Contains Nonbinding Recommendations

Policy for Monkeypox Tests To Address the Public Health Emergency

Guidance for Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff

Document issued on the web on September 7, 2022.

For questions about this document, contact MPXDx@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Preface

Public Comment

You may submit electronic comments and suggestions at any time for Agency consideration to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number FDA-2022-D-1908. Comments may not be acted upon by the Agency until the document is next revised or updated.

Additional Copies

Additional copies are available from the Internet. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please include the document number 22003 and complete title of the guidance in the request.

Table of Contents

Policy for Monkeypox Tests To Address the Public Health Emergency

Guidance for Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the United States from threats such as emerging infectious diseases, including the recent monkeypox outbreak.

On August 9, 2022, the Secretary of the Department of Health and Human Services (HHS) determined[1] under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) that there is a public health emergency, or 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. On September 7, 2022, the Secretary declared[2] that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of monkeypox virus. Rapid detection of monkeypox cases in the United States requires wide availability of diagnostic testing to help control the spread of this contagious infection.

This guidance describes FDA's review priorities of emergency use authorization (EUA) requests for monkeypox diagnostic tests, describes FDA's enforcement policies for certain diagnostic tests that are developed by and performed in a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA) that meets the requirements to perform tests of high

[1] *See* HHS Secretary Section 564 Determination (Aug. 9, 2022), available at Monkeypox | Section 564 Determination (hhs.gov).
[2] *See* HHS Secretary Section 564 Determination (Sept. 7, 2022), available at https://aspr.hhs.gov/legal/Section564/Pages/InVitro-Diagnostics-Monkeypox-7Sept22.aspx

complexity,[3] provides recommendations for diagnostic test validation, describes FDA's enforcement policies for FDA-cleared or authorized monkeypox diagnostic tests that are modified, and describes FDA's enforcement policies for certain serology tests.

In light of the public health emergency, this guidance is being implemented without prior public comment because the FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C)(i) of the FD&C Act and 21 CFR 10.115(g)(2)). This guidance document is being issued without prior public comment, but it remains subject to comment in accordance with the Agency's good guidance practices.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

Cases of monkeypox have been reported from countries, including the United States, where the disease is not endemic and continue to be reported in several endemic countries. Monkeypox virus is a zoonotic infection (a virus transmitted to humans from animals), caused by *Orthopoxvirus* genus of the *Poxviridae* family similar to variola virus (the causative agent of smallpox) and can spread among humans.

On July 23, 2022, the World Health Organization (WHO) declared the global outbreak of monkeypox a Public Health Emergency of International Concern (PHEIC).[4] On August 4, 2022, as cases continued to be reported in the United States, the Secretary of HHS issued a declaration under section 319 of the Public Health Service (PHS) Act that a public health emergency exists nationwide related to monkeypox.[5]

On August 9, 2022, the Secretary of HHS determined that there is a public health emergency, or 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. On September 7, 2022, the Secretary declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of monkeypox virus.

To effectively respond to the monkeypox outbreak, rapid detection of cases and contacts, appropriate clinical management and infection control, and implementation of community mitigation efforts are critical. FDA believes the policies and recommendations set forth in this guidance will help address these urgent public health concerns by helping to quickly increase

[3] In this guidance, references to "high-complexity CLIA-certified laboratories" and "laboratories" are referring to single site laboratories that are certified under CLIA that meet the requirements to perform tests of high-complexity.
[4] Available at https://www.who.int/europe/news/item/23-07-2022-who-director-general-declares-the-ongoing-monkeypox-outbreak-a-public-health-event-of-international-concern
[5] *See* HHS Secretary Section 319 Declaration (Aug. 4, 2022), available at https://aspr.hhs.gov/legal/PHE/Pages/monkeypox-4Aug22.aspx

availability of tests at this stage of the outbreak and expand available testing capabilities in healthcare settings, reference laboratories, and commercial laboratories.

The EUA authorities enable FDA to help strengthen the nation's public health protections against chemical, biological, radiological, and nuclear (CBRN) threats by facilitating the availability and use of medical countermeasures initiatives (MCMs) needed during certain public health emergencies. Under section 564 of the FD&C Act, the FDA Commissioner may allow unapproved medical products or unapproved uses of approved medical products to be used in certain emergency circumstances, after the HHS Secretary has made a declaration justifying authorization of emergency use, to diagnose, treat, or prevent serious or life-threatening disease or conditions caused by CBRN threat agents when certain criteria are met.

