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From General Discretion to Agency Authority? FDA's Bold Bid to Regulate Laboratory Developed Tests

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Introduction

After years of FDA discussion and failed congressional efforts to assert greater oversight of laboratory developed tests (LDTs), FDA has proposed a rule that would require many LDTs to comply with FDA's requirements for in vitro diagnostic devices (IVDs).[1]

Prior Regulatory and Legislative Action on LDTs

The proposed rule is part of an ongoing saga in FDA's efforts to further regulate LDTs. FDA describes LDTs as "[IVDs] that are intended for clinical use and are designed, manufactured, and used within a single clinical laboratory" that meets certain laboratory requirements, including being certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) and authorized to perform high complexity testing. Between 2010 and 2014, FDA proposed further oversight of LDTs through guidance documents, which were met with both strong support and equally strong opposition by various clinical laboratory, IVD, and healthcare groups. After congressional subcommittees held hearings on LDTs, the House Committee on Appropriations asked FDA not to move forward with its plans to assert regulatory oversight because those efforts were outside of the formal rulemaking process and because it would change expectations for relevant parties. Following the 2016 presidential election, FDA announced that it was suspending its work on the guidance documents in favor of allowing for further public discussion and providing Congress with an opportunity to develop relevant legislation. More recently, in 2021, proposed legislation outlined a regulatory framework for LDTs, but this legislation ultimately was not included in the user fee legislation that frequently serves as the vehicle to make significant changes to the Federal Food, Drug, and Cosmetic Act. This year a bill similarly proposing LDT regulation has been reintroduced in the House and is still pending in Committee. Despite these legislative efforts, FDA's proposed rule makes clear that the Agency is taking charge and moving forward in the rulemaking process.

Key Features of FDA's Proposed Rule

Recognizing that the proposed rule will be subject to significant industry scrutiny, and likely litigation, FDA takes great pain in the proposal to provide a detailed explanation for why it is moving from a lengthy period of enforcement discretion for LDTs (i.e., wherein the agency generally has not enforced what it might view as applicable requirements with respect to most LDTs) to an approach that would

apply substantial regulatory requirements to LDTs and FDA oversight. Although some of the discussion is intended to address potential legal weaknesses that the Department of Health and Human Services (HHS) articulated in 2020 (and later withdrew in 2021), other arguments are aimed at justifying FDA's change from its decision to use enforcement discretion. Specifically, FDA emphasizes that the LDT market today differs significantly from the manually processed, lower risk LDTs it assessed decades ago when it began its policy of enforcement discretion. According to the Agency, today, LDTs are both increasingly reliant on complicated instruments and software and used for guiding critical healthcare decisions (including for serious medical conditions such as heart disease and cancer). Significantly, FDA expresses its concern that there is "fundamental uncertainly in the marketplace" about whether LDTs "provide accurate and reliable results." FDA also highlights that LDTs are increasingly seen as a potential commercialization pathway, thereby discouraging innovation through other more traditional regulatory pathways.

If finalized, the rule would begin a four-year phased process to bring LDTs under FDA's medical device oversight. In a change from earlier proposals, FDA is calling for greater regulation of several categories of tests, including low-risk tests, currently available tests, and rare-disease tests. FDA's proposal excludes, however, several groups of LDTs, including, for example, direct-to-consumer tests intended for use without the meaningful involvement by a healthcare professional; Human Leukocyte Antigen (HLA) LDTs when they are used in connection with organ, stem cell, and tissue transplantation to perform HLA allele typing; and tests intended solely for forensic (law enforcement) purposes.

For applicable tests, FDA would end its general enforcement discretion policy over five stages:

- Stage 1: FDA would begin to require medical device reporting and correction and removal reporting (1 year after issuing the final phase-out policy);
- Stage 2: FDA would require registration, listing, labeling, investigational use, and other requirements not covered in other phases (2 years after FDA publishes a final phase-out policy);
- Stage 3: FDA would require compliance with Quality System Regulation requirements (with exceptions for some elements when the test qualifies as a LDT under FDA's more narrow historical definition; 3 years after FDA publishes a final phase-out policy);
- Stage 4: FDA would require premarket review for high-risk IVDs (3½ years after FDA publishes a final phase-out policy, but not before October 1, 2027); and
- Stage 5: FDA would require premarket review for moderate- and low-risk IVDs that need such premarket submissions (4 years after FDA publishes a final phase-out policy, but not before April 1, 2028).

FDA's phased approach is intended to allow companies to work toward compliance and provide industry an opportunity, as needed, to develop additional data, determine appropriate regulatory pathways, and consult with FDA. The stage 4 premarket approval requirements generally would not be enforced until after FDA had completed its review of a Premarket Approval application, and similarly, FDA does not intend to enforce stage 5 requirements until after FDA had completed its review of a company's premarket submission, provided the submission was received by FDA before the announced deadline.

Challenges and Superseding Legislation?

The proposed rule is likely to face challenges as it moves forward. These challenges include FDA's statutory authority over LDTs and challenges related to FDA's apparent change in position on its enforcement discretion and whether the proposed approach meets scrutiny under the "major questions doctrine," which requires that federal agencies have authorization from Congress to impose regulations that have vast economic and political significance.[2] Such judicial challenges may delay the implementation of any finalized rule. Of course, ongoing congressional action could also moot the proposed regulation if legislation establishes a legal framework for LDTs.

Considerations for the Proposed Rule

Although the approach and scope of regulating LDTs is likely to continue to develop, industry stakeholders will likely want to begin to consider a number of key actions related to FDA's proposal:

- The formal rulemaking process will likely set the stage for FDA's eventual final rule, litigation efforts to challenge the rule, or potential legislation to supersede the rule. As a result, FDA is encouraging industry to provide comments in the rulemaking process on the impact of FDA's proposal. Comments must be submitted by December 4, 2023.

- Regardless of what proposal is finalized, it is likely that the LDT industry will be subject to additional FDA oversight in the future, and industry members should consider conducting a readiness assessment to evaluate whether and how their procedures and systems would need to evolve to comply with such future oversight (e.g., Medical Device Reporting). Such an assessment could also inform and otherwise support efforts to provide comments to FDA on the proposed rule.

- Given FDA's focus on the performance, accuracy, and data supporting LDTs, it is important for LDT manufacturers to consider current market feedback related to their LDTs and development files and data supporting the respective tests. Negative customer feedback (e.g., product complaints) will draw FDA scrutiny and place additional pressure on the quality of the data supporting the design and development of the LDT. FDA's focus may also underscore a need for companies to conduct an analysis of their LDT's market feedback and data to understand any past action that may have been undertaken in response to negative customer feedback.

- Because LDT manufacturers may be subject to potential enforcement beyond FDA, consider reviewing existing data that supports the LDT's current uses. If an LDT does not provide accurate, validated results, or is ultimately found not to have sufficient supporting data, third-party payers may raise concerns about the testing, and such testing (and even healthcare services or items that are ordered or arranged for in connection with such testing) may draw scrutiny from government enforcement bodies, such as the Department of Justice.

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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 lawyers:

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[1] Medical Devices; Laboratory Developed Tests, 88 FR 68006-01, https://www.federalregister.gov/documents/2023/10/03/2023-21662/medical-devices-laboratory-developed-tests

[2] The Supreme Court recently invoked the major questions doctrine in holding that the EPA had exceeded its authority in regulating greenhouse emissions. *W. Virginia v. Env't Prot. Agency*, 142 S. Ct. 2587 (2022).