



Centers for Disease Control and Prevention
Julie Villanueva
Laboratory Preparedness and Response Branch Chief
1600 Clifton Road NE, MS-H24-11
Atlanta, Georgia 30329

August 30, 2022

Re: K222558

Trade/Device Name: Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set
Regulation Number: 21 CFR 866.3315
Regulation Name: Nucleic Acid Based Reagents For Detection Of Non-Variola Orthopoxviruses
Regulatory Class: Class II
Product Code: PBK
Dated: August 23, 2022
Received: August 24, 2022

Dear Julie Villanueva:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Noel J. Gerald, Ph.D.
Branch Chief
Bacterial Respiratory and Medical Countermeasures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K222558

Device Name

Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set

Indications for Use (Describe)

The Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set is intended for the in vitro qualitative presumptive detection of non-variola Orthopoxvirus DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to a Centers for Disease Control and Prevention designated laboratory. The assay detects non-variola Orthopoxvirus DNA, including vaccinia, cowpox, monkeypox and ectromelia viruses at varying concentrations. This assay does not differentiate vaccinia virus or monkeypox virus from other orthopoxviruses detected by this assay and does not detect variola virus. Refer to the CDC algorithm, Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States for recommended testing and evaluation algorithms for patients presenting with acute, generalized pustular or vesicular rash illness.

Results of this assay are for the identification of non-variola Orthopoxvirus DNA. These results must be used in conjunction with other diagnostic assays and clinical observations to diagnose Orthopoxvirus infection. The assay should only be used to test specimens with low/moderate risk of smallpox. If a high risk of smallpox exists, viral culture should not be attempted. Negative results obtained with this device do not preclude Variola virus infection and should not be used as the sole basis for treatment or other patient management decisions.

Use is limited to Centers for Disease Control and Prevention designated laboratories.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRASStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

15. **510(k) Summary**

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Assigned 510(k) number:	TBD
Submitted by:	Centers for Disease Control and Prevention 1600 Clifton Road NE Atlanta, GA 30329
Contact Person:	Julie Villanueva, PhD Laboratory Preparedness and Response Branch Chief Division of Preparedness and Emerging Infections National Center for Emerging and Zoonotic Infectious Diseases Centers for Disease Control and Prevention (Registration number: 1050190) 1600 Clifton Road, NE, MS H24-11 Atlanta, GA 30329 (404) 639-3851 (office) Jfv3@cdc.gov
Date prepared:	August 23, 2022
Device trade name:	Non-variola <i>Orthopoxvirus</i> Real-time PCR Primer and Probe Set
Classification name and regulation (if applicable):	21 CFR 866.3315
Predicate device(s):	Non-variola <i>Orthopoxvirus</i> Real-time PCR Primer and Probe Set (K221834)

Background

Variola virus, a member of the *Orthopoxvirus* genus, is the causative agent of smallpox and was certified eradicated in 1980 by the World Health Organization. At that time, smallpox vaccinations were ceased worldwide as a result. However, in recent years, concerns over the potential use of *Variola virus* as a biological weapon led the United States to resume smallpox vaccinations on a limited basis. Since the smallpox vaccine contains live *Vaccinia virus*, it is possible for vaccine recipients and/or their close contacts to develop adverse reactions to the vaccine including the emergence of pustules on the skin.

The Laboratory Response Network (LRN) is part of a national bioterrorism preparedness initiative created to ensure an effective laboratory response to biological threats by helping to improve the nation's public health laboratory infrastructure. Member laboratories must meet specific membership requirements and pass rigorous proficiency tests demonstrating their ability to accurately identify agents of concern. One of the major goals is the development and validation of rapid and specific assays for detection of

biothreat agents and emerging infectious diseases. Accordingly, scientists at the Centers for Disease Control and Prevention have developed several real-time PCR based assays to detect non-variola *Orthopoxvirus* and other potential biothreat agents to meet the need for rapid detection.

The Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set was developed for use in conjunction with clinical observations and other tests as described in the CDC algorithm, Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States. The assay is designed to aid in the identification of the causative agent of a pustular or vesicular rash illness and to help rule out the presence of *Variola virus* in patients presenting with pustular rash illness.

This assay detects most commonly known human pathogenic *Orthopoxviruses* (i.e., *Vaccinia*, *Cowpox*, and *Monkeypox viruses*) but does not detect *Variola virus*, the causative agent of smallpox. *Vaccinia virus* infection in the United States usually occurs in conjunction with smallpox vaccination or contact with a smallpox vaccine recipient. *Monkeypox* and *Cowpox viruses* are enzootic to locations outside the United States, with the exception of the 2003 domestic monkeypox outbreak associated with imported African rodents.

As of August 22, 2022, there are 15,433 cases of *monkeypoxvirus/non-variola orthopoxvirus* in the United States. As case counts continue to rise in the United States where monkeypox is not endemic, there is an urgent need to prepare for larger scale diagnostic testing for *orthopoxviruses*.

Device Description

Unchanged from original submission (K221834).

