

Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised)

Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff

Document issued on the web on May 11, 2020.

This document supersedes “Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency: Immediately in Effect Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff” issued May 4, 2020.

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

Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

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 20010-R3 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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Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency

Immediately in Effect Guidance for Clinical 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

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 a policy to help accelerate the availability of novel coronavirus (COVID-19) tests developed by laboratories and commercial manufacturers for the duration of the public health emergency. Rapid detection of COVID-19 cases in the United States requires wide availability of testing to control the emergence of this rapidly spreading, severe illness. This guidance describes a policy for laboratories and commercial manufacturers to help accelerate the use of tests they develop in order to achieve more rapid and widespread testing capacity in the United States.

This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Secretary of Health and Human Services (HHS) on January 31, 2020, effective January 27, 2020, including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service Act (PHS Act).

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Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020, titled “Process for Making Available Guidance Documents Related to Coronavirus Disease 2019,” available at <https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf>, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency’s good guidance practices.

In general, FDA’s guidance documents, including this guidance, 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

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, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.¹ In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.²

SARS-CoV-2 has demonstrated the capability to spread rapidly, leading to significant impacts on healthcare systems and causing societal disruption. The potential public health threat posed by COVID-19 is high, both globally and to the United States. To respond effectively to the COVID-19 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 set forth in this guidance will help address these urgent public health concerns by helping to expand the number and variety of tests,³ as well as available testing capabilities in reference and commercial laboratories and healthcare settings, while helping ensure these tests are accurate and reliable.

¹ Secretary of Health and Human Services Alex M. Azar II, Determination that a Public Health Emergency Exists, (Jan. 31, 2020), available at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx>. The declaration was renewed on April 21, 2020, effective April 26, 2020.

² Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), available at <https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>.

³ 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. 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. The terms “serological” 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 infection.

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The Centers for Disease Control and Prevention (CDC) laboratories have supported the COVID-19 response, including development of a diagnostic assay that was issued an Emergency Use Authorization (EUA) on February 4, 2020.⁴ Since authorizing CDC's EUA, FDA has been actively working with other SARS-CoV-2 diagnostic test developers to help accelerate development programs and respond to requests for in vitro diagnostic EUAs.⁵ However, the severity and scope of the current COVID-19 situation around the globe necessitates greater testing capacity for the virus than is currently available.⁶

The EUA authorities allow 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 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 disease or conditions caused by CBRN threat agents when certain criteria are met.

III. Scope

The policies described in this guidance for accelerating availability of testing for COVID-19 apply to certain laboratories and commercial manufacturers developing SARS-CoV-2 tests during the public health emergency, as described below.

IV. Policy

This guidance describes policies intended to help rapidly expand testing capacity by facilitating the development and use of SARS-CoV-2 tests during the public health emergency.

This guidance describes two policies for accelerating the development of certain laboratory-developed diagnostic tests for COVID-19 – one leading to an EUA submission to FDA, and the other not leading to an EUA submission when the test is developed under the authorities of the State in which the laboratory resides and the State takes responsibility for COVID-19 testing by laboratories in its State. The policy leading to an EUA remains unchanged from the initial publication of this guidance on February 29, 2020, though some process updates and clarifications have been made as discussed further below. The policy for State oversight remains unchanged from the second publication of this guidance on March 16, 2020.

⁴ See FDA's February 4, 2020, letter authorizing CDC's 2019-nCoV (RT)-PCR Diagnostic Panel for the presumptive qualitative detection of nucleic acid from the 2019-nCoV in upper and lower respiratory specimens, available at <https://www.fda.gov/media/134919/download>. This EUA was re-issued in its entirety on March 15, 2020 to reflect a number of amendments including changes to the intended use and primer and probe materials.

⁵ See FDA's Guidance, 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>.

⁶ Nothing in this guidance is intended to impact or supersede CDC's recommendations regarding which patients should be tested for COVID-19.

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In addition, this guidance describes a policy for commercial manufacturers to more rapidly distribute their SARS-CoV-2 diagnostic tests to laboratories for specimen testing after validation, while an EUA is being prepared for submission to FDA. This policy remains unchanged from the second publication of this guidance on March 16, 2020, though some process updates and clarification have been made as discussed further below.

