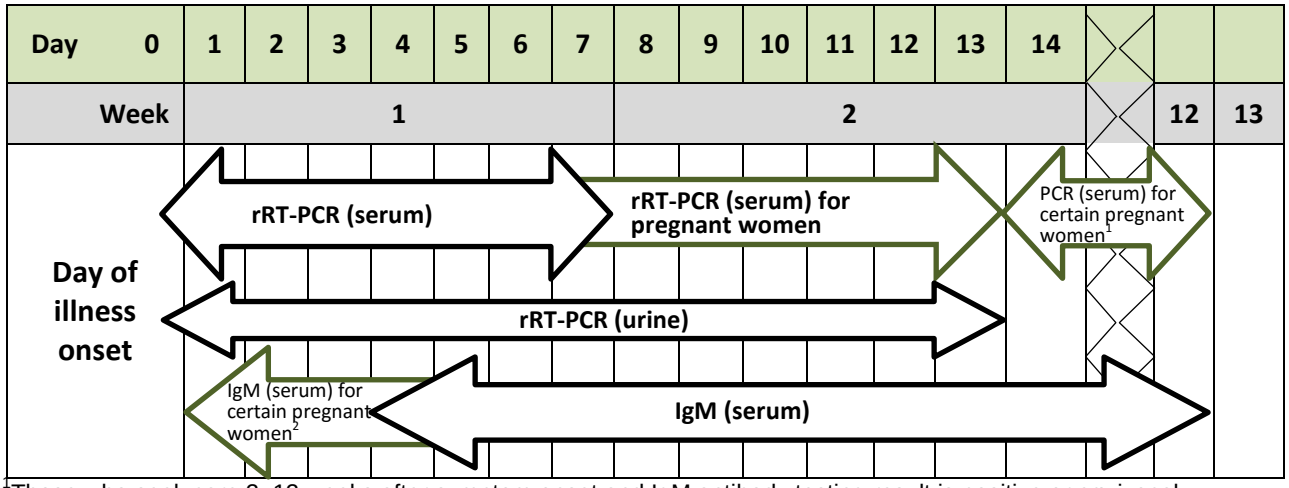
Idaho Public Health Guidance for Zika Virus Testing

Preliminary diagnosis of Zika virus disease is based on a combination of clinical signs and symptoms, travel history, and activities; laboratory diagnosis is determined by laboratory tests of blood or other tissues. Characteristic clinical findings are acute onset of fever with maculopapular rash, arthralgia, or conjunctivitis. Other common symptoms include myalgia and headache. Clinical illness is usually mild with symptoms lasting for several days to a week. Guillain-Barré syndrome following infection with Zika virus has been reported; however, a causal relationship has not been established. Symptoms typically begin 2 to 7 days, but may occur up to two weeks, after being bitten by an infected mosquito.

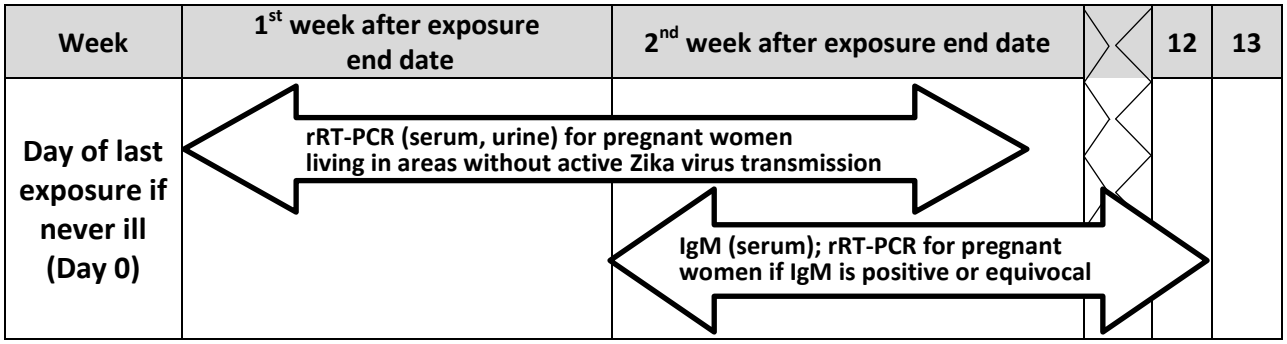
Specimen Collection and Testing (see Figures)

