Fact Sheet for Healthcare Providers: Interpreting TaqPath™ Zika Virus Kit (ZIKV) Test Results
August 2, 2017

Dear Healthcare Provider:

The United States (U.S.) Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to authorize the use of the TaqPath™ Zika Virus Kit (ZIKV) for the *in vitro* qualitative detection of Zika virus with specified instruments. This assay tests for Zika virus RNA in human serum and urine (collected alongside a patient-matched serum specimen). Testing should be conducted on specimens from people who meet Centers for Disease Control and Prevention (CDC) Zika clinical and/or epidemiological criteria for testing and be performed by laboratories in the U.S. that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high complexity tests, or by similarly qualified non-U.S. laboratories (see www.cdc.gov/zika/hc-providers/index.html). This test should be performed according to CDC's procedures for Zika testing (See http://www.cdc.gov/zika/laboratories/lab-guidance.html).

The information in this Fact Sheet is to inform you of the significant known and potential risks and benefits of the emergency use of the TaqPath™ Zika Virus Kit (ZIKV) (See www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm).

Why is this test needed at this time?

Public health officials have determined that Zika virus poses a potential public health emergency. Current information on Zika virus infection for healthcare providers, including case definitions and information about signs and symptoms, is available at www.cdc.gov/zika/hc-providers/index.html. All information and guidance, including those on Zika virus laboratory testing, may change as more data is gathered on this virus. Please check the CDC's Zika virus website regularly for the most current information (www.cdc.gov/zika/index.html).

The U.S. Secretary of Health and Human Services (HHS) has declared that circumstances exist to justify the emergency use of *in vitro* diagnostic tests for the detection of Zika virus and/or diagnosis of Zika virus infection. This EUA will terminate when the HHS Secretary's declaration terminates, unless FDA revokes it sooner.

At this time, there are no FDA approved/cleared tests available that can detect Zika virus in clinical specimens in the U.S. Therefore, Thermo Fisher Scientific has developed the TaqPath™ Zika Virus Kit (ZIKV) to detect evidence of Zika virus infection.

When should the TaqPath™ Zika Virus Kit (ZIKV) test be performed?

If Zika virus infection is suspected based on CDC's published clinical and/or epidemiological criteria, the TaqPath™ Zika Virus Kit (ZIKV) may be ordered and should be performed according to the CDC-issued guidance (http://www.cdc.gov/zika/laboratories/lab-guidance.html). The algorithms included within the guidance illustrate the appropriate Zika

testing approach based on the presence of signs and symptoms, pregnancy status, and the time between onset of symptoms or suspected exposure and specimen collection.

As disease manifestations of dengue and chikungunya virus infections can resemble those of Zika virus infection, additional testing for these viruses should be considered to aid in differentiating dengue and chikungunya virus infections from Zika virus infections or identifying possible co-infections. Please contact your state or local health department to facilitate testing.

Zika virus RNA is typically detectable in serum during the acute phase of infection (generally up to 7 days post-symptom onset). Zika virus RNA has been detected in serum up to 13 days post-symptom onset in non-pregnant patients, and up to 62 days post-symptom onset in pregnant patients. In addition, Zika virus RNA has been detected up to 53 days after the last known possible exposure in an asymptomatic pregnant woman (references 3-4).

As of August 2, 2017, serum is the primary diagnostic specimen for Zika virus RNA and serologic testing, and should be the priority specimen for collection and TaqPath™ Zika Virus Kit (ZIKV) testing. The TaqPath™ Zika Virus Kit (ZIKV) can also be used to test urine (collected alongside a patient-matched serum specimen). While some data from the U.S. suggests that Zika virus RNA may be detectible for longer periods of time in urine than in serum, persistence of Zika virus RNA in urine is not well characterized.

Along with serum specimens, healthcare providers are strongly encouraged to collect and submit additional recommended specimens (per CDC guidance), such as urine, to provide additional opportunities for detection of Zika virus infection. However, a patient-matched serum specimen should always be submitted with a urine specimen to facilitate reflex testing as outlined in the current CDC-issued algorithm (http://www.cdc.gov/zika/laboratories/lab-guidance.html).

Specimens should be collected with appropriate infection control precautions and according to the manufacturer's instructions for the specimen collection device, handling, and storage. Serum should be collected in serum separator tubes and centrifuged after collection to reduce the likelihood of hemolysis. Additional guidance for collection of body fluid specimens for Zika diagnostic testing may be found at: http://www.cdc.gov/zika/laboratories/test-specimens-bodyfluids.html.

If your patient has been symptomatic but is beyond the recommended window for TaqPath™ Zika Virus Kit (ZIKV) testing, serologic testing for antibodies to Zika virus may be helpful.

What does it mean if the specimen tests positive for Zika virus RNA?