This guidance also describes a policy regarding SARS-CoV-2 serological testing, which was modified in the May 4, 2020 publication of this guidance as it pertains to commercial manufacturers but not laboratories. At the time of prior issuance on March 16, 2020, FDA provided flexibility for serology tests to be marketed with notification to FDA and certain labeling information, but without submission of an EUA. FDA's policy was based on the considerations that serology tests are not meant to diagnose active SARS-CoV-2 infection and that early availability and use of these tests could help answer critical questions about the prevalence of COVID-19 infections in different communities, whether the presence of antibodies conveys immunity, and, if so, for how long. That policy succeeded in encouraging development of serology tests.

In addition to this policy, FDA has authorized several serology tests under individual EUAs and has issued an umbrella EUA providing a streamlined approach for EUA authorization of commercial serology tests that are evaluated by the National Institutes of Health's National Cancer Institute (NIH/NCI).⁷ Also since the March 16, 2020 publication of this guidance, FDA has become aware that a concerning number of commercial serology tests are being promoted inappropriately, including for diagnostic use, or are performing poorly based on an independent evaluation by the NIH,⁸ indicating that greater FDA oversight of commercial serology tests is important to protect the public health.

As outlined in the May 4, 2020 update, FDA does not intend to object as described below where commercial manufacturers develop and distribute their serology tests after validation, for a limited period of time, while an EUA is being prepared for submission to FDA. Appendices with templates for such submissions have been added to facilitate and streamline the EUA process.

The policy for serological tests developed and used by *laboratories* that are certified under the Clinical Laboratory Improvement Amendments (CLIA) to perform high-complexity testing has not changed from the March 16, 2020 guidance, though FDA continues to encourage such laboratories to submit EUAs for their laboratory developed tests.

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

⁷ <https://www.fda.gov/media/137470/download>

⁸ The FDA is working with the NIH, the Centers for Disease Control and Prevention (CDC), and the Biomedical Advanced Research and Development Authority (BARDA) to assess the performance of serology tests offered under the policy outlined in the March 16th guidance. As part of this project, the FDA, working with partnering agencies, has designed a performance assessment protocol that offers a mechanism for evaluation of lateral flow SARS-CoV-2 serological tests rapidly in a laboratory environment. Under this protocol, each test submitted to NIH will be evaluated with positive and negative plasma and 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 can be included by the test developer in an EUA submission.

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individual patient but also can have broad public health impact. In this guidance, FDA provides recommendations regarding validation of COVID-19 tests based on the available information. FDA encourages test developers to discuss any alternative technological approaches to validating their test with FDA.

The latest update addresses availability, through download from our website, of a series of templates that developers may choose to use to facilitate the preparation, submission, and authorization of an EUA for various types of COVID-19 tests.

A. Laboratories Certified under CLIA that Meet the CLIA Regulatory Requirements to Perform High-Complexity Testing Using Their Validated Diagnostic Tests Prior to EUA Submission

The policy described in this subsection applies to laboratories certified under CLIA that meet the CLIA regulatory requirements to perform high-complexity testing and that seek to develop and perform diagnostic tests to detect the SARS-CoV-2 virus and pursue an EUA from FDA for those tests. This policy does not apply to home collection of specimens to be sent for testing at a laboratory certified under CLIA for high-complexity testing.

FDA anticipates that clinical laboratories may need to design and manufacture the individual test kit components (e.g., primers, probes, etc.), or to purchase research use only (RUO) components from third party manufacturers, for the development of their assays.

In light of the increasing numbers of COVID-19 cases throughout the country and the urgent need to expand the nation's capacity for COVID-19 testing during the public health emergency, FDA does not intend to object to the use of these SARS-CoV-2 tests for specimen testing for a reasonable period of time, where the test has been validated and while the laboratory is preparing their EUA request, and where the laboratory gives notification of validation to FDA, as described below. FDA believes that 15 business days is a reasonable period of time to prepare an EUA submission for a test that has already been validated.

