



TESTIMONY
OF
LUCIANA BORIO, M.D.
CHIEF SCIENTIST (ACTING)

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS
HOUSE ENERGY AND COMMERCE COMMITTEE
U.S. HOUSE OF REPRESENTATIVES

**U.S. PUBLIC HEALTH RESPONSE TO THE ZIKA VIRUS: CONTINUING
CHALLENGES**

MAY 23, 2017

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Good morning Chairman Murphy, Ranking Member DeGette, and members of the Subcommittee. I am Dr. Luciana Borio, Acting Chief Scientist at the Food and Drug Administration (FDA). Thank you for the opportunity to appear today to discuss FDA's actions in response to the Zika virus outbreak.

Zika virus was first identified in 1947 in Uganda. Since then, sporadic cases and a few outbreaks have been recognized in a number of locations, including parts of Africa, Asia, and the Pacific. However, the situation has changed dramatically since May 2015, when the first local transmission of Zika virus in the Americas was confirmed in Brazil. According to the World Health Organization, from 2015 through March 10, 2017, 61 countries and territories—including the United States, the Commonwealth of Puerto Rico, the U.S. Virgin Islands, and American Samoa—have had ongoing transmission following a new introduction of Zika virus or with a reintroduction into an area where transmission had been interrupted.¹ Additionally, 13 countries have reported evidence of person-to-person transmission, 31 countries or territories have reported microcephaly and other central nervous system malformations that are potentially associated with Zika virus infection, and 23 countries or territories have reported an increase in the incidence of Guillain-Barre Syndrome (GBS) or laboratory confirmation of Zika virus infection among GBS cases.¹

¹ WHO Zika Virus Situation Report, 10 March 2017; <http://apps.who.int/iris/bitstream/10665/254714/1/zikasitrep10Mar17-eng.pdf?ua=1>

In the United States, there have been 5,282 Zika virus disease cases reported in the states [5,010 cases in travelers returning from affected areas, 224 cases acquired through presumed local mosquito-borne transmission in Florida (218 cases) and Texas (6 cases), and 48 cases acquired through other routes, including sexual transmission] and 36,583 Zika virus disease cases reported in the US territories [143 cases in travelers returning from affected areas and 36,440 cases acquired through presumed local mosquito-borne transmission] as of May 17, 2017.² As of May 09, 2017, there are 1,845 pregnant women in the states and District of Columbia and 3,795 pregnant women in the US territories with laboratory-reported evidence of possible Zika virus infection.³

FDA RESPONSE TO THE ZIKA VIRUS OUTBREAK

FDA has taken several steps to rapidly respond to the Zika virus outbreak and remains actively engaged with other components of the Department of Health and Human Services (HHS)—including the Office of the Assistant Secretary for Preparedness and Response (ASPR) and its Biomedical Advanced Research and Development Authority (BARDA), the National Institutes of Health (NIH), and the Centers for Disease Control and Prevention (CDC)—as well as with partners across the U.S. Government, the private sector, and the international community to minimize the impact of this outbreak. FDA’s primary areas of activity include: (1) supporting the development and availability of diagnostic tests that may be useful for identifying the presence of, or prior exposure to, Zika virus; (2) providing advice and consultation to facilitate rapid development of investigational vaccines and therapeutics; (3) advancing the use of innovative

² CDC 2017 Case Counts in the US; <https://www.cdc.gov/zika/geo/united-states.html>, 2016 Case Counts in the US; <https://www.cdc.gov/zika/reporting/2016-case-counts.html>, and 2015 Case Counts in the US; <https://www.cdc.gov/zika/reporting/2015-case-counts.html>.

³ CDC Pregnant Women with Any Laboratory Evidence of Possible Zika Virus Infection in the United States and Territories; <https://www.cdc.gov/zika/geo/pregwomen-uscases.html>

strategies under FDA's regulatory authorities to help suppress the population of Zika virus-carrying mosquitoes; (4) protecting the public from fraudulent products that claim to prevent, diagnose, treat, or cure Zika virus disease; and (5) protecting the safety of the nation's blood supply and human cells, tissues, and cellular and tissue-based products (such as corneas, bone, skin, heart valves, and semen) used for medical, surgical, or reproductive procedures.

