

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

Guidance for Developers and Food and Drug Administration Staff

Document issued on the web on November 15, 2021.

This document supersedes “Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised): Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff” issued May 11, 2020.

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

***This is the fifth edition of this guidance, which originally issued February 29, 2020 and was subsequently revised on March 16, May 4, and May 11, 2020.**

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-R4 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 (Revised)

Guidance for Developers and Food and Drug Administration Staff

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

I. Introduction

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

FDA is issuing this guidance to provide FDA's enforcement policies regarding certain novel coronavirus (COVID-19) tests 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 this rapidly spreading, severe illness. This document supersedes "Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised): Guidance for Clinical Laboratories, Commercial Manufacturers, and Food and Drug Administration Staff" issued May 11, 2020.

The policies in this guidance are 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). FDA continues to assess the evolving situation and intends to update this guidance as appropriate.

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))

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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.

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, 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

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

As of November 15, 2021, FDA has authorized more than 420 tests for COVID-19, including more than 300 diagnostic and 90 serology 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 individual patient but also can have a broad public health impact. False positive results for diagnostic tests, for example, can lead to unnecessary quarantine, wasted contact tracing and testing resources, and delay in accurate diagnosis and appropriate treatment for the individual. False negative results can lead to lack of appropriate treatment for the individual and further spread of the disease.

¹ Secretary of Health and Human Services, Determination that a Public Health Emergency Exists (originally issued on Jan. 31, 2020, and subsequently renewed), *available at* <https://www.phe.gov/emergency/news/healthactions/phe/Pages/default.aspx>.

² Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), *available at* <https://trumpwhitehouse.archives.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>. On February 24, 2021, there was a Presidential Declaration continuing the national emergency concerning the COVID-19 pandemic beyond March 1, 2021. See Continuation of the National Emergency Concerning the Coronavirus Disease 2019 (COVID-19) Pandemic (February 24, 2021), *available at* <https://www.federalregister.gov/documents/2021/02/26/2021-04173/continuation-of-the-national-emergency-concerning-the-coronavirus-disease-2019-covid-19-pandemic>.

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

We are now in a different stage of the COVID-19 pandemic than when the previous versions of this guidance were issued, and many more EUA-authorized COVID-19 tests are available than in May 2020. To facilitate the availability of tests for COVID-19 that FDA believes will be most beneficial at the current stage of the pandemic, FDA has revised this guidance to clarify the types of tests on which the Agency intends to focus its review to facilitate development and authorization of tests that will increase testing capacity, accessibility, and increased understanding of immune responses to SARS-CoV-2. In addition, FDA has revised the enforcement policies in this guidance to reflect that at this stage of the pandemic, the Agency generally expects COVID-19 tests to have been issued an EUA prior to the tests being distributed or offered.

III. Scope

This guidance applies to diagnostic and serology tests for COVID-19.³ The policies and recommendations described in this guidance are intended to facilitate availability of tests for COVID-19 that FDA believes will be most beneficial at the current stage of the public health emergency.

FDA notes that the enforcement policies in this guidance do not address medical device reporting (MDR) under 21 CFR Part 803 for tests offered prior to authorization as described in the guidance. Developers offering such tests are expected to comply with applicable MDR requirements, including reporting of medical device events that reasonably suggest that their device may have caused or contributed to a death or serious injury, and malfunctions that would be likely to cause or contribute to a death or serious injury if they were to recur. Moreover,

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. Screening tests, which are used for testing individuals without symptoms or other reasons to suspect COVID-19, are a subset of diagnostic tests. Molecular tests detect the presence of viral RNA and antigen tests detect the presence of viral proteins that are part of the SARS-CoV-2 virus. The terms "serology" or "antibody" tests are generally used to refer to tests that detect antibodies to the SARS-CoV-2 virus. Because the antibodies are part of the body's immune response to exposure and not the virus itself, such testing cannot be used for diagnosis of acute infection.

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 under CLIA that meet the requirements to perform tests of high-complexity, including testing at the point-of-care when the site is covered by the laboratory's CLIA certificate for high-complexity testing.

IV. Policy

A. Prioritization of Review of EUA Requests for Tests

The issuance of an EUA is discretionary. FDA's decision to review and process an EUA request, and ultimately issue an EUA if the relevant statutory criteria are met, is based on a determination, on a case-by-case basis, that such action is necessary to protect the public health in an emergency. It is an authorization that the government "may" issue when necessary to protect the public health in an emergency (see section 564(a)(1) of the FD&C Act (21 U.S.C. 360bbb-3(a)(1)), which states, in relevant part, "subject to the provisions of this section, the Secretary may authorize the introduction into interstate commerce...a drug, device, or biological product intended for use in an actual or potential emergency"). FDA's January 2017 guidance, *Emergency Use Authorization of Medical Products and Related Authorities*,⁴ describes factors that FDA intends to use in its prioritization of EUA requests, such as the public health need for the product, the availability of the product, the availability and adequacy of the information concerning the likelihood that the product may be safe and effective in preventing, treating, or diagnosing the condition, and whether the product is included in government stakeholder stockpiles. Additionally, given the need to address urgent public health priorities, FDA may need to further prioritize among the EUA requests it receives for COVID-19 tests. At this stage in the pandemic, for SARS-CoV-2 diagnostic tests, FDA intends to encourage development and facilitate the authorization of tests that will significantly increase testing capacity and accessibility. For serology tests, FDA intends to focus on quantitative and neutralizing antibody tests that promote an increased understanding of immune responses to SARS-CoV-2.

