Contains Nonbinding Recommendations

Policy for Coronavirus Disease-2019 Tests (Revised)*

Guidance for Developers and Food and Drug Administration Staff

Document issued January 12, 2023.

This document supersedes "Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised): Guidance for Developers and Food and Drug Administration Staff" issued September 27, 2022.

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

*This is the seventh edition of this guidance, which originally issued February 29, 2020, and was subsequently revised on March 16, May 4, May 11, 2020, November 15, 2021, and September 27, 2022.

Preface

Public Comment

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to https://www.regulations.gov. All comments should be identified with the docket number FDA-2020-D-0987 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders," *available at* https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders, and the FDA webpage titled "Search for FDA Guidance Documents," *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive an additional copy of the guidance. Please include the document number GUI00020010 and complete title of the guidance in the request.

Questions

For questions about this document, contact CDRH-EUA-Templates@fda.hhs.gov.

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Guidance for Developers 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

FDA plays a critical role in protecting the United States from threats such as emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support response efforts to this pandemic.

FDA is issuing this guidance to provide FDA's review priorities and enforcement policies regarding novel coronavirus (COVID-19) tests. Rapid detection of COVID-19 cases in the United States requires wide availability of testing to control the spread of this highly contagious infection.

The policies in this guidance are intended to remain in effect only for the duration of the declaration under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) by the Secretary of Health and Human Services (HHS) on February 4, 2020, declaring that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the novel coronavirus (2019-nCoV).[1] FDA continues to assess the evolving situation and intends to update this guidance as appropriate.

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.

[1] *See* 85 FR 7316; *available at* https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.

II. Background

There is currently a pandemic of respiratory disease caused by a novel coronavirus. The virus has been named "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). On January 31, 2020, the Secretary of HHS issued a declaration of a public health emergency under section 319 of the Public Health Services Act related to COVID-19 and mobilized the Operating Divisions of HHS.[2] On February 4, 2020, the Secretary of HHS issued a declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of SARS-CoV-2 based on the HHS Secretary's public health emergency determination under section 564(b)(1)(C) of the FD&C Act.[3] In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.[4]

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

As of August 15, 2022, FDA has issued EUAs for more than 439 tests for COVID-19, including more than 354 diagnostic and 85 serology or other immune response tests. Further, two molecular diagnostic COVID-19 tests have been granted marketing authorization through the traditional device premarket review pathways. In the context of a public health emergency involving pandemic infectious disease, it is critically important that tests are validated 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 unnecessary quarantine and potential further spread when presumed positive individuals are quarantined together, wasted contact tracing and testing resources, and 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.

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[2] Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued on Jan. 31, 2020, and subsequently renewed), *available at* https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx.

[3] 85 FR 7316; *available at* https://www.federalregister.gov/documents/2020/02/07/2020-02496/determination-of-public-health-emergency.

[4] Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), *available at* https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/. On February 24, 2021, there was a Presidential Declaration continuing the national emergency concerning the COVID-19 pandemic beyond March 1, 2021. See Continuation of the National Emergency Concerning the Coronavirus Disease 2019 (COVID-19) Pandemic (February 24, 2021), *available at* https://www.federalregister.gov/documents/2021/02/26/2021-04173/continuation-of-the-national-emergency-concerning-the-coronavirus-disease-2019-covid-19-pandemic.

Previous versions of this guidance described policies regarding the distribution and offering of certain tests for clinical use prior to or without an EUA. These policies were issued to help quickly increase availability of tests in the early stages of the pandemic. Unless and until an EUA is issued that authorizes additional testing environments for a specific test, under the Clinical Laboratory Improvement Amendments (CLIA), section 353 of the Public Health Service Act (42 USC 263a), use of that test is limited to laboratories that are certified under CLIA, and meet the requirements to perform tests of high complexity, and at the point-of-care (POC) when covered by such a laboratory's CLIA certificate. Throughout this guidance, references to "high-complexity CLIA-certified laboratories" are referring to laboratories that are certified under CLIA and meet the requirements to perform tests of high complexity. These policies did not apply to at-home tests or tests with home specimen collection.

