

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 4, 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 March 16, 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-R2 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 is modified from the policy included in the March 16, 2020 guidance as it pertains to commercial manufacturers but not laboratories. At the time of previous issuance, 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.

Since that policy was issued, FDA has authorized several serology tests under individual EUAs and has issued an umbrella EUA providing a streamlined approach for EUA authorization of serology tests that are evaluated by the National Institutes of Health's National Cancer Institute (NIH/NCI).⁷ The umbrella EUA for NIH-evaluated tests has provided a streamlined pathway for EUA authorization of commercial serology tests. Also since that time, 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.

Under the modified policy, 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.

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

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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.

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

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

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

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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.

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).

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.

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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 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

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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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

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

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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, a template that test kit manufacturers may choose to use to facilitate the preparation, submission, and authorization of an EUA for a molecular diagnostic.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 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

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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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 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.

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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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,

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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.
- 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.

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>.

4. EUA Request

Templates for commercial manufacturers and laboratories are provided in Appendices A and B to facilitate the preparation, submission, and authorization of an EUA.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

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

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>.

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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.

(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

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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.

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.

EUA templates for serology tests for manufacturers and laboratories are provided in Appendices A and B, respectively, to facilitate pre-EUA/EUA submissions. These templates include further

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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.

Appendix A: Serology Template for Manufacturers

This template (the “template”) provides FDA’s current recommendations concerning what data and information should be submitted to FDA in support of a pre-EUA/EUA submission for a SARS-CoV-2 antibody test. As outlined in Section V.C. of this guidance, FDA recommends that the following validation studies be conducted for a SARS-CoV-2 serological assay: Cross-reactivity/Analytical Specificity, Class Specificity, and Clinical Agreement Study. This template is intended to help manufacturers provide these validation data and other recommended information to FDA, but alternative approaches can be used. For more information about EUAs in general, please see the FDA Guidance document: [Emergency Use Authorization of Medical Products and Related Authorities](#).

GENERAL INFORMATION ABOUT THIS TEMPLATE

- Text highlighted in yellow **[Text]** should be completed by the test manufacturer (sponsor) as applicable to their specific test. Text in **bold** outlines the Food and Drug Administration’s (FDA) additional recommendations for the sponsors’ consideration when completing the suggested information in each section.
- Please be reminded that tests for the detection of antibodies against SARS-CoV-2 must not be distributed and/or used for clinical diagnoses.
- This is an EUA interactive review template for Pre-EUA/EUA submissions. The template is subject to change as we learn more about the COVID-19 disease and its risk-benefit profile.
- A test authorized under an EUA is only authorized for emergency use while the EUA is in effect.
- The EUA is not a pathway to permanent marketing of your device. Therefore, we strongly recommend that you consider, in addition to an EUA, a traditional premarket submission for your IVD so that your device can still be legally marketed after termination of the public health emergency declaration. We recommend that you identify as soon as possible in the Pre-EUA review process any consideration of moving your product forward towards De Novo/510(k) clearance.

EXAMPLE TEMPLATE:

A. PURPOSE FOR SUBMISSION

Emergency Use Authorization (EUA) request for distribution of the **[test name]** in **[indicate labs e.g., U.S. laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform moderate complexity and high complexity tests, and U.S. laboratories certified under CLIA to perform high complexity tests, and as applicable, for near patient testing, or point of care use]**, for the detection of **[specify types of antibodies e.g., IgM, IgG, total]** antibodies to SARS-CoV-2 in **[specify matrices]** from individuals with current or prior COVID-19 infection.

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B. MEASURAND

[Specify what the test detects and whether it can differentiate between IgM and IgG or if it detects total antibody without differentiation.]

C. APPLICANT

[Official name, address and contact information of applicant]

D. PROPRIETARY AND ESTABLISHED NAMES

Proprietary Name: *[test name]*

Established Name - *[test name]*

E. REGULATORY INFORMATION

Approval/Clearance Status:

The *[test name]* is not cleared, CLIA waived, approved, or subject to an approved investigational device exemption.

Product Code:

QKO

F. PROPOSED INTENDED USE

1) Intended Use:

The proposed IU will be finalized based on the data provided at the time of authorization.

The *[test name]* is a *[specify technology e.g., Enzyme-Linked Immunosorbent Assay (ELISA)]* intended for qualitative *[or semi-quantitative or quantitative tests, if appropriate validation data is provided. Performance evaluations beyond what is currently described in the template may be necessary]* detection of *[specify the antibody class or classes that are being detected, or indicate whether the test only detects total antibodies]* antibodies to SARS-CoV-2 in human *[specify matrices including anticoagulants]*. The *[test name]* is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. Testing is limited to *[laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C 263a, to perform moderate or high complexity tests and as applicable, Point of Care (POC) testing]*.

