Life Sciences

Emergency Use Authorization for COVID-19 Testing

When a new virus like SARS-CoV-2 arises and causes widespread disease, death, and economic devastation as COVID-19, part of the public health threat is that testing for it doesn't yet exist. Emergency Use Authorization (EUA) from the U.S. Food and Drug Administration (FDA) allows for testing to be developed and authorized very rapidly, within weeks, compared with nonemergency pathways that can take months or years. With the public's health in danger, the FDA's program adjusts the regulatory requirements to facilitate the availability of diagnostic testing and to expand testing capabilities during the declared emergency.

An EUA is not an FDA approval and only applies for as long as the public health emergency is in effect. Additional data to prove safety and effectiveness are required for approval or clearance of the test in transition to full marketing status.

? How Does It Work?

Any entity seeking EUA is advised to speed development by direct advisement from the FDA via email to **CDRH-EUA-Templates@fda.hhs.gov**. For industry questions, companies can contact a hotline 1-888-INFO-FDA, choose option *, or email to **covid19dx@fda.hhs.gov**. Information is updated regularly on FDA websites, including **COVID-19 Diagnostics FAQ** and **EUAs granted**.

Under the EUA for In Vitro Diagnostic Device (IVD) test development, normally exhaustive studies are abbreviated, and simulated clinical samples and *in silico* cross-reactivity analysis are allowed. Since false results can have a broad public health impact during the emergency involving pandemic infectious disease, all clinical tests should be validated prior to use. To ensure analytical and clinical validity for COVID-19 diagnostic assays, the FDA has revised recommendations regarding the minimum testing that should be performed for EUA submissions of tests intended for the detection of SARS-CoV-2.

Depending on the "Indication" of the test, there are four pathways to accelerate the development and availability of testing for COVID-19 during the emergency. The FDA's **Policy for Diagnostic Tests for COVID-19** sets forth four FDA Policies and tests that can be developed and/or offered under the policies outlined in the following four sections:

IV. A	Policy for developing laboratory tests that **lead to an EUA submission.**
IV. B	Policy for developing laboratory tests that **will not lead to** an EUA submission when the state in which the lab resides takes responsibility for such testing.
IV. C	Policy for commercial manufacturers to more rapidly distribute their SARS-CoV-2 diagnostics after validation **while an EUA is being prepared** for submission to the FDA.
IV. D	Policy regarding the use of serological testing **without an EUA**. (This pathway allows developers to market their antibody-based tests without prior FDA review if certain conditions outlined in the guidance document are met).

How Long Is the Process?

It depends on which of the "policies" you decide to pursue and how your test performs. Considering the rapidly evolving conditions in the COVID-19 global pandemic, the number of companies with tests to propose ballooned in response to the crisis. FDA staff, while working with the applicants in interactive pre-EUA/EUA processes, need to ensure the best testing outcomes for the clinical need. While it isn't known how many EUAs will be authorized during this emergency, it is welcome news that testing is coming up to speed rapidly and that the overall process is faster for all applicants.

What is FDA's "EUA Template"?

FDA encourages Pre-EUA submission to ensure good quality tests. Test developers seeking EUA can contact the FDA by email to **CDRH-EUA-Templates@fda.hhs.gov**. The FDA has published two templates to guide the test validation and pre-EUA/EUA submissions.

- The **Accelerated EUA Template** is intended for laboratories certified to perform high-complexity testing under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).
- The **EUA Template for Manufacturers** includes the same clinical validation information but **also addresses information regarding manufacturing, distribution, and stability** for distributed kits.

Currently, the two templates are for molecular-based diagnostic testing that detects the presence of SARS-CoV-2 viral RNA. Products based on any other technology need a direct consultation with the FDA for development guidance.

How Many EUAs in COVID-19 Testing Have Been Granted By the FDA?

As of April 8, the FDA has granted 32 In Vitro Diagnostics EUAs, including 31 EUAs for molecular diagnostic tests and one EUA for serology "SARS-CoV-2 IgM/IgG rapid test." The FDA has also granted six EUAs to molecular-based laboratory-developed tests that are authorized for use by the singular developing laboratory that is certified under CLIA to perform high-complexity tests.

The FDA's **Policy for Diagnostic Tests for COVID-19** as updated on March 16, 2020, outlines a switch in the FDA's approach to EUAs and shows the FDA's flexibility and adaptability during times of public health emergencies. Some of the current EUA authorized commercial tests were launched or distributed prior to the EUA issuance, as set forth in Section IV. C of the FDA's COVID-19 policy.