Specifically, at this stage of the pandemic, FDA intends to focus its review on EUA requests for the following types of tests:

- Diagnostic tests (molecular and antigen) that can be used at the POC or completely at home from developers who have indicated the ability to scale up manufacturing capacity shortly after authorization (e.g., a manufacturing capacity of $\geq 500,000$ tests per week within 3 months of authorization);⁵

⁴ See <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities>.

⁵ Diagnostic tests, including those for screening, that can be manufactured in high volume and used at the POC or completely at home increase accessibility to tests and results from such tests are typically returned faster than other diagnostic tests. FDA believes that 500,000 tests per week is a reasonable and achievable manufacturing capacity for many manufacturers of POC or at home tests.

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- Laboratory-based⁶ molecular diagnostic tests that are: highly sensitive; high throughput⁷; intended for pooling, home specimen collection, screening, or detection of multiple analytes; and from experienced developers⁸ who have indicated the ability to scale up manufacturing capacity shortly after authorization (e.g., a manufacturing capacity of $\geq 500,000$ tests per week within 3 months of authorization);⁹
- Home specimen collection kits intended for use with laboratory-based molecular diagnostic tests, where the manufacturer has indicated the ability to scale up to a manufacturing capacity shortly after authorization (e.g., $\geq 500,000$ kits per week within 3 months of authorization);¹⁰
- Laboratory-based and POC serology tests that are: high throughput, if laboratory-based; intended for the quantitative measurement of antibody titers; and from developers who have indicated the ability to scale up manufacturing capacity shortly after authorization (e.g., a manufacturing capacity of $\geq 500,000$ tests per week within 3 months of authorization);¹¹
- Laboratory-based and POC serology tests that are: intended for the quantitative detection of neutralizing antibodies; and from developers who have indicated the ability to scale up

⁶ For the purposes of this guidance, “laboratory-based tests” are tests intended for use in laboratories certified under CLIA that meet the requirements to perform tests of moderate or high complexity. Such tests do not include POC or at-home tests, which are addressed in the first bullet. As a practical matter, only laboratory-based tests are likely to be the type of highly-sensitive, high throughput tests we are seeking to prioritize here.

⁷ To illustrate, we would generally consider tests that support two 384 well thermocycler runs per 8 hours in combination with an automated extraction and liquid handling platform as “high throughput.”

⁸ For the purposes of this guidance, “experienced developers” refers to developers who have interacted with FDA through an EUA request or pre-EUA submission during the current public health emergency or have similar experience. FDA has interacted with over 1,000 test developers through the EUA and pre-EUA processes during the SARS-CoV-2 pandemic. The Agency has found that EUA requests from inexperienced developers are more resource intensive to review. At this phase of the pandemic, and given our experiences to date, we believe that for high or moderate complexity laboratory tests, FDA’s review resources are more impactful when working with experienced developers given the design and validation complexities associated with such tests. As a result, FDA intends to prioritize the review of EUA requests for high and moderate complexity tests from experienced developers.

⁹ In order for diagnostic tests to significantly increase testing capacity, which has been identified as a US government testing priority, they should be high volume and high throughput and for use on broad patient populations (i.e., not only on symptomatic patients or patients suspected of COVID-19). FDA authorization of high and moderate complexity tests with manufacturing capacities lower than 500,000 tests per week will not sufficiently scale US testing capacity. Furthermore, based on surge manufacturing capacity data received in EUA requests to date, FDA believes that 500,000 tests per week is a reasonable and achievable manufacturing capacity for many manufacturers of high and moderate complexity tests. Similarly, highly manual, low throughput tests will not allow laboratories to scale testing volumes to those needed for large screening programs. With respect to laboratory-based diagnostic tests, FDA intends to prioritize molecular, and not antigen, diagnostic tests that have the other characteristics described since antigen tests are generally not as sensitive as molecular tests, and the primary benefits from antigen tests in this phase of the pandemic come from their ability to scale up for use at POC or completely at home. Reviewing laboratory-based antigen tests would take resources away from reviewing POC and at home antigen tests. Therefore, FDA intends to focus its resources on the types of antigen tests more likely to provide greater benefit to the nation’s COVID-19 response.

¹⁰ Home specimen collection kits intended for use with high volume and high throughput laboratory-based tests will support and enable increased testing with such tests by increasing their accessibility.

¹¹ Laboratory-based and POC serology tests that are high throughput, can be manufactured in high volume, and that are intended for the quantitative measurement of antibody titers promote an increased understanding of immune responses to SARS-CoV-2.

