A Healthcare Provider's Guide to Zika Virus Laboratory Results from the NYSDOH Wadsworth Center

This document is intended to serve as a general reference guide. For assistance with interpretation of results for your specific patient, please consult with the Local Health Department (LHD) where the patient resides.

Test	Possible Results	Interpretation	Discussion/Next Steps
Zika PCR (serum or urine)[1] **Purpose/Indications:** Detects genetic material of Zika virus which is typically found in blood or urine early in infection. **Non-pregnant**, symptomatic patients will receive PCR testing when specimens are collected within 6 weeks of the onset of symptoms. **Pregnant** patients will receive PCR testing on **ALL** submitted specimens, regardless of specimen timing.[2]	'Detected'	Current infection	• **Result is confirmatory.** • **No additional testing for Zika virus is required, though results obtained through concurrent serologic testing may still be reported.**
	'Not Detected'	Indicates the patient does not have detectable virus in the specimen.	• **Zika virus infection cannot be ruled out.** • Antibody testing **(**serology) may still provide evidence of recent or prior Zika infection if specimens were collected outside the timeframe virus is found in the serum/urine (typically a week in serum and a few weeks in urine after onset of symptoms or last exposure)**.** Serology will automatically be performed on this specimen**.** • **Await serology results.**
	'Equivocal'	Result falls within the range between 'detected' and 'not detected'.	• **Obtain additional specimen(s) for repeat PCR testing.** • **Await serology results.**
	'Indeterminate due to compromised specimen'	Interpretation not possible on compromised specimens.[3] Most commonly caused by incorrect specimen transportation conditions.	• **Obtain additional specimen(s) for repeat PCR testing.** • **Await serology results.**

[1] For interpretation of results on specimens other than serum or urine (e.g., amniotic fluid, tissues, infant specimens, etc.), contact the LHD where the patient resides.

[2] Prolonged viremia (virus in the blood ≥14 days after symptom onset or ≥21 days after last exposure) has been observed among some pregnant women.

[3] Some specimens may contain impurities that interfere with or inhibit the PCR testing process such that the PCR assay is unable to provide a result.

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Zika IgM ELISA (serum) **Purpose/Indications:** Screening test to detect IgM antibodies to Zika virus and other flaviviruses[4]. Test will typically be performed on **ALL** specimens. However, Zika IgM testing is ONLY expected to be reactive approximately 2-12 weeks after infection. Results MUST be interpreted in conjunction with the Arbovirus Microsphere Immunofluorescence Assay (MIA) and/or PRN results.	'Presumptive positive'	Result suggests recent exposure to Zika virus or another flavivirus.	• Further testing via Plaque Reduction Neutralization (PRN) is required. • A single specimen PRN test will be automatically performed to help determine whether the Zika IgM positive result is due to recent Zika infection or to another flavivirus infection. • Past exposure to a flavivirus other than Zika (e.g., Dengue) may make PRN results difficult to interpret.
	'Negative'	No evidence of **recent** flavivirus exposure.	• **If the specimen was collected < 8 days after onset of symptoms or < 3 weeks after last exposure[5] additional testing is required**, as IgM might not have developed yet. If the specimen was collected during this early timeframe, collection of a repeat (convalescent) specimen[6] is recommended to rule out infection. • **If the specimen was collected ≥ 8 days after symptom onset or ≥ 3 weeks after last exposure[5],** results should be interpreted in conjunction with the Arbovirus MIA (see Arbovirus MIA section for interpretation).
	'Equivocal'	Results fall within the range between 'Presumptive Positive' and 'Negative'.	• Further testing via PRN is required. • A single specimen PRN test will be automatically performed on the specimen to help determine if it is positive for Zika and/or other flavivirus antibodies. • Collection of a repeat (convalescent) specimen[6] is recommended.
	'Inconclusive'	Unable to interpret laboratory result due to a high level of nonspecific binding in the specimen.	• Further testing via PRN is required. • A single specimen PRN test will be automatically performed on the specimen to help determine if it is positive for Zika and/or other flavivirus antibodies. • **Please collect another specimen.** However, nonspecific reactivity is commonly identified in subsequent specimens.