Results are for the detection of SARS CoV-2 antibodies. *[Specify antibodies detected]* antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

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Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

[As applicable, the sensitivity of [test name] early after infection is unknown.] Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for **[test name]** may occur due to cross-reactivity from pre-existing antibodies or other possible causes. **[For lateral flow devices: Due to the risk of false positive results, confirmation of positive results should be considered using second, different [as appropriate, IgG or IgM] assay].**

The **[test name]** is only for use under the Food and Drug Administration's Emergency Use Authorization.

2) Special Conditions for Use Statements:

For prescription use only

For *in vitro* diagnostic use only

For Emergency Use Authorization only

3) Special Instrument Requirements:

The **[test name]** test is to be used with the **[list all instruments, software requirements, other applicable instrumentation, etc.].**

G. DEVICE DESCRIPTION AND TEST PRINCIPLE

1) Product Overview/Test Principle:

[Describe the technology of the test and how this technology works to identify measurand (i.e., the test principle), the instruments/reader employed/required to perform the test from sample collection to result, and the specimen types for which you claim to have performance characteristics as described below]

The **[test name]** uses the following:

[List the antigen(s) and antibodies used in the assay to detect the antibodies in human specimens]

2) Description of Test Steps: **[Describe in order the steps of the test from specimen collection to result output.]**

3) Control Material

[List all control materials (provided with the test kit and/or required but not provided with the test kit) and describe what they are, how they are expected to work, where in the testing process they are used, and the frequency of use. If a control is commercially available, provide supplier's name and catalog number or other identifier; if your device relies on external controls that are manufactured by a third

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party please note that these controls should also be validated within your analytical and clinical studies described below in Section J.]

Controls that will be provided with the test kit include:

- a) An external positive control for each antibody class claimed (e.g., IgG, IgM) is needed to *[describe need]* and is used *[describe use – please specify the concentration of the positive control relative to the cut-off of your test (note that ideally the positive control concentration should be such that it is close to the cut-off of your test) and specify frequency of use.]*
- b) An external negative control is needed to *[describe need]* and is used *[describe use – please specify the composition of the negative control and specify frequency of use.]*
- c) A *[other (e.g., sample adequacy, internal, etc.)]* control is needed to *[describe need]* and is used *[describe use – please specify the composition of the control and specify frequency of use.]*

Controls that are required but not provided with the test kit include *[describe control – provide recommended sources of the control materials – either a separate control kit for purchase that you develop and market or a control material that can be purchased from a third party]*. This/these control(s) is/are needed to *[describe need]* and is/are used *[describe use – please also specify frequency of use]*.

H. INTERPRETATION OF RESULTS

Assessment of *[test name]* results should be performed after the positive and negative controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted.

[Clearly describe how results are to be interpreted. If applicable, clearly indicate how to interpret numeric test values as positive or negative for the presence of antibodies against SARS-CoV-2. Indicate how to identify indeterminate/equivocal results (if applicable) and how the user should resolve them. Also describe if and when repeat testing may be required.]

If your test is a lateral flow, please describe the results interpretation for each of the test lines. You could consider reporting the results in the form of a table as shown below for a test that detects and differentiates between IgG and IgM:

Table 1. Interpretation of Results

	C Line	M Line	G Line	Test Result Interpretation
1	not present	Any	Any	Invalid Test. The specimen must be retested with another device
2	+	-	-	Valid Test, Negative for antibodies for SARS-CoV-2
3	+	+	-	Valid Test, IgM positive for antibodies for SARS-CoV-2

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4	+	+	+	Valid Test, IgM and IgG positive for antibodies for SARS-Cov-2
5	+	-	+	Valid Test, IgG positive for antibodies for SARS-CoV-2

If you have a lateral flow device, please include a schematic/picture showing the location of the sample well, buffer well, and control and test lines]

I. PRODUCT MANUFACTURING

1) Overview of Manufacturing and Distribution

The product will be manufactured at *[manufacturer’s name and FDA registration number (if applicable)]* by *[manufacturer name]* personnel consistent with practices for the production of *[types of devices]* based on *[type of quality system*]*. Material manufactured by *[manufacturer’s name]* may be bottled and kitted by *[packager name]* manufacturing facility.

The current manufacturing capabilities include the ability to manufacture approximately *[insert the approximate number of units/products that can currently be manufactured per week at the manufacturing facility]* products per week, however in the event of a surge in demand this could be increased to *[please insert the approximate maximum number of units/products that could potentially be manufactured per week at the manufacturing facility if there was a surge in demand]* product per week within a *[please specify in weeks/months the expected timeframe required to increase product production if required]* timeframe.

2) Component Included with the Test: Components manufactured by *[manufacturer’s name and FDA registration number (if applicable)]* and supplied with the test include:

[List all components and reagents provided for your test, including volumes, concentrations, quantities, etc.]

