



## DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring, MD 20993

June 10, 2014

Thomas R. Frieden, MD, MPH  
Director  
Centers for Disease Control and Prevention  
1600 Clifton Rd, MS D-14  
Atlanta, GA 30333

Dear Dr. Frieden:

On June 5, 2013, based on a request by the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA) issued a letter authorizing the emergency use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay for the presumptive detection of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in patients with signs and symptoms of MERS-CoV infection in conjunction with clinical and epidemiological risk factors, pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3), by qualified laboratories.<sup>1</sup> On May 22, CDC submitted a request for an amendment to the Emergency Use Authorization (EUA). In response to that request, and having concluded that revising the June 5, 2013, EUA is appropriate to protect the public health or safety under section 564(g)(2)(C) of the Act (21 U.S.C. § 360bbb-3(g)(2)(C)), the June 5, 2013, letter authorizing the emergency use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay is being reissued in its entirety with the amendments incorporated.<sup>2</sup>

On May 29, 2013, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of Health and Human Services (HHS) determined that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves a biological, chemical, radiological, or nuclear agent or agents, or a disease or condition that may be attributable to such an agent or agents - in this case, MERS-CoV.<sup>3</sup> Pursuant to section 564(b)(1) of the Act (21 U.S.C. § 360bbb-3(b)(1)), and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of the emergency use of

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<sup>1</sup> U.S. Food and Drug Administration. *Authorization of Emergency Use of an In Vitro Diagnostic for Detection of Middle East Respiratory Syndrome Coronavirus; Availability*. 78 Fed. Reg. 42779 (July 17, 2013).

<sup>2</sup> The amendments to the June 5, 2013, letter authorize the expanded use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay to include the *in vitro* qualitative detection of genomic RNA from MERS-CoV in clinical specimens collected from individuals meeting certain epidemiological criteria (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 as part of a public health investigation) who may or may not exhibit clinical signs and symptoms associated with MERS-CoV infection. The amendments also include a new Fact Sheet for Contacts of MERS Cases and revisions to the Instructions for Use, product insert, and Fact Sheets for Health Care Professionals and Patients.

<sup>3</sup> As amended by the Pandemic and All-Hazards Preparedness Reauthorization Act, Pub. L. No. 113-5, under section 564(b)(1)(C) of the Act the Secretary may make a determination of a public health emergency, or of a significant potential for a public health emergency.

*in vitro* diagnostics for the detection of MERS-CoV, subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).<sup>4</sup>

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(c)) are met, I am authorizing the emergency use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay (as described in the scope section of this letter (Section II)) for the presumptive detection of MERS-CoV in individuals meeting MERS-CoV clinical and/or epidemiological criteria (e.g., clinical signs and symptoms associated with MERS-CoV infection, 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 as part of a public health investigation) by qualified laboratories, subject to the terms of this authorization.

## **I. Criteria for Issuance of Authorization**

I have concluded that the emergency use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay for the presumptive detection of MERS-CoV in individuals meeting MERS-CoV clinical and/or epidemiological criteria (e.g., clinical signs and symptoms associated with MERS-CoV infection, 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 as part of a public health investigation) meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. MERS-CoV can cause a serious or life threatening disease or condition, including severe respiratory illness, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay may be effective in diagnosing MERS-CoV, and that the known and potential benefits of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay, when used for diagnosing MERS-CoV infection, outweigh the known and potential risks of such product; and
3. There is no adequate, approved, and available alternative to the emergency use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay for diagnosing MERS-CoV.<sup>5</sup>

## **II. Scope of Authorization**

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay for the presumptive detection of MERS-CoV in individuals meeting MERS-CoV clinical and/or epidemiological criteria (e.g., clinical signs and symptoms associated with MERS-CoV infection, contact with a probable or confirmed MERS-CoV case, history of travel to geographic locations

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<sup>4</sup> U.S. Department of Health and Human Services. *Determination and Declaration Regarding Emergency Use of In Vitro Diagnostics for Detection of Middle East Respiratory Syndrome Coronavirus (MERS-CoV)*. 78 Fed. Reg. 33842 (June 5, 2013).

<sup>5</sup> No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.



where MERS-CoV cases were detected, or other epidemiologic links for which MERS-CoV testing may be indicated as part of a public health investigation).

### **The Authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay:**

The CDC Novel Coronavirus 2012 Real-time RT-PCR Assay is a real-time reverse transcriptase PCR (rRT-PCR) for the *in vitro* qualitative detection of MERS-CoV viral RNA from respiratory specimens (such as nasopharyngeal or oropharyngeal swabs, sputa, lower respiratory aspirates/washes), sera, and stool from individuals meeting MERS-CoV clinical and/or epidemiological criteria (e.g., clinical signs and symptoms associated with MERS-CoV infection, 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 as part of a public health investigation). The testing procedure consists of nucleic acid extraction followed by rRT-PCR on the FDA cleared Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument.

The CDC Novel Coronavirus 2012 Real-time RT-PCR Assay includes the following primer and probe sets:

<b>NCV.N2</b>	targets the MERS-CoV nucleocapsid protein gene
<b>NCV.N3</b>	targets the MERS-CoV nucleocapsid protein gene
<b>NCV.upE<sup>6</sup></b>	targets the MERS-CoV region upstream of envelope protein gene
<b>RP<sup>7</sup></b>	targets the human Ribonuclease P gene. This primer and probe set is included as a control for specimen quality, to confirm that human nucleic acid was successfully extracted from the clinical specimen.

