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Zika Virus — 10 Public Health Achievements in 2016 and Future Priorities

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The introduction of Zika virus into the Region of the Americas (Americas) and the subsequent increase in cases of congenital microcephaly resulted in activation of CDC's Emergency Operations Center on January 22, 2016, to ensure a coordinated response and timely dissemination of information, and led the World Health Organization to declare a Public Health Emergency of International Concern on February 1, 2016. During the past year, public health agencies and researchers worldwide have collaborated to protect pregnant women, inform clinicians and the public, and advance knowledge about Zika virus (Figure 1). This report summarizes 10 important contributions toward addressing the threat posed by Zika virus in 2016. To protect pregnant women and their fetuses and infants from the effects of Zika virus infection during pregnancy, public health activities must focus on preventing mosquito-borne transmission through vector control and personal protective practices, preventing sexual transmission by advising abstention from sex or consistent and correct use of condoms, and preventing unintended pregnancies by reducing barriers to access to highly effective reversible contraception.

1. Issuing Travel Guidance to Warn Pregnant Women Not to Travel to Areas with Ongoing Zika Virus Transmission

On January 15, 2016, CDC issued a travel notice to alert travelers about the risk of Zika virus transmission in 14 countries and territories in Central and South America and the Caribbean, including Puerto Rico. As of December 15, 2016, a total of 60 international Zika travel notices have been issued, including 49 in the Americas. These notices advise pregnant women to avoid travel to areas of active Zika virus transmission, provide recommendations for travelers to avoid exposure to Zika virus, and inform returning travelers about transmission prevention and testing. On August 1, 2016, after the first instance of confirmed mosquito-borne Zika virus transmission in the continental United States, CDC issued domestic travel and diagnostic testing guidance for pregnant women and women of reproductive age living in or traveling to an area of Miami-Dade County, Florida (*1*). On November 28, 2016, local mosquito-borne transmission of Zika virus was reported in Brownsville (Cameron County), Texas, and on December 14, 2016, CDC issued guidance for travel and testing of pregnant women and women of reproductive age living in or traveling to Brownsville (*2*). CDC has continued to collaborate closely with state and local jurisdictions to determine when to issue, revise, or lift domestic travel guidance on the basis of epidemiologic evidence (*3–5*).

2. Publishing Clinical Guidance for the Care of Pregnant Women and Infants

As a newly recognized congenital infection, Zika virus presents unique challenges for obstetric and pediatric health care providers. CDC's first Zika-related clinical guidance outlining evaluation, testing, and clinical management of Zika virus in pregnant women was released on January 19, 2016 (*6*), and on January 26, 2016, guidance for the evaluation and testing of infants with possible congenital Zika virus infection was released (*7*). As new evidence emerged, CDC updated pregnancy and infant guidance and developed guidance for reproductive-aged women (*8–13*). These evidence-based recommendations have been disseminated to health care providers through partnerships with professional organizations, including the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics, and

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FIGURE 1. Timeline of Zika virus response events, by month — worldwide, January–December 2016

