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A Sea Change Looms as FDA Finalizes Its Controversial Regulation Asserting Jurisdiction Over LDTs

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On April 29, 2024, after years of false starts trying to expand oversight of laboratory developed tests ("LDTs") through administrative and legislative actions, FDA announced the much-anticipated—and highly controversial—final rule, Medical Devices; Laboratory Developed Tests. The rule asserts jurisdiction over LDTs more formally than ever before, outlining the agency's new oversight approach to the regulation of LDTs as well as providing a roadmap that directs how and when labs will need to come into compliance. The new oversight approach also includes several limited enforcement discretion policies intended to reduce the rule's impact and burden on the clinical community.

Although the rule will almost certainly be litigated (and likely in the absence of *Chevron* deference to bolster the agency's chances[1]) since it is a game changer for an entire industry, labs should familiarize themselves with its nuances and plan for the rule's potentially broad impact on existing compliance programs. We unpack the events leading up to the rule, analyze the major components of FDA's new enforcement approach, and discuss outstanding controversies and likely next steps below.

Background

FDA considers LDTs to be a type of in vitro diagnostic ("IVD") test. IVDs regulated by FDA include tests performed on samples such as blood or tissue that have been taken from the human body for clinical use (e.g., to diagnose a disease or other condition).[2] LDTs are a category of tests that are intended for clinical use and are designed, manufactured, and used within a single laboratory that is certified under the Clinical Laboratory Improvements Act ("CLIA") to perform high-complexity testing. FDA considers LDTs to be medical devices under the FD&C Act, but the agency has historically relied on a broad enforcement discretion approach to regulation under which the medical device regulatory scheme has not been applied to LDTs. In other words, although FDA has always *said* that it had jurisdiction over LDTs, it has never actually *asserted* such jurisdiction except during declared public health emergencies.

Since the late 1990s, several efforts by FDA and Congress to provide greater regulatory oversight of LDTs have failed. In 2006 and 2014, for instance, FDA attempted to end its enforcement discretion policy through the agency's guidance process—neither of these attempts resulted in any policy changes.[3] Similarly, Congress has undertaken several efforts to pass legislation that would apply a new framework to the oversight of LDTs, the most significant of which is the recent VALID Act.[4]

When Congress failed to pass such legislation in 2022, FDA signaled its intention to pursue rulemaking to achieve its oversight goals,[5] and in October of last year, FDA released its controversial proposed rule. That proposal included only a single line of regulatory text asserting jurisdiction over LDTs but also included a lengthy preamble that outlined FDA's proposed enforcement approach to LDTs. That new approach would be phased in through four stages over a five-year period. The preamble also included FDA's rationale for ending its historic enforcement discretion policies and asserted legal bases for the rule.[6]

The proposed rule was met with much criticism, including arguments that, if finalized, the rule would impose substantial regulatory burdens and costs on labs as well as undermine innovation and access to diagnostic tests. Opponents also argued that FDA lacks jurisdiction over LDTs because LDTs fall outside the scope of the definition of "Device" in the FD&C Act.[7] Specifically, Commenters asserted that "Device" only comprises physical objects, contending that LDTs are not physical objects but are instead healthcare services that rely on tools and devices to facilitate treatment decisions by healthcare professionals.[8] Furthermore, commenters explained that healthcare providers offering these services are exempt from basic requirements of the FD&C Act.[9] Notwithstanding these criticisms (and others), FDA released the text of the final rule this week and the rule is officially scheduled for publication on May 6, 2024.[10]

Overview of the Final Rule

Much of what was outlined in the proposed rule has been included in the final rule. The basic premise remains the same: FDA has amended its regulations to make explicit that it considers IVDs to be devices under the FD&C Act, *including when the manufacturer of the IVD is a laboratory* (i.e., when the test is an LDT).[11] Therefore, LDTs will now be subject to the same oversight approach as other IVDs and will be required to meet the FDA's medical device regulatory requirements. The general phased-in approach to implementation also remains the same, with a few important exceptions regarding additional categories of test for which limited enforcement discretion will continue, including a grandfathering policy for currently marketed tests.