The CDC Novel Coronavirus 2012 Real-time RT-PCR Assay also includes the following control materials:

- **Positive Control:** NCV-2012 rRT-PCR Assay Positive Control (VTC)
- **Negative Controls:** Sterile, nuclease-free water, used as No Template Control (NTC)
  1. **PCR No Template Control (NTC<sub>1</sub>)**
  2. **Extraction control (NTC<sub>2</sub>)**

The above described CDC Novel Coronavirus 2012 Real-time RT-PCR Assay, when labeled consistently with the labeling authorized by FDA, entitled “CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Instructions for Use” (available at <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>), which may be revised with written permission of FDA, is authorized to be distributed to and used by qualified laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

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<sup>6</sup> This a WHO-recommended MERS-CoV primer and probe set. See Corman VM, et al. Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction. *Euro Surveill* 2012;17(39). Available online at: <http://www.eurosurveillance.org/images/dynamic/EE/V17N39/art20285.pdf>.

<sup>7</sup> This primer and probe set is not provided in the CDC Novel Coronavirus 2012 rRT-PCR Assay Kit, but it is required for test performance. Laboratories will utilize the Laboratory Response Network (LRN) RNase P Real-time PCR Primer and Probe Set.

**The above described CDC Novel Coronavirus 2012 Real-time RT-PCR Assay is authorized to be accompanied by the following information pertaining to the emergency use, which is authorized to be made available to health care professionals and patients:**

- **Fact Sheet for Health Care Professionals: Interpreting CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Test Results**
- **Fact Sheet for Patients: Understanding Results from the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay**
- **Fact Sheet for Contacts of MERS Cases: Understanding Results from the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay**

As described in section IV below, CDC is also authorized to make available additional information relating to the emergency use of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay that is consistent with, and does not exceed, the terms of this letter of authorization.

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay in the specified population, when used for presumptive detection of MERS-CoV, outweigh the known and potential risks of such a product.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay may be effective in the diagnosis of MERS-CoV infection pursuant to section 564(c)(2)(A) of the Act. The FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay, when used to diagnose MERS-CoV infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay described above is authorized to diagnose MERS-CoV infection in individuals meeting MERS-CoV clinical and/or epidemiological criteria (e.g., clinical signs and symptoms associated with MERS-CoV infection, 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 as part of a public health investigation).

This EUA will cease to be effective when the declaration of emergency is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

### **III. Waiver of Certain Requirements**

I am waiving the following requirements for the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay during the duration of this EUA:

- Current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay.
- Labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 809.30, except for the intended use statement (21 CFR 809.10(a)(2), (b)(2)), adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5) and (8)), any appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4), and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12).

### **IV. Conditions of Authorization**

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

#### **CDC**

- A. CDC will distribute the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay with the authorized labeling, as may be revised with written permission of FDA, only to qualified laboratories.
- B. CDC will provide to the qualified laboratories the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Health Care Professionals, the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Patients, and the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Contacts of MERS Cases.
- C. CDC will make available on its website the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Health Care Professionals, the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Patients, and the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Contacts of MERS Cases.
- D. CDC will inform state and/or local public health authority(ies) of this EUA, including the terms and conditions herein.
- E. CDC will ensure that qualified laboratories using the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay have a process in place for reporting test results to health care professionals and federal, state, and/or local public health authorities, as appropriate.
- F. CDC will track adverse events and report to FDA as required under 21 CFR Part 803.
- G. Through a process of inventory control, CDC will maintain records of device usage.



- H. CDC will collect information on the performance of the assay, and report to FDA any suspected occurrence of false positive or false negative results of which CDC becomes aware.
- I. CDC is authorized to make available additional information relating to the emergency use of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay that is consistent with, and does not exceed, the terms of this letter of authorization.
- J. Only CDC may request changes to the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Health Care Professionals, the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Patients, or the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay Fact Sheet for Contacts of MERS Cases. Such requests will be made by contacting FDA concerning FDA review and approval.

### **Qualified Laboratories**

- K. Qualified laboratories will make available the authorized Fact Sheet for Health Care Professionals, the authorized Fact Sheet for Patients, and the authorized Fact Sheet for Contacts of MERS Cases.
- L. Qualified laboratories will perform the assay on an Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with the appropriate software.
- M. Qualified laboratories will have a process in place for reporting test results to health care professionals and federal, state, and/or local public health authorities, as appropriate.
- N. Qualified laboratories will collect information on the performance of the assay, and report to CDC any suspected occurrence of false positive or false negative results of which qualified laboratories become aware.

### **CDC and Qualified Laboratories**

- O. CDC and qualified laboratories will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

### **Conditions Related to Advertising and Promotion**

- P. All advertising and promotional descriptive printed matter relating to the use of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay shall be consistent with the Fact Sheets and authorized labeling, as well as the terms set forth in this EUA and other requirements set forth in the Act and FDA regulations.
- Q. All advertising and promotional descriptive printed matter relating to the use of the CDC Novel Coronavirus 2012 Real-time RT-PCR Assay shall clearly and conspicuously state that:
  - This test has not been FDA cleared or approved;


- This test has been authorized by FDA under an Emergency Use Authorization for use by qualified laboratories;
- This test has been authorized only for the detection of MERS-CoV and not for any other viruses or pathogens; and
- This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of MERS-CoV under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1).

No advertising or promotional descriptive printed matter relating to the use of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay may represent or suggest that this test is safe or effective for the diagnosis of MERS-CoV.

The emergency use of the authorized CDC Novel Coronavirus 2012 Real-time RT-PCR Assay as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

#### **V. Duration of Authorization**

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the emergency use of *in vitro* diagnostics for detection of MERS-CoV is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.



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Margaret A. Hamburg, M.D.  
Commissioner of Food and Drugs

Enclosures