



September 23, 2021

To: Developers of Certain Molecular, Antigen and Serology In Vitro
Diagnostics (IVDs) Authorized for Emergency Use for Coronavirus Disease
2019 (COVID-19) as of Today's Date

Re: Establishing additional Conditions of Authorization for the EUAs of Certain
Molecular, Antigen and Serology IVDs related to viral mutations.

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19. Pursuant to Section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of the virus that causes COVID-19 subject to the terms of any authorization issued under Section 564(a) of the Act.¹ FDA subsequently authorized the emergency use of numerous in vitro diagnostics (IVDs) for detection and/or diagnosis SARS-CoV-2, the virus that causes COVID-19.²

Pursuant to Section 564 of the Act, and in response to the continued emergence of new genetic viral variants of SARS-CoV-2,³ FDA is issuing this letter to establish additional Conditions of Authorization on EUAs that are within the Scope of this Revision (Section I).

¹ U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act*, 21 U.S.C. § 360bbb-3. 85 FR 7316 (February 7, 2020)

² In Vitro Diagnostics EUAs: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas>, includes links to tables of currently authorized IVD EUAs for SARS-CoV-2.

³ Like all viruses, the SARS-CoV-2 genome has changed over the course of the COVID-19 pandemic through mutation, with new genetic viral variants of the virus documented in the United States and globally. Sometimes new mutations emerge and disappear, and other times they persist and the resulting new viral variants grow in prevalence. CDRH has been monitoring SARS-CoV-2 genetic viral mutations because of their potential to affect authorized SARS-CoV-2 IVDs. CDRH's monitoring of SARS-CoV-2 genetic viral mutations resulted in FDA releasing a January 8, 2021 [safety alert](https://www.fda.gov/news-events/press-announcements/fda-issues-alert-regarding-sars-cov-2-viral-mutation-health-care-providers-and-clinical-laboratory) (<https://www.fda.gov/news-events/press-announcements/fda-issues-alert-regarding-sars-cov-2-viral-mutation-health-care-providers-and-clinical-laboratory>) to healthcare providers and clinical laboratory staff about the potential impact of viral mutations on the performance of authorized molecular SARS-CoV-2 IVDs. This was subsequently followed by an FDA [guidance document](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-evaluating-impact-viral-mutations-covid-19-tests) (<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-evaluating-impact-viral-mutations-covid-19-tests>), issued in February 2021 - "Policy for Evaluating Impact of Viral Mutations on COVID-19 Tests: Guidance for Test Developers and Food and Drug Administration Staff, February 2021," outlining the FDA's concerns about the impact of viral mutations and recommendations for evaluating molecular, antigen and serology IVDs accordingly. In addition, a webpage was developed to provide information regarding the impact of viral mutations on SARS-CoV-2 tests, including the recommendations for clinical laboratory staff and health care providers from the safety alert, and information about certain tests for which the FDA has identified potential impacts on performance due to SARS-CoV-2 genetic mutations. This website was first posted in March

As set forth throughout, this letter revises the EUAs that are within the scope of this letter to require the additional Conditions of Authorization included in Section III of this letter. These conditions generally concern labeling updates and performance evaluations related to SARS-CoV-2 viral mutations for authorized tests that are within the scope of this revision.⁴ FDA's determination that the Conditions of Authorization established by this revision are necessary or appropriate to protect the public health is based on the available scientific evidence and FDA's continuing efforts to monitor the performance of authorized molecular, antigen, and serology IVDs with respect to emerging SARS-CoV-2 mutations.

Having concluded that establishing these additional conditions on the EUAs that are within the scope of this letter (section I) is appropriate to protect the public health or safety, I am hereby revising all such EUAs pursuant to Section 564(g)(2)(C) to establish the additional conditions set forth in this letter as permitted by Section 564(e) of the Act. This action is based on the available scientific evidence,⁵ including widespread detection of variants of the SARS-CoV-2 virus.

I. Scope of this Revision

Except as provided in the next paragraph, this letter revises the EUAs of the following SARS-CoV-2 IVD devices that have been issued as of today's date by establishing the additional conditions of authorization set forth in Section IV of this letter on such authorizations:

- [Molecular](#) IVD devices⁶
- [Antigen](#) IVD devices⁷
- [Serology](#) IVD devices⁸

This revision does not apply to EUAs for authorized IL-6 assays, EUAs for standalone specimen collection devices, or EUAs for standalone home collection kits. Nor does this revision apply to EUAs that include substantially equivalent viral mutation conditions of authorization.

