NON-VARIOLA ORTHOPOXVIRUS REAL-TIME PCR PRIMER AND PROBE SET -EUA

Centers for Disease Control and Prevention (CDC)

All individuals whose specimens are tested with this product will receive the Fact Sheet for Patients for the product.

March 22, 2024

This Fact Sheet informs you of the significant known and potential risks and benefits of the emergency use of the Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set -EUA.

WHERE CAN I GO FOR GENERAL INFORMATION ON MPOX[1]?

For general information on mpox, including the symptoms of mpox, infection control precautions, and other information please check the CDC Mpox webpage (see links provided in "*Where can I go for updates and more information?*" section at the end of this document) or your local jurisdiction's website for the most up to date information.

WHAT DO I NEED TO KNOW ABOUT MPOX TESTING WITH THIS PRODUCT?

- The Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set -EUA can be **used to test human pustular or vesicular rash specimens and viral cell culture lysates submitted to a Centers for Disease Control and Prevention designated laboratory** obtained from individuals suspected of mpox by their healthcare provider.
- The Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set -EUA is authorized for use with human pustular or vesicular rash specimens collected using authorized home specimen collection kits that are indicated for use with the Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set – EUA when used consistent with their authorization.
- The Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set -EUA is authorized for use in Centers for Disease Control and Prevention designated laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet the requirements to perform high complexity tests.

Specimens should be collected with appropriate infection control precautions. When collecting and handling specimens from individuals suspected of being infected with the virus that causes mpox, appropriate personal protective equipment should be used as outlined on the CDC *Infection Control in Healthcare Settings* webpage. For additional information, refer to the CDC *Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings (2007)* (see links provided in "*Where can I go for updates and more information?*" section at the end of this document).

[1] On November 28, 2022, following a series of consultations with global experts, the World Health Organization (WHO) began using a new preferred term "mpox" as a synonym for monkeypox, the disease caused by the monkeypox virus (MPXV). Refer to: https://www.who.int/news/item/28-11-2022-who-recommends-new-name-for-monkeypox-disease.

WHAT DOES IT MEAN IF THE SPECIMEN TESTS PRESUMPTIVE POSITIVE FOR NON-VARIOLA ORTHOPOXVIRUSES?

The Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set -EUA detects non-variola *Orthopoxvirus* (NVO) gene targets. As the virus that causes mpox (MPXV) clade II is the only member of the *Orthopoxvirus* genus known to be circulating in the US at this time, a presumptive positive result for the NVO gene target most likely represents the presence of the virus that causes mpox, although there is a small possibility that this result could represent the presence of a different NVO, such as vaccinia virus. If clinical concern for such an infection exists, healthcare providers should contact the CDC and their local public health authorities for guidance.

A presumptive positive test result for NVO indicates that DNA from NVO was detected, and therefore the patient is infected with the virus and presumed to be contagious. A presumptive positive test result for NVO does not preclude the possibility of another infectious pathogen (e.g., a bacterial infection or co-infection with other viruses) contributing to the patient's symptoms. Healthcare providers should always consider laboratory test results in the context of clinical observations and epidemiological data (such as local prevalence rates and current outbreak/epicenter locations) in determining individual diagnosis and patient management decisions and should follow current CDC guidelines.

The Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set -EUA has been designed to minimize the likelihood of false positive test results. However, it is still possible that this test can give a false positive result. In the event of a false positive result, risks to patients could include the following: a recommendation for isolation of the patient, monitoring of household or other close contacts for symptoms, patient isolation that might limit contact with family or friends and may increase contact with other potential patients with mpox, limits in the ability to work, delayed diagnosis and treatment for the true infection causing the symptoms, unnecessary prescription of a mpox treatment or therapy, negative impact on mental health and/or interpersonal relationships, or other unintended adverse effects.

All laboratories using this test must follow the standard testing and reporting guidelines according to their appropriate public health authorities.

WHAT DOES IT MEAN IF THE SPECIMEN TESTS NEGATIVE FOR NON-VARIOLA ORTHOPOXVIRUSES?