Example: Table Kit Components

Kit components (example)	Manufacturer
Test Cassette with test strip	
Negative control	
Positive control	
Sample buffer (bottle)	
Transfer pipette	
Lancet (for fingerstick only)	
Instructions for Use leaflet	
Packing materials	

3) Components required but not included with the test:

[List all components (e.g., timer, analyzer/reader) and reagents not included with the test that must be supplied by the user to perform the test, with specific supplier names and catalog numbers or other identifiers for obtaining these components and reagents. Please include here all specific consumables that were validated for use with your device, that are not interchangeable with other products and that are needed to

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guarantee device performance as established in the EUA validation studies listed in section J below].

- 4) The **[test name]** has been validated using only the components referenced above. The **[test name]** was developed using **[briefly describe the capture antigens and antibodies used in the test, how they were designed and purified (e.g., are monoclonal antibodies used, are they manufactured in house or purchased commercially, what species they derive from, what epitope is targeted by the antibodies used in the assay, and if commercial products is there a certificate of analysis, etc.).**
- 5) **Testing Capabilities:** **[Briefly describe current sample throughput capacity, total time required to perform the test (from clinical specimen collection to result), and number of tests that can be performed. Please provide the number of kits you can manufacture per day/week.]**
- 6) **Distribution Plan**
[Describe if you will partner with other companies for the distribution of the device]
- 7) **Reagent Stability**
[Describe the information that supports the stability claims for your device. Please indicate if the test is already in use in other parts of the world.]

J. PERFORMANCE EVALUATION

1) **Analytical Sensitivity and Specificity**

a) **Reactivity/Inclusivity:**

Although mutations in the SARS-CoV-2 genome have been identified as the virus has spread, no serologically unique strains have been described relative to the originally isolated virus (this research is exceptionally limited at present).

b) **Cross-Reactivity:**

If a large number of known negative samples (e.g., ≥ 75 samples collected in the US prior to December 2019) are tested from a population with a high prevalence of vaccination against, and/or infection with, the following viruses, and specificity $>98\%$ is observed, cross-reactivity testing for the following viruses would not be expected at this time:

anti-influenza A (IgG and IgM)
anti-influenza B (IgG and IgM)
anti-HCV (IgG and IgM)
anti-HBV (IgG and IgM)
anti-Haemophilus influenzae (IgG and IgM)
anti-229E (alpha coronavirus)
anti-NL63 (alpha coronavirus)
anti-OC43 (beta coronavirus)
anti-HKU1 (beta coronavirus)

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ANA
anti-respiratory syncytial virus (IgG and IgM)
anti-HIV

[If a large number of known negative samples are not evaluated, or lower than 95% specificity is observed, describe the cross-reactivity testing performed to evaluate the cross-reactants in the table above. Please include in your description the number of samples tested and how samples were prepared.]

If testing of the cross-reactants is needed to demonstrate cross-reactivity of the test, FDA believes testing a minimum of 5 individual samples for each disease/infectious agent/antibody class listed above may be acceptable.

If natural specimens are used, it is important to assess cross reactivity using sera from patients with the underlying diseases in the acute or convalescent stages of infection in order to obtain high levels of IgM or IgG for the underlying condition. If spiked samples with the IgM or IgG antibodies for the underlying conditions are prepared for this study, it is important to confirm that “negative samples” are SARS-CoV-2 IgM and IgG seronegative with the candidate assay **prior** to spiking. Additionally, commercially available IgM or IgG antibodies for the underlying conditions panels may be acceptable if collected prior to the COVID-19 pandemic to ensure the panels are SARS-CoV-2 antibody negative.

We recommend you present your results in the following suggested table and calculate agreement between the candidate test result and the expected result.

Table Cross-Reactivity: **[test name]** example table for wet tested organisms below:

Virus/Bacteria/Parasite Antibody positive	Source/ Sample type	Results*

*If applicable, please include the signal output for your test’s technology.

[If your test exhibits significant cross-reactivity that would produce false positive results for any virus evaluated, please describe a plan to address this risk.]

2) **Class Specificity:**

If your test is intended for the detection of total antibody with no differentiation between different immunoglobulins, then this study does not apply. ***[In this case, please indicate that this study is not applicable.]***

[If your test is intended for the detection of total antibody with no differentiation between different immunoglobulins, then this study does not apply. Please indicate not applicable.]

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If your test is intended to differentiate between different immunoglobulins, describe the approach used to evaluate class specificity.]

[If class specificity testing is needed for your test, please describe the study, or studies, performed to demonstrate that the assay accurately detects each antibody class (e.g., IgG and IgM). This should include a description of the studies performed to evaluate the potential for human IgM to cross react and therefore produce false positive results for IgG, and the reverse, and the potential for IgM to compete with IgG and produce false negative results. Please indicate the number of samples, and the number of replicates per sample, tested. FDA believes that evaluating at least 5 samples positive for both antibody classes (IgM positive while also IgG positive), in duplicate, may be acceptable.]

