May 2024

Laboratory Developed Tests Final Rule

Children's Hospital Association Summary

Internal

On May 6, the FDA published the final rule "Medical Devices; Laboratory Developed Tests," which requires most laboratory developed tests (LDTs)[1] to go through the FDA medical device review process. Prior to the release of this rule, the FDA exercised "enforcement discretion" for LDTs, meaning the agency did not require LDTs to comply with the medical device review and approval requirements that apply to most other in vitro diagnostic tests (IVDs).

The final rule phases in the review and approval requirements over five years, beginning on **May 6, 2025**. The rule also continues partial enforcement discretion for certain LDTs, including the following tests with implications for pediatric medicine:

- LDTs manufactured and performed by a **laboratory integrated within a health care system** to meet an **unmet need** of patients **receiving care within the same healthcare system.**
- **Currently marketed LDTs** that are not modified or that are modified in certain limited ways.
- LDTs approved by the **New York State Clinical Laboratory Evaluation Program (CLEP)**

In our comments on the proposed rule, we highlighted the critical and unique role that LDTs play in pediatric medicine and urged FDA to continue its current general enforcement discretion approach for all pediatric-related tests. While the final rule does not extend full enforcement discretion for pediatric-related tests, the FDA acknowledges the unique pediatric implications of the new regulatory framework in its adoption of the partial enforcement discretion policies.

Provisions with Implications for Children's Hospitals

The following provisions of the final rule have implications for children's hospitals and children's health.

Updates definition of medical devices to include LDTs

The rule amends the Food, Drug, and Cosmetic Act definition to state that IVDs are devices "including when the manufacturer of these products is a laboratory." This gives FDA authority to conduct LDT oversight.

[1] LDTs are diagnostic tests that are developed and offered by high-complexity laboratories certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).

Phases in regulatory oversight of LDTs

The rule establishes a phased in approach to end FDA's policy of enforcement discretion for LDTs and begin regulating them in the same way it regulates medical devices,[2] with some targeted exceptions described in the next section.

Phase-in Timeline

STAGE	COMPLIANCE REQUIREMENTS	TIMELINE
Stage 1	Medical Device Reporting (MDR), correction and removal reporting and complaint file requirements.	May 6, 2025
Stage 2	Requirements not covered in other stages, including establishment registration and device listing, labeling, and investigational use requirements.	May 6, 2026
Stage 3	Current Good Manufacturing Practice requirements in the Quality System (QS) regulation: design controls, purchasing controls, acceptance activities (receiving, in-process and device acceptance), corrective and preventative actions, and records requirements.	May 6, 2027
Stage 4	Premarket review for high-risk LDTS.[3] If a complete application for premarket approval (PMA) has been submitted, or a CLIA-certified lab modifies another manufacturer's 510(k) cleared test,[4] an existing test may remain on the market until FDA completes its review.	Nov. 6, 2027
Stage 5	Premarket review for mid- and low-risk LDTs.	May 6, 2028

[2] Medical devices are subject to a full range of premarket and post-market controls, including requirements related to premarket notification or premarket approval; quality system regulation; medical device reporting; registration and listing; and labeling. They are also generally subject to regulation under CLIA.

[3] The FDA is reclassifying most IVDs so they will be considered moderate risk (Class II), rather than high risk (Class III). Reclassification is intended to allow manufacturers of certain types of tests to seek marketing clearance through the less burdensome premarket notification (510(k)) pathway rather than the premarket approval pathway, the most stringent type of FDA medical device review. FDA aims to complete its reclassification process before Stage 4.

[4] The test modification cannot alter the test's safety and effectiveness and the modified test cannot be a major change from its intended use and must be performed in the lab that made the modification.

	The FDA is applying the same guidelines regarding modifications to an existing test in Stage 5 as it is applying to Stage 4.	

Modifications of approved tests

FDA clarifies that CLIA-certified high-complexity laboratories can make certain modifications (as they can already do under CLIA) to Class II tests without submissions to FDA when:

- The modification does not significantly affect the safety or effectiveness of the test.
- The modification does not constitute a major change or modification in intended use.
- The modified test is performed only in the laboratory making the modification.

LDTs with partial continued enforcement discretion

The final rule establishes a targeted continuation of enforcement discretion for several key types of LDTs that may be developed and used by children's hospitals (see below for more information), meaning these tests would not need to go through the full medical device review and approval process.

