

Proposed Rule Medical Devices: Laboratory Developed Tests

On October 3, 2023, the FDA [published](#) a proposed rule in the Federal Register. Comments are due in 60 days on December 4, 2023.

Summary

The proposed rule amends the definition of in vitro diagnostic products (IVDs) within existing FDA regulations to state that IVDs are devices “including when the manufacturer of these products is a laboratory.” Additionally, FDA intends to phase out its current policy of enforcement discretion on LDTs over the next four years.

Proposed Changes (in red) to 21 CFR 809.3

- (a) 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)(1) 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.**

FDA Rationale For Rulemaking

FDA believes that LDTs offered today differ significantly from those offered in 1976 when the Medical Device Act (MDA) was first enacted, and given their complexity (i.e. used for life-threatening conditions, have complex algorithms, etc.), no longer believes enforcement discretion is appropriate. Acknowledging that the agency does not systematically collect information on LDTs including adverse events, and thus is unable to fully assess the extent of the risk to patients, the FDA cites scientific literature, news articles, and anecdotal reports of poor test quality and patient harm as supporting evidence of problems associated with LDTs.

The agency states that increased oversight would also address business strategies that “take advantage of the current bifurcated system” and remove a disincentive to develop novel tests for non-laboratory manufacturers by stopping laboratories from offering LDTs similar to their FDA authorized IVDs. To further argue that the proposed rule would not disrupt innovation, FDA briefly discusses the several guidance documents already available to determine whether a certain change or modification may require additional FDA review. Additionally, FDA notes it is allowing for the use of previously authorized change control plans for IVDs to allow for certain modifications to be made without further review.

FDA also believes that increased oversight will advance health equity due to concerns that LDTs may “exacerbate health inequities due to higher rates of inaccurate results among underrepresented patient populations, particularly racial and ethnic minorities undergoing genetic testing.” FDA recognizes that LDTs may serve communities in rural, medically underserved areas with disparities in access to diagnostic tests,

however, FDA believes preventing the harms of unsafe or ineffective LDTs will better protect the health of these underserved populations.

In regards to CLIA, the proposed rule says that “FDA has both the authority and the expertise to perform the necessary oversight of IVDs offered as LDTs and is the only Agency for which that is the case.” Further, FDA believes that granting new statutory authorities to CMS would cause a problematic split in oversight, with the same types of tests being reviewed by different agencies depending on where the test is made, leading to confusion and inconsistency.

Legal Basis for Proposed Amendment

FDA is proposing to issue this rule under general rulemaking authorities and statutory authorities related to devices. The proposed rule states that the statutory definition of a device includes in vitro diagnostic (IVD) test systems, which are sets of IVDs, e.g. reagents, instruments, specimen collection devices, etc., that function together to produce a test result. The proposed rule says that the systems “consist of individual parts that have their own regulatory identity, but when combined, constitute a new device” and that the definition of device “encompasses test systems regardless of where or by whom they are manufactured.” FDA argues the word “apparatus,” which is a term included in the statutory definition of “device,” encompasses the concept of test systems.

In detail, the proposed rule summarizes the legislative history of FDA’s authority over IVD test systems since the Food, Drug and Cosmetic (FD&C) Act was first enacted in 1938 as well as cites court cases supporting its position that for more than half of a century, there has been congressional intent for FDA to regulate all IVDs including test systems. The proposed rule even points to the definition of an advanced diagnostic laboratory test in the Protecting Access to Medicare Act of 2014 that specifies that a test offered by a single laboratory must be cleared or approved by the FDA as further affirmation that tests systems manufactured by a laboratory are devices.

The proposed rule points to judicial decisions that support that the scope of the FD&C Act’s practice of medicine provision does not apply to the manufacturer of new test systems and that it only applies in the context of using a “legally marketed device.” Last, FDA argues that FDA maintains jurisdiction over LDTs even if not introduced into interstate commerce or offered for commercial distribution.

Exemptions

For certain test categories, moving forward, FDA will continue to apply current general enforcement discretion:

- **1976-Type LDTs:** This category includes tests that 1) use manual techniques (without automation) performed by laboratory personnel with specialized expertise; 2) use components legally marketed for clinical use; and design, manufacture, and 3) are used within a single CLIA-certified laboratory that meets the requirements under CLIA for high complexity testing.
- **Human Leukocyte Antigen (HLA) LDTs for transplantation**
- **Tests intended solely for forensic purposes**
- **Tests used for public health surveillance:** Results cannot be reported to patients or their healthcare provider

However, for other categories, FDA will not exempt tests from medical device requirements:

- **Rare diseases:** FDA says it is aware of instances where there is high variability in the performance of IVDs offered as LDTs that are currently on the market, so is changing its 2017 position on exempting this category of tests.
- **Low risk/Class I devices:** FDA provides the same reasoning as stated above for rare disease testing.
- **Unmet needs:** FDA explains that it believes the phaseout timeline is sufficient for laboratories to meet premarket review requirements. FDA also notes the Humanitarian Use Devices (HUD)/Humanitarian Device Exemption (HDE) program and Breakthrough Devices program will be applicable to all IVDs.

