FDA Update

Tim Stenzel, Director

Office of In Vitro Diagnostics and Radiological Health (OIR/OHT7)

IVD Roundtable

November 17, 2021

OHT7: Office of In Vitro Diagnostics & Radiological Health (OIR)

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Deputy Director Patient Safety & Product Quality: **Ryan Lubert** (Acting)
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Deputy Director Personalized Medicine: **Wendy Rubinstein**
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Associate Director Strategic Initiatives: Vacant
Associate Director for Regulatory Counsel: **Scott McFarland**
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Deputy – Marianela Perez-Torres

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Director – Lea Carrington
Deputy – Takeesha Taylor-Bell

Division of Microbiology Devices (DMD)

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Deputy – Kristian Roth

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Deputy – Donna Roscoe

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Director – David Lee
Deputy – Preetham Sudhaker

Division of Program Operations and Management (DPOM)

Director – Rob Sauer
Deputy – Vacant

Division of Radiological Health (DRH)

Director – Thalia Mills
Deputy – Michael O'Hara
Deputy – LCDR David Dar (Acting)

We're Constantly Working on COVID Testing Options

FDA continues to work with test developers to make more coronavirus tests available to more people

Increasing Access and Ensuring Reliability of COVID-19 Tests – Now and In the Future

1. U.S. government should invest in the development of truly novel technologies that can be used at POC and at home and for multiple conditions

2. Government should be equipped to independently evaluate the ability of non-laboratorian providers and consumers to use and interpret POC and at-home tests to facilitate validation of and assure confidence in the usability of these products

3. Investing in POC and at-home testing technologies now will allow rapid expansion of national testing capacity and patient access when a new public health threat emerges

4. Widely available FDA-approved POC and at-home tests could create a wealth of data, if complemented by the development of robust telehealth and application-based technologies with appropriate privacy protections

5. To shift the testing landscape, it will also be important to explore and create mechanisms that will allow for reimbursement for prescription at-home tests, over-the-counter tests, pooled testing, and screening tests

* “Bending The Arc Of COVID-19 Test Development To Increase Access And Ensure Reliability—Now And In The Future, " Health Affairs Blog, March 22, 2021. DOI: 10.1377/hblog20210318.9094

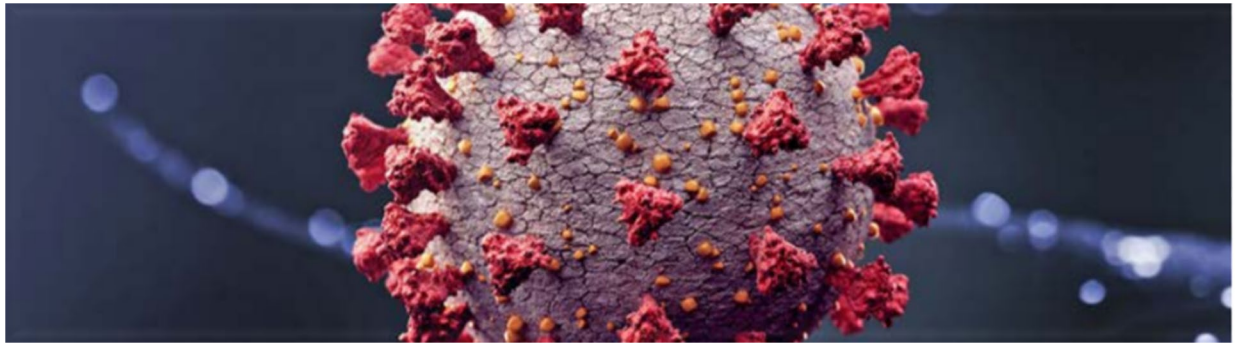
FDA Authorizes Additional OTC Antigen Tests and Provides Updated OTC Antigen Templates

- Including authorizations for use by people with COVID-19 symptoms as a single test
  - Flowflex COVID-19 Antigen Home Test
  - Celltrion Diatrust COVID-19 Ag Home Test
  - Quidel QuickVue At-Home OTC COVID-19 Test
- OTC antigen tests may also be authorized for people with or without symptoms for serial testing based on the same symptomatic validation data

