

Wendi Kuhnert, Ph.D.
Robert Lanciotti, Ph.D.
Emergency Operation Center Laboratory Task Force
Centers for Disease Control and Prevention
1600 Clifton Road NE
Atlanta, GA 30333

Scott Becker, MS
Executive Director
Association for Public Health Laboratories
8515 Georgia Avenue, Suite 700
Silver Spring, MD 20910

RE: Concerns regarding limited capacity for Zika virus Plaque Reduction Neutralization Test

Dear Dr. Kuhnert, Dr. Lanciotti, and Mr. Becker:

The American Society for Microbiology (ASM) and Pan American Society for Clinical Virology (PASCV) are committed to providing education and assistance to their members regarding laboratory testing during public health emergencies.

Clinical laboratories are concerned with the current turnaround time for Plaque Reduction Neutralization Test (PRNT) results. As you are aware, serological testing is an important part of the diagnosis of patients at risk for Zika virus infection, particularly pregnant patients. RNA testing has an important role, but that role is limited, due the relatively brief period of viremia and viruria, and the fact that many returning travelers and immigrants present after viral nucleic acid has been cleared from these specimens. Requests for Zika virus testing are likely to increase for the foreseeable future. The range of Zika virus in the Americas continues to expand, and increasing numbers of pregnant women in the U.S. are at risk for Zika virus infection and will need serologic testing. For these reasons and those listed below, we feel that rapid access to confirmatory PRNT testing is essential for proper diagnosis and management of patients with suspect Zika virus infection.

1. IgM ELISAs have extensive cross-reactivity with other flaviviruses, and therefore, the current serologic testing algorithm relies on the PRNT for final confirmation. While

PRNT may also show cross-reactivity with closely related flaviviruses, titers can help to differentiate these viruses in some cases, particularly when the patient does not have the appropriate travel or exposure history.

Requested action: We are concerned that prior exposure to West Nile virus could cause false-positive results by the Zika IgM capture ELISAs as well as PRNT. Does the CDC have data that it could provide on the extent of cross-reactivity of Zika IgM capture ELISA and PRNT with anti-WNV antibody?

2. Due to the cost and technical complexity of PRNT, it is currently available in select CLIA-certified, public health laboratories. This limited capacity results in large testing volumes and delay in result turnaround time. Results are often not available for 4 weeks, which is especially problematic in high risk populations, such as pregnant women. Increased PRNT capacity is urgently needed to shorten the turnaround time for test results.

Requested action: ASM and PASCV strongly urge the CDC and APHL to identify and support additional laboratory capacity to perform PRNT. Collaborative agreements could be established with CLIA-certified laboratories with current capability to perform PRNT. With support from the CDC, these additional laboratories could increase their PRNT capacity, reduce the testing burden on CDC, and decrease the turnaround time for test results. Laboratories providing PRNT would need to pass a proficiency testing assessment. Furthermore, collaborative agreements could define a process by which specimens flow between local laboratories and PRNT laboratories and provide standardized reporting guidance.

We appreciate your time and attention to this important matter. We hope that the CDC and APHL will consider supporting the expansion of PRNT capacity. Our organizations represent thousands of professionals in clinical laboratory medicine and public health. Providing rapid test results for emerging infectious disease pathogens, such as Zika virus, is critical for clinical laboratory professionals. This will help clinicians make more timely decisions on patient care.

Please send any requests for clarification or additional comments to Kimberly Walker (kwalker@asmusa.org) for immediate attention.

Sincerely,

Alexandra Valsamakis, M.D., Ph.D.
President, Pan American Society for Clinical Virology

Susan E. Sharp, Ph.D., D(ABMM)
President, American Society for Microbiology

cc:

Rima Khabbaz, M.D.
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