FDA has updated these policies when appropriate in response to the changing landscape of this pandemic. The previous update on November 15, 2021, explained FDA's intent to review EUA requests for certain types of tests that FDA believed would be most beneficial at that stage of the pandemic. In addition, in the November 15, 2021, version, FDA revised the previous enforcement policies to reflect that, at that stage of the pandemic, the Agency generally expected COVID-19 tests to have been issued an EUA prior to the tests being distributed or offered.

FDA has continued to closely monitor the COVID-19 testing landscape and believes it is again appropriate to update its policies to reflect the current needs of the pandemic. As explained throughout this guidance, FDA intends to review the EUA requests for a small subset of tests based on the review priorities described in section IV.A. Traditional marketing pathways remain available to all developers and FDA encourages developers of tests that fall outside the scope of the priorities outlined in this guidance to pursue those routes. In sum, in the September 27, 2022, update, FDA revised this guidance to update the types of COVID-19 tests for which the Agency intends to review EUA requests, to discuss the use of the traditional premarket review pathways for other types of COVID-19 tests for which the Agency does not intend to review EUA requests, and to make minor updates to the enforcement policies. In the current version of this guidance, FDA has revised the duration for which the policies in this guidance are intended to remain in effect.

III. Scope

This guidance applies to diagnostic and serology tests for COVID-19.[5] The policies and recommendations described in this guidance are intended to facilitate availability of tests for

[5] 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 infection with the SARS-CoV-2 virus. Diagnostic tests may be designed for use in various settings, such as in a CLIA-certified laboratory, at the point of care at a site covered by a laboratory's CLIA certificate, or at home. Screening tests, which are used for testing individuals without symptoms or other reasons to suspect COVID-19, are a subset of diagnostic tests. Molecular tests detect the presence of viral RNA and antigen tests detect the presence of viral proteins that are part of the SARS-CoV-2 virus. There may also be diagnostic tests that incorporate different technologies, such as breath tests, that have a reasonable expectation of technical and clinical success. While the principles in this guidance are generally still applicable to such tests, there are fewer available, so different approaches may be appropriate. Therefore, FDA recommends that developers of such tests contact FDA at CDRH-EUA-Templates@fda.hhs.gov to discuss the best approach for their test. The terms

COVID-19 that FDA believes will be most beneficial at the current stage of the public health emergency.

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 authorization as described in the guidance. Developers offering such tests 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 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

A. Review of EUA Requests for COVID-19 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. It is an authorization that the government "may" issue when necessary to protect the public health in an emergency (see 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"). FDA's January 2017 guidance, *Emergency Use Authorization of Medical Products and Related Authorities*, [6] describes factors that FDA intends to use in its prioritization of EUA requests, such as the public health need for the product, the availability of the product, the availability and adequacy of the information concerning the likelihood that the product may be safe and effective in preventing, treating, or diagnosing the condition, and whether the product is included in government stakeholder stockpiles.

Given the need to address urgent public health priorities, FDA has and continues to prioritize among the EUA requests it receives for COVID-19 tests.

At this stage of the pandemic, FDA intends to prioritize its review of EUA requests and supplemental EUA requests from experienced developers[7] for diagnostic tests that are likely to

"serology" or "antibody" tests are generally used to refer to tests that detect antibodies to the SARS-CoV-2 virus. Because the antibodies are part of the body's immune response to exposure and not the virus itself, such testing cannot be used for diagnosis of acute infection.

[6] See https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities.

[7] For the purposes of this guidance, "experienced developers" refers to developers who have interacted with FDA through a successful EUA request or have similar experience. FDA has interacted with over 1,000 test developers through the EUA and pre-EUA processes during the SARS-CoV-2 pandemic. The Agency has found that EUA

have a significant public health benefit (e.g., employ innovative technology) or are likely to fulfill an unmet need (e.g., diagnosing infection with a new variant or subvariant).

FDA generally intends to focus its review on EUA requests and supplemental EUA requests for tests that are within these priorities.[8] In addition to the above priorities, FDA also intends to focus its review on EUA requests that are from or supported by a U.S. government stakeholder,[9] such as tests funded by the Biomedical Advanced Research and Development Authority (BARDA) or the National Institutes of Health's Rapid Acceleration of Diagnostics (RADx). FDA intends to notify test developers of its intent by email if FDA declines to review or otherwise decides not to authorize a test/modification in an EUA request or supplemental EUA request.

