



May 22, 2023

Michael J. Wagner, Esq.
Senior Corporate Counsel
Quest Diagnostics Incorporated
33608 Ortega Highway
San Juan Capistrano, CA 92675

Device: Quest Diagnostics Mpox Virus Qualitative Real-Time PCR (2-well)

EUA Number: EUA220415

Company: Quest Diagnostics Nichols Institute (“Quest Diagnostics”)

Indication: This test is authorized for the qualitative detection of DNA from monkeypox virus (Clade II)¹ and non-variola *Orthopoxvirus* in lesion swab specimens (i.e., swabs of acute pustular or vesicular rash) in universal viral transport media (UTM) from individuals suspected of monkeypox virus infection by their healthcare provider.

Emergency use of this test is limited to authorized laboratories.

Authorized Laboratories: Testing is limited to laboratories designated by Quest Diagnostics that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet the requirements to perform high complexity tests.

Dear Mr. Wagner:

On September 7, 2022, based on your² request, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for emergency use of the Quest Diagnostics Monkeypox Virus Qualitative Real-Time PCR, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-3) for the indication stated in the letter.³

¹ On August 12, 2022, following a meeting convened by the World Health Organization (WHO) monkeypox virus variants were renamed to align with current best practices under the International Classification of Diseases and the WHO Family of International Health Related Classifications (WHO-FIC). This letter will refer to the former West African clade as clade two (II). Refer to: <https://www.who.int/news/item/12-08-2022-monkeypox--experts-give-virus-variants-new-names>.

² For ease of reference, this letter will use the term “you” and related terms to refer to Quest Diagnostics Nichols Institute (“Quest Diagnostics”), a subsidiary of Quest Diagnostics Incorporated.

³ The September 7, 2022, letter authorized the Quest Diagnostics Monkeypox Virus Qualitative Real-Time PCR for the qualitative detection of DNA from monkeypox virus (West African clade; clade II) and non-variola Orthopoxvirus in lesion swab specimens (i.e., swabs of acute pustular or vesicular rash) in universal viral transport

Based on your subsequent request, FDA granted an update to the Quest Diagnostics Monkeypox Virus Qualitative Real-Time PCR on December 9, 2022.⁴

On February 14, 2023, you requested to amend your EUA. Based on this request, and having concluded that revising the September 7, 2022, 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)), FDA is reissuing the September 7, 2022, letter in its entirety with the revisions incorporated.⁵ Pursuant to section 564 of the Act and the Scope of Authorization (Section II) and Conditions of Authorization (Section III) of this reissued letter, your product⁶ is now authorized for use consistent with the indication described above.

On August 9, 2022, pursuant to Section 564(b)(1)(C) of the Act, the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency, or a significant potential for a public health emergency, that affects or has a significant potential to affect national security or the health and security of United States citizens living abroad that involves monkeypox virus.⁷ Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared on September 7, 2022 that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of infection with the monkeypox virus, including in vitro diagnostics that detect and/or diagnose infection with non-variola *Orthopoxvirus*, subject to the terms of any authorization issued under Section 564(a) of the Act.⁸

FDA considered the totality of scientific information available in authorizing the emergency use of your product for the indication above. A summary of the performance information FDA relied upon is contained in the EUA Summary (identified below). There is an FDA-cleared test

media (UTM) from individuals suspected of monkeypox virus infection by their healthcare provider. Emergency use of this test was limited to laboratories designated by Quest Diagnostics that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. § 263a, and meet the requirements to perform high complexity tests.

⁴ On December 9, 2022, your request was granted to update the authorized labeling of the Quest Diagnostics Monkeypox Virus Qualitative Real-Time PCR to; (1) include a specimen stability claim of 24 hours at 18-23°C, 7 days at 2-8°C, 30 days at -20°C, and up to three freeze/thaw cycles at -20°C for lesion swab specimens collected in universal viral transport media (UTM) based on data from a specimen stability study performed to fulfill Condition of Authorization O. in the September 7, 2022 Letter of Authorization, (2) add use of leftover deidentified positive patient specimens as an acceptable positive control material, and (3) make some minor edits for clarification.

⁵ The revisions to the September 7, 2022, letter and authorized labeling include: (1) update the name of the EUA product to the “Quest Diagnostics Mpox Virus Qualitative Real-Time PCR (2-well)” assay, (2) update the clinical performance section with results of a clinical study performed using natural clinical specimens to fulfill Condition of Authorization N. in the September 7, 2022 letter, (3) delete Conditions of Authorization N., O. and P. as fulfilled with data and information provided to the Agency, and (4) updating the Fact Sheet for Healthcare Providers and Fact Sheet for Patients with the name of the EUA product and for consistency with more recent authorizations.

⁶ For ease of reference, this letter will use the term “your product” to refer to the Quest Diagnostics Mpox Virus Qualitative Real-Time PCR (2-well) for the indication identified above.

⁷ U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3. 87 FR 50090 (August 15, 2022).

