State of New Jersey
DEPARTMENT OF HEALTH
DIVISION OF EPIDEMIOLOGY, ENVIRONMENTAL AND OCCUPATIONAL HEALTH
PO BOX 369
TRENTON, N.J. 08625-0369

CHRIS CHRISTIE
Governor

www.nj.gov/health

KIM GUADAGNO
Lt. Governor

CATHLEEN D. BENNETT
Acting Commissioner

To: Local health departments and health care providers
From: Shereen Semple, MS
Vectorborne Disease & Ebola Team Lead
New Jersey Department of Health (NJDOH)
Infectious & Zoonotic Disease Program
Date: January 22, 2016
Subject: Zika virus: Updated Guidelines for Diagnostic Testing for Zika Virus

Zika virus disease (Zika) is a mosquito-borne disease that typically occurs in tropical Africa and southeast Asia. In May 2015, the Pan American Health Organization / World Health Organization (PAHO / WHO) reported the first autochthonous (local) transmission of Zika in the Americas. As of January 17, 2016, twenty countries or territories in the South and Central American and Caribbean region are reporting current autochthonous transmission, including Barbados, Bolivia, Brazil, Colombia, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Martinique, Mexico, Panama, Paraguay, Saint Martin, Suriname, Venezuela, and the Commonwealth of Puerto Rico. This list could increase if more countries confirm transmission. Please visit the Zika virus infection webpage at http://www.paho.org/ for the most updated list of current countries and territories with current Zika transmission.

In late December 2015, the NJDOH identified its first laboratory-confirmed case of Zika in a Bergen county woman exposed in Colombia. There is no current risk of transmission in New Jersey. The NJDOH is sending this message to local health departments (LHDs) and health care providers to provide updated testing criteria and the attached interim guidelines for pregnant women during a Zika virus outbreak.

This document replaces any previous guidance for testing. For more background on Zika, as well as recommendations for travel or minimizing the chance of a mosquito bites during travel, please refer to the January 14, 2016 LINCS message #103033-1-15-2016-PHIN: *Zika Virus Disease: Guidelines for Reporting, Testing and Preventing Infection in Travelers* (http://www.njlincs.net/). Clinicians and laboratories must report all confirmed cases of all arboviral diseases (e.g. Zika, chikungunya, West Nile, and dengue) to the LHD where the person resides. A list of LHD can be found at http://localhealth.nj.gov

As more information becomes available, additional guidance will be provided to our public health partners.

Relevant Health Information to Consider

Clinicians and LHDs investigating suspect cases of Zika should obtain the following information: symptom onset date, list of clinical signs and symptoms, travel history including dates and location, co-morbidities and pregnancy status, Japanese encephalitis and yellow fever vaccination history, history of past flavivirus infection (e.g., Dengue, West Nile, St. Louis encephalitis virus) and relevant laboratory testing. Given the possible link between infection with Zika and microcephaly, pregnant woman should be advised to consult with their OB/GYN to discuss further evaluation.

Zika Testing Limitations

Laboratory tests for Zika diagnosis are of limited availability, but include polymerase chain reaction (RT-PCR) for Zika RNA (within 7 days of symptom onset) and Zika virus immunoglobulin M (IgM) and neutralizing antibodies on serum specimens (at least three days after symptom onset). Given the overlap of symptoms and endemic areas with other viral illnesses, patients should also be evaluated for possible dengue or chikungunya virus infection.

Testing has multiple limitations:

- Currently, only the CDC in Fort Collins, Colorado, through approval from state health departments, and a few public health laboratories are able to perform testing.
- There is substantial serological cross-reactivity among the flaviviruses and current IgM antibody assays cannot reliably distinguish between Zika and dengue virus infections. Therefore:
    - An IgM positive result in a dengue or Zika ELISA test should be considered indicative of a recent flavivirus infection.
    - Plaque-reduction neutralization tests (PRNT) are more specific, can be performed to measure virus-specific neutralizing antibodies, and may be able to discriminate between cross-reacting antibodies in primary flavivirus infections.
    - For primary flavivirus infections, a fourfold or greater increase in virus-specific neutralizing antibodies between acute- and convalescent-phase serum specimens collected 2 to 3 weeks apart may be used to confirm recent infection.
- In patients who have been immunized against yellow fever or Japanese encephalitis virus or who have been infected with another flavivirus (e.g., West Nile, St. Louis encephalitis virus) in the past, cross-reactive antibodies in both the IgM and neutralizing antibody assays may make it difficult to identify which flavivirus, if any, is causing the patient's current illness.