Figure.1 Timing of appropriate tests for Zika virus infection in persons who had compatible illness



[1]Those who seek care 2–12 weeks after symptom onset and IgM antibody testing result is positive or equivocal.
[2]Those who have negative rRT-PCR should receive both Zika virus IgM and dengue virus IgM antibody testing.
Note: a transcription-mediated amplification (TMA) assay for Zika virus RNA for serum and plasma is also available.

Figure 2. Timing of appropriate tests for Zika virus infection in persons with no history of acute illness



Indications for Testing

Persons reporting symptoms consistent with Zika virus disease

- Currently ill persons who report symptoms consistent with Zika virus disease with *onset during or within two weeks* of returning from residence in or travel to an area with known Zika virus transmission‡ and for whom test results would aid in differential diagnosis to inform treatment
- Persons who have had possible sexual exposure to Zika virus and develop signs or symptoms consistent with Zika virus disease. Potential sexual exposure is defined as sex (vaginal sex, anal sex, oral sex, and sharing of sex toys) with a person who has traveled to or lives in an area with active Zika virus transmission when the sexual contact did not include a barrier (male or female condoms, dental dams) to protect against infection.

- Pregnant women who report symptoms consistent with Zika virus disease *during or within two weeks* of returning from travel to or residence in an area with Zika virus transmission
- Pregnant woman with possible sexual exposure to Zika virus
- Mothers of infants without microcephaly or intracranial calcifications who had clinical illness consistent with Zika virus disease and residence in or travel history to an area with known Zika virus transmission during pregnancy

‡See http://www.cdc.gov/zika/geo/index.html for areas with active local Zika virus transmission

Persons NOT reporting acute symptoms consistent with Zika virus disease

- Asymptomatic pregnant women
    - *within 2–12 weeks* after returning from travel to or residence in an area with Zika virus transmission while pregnant or after having potential sexual exposure to Zika virus
    - with possible exposure to Zika virus up to 8 weeks before the start of pregnancy, or 6 weeks before the women's last menstrual period, within *2–12 weeks* after possible exposure
    - at the initiation of prenatal care and mid-second trimester if the patient has ongoing risk for Zika virus exposure (i.e., residence in or frequent travel to an area with ongoing Zika virus transmission
- Infants born to women who traveled to or resided in an area with Zika virus transmission during pregnancy who 1) received a diagnosis of microcephaly, intracranial calcifications, or brain and eye abnormalities detected prenatally or at birth, or 2) have mothers with positive or inconclusive test results for Zika virus infection

Testing for Zika virus infection may be considered for the following after discussion with Zika epidemiologists or the Public Health Medical Director, Division of Public Health:

- Infants born to women who, during pregnancy, traveled to or resided in an area with Zika virus transmission, who received a diagnosis of congenital central nervous system abnormalities (other than microcephaly, intracranial calcifications or brain and eye abnormalities) detected prenatally or at birth and not explained by another etiology.
- Currently ill persons who report symptoms consistent with Zika virus disease with onset during or within two weeks of receiving a blood product or organ or tissue transplant.
- Symptomatic and asymptomatic pregnant women who seek care >12 weeks after symptom onset or possible Zika virus exposure.