Approaches to evaluate class specificity depend on the assay format. If you have well-characterized the anti-IgG and anti-IgM reagents, used in your test class specificity testing may not be needed. In this case, please describe how the reagents were characterized and such characterization supports class specificity. One recommended approach includes treating the specimen with dithiothreitol (DTT) where the final IgG result will remain unaffected and the final IgM signal will decrease or be negative. A positive control should also be included that confirms DTT activity.

[Please provide the protocol and results, including line data, from any class specificity testing.]

FDA believes that 100% agreement with expected result would establish antibody class specificity.

If a DTT Treatment approach is followed, below is an example table for IgM and IgG:

Sample ID	Replicates	Result NO DTT Treatment (IgM/IgG)	Result DTT Treatment (IgM/IgG)	Expected result with DTT treatment (IgM/IgG)	Result Agreement
1	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
2	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
3	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
4	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
5	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes

3) *Clinical Agreement Study:*

[Please describe the clinical study used to evaluate the clinical performance of the test. Please note that the exact requirements for the clinical evaluation depend on access to COVID-19 disease clinical specimens at the time of the studies and the nature of the emergency.]

Initial clinical agreement trials typically evaluate all matrices that the sponsor intends to claim in their EUA submission.

The comparator method used to establish clinical truth for the patient at this time is a PCR based assay. Results from the comparator PCR method are obtained using specimens that have been validated for use with the comparator method. Consider collecting nasal swab samples from a patient for PCR and then follow with a fingerstick or blood draw from the same patient. ***[Please identify the PCR comparator that was used. If the PCR comparator is not an EUA-authorized test, please provide Limit of Detection (LoD) and cross-reactivity validation data. If it is an EUA-authorized test, then no validation is needed.]***

Ideally, performance characteristics are established in a clinical study with prospective samples. If a prospective study is not feasible, an acceptable alternative would be to test retrospectively collected SARS-CoV-2 antibody positive specimens from patients that have been previously confirmed infected by SARS-CoV-2 RT PCR, accompanied by basic information such as the population from which the sample was drawn and the comparator method, specimen collection date, date of onset of symptoms (if present/known), and comparator method to confirm patients as SARS-CoV-2 infected or not infected (see above).

Clinical agreement data should be provided using at least 30 antibody positive samples for each immunoglobulin claimed and 75 antibody negative samples from patients tested for SARS-CoV-2 and confirmed as negative and the data should demonstrate a minimum overall 90.0% positive percent agreement and overall 95.0% negative percent agreement, and for tests that report specifically IgM and IgG results, a minimum positive percent agreement for IgM of 70% and a minimum positive percent agreement for IgG of 90%. Point estimates not lower than 93% for combined NPA, not lower than 90% for combined PPA, and for tests that specifically report IgG or IgG and IgM, PPA for IgG not lower than 87%, and PPA for IgM not lower than 67% may be acceptable if a larger number of samples are evaluated and the lower bounds of the 95% confidence intervals are higher than would be demonstrated in a clinical agreement study with 30 antibody positive and 75 antibody negative samples.

For visually read tests, blinding and randomization should be included in the experimental design

If a claim for fingerstick is desired, we believe evaluating a minimum of 30 positive and 30 negative fingerstick whole blood samples may be acceptable to demonstrate

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clinical performance in fingerstick samples. If a claim for near patient testing, or point-of-care (POC) is desired, please see the section specific to POC below.

[Please specify how the samples were generated, collected, and sourced. Please also specify if the samples were fully prospective, mix of prospective, retrospective and/or contrived. Please specify inclusion/exclusion criteria, collection and testing sites, number of samples collected and tested, and number of operators performing the testing, as available.]

[Please clearly describe the data analysis methods used and provide the results from the study, including line data. We suggest calculating positive and negative percent agreement between the candidate device and the comparator method results separately for each claimed matrix, using 2 x 2 tables as follows:]

		Comparator method/Clinical truth	
		Positive	Negative
Your Device	Positive	A	B
	Negative	C	D

*Percent Positive Agreement = $A/(A + C)$ or
True Positives/(True Positives + False Negatives)*

*Negative Percent Agreement = $D/(B + D)$ or
True Negatives/(True Negatives + False positives)*

If you claim that your test can differentiate between IgG and IgM, PPA and NPA for IgG and IgM separately should be calculated separately.]

4) Matrix Equivalency

[Please describe the protocol and provide the results from any matrix equivalency studies performed to support the performance of the assay in claimed sample matrices (serum, EDTA plasma, venipuncture whole blood, different anticoagulants, etc.) that were not evaluated in the initial clinical agreement study.] Please note: Fingerstick whole blood is not considered to be the same sample type as venipuncture whole blood and clinical agreement against PCR should be evaluated (please see Section J.3 above).

Matrix equivalency studies are performed to evaluate specimen matrices for which clinical agreement isn't initially assessed. In these studies, the matrix in which the clinical study(ies) are conducted is the comparator matrix/specimen type and each matrix set (whole blood, plasma, serum) comes from the same donor (i.e., paired samples).