1. Validation

All clinical tests should be validated prior to use. In the context of a public health emergency, it is critically important that tests are validated because false results can negatively impact not only the individual patient but also can have broad public health impact. FDA has provided recommendations regarding testing that should be performed to ensure analytical and clinical validity in section V below. FDA encourages laboratories to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

2. FDA Notification

Following completion of assay validation, laboratories should notify FDA (e.g., email to CDRH-EUA-Templates@FDA.HHS.GOV) that their assay has been validated. This notification should include the name of the laboratory, name of the laboratory director, laboratory address, and contact person in this email. FDA will acknowledge receipt of this notification via auto-reply, and generally will add the laboratory name to FDA's website listing. As noted above, FDA recommends that laboratories submit a completed EUA request within 15 business days of the notification to FDA that the assay has been successfully validated. If an EUA request is not submitted within this timeframe, FDA intends to remove the laboratory from its website listing of laboratories that have notified FDA and may take additional actions as appropriate.

It would be helpful to FDA if laboratories provide information on testing capacity. This information will help the Agency and Department monitor the landscape as we work to ensure adequate testing capacity across the country.

3. Reporting of Results

In order to provide transparency, FDA recommends that test reports include a general statement that the test has been validated but FDA's independent review of this validation is pending.

Laboratories should immediately notify appropriate Federal, State, and local public health agencies of all positive results.

4. EUA Request

FDA has made available, through download from our website, a template that laboratories may choose to use to facilitate the preparation, submission, and authorization of an EUA for a molecular diagnostic test.⁹ Laboratories that intend to use alternative approaches should consider seeking FDA's feedback or recommendation to help them through the pre-EUA and EUA process. FDA encourages laboratories to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

Soon after receiving the EUA request, FDA intends to perform a preliminary review to identify if there are any problems with the performance data. If a problem is identified, FDA intends to work with the laboratory to address the problem (e.g., through labeling or bench testing). If any problems are significant and cannot be addressed in a timely manner, FDA would expect the laboratory to stop testing and issue corrected test reports indicating prior results may not be accurate. In such circumstances, FDA intends to remove the laboratory from the website listing of notifications.

Issued EUAs are posted on FDA's website.

⁹ See <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#coronavirus2019>

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When a laboratory makes a modification to an EUA authorized test for use of a new specimen type, FDA does not intend to object to the use of such a modified test without notification to FDA or a new or amended EUA where the new specimen type has been previously authorized for another test of the same technology¹⁰ and where the EUA authorized test is validated for the new specimen type. Modifications to an EUA authorized test for use of a new specimen type that has *not* been previously authorized for another test of the same technology must be authorized under a new or amended EUA prior to clinical use.

For all other types of modifications, FDA does not intend to object to the use of a test, without notification to FDA or a new or amended EUA, where the test is a modification of an EUA-authorized test and the modified test is validated using a bridging study to the EUA-authorized test.¹¹ One way to bridge to a new component is to establish equivalent performance between parallel testing of the same specimens with the new and original components. We recommend testing 3-fold serial dilutions of SARS-CoV-2 viral materials (e.g., whole genomic viral RNA or inactivated virus, etc.) in a pooled respiratory sample matrix in triplicate until you achieve a hit rate of <100%. If the resultant Limit of Detection (LoD) is the same as the LoD for the unmodified authorized test (i.e., $\leq 3 \times \text{LoD}$), then FDA believes the two tests can be considered to have equivalent performance.

When validating through a bridging study and not pursuing an EUA amendment for the modification, FDA would like to see the laboratory's validation data informally through an email to CDRH-EUA-Templates@FDA.HHS.GOV. If FDA's review of the bridged validation data indicates that it could be applicable to modifications of other tests with an EUA, or to other laboratories modifying the same authorized test, and the laboratory agrees to FDA sharing that information on our website for use by other laboratories, FDA intends to update our FAQs so other laboratories can refer to the validation for their testing, without conducting their own bridging study for the same modification. This informal sharing of data would not be considered to be a notification, as discussed above, or an EUA request.

