HHS Reverses Course on LDTs: COVID-19 LDTs Again Require FDA Premarket Review

USA | December 3 2021

On November 15, 2021, the U.S. Department of Health and Human Services ("HHS") and the Food and Drug Administration ("FDA") issued several policy changes governing the regulation of Laboratory Developed Tests ("LDTs"). These changes resume FDA premarket review of COVID-19 LDTs that HHS halted in August 2020 based on a novel statutory interpretation that FDA lacked legal authority to require premarket review of any LDTs absent notice-and-comment rulemaking. Developers of COVID-19 LDTs that do not yet have FDA Emergency Use Authorization ("EUA") need to be aware of these changes and consider what actions to take in response.

HHS Statement Reversing Prior Administration's LDT Policy

As outlined in a previous Ropes & Gray Alert, on August 19, 2020 HHS published a brief statement on its website explaining that FDA would not require premarket review of LDTs, absent notice-and-comment rulemaking. The announcement reflected a substantial policy reversal both in the COVID-19 context and more generally. Although FDA historically had not enforced premarket review requirements for most LDTs, it had long held the view that it had the legal authority to do so. Further, the agency had previously articulated its view that, in a public health emergency, it was particularly important for FDA to review information related to an LDT's design, validation, and performance characteristics.[1] Thus, in the first iteration of its Policy for COVID-19 Tests During the Public Health Emergency (the "COVID-19 Test Policy") published in February 2020, FDA explained that it would not object to a CLIA-certified high-complexity laboratory offering a COVID-19 LDT after successfully validating its test and notifying FDA, but only if the laboratory submitted an EUA request to FDA within 15 days of such notification.

The August 2020 HHS announcement reversed this FDA position. This reversal was based on an HHS Office of General Counsel legal memorandum, dated June 22, 2020, that asserted that LDTs are not subject to the premarket review provisions in the Food, Drug, and Cosmetic Act ("FDCA") because such provisions are triggered by "commercial distribution" of a medical device and LDTs are a "service" rather than a commercially distributed "good." The memorandum also argued that FDA's past pronouncements that LDTs are regulated medical devices constituted legislative rules issued without notice-and-comment rulemaking and were, therefore, inconsistent with the Administrative Procedure Act. Finally, the memorandum asserted that LDTs offered by laboratories in state universities or public health departments are not subject to the premarket review and certain enforcement provisions of the FDCA that only apply to "persons," because such laboratories do not meet the FDCA's definition of a "person."

On November 15, 2021, HHS issued a statement withdrawing the August 2020 announcement, stating that "HHS no longer has a policy on LDTs that is separate from FDA's longstanding approach in this area." When read in conjunction with the COVID-19 Test Policy, this means that HHS and FDA once again expect developers of COVID-19 LDTs to seek FDA marketing authorization and otherwise comply with FDA device regulations when marketing their tests. LDTs for non-COVID-19 uses are subject to FDA's historical posture of enforcement discretion toward such tests.

FDA's Revised COVID-19 Test Policy

In tandem with the November 2021 HHS statement described above, FDA issued a revised version of its COVID-19 Test Policy, which includes the following changes relevant to LDTs:

Offering Tests Prior to EUA: Previously, as noted above, FDA did not object to a CLIA-certified high-complexity laboratory validating and offering a test provided that it notified FDA of its intent to offer the test and submitted an EUA to FDA within 15 days of the notification. Under the current guidance document, FDA will not continue this policy and has, instead, articulated two new policies for currently unauthorized tests:[2]

- If a test is being offered without an EUA pursuant to FDA's previous notification policies, such tests can continue to be offered if either (1) the laboratory submitted an EUA request after February 1, 2021; or (2) the laboratory submitted an EUA request before February 1, 2021, and the developer confirms to FDA within 45 calendar days from issuance of the guidance that it (a) wants FDA to continue review of the EUA, (b) the EUA is for the current version of the test, and (c) the developer has no new data to add to the submission or new data is submitted within the 45-day period.
- For an LDT that is currently marketed and for which an EUA has not previously been submitted, FDA does not intend to object to continued offering of the test while the laboratory prepares and FDA reviews an EUA request, provided that the laboratory submits the EUA request to FDA within 60 calendar days from issuance of the guidance.
    - If no EUA is submitted within 60 calendar days, FDA generally expects laboratories to cease marketing and offering their tests within that 60-day period. However, if a laboratory that is not able to prepare and submit an EUA within 60 days believes that the continued availability of the test is of significant public health importance, it can provide FDA its rationale, including the continued public health need and reasons why additional time is needed to submit the EUA request.
    - In making an EUA submission, laboratories can use FDA's previously published EUA templates or they can submit an email to FDA with less formal format or substance recommendations, including providing copies of existing validation test reports and data files.
    - If insufficient information is submitted with the EUA submission, FDA may contact the laboratory to request more information. If FDA notifies a laboratory that it will not authorize its LDT, whether due to a lack of adequate data to support authorization or for other reasons, FDA expects the laboratory to cease marketing and offering the test within 15 calendar days of receiving such notification.