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Typically, negative, low positive (e.g., for lateral flow tests, faint test line), and moderate positive (e.g., for lateral flow tests, strong test line) are evaluated. We believe five samples, run in duplicate for each concentration, for a total of 30 results per matrix (assuming 3 concentrations were evaluated) may be acceptable. To allow for comparison, negative samples for each claimed specimen type/matrix are spiked with the same amount of analyte (SARS-CoV-2 IgG and IgM). We believe confirming samples are antibody seronegative with the candidate assay before spiking with SARS-CoV-2 IgG and IgM antibodies is important. For visually read tests, blinding and randomization are important considerations for the experimental design.

For these types of studies, typically, each sample is assayed with the candidate device, and the results obtained for the comparator matrix are compared to the results obtained for each additional matrix under evaluation for each subject. Positive percent agreement and negative percent agreement for each matrix with respect to the comparator matrix are calculated. We believe that at least 95% agreement across all matrices/subject may be acceptable to demonstrate that performance between the matrices can be considered equivalent.

5) Studies to support Point of Care claim, as applicable.

[If the device is intended for near patient testing or Point of Care (POC), please provide data to demonstrate that non-laboratory personnel can perform the test accurately in the intended use environment (i.e. a non-laboratorian healthcare provider accuracy study). Please also provide data to demonstrate robust use of your device for near patient testing (e.g., as applicable, studies to demonstrate the impact of adding different volumes of sample, different volumes of reagents, incorrect order of sample or reagent application).]

K. UNMET NEED ADDRESSED BY THE PRODUCT

This section will be completed by FDA.

L. APPROVED/CLEARED ALTERNATIVE PRODUCTS

Currently no methods for the qualitative detection of SARS-CoV-2 IgM or IgG antibodies have been approved or cleared by FDA.

M. RISKS AND BENEFITS:

This section will be completed by FDA.

N. FACT SHEET FOR HEALTHCARE PROVIDERS AND PATIENTS:

[Include proposed Fact Sheets for Patients and Healthcare Providers] - see examples for authorized EUA tests on our website. During review, FDA will make available Fact Sheet templates.

Contains Nonbinding Recommendations

O. INSTRUCTIONS FOR USE/ PROPOSED LABELING/PACKAGE INSERT:

[Include Instructions for Use, Box Labels, Vial Labels and any other proposed labeling.]

P. RECORD KEEPING AND REPORTING INFORMATION TO FDA:

[Manufacturer Name] will track adverse events and report to FDA under 21 CFR Part 803. A website is available to report on adverse events, and this website is referenced in the Fact Sheet for Health Care providers as well as through the ***[Manufacturer Name]*** Product Support website: ***[link to Manufacturer's website]***. Each report of an adverse event will be processed according to ***[Manufacturer Name]***'s Non-Conformance Reporting Requirements, and Medical Device Reports will be filed with the FDA as required. Through a process of inventory control, ***[Manufacturer Name]*** will also maintain records of device usage/purchase. ***[Manufacturer Name]*** will collect information on the performance of the test, and report to FDA any suspected occurrence of false positive or false negative results of which ***[Manufacturer Name]*** becomes aware. ***[Manufacturer Name]*** will maintain records associated with this EUA and ensure these records are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

Appendix B: Serology Template for Laboratories

This template (the “template”) includes FDA’s current recommendations for laboratories concerning what data and information they should submit to support an EUA request for a SARS-CoV-2 antibody test developed for use in a single CLIA certified high-complexity laboratory. As outlined in Section V.C. of this guidance, FDA recommends that the following validation studies be conducted for a SARS-CoV-2 serological assay: Cross-reactivity/Analytical Specificity, Class Specificity, and Clinical Agreement Study. This template provides one example of how a laboratory can submit these validation data and other recommended information to FDA, but alternative approaches can be used. For more information about EUAs in general, please see the FDA Guidance document: [Emergency Use Authorization of Medical Products and Related Authorities](#).

GENERAL INFORMATION ABOUT THIS TEMPLATE

- This EUA review template (EUA template) is only intended for use by CLIA certified high-complexity laboratories who intend to submit a pre-EUA or EUA to FDA for a SARS-CoV-2 antibody test.
- Text highlighted in yellow **[Text]** should be completed by the laboratory (sponsor) as applicable to their specific test. Text in **bold** outlines the Food and Drug Administration’s (FDA) recommendations for the sponsors’ consideration when providing the suggested information in a specific section. Text in regular font is recommended language provided by FDA as an example. As explained throughout, this template is intended to be a helpful aid that provides FDA’s recommendations to help facilitate the pre-EUA/EUA submission process.
- This is an EUA interactive review template for Pre-EUA/EUA submissions. The template is subject to change as we learn more about the COVID-19 disease and its risk-benefit profile.
- Please be reminded that tests for the detection of antibodies against SARS-CoV-2 must not be distributed and/or used for clinical diagnoses.