5. Clinical Testing

While awaiting an FDA determination on the EUA request, FDA recommends that clinical laboratories obtain confirmation of the first five positive and the first five negative clinical specimens using an EUA-authorized assay. This testing may be performed within the same laboratory using an EUA-authorized assay or may involve sending these ten specimens to another laboratory for confirmation. If any of these results cannot be confirmed, the laboratory should notify FDA at CDRH-EUA-Templates@FDA.HHS.GOV, and take other appropriate actions such as terminating testing patient specimens, and issuing corrected test reports indicating prior test results may not be accurate.

¹⁰ For the purposes of this guidance, all nucleic acid amplification tests are considered to have the same technology.

¹¹ This policy applies to modifications to any EUA-authorized test, including a laboratory's own test with an EUA or a purchased kit from a manufacturer with an EUA.

B. State Authorization of Laboratories Certified under CLIA that Meet the CLIA Regulatory Requirements to Perform High-Complexity Testing

On March 12, 2020, FDA issued enforcement discretion and stated that it was not objecting to the Wadsworth Center authorizing certain laboratories in the State of New York to begin patient testing under certain circumstances to increase availability of COVID-19 testing in response to a request from the Wadsworth Center of the New York State Department of Health (Wadsworth). Wadsworth had informed FDA that it would be willing to have clinical laboratories that currently hold a New York State Department of Health clinical laboratory permit to notify Wadsworth that they have validated a test for COVID-19, and to submit validation studies to Wadsworth. Wadsworth likewise said it would notify the laboratory if it identified any concerns, and request that the laboratory terminate testing patient specimens and issue corrected test reports indicating prior test results might not be accurate.

On March 13, 2020, the President issued a “Memorandum on Expanding State-Approved Diagnostic Tests” (Memorandum), which refers to the flexibility that FDA allowed New York State and states as follows:

“Should additional States request flexibility to authorize laboratories within the State to develop and perform tests used to detect COVID-19, the Secretary shall take appropriate action, consistent with law, to facilitate the request.”

In accordance with the Memorandum, FDA describes below its 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.

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 establishes. FDA does not intend to object to the use of such tests for 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, and where instead the State or territory takes responsibility for COVID-19 testing by laboratories in its State during the COVID-19 outbreak.

FDA requests that the State or territory notify us if they choose to use this flexibility to expedite COVID-19 testing.¹² FDA will not be reviewing the process adopted by the State or territory, which we understand may be different than the process adopted by New York State. FDA expects that such states as part of their oversight process will require laboratories developing SARS-CoV-2 tests to validate those tests prior to use. FDA encourages laboratories that develop and perform a test for COVID-19 under this policy to notify FDA that they have started clinical testing by sending an email to that effect to CDRH-EUA-Templates@FDA.HHS.GOV. It would be helpful to FDA if laboratories provide information on testing capacity. This information will

¹² A list of States who have notified FDA under this policy is available on FDA’s FAQ website at: <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic-testing-sars-cov-2>.

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help the Agency and Department monitor the landscape as we work to ensure adequate testing capacity across the country.

C. Commercial Manufacturer Development and Distribution of Diagnostic Tests Prior to EUA Submission

The policy described in this subsection applies to commercial manufacturers that seek to develop and distribute diagnostic test kits to detect the SARS-CoV-2 virus to clinical laboratories or to healthcare workers for point-of-care testing. 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 laboratories certified to perform high complexity testing, including testing at the point-of-care when the site is covered by the laboratory's CLIA certificate for high-complexity testing.

This policy does not apply to at-home testing, including at-home specimen collection.

In light of the increasing numbers of COVID-19 cases throughout the country and the urgent need to expand the nation's capacity for COVID-19 testing during the public health emergency, FDA does not intend to object to a commercial manufacturer's development and distribution of SARS-CoV-2 test kits for specimen testing for a reasonable period of time, where the test has been validated and while the manufacturer is preparing its EUA request, where the manufacturer gives notification of validation to FDA as described below, and where the manufacturer provides instructions for use of the test and posts data about the test's performance characteristics on the manufacturer's website. Transparency can help mitigate potential adverse impacts from a poorly designed test by facilitating better informed decisions by potential purchasers and users.

