who contract Zika but are asymptomatic will have any negative effects for themselves or their children, nor do we know if previous infection from a related virus, such as dengue or yellow fever, has an impact on the effects of Zika on an individual.

Another challenge is the lack of modeling for infectious diseases. Modeling is crucial to combat a virus such as Zika because it would help both public health officials and vector control units prepare for, identify, detect, and predict where the disease is likely to spread. Modeling would also help predict the need for lab and testing capacity in a given region, the demand for vaccines if and when they come to market, and where to prioritize effective mosquito control. The lack of sufficient data, methods, and the unique aspects of the Zika virus pose challenges for conducting modeling and simulation studies. According to CDC documents and officials interviewed by the GAO, the CDC has not been able to predict how much the Zika virus will spread in the continental United States.⁴⁴ On May 5, 2017, NIH issued a grant opportunity for “Modeling of Infectious Disease Agent Study Research Projects.”⁴⁵ According to the announcement, the purpose of this funding opportunity “is to support innovative research that will develop and apply computational tools and methods for modeling interactions between infectious agents and their hosts, disease spread, prediction systems and response strategies.”⁴⁶

Finally, challenges remain regarding the development and use of diagnostic tools. Despite the fact that the U.S. has known about the Zika virus, at the time of the discovery that Zika infection during pregnancy could lead to severe birth defects, there were no accurate and reliable authorized diagnostic tools for the Zika virus disease. As previously noted, by April 12, 2017, FDA had authorized 15 diagnostic tests for the Zika virus (12 molecular tests and three serologic tests) under EUAs following the public health emergency declaration. One major issue with these tests is that it is not possible to compare the tests with one another based on the information on the product insert. Communicating such information could have enabled users to more easily identify the test that could detect the smallest amount of virus in a sample.⁴⁷

Manufacturers of diagnostic tests faced several challenges, including: (1) lack of knowledge of key scientific aspects of the virus; (2) difficulty in accessing well-characterized clinical samples; (3) gaining access to EUA tests for use as a comparator assay; (4) gaining cooperation with international entities; and (5) manufacturers’ mixed opinions about the effectiveness of communication from FDA.⁴⁸ Users of the tests also identified challenges, including: (1) complying with the test’s EUA label, which specifies equipment required to perform the test, and (2) determining the most accurate test, in part because of challenges

⁴³ *Id.*

⁴⁴ GAO Report.

⁴⁵ Grants.gov, Department of Health and Human Services, National Institutes of Health, May 5, 2017, *available at* <https://www.grants.gov/web/grants/view-opportunity.html?oppId=293636>.

⁴⁶ *Id.*

⁴⁷ GAO Report.

⁴⁸ *Id.*

comparing performance characteristics reported in the EUA labels.⁴⁹ GAO found that the CDC and FDA did not follow their guidance in communicating information about Zika virus diagnostic tests that could have enabled users to more easily identify the test that could detect the smallest amount of virus in a sample.⁵⁰

In particular, there were issues with CDC communications about molecular diagnostic test sensitivity. Last year, a CDC scientist and expert on arboviruses, who later became a whistleblower, alleged that CDC endangered public health when it failed to disclose that the CDC test used to detect the Zika virus, known as a Trioplex (an FDA EUA), was less sensitive than another CDC laboratory-developed test (not authorized under FDA EUA), known as a Singleplex.⁵¹ Following an Office of Special Counsel investigation, CDC agreed to reinstate the scientist. An internal CDC investigation about the allegations found that the evidence did not support the allegations.⁵²

The GAO found, however, that the CDC investigation did not attempt to gather additional information on comparing the tests from public health laboratories using the Singleplex.⁵³ Further, later actions taken by the CDC appear to validate the whistleblower's concerns regarding the Trioplex test. The original Trioplex test was authorized using a smaller input volume, while the Singleplex was not subject to the limitation because it had not been submitted to the FDA for review.⁵⁴ Smaller input volume lessens the sensitivity of the test. CDC submitted a substantial amendment to the Trioplex test for FDA authorization to increase the input volume of the test in August 2016, and in January 2017, the authorization was amended again to allow laboratories to use a Singleplex reaction on the Trioplex assay.⁵⁵ The larger input volume has been demonstrated to increase the sensitivity of the Trioplex assay, according to CDC. A journal article later showed that the original Trioplex test was less sensitive than the Singleplex test.⁵⁶ Representatives of three scientific professional societies told GAO that information about the development and verification of CDC's diagnostic tests should be made available to the scientific and medical communities.⁵⁷

f. GAO Recommendations

The GAO recommended two actions for FDA: (1) Consolidate information from individual diagnostic test labels and make this information available in a form that enables users to more readily compare information across tests; and (2) Require manufacturers to list the

⁴⁹ *Id.*

⁵⁰ *Id.*

⁵¹ Lena H. Sun, CDC whistleblower claims agency has been using wrong Zika test, Washington Post, September 28, 2016.