There is an FDA-cleared diagnostic test for non-variola orthopoxviruses, including monkeypox virus, which the Centers for Disease Control and Prevention (CDC) developed.[6] That test has been helping address critical testing needs. However, the United States Government believes there are additional, critical needs for monkeypox tests at this stage of the outbreak. The policies in this guidance are designed to address those testing needs and account for the importance of expanding availability of tests and addressing future potential testing needs. FDA will continue to monitor and assess the testing landscape in the United States and other relevant factors regarding this outbreak, and will revise its policies and recommendations as appropriate.

III. Scope

The policies described in this guidance for expanding testing availability for monkeypox or other non-variola orthopoxviruses[7] apply to certain laboratories[8] and commercial manufacturers that are developing monkeypox tests[9] during the public health emergency, as described below. The policies, validation recommendations, and other recommendations discussed below should be considered for initial testing of patient specimens, with subsequent confirmatory testing performed as appropriate.

FDA notes that the enforcement policies in this guidance do not address medical device reporting (MDR) under 21 CFR Part 803 for tests offered prior to or without authorization as described in

[6] CDC Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set (K181205, K221658, K221834 and K222558).

[7] For purposes of this guidance, "monkeypox tests" means tests for monkeypox or other non-variola orthopoxviruses.

[8] As described in Section I. Introduction and the policies in Section IV of this guidance, the guidance describes FDA's enforcement policies for certain diagnostic tests that are developed by and performed in a laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA) that meets the requirements to perform tests of high complexity. In this guidance, references to "high-complexity CLIA-certified laboratories" and "laboratories" are referring to single site laboratories that are certified under CLIA that meet the requirements to perform tests of high-complexity.

[9] Throughout this guidance, the term "diagnostic test" is generally used to refer to molecular or antigen tests, both of which can be used to diagnose active infection with monkeypox virus. Molecular tests detect the presence of viral DNA and antigen tests detect the presence of viral proteins that are part of monkeypox virus. The terms "serology" or "antibody" tests are generally used to refer to tests that detect antibodies to monkeypox virus. Because the antibodies are part of the body's immune response to exposure and not the virus itself, such testing cannot be used to diagnose an active infection.

the guidance. Developers offering monkeypox tests during the public health emergency are expected to comply with applicable MDR requirements, including reporting of medical device events that reasonably suggest that their device may have caused or contributed to a death or serious injury, and malfunctions that would be likely to cause or contribute to a death or serious injury if they were to recur. Moreover, unless and until an EUA (or marketing authorization with accompanying CLIA categorization) is issued that authorizes additional testing environments for a specific test, under CLIA, use of that test is limited to high-complexity CLIA-certified laboratories, including testing at the point-of-care when the site is covered by the laboratory's CLIA certificate for high-complexity testing.

IV. Policy

FDA generally expects developers of tests that are outside the scope of the policies described below to submit an EUA request or a premarket submission and receive authorization or clearance prior to offering or distributing a monkeypox test.

A. Diagnostic Tests

The following policies are intended to help facilitate the availability and accessibility of diagnostic tests that detect monkeypox virus in the United States at this stage in the outbreak.

The policies described in this section apply to diagnostic tests that detect monkeypox virus – whether they be for monkeypox specifically or for non-variola orthopoxviruses – and are intended for use on individuals suspected of having monkeypox by a healthcare provider.

1. Prioritization of Review of EUA Requests for Tests

The issuance of an EUA is discretionary. FDA's decision to review and process an EUA request, and ultimately issue an EUA if the relevant statutory criteria are met, is based on a determination, on a case-by-case basis, that such action is necessary to protect the public health in an emergency. EUAs "may" be issued by the government when necessary to protect the public health in an emergency, as described in section 564(a)(1) of the FD&C Act (21 U.S.C. 360bbb-3(a)(1)), which states, in relevant part, "subject to the provisions of this section, the Secretary may authorize the introduction into interstate commerce…a drug, device, or biological product intended for use in an actual or potential emergency."

At this stage in the outbreak, for monkeypox diagnostic tests, FDA intends to prioritize review of EUA requests for high-throughput diagnostic tests, tests with home specimen collection, or rapid[10] diagnostic tests,[11] all from experienced developers[12] with high manufacturing capacity that inform FDA within 30 days after publication of the notice of availability of this guidance in the Federal Register of their intent to submit an EUA request. FDA will monitor the situation and may adjust this prioritization, including shortening or lengthening this time period, as appropriate.