FDA believes that 15 business days is a reasonable period of time to prepare an EUA submission for a test that has already been validated. Soon after receiving the EUA request, FDA will perform a preliminary review to identify if there are any problems with the performance data. If a problem is identified, FDA intends to work with the manufacturer to address the problem (e.g., through labeling or bench testing). If the problem is significant and cannot be addressed in a timely manner, and the manufacturer has already distributed the device, FDA would expect the manufacturer to suspend distribution and conduct a recall of the test.

1. Validation

All clinical tests should be validated prior to use. In the context of a public health emergency, it is critically important that tests are validated because false results can negatively impact not only the individual patient but also can have broad public health impact. FDA has provided recommendations regarding testing that should be performed to ensure analytical and clinical validity in section V below. FDA encourages manufacturers to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

2. FDA Notification

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Following completion of assay validation, manufacturers should notify FDA (e.g., e-mail to CDRH-EUA-Templates@FDA.HHS.GOV) that their assay has been validated and they intend to begin distribution. This notification should include the name of the manufacturer, address, contact person, a website link, and a copy of the instructions for use including a summary of assay performance. FDA will acknowledge receipt of this notification via auto-reply, and generally will add the name of the manufacturer and test to FDA's website listing.

In circumstances where manufacturers use distributor(s) for their product, the manufacturers should identify the names of all distributors in their notification. Distributors and laboratories using these tests should not provide separate notification. As noted above, FDA recommends that manufacturers submit a completed EUA request within 15 business days of the notification to FDA that the assay has been successfully validated.¹³ If an EUA request is not submitted within this timeframe, FDA intends to remove the manufacturer/test from its website listing of notified tests and may take additional actions as appropriate.

It would be helpful to FDA if manufacturers provide information on testing capacity, as well as the number of laboratories in the U.S. with the required platforms installed. This information will help the Agency and Department monitor the landscape as we work to ensure adequate testing capacity across the country.

3. Reporting of Results

In order to provide transparency, FDA recommends that instructions for use and test reports include a general statement that the test has been validated but FDA's independent review of this validation is pending.

4. EUA Request

FDA has made available, through download from our website, templates that test kit manufacturers may choose to use to facilitate the preparation, submission, and authorization of EUAs for molecular and antigen diagnostics.¹⁴ Manufacturers can use alternative approaches. Manufacturers who intend to use alternative approaches should consider seeking FDA's feedback or recommendations to help them through the pre-EUA and EUA process. FDA encourages manufacturers to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

Soon after receiving the EUA request, FDA intends to perform a preliminary review to identify if there are any problems with the performance data. If a problem is identified, FDA intends to work with the manufacturer to address the problem (e.g., through labeling or bench testing). If any problems are significant and cannot be addressed in a timely manner, FDA would expect the manufacturer to suspend distribution and conduct a recall of the test, which should include a

¹³ See FDA's Guidance, 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>.

¹⁴ See <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#coronavirus2019>

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notification concerning corrected test reports indicating prior test results may not be accurate. In such circumstances, FDA intends to remove the manufacturer/test from the website listing of notifications.

Issued EUAs are posted on FDA's website.

A manufacturer may request certain modifications to its EUA-authorized test as an amendment to the EUA as specified in the EUA's Conditions of Authorization. Where validation data supporting the modification have been submitted in the amendment, FDA does not intend to object to implementation of the modification while FDA conducts its review, except for modifications to add specimen types that have not been previously authorized with another test of the same technology.

5. Clinical Testing

While awaiting FDA determination on the EUA request, FDA recommends that manufacturers make publicly available on their website the instructions for use, including a summary of assay performance.

D. Commercial Manufacturer Development and Distribution and Laboratory Development and Use of Serology Tests Prior to or Without an EUA

The policy described in this subsection applies to developers of serology tests that identify antibodies (e.g., IgG, IgM) to SARS-CoV-2 from clinical specimens. 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 laboratories certified to perform high complexity testing, and at the point-of-care when covered by the laboratory's CLIA certificate for high-complexity testing.¹⁵ This policy does not apply to at-home testing, including at-home specimen collection, due to additional considerations that require FDA review.¹⁶

FDA does not intend to object to a commercial manufacturer's development and distribution of serology tests to identify antibodies to SARS-CoV-2 for a reasonable period of time, where the test has been validated and while the manufacturer is preparing its EUA request, where the manufacturer gives notification of validation to FDA as described in subsection D.2 below, and

¹⁵ Under CLIA, a new test is automatically categorized as high complexity and must be performed in a laboratory that is certified under CLIA to perform high complexity testing. When authorizing an EUA under Section 564(m) of the FD&C Act, FDA can authorize the test to be performed in a particular setting and it is deemed to be in that particular categorization under CLIA (e.g., moderate complexity or point of care).