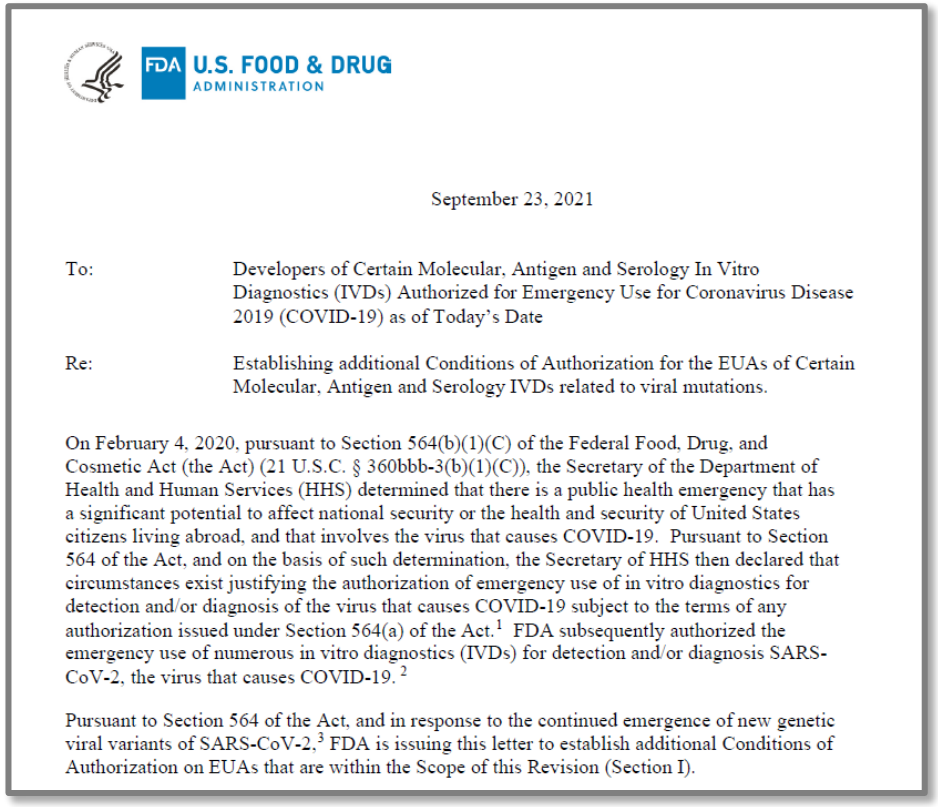
Coronavirus (COVID-19) Update: FDA Authorizes Additional OTC Home Test to Increase Access to Rapid Testing for Consumers

Updated EUA templates include flexible study recommendations about how to demonstrate that different types and ages of consumers can use OTC antigen tests appropriately

EUA Revision Concerning Viral Mutations



- In response to the continued emergence of new variants of SARS-CoV-2:
  - FDA revised the EUAs of molecular, antigen, and serology tests to establish additional Conditions of Authorization
  - Test developers are required to update their authorized labeling and evaluate the impact of SARS-CoV-2 viral mutations on their test's performance as outlined in the letter



U.S. FOOD & DRUG ADMINISTRATION

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.

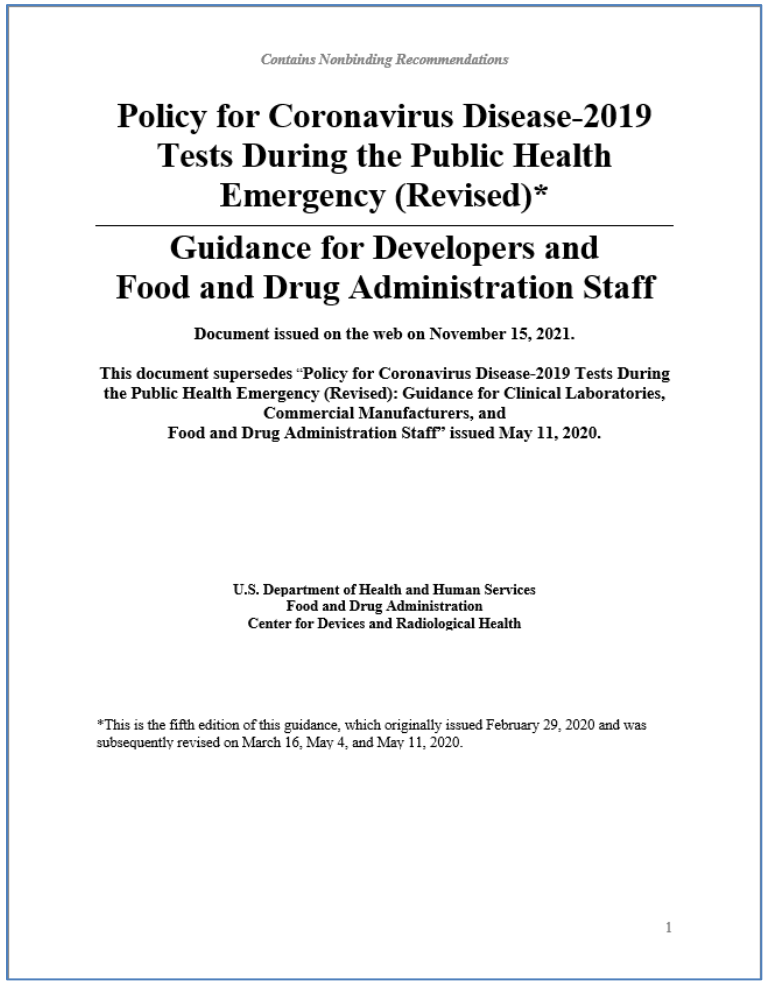
On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect 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).