EXAMPLE TEMPLATE

A. PURPOSE OF SUBMISSION

Emergency Use Authorization (EUA) request for **[test name]** to be performed for the detection of **[specify types of antibodies e.g., IgG, IgG/IgM or total]** antibodies to SARS-CoV-2 in **[specify matrices]** from individuals with current or prior COVID-19 infection. The test will be performed in CLIA certified high-complexity laboratories. Additional testing and confirmation procedures should be performed in consultation with public health and/or other authorities to whom reporting is required. Positive results should also be reported in accordance with local, state, and federal regulations.

B. MEASURAND

[Specify what the test detects and whether it can differentiate between IgM and IgG or if the test detects total antibody without differentiation]

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C. LABORATORY/SPONSOR

[Include the following information: Official name, address and contact information of applicant and all locations where specimen testing will be performed]

D. REGULATORY INFORMATION

D. Approval/Clearance Status:

The **[test name]** is not cleared, CLIA waived, approved, or subject to an approved investigational device exemption.

E. PROPOSED INTENDED USE

1) **Intended Use (IU):**

The proposed IU will be finalized based on the data provided at the time of authorization. An example IU is provided below.

The **[test name]** is a **[specify technology e.g., Enzyme-Linked Immunosorbent Assay (ELISA)]** intended for qualitative **[or semi-quantitative or quantitative tests, if appropriate validation data is provided. Performance evaluations beyond what is currently described in the template may be necessary]** detection of **[specify the antibody class or classes that are being detected, or indicate whether the test only detects total antibodies]** antibodies to SARS-CoV-2 in human **[specify matrices including anticoagulants]**. The **[test name]** is intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection. At this time, it is unknown for how long antibodies persist following infection and if the presence of antibodies confers protective immunity. The **[test name]** should not be used to diagnose acute SARS-CoV-2 infection. Testing is limited to **[Name of Clinical Laboratory(s)]** that are Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a certified high-complexity laboratories.

Results are for the detection of SARS CoV-2 antibodies. **[Specify antibodies detected]** antibodies to SARS-CoV-2 are generally detectable in blood several days after initial infection, although the duration of time antibodies are present post-infection is not well characterized. Individuals may have detectable virus present for several weeks following seroconversion.

Laboratories within the United States and its territories are required to report all positive results to the appropriate public health authorities.

[As applicable, the sensitivity of [test name] early after infection is unknown.] Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct testing for SARS-CoV-2 is necessary.

False positive results for **[test name]** may occur due to cross-reactivity from pre-existing antibodies or other possible causes.

The **[test name]** is only for use under the Food and Drug Administration's Emergency Use Authorization.

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2) **Special Conditions for Use Statements:**

For prescription use only
For *in vitro* diagnostic use only
For Emergency Use Authorization only

3) **Instruments Used:**

The *[test name]* test is to be used with the *[list all instruments, software requirements, other applicable instrumentation, etc.]*.

F. DEVICE DESCRIPTION AND TEST PRINCIPLE

1) **Product Overview/Test Principle:**

[Briefly describe the technology of the test and how this technology identifies the measurand (i.e., the test principle), and the instruments/reader employed/required to perform the test from sample collection to result and the specimen types for which you claim to have performance characteristics as described below.]

The *[test name]* uses the following: *[List the antigen(s) and antibodies used in the assay to detect the antibodies in human specimens]*

2) **Description of Test Steps:** *[Describe in order the steps of the test from specimen collection to result output.]*

3) **Control Material**

[Please describe the assay controls to be performed in the laboratory, including the positive control for each antibody class the test is intended to detect, the negative control, and any other necessary controls. Please also describe the frequency with which controls will be performed.]

G. INTERPRETATION OF RESULTS

Assessment of *[test name]* results should be performed after the positive and negative controls have been examined and determined to be valid and acceptable. If the controls are not valid, the patient results cannot be interpreted.

[Clearly indicate how to interpret numeric test values as positive or negative for the presence of antibodies against SARS-CoV-2. If applicable, indicate how to identify indeterminate/equivocal results and how the user should resolve them. Also describe if and when repeat testing may be required.]

H. PERFORMANCE EVALUATION

1) **Analytical Sensitivity and Specificity**

a) Reactivity/Inclusivity:

Although mutations in the SARS-CoV-2 genome have been identified as the virus has spread, no serologically unique strains have been described relative to the originally isolated virus (this research is exceptionally limited at present).