¹⁶ Different risks are presented with specimen collection in the home versus 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.

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where the manufacturer includes information in the instructions for use as described in subsection D.3 below. FDA provided early market access through its March 16, 2020, updated guidance, but that access was premised on the understanding that tests should be validated before being marketed to fall under the enforcement discretion policy. Given that any test on the market under the March 16 enforcement discretion policy or this policy should already be validated by the manufacturer before being marketed, FDA believes that 10 business days (from the date of notification or the date of publication of this guidance, whichever is later) is a reasonable period of time to prepare an EUA submission for a test whose performance characteristics have already been validated.

If FDA becomes aware of questions or concerns about a test after notification, such as poor performance or misleading statements about the test, FDA will communicate those concerns to the manufacturer and provide the manufacturer an opportunity to address the questions or concerns. If the concerns cannot be or have not been addressed in a timely manner, and the manufacturer has already distributed the test, FDA would expect the manufacturer to suspend distribution of the test. FDA also intends to remove the test from the website listing of notifications and may take additional actions as appropriate.

While laboratories are encouraged to submit EUA requests for serology tests, FDA does not intend to object to the development and use of serology tests to identify antibodies to SARS-CoV-2 by laboratories that are certified under CLIA to perform high-complexity testing, where the test has been validated, notification is provided to FDA, and information is included in the test reports as described in subsection D.3 below. At this time, we believe it is most beneficial to focus our EUA review and authorization efforts on tests from commercial manufacturers, which have the potential to be distributed more broadly, rather than laboratory-developed serology tests that are not for diagnostic purposes, are being performed at one laboratory that is CLIA-certified to perform high-complexity testing, and that are validated in-house. However, if FDA becomes aware of questions or concerns about a laboratory-developed 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 intends to remove the laboratory from the website listing of notifications and may take additional actions as appropriate.

1. Validation

All clinical tests should be validated prior to use. In the context of a public health emergency, it is critically important that tests are validated because false results can negatively impact not only the individual patient but also can have broad public health impact. FDA has provided recommendations regarding testing that should be performed to ensure analytical and clinical validity in section V below. FDA encourages developers to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV and additionally encourages developers to refer to the templates provided as examples in the Appendices to this guidance for serology test manufacturers and laboratories.

2. FDA Notification

Following completion of assay validation, developers should notify FDA by email to CDRH-EUA-Templates@FDA.HHS.GOV that their assay has been validated and they intend to begin distribution or testing.

- a. For tests developed and used by laboratories certified under CLIA that meet the CLIA regulatory requirements to perform high-complexity testing, this notification should include the name of the laboratory, name of the laboratory director, laboratory address, and contact person in this email. FDA will acknowledge receipt of this notification via auto-reply, and generally will add the laboratory name to FDA's website listing.

It would be helpful to FDA if laboratories provide information on testing capacity. This information will help the Agency and Department monitor the landscape as we work to ensure adequate testing capacity across the country.

- b. For tests developed and distributed by commercial manufacturers, this notification should include the name of the manufacturer, address, contact person, and a copy of the instructions for use that includes a summary of assay performance. FDA will acknowledge receipt of this notification via auto-reply, and generally will add the name of the manufacturer and test to FDA's website listing. As noted above, FDA recommends that manufacturers submit a completed EUA request within 10 business days of the notification to FDA that the assay has been successfully validated, or the date of publication of this guidance, whichever is later.¹⁷ If an EUA request is not submitted within this timeframe, FDA intends to remove the manufacturer/test from its website listing of notified tests and may take additional actions as appropriate.

In circumstances where manufacturers use distributor(s) for their test, the manufacturer should identify the names of all distributors in their notification. Distributors should not provide separate notification.