Implementation Timeline

The rule phases out FDA's historic enforcement discretion approach over the course of a four-year period beginning one year from publication of the rule.[12] During this period, LDT manufacturers will be incrementally required to comply with FDA's typical framework for device regulation in five stages:

1. *Stage 1:* One year after publication of the final rule, FDA will end the general enforcement discretion approach with respect to medical device reporting ("MDR") (i.e., reporting of adverse events), correction and removal reporting requirements, and certain quality systems ("QS") requirements related to complaint files.[13]

2. *Stage 2:* Two years after publication of the final rule, FDA will end the general enforcement discretion approach with respect to requirements other than MDR, correction and removal reporting, most QS requirements, and premarket review. This means that the FDA will begin enforcement of registration and listing, labeling, and investigational use requirements for LDTs.[14]

3. *Stage 3:* Three years after publication of the final rule, FDA will end the general enforcement discretion approach with respect to QS requirements, including device current good manufacturing practice ("CGMP") requirements.[15]

4. *Stage 4:* Three and a half years after publication of the final rule, FDA will end the general enforcement discretion approach with respect to premarket review requirements for high-risk IVDs.[16]

5. *Stage 5:* Four years after publication of the final rule, FDA will end the general enforcement discretion approach with respect to premarket review requirements for moderate -risk and low-risk IVDs.[17]

Limited Enforcement Discretion Policies in the Final Rule

The enforcement approach outlined in the rule's preamble includes several limited enforcement discretion policies that are intended to reduce the burden on entities who must come into compliance. Most notable are the following:

- *Grandfathering for currently marketed IVDs offered as LDTs*: The rule outlines an approach to allow enforcement discretion with respect to premarket review and most QS requirements for currently marketed IVDs offered as LDTs.[18] Retaining limited enforcement discretion for currently marketed tests is intended to reduce the high cost that would otherwise be associated with bringing these tests into compliance, and to prevent patients from losing access to tests upon which they currently rely. Notably, this enforcement discretion policy does not extend to other regulatory requirements such as adverse event reporting, records keeping, and registration and listing.[19] Additionally, manufacturers will need to submit current labeling for these products to the FDA, and certain modifications to the test will result in it falling outside of the enforcement discretion policy.[20] Specifically, modifications that could affect the test's basic safety and effectiveness profile would generally push it outside of this grandfathering provision; the preamble outlines certain modifications that would trigger this threshold.[21]

- *Tests performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within the same healthcare system*: In recognition of the importance of maintaining and enabling the development of tests for unmet needs, the rule outlines a limited enforcement discretion approach under which FDA will not enforce premarket review and QS requirements for certain such tests.[22] Similar to the enforcement discretion policy for currently marketed tests, this enforcement discretion policy does not extend to other regulatory requirements such as adverse event reporting, records keeping, and registration and listing, and manufacturers will need to submit current labeling for these products to the FDA.[23]

  There are two requirements that must be met for this "integrated medical care" enforcement discretion policy to apply. First, the LDT must be manufactured and performed by a laboratory that is integrated within the same healthcare system where the patient is receiving care (e.g., academic medical centers, hospitals).[24] Among other limitations, the preamble indicates that it will not extend to tests performed on patients that are being treated at *affiliated* hospitals.[25] FDA also said that the agency intends to look at corporate ownership in assessing whether a lab is part of an integrated healthcare system, explaining that the agency has greater confidence in the safety and accuracy of LDTs performed by labs that are integrated within healthcare systems because they have built-in communication mechanisms that non-integrated labs lack.[26] FDA's willingness to provide this enforcement discretion policy is likely in response to hundreds of comments to the proposed rule received from the academic medical center community.

Second, the LDT must be intended for use with respect to an unmet need. The preamble indicates three circumstances under which FDA will find an unmet medical need: 1) there is no FDA-authorized IVD for the disease or condition; 2) an FDA-authorized IVD for the disease or condition exists, but it is not approved for use by the patient; or 3) there is an FDA-authorized IVD, but it is not available to the patient.[27] Although the preamble provides examples, determining whether an LDT meets these criteria will likely require a case-by-case analysis.