Intended Use

The Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set is intended for the *in vitro* qualitative presumptive detection of non-variola *Orthopoxvirus* DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to a Centers for Disease Control and Prevention designated laboratory. The assay detects non-variola *Orthopoxvirus* DNA, including *Vaccinia*, *Cowpox*, *Monkeypox* and *Ectromelia viruses* at varying concentrations. This assay does not differentiate *Vaccinia virus* or *Monkeypox virus* from other *Orthopoxviruses* detected by this assay and does not detect *Variola virus*. Refer to the CDC algorithm, Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States for recommended testing and evaluation algorithms for patients presenting with acute, generalized pustular or vesicular rash illness.

Results of this assay are for the presumptive identification of non-variola *Orthopoxvirus* DNA. These results must be used in conjunction with other diagnostic assays and clinical observations to diagnose *Orthopoxvirus* infection. The assay should only be used to test specimens with low/moderate risk of smallpox. If a high risk of smallpox exists, viral culture should **not** be attempted. Negative results obtained with this device do not preclude *Variola virus* infection and should not be used as the sole basis for treatment or other patient management decisions.

Use is limited to Centers for Disease Control and Prevention designated laboratories.

Device Comparison

The following table summarizes the similarities and differences between the cleared assay and the new submission for this device.

	New Submission	Original Submission (K221834)
Device Name	Non-variola <i>Orthopoxvirus</i> Real-time PCR Primer and Probe Set	Non-variola <i>Orthopoxvirus</i> Real-time PCR Primer and Probe Set
Intended Use	<p>The Non-variola <i>Orthopoxvirus</i> Real-time PCR Primer and Probe Set is intended for the in vitro qualitative presumptive detection of non-variola <i>Orthopoxvirus</i> DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to a Centers for Disease Control and Prevention designated laboratory. The assay detects non-variola <i>Orthopoxvirus</i> DNA, including vaccinia, cowpox, monkeypox and ectromelia viruses at varying concentrations. This assay does not differentiate vaccinia virus or monkeypox virus from other <i>orthopoxviruses</i> detected by this assay and does not detect variola virus. Refer to the CDC algorithm, Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States for recommended testing and evaluation algorithms for patients presenting with acute, generalized pustular or vesicular rash illness.</p>	<p>The Non-variola <i>Orthopoxvirus</i> Real-time PCR Primer and Probe Set is intended for the in vitro qualitative presumptive detection of non-variola <i>Orthopoxvirus</i> DNA extracted from human pustular or vesicular rash specimens and viral cell culture lysates submitted to a Laboratory Response Network (LRN) reference laboratory. The assay detects non-variola <i>Orthopoxvirus</i> DNA, including vaccinia, cowpox, monkeypox and ectromelia viruses at varying concentrations. This assay does not differentiate vaccinia virus or monkeypox virus from other <i>orthopoxviruses</i> detected by this assay and does not detect variola virus. Refer to the CDC algorithm, Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States for recommended testing and evaluation algorithms for patients presenting with acute, generalized pustular or vesicular rash illness.</p>

Centers for Disease Control and Prevention
 Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set
 Special 510(k)

	<p>Results of this assay are for the identification of non-variola <i>Orthopoxvirus</i> DNA. These results must be used in conjunction with other diagnostic assays and clinical observations to diagnose <i>Orthopoxvirus</i> infection. The assay should only be used to test specimens with low/moderate risk of smallpox. If a high risk of smallpox exists, viral culture should not be attempted. Negative results obtained with this device do not preclude <i>Variola virus</i> infection and should not be used as the sole basis for treatment or other patient management decisions.</p>	<p>Results of this assay are for the identification of non-variola <i>Orthopoxvirus</i> DNA. These results must be used in conjunction with other diagnostic assays and clinical observations to diagnose <i>Orthopoxvirus</i> infection. The assay should only be used to test specimens with low/moderate risk of smallpox. If a high risk of smallpox exists, viral culture should not be attempted. Negative results obtained with this device do not preclude <i>Variola virus</i> infection and should not be used as the sole basis for treatment or other patient management decisions.</p>
	<p>Use is limited to Centers for Disease Control and Prevention designated laboratories.</p>	<p>Use is limited to Centers for Disease Control and Prevention designated laboratories.</p>
<p>Principle of Operation</p>	<p>Unchanged</p>	<p>Nucleic acid amplification and fluorescent probe detection</p>
<p>Sample Types</p>	<p>Unchanged</p>	<ul style="list-style-type: none"> • Skin or crust from roof of vesicle • Dry or wet swab of lesion (dry swab is preferred). Wet swabs include swabs in transport media. • Touch prep (slide) of vesicular or pustular lesion fluid • Fresh biopsy of pustule or vesicle (no formalin) • Cellular material from tissue culture demonstrating cytopathic effect (Viral cell culture lysates)

Instrumentation and Software	Unchanged	<ul style="list-style-type: none">• Real-time PCR instrumentation and software
-------------------------------------	-----------	--

Establishment of Performance Characteristics

Inquiries regarding performance characteristics for the Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set should be directed to the Centers for Disease Control and Prevention.

Analytical Limit of Detection (LOD)

The limit of detection for the Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set was determined through an analytical sensitivity study.

Analytical Sensitivity and Specificity

Inquiries regarding performance characteristics for the Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set should be directed to the Centers for Disease Control and Prevention.

Clinical Performance

Inquiries regarding clinical performance characteristics for the Non-variola *Orthopoxvirus* Real-time PCR Primer and Probe Set should be directed to the Centers for Disease Control and Prevention.