Diagnostic Tests

At the start of the Zika virus outbreak in the Americas, there were no diagnostic tests for the detection of Zika virus authorized for use in the United States. FDA worked with CDC, which was developing diagnostic tests, to make Zika diagnostic tests rapidly available. FDA was able to authorize the use of two CDC tests under FDA's Emergency Use Authorization (EUA) authority in February and March of 2016. FDA also—in keeping with FDA's normal practice for responding to emerging infectious disease outbreaks—reached out to diagnostic manufacturers to encourage them to develop needed diagnostic tests for Zika virus. FDA immediately began working interactively with manufacturers interested in developing diagnostic tests for Zika virus to help accelerate development programs—including clarifying EUA data requirements for the Zika diagnostic tests—and to ensure that their tests are properly validated before they are used to inform patient care. FDA granted an EUA for the first commercial test in April 2016.

FDA has taken several proactive steps to help advance the development of diagnostic tests for Zika virus. For example, FDA developed and made available EUA review templates delineating data requirements for a Zika virus diagnostic EUA. FDA has fulfilled more than 100 requests for the EUA templates. In addition, to help Zika diagnostic manufacturers develop nucleic acid testing-based diagnostic devices, FDA created Zika virus reference materials that are available to

Zika diagnostic manufacturers that have a pre-EUA submission with FDA and have established the analytical performance of their assay.⁴ FDA has fulfilled 17 requests for the reference materials.

FDA has continued to work interactively with Zika virus diagnostic manufacturers throughout the product development process to address scientific challenges, review data, and provide feedback based on the latest available scientific information. For example, FDA has had more than 15 face-to-face meetings, 150 teleconferences, and more than 3,500 emails with diagnostic developers or Zika experts to support the development of Zika diagnostics. This collaboration has been extremely successful, and to date, FDA has authorized the use of sixteen diagnostic tests for Zika virus under FDA's EUA authority—13 nucleic acid testing-based tests to diagnose active infection (12 of which are currently available⁵) and 3 serological tests to assess whether individuals who may have recently been exposed to Zika had actually been infected. It is important to note that, as a result of these efforts, diagnostic tests for Zika virus are now available in laboratories throughout the United States including automated, high throughput tests. The serological tests to assess whether individuals who may have been exposed to Zika recently had actually been infected are especially important for women given the link between Zika virus infection and congenital Zika syndrome, including microcephaly and other birth defects, in babies of mothers who were infected with Zika virus during their pregnancy.

FDA continues to work with diagnostic manufacturers once their tests are authorized under EUA to further product development, improve product performance, and make sure that authorized

⁴ FDA has created an email account specifically for requesting the EUA review templates (CDRH-ZIKA-Templates@fda.hhs.gov).

⁵ At the request of Roche Molecular Systems, Inc., on March 13, 2017, FDA revoked the EUA for emergency use of the company's *LightMix*® Zika rRT-PCR Test that was issued on 26 August 2016, reducing the number of tests to diagnose active infection to 12.

tests continue to meet EUA standards and public health needs. For example, FDA has issued 21 amendments to EUAs for the authorized Zika diagnostic tests—upon request from the product manufacturers—to add additional instruments or specimen types for testing. In addition, FDA is continuing to work to help advance the development of diagnostic tests for Zika virus. For example, FDA is supporting the validation and use of a World Health Organization reference panel to be developed into an international standard for serological assays. FDA also monitors the performance of Zika diagnostic tests authorized under EUA and works with manufacturers and laboratory personnel to quickly resolve any issues that may arise. Toward that end, FDA has established an email account that laboratory personnel using Zika diagnostic assays under EUA are encouraged to use to report performance concerns directly to FDA (CDRH-EUA-Reporting@fda.hhs.gov), in addition to reporting concerns to the manufacturer.