It would be helpful to FDA if manufacturers provide information on test production capacity, the number of laboratories in the U.S. with the required platforms installed. This information will help the Agency and Department monitor the landscape as we work to ensure adequate testing capacity across the country.

3. Labeling and Reporting of Results

In order to provide important information about the intended use of the test and its limitations, FDA recommends that instructions for use and patient test reports include information that helps users and patients understand the test results, such as the following:

- This test has not been reviewed by the FDA.

¹⁷ See FDA's Guidance, 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>.

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- Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct 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.

4. EUA Request

FDA has made available through download from our website templates that commercial manufacturers and laboratories may choose to use to facilitate the preparation, submission, and authorization of an EUA for a serology test.¹⁸ 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 CDRH-EUA-Templates@FDA.HHS.GOV.

FDA may leverage data from testing at the National Institutes of Health’s National Cancer Institute (NIH/NCI), or at another federal government laboratory designated by FDA, to inform decisions on EUA requests and other actions. FDA has issued an EUA for certain serology tests evaluated in the NIH/NCI independent validation study, or by another government agency designated by FDA, that are confirmed by FDA to meet certain specific performance and other criteria, and added to the EUA.¹⁹

FDA will communicate any questions or concerns regarding a pre-EUA or EUA submission to the developer. FDA will also work collaboratively to address any potential concerns or safety considerations raised in the pre-EUA submission or EUA request and will contact the developer regarding a final determination on the EUA request.

Issued EUAs are posted on FDA’s website.

If FDA is not able to issue an EUA, FDA intends to notify the manufacturer. Where the manufacturer has distributed tests, FDA also would expect the manufacturer to suspend distribution of the test, which should include a notification indicating that prior test results may not be accurate. FDA intends to remove the manufacturer/test from the website listing of notifications. FDA may also take other action as may be appropriate in the circumstances.

V. Validation Study Recommendations Based on the Technological Principles of Tests

¹⁸ See <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#coronavirus2019>.

¹⁹ See <https://www.fda.gov/media/137470/download>.

Contains Nonbinding Recommendations

In this section, FDA provides recommendations for developers regarding testing that should be performed to demonstrate that a SARS-CoV-2 test is validated based upon the underlying technological principles of the test. Depending on the characteristics of your test, additional validation studies may be recommended. FDA encourages test developers to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-templates@FDA.HHS.GOV.

A. Molecular Diagnostic Tests

FDA defines SARS-CoV-2 molecular diagnostic tests as tests that detect SARS-CoV-2 nucleic acids from human specimens. FDA recommends that the following validation studies be conducted for molecular SARS-CoV-2 diagnostic tests:

(1) Limit of Detection

FDA recommends that developers document the limit of detection (7) of their SARS-CoV-2 assay. FDA generally does not have concerns with spiking RNA or inactivated virus into artificial or real clinical matrix (e.g., Bronchoalveolar lavage [BAL] fluid, sputum, etc.) for LoD determination.

FDA recommends that developers test a dilution series of three replicates per concentration with inactivated virus on actual patient specimen, and then confirm the final concentration with 20 replicates. For this guidance, FDA defines LoD as the lowest concentration at which 19/20 replicates are positive. If multiple clinical matrices are intended for clinical testing, FDA recommends that developers submit in their EUA requests the results from the most challenging clinical matrix to FDA. For example, if testing respiratory specimens (e.g., sputum, BAL, nasopharyngeal (NP) swabs, etc.), laboratories should include only results from sputum in their EUA request.

(2) Clinical Evaluation

The availability of positive samples has increased as the pandemic has progressed. As such, FDA now recommends that developers use positive clinical samples for clinical validation. Moreover, due to the increased availability of clinical samples, FDA recommends that developers confirm performance of their assay by testing a minimum of 30 positive specimens and 30 negative specimens as determined by an authorized assay. If you do not have access to clinical samples as determined by an authorized assay, contrived clinical specimens may be considered. Contrived reactive specimens can be created by spiking RNA or inactivated virus into leftover clinical specimens, of which the majority can be leftover upper respiratory specimens such as NP swabs, or lower respiratory tract specimens such as sputum, etc. If contrived samples are used, FDA recommends that twenty of the contrived clinical specimens be spiked at a concentration of 1x-2x LoD, with the remainder of specimens spanning the assay testing range. For this guidance, FDA defines the acceptance criteria for the performance as 95% agreement at 1x-2x LoD, and 100% agreement at all other concentrations and for negative specimens.

