

Fact Sheet for Health Care Providers: Interpreting CDC's Enterovirus D68 2014 Real-time RT-PCR Assay (EV-D68 2014 rRT-PCR) Results

May 12, 2015

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 Centers for Disease Control and Prevention's (CDC) Enterovirus D68 2014 Real-time RT-PCR Assay (EV-D68 2014 rRT-PCR) for the *in vitro* qualitative detection of RNA from the enterovirus D68 strains detected in North America in 2014 (EV-D68). It is intended for use with upper respiratory specimens (such as nasopharyngeal (NP) swabs, oropharyngeal (OP) swabs, dual NP/OP swabs, and/or nasal washes) and sera in conjunction with patient-matched upper respiratory specimen(s) from individuals with signs and symptoms of EV-D68 infection and/or epidemiologic risk factors by qualified laboratories designated by CDC.

FDA issued this EUA based on data submitted by CDC to FDA and on the U.S. Secretary of Health and Human Services' (HHS) declaration that circumstances exist to justify the emergency use of *in vitro* diagnostic tests for the detection of EV-D68. 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 EV-D68 2014 rRT-PCR. For more information on this EUA, please see FDA's website at <http://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 can detect EV-D68 in clinical specimens are available. CDC has developed the EV-D68 2014 rRT-PCR to detect EV-D68 infections in the specified population.

If infection with EV-D68 is suspected based on current clinical and/or epidemiological screening criteria recommended by public health authorities, the EV-D68 2014 rRT-PCR should be ordered only to presumptively diagnose EV-D68 infection. This test is authorized for use with upper respiratory specimens. As of December 2014, consider upper respiratory specimens a priority for collection and testing for patients presenting with respiratory symptoms and suspected of EV-D68 infection. Viremia has been detected in a small number of individuals and serum may be collected in addition to upper respiratory specimens. Expected diagnostic yield of sera is low, and therefore sera may only be tested in conjunction with patient-matched upper respiratory specimen(s). Specimens should be collected with appropriate infection control precautions (see <http://www.cdc.gov/non-polio-enterovirus/lab-testing/specimen-collection.html> and <http://www.cdc.gov/non-polio-enterovirus/hcp/EV-D68-hcp.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 designated by CDC for analysis.

Current information on EV-D68, including case definitions and infection control guidelines, is available at: <http://www.cdc.gov/non-polio-enterovirus/about/ev-d68.html>. All information and guidelines, including those on EV-D68 laboratory testing, may change as the U.S. outbreak evolves. Please check the CDC EV-D68 website regularly for the most current information.

What are the symptoms of EV-D68?

Mild symptoms may include runny nose, sneezing, cough, and body and muscle aches. Severe symptoms may include wheezing and difficulty breathing. Some patients with EV-D68 infection developed severe acute respiratory illness with symptoms of fever, cough, and shortness of breath. Other patients experienced milder respiratory illnesses or no symptoms. Many patients with EV-D68 infection had a history of asthma or wheezing.

From mid-August to January 15, 2015, a total of 1,153 confirmed cases of respiratory illness caused by EV-D68, including 12 deaths, have been identified in the United States. These cases have occurred across 49 states and the District of Columbia. Almost all of the confirmed cases have been identified among children.

How does the virus spread?

Since EV-D68 causes respiratory illness, the virus can be found in an infected person's respiratory secretions, such as saliva, nasal mucus, or sputum. EV-D68 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 EV-D68?

A positive test result from the EV-D68 2014 rRT-PCR indicates that the patient is presumptively infected with EV-D68. 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.

Although a very small chance exists that this test can give a positive result that is wrong (false positive), it is unlikely. The EV-D68 2014 rRT-PCR has been designed to minimize the likelihood of false positive test results.

What does it mean if the specimen tests negative for EV-D68?

A negative test presumes that EV-D68 was not present at the detection level of the assay. However, negative results do not preclude EV-D68 infection, and should not be

used as the sole basis for treatment, public health, 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 decisions. A negative EV-D68 2014 rRT-PCR test result should not be interpreted as demonstrating that the patient does not have an EV-D68 infection. A very small chance exists that this test can give a negative result that is wrong (false negative), meaning a patient could still have EV-D68 infection even though the test is negative. While the EV-D68 2014 rRT-PCR 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 patient’s recent exposures or clinical presentation indicate EV-D68 infection is likely, and diagnostic tests for other causes of acute respiratory illness are negative. A false positive or a false negative 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 (www.fda.gov/medwatch) by submitting a MedWatch Form 3500 (available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM163919.pdf>) or by calling 1-800-FDA-1088.

Give patients the *Fact Sheet for Patients: Understanding Results from the Enterovirus-D68 2014 Real-time RT-PCR Assay (EV-D68 rRT-PCR)*.

Contact information for technical assistance for the EV-D68 2014 rRT-PCR:

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Any significant new findings observed during the course of the emergency use of the EV-D68 2014 rRT-PCR will be made available at:
<http://www.cdc.gov/non-polio-enterovirus/hcp.html>