- *Tests reviewed by New York State Department of Health Clinical Laboratory Evaluation Program (NYS CLEP)*: In the proposed rule, FDA requested comments on whether it may be appropriate to continue an enforcement discretion approach for tests that have been reviewed by NYS CLEP.[28] The final rule adopts an approach intended to leverage NYS CLEP's existing program by not requiring premarket review of certain moderate-risk LDTs that have conditional or full approval by NYS CLEP.[29] These tests will, however, need to meet other FDA requirements such as registration and listing, adverse event reporting, and certain QS and labeling requirements.[30]

- *"1976-type LDTs"*: The FDA will continue broad enforcement discretion for certain tests that have characteristics similar to LDTs that were offered in 1976. This test category is described in the final rule as tests that: 1) use manual techniques (without automation) performed by laboratory personnel with specialized expertise; 2) use components legally marketed for clinical use; and 3) are designed, manufactured, and used within a single laboratory that meets the CLIA requirements for high-complexity testing.[31] Although somewhat ambiguous, FDA provided several examples of tests that would fall into this category (e.g., various tests that use staining antibodies and general-purpose reagents for cytology, hematology, and bacterial infections; cystic fibrosis sweat tests; certain colorimetric newborn screening tests; etc.) and indicated it would consider issuing guidance on this topic in the future.[32]

Additionally, the rule outlines several more limited enforcement discretion policies that are applicable to various categories of tests. These include enforcement discretion policies for non-molecular antisera LDTs for rare red blood cell antigens, human leukocyte antigen tests, tests intended solely for forensic purposes that are used in the context of law enforcement, and tests manufactured and performed within the Veterans Health Administration or Department of Defense.[33]

Separate from enforcement discretion policies, FDA has concurrently issued new guidance documents outlining the approach it will take in overseeing tests used in public health emergencies.[34] Additionally, the preamble clarifies that certain categories of tests—such as those used for public health surveillance purposes, direct-to-consumer tests, and certain blood donor screening tests—will not be impacted by the rule because FDA has never classified these tests as LDTs.[35]

What the Final Rule Will Mean in Practice

Although the final rule has been published, there is a lot of outstanding uncertainty about what will happen next. Legal challenges aimed at preventing the rule from taking effect are imminent, though it remains to be seen whether a court will grant an injunction preventing FDA from implementing the rule while the litigation is pending. This could delay implementation of the rule for months, if not years.

Rumblings of potential Congressional action also create uncertainty. As evidenced by a recent House Energy and Commerce Committee hearing on LDTs and a request for information from the Ranking Member of the Senate Committee on Health, Education, Labor and Pensions, bipartisan and bicameral interest remains on this topic.[36,37] Whether Congress will act remains to be seen, but the call for a

legislative solution is likely to be stronger now that stakeholders see FDA oversight is seemingly imminent.

Despite the potential slow pace of litigation or legislation that may impact the rule's implementation, FDA has already indicated through issuance of recent warning letters that it is taking a closer look at behavior surrounding IVDs in the meantime. This is especially true as it relates to Research Use Only tests versus those intended for clinical use. Thus, there are still many moving pieces to be considered, and needless to say, entities who have historically enjoyed enforcement discretion with respect to oversight of their LDTs will grapple with how to proceed.

There are, however, concrete steps that we are recommending to clients as they, and we, prepare for impending changes in this area—and with a heightened sense of caution given the heighten scrutiny of IVDs we've seen in recent FDA warning letters. Understanding the complex implications of the rule (including the rule's built-in enforcement discretion mechanisms) will be critical to successfully navigating heightened oversight. Understanding FDA's device reporting requirements, quality systems and labeling is similarly crucial, as is careful study of planned or proposed LDT and IVD modifications. Promotional materials should be carefully reviewed to avoid indications of new intended use(s) and to stay squarely under the enforcement discretion policy umbrella. IVD manufacturers who still have products authorized for emergency use will want to tread carefully while they seek marketing authorization for those products.

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If you have any questions concerning these developing issues, please do not hesitate to contact any of the following Paul Hastings Washington D.C. lawyers:

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[1] *See Loper Bright Enterprises v. Raimondo*, SCOTUSBLOG, https://www.scotusblog.com/case-files/cases/loper-bright-enterprises-v-raimondo/ (U.S. Supreme Court Docket No. 22-451)*; Relentless, Inc. v. Department of Commerce*, SCOTUSBLOG, https://www.scotusblog.com/case-files/cases/relentless-inc-v-department-of-commerce/ (U.S. Supreme Court Docket No. 22-1219) two cases that challenge the *Chevron* framework.