⁸ U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorization Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3.

for the qualitative detection of non-variola *Orthopoxvirus*, that includes monkeypox virus, but this is not an adequate and available alternative to your product.⁹

Having concluded that the criteria for issuance of this authorization under Section 564(c) of the Act are met, I am authorizing the emergency use of your product, described in the Scope of Authorization of this letter (Section II), subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of your product meets the criteria for issuance of an authorization under Section 564(c) of the Act, because I have concluded that:

1. The monkeypox virus can cause a serious or life-threatening disease or condition, to humans infected by this virus;
2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that your product may be effective in diagnosing infection with the monkeypox virus, and that the known and potential benefits of your product when used for diagnosing monkeypox virus, outweigh the known and potential risks of your product; and
3. There is no adequate, approved, and available alternative to the emergency use of your product.¹⁰

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 indication above.

Authorized Product Details

Your product is a real-time PCR test intended for the qualitative detection of DNA from monkeypox virus (Clade II) and non-variola *Orthopoxvirus* in lesion swab specimens (i.e., swabs of acute pustular or vesicular rash) in universal viral transport media (UTM) from individuals suspected of monkeypox virus infection by their healthcare provider. Testing is limited to laboratories designated by Quest Diagnostics that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meet the requirements to perform high complexity tests.

The monkeypox virus (Clade II) and non-variola *Orthopoxvirus* nucleic acid is generally detectable in human pustular or vesicular rash specimens during the acute phase of infection.

⁹ To date, the FDA-cleared CDC Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set (Product Code: PBK; DEN070001, K181205, K221658, K221834, K222558) is the only test available in the United States with FDA clearance for the detection of non-variola *Orthopoxvirus* DNA, including vaccinia, cowpox, monkeypox and ectromelia viruses at varying concentrations. Available information indicates that timely detection of monkeypox cases in the United States requires wide availability of diagnostic testing to control the spread of this contagious infection and there is currently a need for additional diagnostic testing for monkeypox virus in the United States.

¹⁰ No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

Positive results are indicative of the presence of monkeypox virus (Clade II) and/or other non-variola *Orthopoxvirus* DNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses. Negative results obtained with this device do not preclude monkeypox virus (Clade II) or non-variola *Orthopoxvirus* infection and should not be used as the sole basis for treatment or other patient management decisions.

To use your product, monkeypox virus (Clade II) or non-variola *Orthopoxvirus* nucleic acid is first extracted, isolated and purified from lesion swab specimens; these processes are followed by PCR amplification and detection using an authorized real-time (RT) PCR instrument described in the authorized labeling (described below).

Your product uses all commercially sourced materials or other authorized materials and authorized ancillary reagents (as may be requested under Condition J. below) commonly used in clinical laboratories, as described in the authorized labeling (described below).

Your product requires use of control materials or other authorized control materials (as may be requested under Condition J. below) that are described in the authorized labeling (described below). All controls must generate expected results in order for the test result to be valid, as outlined in the authorized labeling (described below).

The labeling entitled “Mpox Virus Qualitative Real-Time PCR (2-well) (Test Code 12084) Package Insert”, the EUA Summary (available at <https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/monkeypox-emergency-use-authorizations-medical-devices>), and the following fact sheets pertaining to the emergency use, are required to be made available as set forth below and in the Conditions of Authorization (Section IV), and are collectively referred to as “authorized labeling:”

- Fact Sheet for Healthcare Providers: Quest Diagnostics Nichols Institute - Quest Diagnostics Mpox Virus Qualitative Real-Time PCR (2-well)
- Fact Sheet for Patients: Quest Diagnostics Nichols Institute - Quest Diagnostics Mpox Virus Qualitative Real-Time PCR (2-well)

The above described product, when accompanied by the authorized labeling as set forth in the Conditions of Authorization (Section IV), is authorized to be distributed to and used by the authorized laboratories under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

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 your product, when used consistent with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of your 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 your product may be effective in diagnosing infection with the monkeypox virus, when used consistent with the Scope of

Authorization of this letter (Section II), pursuant to Section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that your product (as described in the Scope of Authorization of this letter (Section II)) meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of your product under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). 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) of the Act described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1) of the Act, your product is authorized for the indication above.

III. Waiver of Certain Requirements

I am waiving the following requirements for your product 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 your product.

IV. Conditions of Authorization

Pursuant to Section 564(e) of the Act, I am establishing the following conditions on this authorization:

Quest Diagnostics Nichols Institute (You)

- A. Your product must comply with the following labeling requirements: 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), (7), and (8)); 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).
- B. You must inform authorized laboratories and relevant public health authorities of this EUA, including the terms and conditions herein, and any updates made to your product and authorized labeling.
- C. You must make your product available with the authorized labeling to authorized laboratories.
- D. You must make available on your website(s) the Fact Sheet for Healthcare Providers and Fact Sheet for Patients.