2015

- **Dec 31:** First local Zika virus transmission reported in Puerto Rico

2016

- **Jan 15:** Zika travel notice for 14 countries in the Americas issued
- **Jan 19:** First clinical guidance for pregnant women
- **Jan 22:** Activation of CDC Emergency Operations Center
- **Jan 26:** Clinical guidance for infants
- **Feb 1:** WHO declares Zika Public Health Emergency of International Concern
- **Feb 5:** First case of sexual transmission confirmed (Texas)
- **Feb 16:** FDA recommends cessation of blood collection in U.S. areas with local transmission
- **Feb 26:** Zika MAC-ELISA IgM test receives FDA emergency use authorization
- **Mar 4:** U.S. Zika Pregnancy Registry (USZPR) & Puerto Rico Zika Active Pregnancy Surveillance System (ZAPSS) launched
- **Mar 17:** Trioplex PCR test receives FDA emergency use authorization
- **Apr 1:** Zika Action Plan Summit for local, state, & federal officials to improve Zika preparedness & response (Atlanta)
- **Apr 13:** Zika determined to be a cause of microcephaly and brain defects
- **Apr 30:** Zika-Contraception Access Network launched; first provider training in Puerto Rico
- **May 20:** Regular reporting of pregnant women with Zika virus infection begins (USZPR & ZAPSS)
- **Jun 14:** First Zika Interim Response Plan to prepare for local transmission
- **Jul 18:** Investigation of Zika infection not linked to travel (Utah)
- **Jul 21–22:** Meeting to inform updated infant guidance (CDC and AAP)
- **Jul 29:** Florida announces first cases of local transmission (Miami)
- **Aug 1:** Travel and testing guidance issued for Wynwood neighborhood, Miami-Dade County (Florida)
- **Aug 26:** FDA recommends screening of all donated blood in the United States
- **Sep 19:** Vector control efforts successful in Wynwood neighborhood, Miami-Dade County
- **Sep 30:** Updated clinical guidance on preconception counseling and sexual transmission prevention
- **Nov 16:** Updated guidance for U.S. laboratories testing for Zika virus infection
- **Nov 22:** Report of congenital Zika infection without microcephaly at birth (CDC & Brazil)
- **Nov 28:** Texas reports first case of local Zika transmission
- **Dec 14:** Travel and testing guidance issued for Brownsville, Cameron County (Texas)

Abbreviations: AAP = American Academy of Pediatrics; FDA = Food and Drug Administration; MAC-ELISA = immunoglobulin M-capture enzyme-linked immunosorbent assay; PCR = polymerase chain reaction; WHO = World Health Organization.

have provided clear guidance for providers monitoring and caring for pregnant women and fetuses and infants affected by Zika virus infection.

3. Identifying Sexual Transmission of Zika Virus Infection

In late January, CDC, in collaboration with Texas health officials, confirmed sexual contact as the source of Zika virus infection in a Dallas man whose partner had traveled to Brazil (*14*) and issued guidance for the prevention of sexual transmission of Zika virus in February (*15*). To date, 38 cases of sexually transmitted Zika virus infection have been confirmed in the United States (*16*). Most cases have involved transmission from symptomatic men to women (*17*); however, cases of male-to-male (*14*), female-to-male (*18*), and asymptomatic male-to-female (*19*) sexual transmission have also been documented. In April and May, CDC initiated two studies to determine the frequency and duration of Zika virus shedding in the semen and urine of infected men. CDC continues to work closely with state, local, and territorial health officials to identify and investigate possible cases of sexual transmission of Zika virus. As new information regarding sexual transmission emerges, one recommendation remains consistent: men who live in or have traveled to an area with active Zika virus transmission should prevent sexual transmission to their pregnant partners by abstaining from sex or consistently and correctly using condoms for the duration of their partner's pregnancy (*10*,*12*,*13*,*15*).

4. Monitoring Blood Safety and Availability

Because of known transfusion-transmission risks associated with other flaviviruses, Zika virus was recognized as a potential threat to blood safety. The Food and Drug Administration (FDA) and CDC collaborated to recommend travel and risk factor–related deferrals for all U.S. blood donors; in February 2016, FDA issued guidance recommending that, until laboratory screening of blood donations or pathogen-reduction technology could be implemented, blood centers in areas with active mosquito-borne Zika virus transmission cease local blood collection and import blood from U.S. areas without active transmission (*20*). Because of ongoing local transmission of Zika virus in Puerto Rico and unavailability of either screening or pathogen-reduction technology for all blood products, CDC, in collaboration with the Puerto Rico Department of Health, conducted a rapid assessment of blood collection and use on the island to help guide blood importation measures (*21*). Blood importation, supported by the Biomedical Advanced Research and Development Authority, continued for Puerto Rico until April 2016, when Zika virus screening of blood donations was implemented under an FDA-approved investigational new drug application (*21*–*23*). Based on increasing reports of persons infected through travel as well as local transmission, FDA expanded its blood screening recommendations in August 2016 to include all areas of the United States (*24*). As of December 10, 2016, products from 78 donations in the continental United States and Hawaii and 353 donations in Puerto Rico have been prevented from entering the blood supply as a result of screening.