To facilitate FDA's prioritization efforts, FDA recommends that developers send the following preliminary information to FDA to indicate their intent to submit an EUA request for a monkeypox diagnostic test:

- Description of the test technology,
- Manufacturing capacity, including ramp up timeframes,
- Test throughput,
- Expected timeline for development, validation, and submission of an EUA request, and
- Any available validation data, including data supporting the validity of testing any non-lesion based sample types, if used.

FDA recommends providing this information in an email to MPXDx@fda.hhs.gov titled "Diagnostic Test for Monkeypox – Intent to Submit EUA Request - Test Summary Information." FDA's goal will be to respond promptly by return email on a rolling basis to inform developers whether FDA intends to prioritize review of the proposed test at that time. FDA intends for this response to inform the developer's plans and decisions regarding whether to submit an EUA request.

After an EUA request has been submitted, FDA intends to notify test developers by email if FDA authorizes a test or declines to review, declines to issue, or otherwise decides not to authorize a test for any reason, including lack of response or a determination that there is a lack of adequate data to support authorization.

[10] Rapid tests are generally considered to be diagnostic tests (molecular or antigen) that can be used at the Point of Care (POC) with a result in 30 minutes.

[11] High-throughput tests may help to significantly increase testing capacity, tests with home specimen collection may help to make testing more accessible to a broader patient population (e.g., to individuals who are unable or not likely to have their specimen collected in a healthcare or similar setting), and rapid diagnostic tests also may help with accessibility as these tests are often relatively simple to perform and so are often authorized for point-of-care.

[12] For the purposes of this guidance, "experienced developers" refers to developers who have successfully been issued an EUA for a test during a public health emergency, received approval or clearance for a diagnostic test, or have similar experience and are developers for whom FDA does not have current compliance concerns. Given our experiences to date, we believe that FDA's review resources are more impactful when working with experienced developers given the design and validation complexities associated with such tests.

2. Monkeypox Diagnostic Tests Developed and Performed by Laboratories

At this time, FDA does not intend to object to the offering of monkeypox tests developed and performed in a CLIA-certified laboratory that meets the requirements to perform tests of high complexity where:

- the test uses molecular PCR technology;
- the test uses lesion swabs;
- the test has been appropriately validated; and,
- the laboratory notifies FDA of validation within five business days of offering the test (or, for currently-offered tests within this scope, notifies FDA within five business days from the date of this guidance) that it has appropriately validated such test.

For recommended notification content, see section IV.A.4.

The policy described in this section does not apply to tests with home specimen collection or at-home tests[13] or to tests using specimen types other than lesion swabs or technologies other than PCR.[14] As always, FDA retains discretion and may decide not to object to the offering of tests in other circumstances on a case-by-case basis, such as not objecting to the offering of tests using a different specimen type or a different technology for laboratories directly involved in patient care, like those in academic medical centers, if important for providing patient care. Laboratories that want to discuss should contact FDA at MPXDx@fda.hhs.gov.

FDA believes the policy described in this section is appropriate at this time in light of the increasing numbers of monkeypox cases throughout the country and the urgent need to continue to expand the nation's capacity for monkeypox testing at this stage of the public health emergency. There is currently an FDA-cleared diagnostic test developed by CDC, but available information indicates that there is a need for additional diagnostic testing for monkeypox in the

[13] Different risks are presented with specimen collection in the home versus the healthcare setting. Home collection raises several issues of importance, including whether the lay user can safely and properly collect the specimen, whether the components of the specimen transport media are safe for use in the home environment (since some may be toxic), proper shipment, and adequate stability of the specimen given the time lapse between collection and testing and the potential impact of shipping conditions (such as, if the specimen sits in a hot truck). Tests that are also interpreted in the home require demonstration of the ability of a lay user to collect their specimen, run the test, and interpret their results accurately.

