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Key Takeaways From FDA Final Rule On Lab-Developed Tests

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The U.S. Food and Drug Administration on April 29 announced its final rule on laboratory-developed tests. This move marks the beginning of the end of the FDA's broad and long-established enforcement discretion policy for tests, which are known as LDTs and are mostly not expected to meet the premarket or post-market regulatory requirements.

The final rule makes clear that LDTs are now considered regulated medical devices and that the FDA will phase out its LDT enforcement discretion policy over a four-year period.

This article discusses the key takeaways from the LDT final rule, the FDA's phaseout policy for LDT enforcement discretion, and potential consequences.

IVD Definition Revised to Make Clear LDTs Are Regulated Devices

Although the Federal Register notice announcing this monumental regulatory shift for LDTs is well over a hundred pages, the change to the FDA's regulations consisted of adding only 10 words to the end of the regulatory definition for in vitro diagnostic, or IVD, products:

> In vitro diagnostic products are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. These products are devices as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the act), and may also be biological products subject to section 351 of the Public Health Service Act, including when the manufacturer of these products is a laboratory.

As revised, this regulation now makes clear that LDTs are included within the definition of IVDs and thus qualify as devices subject to the FDA's oversight and regulation under the Federal Food, Drug, and Cosmetic Act.

Scope of Phaseout Policy

The scope of tests eligible for the LDT phaseout program include not only tests that qualify as LDTs per the FDA's traditional definition — i.e., tests designed, manufactured and used at a single laboratory

certified for high-complexity testing by the Clinical Laboratory Improvement Amendments tests — but also tests that were manufactured by high complexity, CLIA-certified labs and offered as LDTs by the lab.

The latter category includes tests that may not have fully met the agency's definition for an LDT — e.g., because the test was designed at a different laboratory location.

However, the FDA explicitly states that the following types of tests are not eligible for the phaseout program, as the FDA has previously stated that such tests do not qualify for LDT enforcement discretion.

As such, the FDA has and continues to require these types of tests to fully meet the applicable FDA requirements:

- Direct-to-consumer tests;
- Tests intended for donor screening for blood or for human cells, tissues, and cellular and tissue-based products;
- Tests intended for emergency use per Section 564 of the FDCA; and
- Tests manufactured or used outside of a clinical laboratory.

Four-Year Phaseout Approach

The FDA is phasing out its blanket enforcement discretion policy for LDTs over the course of four years in five stages. At each stage, the FDA expects LDTs to come into compliance with specific regulatory requirements, as set forth below:

- Stage 1: Compliance with requirements for medical device reporting, corrections and removals reporting, and complaint handling starting one year after the final rule publication date;
- Stage 2: Compliance with other regulatory requirements — including establishment registration, device listing, labeling and investigational use — required starting two years after the final rule publication date;
- Stage 3: Compliance with the quality system regulation, which sets forth the good manufacturing practices for medical devices, starting three years after the final rule publication date;
- Stage 4: Compliance with premarket review requirements for high-risk LDTs, starting three and a half years after the final rule publication date; and
- Stage 5: Compliance with premarket review requirements for low- and moderate-risk LDTs, starting four years after the final rule publication date.

New Enforcement Discretion for Grandfathered LDTs

In a move certain to provide relief for many laboratories that offer LDT testing services, the FDA added a new, limited enforcement discretion policy for LDTs that "were first marketed prior to the date of issuance of the rule and that are not modified, or that are modified in certain limited ways."

These preexisting LDTs will not be required to comply with the FDA's premarket review or quality system regulation requirements, but other regulatory requirements will apply — e.g., medical device reporting, complaint handling, registration and listing.

In addition, the FDA states that it will request that laboratories offering preexisting LDTs submit labeling to the FDA.

The FDA also has created several other new, limited enforcement discretion policies for certain other types of LDTs, including, for example:

- 1976-type LDTs — i.e., tests that have certain characteristics common among LDTs offered in 1976;
- LDTs approved by the New York State Department of Health's Clinical Laboratory Evaluation Program; and
- LDTs manufactured and performed solely within the Veteran's Health Administration or U.S. Department of Defense.

More Scrutiny Possible for Suppliers of LDT Components

In the preamble to the final rule, the FDA made clear that a laboratory manufacturing or assembling an LDT from third-party components — such as software, kits, instruments and reagents — is responsible for determining the necessary specifications for such components and implementing purchasing and acceptance controls.

Thus, third parties that supply components used for LDTs should be aware that their laboratory customers may seek to impose more requirements — including quality requirements — and controls via contract in order to meet these obligations.

For example, software developers that provide software products or services used in LDTs may find customers imposing requirements for software validation, the sharing of other data or information to support that the software functions as intended, and reporting of changes that could affect an LDT subject to the grandfathered enforcement discretion policy — e.g., addition of artificial intelligence or machine learning to the software algorithm.

The Valid Act and Potential Litigation

It is unclear whether — or to what extent — the FDA's new final rule will affect efforts to pass the Verifying Accurate, Leading-edge IVCT Development, or VALID, Act currently pending in Congress.

The VALID Act would create a new regulatory framework for IVDs, including LDTs, separate from the current regulatory scheme for medical devices. The VALID Act has been introduced in Congress for several years in a row but has not yet had sufficient support to move forward.

It has generally had the support of the medical device industry, and it is possible that clinical laboratory stakeholders, now faced with a timeline for LDTs to start complying with the FDA's medical device regulations, may view an alternative IVD regulatory scheme more favorably and throw their support in

as well.

In addition, comments to the proposed rule suggested that the FDA does not have the authority under the FDCA to regulate LDTs. Considering pending U.S. Supreme Court litigation questioning deference afforded to regulatory agencies in rulemaking — Loper Bright Enterprises v. Raimondo and Relentless Inc. v. Department of Commerce — it is possible that private litigants will challenge the LDT rulemaking, thereby at a minimum potentially delaying implementation of the rule.

The LDT rule becomes final on July 5.

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