In general, FDA believes these priorities are appropriate to address the public health needs at the current stage of the public health emergency based on the available information and may adjust these priorities as public health needs change. Specifically, there is generally sufficient availability of authorized high-throughput laboratory-based diagnostic tests intended for use with pooled samples and authorized home-use antigen tests that are available for over the-counter (OTC) or prescription use.

FDA believes that the number of EUA requests that fall within FDA's current review priorities described in this guidance are likely limited and generally encourages developers to submit COVID-19 tests through traditional premarket review pathways. If you are unsure whether your test may be prioritized for review, we encourage you to reach out to CDRH-EUA-Templates@fda.hhs.gov; however, at this stage, FDA strongly encourages developers of new tests and existing tests for which modifications are sought to pursue traditional pre-market pathways.

B. State Authorization of High-Complexity CLIA-Certified Laboratories

Versions of this guidance prior to November 15, 2021, described a policy regarding States and territories that authorize laboratories within their State or territory to develop their own COVID-19 tests and perform specimen testing, where the notification of SARS-CoV-2 test validation is not submitted to FDA and the laboratory does not submit an EUA request to FDA.

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requests from inexperienced developers are more resource intensive to review. At this phase of the pandemic, and given our experiences to date, we believe that for COVID-19 tests, FDA's review resources are more impactful when working with experienced developers given the design and validation complexities associated with such tests. As a result, FDA intends to prioritize the review of EUA requests for tests from experienced developers.

[8] Developers of tests that are not within these priorities should consider pursuing marketing authorization through a traditional premarket review pathway. Test developers are welcome to reach out to the team at CDRH-EUA-Templates@fda.hhs.gov to discuss whether review of their EUA request may be prioritized.

[9] Prioritization of EUA requests from (or supported by) government stakeholders is discussed in the Guidance for Industry and Other Stakeholders: Emergency Use Authorization of Medical Products and Related Authorities, *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities.

Under such policy, a State or territory choosing to authorize laboratories within that State or territory to develop and perform a test for COVID-19 would do so under authority of its own State law, and under a process that it established, and FDA did not intend to object to the use of such tests for specimen testing where the notification of SARS-CoV-2 test validation was not submitted to FDA and the laboratory did not submit an EUA request to FDA, and where instead the State or territory took responsibility for COVID-19 testing by laboratories in its State during the COVID-19 outbreak. This policy applied only to tests designed, developed, and used within a single, high-complexity, CLIA-certified laboratory. The policy did not apply to at-home tests or tests with home specimen collection, or any testing outside of a high-complexity CLIA-certified laboratory.[10]

In versions of this guidance prior to November 15, 2021, FDA requested that the State or territory notify us if it chose to use this flexibility to expedite COVID-19 testing.[11] FDA indicated that it would not be reviewing the process adopted by the State or territory. FDA expected that such States and territories as part of their oversight process would require laboratories developing SARS-CoV-2 tests to validate those tests prior to use. FDA encouraged laboratories that developed and performed a test for COVID-19 that was authorized by a State or territory to notify FDA that they have started clinical testing by sending an email to that effect to CDRH-EUA-Templates@FDA.HHS.GOV, and provide information on testing capacity.

In the November 15, 2021, version of this guidance, FDA revised this policy such that FDA no longer intended to apply the policy to any additional States or territories going forward.[12] The FDA is maintaining the policy in Section IV.B. of the November 15, 2021, policy, without further revision. For the States and territories listed on the notification list on FDA's website prior to November 15, 2021, that are continuing to authorize laboratories within that State or territory to develop and perform a test for COVID-19, FDA does not intend to object to the use of such tests for specimen testing where notification of SARS-CoV-2 test validation is not submitted to FDA and the laboratory does not submit an EUA request to FDA, and where instead the State or territory takes responsibility. This policy applies only to tests designed, developed, and used within a single, high-complexity CLIA-certified laboratory. This policy does not apply to at-home tests or tests with home specimen collection, or any testing outside of a high-complexity CLIA-certified laboratory.[13]

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[10] There are different risks associated with testing in different settings and different issues need to be addressed. For example, 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 (because 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 performed fully at home raise additional issues such as whether the lay user can safely and properly perform the test and read and accurately interpret the results.