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manufacturing capacity shortly after authorization (e.g., a manufacturing capacity of $\geq 500,000$ tests per week within 3 months of authorization);¹² and

- Tests for which the EUA request is from (or supported by) a US government stakeholder,¹³ such as tests funded by the Biomedical Advanced Research and Development Authority (BARDA) or the National Institutes of Health's Rapid Acceleration of Diagnostics (RADx).

Further, for tests intended for use on instruments not used for previously authorized tests, FDA intends to prioritize those tests where the developer indicates sufficient instrument and kit production capacity.¹⁴ For tests intended for use with home collection kits, FDA intends to prioritize those tests where there is sufficient assay and collection kit production capacity.

In order to make effective use of FDA resources, FDA generally intends to focus its review on EUA requests for tests that are within these priorities.¹⁵ Appendix A includes a visual overview of these review priorities. FDA believes these priorities are appropriate to address the public health needs at the current stage of the public health emergency and may adjust these priorities as more tests are authorized or public health needs change. FDA encourages test developers to consider these priorities and focus on these areas of need as they develop and validate their tests.

For tests not authorized and not being offered at the time this updated guidance issues, FDA expects it will only review EUA requests for priority tests. FDA intends to notify test developers of such tests by email if FDA declines to review or otherwise decides not to authorize the test.¹⁶

¹² Laboratory-based and POC serology tests that can be manufactured in high volume and that are intended for the quantitative detection of neutralizing antibodies promote an increased understanding of immune responses to SARS-CoV-2.

¹³ Prioritization of EUA requests from (or supported by) government stakeholders is discussed in the Guidance for Industry and Other Stakeholders: Emergency Use Authorization of Medical Products and Related Authorities, available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities>.

¹⁴ FDA has received EUA requests for tests that require a new instrument to perform the test, but the instrument production capacity is such that the test developers would not be able to produce and distribute in a timely manner enough instruments to perform all the tests they are planning to offer. The addition of an instrument greatly increases the complexity of an EUA review. In addition, laboratories, including POC sites, are unlikely to purchase new instruments that will only be able to run a single test and will potentially not be able to run any tests after the pandemic.

¹⁵ Developers of tests that are not within these priorities may consider modifications to their test prior to submitting an EUA request to FDA to better align with the current public health needs. Alternatively, they may consider pursuing marketing authorization through a traditional premarket review pathway. If developers of tests that are not within these priorities and are a new type of test where the developer believes the test can help address current public health needs, the developers and/or laboratories are welcome to provide FDA their rationale for the public health need for the individual test and the reasons why FDA review of an EUA request should be considered, by sending an email to CDRH-EUA-Templates@fda.hhs.gov.

¹⁶ FDA may decline to review or otherwise decide not to authorize a test based on any number of factors, including lack of adequate data to support emergency use authorization, as discussed in Guidance for Industry and Other Stakeholders: Emergency Use Authorization of Medical Products and Related Authorities, available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities>.

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For tests on one of the notification lists on FDA’s website at the time this guidance issues and laboratory developed tests (LDTs)¹⁷ being offered following the HHS August 2020 Web Statement entitled “Recission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests” (“August 2020 HHS Announcement”), FDA generally intends to review EUA requests as outlined in Section IV.C of this guidance.

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

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

Under such policy, a State or territory choosing to authorize laboratories within that State or territory to develop and perform a test for COVID-19 would do so under authority of its own State law, and under a process that it established, and FDA did not intend to object to the use of such tests for specimen testing where the notification of SARS-CoV-2 test validation was not submitted to FDA and the laboratory did not submit an EUA request to FDA, and where instead the State or territory took responsibility for COVID-19 testing by laboratories in its State during the COVID-19 outbreak. This policy applied only to tests designed, developed, and used within a single, high-complexity, CLIA-certified laboratory. The policy did not apply to at-home tests or tests with home specimen collection, or any testing outside of a high-complexity CLIA-certified laboratory.¹⁸

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

¹⁷ LDTs are typically considered tests that are designed, manufactured, and used within a single laboratory that is certified under CLIA and meets the requirements to perform tests of high-complexity.

¹⁸ There are different risks associated with testing in different settings and different issues need to be addressed. For example, home collection raises several issues of importance, including whether the lay user can safely and properly collect the specimen, whether the components of the specimen transport media are safe for use in the home environment (because some may be toxic), proper shipment, and adequate stability of the specimen given the time lapse between collection and testing and the potential impact of shipping conditions (such as, if the specimen sits in a hot truck). Tests performed fully at home raise additional issues such as whether the lay user can safely and properly perform the test and read and accurately interpret the results.

¹⁹ A list of States and territories that have notified FDA under this policy is available on FDA’s FAQ website at: <https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-diagnostic-testing-sars-cov-2>.