Importantly, neither of the policies outlined above applies to at-home tests, home collection, or testing conducted outside a CLIA-certified high-complexity environment. Thus, test offerings that incorporate "home collection" of specimens are not subject to a grace period during which they may be marketed while an EUA is being prepared or is under FDA review. The phrase "home collection" in this context generally refers to specimens that are self-

collected without healthcare practitioner (HCP) supervision, although in some cases it can apply to specimens that are self-collected outside a healthcare setting with HCP supervision via telehealth, meaning that a test incorporating telehealth-proctored specimen collection would not be subject to the 60-day grace period.

Review Priorities: Sets forth FDA's review priorities for new EUA submissions, which focus on tests with the following characteristics: point of care, at-home testing or specimen collection, high throughput, pooling capabilities, screening indication, ability quickly to scale capacity, or support or submission by a U.S. government stakeholder.

State Authorization: FDA will continue to exercise enforcement discretion with respect to LDTs authorized by states or territories that previously notified FDA that they would take responsibility for review of COVID-19 LDTs, but FDA will not permit additional states to establish their own LDT review and authorization pathway. The list of states and territories that previously notified FDA that they will take responsibility for review of COVID-19 LDTs includes Puerto Rico, Colorado, Connecticut, Maryland, Mississippi, Nevada, New Jersey, New York, and Washington (state).

Test Modifications: When a CLIA-certified high-complexity lab modifies a test, including when it is not the developer of the original EUA-authorized test, FDA does not intend to object to implementation of such test without notification to FDA or a new or amended EUA, where the lab has validated the modification and confirmed performance is equivalent to the authorized test, and use of the test is limited to the lab in which the modification was made.

Medical Device Reporting (MDR): Developers offering tests prior to authorization are expected to comply with applicable FDA MDR requirements.

Umbrella EUA for Certain PCR LDTs

In addition to the revised COVID-19 Test Policy, FDA issued a new "Umbrella EUA" for certain RT-PCR molecular-based tests intended to detect SARS-CoV-2 from nasal specimens as part of a serial testing program. An LDT that meets the requirements laid out in the Umbrella EUA is deemed to be authorized under the Umbrella EUA and, therefore, does not need a separate EUA.

To fall within the Umbrella EUA, a test must be:

- a qualitative test for detection of nucleic acid from SARS-CoV-2 in individual or pooled anterior nasal respiratory specimens;
- intended for use as part of a serial testing program in which asymptomatic or symptomatic individuals are tested at least once per week;
- designed, manufactured, and used within a single CLIA-certified high-complexity laboratory;
- for detecting only SARS-CoV-2; and
- validated in accordance with various appendices to the Umbrella EUA.

The validation requirements for a given test to fall under the Umbrella EUA vary based on the test's indications for use. Options for such indications include whether the test is intended for individual specimen testing or various types of pooled testing and whether it is intended for use with specimens collected by a healthcare practitioner ("HCP"),

self-collected under HCP observation, or self-collected "at home" (i.e., without HCP observation) using an authorized home collection kit. The Umbrella EUA also establishes additional technical and other requirements for a test to be covered by the EUA, including that the test must be for prescription (Rx) use only, detect two or more viral targets on the SARS-CoV-2 genome, and include a chemical lysis step followed by a nucleic acid isolation step.

After validating the LDT according to the FDA-specified criteria, laboratories submit the data and other information in a "notification" to FDA. Once FDA has determined that a complete notification has been submitted, but prior to FDA's review of the validation data, FDA will notify the developer that the test been added to a public "Exhibit." A test is considered authorized once it has met the eligibility criteria in the Umbrella EUA, even if FDA has not yet reviewed the validation data. If, after review, FDA determines that a test listed on the Exhibit does not meet one or more of the eligibility criteria, it will remove the test from the Exhibit, and the test will no longer be considered authorized under the Umbrella EUA.

Takeaways for Clinical Laboratories

FDA's authority to regulate LDTs has been a complex and controversial topic for years. If the government were to seek to enforce premarket review requirements as articulated in the COVID-19 Testing Policy, it would have to contend with HHS's 180-degree policy changes during the COVID-19 pandemic as well as the legal issues raised by the HHS OGC in the June 22, 2020 memorandum detailed above. Nevertheless, we expect in general that laboratories offering currently unauthorized COVID-19 LDTs would want to pursue one of the available EUA pathways rather than face the costs and legal risks associated with FDA enforcement action.

Laboratories offering currently unauthorized LDTs for COVID-19 should therefore evaluate FDA's COVID-19 Testing Policy to determine the EUA notification or submission pathways and timelines applicable to their tests. Laboratories should consider whether submission of an individual EUA in accordance with one of FDA's templates, making a streamlined submission as contemplated by the COVID-19 Testing Policy, or using the Umbrella EUA offers the optimal path to authorization based on the desired indications and available data.

Ropes & Gray LLP - Beth P. Weinman, Gregory H. Levine, David Peloquin and Steven J. Gonzalez