Viral Mutation Revision Letter – September 23, 2021

SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests

Policy for Coronavirus Disease-2019 Tests Update: Notifications and EUA Priorities



Contains Nonbinding Recommendations

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.

1

- Notification policy has ended
  - Currently notified tests should confirm they are still seeking authorization
  - Notified tests can continue to be offered until they receive an EUA decision
- EUA priorities:
  - At-home and point-of-care (POC) diagnostic tests for use with or without a prescription and that can be manufactured in high volumes;
  - Certain high-volume, lab-based molecular diagnostic tests (and home collection kits for use with such tests) that expand testing capacity or accessibility such as through pooling of specimens to increase throughput, testing specimens collected at home and shipped to the lab, screening asymptomatic individuals or detecting multiple different respiratory viruses at once;
  - Certain lab-based and POC high volume antibody tests that can measure the amount of antibodies (fully quantitative antibody tests) or the amount of neutralizing antibodies; and
  - Tests for which the request is from, or supported by, a U.S. government stakeholder
  - EUA prioritization flowcharts are available in the revised guidance

HHS Statement on Laboratory Developed Tests

FOR IMMEDIATE RELEASE
November 15, 2021

Contact: HHS Press Office
202-690-6343
media@hhs.gov

Statement by HHS Secretary Xavier Becerra on Withdrawal of HHS Policy on Laboratory-Developed Tests

The U.S. Department of Health and Human Services and the Food and Drug Administration are committed to helping ensure that COVID-19 tests are accurate, reliable, and available. Today, as part of that commitment, HHS is withdrawing a policy established during the previous administration that limited FDA's ability to address certain problematic COVID-19 tests.

The policy, first announced on August 19, 2020, related specifically to "laboratory developed tests" (LDTs). An LDT is a type of test that is generally designed, manufactured, and used in a single laboratory. The policy directed FDA not to require premarket review for LDTs, including premarket approval (PMA) or clearance (510(k)), and emergency use authorization (EUA), even in situations where they have poor performance.

By withdrawing the policy, HHS is helping to ensure that COVID-19 tests work as intended. Effective today, HHS no longer has a policy on LDTs that is separate from FDA's longstanding approach in this area.

Today, FDA also updated its policies for COVID-19 tests, including COVID-19 LDTs. These policies take into account the importance of test availability, reliability, and accuracy.

To read the FDA press release, please visit: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-updates-test-policies-help-ensure-accuracy-and-reliability-tests-and