[14] FDA believes limiting this policy to laboratories that develop tests that use PCR technology is appropriate because PCR is an established technology for which high-complexity CLIA-certified laboratories have experience developing tests. FDA is further limiting this policy to PCR tests that test lesion swab specimens because FDA is confident that appropriately validated tests can detect the monkeypox DNA from lesion swabs. Use of lesion swabs has been shown to be effective when using the FDA-cleared CDC Non-variola Orthopoxvirus Real-time PCR test and FDA is not aware of other validated specimen types for diagnosing monkeypox at this time. Moreover, the CDC published a Real-Time PCR test procedure to detect non-variola *Orthopoxvirus*, which can help guide laboratories in the development and validation of their tests (See https://www.cdc.gov/poxvirus/monkeypox/pdf/Non-variola-Orthopoxvirus-Generic-Real-Time-PCR-Test.pdf).

United States.[15, 16] To address the immediate capacity needs, FDA does not intend to object to the development and offering of additional diagnostic tests, as described in this section, for a period long enough to address availability and accessibility concerns, which FDA believes should be addressed by laboratories that notify FDA within 30 days given current signals. As such, we intend to accept notifications for 30 days after publication of the notice of availability of this guidance in the Federal Register but FDA will monitor the situation and may adjust, including shortening or lengthening this time period, as appropriate. In addition, FDA will monitor the situation for whether to make any other revisions to this policy. This policy should help foster continued and immediate access to already-offered diagnostic tests for monkeypox, help increase wider access to diagnostic tests in local communities across the United States through the development of new tests, and help expedite turnaround times for test results, while FDA-cleared and authorized tests become increasingly available.

For tests described in this section, if FDA identifies a significant problem or concern with a test, FDA intends to notify the laboratory by email and work with the laboratory to address the concerns. If the concerns cannot be adequately addressed in a timely manner, FDA generally would expect the laboratory to take appropriate steps, which could include that the laboratory stop offering the test, conduct a recall of the test whether modified or not, and/or notify end users by issuing corrected test reports indicating prior test results may not be accurate.

3. Modifications to FDA-cleared or EUA-authorized Diagnostic Tests

When a high-complexity CLIA-certified laboratory is modifying a cleared or authorized monkeypox molecular diagnostic test, including one for which such laboratory is not the developer of the original test, and the modifications do not change the indication for use set forth in the 510(k) or EUA (e.g., including new/different extraction kits or instruments that would not be expected to change the indication for use) and do not change the analyte specific reagents (e.g., the modifications do not change the PCR primers and/or probes or enzymes),[17] FDA does not intend to object to implementation of the modification to the diagnostic test without a new or amended EUA or a new premarket submission (e.g., 510(k)) where the test has been validated, the validation demonstrates that the modifications do not adversely affect test performance,[18] and the laboratory submits notification of validation to FDA, as described in section IV.A.4.

If a laboratory modifies a test for which the laboratory is not the developer, FDA encourages the laboratory to collaborate with the original developer so that validation data supporting the modifications can be submitted by the original developer to FDA in a supplemental EUA request

[15] To date, the FDA-cleared CDC Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set (Product Code: PBK; Regulation Number: 21 CFR 866.3315; 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.

[16] For additional information, refer to https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/fda-monkeypox-response.

[17] Other modifications, including to specimen types, test settings (e.g., point-of-care), and new patient populations, among others, do not fall under this policy.

[18] FDA generally considers equivalent performance to be where the LoD of the modified test (using the same validation material used in the LoD study described in the authorized test's Instructions For Use (IFU)) is within 3x of the LoD established in the authorized test's IFU or that the LoD of the modified test is within 3x of the LoD of the authorized test in a direct comparison LoD study.

or new premarket submission, as applicable. Supplemental EUA requests or premarket submissions such as this have the potential to increase testing capacity by allowing more laboratories to use the test with additional components.

When a commercial manufacturer is modifying its own cleared or authorized monkeypox molecular diagnostic test to make modifications that do not change the indication for use set forth in the 510(k) or EUA (e.g., including new/different extraction kits or instruments that would not be expected to change the indication for use) and do not change the analyte specific reagents (e.g., the modifications do not change the PCR primers and/or probes or enzymes),[19] where the commercial manufacturer has submitted validation data supporting the modification to FDA in a supplemental EUA request or a new premarket submission, FDA does not intend to object to implementation of the modification to the diagnostic test while FDA conducts its review of the supplemental EUA request or premarket submission.

