Navigating the Future of Laboratory Developed Tests (LDTs)

November 2024

Laboratory Developed Tests (LDTs) have long been an essential part of diagnostic healthcare in the USA empowering laboratories to develop in-house tests that address unique patient needs and emerging health issues. While these tests have historically operated with minimal regulatory oversight, allowing for considerable flexibility and innovation, recent FDA initiatives have introduced a wave of uncertainty across the field. Researchers, clinicians, and companies involved in developing, manufacturing, and utilizing LDTs are now questioning how potential regulatory shifts might impact their work. The FDA's proposed framework aims to modernize LDT oversight, balancing safety and innovation in a way that could significantly influence the future of precision medicine, where these tests are vital for diagnosing rare and complex conditions and tailoring treatments to individual patients. As regulatory bodies and stakeholders deliberate, the stakes are high for both the laboratories that create these tools and the patients who depend on them.

What is a LDT?

LDTs are often developed in response to a specific public health need when no (or limited) FDA-approved tests are available. LDTs are **in vitro diagnostic products (IVDs)** that are intended for clinical use and are designed, manufactured, and used within a single laboratory that is certified under the Clinical Laboratory Improvement Amendments of 1988 **(CLIA)** and meets the regulatory requirements under CLIA to perform high complexity testing. LDTs, like other IVDs, can be used to measure or detect a wide variety of substances or analytes in the human body, such as proteins, glucose, cholesterol, or DNA, to provide information about a patient's health, including to diagnose, monitor, or determine treatment for diseases and conditions. **LDTs offer significant benefits** by enabling laboratories to swiftly develop diagnostic tests tailored to specific patient populations and unique health challenges. These tests are often crucial when commercial options are unavailable, particularly for diagnosing rare diseases, responding to emerging public health threats, or addressing complex conditions where a tailored approach is essential. By fostering rapid innovation within labs, LDTs contribute to advances in precision medicine, helping clinicians make more personalized treatment decisions that can improve patient outcomes. This flexibility supports a responsive, patient-centred approach to healthcare that can adapt quickly to evolving diagnostic needs.

How are LDTs enforced?

Since the Medical Device Amendments of 1976, the FDA has largely exercised enforcement discretion for Laboratory Developed Tests (LDTs), opting not to enforce most regulatory requirements for these in-house diagnostics. Originally, this approach reflected the lower risk associated with LDTs, which were typically small-scale, localized, and specialized for specific patient groups. However, the role of LDTs has since expanded: with advancements in technology, many LDTs now leverage complex software and high-tech instrumentation, process large volumes of specimens, and serve patients nationwide. This broader scope introduces new risks, as LDTs are increasingly used to guide critical healthcare decisions for diverse and widespread populations. In response, **the FDA is moving away from its historic enforcement** discretion, signalling a shift toward stricter oversight to enhance the safety, effectiveness, and reliability of LDTs in today's healthcare landscape while still considering public health needs such as patient access.

On May 6, 2024, the FDA issued a final rule to regulated LDTs as medical devices, aimed at helping to ensure the safety and effectiveness of laboratory developed tests (LDTs).

The FDA has developed a structured "phase-out" policy for its enforcement discretion regarding LDTs, moving towards comprehensive regulatory oversight. This gradual transition is planned over four years and consists of five distinct stages, each introducing more stringent requirements. The FDA's goal with this phased approach is to facilitate a manageable transition for laboratories, enabling them to comply with the statutory and regulatory premarket and post-market requirements for devices.

What are the 5 phase-out stages?

1. 1 year after publication, the FDA will require laboratories to comply with MDR requirements under 21 C.F.R. correction and removal reporting requirements and complaint handling requirements.
2. Starting 2 years after publication the FDA will require compliance with regulatory standards not addressed in other stages of the phase-out. These include registration and listing requirements, labelling standards, and investigational use regulations.
3. Beginning 3 years after the publication of the final rule, the FDA will require compliance with quality system requirements under 21 C.F.R. Part 820.
4. Beginning 3½ years after publication, the FDA will require compliance with premarket review requirements for high-risk IVDs offered as LDTs.
5. Starting 4 years after the publication, the FDA will require compliance with premarket review requirements for moderate- and low-risk IVDs offered as LDTs that need premarket submissions.

What does this mean and what should be your next steps?

Below is a concise guide to help laboratories prepare for compliance, including timelines for planning and execution:

Stage 1: Preparing for MDR and Reporting Compliance (1 Year Post-Publication)

By one year post-publication, laboratories must align their incident and adverse event reporting systems with MDR requirements. Immediate actions should include reviewing reporting mechanisms, identifying data gaps, and refining procedures for adverse events and corrections. Staff training on new protocols and establishing a regular review process for compliance documentation is essential.

Stage 2: Registration, Listing, and Labelling Compliance (2 Years Post-Publication)

Two years after publication, laboratories need to prepare for FDA registration as a device establishment and compile necessary LDT listings. This stage also requires updating labelling processes to meet FDA standards and ensuring compliance with investigational device exemption (IDE) requirements.

Stage 3: Quality System Regulation Compliance (3 Years Post-Publication)

By three years post-publication, laboratories must develop a compliant quality system, a process that should begin 18 months before this stage. Adequate time should be allowed for documentation and facility registration, typically taking 8-10 months.

Stage 4: Premarket Approval for High-Risk LDTs (3.5 Years Post-Publication)

At 3.5 years post-publication, laboratories should gather data and prepare premarket approval applications for high-risk LDTs, ensuring that submissions are made by the start of this stage.

Stage 5: Premarket Notification for Moderate- and Low-Risk LDTs (4 Years Post-Publication)

Four years after publication, laboratories must prepare and submit 510(k) premarket notifications for moderate- and low-risk LDTs that require them, unless they are exempt from this requirement.

So, what's next?

The FDA's release of the LDT Final Rule reaffirms its stance that laboratory-developed tests (LDTs) fall under the definition of a "device," placing them within the FDA's jurisdiction. This interpretation has sparked controversy, as the laboratory community argues that LDTs, considered professional services, should not be subject to device regulations. This situation highlights the ongoing complexity of balancing regulatory authority, industry capabilities, and legislative intent in governing LDTs.

How can Apotech can help?

Apotech is uniquely positioned to support laboratories during the transition away from LDT enforcement discretion. Our tailored services are designed to help navigate the complexities of the new regulatory framework effectively.

- **Regulatory Gap Assessment and Strategic Planning**
- **Quality Management System (QMS) Development**
- **Submission and Registration Support**
- **Training and Ongoing Regulatory Vigilance**

By partnering with Apotech early in the process, laboratories can confidently navigate each regulatory milestone and maintain their ability to provide safe and effective diagnostic tools under the new LDT regulations.

Apotech can support you during your LDT navigation by providing expert guidance and hands-on assistance.

Please don't hesitate to reach out to use at

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