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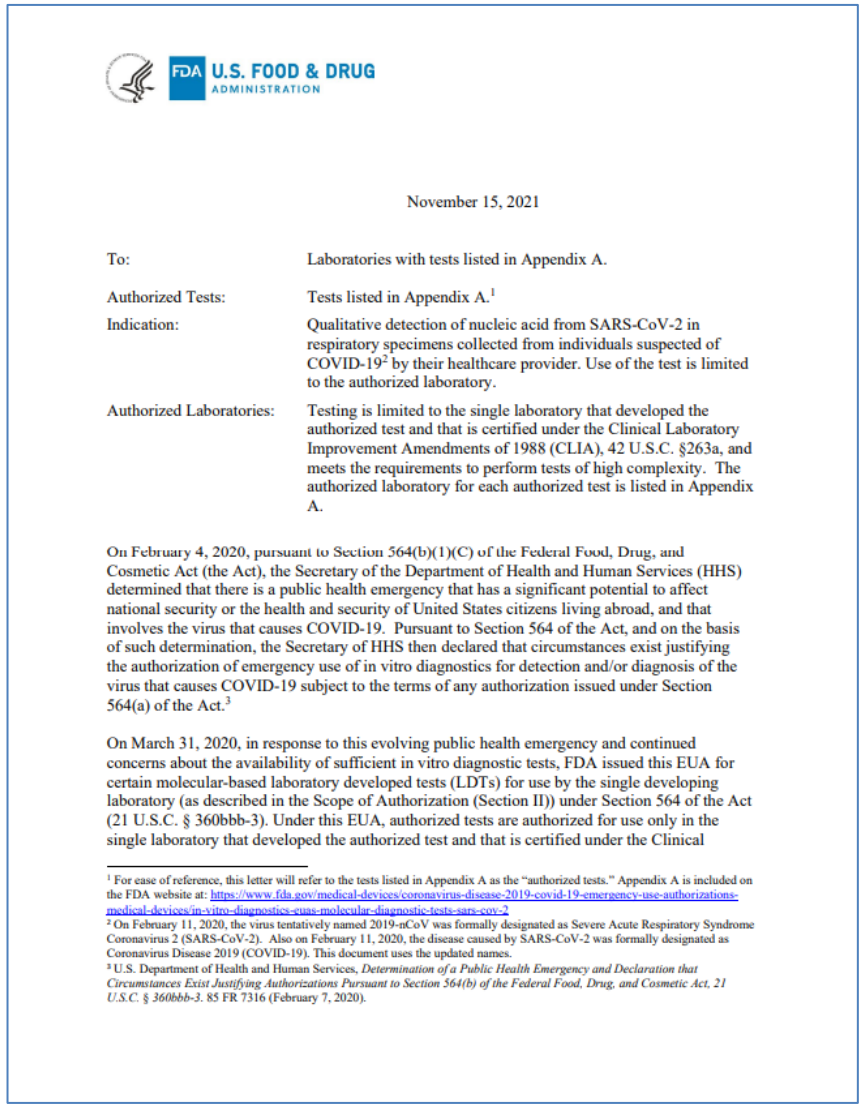
"Effective today, HHS no longer has a policy on LDTs that is separate from FDA's longstanding approach in this area."

New Umbrella EUA for Laboratories with Tests for Serial Testing Programs

- FDA issued an umbrella EUA for serial testing with certain molecular diagnostic tests developed by laboratories.
- These tests will be able to be used for testing at regular intervals as part of serial testing programs, such as those established at places like schools, workplaces or community groups.
- The umbrella EUA efficiently authorizes certain tests to help increase access to accurate and reliable molecular diagnostic tests.



U.S. FOOD & DRUG ADMINISTRATION

November 15, 2021

To:	Laboratories with tests listed in Appendix A.
Authorized Tests:	Tests listed in Appendix A.[1]
Indication:	Qualitative detection of nucleic acid from SARS-CoV-2 in respiratory specimens collected from individuals suspected of COVID-19[2] by their healthcare provider. Use of the test is limited to the authorized laboratory.
Authorized Laboratories:	Testing is limited to the single laboratory that developed the authorized test and that is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, and meets the requirements to perform tests of high complexity. The authorized laboratory for each authorized test is listed in Appendix A.

On February 4, 2020, pursuant to Section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act), 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.[3]

On March 31, 2020, in response to this evolving public health emergency and continued concerns about the availability of sufficient in vitro diagnostic tests, FDA issued this EUA for certain molecular-based laboratory developed tests (LDTs) for use by the single developing laboratory (as described in the Scope of Authorization (Section II)) under Section 564 of the Act (21 U.S.C. § 360bbb-3). Under this EUA, authorized tests are authorized for use only in the single laboratory that developed the authorized test and that is certified under the Clinical