5. Developing and Distributing Laboratory Test Kits and Reagents

Working with FDA, CDC obtained the first two emergency use authorizations for CDC-developed in vitro tests to diagnose Zika virus infection: the Zika immunoglobulin M capture enzyme-linked immunosorbent assay (MAC-ELISA) on February 26, 2016 and the Trioplex real-time reverse transcription–polymerase chain reaction assay for the detection and differentiation of RNA from dengue, chikungunya, and Zika viruses on March 17, 2016. CDC manufactured and conducted quality control testing of reagents required for both tests and distributed them domestically and to approximately 100 countries (Figure 2). CDC continues to provide guidance to laboratories on all aspects of testing and interpretation of test results for all Zika virus emergency use authorization tests (*25*). CDC has continued to work to expand Zika immunoglobulin M testing capacity by entering into material transfer agreements and biologic material licensing agreements with commercial laboratories.

6. Establishing a Causal Link Between Zika Virus Infection During Pregnancy and Serious Brain Abnormalities, Including Microcephaly

In collaboration with colleagues from Brazil, CDC pathology experts identified the first evidence of Zika virus infection in the fetal brain and in placental tissues, providing evidence of the possible role of Zika virus infection during pregnancy in adverse fetal and infant outcomes (*26*,*27*). In April 2016, CDC authors published a comprehensive analysis of the data, concluding that sufficient evidence existed to support a causal relationship between Zika virus infection during pregnancy and microcephaly and other brain abnormalities (*28*). As of December 15, 2016, 29 countries and territories have reported potential cases of congenital Zika syndrome.*

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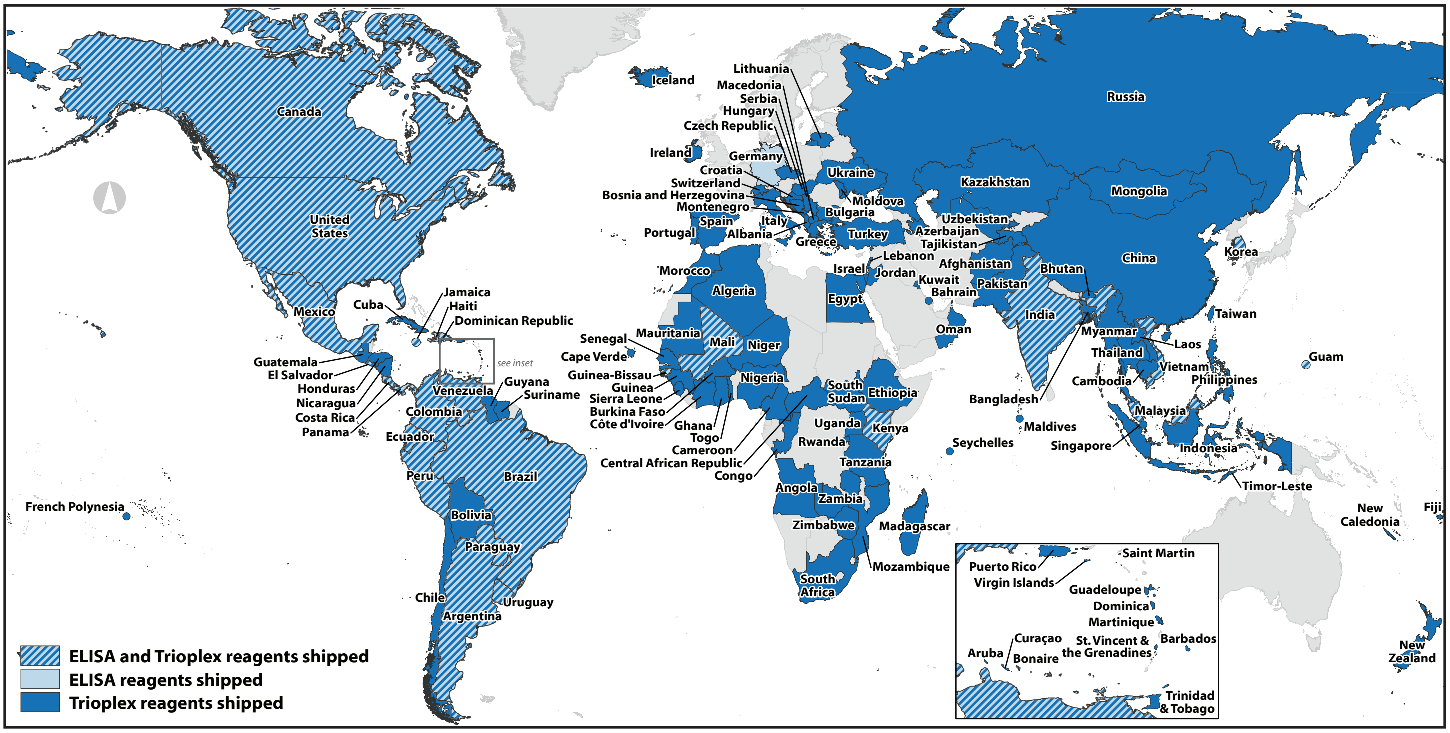
* http://apps.who.int/iris/bitstream/10665/252533/1/zikasitrep15Dec2016-eng.pdf?ua=1.