All information about diagnostic tests for Zika virus authorized under EUA, such as letters of authorization, labeling that includes the tests' performance data, and fact sheets for patients and health care providers, are readily available on the FDA website.⁶

Vaccines and Therapies

There are no vaccines or treatments for Zika virus at this time. Development programs are in the relatively early stages, but several vaccine candidates continue to progress at an expedited pace. FDA is actively engaged with NIH and BARDA, the international community, and product developers to help accelerate development programs. FDA is working with medical product developers to provide technical support and clarify regulatory and data requirements necessary to move products forward in development as quickly as possible. One of our highest priorities is to facilitate the development and availability of an effective Zika virus vaccine as quickly as

⁶ Zika Virus Emergency Use Authorizations; <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika>

possible and we are working closely with NIH, BARDA, CDC, and the private sector on this. Although therapeutic development proposals are generally at an earlier stage than for vaccines, FDA has also engaged in preliminary discussions of potential approaches to the development of therapeutics and is open to ongoing interactions to provide input on such development proposals.

Vector Control

In the United States, mosquito control is typically achieved by a multi-faceted approach that relies on a range of tools, including surveillance of mosquito activity, reduction in breeding sites, and the use of chemical and biological control methods. FDA's involvement in mosquito control is through the oversight of products that help suppress the population of virus-carrying mosquitoes that fall under FDA's regulatory authorities. With respect to Zika virus, there has been public discussion of a new method to potentially help control mosquito populations through the use of a genetically engineered (GE) line of the mosquito *Aedes aegypti* (OX513A) developed by Oxitec, Ltd. The release of male Oxitec GE mosquitoes is intended to cause suppression of the mosquito population in a release area over time because the offspring resulting from the mating of male GE mosquitoes with wild-type females do not develop to adulthood.

FDA reviewed information in an Investigational New Animal Drug (INAD) file from Oxitec Ltd. regarding the potential use of the company's GE mosquito with the intent of suppressing the population of *Aedes aegypti* mosquitoes at the release site in Key Haven, Florida.⁷ On August 5, 2016, FDA completed the environmental review for a proposed field trial of Oxitec's GE

⁷ FDA ordinarily cannot acknowledge or discuss INAD files due to confidentiality concerns; however FDA is able to do so in this case because Oxitec has publicly announced that they have opened an INAD file.

mosquitoes in Key Haven, Florida, and published a final environmental assessment—or EA—and finding of no significant impact—or FONSI—stating that the proposed field trial will not have significant impacts on the environment. This enabled the field trial to proceed, provided all other local, state, and federal requirements are met. Ultimately, Oxitec, together with its local partner, the Florida Keys Mosquito Control District, decided not move forward with the Key Haven field trial as the result of a November 8, 2016, referendum on the use of GE mosquitoes that found Key Haven residents did not support the trial. Since then, FDA and Oxitec have maintained an open line of communication and FDA stands ready to promptly review any submissions should, for example, Oxitec decide to pursue a field trial in another location.

Meanwhile, in January 2017, FDA issued draft guidance (developed in coordination with the Environmental Protection Agency (EPA)) that clarifies that mosquito-related products intended to function as pesticides by preventing, destroying, repelling, or mitigating mosquitoes for population control purposes are not “drugs” under the Federal Food, Drug, and Cosmetic Act (FD&C Act). If the guidance is finalized, these products will be regulated by EPA as “pesticides” under the Federal Insecticide, Fungicide, and Rodenticide Act. FDA would continue to have jurisdiction over mosquito-related products that otherwise meet the FD&C Act drug definition, such as those intended to prevent, treat, or cure a disease or to reduce the viral or pathogen load in a mosquito. The 30-day public comment period for the draft guidance closed on February 21, 2017. FDA is currently considering the comments.

Fraudulent Product Claims

Unfortunately, during emerging infectious disease outbreaks such as this, fraudulent products that claim to prevent, treat, or cure a disease frequently appear on the market. FDA is actively

monitoring for fraudulent products and false product claims related to Zika virus and will implement enforcement actions, as warranted, to protect the public health.

