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CLIENT ALERT: FDA Taking Overdue Steps to Accelerate COVID-19 Diagnostic Testing

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In response to the COVID-19 pandemic, and in light of the persistent shortage of diagnostic tests for the SARS-CoV-2 virus, the U.S. Food and Drug Administration (FDA) provided recent but overdue guidance on the use of its Emergency Use Authorization (EUA) authority and has taken additional steps to liberalize its oversight of clinical laboratory diagnostic testing tor the SARS-CoV-2 virus.

Under section 564 of the Federal Food, Drug, and Cosmetic Act (FFDCA, 21 U.S.C. 360bbb-3), the FDA may authorize "emergency use" of unapproved products or unapproved uses of approved products to diagnose, treat, or prevent serious or life-threatening diseases or conditions when there are no adequate, approved, and available alternatives. An Emergency Use Authorization (EUA) is possible only upon an emergency declaration or a threat justifying emergency authorized use, such as "heightened risk of attack with a biological, chemical, radiological, or nuclear agent or agents" or, in the present case, "a public health emergency… that involves a biological, chemical, radiological, or nuclear agent or agents."

Even without an emergency use declaration, FDA is authorized to approve expanded access of investigational drugs. FDA approves expanded access for a patient with an immediately life-threatening condition or serious disease or condition to gain access to an investigational medical product (drug, biologic, or medical device) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available. For example, FDA has granted over 250 patients expanded access to Gilead Science's investigational antiviral drug remdesivir.

Today, FDA also issued a new guidance implementing a policy to expand the availability and capability of non-invasive remote monitoring devices to facilitate patient monitoring while reducing patient and healthcare provider contact and exposure to COVID-19 during this pandemic.

COVID-19 Diagnostic Testing "Failing"

FDA's announcements are urgently needed to address the protracted nationwide shortages of SARS-CoV-2 diagnostic tests in the United States, which Dr. Tony Fauci, director of the National Institute of Allergy and Infectious Diseases at the U.S. National Institutes of Health (NIAID/NIH), conceded on March 12 was "a failing" of the Federal government.[1]

The ongoing shortage of tests is attributable at least in part to the U.S. Centers for Disease Control and Prevention (CDC) decision to forego use of molecular assays rapidly

[1] G. Kessler, What did Dr. Anthony Fauci say about coronavirus testing 'failing'? *Washington Post,* March 18, 2020.

developed abroad after the SARS-CoV-2 virus genome was published, and endorsed for use by the World Health Organization (WHO) as early as late January. Following Health and Human Services (HHS) Secretary Alex Azar's January 31 declaration of a public health emergency,[2] CDC's own real-time RT-polymerase chain reaction (rRT-PCR) test received an EUA from FDA on February 4, but manufacturing and quality problems with the test's negative control resulted in distribution of faulty tests to State and local health departments.[3]

FDA Issues, Then Revises Guidance for Clinical Laboratories

Despite the delays in distributing CDC's diagnostic tests to States and cities, the FDA took several weeks to issue its first policy change via a guidance document to permit clinical laboratories to conduct SARS-CoV-2 diagnostic tests on February 29. During this period, "[f]rom mid-January until February 28, *fewer than 4,000 tests* from the CDC were used out of more than 160,000 produced."[4] (italics added) It is unknown why, given its knowledge of the small numbers of tests being distributed by CDC and used in the field, FDA delayed so conspicuously in liberalizing its guidance to States and to private clinical laboratories, who operated under heightened regulatory uncertainty in the absence of clear and flexible guidance.

The FDA's first guidance, available here, newly allowed high complexity laboratories to conduct such tests while pursuing EUA authorization from the FDA for 15 days, which the Agency characterized as "a reasonable period of time" after validation and while preparing an EUA submission.[5]

On March 12 and in response to pressure from the State of New York, FDA issued a new policy statement of enforcement discretion that the Agency "was not objecting" to labs licensed by the State of New York to test patients for SARS-CoV-2 infection. The laboratories would provide validation data to New York, "in lieu of pursuing an EUA with FDA" and the State would monitor laboratory quality, terminating operations on the basis of any concerns.[6] (The FDA had previously issued an EUA to the State of New York for its RT-PCR SARS-CoV-2 panel on February 29.)

On the basis of this precedent, FDA issued a broader policy statement on March 16, significantly expanding the scope of liberalized testing possible for clinical laboratories nationwide to reflect the realities of the pandemic. Claiming the "ability to pivot and adapt as

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[2] HHS, Secretary Azar Declares Public Health Emergency for United States for 2019 Novel Coronavirus, January 31, 2020.