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At the current stage of the pandemic, FDA is revising this policy such that FDA no longer intends to apply the policy to any additional States or territories going forward.²⁰ For the States and territories listed on the notification list on FDA's website prior to the date of issuance of this updated guidance that are continuing to authorize laboratories within that State or territory to develop and perform a test for COVID-19, FDA does not intend to object to the use of such tests for specimen testing where 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. This policy applies only to tests designed, developed, and used within a single, high-complexity CLIA-certified laboratory. This policy does not apply to at-home tests or tests with home specimen collection, or any testing outside of a high-complexity CLIA-certified laboratory.²¹

FDA notes that laboratories offering testing authorized by States or territories should be aware of requirements to report test results to appropriate federal, state, and local public health agencies in accordance with applicable federal, state, and local laws.²²

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

For the enforcement policies in the May 2020 editions of this guidance, where a developer notified FDA that it intended to distribute or offer its validated test as outlined in the guidance, FDA would generally add the developer/test to one of the notification lists on FDA's website. As discussed in those policies, FDA generally did not intend to object to developers distributing and offering a test on the notification list as described in the policies.

FDA is revising the prior policies because we are at a different stage of the pandemic, and there are many more EUA-authorized COVID-19 tests available now. In addition, experience has shown that many of the COVID-19 tests offered prior to FDA review were determined to have poor performance, either upon FDA review of the EUA request or, for some serology tests, upon evaluation by the National Institutes of Health's National Cancer Institute (NIH/NCI).

²⁰ A State or territory that believes there would be a particular benefit to the policy applying to the State or territory is welcome to reach out to FDA to discuss further by sending an email to CDRH-EUA-Templates@fda.hhs.gov.

²¹ There are different risks associated with testing in different settings and different issues need to be addressed. For example, home collection raises several issues of importance, including whether the lay user can safely and properly collect the specimen, whether the components of the specimen transport media are safe for use in the home environment (because some may be toxic), proper shipment, and adequate stability of the specimen given the time lapse between collection and testing and the potential impact of shipping conditions (such as, if the specimen sits in a hot truck). Tests performed fully at home raise additional issues such as whether the lay user can safely and properly perform the test and read and accurately interpret the results.

²² Under section 18115 of the CARES Act (Public Law 116-136), laboratories, including those in patient care settings operating under a CLIA Certificate of Waiver, Certificate of Compliance or Certificate of Accreditation, must report the results of COVID-19 tests to HHS or its designee, in such form and manner as the Secretary may prescribe, during the declared public health emergency. For additional information on the laboratory data reporting guidance and FAQs from HHS, please see: <https://www.hhs.gov/coronavirus/testing/covid-19-diagnostic-data-reporting/index.html>.

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As outlined below, among other things, FDA no longer intends to add tests to the notification lists. Further, for tests already on the notification lists, FDA intends to remove tests for which FDA has either issued an EUA or has notified the test developer by email that FDA declines to review, declines to issue, or otherwise decides not to authorize the test for any reason.

(1) Diagnostic and Serology Tests on Notification Lists for which an EUA Request was Submitted²³

For SARS-CoV-2 diagnostic or serology tests on one of the notification lists and for which an EUA request was submitted prior to issuance of this updated guidance, FDA does not intend to object to continued distribution or offering of those tests for a period of time while FDA reviews the EUA requests for the tests where:

- 1) The developer submitted its EUA request after February 1, 2021; or
- 2) The developer submitted its EUA request prior to February 1, 2021 and the developer confirms to FDA (through an email to CDRH-EUA-Templates@fda.hhs.gov), within 45 calendar days from the date of issuance of this updated guidance, that:
 - a. the developer wants FDA to continue reviewing its EUA request;
 - b. the EUA request is for the current version of the test; and
 - c. either the developer does not have additional data to add, or the developer submits updated information to FDA within that 45 calendar-day timeframe including, if not previously provided, validation with clinical specimens using an appropriate comparator.²⁴ FDA believes that 45 calendar days is reasonable for this.

If FDA does not receive confirmation from a test developer that submitted its EUA request prior to February 1, 2021 confirming that the developer wants FDA to continue reviewing its EUA request, FDA intends to decline to review (or decline to further review where review has already begun) the EUA request.

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

²³ There may be a number of tests for which notification was submitted to FDA prior to May 2020 that are not listed on the notification lists on the FDA's website. FDA generally intends to consider such tests similarly as tests on the notification lists at the time this updated guidance issues, provided they are not listed on the removal lists on the FDA's website.

²⁴ If submitting new information to FDA, developers should consider submitting information relating to the priorities outlined in Section IV.A as tests falling under those priorities reflect the public health needs at the current stage of the public health emergency and the tests for which FDA will be prioritizing review.