[4] Flavivirus is the family of viruses which includes, but is not limited to, Zika, Dengue, West Nile, and Yellow Fever viruses.

[5] Date of last exposure could refer to last date of travel to an area with active mosquito-borne transmission of Zika virus or last date of unprotected sexual contact with a partner who traveled to an area with active mosquito-borne transmission of Zika virus.

[6] When collecting specimens for convalescent testing, only a serum specimen is required. No urine collection is necessary. It is recommended that repeat (convalescent) specimens be collected approximately 3 weeks after the original (acute) specimen was collected.

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Microsphere Immunofluorescence Assay (MIA) (West Nile E polyvalent MIA) **Purpose/Indications:** Screening test to detect total antibodies (IgM, IgG & IgA) to flaviviruses.[4] Test will typically be performed on **ALL** serum specimens. Results should be interpreted with the Zika IgM ELISA.	'Reactive'	Result suggests exposure to a flavivirus at an undetermined time.	• Further testing via PRN is required. A single specimen PRN test will be automatically performed on the specimen to help determine if it is positive for Zika or other flavivirus antibodies. • Past exposure to a flavivirus other than Zika (e.g., dengue) may make PRN results difficult to interpret.
	'Nonreactive'	No evidence of flavivirus exposure.	• **If the specimen was collected < 8 days after onset of symptoms or < 3 weeks after last exposure[5], additional testing is required**, as antibodies might not have developed yet. If the specimen was collected during this early timeframe, collection of a repeat (convalescent) specimen[6] is recommended to rule out infection. • **If the specimen was collected ≥ 8 days after symptom onset OR ≥ 3 weeks after last exposure[5]**, result suggests no exposure to a flavivirus. If the Zika IgM ELISA and PCR are also negative, laboratory testing does not detect any evidence of Zika infection. No additional testing is required.
	'Indeterminate'	Unable to interpret laboratory result.	• **Further testing via PRN may be done based on the Zika IgM ELISA result** (see Zika IgM ELISA section for interpretation). • **If Zika IgM ELISA is negative, a repeat (or convalescent)[6] specimen may be required.**
	'Weakly reactive'	Results close to cutoff value of the assay.	• **Further testing via PRN may be done based on the Zika IgM ELISA result** (see Zika IgM ELISA section for interpretation). • **Weakly reactive results *alone* do not correlate with a serologic response to Zika virus infection.** A repeat (or convalescent)[6] specimen may be required**.**

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Plaque Reduction Neutralization (PRN) Testing (serum) **Purpose/Indications:** Identifies neutralizing antibodies to viruses. Requires virus to grow in culture which is then exposed to the patient's antibodies found in serum to see if they neutralize the virus. Note, previous exposure to a flavivirus may make results difficult to interpret. If Zika IgM ELISA OR Arbovirus MIA are positive or equivocal, a PRN will automatically be performed. Past exposure to a flavivirus other than Zika (e.g., Dengue) may make PRN results difficult to interpret.	'Positive' for Zika virus	Results indicate the presence of Zika virus neutralizing total antibodies.	• Suggests Zika virus infection at an undetermined time. • **No further Zika testing is required.**
	'Positive' for Dengue virus	Results indicate the presence of Dengue virus neutralizing total antibodies.	• Suggests Dengue infection at an undetermined time. • **If the specimen was collected ≥3 weeks after last exposure[5], then no further dengue testing is required.**
	'Positive' for Dengue and Zika viruses	Results indicate the presence of Dengue and Zika virus neutralizing total antibodies.	• This result can occur in specimens from patients who have been infected with Zika and/or Dengue virus in the past OR with cross reactivity between Zika and Dengue viruses. • **Zika virus infection cannot be ruled out.** • **No further testing is required.**
	'Negative' for Zika virus (regardless of dengue virus result)	Result suggests no evidence of Zika virus infection.	• **If the specimen was collected ≥3 weeks after last exposure[5], then no further Zika testing is required.** • **If Zika virus infection is still clinically suspected, consider ordering Zika serology on another specimen[6] collected approximately 3 weeks after the original (acute) specimen.**