

LABSTRACT – May 2019

Zika Virus Serology Testing: Implementation of Screening Serology at Public Health Ontario Laboratory

Audience

Health care providers caring for patients suspected of having Zika virus infection and laboratories involved in submission of specimens for Zika virus testing.

Overview

Beginning May 6, 2019, Public Health Ontario (PHO) Laboratory will commence performing Zika virus IgM and IgG serology, using the following commercial assays: InBiOS ZIKV Detect™ 2.0 IgM Capture ELISA (MAC-ELISA) and Euroimmun Anti-Zika Virus ELISA (IgG). This serology testing was previously provided by the National Microbiology Laboratory (NML), Winnipeg.

Specimens that screen positive or inconclusive for IgM or IgG antibodies at PHO Laboratory will be forwarded to NML for confirmatory plaque reduction neutralization test (PRNT), as per the current recommended Zika virus serology testing algorithm.

This transition to serology testing being performed by PHO Laboratory instead of NML will enable shorter turnaround time for screening serology results, facilitating earlier diagnosis for patients being tested for Zika virus infection.

Background information

Zika virus, a flavivirus first detected in Uganda in 1947, emerged in 2015 in South and Central America, resulting in a large multinational outbreak. Clinical manifestations, which only occur in 20% of persons infected, include low grade fever, maculopapular rash, conjunctivitis and arthralgia.

In late 2015, associations were made between Zika virus infection and both Guillain-Barré Syndrome and congenital infection (Congenital Zika Syndrome), the latter characterized by microcephaly, intracranial calcifications, other brain anomalies, and eye abnormalities.

Laboratory testing assays for the detection and diagnosis of Zika virus infection include molecular testing (by PCR) and serology. Since March 2016, PCR is being performed at the PHO Laboratory; a positive PCR

is considered confirmatory. Serology testing is performed by using two assays for initial screening, one for Zika virus IgM and another assay for IgG. If either test is reactive or inconclusive, a more specific, PRNT is done for serological confirmation. Confirmatory serology is required due to the high cross reactivity among different flaviviruses (e.g. Zika virus, dengue virus, and West Nile virus) in serological IgM and IgG screening assays.

Zika Virus Serology Screening Assays and Testing Algorithm

PHO Laboratory will be implementing the following assays for Zika virus serology screening:

- 1. InBios ZIKV Detect™ 2.0 IgM Capture ELISA (MAC-ELISA)** – possible results include Zika virus reactive, Zika virus indeterminate (antibody status inconclusive), flavivirus (non-Zika) reactive, or Zika virus non-reactive.
- 2. Euroimmun Anti-Zika Virus ELISA (IgG)** – possible results include Zika virus IgG reactive, indeterminate (antibody status inconclusive) or non-reactive.

Specimens which are reactive or inconclusive in either of the above tests may indicate a recent or previous flavivirus infection. All IgM and/or IgG reactive or inconclusive specimens will be forwarded to NML for confirmatory Zika virus PRNT.

For detailed information on the Zika virus testing at PHO Laboratory, including testing indications, specimen collection, submission guidance and the Zika virus testing algorithm, please refer to the PHO Laboratory [Zika Virus Test Information Sheet](#).

There is no change in the current algorithm being used for Zika virus testing, which is based on current Canadian guidelines, featured in the [Canadian Zika Virus Prevention and Treatment Guidelines](#), developed by the [Committee to Advise on Tropical Medicine and Travel \(CATMAT\)](#). Additional information provided by the Public Health Agency of Canada on Zika virus, including laboratory testing, is available within the document [Zika virus: For Health Professionals](#).

Test Performance

During PHO Laboratory's verification, InBios ZIKV Detect™ 2.0 IgM Capture ELISA in combination with the Euroimmun Anti-Zika Virus ELISA (IgG) demonstrated a sensitivity of 100% for detection of Zika virus antibodies when compared to PRNT as the gold standard. In an evaluation by NML, the InBios ZIKV Detect IgM Capture ELISA (an earlier version of the assay PHO Laboratory is implementing) in combination with the Euroimmun Anti-Zika Virus ELISA (IgG) demonstrated sensitivity of 97.2%, and specificity of 96.0% when compared to PRNT. Cross-reactivities of InBios ZIKV Detect IgM Capture ELISA and Euroimmun Anti-Zika Virus ELISA (IgG) were 71.5% and 50.0%, respectively, with sera positive for dengue virus antibodies (see reference #1 below). Based on their evaluation, NML has recommended

that provincial laboratories use these two assays in combination to perform Zika virus serology screening. The estimated turnaround time for Zika virus screening serology at PHO Laboratory is up to 5 days.

References

1. Establishment of a comprehensive and high throughput serological algorithm for Zika virus diagnostic testing. *Diagn Microbiol Infect Dis*. 2019 Jan 14. pii: S0732-8893(18)30423-1. doi: 10.1016/j.diagmicrobio.2019.01.004. [Epub ahead of print]. Mendoza EJ, Makowski K, Barairo N, Holloway K, Dimitrova K, Sloan A, Vendramelli R, Ranadheera C, Safronetz D, Drebot MA, Wood H.
2. [Zika Virus Test Information Sheet](#).
3. [Canadian Zika Virus Prevention and Treatment Guidelines](#),
4. [Zika virus: For Health Professionals](#)
5. [CDC Zika Virus Web Page](#)

For further information

- Contact the PHO Customer Service Centre at 416-235-6556 or 1-877-604-4567 (toll-free), or by email at customerservicecentre@oahpp.ca
- For PHO Laboratory specimen collection information and previous Lababstracts, refer to [publichealthontario.ca/test directory](http://publichealthontario.ca/test-directory)
- The current version of the PHO Laboratory General Test Requisition and other forms are available at publichealthontario.ca/Requisitions
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