(2) Laboratory Serology Tests on the Notification List and Certain LDTs for Which an EUA Request was Not Submitted

Certain serology tests developed by laboratories are being offered without FDA authorization after the developer notified FDA as described in the previous version of this guidance. In addition, FDA understands that some LDTs for SARS-CoV-2 are being offered without FDA authorization or submission of an EUA request following the August 2020 HHS Announcement. The policy below applies to serology tests developed by laboratories offered without submission of an EUA request after notifying FDA as described in the previous version of this guidance and LDTs being offered without submission of an EUA request following the August 2020 HHS Announcement.²⁵

For such tests, FDA does not intend to object to continued offering of the tests while FDA reviews the EUA requests where the developer submits the EUA request to FDA through an email to CDRH-EUA-Templates@fda.hhs.gov within 60 calendar days from the date of issuance of this updated guidance.^{26, 27} FDA believes this is sufficient time for a test developer to prepare and submit an EUA request, considering that the validation recommendations included in the EUA templates²⁸ have been publicly available and generally consistent since Spring 2020, and such tests should have already been validated prior to being offered. As for all test developers seeking an EUA, these laboratories may use the optional EUA templates, which generally recommend providing information on the indication of the test, a description of the test, the validated performance of the test, a description of how the test was validated, and validation data. FDA understands that developers of these tests may not have familiarity with the templates or EUA process. As such, FDA is clarifying that, because the EUA templates are optional, instead of using the EUA templates, laboratories may submit an email to FDA with supporting information, such as a description of their test and intended use and attach existing validation test reports and excel data files that they already have on file in accordance with their internal procedures. Laboratories should submit this and any additional information they believe would support authorization.²⁹ If the test developer does not submit an EUA request within 60 calendar days from the date of issuance of this updated guidance, FDA generally expects developers to cease marketing and offering their tests within 60 calendar days from the date of issuance of the updated guidance.³⁰

²⁵ If developers of these serology tests and LDTs submitted an EUA request to FDA prior to issuance of this guidance, the policy discussed in Section IV.C.1 of this guidance applies.

²⁶ This policy does not apply to at-home tests or tests with home specimen collection, or any testing outside of a laboratory certified under CLIA that meets the requirements to perform tests of high-complexity.

²⁷ When submitting such an EUA request, developers should consider submitting information relating to the priorities outlined in Section IV.A as tests falling under those priorities reflect the public health needs at the current stage of the public health emergency and the tests for which FDA will be focusing its review.

²⁸ Available at: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>.

²⁹ If sufficient information is not submitted to support authorization, FDA may reach out to laboratories to request additional information.

³⁰ If developers are not able to prepare and submit an EUA request within 60 calendar days, but they believe it is of significant public health importance that they continue to offer their unauthorized test beyond that timeframe, the developer is welcome to provide FDA their rationale for the continued public health need for their individual test and the reasons why additional time is needed to prepare and submit an EUA request, by sending an email to CDRH-EUA-Templates@fda.hhs.gov.

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

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

FDA continues to recommend the following:

1. Test reports should prominently disclose that the test has not been reviewed by FDA. Until the test is authorized by FDA, any statements in the test reports and other labeling that expressly state or imply that the test has been authorized by FDA would be false. Similarly, any statements in the test reports and other labeling that state or imply that EUA issuance or FDA authorization are imminent or pending could be misleading.
2. Developers should make publicly available on their website the instructions for use for the test and data about the test's performance characteristics, including a summary of assay performance.
3. Instructions for use and patient test reports for serology tests should include information that helps users and patients understand the test results, including the following:
 - Negative results do not preclude acute SARS-CoV-2 infection. If acute infection is suspected, direct (i.e., diagnostic) testing for SARS-CoV-2 is necessary.
 - Results from antibody testing should not be used to diagnose or exclude acute SARS-CoV-2 infection.
 - Positive results may be due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.

In addition, as noted in the May 2020 editions of this guidance and earlier in this updated guidance, unless and until an EUA is issued that authorizes additional testing environments for a specific test, under CLIA, use of that test is limited to laboratories certified under CLIA that meet the requirements to perform tests of high-complexity, including testing at the POC when the site is covered by such a laboratory's CLIA certificate.

(4) FDA Review of EUA Requests

For tests described in Sections IV.C.1 and IV.C.2 of this guidance, FDA generally intends not to authorize a test where the EUA request does not demonstrate that the test has been appropriately

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validated, including validation with clinical specimens using an appropriate comparator as described in Section V of this guidance. FDA's recommendations for validation, including descriptions of appropriate comparators for different types of tests, can be found in the EUA templates³¹ for different types of tests.

For tests described in Sections IV.C.1 and IV.C.2 of this guidance, FDA intends to consider the priorities outlined in Section IV.A, as well as other relevant considerations for these currently available tests (e.g., safety concerns), to inform the Agency's review and prioritization of EUA requests for these tests. Appendix B includes a visual overview of the review policies for tests described in section IV.C.1 and IV.C.2.

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

A developer may request certain modifications to its EUA-authorized test that was authorized in an individual EUA, and such changes shall be implemented as specified in the EUA's Conditions of Authorization, including having concurrence from FDA prior to modification.³² FDA also has discussed various modification policies in previous editions of the guidance relating to authorized COVID-19 tests. As discussed further below, FDA is updating these policies.

The policies in this section do not apply to at-home testing, including at-home specimen collection.

In addition, as noted in the May 2020 editions of this guidance and earlier in this updated guidance, unless and until an EUA is issued that authorizes additional testing environments for a specific test, under CLIA, use of that test is limited to laboratories certified under CLIA that meet the requirements to perform tests of high-complexity, including testing at the POC when the site is covered by such a laboratory's CLIA certificate.