In addition, the FDA has been notified by more than 145 laboratories that they have begun testing under the policies set forth in Section IV. A of the FDA COVID-19 policy. CLIA-certified laboratories can now manufacture key components such as primers and probes and begin using on patient samples after the tests are validated but before the EUA is submitted. The FDA "does not intend to object to the use" of validated tests for specimen testing for up to 15 business days after validation while the EUA request is being prepared.

What Are the Types of Molecular Tests and Serology Tests for COVID-19?

SARS-CoV-2 molecular diagnostic tests detect SARS-CoV-2 nucleic acids from human respiratory specimens such as Nasopharyngeal, Oropharyngeal, throat, or nasal swab. The reverse transcription polymerase chain reaction (RT-PCR) is used in most molecular tests. The nucleic acid amplification technologies employed by authorized tests include real-time RT-PCR, RT-digital PCR, and the isothermal amplification used by the EUA for a "rapid" molecular test.

SARS-CoV-2 serological tests are indicated for the qualitative detection of antibodies (e.g., IgM, IgG) against SARS-CoV-2 in blood-based clinical specimens such as serum, plasma, and whole blood. The technologies for serology testing include Lateral Flow Immunoassay-based "rapid" tests and Enzyme-linked Immunosorbent Assay.

Serology tests detect the body's immune response to the infection caused by the virus rather than detecting the virus itself. Currently, it is unknown for how long IgM or IgG antibodies may persist following infection and hence the tests should not be used as the sole basis to diagnose COVID-19. Serology tests can be useful in surveying the population exposure or informing vaccine development. Serology tests may soon play a significant role in the fight against COVID-19 by helping to identify individuals who have overcome an infection and have developed an immune response, whether they had developed COVID-19 symptoms or were asymptomatic.

Considerations for Marketing Diagnostic Tests Via EUA

Developers would be prudent to include the risk of rapid market changes when considering the EUA pathway for their SARS-CoV-2 or serological tests. Close communication with the FDA is crucial to managing that risk.

Development activities:

- Contact the FDA if clarification is needed on any point.
- Develop, manufacturer, and validate tests.
- Conduct stability studies.
- Develop instructions for use.
- Develop a procedure for complaint-handling and adverse event reporting.

Day 1 activities:

- Notify the FDA that your diagnostic test has been validated and you intend to begin distribution.
- Register your company.
- List the device.
- Begin distributing devices.

Activities that need to be completed within 15 days of distribution:

- Submit EUA application using the most logical template published at the time (we expect additional templates to be published on the FDA's EUA web page).

Ongoing activities:

- Work collaboratively with the FDA to address any concerns or safety considerations raised. (Note that this could include a recall of your product.)
- Update intended use statements based on EUA authorization.
- Continue real-time stability studies.
- Report all events of false positive and false negative results to the FDA.

Contacts

Marilyn Gatin, PhD, RAC
Associate Director
Life Sciences Regulatory,
Quality & Patient Safety
(317) 922-5750
Marilyn.Gatin@guidehouse.com

Min Yao, PhD, RAC
Associate Director
Life Sciences Regulatory,
Quality & Patient Safety
(213) 545-7804
min.yao@guidehouse.com

Dorothy Henckel, BS
Senior Consultant
Life Sciences Regulatory,
Quality & Patient Safety
(317) 272-5433
dorothy.henckel@guidehouse.com

Special thanks for key contribution by **Jane SC Tsai, PhD, FAACC, PMP**

linkedin.com/showcase/guidehouse-health

twitter.com/GuidehouseHC

guidehouse.com

About Guidehouse

Guidehouse is a leading global provider of consulting services to the public and commercial markets with broad capabilities in management, technology, and risk consulting. We help clients address their toughest challenges with a focus on markets and clients facing transformational change, technology-driven innovation and significant regulatory pressure. Across a range of advisory, consulting, outsourcing, and technology/analytics services, we help clients create scalable, innovative solutions that prepare them for future growth and success. Headquartered in Washington DC, the company has more than 7,000 professionals in more than 50 locations. Guidehouse is a Veritas Capital portfolio company, led by seasoned professionals with proven and diverse expertise in traditional and emerging technologies, markets, and agenda-setting issues driving national and global economies. For more information, please visit: www.guidehouse.com.

Guidehouse