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b) *Cross-Reactivity:*

If a large number of known negative samples (e.g., ≥ 75 samples collected in the US prior to December 2019) are tested from a population with a high prevalence of vaccination against, and/or infection with, the following viruses, and specificity $>98\%$ is observed, cross-reactivity testing for the following viruses would not be expected at this time:

anti-influenza A (IgG and IgM)
anti-influenza B (IgG and IgM)
anti-HCV (IgG and IgM)
anti-HBV (IgG and IgM)
anti-Haemophilus influenzae (IgG and IgM)
anti-229E (alpha coronavirus)
anti-NL63 (alpha coronavirus)
anti-OC43 (beta coronavirus)
anti-HKU1 (beta coronavirus)
ANA
anti-respiratory syncytial virus (IgG and IgM)
anti-HIV

[If a large number of known negative samples are not evaluated, or lower than 95% specificity is observed, describe the cross-reactivity testing performed to evaluate the cross-reactants in the table above.]

If testing of the cross-reactants on above is needed to demonstrate cross-reactivity for the test, FDA believes testing a minimum of 5 individual samples for each disease/infectious agent/antibody class listed above may be acceptable.

If natural specimens are used, it is important to assess cross reactivity using sera from patients with the underlying diseases in the acute or convalescent stages of infection in order to obtain high levels of IgM or IgG for the underlying condition. If spiked samples with the IgM or IgG antibodies for the underlying conditions are prepared for this study, it is important to confirm that “negative samples” are SARS-CoV-2 IgM and IgG seronegative with the candidate assay prior to spiking. Additionally, commercially available IgM or IgG antibodies for the underlying conditions panels may be acceptable if collected prior to the COVID-19 pandemic to ensure the panels are SARS-CoV-2 antibody negative.

We recommend you present your results in the following suggested table and calculate agreement between the candidate test result and the expected result.

Cross-Reactivity: **[test name]** example table for wet tested organisms below:

Virus/Bacteria/Parasite Antibody positive	Source/ Sample type	Results*

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***If applicable, please include the signal output for your test's technology.**

[If your test exhibits significant cross-reactivity that would produce false positive results for any virus evaluated, please describe a plan to address this risk.]

2) Class Specificity:

If your test is intended for the detection of total antibody with no differentiation between different immunoglobulins, then this study does not apply. *[In this case, please indicate that this study is not applicable.]*

[If your test is intended for the detection of total antibody with no differentiation between different immunoglobulins, then this study does not apply. Please indicate not applicable.]

If your test is intended to differentiate between different immunoglobulins, describe the approach used to evaluate class specificity.]

[If class specificity testing is needed for your test, please describe the study, or studies, performed to demonstrate that the assay accurately detects each antibody class (e.g., IgG and IgM). This should include a description of the studies performed to evaluate the potential for human IgM to cross react and therefore produce false positive results for IgG, and the reverse, and the potential for IgM to compete with IgG and produce false negative results. Please indicate the number of samples, and the number of replicates per sample, tested. FDA believes that evaluating at least 5 samples positive for both antibody classes (IgM positive while also IgG positive), in duplicate, may be acceptable.]

Approaches to evaluate class specificity depend on the assay format. If you have well-characterized the anti-IgG and anti-IgM reagents, used in your test class specificity testing may not be needed. In this case, please describe how the reagents were characterized and such characterization supports class specificity. One recommended approach includes treating the specimen with dithiothreitol (DTT) where the final IgG result will remain unaffected and the final IgM signal will decrease or be negative. A positive control should also be included that confirms DTT activity.

[Please provide the protocol and results, including line data, from any class specificity testing.]

FDA believes that 100% agreement with expected result would establish antibody class specificity.

If a DTT Treatment approach is followed, below is an example table for IgM and IgG:

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Sample ID	Replicates	Result NO DTT Treatment (IgM/IgG)	Result DTT Treatment (IgM/IgG)	Expected result with DTT treatment (IgM/IgG)	Result Agreement
1	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
2	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
3	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
4	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes
5	1	+/+	-/+	-/+	yes
	2	+/+	-/+	-/+	yes

3) **Clinical Agreement Study:**

[Please describe the clinical study used to evaluate the clinical performance of the test. Please note that the exact requirements for the clinical evaluation depend on access to COVID-19 disease clinical specimens at the time of the studies and the nature of the emergency.]

Initial clinical agreement trials typically evaluate all matrices that the sponsor intends to claim in their EUA submission.

The comparator method used to establish clinical truth for the patient at this time is a PCR based assay. Results from the comparator PCR method are obtained using specimens that have been validated for use with the comparator method. Consider collecting nasal swab samples from a patient for PCR and then follow with a fingerstick or blood draw from the same patient. *[Please identify the PCR comparator that was used. If the PCR comparator is not an EUA-authorized test, please provide Limit of Detection (LoD) and cross-reactivity validation data. If it is an EUA-authorized test, then no validation is needed.]*

Ideally, performance characteristics are established in a clinical study with prospective samples. If a prospective study is not feasible, an acceptable alternative would be to test retrospectively collected SARS-CoV-2 antibody positive specimens from patients that have been previously confirmed infected by SARS-CoV-2 RT PCR, accompanied by basic information such as the population from which the sample was drawn and the comparator method, specimen collection date, date of onset of symptoms (if present/known), and comparator method to confirm patients as SARS-CoV-2 infected or not infected (see above).