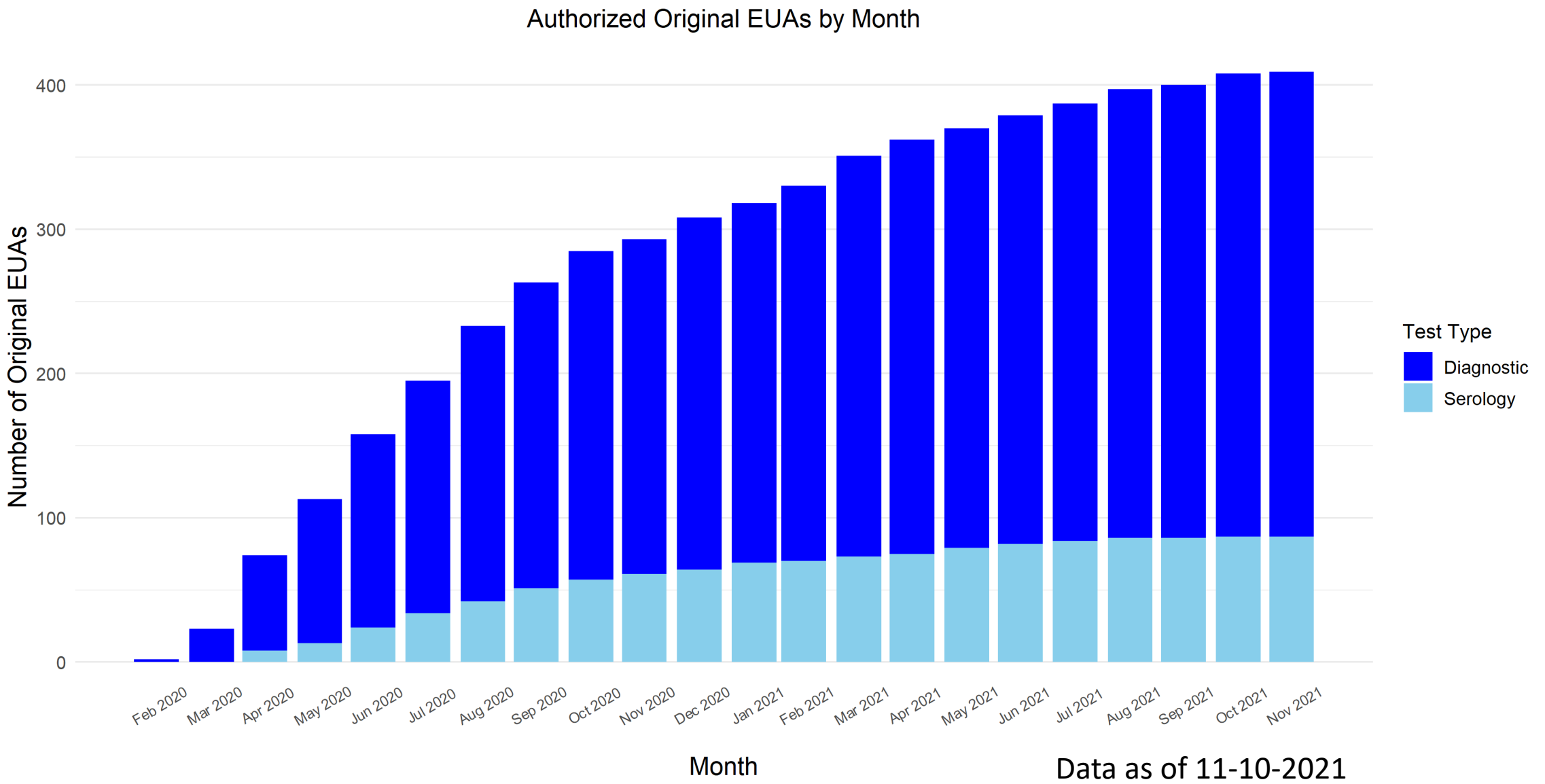
[1] For ease of reference, this letter will refer to the tests listed in Appendix A as the "authorized tests." Appendix A is included on the FDA website at: https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-molecular-diagnostic-tests-sars-cov-2

[2] On February 11, 2020, the virus tentatively named 2019-nCoV was formally designated as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Also on February 11, 2020, the disease caused by SARS-CoV-2 was formally designated as Coronavirus Disease 2019 (COVID-19). This document uses the updated names.

[3] 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).


"In addition to vaccination efforts, testing remains a cornerstone of the national response to the pandemic and plays a central role in helping Americans get back to work, school and other important activities. The FDA remains committed to helping to increase the availability of tests that will have the biggest impact on the nation's ongoing COVID-19 testing needs."
—Jeff Shuren, M.D., J.D.
Director, Center for Devices and Radiological Health
FDA

EUA Authorizations



Data as of 11-10-2021

Tests Authorized as of November 16, 2021

293

Molecular diagnostic tests

- 32 Pooling
- 50 Asymptomatic single use screening
- 9 Serial screening
- 20 Multi-analyte (i.e., SARS-CoV-2 + Influenza)
- 17 Point-of-care
- 66 Home collection
  - 13 Direct-to-consumer
  - 3 Multi-analyte
  - 14 Saliva home collection
- 17 Standalone home collection kits
- 3 Standalone saliva collection devices
- 1 Prescription at-home test
- 3 Over-the-counter at-home test

39

Antigen diagnostic tests

- 33 Point-of-care
- 3 Prescription at-home tests
- 10 Over-the-counter (OTC) at-home tests
- 19 Serial Screening
- 3 Multi-Analyte