Updated Testing Guidance

Health care providers may consult with their local health department or the NJDOH regarding laboratory testing in the following circumstances:

- Pregnant women who present within two weeks of travel to a country with current Zika transmission and have two or more of the following symptoms:
    - Acute onset of fever
    - Maculopapular rash
    - Arthralgia
    - Conjunctivitis

- Asymptomatic pregnant women with travel to a country with current Zika transmission who have a fetal ultrasound suggestive of microcephaly or intracranial calcifications

Pregnant women with a history of travel to an area with Zika transmission, but who do not present with symptoms, are not currently being recommended for testing.

Non-pregnant individuals with a history of travel to an area with Zika transmission are not currently being recommended for testing, even if symptoms are present. In these individuals, Zika is typically a mild illness with no specific treatment, so while Zika should still be considered in the differential, it is not clinically important to make a definitive diagnosis.

Considerations for follow up: Asymptomatic pregnant women with a history of travel to an area of Zika transmission while pregnant, regardless of past symptoms, should consult with their health care provider. Providers may refer to the CDC MMWR Interim Guidelines for Pregnant Women During a Zika Virus Outbreak: http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1er.htm

Testing is not indicated for women without a recent travel history to an area with Zika transmission, or for pregnant women who traveled before becoming pregnant.

Requests for Testing

At this time, all testing will be performed at the CDC. Testing capacity is very limited. For those with recent travel to countries with identified transmission, CDC is accepting samples from symptomatic pregnant women, and may consider accepting samples from asymptomatic pregnant women who have a fetal ultrasound suggestive of microcephaly or intracranial calcifications.

Clinicians considering testing a pregnant woman for Zika based on the testing considerations above should contact their LHD or the NJDOH Vectorborne Disease Program during normal business hours at (609) 826-5964. The CDC will not accept specimens sent without pre-approval from state health departments. If the testing requested meets current CDC capacity and priority, testing can be approved. Availability of testing may increase in the future, and criteria for approval may change.

Specimen Collection Guidance

If testing is approved, the NJDOH or LHD will provide guidelines for sample collection and shipment to the CDC. Collect serum ($\geq$ 3 mL) in a large, red top tube. Refrigerate serum at 4°C or maintain on ice for no longer than 24 hrs. Samples collected and shipped with expected arrival the same day, can be shipped on cold packs (4°C). If storage/transport will exceed 24 hrs., serum

should be frozen at -20°C or lower. These samples should be shipped on dry ice. Follow packing and shipping instructions for Category B, Biological Substances.

Acute serum (≥ 3 mL) collected within the first 7 days following symptom onset can be tested by RT-PCR. IgM antibodies may be detectable by day 4 of illness but are more reliably identified later on in the course of infection; convalescent specimens, collected 2-3 weeks later, may be necessary to confirm or rule-out infection.

For More Information

- Contact the NJDOH Vectorborne Disease Program by phone at (609) 826-5964
- CDC Zika virus website: http://www.cdc.gov/zika/
- CDC's Interim Guidelines for Pregnant Women During a Zika Virus Outbreak: http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1er.htm
- CDC health advisories on Zika and other travel-related health risks: http://wwwnc.cdc.gov/travel/notices
- Protection against mosquitoes for travelers: http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-2-the-pre-travel-consultation/protection-against-mosquitoes-ticks-and-other-insects-and-arthropods
- CDC's Clinician Outreach and Communication Activity (COCA): http://emergency.cdc.gov/coca/calls/
- Pan American Health Organization: http://www.paho.org/