

## Quick Guide for Clinicians: How to Interpret Zika Test Results

Below is a summary of the tests that CDC is currently performing on persons potentially exposed to Zika virus. For a more detailed discussion of the tests and how to interpret results, please visit the CDC fact sheets for [clinicians](#) and for [laboratories](#).

There are three types of Zika virus tests currently being performed by CDC:

- **Nucleic acid testing:** Reverse transcriptase-polymerase chain reaction (RT-PCR). This test determines if Zika RNA is present in the specimen, indicating that the patient is viremic.
- **Antibody testing:** Zika virus IgM Capture Antibody (MAC-ELISA). The presence of IgM antibody suggests that a fairly recent infection has resulted in the production of antibodies against Zika. However, due to cross-reactivity, recent infection with dengue may result in a false-positive Zika IgM.
- **Antibody effectiveness testing:** Plaque-reduction neutralization test (PRNT). This is a difficult test to perform as it requires mixing the patient's serum with live virus to determine how effective the serum is at neutralizing the virus. It is a measure of total antibody rather than IgM specifically. Cross-reactivity is also an issue with PRNT.

The specific tests performed by CDC depend on whether or not the patient is symptomatic and when the specimen was collected in relation to the patient's illness and/or possible exposure.

If the patient is symptomatic, viral RNA can usually be identified in serum during the first 7 days of illness. However, because viremia decreases over time, a negative RT-PCR on a specimen collected  $\geq 5$  days after symptom onset does not exclude infection. The serologic (antibody) test results should be evaluated in this situation. Virus-specific IgM antibodies may be detectable  $\geq 4$  days after onset of illness, and should be detectable  $> 7$  days after onset of illness.

In symptomatic or asymptomatic persons, IgM antibodies typically are present from 2-12 weeks after infection. IgM antibodies usually wane below the level of detection  $> 12$  weeks after infection. In asymptomatic persons, the last date of travel is used as a stand-in for the last possible date of infection.

Since there is substantial cross-reactivity between Zika and dengue, and Zika, dengue and chikungunya all share the same mosquito vector and have similar symptoms, CDC is also performing tests for dengue and chikungunya. A history of vaccination against yellow fever, Japanese encephalitis, or tickborne encephalitis may also create antibodies that cross-react with Zika antibodies. We recommend consulting with the Bureau of Epidemiology (717-787-3350) on interpretation of results in persons who have received these vaccinations.

**A table of various test result scenarios is on the next page.**

**Examples of Zika test result scenarios with interpretation, caveats, and comments.**

TEST	RESULT	INTERPRETATION	CAVEATS/COMMENTS
Zika RT-PCR	Detected	Current Zika virus infection	
Zika RT-PCR	Not Detected	No evidence of <u>current</u> Zika infection	If collected $\geq 5$ days after onset, virus may have declined below detectable levels. Serology should be performed.
Zika IgM Capture ELISA	Not Detected	No evidence of recent infection with Zika	If collected $\leq 7$ days from onset (or date of last potential exposure if asymptomatic), IgM may not yet have reached detectable levels. If collected $> 12$ weeks after last date of travel, IgM may have waned.
Zika IgM Capture ELISA	Detected	No evidence of Zika virus infection  The PRNT detection limit may vary, but usually negatives are expressed as " $< 10$ "	If a positive Zika IgM is not confirmed by Zika PRNT, the IgM is a false positive and Zika virus infection is ruled out
Zika PRNT	Not Detected ( $<$ detection limit)		
Zika IgM Capture ELISA	Detected	Evidence of recent Zika virus infection	Interpretation of positive Zika PRNT results is difficult in patients with a history of vaccination against yellow fever, Japanese encephalitis, or tickborne encephalitis. Consider requesting a consultation for vaccinated patients.
Zika PRNT	Detected		
Dengue PRNT	Not Detected ( $<$ detection limit)		
Zika IgM Capture ELISA	Detected	Evidence of recent Zika virus infection.	Patient may have had dengue in the past, or Zika antibodies may be cross-reacting with the dengue PRNT. May wish to consult with Bureau of Epidemiology to ensure that interpretation is correct.
Zika PRNT	PRNT value $\geq 4$ times higher than the dengue PRNT value		
Dengue PRNT	Detected		
Zika IgM Capture ELISA	Detected	Probable, but not confirmed, evidence of recent Zika infection	Patient may have had dengue in the past. May wish to consult with Bureau of Epidemiology to ensure that interpretation is correct.
Dengue IgM Capture ELISA	Not Detected		
Zika PRNT	Detected but $< 4$ times higher than the dengue PRNT value		
Dengue PRNT	Detected		
Zika IgM Capture ELISA	Detected	Probable evidence of Zika virus infection	Right now CDC is doing PRNTs whenever appropriate. However, this scenario may arise when commercial labs begin testing.
Dengue IgM Capture ELISA	Not Detected		
Zika PRNT	Not done		