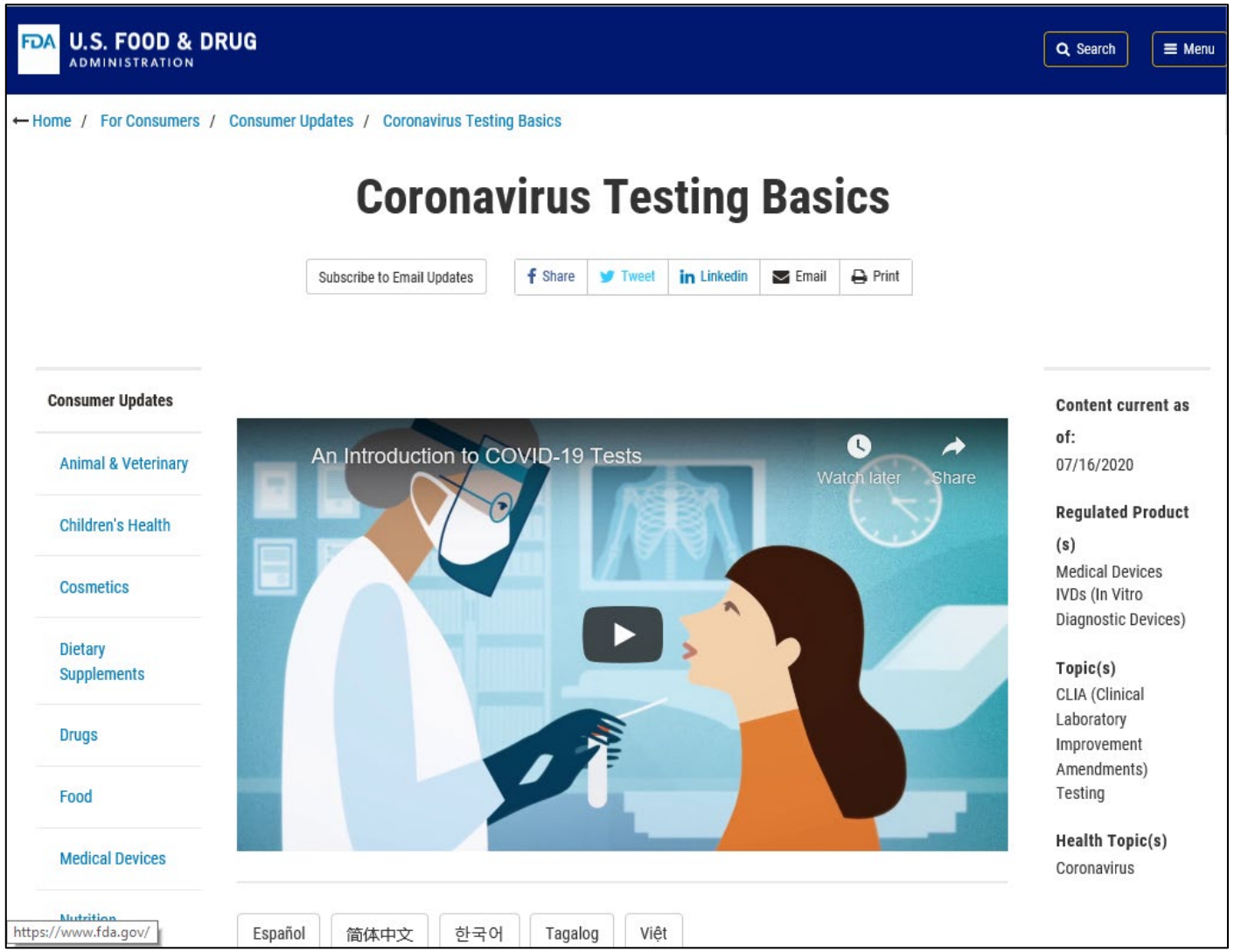
90

Serology and other immune response tests

- 13 Point-of-care
- 2 Neutralizing antibody tests
- 19 Semi-quantitative
- 1 Quantitative
- 1 Home Collection

The FDA has also authorized 685 revisions to test EUA authorizations.

Outreach



- 72 Virtual Town Halls (>49,000 participants)
- FAQs on Testing for SARS-CoV-2
- Safety Communications
- Resources for Patients, Healthcare Providers, and Developers
- COVID-19 Diagnostics Mailbox (185,000+ inquiries)
- 2 stakeholder calls to discuss the guidance/policy
- 1 virtual town hall to discuss 3D Swabs