Partial enforcement discretion

Category of Test	Stage 1 (beginning May 6, 2025): MDR, Correction & Removal Reporting, Etc.	Stage 2 (beginning May 6, 2026): Registration & Listing, Labelling	Stage 3 (beginning May 6, 2027): QS	Stages 4 & 5: (beginning Nov. 6, 2027, and May 6, 2028): Premarket Reviews
LDTs for **unmet need** manufactured and performed by a laboratory integrated within a health care system for patients receiving care within the same system.	Required	Required	**Exempt, but must comply with QS requirements**[5].	**Exempt**
Currently marketed (prior to May 6, 2024) LDTs	Required	Required	**Exempt, but must comply with QS requirements**[6]**:**	**Exempt**
LDTs **approved by the NYS**	Required	Required	Required	**Exempt**

[5] QS requirements: design controls, purchasing controls, acceptance activities (receiving, in-process and device acceptance), corrective and preventative actions, and records requirements.

[6] See above.

Clinical Laboratory Evaluation Program (CLEP), including those that are approved, conditionally approved, or within an approved exemption from full technical documentation				

- **"Unmet need"**
  - The final rule extends partial enforcement discretion to an **LDT that is developed and manufactured by a laboratory integrated within a health care system to meet an unmet need of patients receiving care within the same system.**
  - The "unmet need" standard is met when there is no available FDA-authorized IVD that meets the patient's needs[7] for any of the following reasons:
    - There is no FDA-authorized test for the disease or condition (for example, because it is for a rare disease or condition).
    - There is an FDA-authorized test for the disease or condition, but it is not indicated for use on the patient, or a unique attribute needs to be added to the LDT to meet the patient's needs (for example, no test for a pediatric indication).
    - There is an FDA-authorized test but it is not available to the patient. (For example, there is an FDA-authorized test that is offered only in another health care system but it is not accessible to the patient and the developing laboratory will not make the IVD available outside its system).
  - Laboratories associated with an affiliated hospital with different corporate ownership than the laboratory will not be considered an "integrated health care system" for purposes of the unmet need continued enforcement discretion policy.
  - The unmet need policy applies only to LDTs that are validated. FDA may issue additional guidance regarding validation of tests, including those for rare diseases, that takes into consideration the challenges of obtaining a robust number of samples for validation.
  - FDA also plans to issue further guidance on the overall implementation of the unmet need standard.
- **Currently marketed LDTs**
  - Partial enforcement discretion is given to **currently marketed IVDs that were first marketed prior to the date of issuance of the final rule (May 6, 2024).**
  - The partial enforcement discretion for a "grandfathered" LDT is in effect as long as there are no adverse changes to the performance or safety specifications and it is not modified in a significant way, such as:
    - An update to the indication.
    - A change/update to its operating principle.

[7] An LDT would not be eligible for continued enforcement discretion if there is an available FDA-authorized test that would meet the patient's needs with potential improvements in performance or lower cost in comparison.

    - The addition of new technology.
  - FDA will request submission of the labeling for currently marketed LDTs and use this information, along with information obtained through laboratory compliance with other relevant requirements (including adverse event reporting) to identify currently marketed LDTs that raise concerns.
  - If the LDT is modified in any way the laboratory must comply with QS and premarket review requirements.
- **LDTs approved by the New York State CLEP**
  - Includes LDTs that are approved, conditionally approved, or within an approved exemption from full technical documentation by the CLEP.
    - The CLEP evaluates high-risk and moderate-risk LDTs for analytical and clinical validity. High-risk LDTs require full technical review and approval prior to testing on specimens from New York State; moderate-risk LDTs require full technical review but may receive conditional approval if the laboratory holds a permit in the appropriate category.
  - FDA acknowledges that some laboratories may offer different versions of an LDT depending on whether a patient specimen comes from New York State or from elsewhere.

LDTs with full continued enforcement discretion

- The final rule fully exempts certain types of LDTs from the medical device regulatory reviews:
  - "1976-Type LDTs," which are tests that use manual techniques without automation.
  - Human leukocyte antigen tests for transplantation that are designed, manufactured, and used within a single laboratory appropriately certified under CLIA.
  - Tests for forensic (law enforcement) and public health purposes.
  - LDTs performed within the Veteran's Health Administration or the Department of Defense.

Fully regulated LDTs

- Tests that are not currently subject to the LDT enforcement discretion policy and will continue to be actively regulated as medical devices include:
  - Direct-to-consumer tests.
  - Tests that have been issued an emergency use authorization (e.g., COVID-19 Antigen Diagnostic Tests).
    - FDA also released two draft guidance documents that establish a different system of regulatory expectations and enforcement discretion in the case of emergencies for immediate response to chemical, biological, radiological, or nuclear agents. One addresses use of LDTs in the absence of a formal emergency declaration and one addresses their use after a declaration has been issued.
  - Tests intended as donor screening tests required for infectious disease testing, or required for determination of blood group and Rh factor.
- The manufacturing of test components outside of a lab—for example, when the same entity owns both the lab and a manufacturing facility separate from the lab—does not fall within FDA's general enforcement discretion and the components will continue to be regulated as medical devices.