All updated labeling will be added to FDA's webpage and posted with the EUA after it is submitted to FDA as required by Condition of Authorization (1) of this letter.

2021 and updated in June 2021: [SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests | FDA](https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests) (<https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests>).

⁴ Authorized labeling potentially impacted by the additional conditions established by this letter include some combination of the following documents: Instructions for Use (IFU), laboratory Standard Operating procedures (SOPs), EUA Summary and/or Fact Sheet for Healthcare Providers. Note that the EUA Summary is generated by FDA who will update the document after it receives the supplement request to update the test's other labeling consistent with this revision.

⁵ [SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests | FDA](https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests): <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests>.

⁶ Molecular IVD devices: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2>.

⁷ Antigen IVD devices: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-antigen-diagnostic-tests-sars-cov-2>.

⁸ Serology IVD devices: <https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-serology-and-other-adaptive-immune-response-tests-sars-cov-2>.

II. Waiver of Certain Requirements

This revision does not change the waiver of any requirements included in the EUAs being amended.

III. Conditions of Authorization

Pursuant to Section 564(e) of the Act, I am establishing the additional conditions below with respect to SARS-CoV-2 viral mutations.

Developer (You)

- (1) You must update your authorized labeling as set forth in Appendix A and B of this letter within 3 months of today's date by submitting the updated labeling to FDA as a supplement to your EUA, unless otherwise agreed to by the Division of Microbiology (DMD)/Office of Health Technology 7 (OHT7)-Office of In Vitro Diagnostics and Radiological Health (OIR)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH).⁹
- (2) You must evaluate the impact of SARS-CoV-2 viral mutations on your product's performance. For multi-analyte tests, you must evaluate the impact of SARS-CoV-2 viral mutations **and** all other target analytes. Such evaluations must occur on an ongoing basis and must include any additional data analysis that is requested by FDA in response to any performance concerns you or FDA identify during routine evaluation. Additionally, if requested by FDA, you must submit records of these evaluations for FDA review within 48 hours of the request. If your evaluation identifies viral mutations that affect the stated expected performance of your device, you must notify FDA immediately (via email: CDRH-EUA-Reporting@fda.hhs.gov).
- (3) If requested by FDA, you must update your labeling within 7 calendar days to include any additional labeling risk mitigations identified by FDA regarding the impact of viral mutations on test performance. Such updates will be made in consultation with, and require concurrence of, DMD/OHT7-OIR/OPEQ/CDRH.

Sincerely,

/S/

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosure

⁹ FDA will update the Healthcare Provider Fact Sheet for the "Umbrella EUA for Molecular Diagnostic Tests for SARS-CoV-2 Developed and Performed By Laboratories Certified Under CLIA To Perform High Complexity Tests." Test developers that use this Fact Sheet for their tests should begin using the updated version no later than 3 months from today's date.

Appendix A

Required Changes to Authorized Labeling – IFU/Laboratory SOP and/or EUA Summary⁴

As required by Condition of Authorization (1), you must update your authorized labeling (e.g., IFU, Laboratory SOPs and/or EUA Summary) to include the limitation below:

The performance of this test was established based on the evaluation of a limited number of clinical specimens. Clinical performance has not been established with all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

Appendix B

Required Changes to Authorized Labeling – Fact Sheet for Healthcare Providers¹⁰

As required by Condition of Authorization (1), you must update the Fact Sheet for Healthcare Providers as follows:

- 1) For molecular and antigen IVDs at the end of the section titled “What does it mean if the specimen tests negative for the virus that causes COVID-19?” add the following paragraph:

The performance of this test was established based on the evaluation of a limited number of clinical specimens. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

- 2) For serology IVDs at the end of the section titled “What does it mean if the specimen tests negative for antibodies against virus that causes COVID-19?” add the following paragraph:

The performance of this test was established based on the evaluation of a limited number of clinical specimens. The clinical performance has not been established in all circulating variants but is anticipated to be reflective of the prevalent variants in circulation at the time and location of the clinical evaluation. Performance at the time of testing may vary depending on the variants circulating, including newly emerging strains of SARS-CoV-2 and their prevalence, which change over time.

¹⁰ The Fact Sheet for Patients/Individuals/Recipients does not include language specific to viral mutations and therefore does not need to be updated as part of this revision.