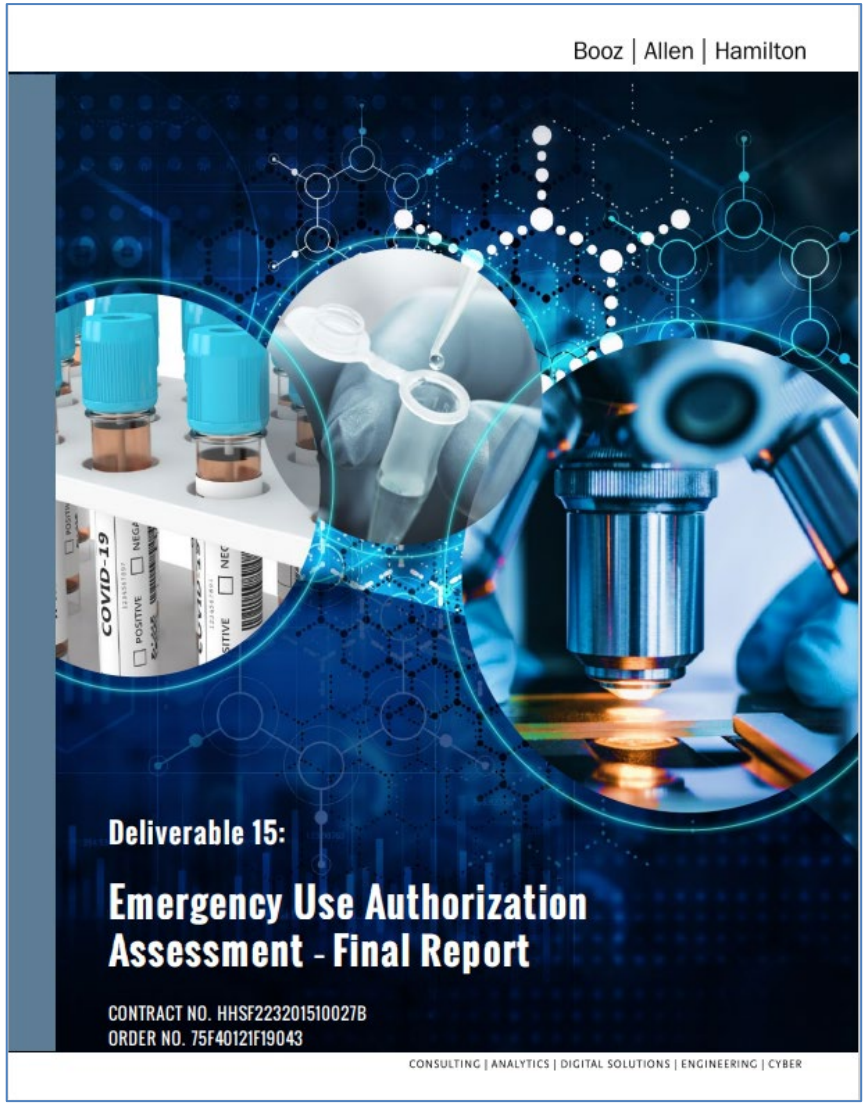
The 510(k) Pathway is Available for Molecular COVID-19 Tests

BioFire Respiratory Panel 2.1 (RP2.1), which had an Emergency Use Authorization (EUA), was granted marketing authorization using the De Novo premarket review pathway, a regulatory pathway for low- to moderate-risk devices of a new type.

- With granting of the De Novo, the FDA also revoked the EUA for this device
- This EUA revocation and De Novo authorization do not impact the availability other tests under EUA
- Other manufacturers may apply for 510(k) clearance under Product Code QOF (Multi-target respiratory specimen nucleic acid test including sars-cov-2 and other microbial agents)
- First 510(k) cleared on November 1, 2021 for the BioFire COVID-19 Test 2

https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-first-sars-cov-2-diagnostic-test-using-traditional-premarket-review-process

Independent Evaluation of FDA's EUA Response: Testing



https://www.fda.gov/media/152992/download)

- Assessment Objectives
  - Evaluate how the Agency prioritized the processing of EUA requests
  - Evaluate review times
  - Report on the accuracy and reliability of diagnostic tests
  - Evaluate how the Agency's response to EUAs for COVID-19 tests compares to prior PHEs
  - Evaluate EUA requestor perspectives
- Evaluation through Spring 2021

Independent Evaluation: Best Practices

	Focus Area
Best Practices	• Rapid updates to guidance and policy regarding different test types and developers, allowing CDRH to strike a balance between urgent need for tests and assurance of test performance • Use of publicly available templates to provide guidance on the EUA requests and continue to gather feedback from • stakeholders on the templates • Factors to prioritize submission review, including test capacity, accessibility, novelty, and supply chain considerations, • to focus review resources on the most impactful requests • Development and required use of a reference panel for assurance of performance • Collaboration on validation and performance testing; generation and evaluation of RWD; and supply chain monitoring • Hosting Town Halls to communicate interactively and frequently • Electronic submission to facilitate the process for EUA requestors