Contains Nonbinding Recommendations

(3) Inclusivity

developers should document the results of an *in silico* analysis indicating the percent identity matches against publicly available SARS-CoV-2 sequences that can be detected by the proposed molecular assay. FDA anticipates that 100% of published SARS-CoV-2 sequences will be detectable with the selected primers and probes.

(4) Cross-reactivity

FDA recommends cross-reactivity wet testing on common respiratory flora and other viral pathogens at concentrations of 10^6 CFU/ml or higher for bacteria and 10^5 pfu/ml or higher for viruses, except for SARS-Coronavirus and MERS-Coronavirus, which can be accomplished by *in silico* analysis. As an alternative, FDA believes an *in silico* analysis of the assay primer and probes compared to common respiratory flora and other viral pathogens can be performed. For this guidance, FDA defines *in silico* cross-reactivity as greater than 80% homology between one of the primers/probes and any sequence present in the targeted microorganism. In addition, FDA recommends that developers follow recognized laboratory procedures in the context of the sample types intended for testing for any additional cross-reactivity testing.

Additional information for the validation of molecular diagnostics is included in the manufacturer and developers EUA templates available for download on our website.

B. Antigen Detection Tests

FDA defines SARS-CoV-2 antigen tests as those that detect proteins that are part of the SARS-CoV-2 virus directly from clinical specimens. FDA recommends that the following validation studies be conducted for a SARS-CoV-2 antigen test:

- Limit of Detection/Analytical Sensitivity
- Cross-reactivity/Analytical Specificity
- Microbial Interference
- Clinical Agreement Study

The clinical agreement study is intended to establish the performance characteristics (e.g., sensitivity/PPA, specificity/NPA) of the test. FDA believes that clinical agreement should be established on human specimens, preferably leftover specimens from patients with or without SARS-CoV-2 infection.

FDA has made available through download from our website, a template that antigen test developers may choose to use to facilitate the preparation, submission, and authorization of an EUA for an antigen test. See more information in Section VI. For antigen tests, the template includes further recommendations concerning the above validation studies and make additional recommendations about other information that should be provided to FDA as part of the pre-EUA/EUA submission process. Developers can use alternative approaches. FDA encourages developers to discuss any alternative approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

C. Serological Tests

FDA defines SARS-CoV-2 serological tests as tests that identify antibodies (e.g., IgG, IgM) to SARS-CoV-2 from clinical specimens. FDA recommends that the following validation studies be conducted for a SARS-CoV-2 serological assay:

- Cross-reactivity/Analytical Specificity
- Class Specificity
- Clinical Agreement Study

The clinical agreement study is intended to establish the performance characteristics (e.g., sensitivity/PPA, specificity/NPA) of the test. FDA recommends that clinical accuracy should be established on human specimens from patients with microbiologically confirmed COVID-19 infection.

FDA has made available through download from our website templates that commercial manufacturers and laboratories may choose to use to facilitate the preparation, submission, and authorization of an EUA for a serology test. See more information in Section VI. For serological tests, these templates include further recommendations concerning the above validation studies and make additional recommendations about other information that should be provided to FDA as part of the pre-EUA/EUA submission process. Developers can use alternative approaches. FDA encourages developers to discuss any alternative approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

VI. Availability of EUA Templates

FDA has made available through download from our website²⁰ a series of templates that developers may choose to use to facilitate the preparation, submission, and authorization of an EUA for various types of COVID-19 tests. The templates reflect FDA's current thinking on the data and information that developers should submit to facilitate the EUA process. The templates provide information and recommendations, and we plan to update them as appropriate as we learn more about the COVID-19 disease and gain experience with the EUA process for the various types of COVID-19 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 CDRH-EUA-Templates@FDA.HHS.GOV.

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.

²⁰ See <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#coronavirus2019>.