In order to provide transparency, when a developer is distributing or offering a test that is a modification of an EUA-authorized diagnostic test prior to or without authorization of the modified test, as discussed in this section, the recommendations in Section IV.C.3 of this updated guidance apply. FDA further recommends that the developer post data about the modified test's performance characteristics on the developer's website, and that the instructions for use or test protocol and the test reports accurately reflect the modification and prominently disclose that the test has been modified since authorization by FDA and that the modified test has not been reviewed by FDA.

If FDA identifies a significant problem or concern with a modified test, based either on the provided information or external reports, that cannot be addressed in a timely manner, FDA generally would expect the developer to cease distribution, marketing and offering the modified

³¹ Available at: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>.

³² We note that modifications to a test authorized under an umbrella EUA are handled differently given the nature of umbrella EUAs. As such, the policy set forth in this subsection regarding modifications does not apply to tests authorized under an umbrella EUA.

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

(1) Certain Modifications Made After Issuance of this Updated Guidance

When a commercial manufacturer is modifying its authorized COVID-19 molecular diagnostic test to make modifications that do not change the indication for use set forth in the EUA (e.g., including new/different extraction kits or instruments) and do not change the analyte specific reagents (e.g., PCR primers and/or probes),³³ where the developer has submitted validation data supporting the modification to FDA in a supplemental EUA request, FDA does not intend to object to implementation of the modification to the diagnostic test while FDA conducts its review.

When a high-complexity CLIA-certified laboratory is modifying an authorized COVID-19 molecular diagnostic test, including one for which such laboratory is not the developer of the original, EUA-authorized test, and the modifications do not change the indication for use set forth in the EUA (e.g., including new/different extraction kits or instruments) and do not change the analyte specific reagents (e.g., PCR primers and/or probes),³⁴ FDA does not intend to object to implementation of the modification to the diagnostic test without notification to FDA or a new or amended EUA where the laboratory has validated the modification and confirmed that the performance of the modified test is equivalent to the performance of the authorized test, and use of the test is limited to the high-complexity CLIA-certified laboratory in which the modification was made.³⁵

FDA encourages the laboratory to collaborate with the developer of the authorized test so that validation data supporting the modifications can be submitted by the original developer to FDA in a supplemental EUA request. Supplemental EUA requests such as this, which have the potential to increase testing capacity by allowing more laboratories to use the test with additional components, are more likely to meet FDA's review priorities, discussed in Section IV.A of this guidance.

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

Under the previous version of the guidance, when a commercial manufacturer made certain modifications to its EUA-authorized COVID-19 diagnostic test, and where validation data

³³ Other modifications, including new claimed specimen types, test settings (e.g., point-of-care, home testing), and new patient populations (e.g., asymptomatic individuals), among others, do not fall under this policy.

³⁴ Other modifications, including new claimed specimen types, test settings (e.g., point-of-care, home testing), and new patient populations (e.g., asymptomatic individuals), among others, do not fall under this policy.

³⁵ FDA generally considers equivalent performance to be where the LoD of the modified test (using the same validation material used in the LoD study described in the authorized test's Instructions For Use (IFU)) is within 3x of the LoD established in the authorized test's IFU or that the LoD of the modified test is within 3x of the LoD of the authorized test in a direct comparison LoD study.

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

Under the previous version of the guidance, when a high-complexity CLIA-certified laboratory modified an EUA-authorized COVID-19 diagnostic test³⁶ for use with a new specimen type, where the new specimen type has been previously authorized for another test of the same technology³⁷ and where the lab had validated the test for the new specimen type, FDA stated that it did not intend to object to the use of such a modified test without notification to FDA or a new or amended EUA. For all other types of modifications made by a high-complexity CLIA-certified laboratory for an EUA-authorized COVID-19 diagnostic test, in the previous version of the guidance, FDA stated that it did not intend to object to the use of the test by high-complexity CLIA-certified laboratories, without notification to FDA or a new or amended EUA, where the test is a modification of an EUA-authorized diagnostic test and the modified test is validated using a bridging study to the EUA-authorized test.

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

In such cases, where the laboratory performing the modified test is not the developer of the original, EUA-authorized test, FDA encourages the laboratory to share its validation data with the developer of the original, EUA-authorized test so that the developer of the original, EUA-authorized test can use the validation data in support of a supplemental EUA request to add the modification. Supplemental EUA requests such as this, which have the potential to increase testing capacity by allowing more laboratories to use the test with additional components, are more likely to meet FDA's review priorities, discussed in Section IV.A of this guidance.

V. Validation

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

In the context of a public health emergency, it is critically important that tests be validated prior to use because false results not only can negatively impact the individual patient but also can have a broad public health impact. FDA has provided recommendations regarding testing that should be performed to ensure analytical and clinical validity, including descriptions of appropriate comparators for different types of tests, in the EUA templates available through

³⁶ This applies to modifications to any EUA-authorized diagnostic test, including a laboratory's own test with an EUA or a purchased kit from a commercial manufacturer with an EUA.