Blood Supply and Tissue Safety

One of FDA's first actions in response to the Zika virus outbreak was to take important steps to help protect the safety of the blood supply. FDA issued guidance in February 2016 that recommended the deferral of individuals from donating blood if they had been to areas with active Zika virus transmission, were potentially exposed to the virus, or had a confirmed infection. The guidance also recommended that areas with active Zika virus transmission, like Puerto Rico, obtain whole blood and blood components from areas of the United States without active virus transmission until a blood donor screening test for Zika virus became available to ensure the safety of their blood supply. Until blood donor screening tests for Zika virus became available, HHS arranged for and funded shipments of blood products from the continental United States to Puerto Rico to ensure an adequate supply of safe blood for its residents during this interim period. Concomitantly, FDA worked closely with the test kit developers in a highly accelerated time frame to make available the first investigational test for blood screening in March 2016. The availability of this investigational test, which has been in use in Puerto Rico since early April 2016, enabled blood establishments to resume safe blood collection in areas with active Zika virus transmission. A second investigational blood screening test was made available in June 2016. Together, these tests enabled blood donor screening to be put in place across the United States where active Zika virus transmission was established as well as in areas where local virus transmission was anticipated, helping to maintain an adequate and safe blood supply.

In August 2016, after careful consideration of the evolving scientific and epidemiologic data (including the significant number of travel-associated cases of Zika across the continental US), consultation with other public health agencies, and taking into consideration the potential serious health consequences of Zika virus infection to pregnant women and children born to women exposed to Zika virus during pregnancy, FDA issued updated guidance recommending that all states and U.S. territories screen blood with an approved investigational blood screening test. The guidance recommended a staggered implementation of blood screening across the nation, with immediate implementation in states and territories with one or more locally-acquired mosquito-borne cases of Zika virus, implementation within four weeks in states with proximity to areas with locally-acquired Zika virus cases or other epidemiological linkages to Zika virus (such as a high number of travel-associated Zika cases), and implementation within 12 weeks in all other states and territories.

FDA worked with blood collection establishments to facilitate implementation of the revised guidance across the U.S. and its territories. As of May 2, 2017, 376 presumptive viremic blood donations have been prevented from entering the blood supply in the United States and its territories.⁸

FDA is continuing to monitor the evolving scientific and epidemiologic data on Zika virus and will update its guidance for blood donor testing as necessary based on additional information that may become available that would support reassessing the blood donor testing situation while adequately protecting the blood supply.

⁸ CDC Zika Virus Case Counts in the US; <https://www.cdc.gov/zika/geo/united-states.html>

Zika virus also poses a risk for transmission by human cells, tissues, and cellular and tissue-based products (HCT/Ps) such as corneas, bone, skin, heart valves, and semen used for medical, surgical, or reproductive procedures. Because of this risk, FDA issued guidance in February 2016 recommending that donors of HCT/Ps be considered ineligible if they were diagnosed with Zika virus infection, were in an area with active Zika virus transmission, or had sex with a male with either of those risk factors, within the past six months. FDA is continuing to assess the evolving scientific and epidemiologic data on Zika virus as well as supporting research to help better understand the persistence of Zika virus in cells and tissues, and will update its guidance if necessary to better reduce the risk of Zika virus transmission through HCT/Ps used for medical, surgical, or reproductive procedures.

CONCLUSION

FDA is fully committed to remaining highly responsive and adaptive to the complex range of issues the Zika virus outbreak has presented and will continue to present. Developing the medical products necessary to help bring this outbreak under control is highly complex and will require a sustained effort. Close cooperation and collaboration within FDA, within the U.S. Government, with our international partners, and with product developers is essential to help facilitate the development and availability of medical products to respond to Zika virus as quickly as possible. FDA is wholly prepared to leverage its authorities to the fullest extent practicable to help accelerate the development and availability of safe and effective products with the potential to help mitigate the Zika virus outbreak as quickly as the science will allow.

Thank you. I am happy to answer your questions.