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Sunsetting Enforcement Discretion for CLIA-Certified High-Complexity Tests – FDA Presses Ahead With LDT Final Rule

May 6, 2024

On May 6, 2024, the US Food and Drug Administration (FDA) published its final rule to overhaul FDA's approach for laboratory-developed tests (LDTs). The final rule – issued seven months after the proposed rule was published[1] – amends FDA's regulations to make clear that in vitro diagnostics (IVDs) include LDTs under the Federal Food, Drug, and Cosmetic Act (FDCA). The final rule also sets forth FDA's policy to phase in enforcement of the FDCA requirements for most LDTs. FDA will host a webinar on the final rule on May 14, 2024.

Main elements of the final rule

The final rule amends the definition of "in vitro diagnostic products,"[2] which states that "[t]hese products are devices as defined under section 201(h) of the [FDCA]." To emphasize that the IVD definition includes LDTs, FDA adds to the end of this definition the phrase "including when the manufacturer of these products is a laboratory."[3]

A key component to implementing the final rule is sunsetting FDA's current LDT enforcement discretion policy[4] over the next four years as follows:

Stage	Date effective for most LDTs	FDCA requirements
1	**May 6, 2025**	Medical device reporting (MDR), corrections and removals, and complaint files[5]
2	**May 6, 2026**	Establishment registration and device listing, labeling and investigational use requirements[6]
3	**May 6, 2027**	Quality system (other than complaint files, which have an earlier effective date)
4	**November 6, 2027**	Premarket approval (PMA) for high-risk IVDs offered as LDTs (IVDs in class III or subject to licensure under section 351 of the Public Health Service Act)[7]
5	**May 6, 2028**	Premarket review requirements for low-risk (nonexempt class I devices) and moderate-risk (nonexempt class II devices) IVDs offered as LDTs that require premarket submissions (510(k) or De Novo)[8]

Thus, at the end of four years, FDA will generally expect FDCA compliance for the majority of LDTs, including companion diagnostics used in oncology.[9] But the final rule also outlines certain categories of LDTs for which

FDA will follow a different approach – requiring full and immediate FDCA compliance, continued exercise of full enforcement discretion, or a hybrid approach, namely, not requiring compliance with premarket review and quality system requirements except recordkeeping. This last category includes currently marketed LDTs that were first marketed before May 6, 2024. Such tests will be exempted from the new program, though they will have to comply with requirements other than premarket review and quality system requirements (except recordkeeping). [10]

LDTs carved out from the four-year sunsetting

High-risk tests that must immediately comply with the FDCA and Public Health Service Act	Tests for which FDA will continue to apply existing enforcement discretion policy	Exempted tests for which FDA will not enforce premarket review and quality system requirements except recordkeeping

• Blood donor screening tests, or human cells, tissues, and cellular- and tissue-based product (HCT/P) donor screening tests, required for infectious disease testing,[11] respectively, or tests for the determination of blood group and Rh factors.[12]
• Tests intended for actual or potential emergencies or material threats declared under section 564 of the FDCA.
• Direct-to-consumer tests (i.e., tests intended for consumer use without meaningful involvement by a licensed healthcare professional).
	• 1976-type LDTs, which have certain characteristics that were commonly associated with LDTs offered in 1976, including:
	  ○ Use of manual techniques (without automation) performed by laboratory personnel with specialized expertise.
	  ○ Use of components legally marketed for clinical use.
	  ○ Design, manufacture and use within a single CLIA-certified laboratory that meets the requirements under CLIA for high-complexity testing.
	• Human leukocyte antigen (HLA) tests for transplantation used in histocompatibility laboratories that meet the regulatory requirements under CLIA to perform high-complexity histocompatibility testing, when used in connection with organ, stem cell, and tissue transplantation to perform HLA allele typing, for HLA antibody screening and monitoring, or for conducting real and "virtual" HLA crossmatch testing.
	• Forensic tests (i.e., tests
		• Currently marketed IVDs offered as LDTs that were first marketed prior to the date of issuance of this rule (May 6, 2024), and that are not later modified or modified with minor changes.
		• LDTs manufactured and performed by a laboratory integrated within a healthcare system to meet an unmet need of patients receiving care within the same healthcare system.
		• Nonmolecular antisera LDTs for rare red blood cell (RBC) antigens, where such tests are manufactured and performed in blood establishments, including transfusion services and immunohematology laboratories, and where there is no alternative available to meet the patient's need for a compatible blood transfusion.

intended solely for law enforcement purposes).