³⁷ For the purposes of this guidance, all nucleic acid amplification tests are considered to have the same technology.

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download from our website.³⁸ Depending on the characteristics of a developer's test, additional validation studies may be recommended.

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

Additionally, FDA continues to expect certain serology tests to be independently evaluated by NIH/NCI,³⁹ prior to authorization, when requested by the FDA. When performed, this additional testing can assist FDA in determining whether the EUA issuance criteria in section 564 of the FD&C Act have been met and whether FDA should authorize the test.

VI. Availability of EUA Templates

FDA has made available through download from our website⁴⁰ a series of templates that developers may choose to use to facilitate the preparation and submission of an EUA request for various types of COVID-19 tests. The templates reflect FDA's current thinking on validation recommendations for SARS-CoV-2 tests and the data and information that developers should submit to facilitate the EUA process. The templates provide information and recommendations, and FDA plans to update them as appropriate as more is learned about COVID-19 and more experience is gained with the EUA process for the various types of COVID-19 tests.

Developers can use alternative approaches. Developers who intend to use alternative approaches should consider seeking FDA's feedback or recommendations to help them through the EUA process. FDA encourages developers to discuss any alternative technological approaches to validating their test with FDA through CDRH-EUA-Templates@FDA.HHS.GOV.

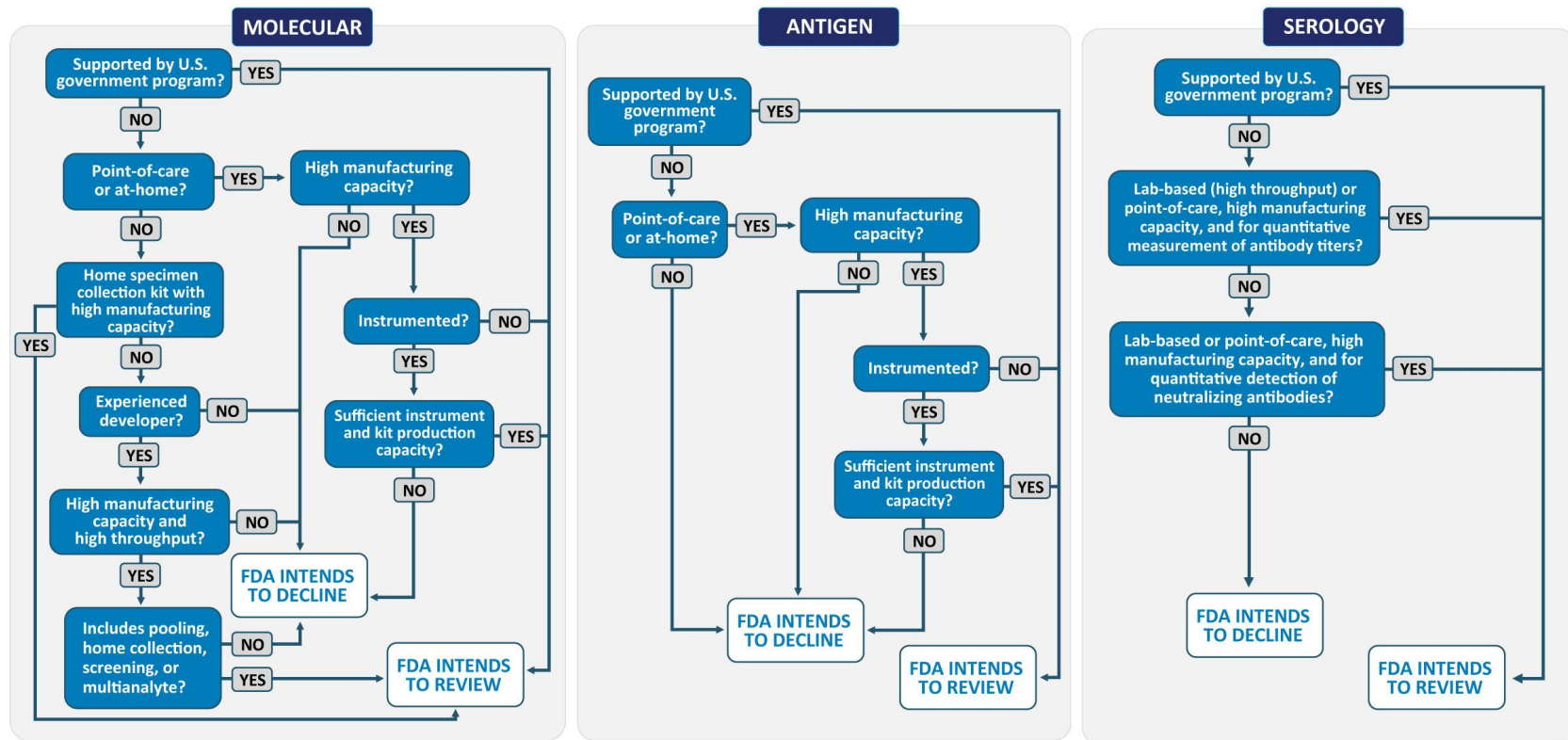
Members of the public can submit questions about the templates to CDRH-EUA-Templates@FDA.HHS.GOV, or they can submit comments regarding the templates to the public docket established for this guidance.