FIGURE 2. Distribution of reagents for CDC Zika diagnostic tests* for use under an emergency use authorization as of December 6, 2016



* Enzyme-linked immunosorbent assay (ELISA) and Trioplex real-time reverse transcription–polymerase chain reaction (Trioplex).

7. Gathering and Analyzing Zika Pregnancy Surveillance Data to Understand the Magnitude of the Risk and the Full Range of Fetal and Infant Outcomes

To monitor the effect of Zika virus infection during pregnancy, pregnancy and infant surveillance was put in place in U.S. states and territories (*29*). The U.S. Zika Pregnancy Registry was established in coordination with state, local, tribal, and territorial health departments to monitor all states and territories except Puerto Rico. In Puerto Rico, the Zika Active Pregnancy Surveillance System was established to address specific needs resulting from the anticipated large outbreak (*30*). CDC also collaborated with the *Instituto Nacional de Salud* (National Institute of Health) in Colombia to conduct enhanced surveillance of pregnant women with symptomatic Zika virus disease in three cities (*31*). These surveillance systems continue to provide information about the magnitude of risk, the gestational timing of highest risk, and the spectrum of congenital Zika syndrome. Data reported to the U.S. Zika Pregnancy Registry from the continental United States and Hawaii suggest that among pregnant women with laboratory evidence of possible Zika virus infection, approximately 6% of fetuses or infants have a birth defect potentially related to Zika virus, and among women with first-trimester Zika infection, 11% of fetuses or infants have evidence of Zika-associated birth defects (*32*). The proportion of completed pregnancies affected by birth defects was similar following either symptomatic or asymptomatic infection during pregnancy (*32*). This estimate is consistent with models based on the outbreak in Bahia, Brazil, which estimated a 1%–13% risk for microcephaly after a Zika virus infection during the first trimester (*33*).

8. Improving Access to the Full Range of Voluntary, Reversible Contraception Methods to Decrease Unintended Pregnancies as a Strategy to Reduce the Impact of Zika Virus Infection

Prevention of unintended pregnancies is a primary strategy to reduce births of infants with Zika-related birth defects. A review of contraception use in Puerto Rico demonstrated limited supply, few trained providers, a cumbersome referral process, and limited provider reimbursement (*34*). The CDC Foundation, in collaboration with local partners and CDC, established the Zika Contraceptive Access Network (Z-CAN), with the aim of building a network of providers trained in contraception counseling and provision, securing sufficient contraceptive products to meet the needs of women in Puerto Rico, and raising awareness about the role of contraception in the context of Zika. By the end of 2016, among the 150 physicians actively providing obstetrical services in Puerto Rico, 105 (70%) had been trained and mentored on provision of all reversible methods of contraception. After approximately 3,000 initial Z-CAN visits, 96% of patients have received same-day contraceptive services, and 64% have chosen a long acting reversible contraceptive method. On August 2, 2016, CDC published a review of contraception use among women of reproductive age at risk for unintended pregnancy in states at potential risk for local Zika transmission; the review identified barriers to the use of highly effective contraception and described key strategies states can implement to increase access to contraception during periods of local Zika virus transmission (*35*).