Requests for Comment on Exemptions

- **Public health scenarios:** FDA intends to issue draft guidance with an enforcement policy for IVDs for emerging outbreaks offered prior to FDA review to address the immediate public health need and seeks comment on whether this would be appropriate for other public health scenarios.
- **Grandfathered tests:** FDA asks several questions to understand why currently marketed tests should continue to be exempt from certain medical device requirements (such as premarket review and some or all QS requirements) as long as they are not changed with respect to indications for use or performance.
- **Small laboratories:** FDA asks whether there is a rationale to have a longer phaseout period for IVDs offered as LDTs by laboratories with annual receipts below a certain threshold (e.g., \$150,000).
- **Academic Medical Centers (AMCs):**
 - FDA suggests a definition for AMC laboratories –
 - a laboratory for which a certificate is in effect under CLIA and that meets the requirements under CLIA to perform tests of high-complexity;
 - that is part of an accredited public or nonprofit private AMC that has a medical residency training program or fellowship program related to test development, application, and interpretation; and
 - that is integrated into the direct medical care for a patient, including specimen collection, testing, interaction with the treating provider, and, as appropriate, patient treatment based on the test, all at the same physical location.
 - FDA asks several questions including whether the definition reflects the characteristics of an AMC lab. FDA also asks about whether an exemption for a test provided by an AMC should exist if there is an FDA cleared or approved test with the same intended use currently available.
- **Laboratories that are subject to certain programs:** New York State Department of Health Clinical Laboratory Evaluation Program (NYSDOH CLEP) and laboratories within the Veterans Health Administration (VHA) are specifically mentioned. FDA would like to know about what the characteristics of outside programs should be and what the scope of the exemption might be (e.g., just premarket review, all medical device requirements, or some other alternative).

Stages for Ending Enforcement Discretion for LDTs

- After the end of enforcement discretion of the premarket review requirements, FDA anticipates that approximately 50 percent of IVDs offered as LDTs would require premarket review.
- FDA requests public comment on unintended consequences to certain patient populations (e.g. Medicare, rural, etc.) that may result from the proposed phaseout policy and steps to mitigate them.

<u>Stage</u>	<u>Timeline*</u>	<u>Details</u>
	Final phaseout policy published	
Stage 1: End of enforcement discretion for medical device reporting (MDR) and correction and removal reporting requirements	1 year	MDR requirements would include 21 U.S.C. 360i(a) through (c) and 21 CFR part 803 Correction and removal requirements include 21 U.S.C. 360i(g) and part 806 (21 CFR part 806)
Stage 2: End of enforcement discretion for most other medical device requirements except those associated with QS and premarket review	2 years	Requirements include registration and listing requirements under 21 U.S.C. 360 and part 807 (excluding subpart E); labeling requirements under 21 U.S.C. 352 and parts 801 and 809, subpart B; and investigational use requirements under 21 U.S.C. 360j(g) and part 812.
Stage 3: End enforcement discretion for quality system (QS) requirements	3 years	FDA would expect compliance with the device Current Good Manufacturing Practice requirements of the QS requirements under 21 U.S.C. 360j(f) and part 820 (21 CFR part 820). For LDTs performed in a single CLIA certified, high complexity laboratory, CLIA regulations will account for some but not all QS requirements. These labs will need to comply with: <ul style="list-style-type: none"> • Design controls under 21

		<p>CFR 820.30;</p> <ul style="list-style-type: none"> ● Purchasing controls (including supplier controls) under 21 CFR 820.50; ● Acceptance activities (receiving, in-process, and finished device acceptance) under 21 CFR 820.80 and 21 CFR 820.86; ● Corrective and preventative actions (CAPA) under 21 CFR 820.100; and ● Records requirements under part 820, subpart M <p>Note: FDA is working on finalizing proposed amendments to 21 CFR part 820 to align with international consensus standards and the phaseout would apply to the new/changes regulations.</p>
<p>Stage 4: Premarket review required for all high risk IVDs unless exempt</p>	<p>3.5 years after but not before October 1, 2027.</p> <p>Note: this is the start of FY28 and MDUFA VI performance goals and procedures would be in effect.</p>	<p>If an application has been submitted, an existing test may remain on the market until FDA completes its review.</p>
<p>Stage 5: Premarket review for all moderate and low risk IVDs required unless exempt</p>	<p>4 years after but not before April 1, 2028</p>	<p>If an application has been submitted, an existing test may remain on the market until FDA completes its review.</p> <p>Laboratories may utilize FDA's Third Party review Program. FDA says it anticipates interest from new Third Party review organizations including existing CLIA accreditation organizations.</p>

* While the final rule will be effective 60 days after publication date, the requirements in each stage and their corresponding timeline will take effect on the date the final phaseout policy is published.

Economic Impact

The White House Office of Information and Regulatory Affairs (OIRA) has determined that this proposed rule is a significant regulatory action under Executive Order 12866 Section 3(f)(1), which means that the proposed rule would have an annual effect on the economy of \$200 million or more or it would adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, territorial, or tribal governments or communities. Also, the Regulatory Flexibility Act requires Agencies to analyze regulatory options to minimize any significant impact of a rule on small entities, and because most facilities affected by this rule are defined as small businesses, the FDA found that the proposed rule will have a significant economic impact on a substantial number of small entities.

The proposed rule argues there will be significant savings from “a reduction in healthcare costs associated with unsafe or ineffective tests, including tests promoted with false or misleading claims, and from therapeutic decisions based on the results of those tests.” The full preliminary analysis of economic impacts is available [here](#).

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