A positive test result for Zika virus from the TaqPath™ Zika Virus Kit (ZIKV) indicates that RNA from Zika virus was detected in the patient's specimen. A positive test result in any authorized specimen collected from a patient is indicative of Zika virus infection. Laboratory test results should always be considered in the context of clinical observations, epidemiological data, and travel history in making a final diagnosis and patient management

decisions. For guidance on Zika virus, please refer to: www.cdc.gov/zika/hc-providers/index.html.

The TaqPath™ Zika Virus Kit (ZIKV) has been designed to minimize the likelihood of false positive test results. Cross-reactivity of any of the components of this test resulting in false positive results is not expected. However, in the event of a false positive result, risks to patients could include any or all of the following: impaired ability to detect and receive appropriate medical care for the true source of symptoms; in the case of pregnant women, an unnecessary increase in the monitoring of a woman's pregnancy; other unintended adverse effects.

In the U.S. and its territories, Zika virus infection and disease (non-congenital and congenital) are nationally notifiable conditions and should be reported to the local or state health department. For guidance on Zika virus, please refer to: http://www.cdc.gov/zika/hc-providers/index.html.

While there is an established association between Zika virus infection during pregnancy and microcephaly, detection of Zika virus RNA in specimens collected from a pregnant woman does not provide definitive information about the health of her fetus and does not indicate imminent harm to her fetus. If a pregnant woman is diagnosed with Zika virus infection based on detection of Zika virus RNA, issues such as timing of infection during the course of pregnancy, presence of symptoms, and other factors may help determine the risk to her fetus.

What does it mean if the specimen tests negative for Zika virus RNA?

A negative test result for Zika virus in the specimen means that RNA from Zika virus is not present in the specimen above the test's limit of detection. However, a negative result does not rule out Zika virus infection and should not be used as the sole basis for treatment or patient management decisions.

It is especially important to note that negative results in urine, which is not the recommended primary diagnostic specimen type, do not necessarily mean that a person is not infected. When results are negative for urine, the patient-matched serum specimen should be tested as outlined in the current CDC-issued algorithm (http://www.cdc.gov/zika/laboratories/lab-guidance.html).

A negative TaqPath™ Zika Virus Kit (ZIKV) result does not exclude the possibility of Zika virus infection. In serum, negative rRT-PCR test results are known to occur in Zika virus infection, particularly if testing is conducted outside the acute phase of infection (generally up to 7 days post symptom-onset) or in asymptomatic people. When diagnostic testing is negative, the possibility of a false negative result should be considered in the context of a patient's recent exposures and the presence of clinical signs and symptoms consistent with Zika virus infection. Such patients should have antibody testing performed on their serum sample, as per the CDC testing algorithm (found at http://www.cdc.gov/zika/laboratories/lab-guidance.html).

Absence of laboratory evidence of Zika virus infection cannot definitively rule out Zika virus infection in persons with epidemiological risk factors. All results should be considered in the context of clinical signs and symptoms, exposure risk, and time since symptom onset, or in the absence of symptoms, time since exposure.

Guidance for healthcare providers, including those caring for pregnant women and women of reproductive age with possible Zika virus exposure, is available on the CDC website: www.cdc.gov/zika/hc-providers/index.html.

Reporting Adverse Events

You should report adverse events, including problems with test performance or results, to MedWatch at http://www.fda.gov/Safety/MedWatch/default.htm, by submitting the online FDA Form 3500 for Health Professionals (available at https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home) or by calling 1-800-FDA-1088.

All patients should receive the Fact Sheet for Patients: Understanding Results from the TaqPath™ Zika Virus Kit (ZIKV)

Contact Information for the Manufacturer:
Thermo Fisher Scientific
6055 Sunol Boulevard
Pleasanton, CA 94566
Phone: 800.955-6288

Contact Information for Technical Assistance for the TaqPath™ Zika Virus Kit (ZIKV):
E-Mail: techsupport@lifetech.com

Any significant new findings that negatively impact the performance of the test and that are observed during the course of the emergency use of the TaqPath™ Zika Virus Kit (ZIKV) will be made available on the Thermo Fisher Scientific website: http://www.thermofisher.com

References

1. Rasmussen, S.A., Jamieson, D.J., Honein, M.A., Petersen, L.R. Zika Virus and Birth Defects – Reviewing the Evidence for Causality. New England Journal of Medicine, May 19, 2016; 374:1981-1987. DOI: 10.1056/NEJMsr1604338.
2. CDC Website - http://www.cdc.gov/zika/
3. Driggers, R.W., et al. Zika virus Infection with Prolonged Maternal Viremia and Fetal Brian Abnormalities. New England Journal of Medicine, June 2, 2016; 374:2142-2151. DOI: 10.1056/NEJMoa1601824.
4. Meaney-Delman et al. Prolonged Detection of Zika Virus RNA in Pregnant Women. Obstetrics and Gynecology, 2016, 128:724-730. DOI: 10.1097/AOG.0000000000001625.