Fact Sheet for Health Care Professionals: Interpreting CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Test Results

June 10, 2014

Dear Health Care Professional:

If you have received this Fact Sheet, it is because the Secretary of Health and Human Services (HHS) has declared that circumstances exist to justify authorization of emergency use of *in vitro* diagnostic (IVD) tests for the detection of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) because of a significant potential for a public health emergency involving this virus. Based on the HHS declaration, the Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) for the Centers for Disease Control and Prevention (CDC) Novel Coronavirus 2012 Real-time RT-PCR Assay (CDC NCV-2012 rRT-PCR Assay) to test for the presumptive presence of MERS-CoV in the following clinical specimens: upper respiratory specimens, such as nasopharyngeal swabs (NPS) and oropharyngeal swabs (OPS); lower respiratory specimens, such as bronchoalveolar lavage (BAL), bronchial wash (BW), tracheal aspirate (TA), and sputum; serum; and stool. This EUA will terminate when the Secretary's declaration terminates, unless it is revoked sooner.

This Fact Sheet contains the minimum information necessary to inform you of the significant known and potential risks and benefits of the emergency use of the CDC NCV-2012 rRT-PCR Assay. For more information on this EUA, please see FDA's website (www.fda.gov).

This EUA is needed because, at this time, no FDA-approved/cleared tests that identify the existence of MERS-CoV in clinical specimens are available in the United States. Therefore, CDC has developed this test to detect MERS-CoV infections. Current information on MERS, including case definitions and infection control guidelines, is available at http://www.cdc.gov/coronavirus/mers/index.html. All information and guidelines, including those on MERS-CoV laboratory testing, may change as we continue to learn more about this virus. Please check CDC's MERS website regularly for the most current information.

If infection with MERS-CoV is suspected based on current clinical and/or epidemiological screening criteria recommended by public health authorities, the CDC NCV-2012 rRT-PCR Assay test should be ordered only to presumptively diagnose MERS. This test is authorized for use with both upper respiratory specimens (such as NPS and OPS), lower respiratory specimens (such as BAL, BW, TA, and sputum), serum, and stool. To date, little is known about pathogenic potential and transmission dynamics of MERS-CoV. To increase the likelihood of detecting infection, it is recommended to collect multiple specimens from different sites at different times after symptom onset, if possible. As of May 2014, consider lower respiratory tract, NP/OP swab (combined), and serum specimens a priority for collection and testing. Specimens should be collected with appropriate infection control precautions (http://www.cdc.gov/coronavirus/mers/guidelines-clinical-specimens.html and http://www.cdc.gov/coronavirus/mers/guidelines-lab-biosafety.html), following CDC guidance

for case investigation and specimen collection and according to the manufacturer's instructions for the specimen collection device, and sent to a qualified laboratory for analysis.

What are the symptoms of Middle East Respiratory Syndrome?

Most confirmed cases of MERS developed severe acute respiratory illness with symptoms of fever, cough, and shortness of breath. Some confirmed cases experienced mild respiratory illness or no symptoms. From April 2012 to May 2014, approximately 30 percent of confirmed MERS cases have died.

In May 2014, public health laboratories identified the first two human cases of MERS in the United States using this test. Public health officials have determined that MERS-CoV has a potential to spread to the United States and pose risks for the public health. All MERS cases confirmed through May 2014 have been directly or indirectly linked through residence in or travel to the Arabian Peninsula and surrounding countries, particularly the Kingdom of Saudi Arabia and the United Arab Emirates.

What does it mean if the specimen tests positive for MERS-CoV?

A positive test result from the CDC NCV-2012 rRT-PCR Assay indicates that the patient is presumptively infected with MERS-CoV. The test does not indicate the stage of infection. Laboratory test results should always be considered in the context of clinical observations and epidemiologic data in making a final diagnosis. For guidelines on MERS, please refer to http://www.cdc.gov/coronavirus/mers/index.html.

Although a very small chance exists that this test can give a positive result that is wrong (false positive), it is unlikely. The CDC NCV-2012 rRT-PCR Assay has been designed to minimize the likelihood of false positive test results. However, in the event of a false positive result, risks to patients could include any or all of the following: a recommendation for quarantine of household or other close contacts, patient isolation that might limit contact with family or friends, the ability to work, the impaired ability to detect and receive appropriate medical care for the true infection causing the symptoms, unnecessary prescription of a treatment or therapy, or other unintended adverse effects. Any positive test result for MERS-CoV should be immediately reported to and discussed with your local and state health departments.

What does it mean if the specimen tests negative for MERS-CoV?

A very small chance exists that this test can give a negative result that is wrong (false negative), meaning a patient could still have MERS-CoV even though the test is negative. Negative results do not rule out MERS-CoV infection, and should not be used as the sole basis for treatment or other patient management decisions. The clinical features of the illness and the type and risk of exposure are the keys to making patient management and isolation decisions. A negative CDC NCV-2012 rRT-PCR Assay test result should not be interpreted as demonstrating that the patient does not have MERS-CoV infection. While expected to be very sensitive, there is limited experience testing patient samples and so the actual sensitivity of the test in diagnosing MERS-CoV, and the frequency of false negatives, is not clearly understood. In addition, the late

collection of a specimen relative to symptom onset and/or improper specimen collection and handling can result in a false negative test result. For these reasons, the possibility of a false negative result should especially be considered if the patient's recent exposures or clinical presentation indicate MERS-CoV infection is likely, and diagnostic tests for other causes of acute respiratory illness are negative. Risks to a patient of a false negative result include: delayed treatment, potential lack of treatment, or stopping treatment too soon.

Some individuals may meet CDC's testing criteria due to certain epidemiological risk factors (for example, close contact with a confirmed MERS case), but may not demonstrate clinical signs and symptoms associated with MERS. Negative results for these individuals do not rule out future illness and do not demonstrate that an individual is not infectious. Negative results with the NCV-2012 rRT-PCR assay do not preclude infection with MERS-CoV. Persons who meet epidemiological criteria and test negative by the NCV-2012 rRT-PCR should still monitor their health for the full term recommended by CDC.

Reporting Adverse Events

You should report adverse events, including problems with test performance or results, to MedWatch at www.fda.gov/medwatch, by submitting a MedWatch Form 3500 (available at http://www.fda.gov/medwatch/safety/FDA-3500_fillable.pdf) or by calling 1-800-FDA-1088.

Give patients the *Fact Sheet for Patients: Understanding Results from the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay.*

Give persons tested due to epidemiological risk factors who do not display clinical signs and symptoms associated with MERS the *Fact Sheet for Contacts of MERS Cases: Understanding Results from the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay.*

Contact Information for the Manufacturer:

Eileen Schneider, MD, MPH
Respiratory Virus and Picornavirus Team
CDC/NCIRD/DVD/EB
1600 Clifton Road, MS-A34
Atlanta, Georgia, USA, 30333
Office phone: 404.639.5345
Cell phone: 404.784.0980
Fax: 404.315.4932
E-mail: ees2@cdc.gov

Any significant new findings observed during the course of the emergency use of the NCV-2012 rRT-PCR Assay will be made available at http://www.cdc.gov/coronavirus/mers/index.html.