Interpretation of Zika Virus Serology
Performed at the New York State Department of Health Wadsworth Center

If Zika virus PCR of serum or urine is positive (ie, "detected"), the test is conclusive for Zika virus infection. No serologic testing is required for the diagnosis of Zika virus infection.

In the absence of detectable virus in urine or serum by PCR, serologic testing should be performed. A second "convalescent" specimen may be needed for comprehensive laboratory assessment. This document provides guidance on common combinations of serologic test results. This interpretative information is intended as a guide and should not be considered definitive for any given patient. Laboratory test results for Zika virus should always be interpreted in conjunction with the patient's clinical information and the history of potential Zika and other flavivirus exposure. Additional information on individual tests and immunological response can be found in the documents entitled "**A Healthcare Provider's Guide to Zika Virus Laboratory Results from the NYSDOH Wadsworth Center"** and **"Detecting Zika virus RNA and Antibodies"** available at http://www.health.ny.gov/diseases/zika_virus/providers.htm.

Of note, the algorithm for serologic testing changed in June, 2017, to incorporate a new Flavivirus MIA assay with specificity for both Zika and Dengue antibodies.[1] The MIA used before June, 2017, known as the West Nile Virus MIA, served as a screening test for flavivirus infection. It was not a measure of virus-specific antibody. Therefore, this document is divided into two major sections:

I. Serologic Testing as of June, 2017 to present (pages 2-3)
II. Serologic Testing from January, 2016 to June, 2017 (pages 4-5)

Assistance with laboratory test interpretation can be obtained by calling the New York State Department of Health Zika Information Line Monday through Friday 9 am to 5 pm at 888-364-4723.

Abbreviations used in this document

PCR – polymerase chain reaction
IgM – refers to laboratory tests measuring IgM antibodies
MIA – microsphere immunofluorescence assay, which measures total antibody (primarily IgG)
PRNT – plaque reduction neutralization testing, which measures total antibody (primarily IgG)

[1] Wong SJ, Furuya A, Zou J, Xie X, Dupuis AP, Kramer LD, Shi PY. A Multiplex Microsphere Immunoassay for Zika Virus Diagnosis. EBioMedicine 16(2017) 136-140. Available at http://www.ebiomedicine.com/article/S2352-3964(17)30008-7/fulltext.

Serologic Testing as of June, 2017 - Present

Combinations of Test Results that **MAY REPRESENT** Zika Virus Infection

Test Results			Possible Interpretation	Conclusion
Zika IgM	Zika MIA	Zika PRNT		
presumptive positive	reactive for Zika antibodies	positive	The serologic testing provides evidence for recent Zika infection, likely within the previous 3 months. Women who are currently or have recently become pregnant with this testing pattern may have had Zika virus in a timeframe which poses a risk of congenital Zika syndrome. Correlation with exposure history is needed.	Zika virus infection, probably recent, is likely.
negative	reactive for Zika antibodies	positive	The serologic testing provides evidence for Zika infection. Women who are currently or have recently become pregnant with this testing pattern may have had Zika in a timeframe which poses a risk of congenital Zika syndrome. Correlation with exposure history is needed.	Zika virus infection at an undetermined time is likely.

Serologic Testing as of June, 2017 - Present

Combinations of Test Results **UNLIKELY TO REPRESENT** Zika Virus Infection

Test Results			Possible Interpretation	Conclusion
Zika IgM	Zika MIA	Zika PRNT		
presumptive positive	nonreactive for Zika antibodies	negative	Cross-reactivity is likely, with the immunologic response to another flavivirus such as Dengue leading to the positive IgM results.	If testing has been obtained in a timeframe in which a serologic response is expected, the patient is not likely to have been infected with Zika virus, and no further testing is required. [2]
negative	nonreactive for Zika antibodies	not performed or negative	No serologic evidence of Zika virus infection is seen.	If testing has been obtained in a timeframe in which a serologic response is expected, the patient is not likely to have been infected with Zika virus, and no further testing is required.[2]
negative	nonreactive for Zika antibodies	positive	If the MIA is reactive for Dengue antibodies or the patient has been exposed to another flavivirus, cross-reactivity is possible.	Cross-reactivity may explain the conflicting MIA and PRNT results. Clinical correlation is needed in the management of women with this testing pattern who are currently or have recently been pregnant.

[2] **If this specimen was collected < 8 days after symptom onset or < 3 weeks after exposure, negative results should be confirmed by collecting another specimen for serology in 3 weeks.**

Serologic Testing from January, 2016 – June, 2017

Combinations of Test Results that **MAY REPRESENT** Zika Virus Infection

Test Results			Possible Interpretation	Conclusion
Zika IgM	MIA	Zika PRNT		
presumptive positive	reactive	positive	The serologic testing provides evidence for recent Zika virus infection, likely within the previous 3 months. If the Dengue PRNT is also positive or the patient has been exposed to another flavivirus, cross-reactivity is possible.	If the Dengue PRNT is also positive, it is unclear if the patient has had Zika virus infection, a dual flavivirus infection, or is merely cross-reacting to Dengue. Women who are currently or have recently become pregnant with this testing pattern may have had Zika virus infection in a timeframe which poses a risk of congenital Zika syndrome. Correlation with exposure history is needed.
negative	reactive	positive	The serologic testing provides evidence for Zika virus infection, likely more than 3 months prior to testing. If the Dengue PRNT is also positive or the patient has been exposed to another flavivirus, cross-reactivity is possible.	If the Dengue PRNT is also positive, it is unclear if the patient has had Zika virus infection, a dual flavivirus infection, or is merely cross-reacting to Dengue. Women who are currently or have recently become pregnant with this testing pattern may have had Zika virus infection in a timeframe which poses a risk of congenital Zika syndrome. Correlation with exposure history is needed.

Serologic Testing from January, 2016 – June, 2017

Combinations of Test Results **UNLIKELY TO REPRESENT** Zika Virus Infection

Test Results			Possible Interpretation	Conclusion
Zika IgM	MIA	Zika PRNT		
presumptive positive	reactive	negative	Cross-reactivity is likely, with the immunologic response to another flavivirus such as Dengue leading to the positive IgM and reactive MIA results.	If testing has been obtained in a timeframe in which a serologic response is expected, the patient is not likely to have been infected with Zika virus, and no further testing is required.[2]
negative	nonreactive	not performed	No serologic evidence of Zika virus infection.	If testing has been obtained in a timeframe in which a serologic response is expected, the patient is not likely to have been infected with Zika virus, and no further testing is required. [2]
negative	weakly reactive	not performed	This serologic testing pattern does not correlate with Zika virus infection. The weakly reactive MIA may indicate past infection with or vaccination against a flavivirus.	If testing has been obtained in a timeframe in which a serologic response is expected, Zika virus infection is unlikely, and no further testing is required. [2]
negative	reactive	negative	There is no serologic evidence of infection with Zika virus.	If testing has been obtained in a timeframe in which a serologic response is expected, Zika virus infection is unlikely, and no further testing is required. [2] Exposure to another flavivirus (e.g, Dengue) at an undetermined time is likely.