- Public health surveillance tests, which are intended solely for use on systematically collected samples for analysis and interpretation of health data in connection with disease prevention and control, and test results are not reported to patients or their healthcare providers.
- Tests manufactured and performed within the Veterans Health Administration (VHA) or the Department of Defense (DoD).

In addition, FDA does not intend to enforce premarket review requirements with respect to LDTs approved by the New York State Clinical Laboratory Evaluation Program, although these tests are still subject to requirements other than premarket review requirements.

Moreover, along with this final rule, FDA issued contemporaneously two new draft guidance documents to outline FDA's policy on how it will approach tests responding to an "emergent situation," such as the outbreak of an infectious disease or other public health emergencies.

A word about enforcement discretion

Enforcement discretion is not the same as a full carve out from FDA's oversight, as we saw with certain categories of software in the 21st Century Cures Act. Thus, for all LDTs subject to enforcement discretion, it is important to remember that FDA retains jurisdiction over the products as medical devices, particularly in light of the final rule's changes to the IVD definition. For a product subject to enforcement discretion, FDA may enforce the FDCA and pursue enforcement action for violations of the FDCA at any time it deems appropriate.

What comes next?

This final rule implements some of the policies the agency already had in place during the COVID-19 pandemic, such as requiring immediate compliance with the FDCA for tests intended for actual or potential emergencies or material threats declared under section 564 of the FDCA, and the continued exercise of enforcement discretion with respect to premarket review requirements for LDTs approved by the New York State Clinical Laboratory Evaluation Program. This enforcement discretion approach for the state of New York begs the question of whether other states were considered for this policy, or entities approved by other state clinical laboratory evaluation programs will challenge the rule.

As discussed in our November 2023 alert on the proposed rule, for this and other reasons, we anticipate litigation as FDA begins to enforce this new rule. Interestingly, the timing of this new rule coincides well with FDA's rollout of the new Quality Management System Regulation (QMSR), which becomes effective on February 2, 2026. Therefore, LDT developers can focus on aligning their quality systems to the QMSR, without the uncertainty of whether it will be in effect when LDTs and LDT developers will be expected to comply with the quality system regulations.

Cooley senior regulatory analyst Kelly Marco also contributed to this alert.

Notes

1. See Medical Devices; Laboratory Developed Tests, 88 FR at 68006 (October 3, 2023).
2. 21 CFR § 809.3(a).
3. Id.
4. This policy applies to IVDs that are manufactured and offered as LDTs by laboratories that are certified under the Clinical Laboratory Improvement Amendments (CLIA), meet the regulatory requirements under CLIA to perform high-complexity testing, and used within such laboratories.
5. See 21 CFR § 820.198.
6. See 21 USC § 360 and 21 CFR Part 807 (establishment registration and device listing requirements); 21 USC § 352 and 21 CFR Parts 801 and 809 (labeling requirements); and 21 USC § 360j(g) and 21 CFR Part 812 (investigational use requirements).
7. LDTs may continue to be offered after this date while a PMA is under review by FDA.
8. LDTs may continue to be offered after this date while a 510(k) or De Novo is under review by FDA.
9. See FDA's June 2023 guidance, Oncology Drug Products Used with Certain In Vitro Diagnostics: Pilot Program.
10. 21 CFR, Part 820, Subpart M.
11. 21 CFR §§ 610.40, 1271.80(c).
12. 21 CFR § 640.5.
13. With the amendment, 21 CFR § 809.3(a) is amended as follows: "These products are devices as defined in section 201(h) of the [FDCA] 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**." (emphasis added)

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Key Contacts

Sonia Nath **Washington, DC**	**snath@cooley.com** **+1 202 776 2120**
Son Nguyen Washington, DC	snguyen@cooley.com +1 202 728 7100

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