[2] 21 C.F.R. § 809.3.

[3] FDA, "In Vitro Diagnostic Multivariate Index Assays; Draft Guidance for Industry, Clinical Laboratories, and FDA Staff," September 7, 2006. Available at *https://downloads.regulations.gov/FDA-2006-D-0233-0002/attachment_1.pdf.;* FDA, "Framework for Regulatory Oversight of Laboratory Developed Tests (LDTs); Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories," October 3, 2014. Available at *https://www.fda.gov/media/89841/download.;* FDA, "FDA Notification and Medical Device Reporting for Laboratory Developed Tests (LDTs); Draft Guidance for Industry, Food and Drug Administration Staff, and Clinical Laboratories," October 3, 2014. Available at *https://www.fda.gov/media/89837/download*.

[4] S.2209 - 117th Congress (2021-2022): VALID Act of 2021, S.2209, 117th Cong. (2021), https://www.congress.gov/bill/117th-congress/senate-bill/2209.

[5] *See* Al-Faruque, *Califf: FDA may use rulemaking for diagnostics reform if VALID isn't passed*, RAPS (2022), https://www.raps.org/news-and-articles/news-articles/2022/10/califf-fda-may-use-rulemaking-for-diagnostics-refo.

[6] Proposed Rule, *Medical Devices; Laboratory Developed Tests,* 88 Fed. Reg. 68006 (Oct. 03, 2023), *available at* https://www.federalregister.gov/documents/2023/10/03/2023-21662/medical-devices-laboratory-developed-tests#citation-12-p68016.

[7] See, e.g., Van Meter, ACLA Comments on Proposed Rule, "Medical Devices; Laboratory Developed Tests" (Docket No. FDA-2023-N-2177), American Clinical Laboratory Association (2023), 59-61, available at https://www.acla.com/aclas-comments-on-fdas%20proposed-regulation%20of%20laboratory-developed%20tests-as-medical-devices/.

[8] *See Id*. at 5.

[9] *See* § 510(g) of the FD&C Act [21 U.S.C. § 360(g)], generally exempting healthcare providers from certain requirements for devices such as registration and listing, recordkeeping, inspection, and reporting.

[10] *See* Final Rule, *Medical Devices: Laboratory Developed Tests*, Docket No. FDA-2023-N-2177 (Apr. 29, 2024), *available at* https://www.federalregister.gov/public-inspection/2024-08935/medical-devices-laboratory-developed-tests.

[11] *Id*. at 1.

[12] *Id*. at 26.

[13] *Id*.

[14] *Id*. at 27.

[15] *Id*.

[16] *Id*.

[17] *Id*.

[18] *Id*. at 28.

[19] *Id*. at 64-65.

[20] *Id*.

[21] *Id*. at 63.

[22] *Id*. at 49.

[23] *Id*. 53.

[24] *Id*. at 49.

[25] *Id*. at 54.

[26] *Id*.

[27] *Id*. at 55.

[28] See Proposed Rule at 68024.

[29] *See Final Rule* at 41, 43.

[30] *Id*. at 47.

[31] *Id*. at 37.

[32] *Id*. at 37, 402.

[33] *Id*. at 27-28.

[34] *Id*. at 32-33.

[35] *Id*. at 32-34.

[36] *See Hearing Announcement, Evaluating Approaches to Diagnostic Test Regulation and the Impact of the FDA's Proposed Rule*, *Before the Subomm. on Health of the H. Comm. on Energy & Commerce*, Mar. 21, 2024, *available at* https://energycommerce.house.gov/events/health-subcommittee-hearing-evaluating-approaches-to-diagnostic-test-regulation-and-the-impact-of-the-fda-s-proposed-rule

[37] *See* Press Release, *Ranking Member Cassidy Seeks Information from Stakeholders on Regulation of Clinical Tests,* U.S. Sen. Comm. on Health, Edu., Labor & Pensions (Mar. 13, 2024), *available at* https://www.help.senate.gov/ranking/newsroom/press/ranking-member-cassidy-seeks-information-from-stakeholders-on-regulation-of-clinical-tests