[11] A list of States and territories that have notified FDA under this policy is available on FDA's FAQ website at: https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/notifications-and-emergency-use-authorizations-faqs-testing-sars-cov-2.

[12] A State or territory that believes there would be a particular benefit to the policy applying to the State or territory is welcome to reach out to FDA to discuss further by sending an email to CDRH-EUA-Templates@fda.hhs.gov.

[13] As discussed in FN [8], there are different risks associated with testing in different settings and different issues need to be addressed.

FDA notes that laboratories should be aware of requirements to report test results to appropriate federal, state, and local public health agencies in accordance with applicable federal, state, and local laws.[14]

C. Distribution and Offering of SARS-CoV-2 Diagnostic and Serology Tests During FDA Review

Previous versions of this guidance document described enforcement policies where FDA generally did not intend to object to developers distributing and offering certain tests prior to FDA authorization, as described in the policies. Those policies were updated in the November 15, 2021, version of the guidance, and FDA is generally continuing those updated policies and clarifying them, as discussed below.

(1) FDA Review of EUA Requests

For the following tests, FDA does not intend to object to the continued distribution or offering of the test while FDA reviews the EUA request for the test:

- Tests on one of the notification lists[15] on FDA's website at the time of issuance of this updated guidance; and,
- Laboratory developed tests (LDTs)[16] offered following the HHS August 2020 Web Statement entitled, "Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests" ("August 2020 HHS Announcement") and prior to November 15, 2021, where an EUA request was submitted to FDA as described in Section IV.C.2 of the November 15, 2021 version of this guidance document.[17]

For tests described in this section, FDA intends to notify test developers by email if FDA declines to review, declines to issue, or otherwise decides not to authorize the test for any reason, including lack of response or a determination that there is a lack of adequate data to support authorization. If so notified, FDA generally expects developers to cease distributing, marketing, and offering their tests within 15 calendar days. Moreover, if FDA identifies a significant problem or concern with a test, based either on the provided information or external reports, FDA generally would expect the developer to take appropriate steps to address such problems,

[14] Under section 18115 of the CARES Act (Public Law 116-136), laboratories, including those in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance or Certificate of Accreditation, must report the results of COVID-19 tests to HHS or its designee, in such form and manner as the Secretary may prescribe, during the declared public health emergency. For additional information on the laboratory data reporting guidance and FAQs from HHS, please see: https://www.hhs.gov/coronavirus/testing/covid-19-diagnostic-data-reporting/index.html.

[15] https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/notifications-and-emergency-use-authorizations-faqs-testing-sars-cov-2

[16] LDTs are typically considered tests that are designed, manufactured, and used within a single laboratory that is certified under CLIA and meets the requirements to perform tests of high complexity.

[17] This does not apply to EUA requests for which FDA has already notified the test developer by email that FDA declines to review, declines to issue, or otherwise decides not to authorize the test for any reason, including lack of response or a determination that there is a lack of adequate data to support authorization. Developers of such tests were generally expected to cease distributing, marketing, and offering their tests within 15 calendar days of receiving such an email.

which could include conducting a recall of the test and/or notification concerning corrected test reports indicating prior test results may not be accurate.

(2) Recommendations Regarding Test Reports and Other Information for Tests Offered During FDA Review of EUA Requests

FDA continues to recommend the following:

1. Test reports should prominently disclose that the test has not been reviewed by FDA. Until the test is authorized by FDA, any statements in the test reports and other labeling that expressly state or imply that the test has been authorized by FDA would be false. Similarly, any statements in the test reports and other labeling that state or imply that EUA issuance or FDA authorization are imminent or pending could be misleading.

2. Developers should make publicly available on their website the instructions for use for the test and data about the test's performance characteristics, including a summary of assay performance.

3. Instructions for use and patient test reports for serology tests should include information that helps users and patients understand the test results, including the following:

    - Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct (i.e., diagnostic) testing for SARS-CoV-2 is necessary.
    - Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection.
    - Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.

In addition, as noted in previous versions of this guidance and earlier in this updated guidance, unless and until an EUA 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 POC when the site is covered by such a laboratory's CLIA certificate.