Clinical agreement data should be provided using at least 30 antibody positive samples for each immunoglobulin claimed and 75 antibody negative samples from patients tested for SARS-CoV-2 and confirmed as negative and the data should

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demonstrate a minimum overall 90.0% positive percent agreement and overall 95.0% negative percent agreement, and for tests that report specifically IgM and IgG results, a minimum positive percent agreement for IgM of 70% and a minimum positive percent agreement for IgG of 90%. Point estimates not lower than 93% for combined NPA, not lower than 90% for combined PPA, and for tests that specifically report IgG or IgG and IgM, PPA for IgG not lower than 87%, and PPA for IgM not lower than 67% may be acceptable if a larger number of samples are evaluated and the lower bounds of the 95% confidence intervals are higher than would be demonstrated in a clinical agreement study with 30 antibody positive and 75 antibody negative samples.

If a claim for fingerstick is desired, we believe evaluating a minimum of 30 positive and 30 negative fingerstick whole blood samples may be acceptable to demonstrate clinical performance in fingerstick samples.

[Please specify how the samples were generated, collected, and sourced. Please also specify if the samples were fully prospective, mix of prospective, retrospective and/or contrived. Please specify inclusion/exclusion criteria, collection and testing sites, number of samples collected and tested, and number of operators performing the testing, as available.]

[Please clearly describe the data analysis methods used and provide the results from the study, including line data. We suggest calculating positive and negative percent agreement between the candidate device and the comparator method results separately for each claimed matrix, using 2 x 2 tables as follows:]

		<i>Comparator method/Clinical truth</i>	
		<i>Positive</i>	<i>Negative</i>
<i>Your Device</i>	<i>Positive</i>	A	B
	<i>Negative</i>	C	D

Percent Positive Agreement = $A/(A + C)$ or True Positives/(True Positives + False Negatives)

Negative Percent Agreement = $D/(B + D)$ or True Negatives/(True Negatives + False positives)

If you claim that your test can differentiate between IgG and IgM, PPA and NPA for IgG and IgM separately would be calculated separately.]

4) Matrix Equivalency

[Please describe the protocol and results from any matrix equivalency studies performed to support the performance of the assay in claimed sample matrices (serum,

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EDTA plasma, venipuncture whole blood, different anticoagulants, etc.) that were not evaluated in the initial clinical agreement study.]

Matrix equivalency studies are performed to evaluate specimen matrices for which clinical agreement isn't initially assessed. In these studies, the matrix in which the clinical study(ies) are conducted is the comparator matrix/specimen type and each matrix set (whole blood, plasma, serum) comes from the same donor (i.e., paired samples).

Typically, negative, low positive, and moderate positive samples are evaluated. We believe five samples, run in duplicate for each concentration for a total of 30 results per matrix (assuming 3 concentrations were evaluated) may be acceptable. To allow for comparison, negative samples for each claimed specimen type/matrix are spiked with the same amount of analyte (SARS-CoV-2 IgG and IgM). We believe confirming samples are antibody seronegative with the candidate assay before spiking with SARS-CoV-2 IgG and IgM antibodies is important.

For these types of studies, typically, each sample is assayed with the candidate device, and the results obtained for the comparator matrix are compared to the results obtained for each additional matrix under evaluation for each subject. Positive percent agreement and negative percent agreement for each matrix with respect to the comparator matrix are calculated. We believe that at least 95% agreement across all matrices/subject may be acceptable to demonstrate that performance between the matrices can be considered equivalent.

I. UNMET NEED ADDRESSED BY THE PRODUCT

This section will be completed by FDA.

J. APPROVED/CLEARED ALTERNATIVE PRODUCTS

Currently no methods for the qualitative detection of SARS-CoV-2 IgM or IgG antibodies have been approved or cleared by FDA.

K. RISKS AND BENEFITS:

This section will be completed by FDA.

L. FACT SHEET FOR HEALTHCARE PROVIDERS AND PATIENTS:

[Include proposed Fact Sheets for Patients and Healthcare Providers] - see examples for authorized EUA tests on our website. During review, FDA will make available Fact Sheet templates.

M. INSTRUCTIONS FOR USE/ PROPOSED LABELING/PACKAGE INSERT:

[In lieu of a package insert or labeling, please include your Laboratory SOP/protocol.]

Contains Nonbinding Recommendations

N. RECORD KEEPING AND REPORTING INFORMATION TO FDA:

The laboratory will track adverse events and report to FDA under 21 CFR Part 803. A website is available to report on adverse events, and this website is referenced in the Fact Sheet for Health Care providers. The laboratory will maintain will information on the performance of the test, and report to FDA any suspected change in performance of which they become aware. The laboratory will maintain records associated with this EUA and ensure these records are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.