A negative test result for this test means that non-variola *Orthopoxvirus* DNA, including the virus that causes mpox, was not present in the specimen above the limit of detection. However, a negative result does not rule out mpox and should not be used as the sole basis for treatment or patient management decisions. It is possible for a test to miss infection with the virus that causes mpox if testing a person occurs too early or too late during their illness, or if the specimen is not collected from a site carrying adequate concentration of virus. Inadequate or improper specimen collection and handling may yield false negative results via the Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set -EUA.

When diagnostic testing is negative, the possibility of a false negative result should be considered in the context of an individual's recent exposures and the presence of clinical signs and symptoms consistent with mpox. The possibility of a false negative result should especially be considered if the individual's recent exposures or clinical presentation indicate that mpox is likely,

and diagnostic tests for other causes of illness (e.g., other illnesses with similar symptoms) are negative. Special consideration should be given to patients who are immunocompromised, pregnant, very young, or otherwise at increased risk of severe or complicated disease.

If mpox is still suspected based on exposure history together with other clinical findings, re-testing with an alternative method should be considered by healthcare providers in consultation with public health authorities. Additional testing may be helpful to ensure testing was not conducted too early and that an adequate specimen was collected from the appropriate anatomical site(s).

Risks to a patient of a false negative test result include delayed or lack of supportive treatment, lack of monitoring of infected individuals and their household or other close contacts for symptoms resulting in increased risk of spread of mpox within the community, or other unintended adverse events.

The performance of this test was established based on the evaluation of a limited number of clinical specimens. As the ongoing global outbreak of mpox is actively evolving, new epidemiological, microbiological, and clinical information may emerge over time requiring updates to best practices in testing, prevention, and treatment of this virus.

WHAT IS AN EUA?

The U.S. FDA has made this test available under an emergency access mechanism called an Emergency Use Authorization (EUA). The EUA is supported by the Secretary of Health and Human Service's (HHS's) declaration that circumstances exist to justify the emergency use of in vitro diagnostics (IVDs) for the detection and/or diagnosis of the virus that causes mpox.

An IVD made available under an EUA has not undergone the same type of review as an FDA-approved or cleared IVD. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives, and based on the totality of scientific evidence available, it is reasonable to believe that this IVD may be effective in diagnosing mpox.

The EUA for this test is in effect for the duration of the mpox declaration justifying emergency use of IVDs, unless the declaration is terminated or authorization is revoked sooner.

WHAT ARE THE APPROVED AVAILABLE ALTERNATIVES?

Any tests that have received full marketing status (e.g., cleared, approved), as opposed to an EUA, by FDA can be found by searching the medical device databases here: https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases. As of the date of this fact sheet, there is only one cleared test.[2] A cleared or approved test should be used instead of a test made available under an EUA, when appropriate and available. FDA has issued EUAs for other tests that can be found at: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization.

[2] There is an FDA-cleared diagnostic test for non-variola orthopoxviruses, including the virus that causes mpox, which the Centers for Disease Control and Prevention (CDC) developed.

WHERE DO I REPORT ADVERSE EVENTS?

Report Adverse events, including problems with test performance or results, to MedWatch by submitting the online FDA Form 3500 (https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home) or by calling **1-800-FDA-1088**

WHERE CAN I GO FOR UPDATES AND MORE INFORMATION?

CDC WEBPAGES:

Mpox Home Page: https://www.cdc.gov/poxvirus/mpox/index.html

2022 U.S. Outbreak Information: https://www.cdc.gov/poxvirus/mpox/response/2022/index.html

Symptoms: https://www.cdc.gov/poxvirus/mpox/symptoms/index.html

Healthcare Professionals: https://www.cdc.gov/poxvirus/mpox/clinicians/index.html

Information for Laboratories: https://www.cdc.gov/poxvirus/mpox/lab-personnel/index.html

Laboratory Biosafety: https://www.cdc.gov/poxvirus/mpox/lab-personnel/lab-procedures.html

Isolation Precautions in Healthcare Settings: https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html

Specimen Collection: https://www.cdc.gov/poxvirus/mpox/clinicians/prep-collection-specimens.html

Infection Control: https://www.cdc.gov/poxvirus/mpox/clinicians/infection-control-healthcare.html

FDA WEBPAGES:

General: https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/fda-mpox-response

EUAs: (includes links to patient fact sheet and manufacturer's instructions) https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/monkeypox-mpox-emergency-use-authorizations-medical-devices

CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC):

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