

# Utah Department of Health

## Instructions for Submitting Diagnostic Specimens for Zika Virus Testing

*Updated on February 8, 2016*

### **ZIKA VIRUS AND PREGNANT WOMEN**

Zika virus is a flavivirus that is transmitted to humans primarily by *Aedes* species mosquitoes; in the Americas, *Aedes aegyptii*, is the most common vector. Other documented modes of transmission include intrauterine resulting in congenital infection, intrapartum from a viremic mother to her newborn, sexual, blood transfusion and laboratory exposure. Human disease has been seen in African, Asia, and the Pacific islands. In May 2015, the first locally-acquired cases in the Americas were reported in Brazil. Local transmission has been reported in several countries and territories in the Americas, including Puerto Rico (<http://wwwnc.cdc.gov/travel/notices>). To date, there has been one case of sexual transmission documented in the U.S. All other Zika virus infections documented in U.S. citizens have been in travelers returning from other countries; no endemic Zika transmission from mosquitoes has been documented in the continental United States. In Brazil, a substantial increase in the number of infants born with microcephaly was noted in 2015, and Zika virus infection has been identified in several infants born with microcephaly and other fetal losses. Although a definite causal association has not yet been established, the U.S. Centers for Disease Control and Prevention (CDC) is recommending that pregnant women who traveled to areas with Zika virus transmission while they were pregnant be evaluated according to the guidance found at the following websites:

<http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1.htm>

[http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm?s\\_cid=mm6505e2er.htm\\_w](http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm?s_cid=mm6505e2er.htm_w).

Initial diagnostic testing for Zika virus is recommended for pregnant women with a history of travel to an area with Zika virus transmission during pregnancy. Symptoms only occur in about 1 in 5 people and include fever, rash, joint pain, conjunctivitis (red eyes), muscle pain, and headache (<http://www.cdc.gov/zika/symptoms/>). Symptoms typically begin 2 to 7 days after being bitten by an infected mosquito. Otherwise, the decision to test for Zika virus should be made based on results of fetal ultrasound.

### **INFANTS WITH MICROCEPHALY**

Interim guidance for evaluation and testing of infants with microcephaly or intracranial calcifications whose mothers traveled to or resided in an area with Zika virus transmission during pregnancy can be found at [http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3.htm#F1\\_down](http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3.htm#F1_down).

## DIAGNOSTIC TESTING FOR ZIKA VIRUS

Laboratory tests for Zika virus infection diagnosis are of limited availability, but include polymerase chain reaction (RT-PCR) for Zika RNA and Zika virus immunoglobulin M (IgM) and neutralizing antibodies on serum specimens. Given the overlap of symptoms and endemic areas with other viral illnesses, patients should also be evaluated for other possible flavivirus infections.

Testing for Zika virus has multiple limitations.

- Currently, only the CDC in Fort Collins, Colorado and a few public health laboratories are able to perform testing. The Utah Public Health Laboratory (UPHL) does not currently perform this test. CDC is working with laboratories to expand availability of testing.
- There may be serological cross-reactivity among the flaviviruses and current IgM antibody assays may not reliably distinguish between Zika and dengue virus infections. CDC has been looking for cross-reactivity on recent samples submitted for Zika testing and has found that the Zika IgM test is performing better than expected.
- 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 or 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 is causing the patient's current illness. Because antibody tests may cross-react with other flaviviruses (e.g., dengue, yellow fever, Chikungunya, or Japanese B encephalitis) and produce false positives, it is recommended that the patient be tested for these viruses as well. CDC is currently performing dengue and Chikungunya antibody tests on Zika IgM-positive specimens only. If clinicians need to rule out these infections regardless of Zika results, these tests are available through commercial laboratories.
- Acute serum ( $\geq 3$  mL) collected within the first 7 days following symptom onset can be tested by 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.

Consultation about laboratory testing is available through the Utah Department of Health (UDOH) in the following circumstances:

1. A pregnant woman (regardless of symptoms) with a history of travel to an area with ongoing Zika virus transmission may be offered testing up to 12 weeks after her return. At present, CDC will perform testing according to the following algorithm:
  - a) If a pregnant woman is within 7 days of onset of symptoms, the maternal serum will be tested for reverse transcription-polymerase chain reaction (RT-PCR).
  - b) If a pregnant woman is asymptomatic or  $\geq 4$  days from onset of symptoms, her serum will be tested for anti-Zika IgM antibody.
  - c) If Zika IgM antibody testing is positive, her serum will also be tested for dengue and Chikungunya to rule out cross-reactive antibodies with these diseases. (These tests will not be performed on Zika IgM-negative women.)

If the test results are either positive or inconclusive, fetal ultrasound(s) should be performed to detect microcephaly or intracranial calcifications. If the test results are negative, the patient should be monitored with serial ultrasounds as indicated by clinical judgement and level of concern.

2. Pregnant women residing in areas with ongoing Zika virus transmission are at risk throughout pregnancy. For these women, testing is recommended during the first week of illness if symptoms occur. For asymptomatic women, testing is recommended at the initiation of prenatal care with follow-up testing mid-second trimester.
3. Zika virus testing may also be requested for men returning from a Zika-endemic area if their spouse is pregnant. Testing can be requested up to 12 weeks after return. Other guidance for prevention of sexual transmission can be found at:  
<http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e1er.htm>.

For other questions about testing, please consult the State Epidemiologist or Medical Officer on call at the UDOH (see contact information below).

## **ZIKA-AFFECTED AREAS/ TRAVEL INFORMATION**

<http://wwwnc.cdc.gov/travel/page/zika-travel-information>

## **REQUESTING LABORATORY TESTING**

At this time, Zika virus testing for Utah residents will be performed at the CDC free of charge. However, testing capacity is very limited, so CDC is requesting that the State Epidemiologist or Medical Officer on-call at the UDOH approve testing requests. **To discuss testing, please contact the UDOH, Bureau of Epidemiology at 801-538-6191.**

Once testing is approved by the UDOH, follow these instructions:

- 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 hours.
- Samples collected and shipped with expected arrival the same day can be shipped on cold packs (4°C).
- If storage/transport will exceed 24 hours, serum should be frozen at -20°C or lower. These samples should be shipped on dry ice.
- Follow packaging and shipping instructions for Category B, Biological Substances.
- There are three forms that must be completed by the provider. These forms will be emailed directly to the provider by the UPHL once testing is approved by the state epidemiologist. If a provider needs assistance with completing these forms, s/he should work with local health department or UDOH epidemiology staff. Samples with incomplete information will result in delayed testing and reporting of results.
- Arrangements must be made with the UDOH for specimen shipping and delivery to the UPHL.
- UPHL will ship specimens to CDC on Monday, Tuesday and Wednesday. Specimens received later in the week will not be shipped until the following week.
- At this time, it is unclear what the turnaround time for testing will be.