[3] According to CDC, "performance issues were identified related to a problem in the manufacturing of one of the reagents which led to laboratories not being able to verify the test performance." CDC, CDC Tests for COVID-19. See also, J. Cohen, "The United States badly bungled coronavirus testing—but things may soon improve," *Science*, February 28, 2020.

[4] P. Whoriskey and N. Satija, How U.S. coronavirus testing stalled: Flawed tests, red tape and resistance to using the millions of tests produced by the WHO, *Washington Post,* March 16, 2020.

[5] FDA, Policy for Diagnostics Testing in Laboratories Certified to Perform High-Complexity Testing under CLIA prior to Emergency Use Authorization for Coronavirus Disease-2019 during the Public Health Emergency, February 29, 2020; also, 85 FR 13169, March 6, 2020.

[6] FDA, FDA gives flexibility to New York State Department of Health, FDA issues Emergency Use Authorization diagnostic, March 13, 2020.

the situation warrants in light of a public health emergency",[7] FDA's policy statement "describes two policies for accelerating the development of certain laboratory tests for COVID-19 – one leading to an EUA submission to FDA, and the other not leading to an EUA submission" under which a State authority "takes responsibility for COVID-19 testing by laboratories in its State" using a test developed and validated "under the authorities of the State in which the lab resides."[8]

In sum, the first policy leading to an EUA submission to FDA is identical to that of the February 29 policy, while the second policy formally recognizes the urgent and practical steps already taken by New York in the absence of validated, FDA-authorized tests.

FDA also clarified for laboratories and providers conducting antibody tests that the Agency "recognizes that serology tests are less complex than molecular tests and are solely used to identify antibodies, which limits their effectiveness for diagnosis; however… the FDA does not intend to object to the distribution and use of serology tests to identify antibodies to SARS-CoV-2 where the test has been validated, notification is provided to the FDA, and warning statements are included with the tests."[9]

Testing on High Volume Platforms Authorized in Mid-March

On the same day as its announcement regarding the State of New York, FDA also reviewed and approved within 24 hours an EUA for Roche Molecular Systems of its SARS-CoV-2 test on a high-volume molecular diagnostic platform-- "the first commercially distributed diagnostic test to receive an EUA during the COVID-19 outbreak."[10] The next day, a similar EUA was issued to Thermo Fisher for the "second commercially distributed" COVID-19 diagnostic test, and EUAs were issued to Hologic and LabCorp on March 16. [11] An updated list of SARS-CoV-2 diagnostic EUAs is maintained by the FDA.

Next Steps with FDA

Diagnostic sponsors, clinical laboratories and States now have two FDA-sanctioned policies under which to develop, validate, and distribute COVID-19 diagnostic tests – the EUA pathway and a State-based regulatory model. On March 16, FDA Commissioner Hahn stated that "more than 100 test developers have sought FDA guidance … [on] the EUA process.

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[7] FDA, FDA Provides More Regulatory Relief During Outbreak, Continues to Help Expedite Availability of Diagnostics, March 16, 2020.
[8] FDA, Policy for Diagnostic Tests for Coronavirus Disease-2019 during the Public Health Emergency, March 16, 2020.
[9] See infra, FDA, Regulatory Relief, March 16, 2020.
[10] See infra, FDA, March 13, 2020.
[11] FDA, FDA Issues Emergency Use Authorization to Thermo Fisher, March 13, 2020; FDA Issues Diagnostic Emergency Use Authorization to Hologic and LabCorp, March 16, 2020.

Additionally, more than 80 laboratories have notified us that they are testing or intend to begin testing soon under our new policy."[12]

For companies, laboratories, and investigators interested in helping to address the pandemic, the FDA provides information on how to submit a pre-EUA application for SARS-CoV-2 diagnostic tests.[13] A pre-EUA template is available, which sponsors should complete and include:

- A detailed description of your IVD (target pathogen, device technology- assay based on molecular, antigen or antibody detection, etc.);
- The proposed intended use;
- Summary of any analytical (LoD, inclusivity, exclusivity, Interfering substances, Hook effect, etc.) and clinical data collected for this device to date; and
- Summary of any analytical or clinical studies planned but not yet started.

FDA also maintains a toll-free number, 1-888-INFO-FDA, to respond to laboratory or sponsor questions about the EUA application process.

Despite substantial delays in the Federal regulatory response to the urgent public health need for widespread, reliable diagnostic testing during the COVID-19 pandemic, the recent changes in FDA policy will hopefully help produce "more rapid testing capacity in the U.S.", in the words of Commissioner Hahn.

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[12] See infra, FDA, Regulatory Relief, March 16, 2020.

[13] FDA, How to Submit a Pre-EUA for In vitro Diagnostics to FDA, accessed March 20, 2020.