Table 4-1. Best Practices Identified by Booz Allen to Support the EUA Process
https://www.fda.gov/media/152992/download

Independent Evaluation: FDA Agrees with Priority Recommendations

Consider ways to optimize the IT system to account for EUA processes
"Fully automate submission and tracking of EUA requests (e.g., linking Pre-EUA to EUA; lags while awaiting additional information from requestors; lags due to backlog or priority designation) to provide more comprehensive picture of review time from EUA submission to decision for review efficiency, performance monitoring, prioritization, process improvements, and workload management"

Consider developing a systematic approach (that is, a strategy and plan) for allocation and tracking of staff during public health emergencies (PHEs)
"Quick determination of staffing needs and deployment of the right staff to the right place at the right time to maximize review efficiency. Identification of most likely areas for future PHEs (e.g., emerging infectious diseases) and development of process for cross-training to prepare a subset of staff in those areas in the event of a PHE"

Consider developing a framework for how to conduct validation of diagnostic tests for emerging pathogens in the setting of a declared PHE
"[This should result in] Earlier access to accurate and reliable diagnostic tests"

Priority Recommendations and Intended Impact from Table 4-2
https://www.fda.gov/media/152992/download

Collaborative Communities: Addressing Health Care Challenges Together

A collaborative community is a continuing forum in which private- and public-sector members, which can include the FDA, work together on medical device challenges to achieve common objectives and outcomes

Collaborative Communities with CDRH Participation

- Collaborative Community on Ophthalmic Imaging
- National Evaluation System for health Technology Coordinating Center (NESTcc) Collaborative Community
- Standardizing Laboratory Practices in Pharmacogenomics Initiative (STRIPE) Collaborative Community
- International Liquid Biopsy Standardization Alliance (ILSA)
- Xavier Artificial Intelligence (AI) World Consortium
- Case for Quality Collaborative Community
- Heart Valve Collaboratory (HVC)
- Wound Care Collaborative Community
- Pathology Innovation Collaborative Community (PICC)
- RESCUE (REducing SuiCide Rates Amongst IndividUals with DiabEtes) Collaborative Community)
- MedTech Color Collaborative Community
- Digital Health Measurement Collaborative Community (DATAcc)

International Liquid Biopsy Standardization Alliance (ILSA)

Members/Stakeholders:

- Public and private sector - representing academia, industry, government, patients, end users
- International representation - US, UK, EU, Japan

A number of non-profit efforts and consortia, dialogue with the FDA and EMA

Measurement of different cancer biomarkers in blood key to fully realize benefits of precision medicine as a safe alternative to traditional invasive tumor biopsies – can be used to help find cancer at an early stage, help plan treatment, find out how well treatment is working or if cancer has come back.

Updates for ILSA Collaborative Community

- August 2020 - FDA joined
- **ILSA landing page** created at https://fnih.org/our-programs/biomarkers-consortium/programs/ilsa and shared language used across ILSA members' websites
- **The ILSA White Paper** published in Critical Reviews in Oncology/Hematology Volume 156, December 2020, 103112; titled "International liquid biopsy standardization alliance white paper“
- **ILSA public webinar** “International Liquid Biopsy Standardization Alliance (ILSA) Collaborative Community Public Webinar” held on June 17, 2021, with over 1000 participants over the course of the meeting
- ISLB Liquid Biopsy Congress October 22, 2021 (virtual, free), with ILSA participation
- ILSA to provide a plenary presentation at the 6th Liquid Biopsy for Precision Oncology Summit in San Diego, February 9, 2022, to discuss our international efforts in standardization and best practices

Challenges and Solutions to Workload Impact: IVDs

A Year Into the Pandemic: How the FDA's Center for Devices and Radiological Health is Prioritizing its Workload and Looking Ahead

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- Staff and managers from every division of OHT7/OIR have been directly involved in the COVID-19 response
- Review timelines were impacted for non-COVID IVD submissions due to reallocation of review resources
  - Paused submissions have resumed active review as of June 10, 2021, under extended review timelines
  - Review of IVD Pre-Submissions remains suspended in 2021 unless they fall into one of four categories:
    - COVID-19 related
    - Companion Diagnostics
    - Breakthrough Designation Request
    - Significant Public Health Impact
- Expect to implement a phased approach to standard review times starting in early CY 2022

https://www.fda.gov/news-events/fda-voices/year-pandemic-how-fdas-center-devices-and-radiological-health-prioritizing-its-workload-and-looking

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Thank You