FDA intends to notify developers by email if FDA declines to review, declines to issue, or otherwise decides not to authorize a supplemental EUA request for any reason, including lack of response or a determination that there is a lack of adequate data to support such request. If so notified, FDA generally expects developers to cease distributing and offering their modified test within 15 calendar days of the date of the FDA notification. Moreover, if FDA identifies a significant problem or concern with a test, FDA generally expects the developer to take appropriate steps to address such problems, which could include conducting a recall of the test and/or notification concerning corrected test reports indicating prior test results may not be accurate.

In order to provide transparency, when a developer is distributing or offering a test that is a modification of a cleared or EUA-authorized diagnostic test as discussed in this section, the recommendations in Section IV.A.5 of this guidance apply. FDA further recommends that the developer post data about the modified test's performance characteristics on the developer's website, and that the instructions for use or test protocol and the test reports accurately reflect the modification and prominently disclose that the test has been modified since clearance/authorization by FDA and that the modified test has not been reviewed by FDA.

4. Notification Content

The information contained in this section applies to laboratories notifying as described in sections IV.A.2 or IV.A.3. Notification should be sent by email to MPXDx@fda.hhs.gov with a subject line "FDA Notification of Development and Validation of Monkeypox Test." Providing certain information in this notification would be helpful to FDA in assessing potential testing capacity. As such, we encourage laboratories to include all of the following types of information, as applicable:

1. The policy in this guidance for which you are providing notification (e.g., whether it is a test developed as described in Section IV.A.2. or a modified test as described in Section IV.A.3.)
2. Laboratory name

[19] See fn. 17 above.

3. Test name
4. Test methodology, including specimen type
5. Name of the laboratory director
6. Address
7. Laboratory CLIA ID#
8. The date you began, or intend to begin, patient testing
9. Contact individual's name, address, phone number, email address
10. Estimated initial testing capacity (e.g., in tests per week)
11. For notifications of modifications as described in section IV.A.3 of this guidance, please include the test name and developer of the FDA-cleared or authorized unmodified test and a short description of the modifications made to that test.

You will receive an autoreply email acknowledging receipt of your email and FDA intends to provide a unique reference number for you in a subsequent response to your notification email.

5. Reporting of Results

In order to provide transparency, test reports should prominently disclose that the test has not been reviewed by FDA if the test is offered as described in the policy described in section IV.A.2. or as applicable in section IV.A.3. Unless a test is authorized by FDA, any statements that expressly state or imply that the test has been reviewed or authorized by FDA would be false. Similarly, any statements that state or imply that FDA will authorize a test could be misleading.

Laboratories should immediately notify appropriate Federal, State, or local public health agencies of test results in accordance with applicable laws.

B. Validation of Diagnostic Tests

In the context of a public health emergency, it is critically important that tests be appropriately validated prior to use because false results not only can negatively impact the individual patient but also can have a broad public health impact. False positive results for diagnostic tests, for example, can lead to delay in accurate diagnosis and appropriate treatment for the individual. False negative results can lead to lack of appropriate treatment for the individual and further spread of the disease.

Given the importance of test validation, FDA is providing in templates on its website recommendations regarding validation testing that should be performed for diagnostic monkeypox tests. The recommendations in the templates are voluntary, and developers may use alternative approaches to validation to address the analytical and clinical validation principles discussed in FDA's recommendations.

FDA has provided on its website two types of voluntary templates that developers may opt to use to facilitate an EUA request.[20] One is a summary template with recommendations regarding validation testing that should be performed to provide information on the analytical and clinical validity of the test. The other is a voluntary comprehensive template that provides additional

20 https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/monkeypox-emergency-use-authorizations-medical-devices

details, including study design considerations and fill-in-the-blank responsive text. Depending on the characteristics of the test, additional validation studies may be recommended. However, developers do not need to use either template when submitting an EUA request.

To show validation for tests developed using primers and probes[21] that are identical to the FDA-cleared CDC test[22], FDA generally recommends that an evaluation of the Limit of Detection (LoD) and a clinical agreement study demonstrate performance consistent with the FDA-cleared test. For additional information on FDA's recommendations for these performance evaluations, please see the voluntary templates on FDA's website.

FDA intends to update its recommendations regarding validation testing as the outbreak evolves. At this time, FDA's initial validation recommendations are for clinical validation with contrived specimens, but if clinical samples become more widely available, FDA may revise this recommendation.

Developers can use alternative approaches. FDA encourages developers to discuss any alternative technological approaches to validating their test with FDA through submission of a pre-EUA to MPXDx@fda.hhs.gov. FDA may make other templates available throughout the emergency.

