Fact Sheet for Health Care Providers: Interpreting RealStar® MERS-CoV RT-PCR Kit U.S. Test Results

February 12, 2016

Dear Health Care Provider:

The U.S. Food and Drug Administration (FDA) has issued an Emergency Use Authorization (EUA) to authorize the use of the RealStar® MERS-CoV RT-PCR Kit U.S. for the *in vitro* qualitative detection of RNA from the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). It is intended for use with:

- **lower respiratory specimens** (tracheal aspirate/tracheal secretions) from **individuals with signs and symptoms** of infection with MERS-CoV in conjunction with epidemiological risk factors for the presumptive detection of MERS-CoV; and,

- **nasopharyngeal swabs** from **asymptomatic individuals** suspected of exposure to MERS-CoV based on epidemiological risk factors (e.g., contact with a probable or confirmed MERS-CoV case, history of travel to geographic locations where MERS-CoV cases were detected, or other epidemiologic links for which MERS-CoV testing may be indicated) for the presumptive detection of MERS-CoV.

FDA issued this EUA based on data submitted by altona Diagnostics GmbH to FDA and on the U.S. Secretary of Health and Human Services' (HHS) declaration that circumstances exist to justify the authorization of the emergency use of *in vitro* diagnostic tests for the detection of MERS-CoV. This EUA will terminate when the HHS Secretary's declaration terminates, unless FDA revokes it sooner.

The information in this Fact Sheet is the minimum necessary to inform you of the significant known and potential risks and benefits of the emergency use of the RealStar® MERS-CoV RT-PCR Kit U.S. For more information on this EUA, please see FDA's website at www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm.

Why is this test needed at this time?

At this time, no FDA-approved/cleared tests that identify the existence of MERS-CoV in clinical specimens are available. altona Diagnostics GmbH has developed the RealStar® MERS-CoV RT-PCR Kit U.S. to detect MERS-CoV infections in the specified population.

If infection with MERS-CoV is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, the RealStar® MERS-CoV RT-PCR Kit U.S. should be ordered only to presumptively diagnose MERS-CoV infection. This test is authorized for use with lower respiratory specimens (tracheal aspirate/tracheal secretions) from symptomatic patients. 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.

This test is also authorized for use with nasopharyngeal swabs taken from asymptomatic individuals suspected of exposure to MERS-CoV (e.g., patient contacts or individuals who traveled from countries where this infection is relatively frequent). As of January 2016, little is known about the pathogenic potential of MERS-CoV. Transmission is mainly through close contact and no sustained community transmission has been observed.

All 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 CLIA High Complexity Laboratory or similarly qualified non-U.S. laboratories for analysis.

Current information on MERS-CoV, including case definitions and infection control guidelines, is available at 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-CoV website regularly for the most current information.

What are the symptoms of MERS-CoV Infection?

Most confirmed cases of MERS-CoV infection developed severe acute respiratory illness with symptoms of fever, cough, and shortness of breath. MERS-CoV in humans could vary in severity from mild to severe. Very few confirmed cases to date experienced mild respiratory illness. As of January 2016, two individuals in the U.S. have tested positive for MERS-CoV infection, one in Indiana, the other in Florida—both in May 2014—while more than 750 have tested negative. However, public health officials have determined that MERS-CoV has a potential to spread to the United States and pose risks for the public health.

From April 2012 to January 2016, all cases of MERS-CoV have been directly or indirectly linked through travel to or residence in the Arabian Peninsula and surrounding countries, particularly the Kingdom of Saudi Arabia and the United Arab Emirates. Starting in May 2015 there have been additional cases linked to an outbreak in South Korea. This outbreak stems from a single traveler from the Arabian Peninsula.

How does the virus spread?

Since MERS-CoV causes respiratory illness, the virus can be found in an infected person's respiratory secretions, such as saliva, nasal mucus, or sputum. MERS-CoV likely spreads from person to person when an infected person coughs, sneezes, or touches a surface that is then touched by others.

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

A positive test result from the RealStar® MERS-CoV RT-PCR Kit U.S. indicates that the individual 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 further information on MERS-CoV, please refer to 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 RealStar® MERS-CoV RT-PCR Kit U.S. has been designed to minimize the likelihood of false positive test results. However, in the event of a false positive result, risks to individuals could include any or all of the following: a recommendation for quarantine of household or other close contacts, individual isolation that might limit contact with family or friends, limitations on one's 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 negative test presumes that MERS-CoV was not present at the detection level of the assay. However, negative results do not preclude MERS-CoV infection, and should not be used as the sole basis for treatment, public health, or other individual management decisions. The clinical features of the illness and the type and risk of exposure are the keys to making individual management decisions. A negative RealStar® MERS-CoV RT-PCR Kit U.S. test result should not be interpreted as demonstrating that the individual does not have a MERS-CoV infection.

A very small chance exists that this test can give a negative result that is wrong (false negative), meaning an individual could still have MERS-CoV infection even though the test is negative. While the RealStar® MERS-CoV RT-PCR Kit U.S. test is expected to be very sensitive, the late collection of a specimen relative to symptom onset, collection of specimens prior to symptoms 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 be considered—especially if the individual's recent exposures or clinical presentation indicate MERS-CoV infection is likely, and diagnostic tests for other causes of acute respiratory illness are negative. A false positive or a false negative test result has the potential to delay a correct diagnosis.

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 www.fda.gov/Safety/MedWatch/HowToReport/DownloadForms/default.htm)
or by calling 1-800-FDA-1088.

Give patients the *Fact Sheet for Patients: Understanding Results from the RealStar® MERS-CoV RT-PCR Kit U.S.*

Give persons tested due to epidemiological risk factors who do not display clinical signs and symptoms associated with MERS the *Fact Sheet for Asymptomatic Individuals*

Suspected of Exposure to MERS-CoV Cases: Understanding Results from the RealStar® MERS-CoV RT-PCR Kit U.S.

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Any significant new findings observed during the course of the emergency use of the RealStar® MERS-CoV RT-PCR Kit U.S. will be made available at www.altona-diagnostics.com.