9. Implementing Vector Control Strategies and Building the Evidence Base for Best Practices

Successful control of *Aedes aegypti,* the primary mosquito vector of Zika virus, has proven extremely difficult using existing control methods. CDC's technical assistance during the Zika response has therefore included support for improved mosquito control infrastructure, novel mosquito control techniques, and integrated vector management that uses existing control methods. During the Zika virus outbreak in the Wynwood neighborhood of Miami-Dade County, Florida, aggressive ground-based integrated vector management was supplemented by sequential aerial applications of adulticide and larvicide, which rapidly reduced adult mosquito counts in surveillance traps by approximately 90% and helped to end this local outbreak (*36*). A similar approach in Miami Beach, Florida, using aerial applications of adulticide and ground-based applications of larvicide, also substantially reduced adult mosquito counts. Recent advances in aerial insecticide application methods, and the fact that, in the continental United States, *Aedes aegypti* lives primarily outdoors, likely contributed to the success of the aerial approach in Miami-Dade County. Public opposition to aerial pesticide application in Puerto Rico precluded a similar approach there; instead, lethal mosquito traps have been deployed as part of large community trials that aim to evaluate this method of preventing future outbreaks of mosquito-borne disease on the island (*37*).

10. Improving Understanding of the Link Between Guillain-Barré Syndrome and Zika Virus Infection

Many countries have reported increases in the occurrence of severe neurologic illness, particularly Guillain-Barré syndrome (GBS), after Zika virus outbreaks, with reported rates two to 10 times higher than those reported before Zika virus disease outbreaks (*38–40*). During the past year, the Puerto Rico Department of Health and CDC established an enhanced surveillance system for GBS in Puerto Rico. Initial analyses have demonstrated that among 56 patients with suspected GBS during January 1–July 31, 2016, a total of 26 (47%) had confirmed (n = 10, 18%) or presumptive (16, 29%) Zika virus infection (*41*). Other work related to GBS includes retrospective case-control investigations in Puerto Rico, Brazil, and Colombia, which will help improve understanding of the association between Zika virus infection and GBS.

Summary

What is already known about this topic?

The introduction of Zika virus into the Region of the Americas and the subsequent increase in cases of congenital microcephaly resulted in activation of CDC's Emergency Operations Center and the declaration of a Public Health Emergency of International Concern by the World Health Organization. As of December 15, 2016, 61 countries and territories have reported local Zika virus transmission as part of the current outbreak; 29 countries and territories have reported potential cases of congenital Zika syndrome.

What is added by this report?

CDC's emergency response to Zika virus rapidly addressed many acute public health needs associated with the outbreak and developed new public health surveillance and infection control tools, including issuing travel and clinical guidance; identifying sexual transmission; monitoring blood safety; developing and distributing laboratory test kits; establishing the causal link between in utero infection and congenital Zika syndrome and assessing the range of outcomes and the magnitude of risk; improving access to contraception to prevent unintended pregnancies; implementing vector control strategies; and improving the understanding of the link between and Zika virus infection and other neurological illnesses.

What are the implications for public health practice?

To protect pregnant women and their fetuses and infants from the effects of Zika virus infection during pregnancy, public health activities must focus on preventing mosquito-borne transmission through vector control and personal protective practices, preventing sexual transmission by advising abstention from sex or consistent and correct use of condoms, and preventing unintended pregnancies by reducing barriers to access to highly effective reversible contraception. Collectively, these critical strategies can reduce the effect of the virus on infants, families, and communities.

Future Priorities

Zika virus remains a serious threat to world health that is likely to continue until a safe and effective vaccine becomes available and is widely implemented. Threats from mosquito-borne infection are likely to continue until better vector control interventions are developed. The severe consequences of Zika virus infection require a long-term approach with dedicated resources (*42*). Important future priorities include continuing to protect pregnant women and fetuses and infants from Zika virus infection; developing improved diagnostics, including the ability to distinguish among flaviviruses serologically; collaborating among government and private partners to accelerate vaccine development; developing and implementing improved vector surveillance and control strategies and capacities; improving contraceptive access to reduce unintended pregnancies; and improving understanding of the long-term outcomes for infants exposed to Zika virus in utero. Much remains to be done to protect pregnant women and fetuses and infants from Zika virus infection; the rapid action, dedication, and collaboration demonstrated by the global public health community during the past year provide a solid foundation for future work.

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