C. Serology Tests

In an emerging outbreak, use of serology tests can provide information that may further our understanding of the disease process. While monkeypox serology tests can be helpful, there is great potential for their misuse. At least at this time, monkeypox serology tests cannot be used to diagnose, or aid in the diagnosis of, an active infection and are not tests of immunity. Therefore, it is important that results from monkeypox serology tests be used for appropriate purposes and the result be properly communicated.

At this time, FDA does not intend to object to the use of monkeypox serology tests that are developed and performed by a high-complexity, CLIA-certified laboratory that is part of an entity that conducts research on diseases and is integrated into the direct medical care of the patient (often referred to as academic medical center laboratories), where the laboratory gives notification of validation to FDA as described in section IV.C.2., and certain information is included in the test reports as described in section IV.C.1. This should mitigate the potential misuse of monkeypox serology test results while also fostering research from availability of data from serology testing of patients. For example, these laboratories can test their patients daily or frequently over a period of time to monitor immune response and are most likely to benefit from the information learned from serology testing at this stage of the monkeypox outbreak.

FDA encourages the laboratories to share their validation data with FDA as well as what they learn about the utility of such tests. Should clinical utility be demonstrated for monkeypox

[21] The sequences used in the FDA-cleared CDC assay can be found on CDC's website: https://www.cdc.gov/poxvirus/monkeypox/pdf/Non-variola-Orthopoxvirus-Generic-Real-Time-PCR-Test.pdf

[22] FDA's decision summary for the FDA-cleared CDC *Orthopoxvirus* test can be found on FDA's website at: https://www.accessdata.fda.gov/cdrh_docs/reviews/K221658.pdf.

serology tests in the future, FDA may decide it is in the best interest of public health to review EUA requests for serology tests.

If FDA becomes aware of questions or concerns about a notified serology test, such as poor performance or misleading statements about the test, FDA will communicate those concerns to the laboratory and provide the laboratory an opportunity to address the questions or concerns. If the concerns cannot be, or have not been, addressed in a timely manner, FDA would expect the laboratory to stop offering their test, and FDA may take additional actions as appropriate.

1. Reporting of Results

FDA recommends including certain clarifying information in the test reports for serology tests to help patients understand the test results, such as the information in the following statements:

- Not for use to diagnose an active infection.
- Negative results do not preclude monkeypox virus infection. If active infection is suspected, viral testing for monkeypox virus or *Orthopoxvirus* is necessary.
- Results from antibody testing should not be used to diagnose or exclude *Orthopoxvirus* infection.
- The clinical significance of a positive or negative antibody result following smallpox vaccination has not been established.

2. Content of Notification

Laboratories notifying FDA that their assay has been validated as discussed immediately above should send an email to MPXDx@fda.hhs.gov with a subject line "FDA Notification of Serologic Monkeypox Test." For example, the notification should include all of the following types of information, as applicable:

1. Laboratory name
2. Test name
3. Test methodology, including specimen type
4. Name of the laboratory director
5. Laboratory address
6. Laboratory CLIA ID#
7. The date you intend to begin patient testing
8. Contact individual's name, address, phone number, email address
9. Estimated initial testing capacity (e.g., in tests per week)

You will receive an autoreply email acknowledging receipt of your email and FDA intends to provide a unique reference number for you in a subsequent response to your notification email.

V. Availability of EUA Templates

FDA has made available through download from our website[23] a series of templates that developers may choose to use to facilitate the preparation and submission of an EUA request for various types of monkeypox tests. The templates reflect FDA's current thinking on validation recommendations for monkeypox tests and the data and information that developers should submit to facilitate the EUA process. The templates provide information and recommendations, and FDA plans to update them as appropriate as more is learned about monkeypox virus and more experience is gained with the EUA process for the various types of monkeypox tests.

Developers can use alternative approaches. Developers who intend to use alternative approaches should consider seeking FDA's feedback or recommendations to help them through the EUA process. FDA encourages developers to discuss any alternative technological approaches to validating their test with FDA through MPXDx@fda.hhs.gov.

Members of the public can submit questions about the templates to MPXDx@fda.hhs.gov, or they can submit comments regarding the templates to the public docket established for this guidance.

[23] https://www.fda.gov/medical-devices/emergency-use-authorizations-medical-devices/monkeypox-emergency-use-authorizations-medical-devices