D. Modifications to EUA-Authorized Diagnostic COVID-19 Tests

Throughout the course of the pandemic, FDA has issued various policies with respect to modifications and, as discussed further below, FDA is updating these policies. The policies in this section do not apply to at-home tests or tests with at-home specimen collection.

In order to provide transparency, when a developer is distributing or offering a test that is a modification of an EUA-authorized diagnostic test prior to or without authorization of the modified test, as discussed in this section, the recommendations in Section IV.C.2 of this updated 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 authorization by FDA and that the modified test has not been reviewed by FDA.

If FDA identifies a significant problem or concern with a modified test, based either on the provided information or external reports, that cannot be addressed in a timely manner, FDA generally would expect the developer to cease distribution, marketing and offering the modified test and address such problem, which could include conducting a recall of the modified test and/or notification concerning corrected test reports indicating prior test results may not be accurate.

(1) Modifications Made After Issuance of this Updated Guidance

In addition to the priorities above, FDA intends to review supplemental EUA requests that fulfill a condition of an EUA. For other supplemental requests, such as those that are beyond the priorities outlined above, FDA encourages developers to consider including the modification in a submission through a traditional premarket review pathway. In general, FDA expects such modified tests to be authorized under an EUA or pursuant to a traditional premarket review pathway before being distributed or offered.

When a high-complexity CLIA-certified laboratory is modifying an authorized COVID-19 molecular diagnostic test, including one for which such laboratory is not the developer of the original, EUA-authorized test, and the modifications do not change the indication for use set forth in the 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),[18] FDA does not intend to object to implementation of the modification to the diagnostic test without notification to FDA or a new or amended EUA where the laboratory has validated the modification and confirmed that the performance of the modified test is equivalent to the performance of the authorized test, and use of the test is limited to the high-complexity CLIA-certified laboratory in which the modification was made.[19]

In such cases, where the laboratory modifying and performing the test is not the developer of the original, EUA-authorized test, FDA encourages the laboratory to collaborate with the developer of the authorized test so that validation data supporting the modifications can be submitted by the original developer to FDA in a supplemental EUA request or incorporated into a future submission through the traditional premarket review pathways.

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

[19] 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.

(2) Certain Modifications Made Before Issuance of this Updated Guidance

Under previous versions of this guidance, when a commercial manufacturer made certain modifications to its EUA-authorized COVID-19 diagnostic test, and where validation data supporting the modification had been submitted in a supplemental EUA request, FDA stated that it did not intend to object to implementation of the modification while FDA conducted its review, except for modifications to add specimen types that have not been previously authorized with another test of the same technology. For such modifications made and implemented as discussed in the policies in the previous version of the guidance, FDA does not intend to object to such commercial manufacturers continuing to implement the modification while FDA conducts its review.

Under previous versions of the guidance, when a high-complexity CLIA-certified laboratory modified an EUA-authorized COVID-19 diagnostic test[20] prior to November 15, 2021, for use with a new specimen type, where the new specimen type has been previously authorized for another test of the same technology[21] and where the laboratory had validated the test for the new specimen type, FDA stated that it did not intend to object to the use of such a modified test without notification to FDA or a new or amended EUA. For all other types of modifications made by the high-complexity CLIA-certified laboratory prior to November 15, 2021, for an EUA-authorized COVID-19 diagnostic test, in previous versions of the guidance, FDA stated that it did not intend to object to the use of the test by high-complexity CLIA-certified laboratories, without notification to FDA or a new or amended EUA, where the modified test is validated using a bridging study to the EUA-authorized test.

For high-complexity CLIA-certified laboratories that modified an authorized COVID-19 molecular diagnostic test after November 15, 2021, but before issuance of the September 27, 2022, version of the guidance, including one for which such laboratory is not the developer of the original, EUA-authorized test, and the modifications do not change the indication for use set forth in the 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),[22] FDA stated that it did not intend to object to implementation of the modification to the diagnostic test without notification to FDA or a new or amended EUA where the laboratory has validated the modification and confirmed that the performance of the modified test is equivalent to the performance of the authorized test, and use of the test is limited to the high-complexity CLIA-certified laboratory in which the modification was made.[23]

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[20] This applies to modifications to any EUA-authorized diagnostic test, including a laboratory's own test with an EUA or a purchased kit from a commercial manufacturer with an EUA, but does not apply to modifications of authorized home collection kits.