⁵² U.S. Department of Health and Human Services, Report of Investigation, OSC File Number DI-16-3709, attached to September 2, 2016 from HHS Secretary Sylvia M. Burwell to The Honorable Carolyn N. Lerner, Special Counsel, Office of the Special Counsel.

⁵³ GAO Report.

⁵⁴ *Id.*

⁵⁵ *Id.*

⁵⁶ *Id.*

⁵⁷ *Id.*

identity of comparator assays on their diagnostic test labels. The FDA concurred with both recommendations.

The GAO recommended three actions for CDC: (1) Establish a transparent process to provide CDC diagnostic tests, upon request, to manufacturers that are in the final stages of diagnostic test authorization; (2) Include information on CDC-developed tests distributed to public health laboratories on CDC's website, including any laboratory-developed tests; and (3) Provide details such as collection records, dates, and data limitations on posted and disseminated mosquito distribution maps to better inform mosquito control experts and the general public. CDC concurred with Recommendations (1) and (3), and partially concurred with Recommendation (2).

In recent decades, emerging infectious diseases have continued to garner global attention. Diseases such as SARS, H1N1, Ebola, pandemic influenza, and now Zika have continued to surface leaving little time for public health officials to react. In each of the aforementioned cases, the GAO found that HHS was reactive in its response to outbreak prevention, preparedness, detection, and response. This was the theme of the Subcommittee's hearing on biodefense preparedness held on February 12, 2016, focused on the bipartisan report of the Blue Ribbon Study Panel on Biodefense.⁵⁸ Given global travel and migration patterns, infectious diseases spread more easily than ever before. With the emergence of more infectious diseases around the corner, the federal government needs to find ways to be more proactive instead of reactive.

g. Status of Zika Funding

Funding for federal government spending on the Zika virus has come from multiple sources. On April 6, 2016, the White House Office of Management and Budget and the Secretary of HHS identified \$589 million that could be redirected and spent on the response to the Zika virus.⁵⁹

In addition, through the Zika Response and Preparedness Act, 2017, Congress provided an additional \$1.1 billion in supplemental funds to the U.S. Department of Health and Human Services, the U.S. Department of State, and the U.S. Agency for International Development. HHS received \$933 million of the \$1.1 billion. Of the \$933 million, the CDC received \$394 million, the NIH received \$152 million, and the Public Health and Social Services Emergency Fund received \$387 million, with \$245 million of that going to the Biomedical Advanced Research and Development Authority (BARDA).⁶⁰

As of April 30, 2017, HHS has obligated \$635 million of the \$933 million appropriated in the Zika Response and Preparedness Act.⁶¹ The breakdown by agency is as follows:

⁵⁸ *Outbreaks, Attacks, and Accidents: Combating Biological Threats, Hearing Before the H. Comm. on Energy & Commerce*, 114th Cong. (Feb. 12, 2016), available at <https://energycommerce.house.gov/hearings-and-votes/hearings/outbreaks-attacks-and-accidents-combatting-biological-threats>.

⁵⁹ Congressional Research Service, *Zika Response Funding: Request and Congressional Action*, Sept. 30, 2016.

⁶⁰ U.S. Dep't of Health & Human Servs., *Zika Supplemental Funding Spend Plan*, Oct. 26, 2016.

⁶¹ Email from HHS staff to Committee staff, May 18, 2017.

- CDC: \$332.2 million obligated;
- NIH: \$68.8 million obligated;
- ASPR/BARDA: \$110.6 million obligated;
- HRSA: \$57.3 million obligated; and
- CMS: \$66.1 million obligated.

HHS has informed the Committee that remaining funds not yet obligated have been committed, and that the funding will last through the end of the fiscal year.

III. ISSUES

The following issues will be examined at the hearing:

- How can the CDC and the states be better equipped to respond to any potential Zika outbreaks in the U.S. this summer?
- How can the FDA and CDC establish a transparent process for providing test manufacturers access to diagnostic tests for comparison purposes and provide information to help ensure that users of diagnostic tests can compare performance?
- How can state and local implementation of mosquito control programs be improved and more effectively supported by federal agencies?
- What is the current state of research into (a) the causal link between Zika and other health conditions, including microcephaly and GBS; and (b) the efficacy and availability of currently available rapid diagnostic testing for Zika?
- What is the status of diagnostic testing development, vaccine development, or other therapeutics for Zika?

IV. STAFF CONTACTS

If you have any questions regarding the hearing, please contact Alan Slobodin, Brittany Havens, or Jennifer Barblan at (202) 225-2927.