³⁸ See <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>.

³⁹ The FDA is working with the NIH, the Centers for Disease Control and Prevention (CDC), and BARDA to assess the performance of certain commercial manufacturers' serology tests. As part of this project, the FDA, working with partnering agencies, has designed a performance assessment protocol that offers a mechanism for an independent evaluation of certain lateral flow and certain enzyme-linked immunosorbent assay (ELISA) or similar technology-based SARS-CoV-2 antibody tests in a laboratory environment. Under this protocol, each test evaluated at the NIH/NCI will be evaluated with a well-characterized sample panel consisting of positive and negative plasma and/or serum samples. The approach represents a balanced attempt to provide a reasonable understanding of the potential performance of a significant number of the tests within a short time period. Performance results are considered during FDA's review of an EUA request for the test.

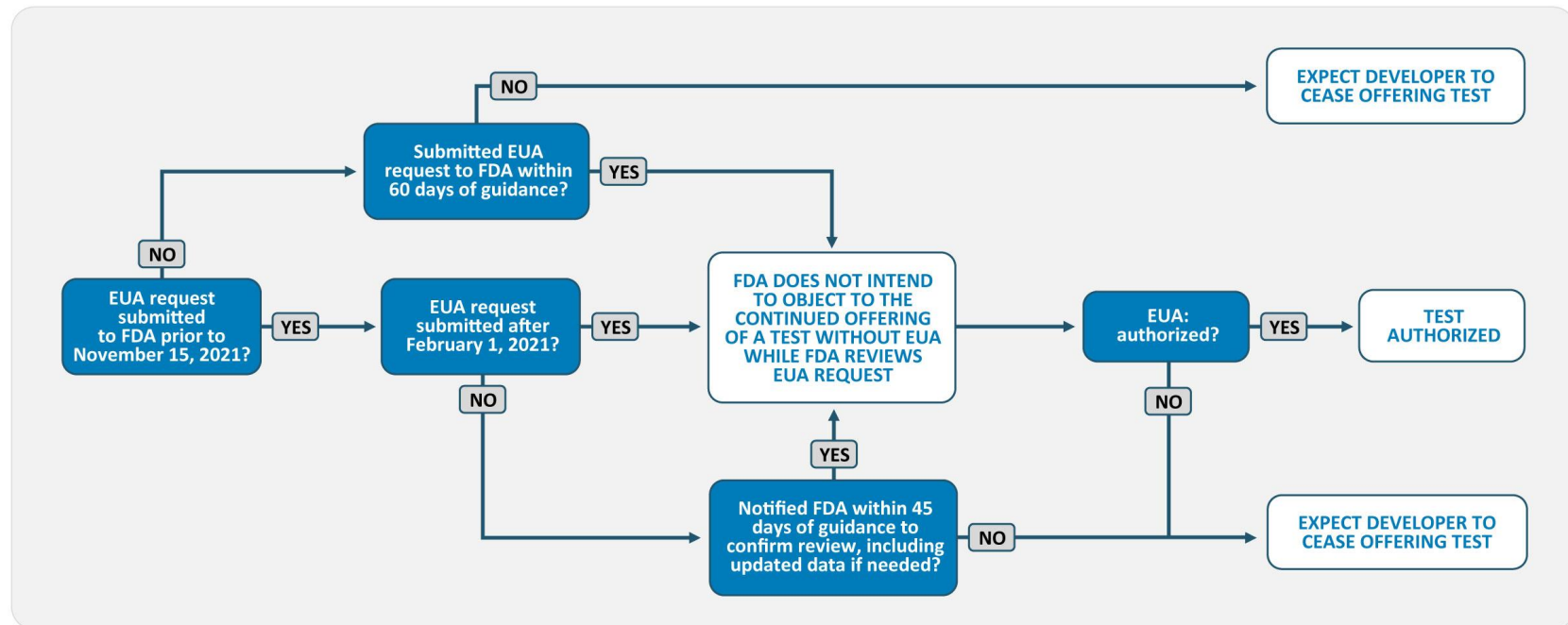
⁴⁰ See <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>.

Appendix A – FDA Review of EUA Requests for COVID-19 Tests Not Offered Prior to November 15, 2021*



*The flowcharts above give a general overview of the policies in Section IV.A of this guidance. Readers should refer to that section for the policies themselves. The flowcharts do not address policies discussed in other sections of this guidance.

Appendix B – FDA Review of EUA Requests for COVID-19 Tests Offered Prior to November 15, 2021 and Policies for Distribution and Offering of Such Tests During FDA Review *



*The flowchart above gives a general overview of the policies in Section IV.C of this guidance. Readers should refer to that section for the policies themselves. The flowchart does not address policies discussed in other sections of this guidance.