- E. You must ensure that the authorized laboratories using your product have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- F. You must maintain records of the laboratories you designate as authorized laboratories and you must also maintain records of test usage by all such authorized laboratories.
- G. You are authorized to make available additional information relating to the emergency use of your product that is consistent with, and does not exceed, the terms of this letter of authorization.
- H. You must maintain customer complaint files concerning your product and must report to the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7): Office of In Vitro Diagnostics /Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH) (via email: CDRH-EUAReporting@fda.hhs.gov) any significant deviations from the established performance characteristics of your product of which you become aware.
- I. You must have a process in place to track adverse events and report to FDA pursuant to 21 CFR Part 803.
- J. You may request changes to this EUA for your product, including to the Scope of Authorization (Section II in this letter) or to the authorized labeling. Any request for changes to this EUA should be submitted to DMD/OHT7/OPEQ/CDRH and requires appropriate authorization from FDA prior to implementation.
- K. You must evaluate the analytical limit of detection and assess traceability of your product with any FDA-recommended reference material(s), if requested by FDA.¹¹ After submission to and concurrence with the data by FDA, you will update the authorized labeling to reflect the additional testing. Such labeling updates will be made in consultation with, and require concurrence of, DMD/OHT7/OPEQ/CDRH. FDA will update the EUA Summary to reflect the additional testing.
- L. You must evaluate the impact of monkeypox viral mutations on your product’s performance. Such evaluations must occur on an ongoing basis and must include any additional data analysis that is requested by FDA in response to any performance concerns you or FDA identify during routine evaluation. Additionally, if requested by FDA, you must submit records of these evaluations for FDA review within 48 hours of the request. If your evaluation identifies viral mutations that affect the stated expected performance of your device, you must notify FDA immediately (via email: CDRH-EUA-Reporting@fda.hhs.gov).

¹¹ Traceability refers to tracing analytical sensitivity/reactivity back to an FDA-recommended reference material. FDA may request, for example, that you perform this study in the event that we receive reports of adverse events concerning your product.

- M. If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA regarding the impact of viral mutations on test performance. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7/OPEQ/CDRH.

Authorized Laboratories

- N. Authorized laboratories that receive your product must notify the relevant public health authorities of their intent to run your product prior to initiating testing.
- O. Authorized laboratories using your product must have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- P. Authorized laboratories using your product must include with test result reports, all authorized Fact Sheets. Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Q. Authorized laboratories using your product must use your product as outlined in the authorized labeling. Deviations from the authorized procedures, including the authorized instruments, authorized extraction methods, authorized clinical specimen types, authorized control materials, authorized other ancillary reagents and authorized materials required to use your product are not permitted.
- R. Authorized laboratories must collect information on the performance of your product and report to DMD/OHT7/OPEQ/CDRH (via email: CDRH-EUA-Reporting@fda.hhs.gov) and you (michael.j.wagner@questdiagnostics.com) any significant deviations from the established performance characteristics of your product of which they become aware.
- S. Authorized laboratories must have a process in place to track adverse events and report to you (via email: michael.j.wagner@questdiagnostics.com) and to FDA pursuant to 21 CFR Part 803.
- T. All laboratory personnel using your product must be appropriately trained in RT-PCR techniques and use appropriate laboratory and personal protective equipment when handling your product and use your product in accordance with the authorized labeling.

Quest Diagnostics Nichols Institute (You) and Authorized Laboratories

- U. You and authorized laboratories must ensure that any records associated with this EUA, including test usage, are maintained until otherwise notified by FDA. Such records must be made available to FDA for inspection upon request.

Conditions Related to Printed Materials, Advertising and Promotion

- V. All descriptive printed matter, advertising and promotional materials relating to the use of your product shall be consistent with the authorized labeling, as well as the terms set forth in this EUA and meet the requirements set forth in section 502(a), (q)(1), and (r) of the Act, as applicable, and FDA implementing regulations.
- W. No descriptive printed matter, advertising or promotional materials relating to the use of your product may represent or suggest that this test is safe or effective for the detection of monkeypox virus or other non-variola orthopoxviruses.
- X. All descriptive printed matter, advertising and promotional materials relating to the use of your product shall clearly and conspicuously state that:
- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA for use by the authorized laboratories;
 - This product has been authorized only for the detection of nucleic acid from monkeypox virus or other non-variola orthopoxviruses, not for any other viruses or pathogens; and
 - The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of infection with the monkeypox virus, including in vitro diagnostics that detect and/or diagnose infection with non-variola *Orthopoxvirus*, under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.

The emergency use of your product as described in this letter of authorization must comply with the conditions 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 and/or diagnosis of infection with the monkeypox virus, including in vitro diagnostics that detect and/or diagnose infection with non-variola *Orthopoxvirus*, is terminated under Section 564(b)(2) of the Act or the EUA is revoked under Section 564(g) of the Act.

Sincerely,

Jeffrey E. Shuren, M.D., J.D.
Director
Center for Devices and Radiological Health
Food and Drug Administration

Enclosure