Testing for Zika virus infection through public health agencies is NOT recommended and will not be performed at CDC for:

- Asymptomatic pregnant women who completed travel to an area with Zika virus transmission more than 8 weeks *before* becoming pregnant and mosquito bites during travel is the only potential exposure
- Infants without microcephaly, intracranial calcifications, brain and eye abnormalities detected at birth who were born to mothers with negative test results for Zika virus infection
- Currently ill persons who report onset of symptoms consistent with Zika virus disease two or more weeks after returning from travel to an area with Zika virus transmission and whose potential exposure was from travel
- Well persons with a history of residence in or travel to an area with Zika virus transmission and for whom test results will not aid in clinical evaluation
- Persons with a history of residence in or travel to an area with Zika virus transmission for the purpose of assessing risk for sexual transmission
- Semen from semen donors

Testing Through the Idaho Bureau of Laboratories (IBL)

IBL conducts PCR testing on serum, CSF, and urine; other specimens and tests are conducted at CDC. Results of tests conducted at CDC could take 30 or more days to receive.

Table. Zika virus testing through the Idaho Bureau of Laboratories

Test Name	Specimen Type	Minimum Volume
Reverse transcriptase-polymerase chain reaction (RT-PCR)* or virus isolation	Serum* Cerebrospinal fluid* Urine* Amniotic fluid*†	Submit 0.5 mL of serum or urine, or 1 mL of CSF
	Saliva† Semen† Umbilical cord blood†	1 mL (place swab of saliva in tube with 1 mL media)
	Fresh frozen tissue (placenta, umbilical cord, fetal tissue, other products of conception) †	1 cm^3
Serology: Zika virus-specific IgM and plaque-reduction neutralization testing (PRNT)	Serum Umbilical cord blood†	0.5 mL
	Cerebrospinal fluid	1 mL
Histopathology and immunohistochemistry	Fixed tissue (placenta, umbilical cord, fetal tissue, other products of conception) †	1 cm^3

*PCR is the preferred test for Zika virus infection. CSF, urine, and amniotic fluid may only be tested alongside a patient-matched serum specimen. †Contact IBL before submitting these samples.

Guidance for Completing Test Request Forms for Public Health Testing

Please review the Instructions for CDC Form 50.34 for Zika Testing and ensure that CDC Form 50.34 for Idaho is filled out completely as indicated on the instructions prior to specimen submission to IBL. Specimens will not be tested or forwarded for testing until all required information is on the form, including pregnancy status, onset of illness date, clinical description, and travel history (including dates). Public health officials will contact provider offices if necessary to obtain the required information.

Testing at Commercial Laboratories

Testing for Zika virus infection by RNA amplification assays (PCR, TMA), but not by IgM or PRNT, is commercially available for testing serum, plasma, and urine specimens from patients meeting clinical criteria. Contact your commercial laboratory to ascertain which samples may be tested by that laboratory. Providers who request Zika virus RNA amplification assay testing from a commercial laboratory are advised to store a serum aliquot for subsequent Zika IgM ELISA testing if the assay is negative.

Interpretation of Serologic Test Results

Cross-reaction with IgM antibodies against related flaviviruses is common in areas where there is co-circulation of viruses. See http://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm?s_cid=mm6521e1_e published 5/31/2016, for updated interpretation of Zika virus PCR and antibody test results. Because IgM and PRNT test results are not normally received until 30 days or more after specimen receipt, antibody testing for other flaviviruses (*e.g.*, dengue) for clinical evaluation and diagnosis should be ordered from a commercial laboratory to ensure timely results. If the first of paired samples is diagnostic, testing of the second sample is not expected.

Healthcare providers who have questions about testing may contact the following for more information:

Idaho Local Public Health Districts
http://healthandwelfare.idaho.gov/Health/HealthDistricts/tabid/97/Default.aspx

Division of Public Health
Bureau of Communicable Disease Prevention, Epidemiology Program: 208-334-5939

Idaho Bureau of Laboratories
Clinical Section: 208-334-0589

References

CDC Guidance for Health Care Providers:
http://www.cdc.gov/zika/hc-providers/index.html

CDC instructions for submitting diagnostic specimens:
http://www.cdc.gov/ncezid/dvbd/specimensub/arboviral-shipping.html