[21] For the purposes of this guidance, all nucleic acid amplification tests are considered to have the same technology.

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

[23] 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.

For such modifications made and implemented by high-complexity CLIA-certified laboratories as discussed in the policies in the previous versions of the guidance, FDA does not intend to object to such laboratories continuing to offer any of those modified tests.

In such cases, where the laboratory performing the modified test is not the developer of the original, EUA-authorized test, FDA encourages the laboratory to share its validation data with the developer of the original, EUA-authorized test so that the developer of the original, EUA-authorized test can use the validation data in support of a supplemental EUA request to add the modification or can incorporate it into a future submission through the traditional premarket review pathways.

V. Validation

All clinical tests should be validated using clinical specimens and an appropriate comparator test prior to use.

In the context of a public health emergency, it is critically important that tests be validated prior to use because false results not only can negatively impact the individual patient but also can have a broad public health impact. However, FDA also generally accepts a lower level of evidence of validation for an EUA than for traditional premarket review pathways. FDA has provided recommendations regarding testing that should be performed to ensure analytical and clinical validity to the level of evidence expected for an EUA, including descriptions of appropriate comparators for different types of tests, in the EUA templates available through download from our website.[24] Depending on the characteristics of a developer's test, additional validation studies may be recommended.

Because the level of evidence required for authorization under traditional premarket review pathways is higher than that required for an EUA, the recommendations in the EUA templates may not be sufficient for developers seeking marketing authorization of their tests through traditional premarket review pathways. FDA can provide recommendations specific to a test developer's situation through inquiries to CDRH-EUA-Templates@fda.hhs.gov or through pre-submission interactions.[25]

Developers can use alternative approaches. FDA encourages developers to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

[24] See https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas.

[25] See FDA Guidance document "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program," available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.

Additionally, FDA continues to expect certain serology tests to be independently evaluated by NIH/NCI,[26] prior to authorization, when requested by the FDA. When performed, this additional testing can assist FDA in determining whether the EUA issuance criteria in section 564 of the FD&C Act have been met and whether FDA should authorize the test. This independent evaluation may also be used to assist FDA in determining whether the criteria for marketing authorization have been met for tests submitted through traditional premarket review pathways.

VI. Availability of EUA Templates and Inquiries Regarding Validation

FDA has made available through download from our website[27] a series of templates that developers may choose to use to facilitate the preparation and submission of an EUA request for various types of COVID-19 tests. The templates reflect FDA's current thinking on validation recommendations for SARS-CoV-2 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 COVID-19 and more experience is gained with the EUA process for the various types of COVID-19 tests. Developers may use alternative approaches. Developers who are considering alternative approaches should consider seeking FDA's feedback.

FDA can provide validation recommendations specific to a test developer's situation both for those seeking EUA and for those seeking marketing authorization through traditional review pathways. Developers can send simple inquiries to CDRH-EUA-Templates@fda.hhs.gov or submit a pre-EUA or pre-submission for more complex inquiries.[28] For tests seeking marketing authorization through traditional premarket review pathways, FDA may recommend validation studies or supportive evidence in addition to the recommendations in the EUA templates.

Members of the public can submit questions about the templates to CDRH-EUA-Templates@FDA.HHS.GOV, or they can submit comments regarding the templates to the public docket established for this guidance.

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[26] The FDA is working with the NIH, the Centers for Disease Control and Prevention (CDC), and BARDA to assess the performance of certain commercial manufacturers' serology tests. As part of this project, the FDA, working with partnering agencies, has designed a performance assessment protocol that offers a mechanism for an independent evaluation of certain lateral flow and certain enzyme-linked immunosorbent assay (ELISA) or similar technology-based SARS-CoV-2 antibody tests in a laboratory environment. Under this protocol, each test evaluated at the NIH/NCI will be evaluated with a well-characterized sample panel consisting of positive and negative plasma and/or serum samples. The approach represents a balanced attempt to provide a reasonable understanding of the potential performance of a significant number of the tests within a short time period. Performance results are considered during FDA's review of an EUA request for the test.

[27] See https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas.

[28] See FDA Guidance document "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program," available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.