King & Spalding

Client Alert

FDA and Life Sciences

JULY 5, 2024

For more information, contact:

Lisa Dwyer
+1 202 626 2393
ldwyer@kslaw.com

Seth Lundy
+1 202 626 2924
slundy@kslaw.com

Jessica Ringel
+1 202 626 9259
jringel@kslaw.com

Jeffrey Shapiro
+1 202 626 2927
jshapiro@kslaw.com

Brian Bohnenkamp
+1 202 626 5413
bbohnenkamp@kslaw.com

Elaine Tseng
+1 415 318 1240
etseng@kslaw.com

McKenzie Cato
+1 202 626 9270
mcato@kslaw.com

King & Spalding

Washington, D.C.
1700 Pennsylvania Avenue, NW
Suite 900
Washington, D.C. 20006
Tel. +1 202 737 0500

The LDT Final Rule Goes Into Effect Today

The highly anticipated laboratory developed test final rule ("LDT Final Rule"), which was published in the Federal Register on May 6, 2024, goes into effect today—60 days after the publication date (see our Client Alert analyzing the final rule).

While the first compliance date for the Food and Drug Administration's ("FDA's") phase-out of its enforcement discretion policy for LDTs is not until May 6, 2025, as of today, all LDTs are, by regulation, considered by FDA to be medical devices. As a result, there are activities that those laboratories FDA considers to be "manufacturing" LDTs should consider starting as soon as possible, in preparation for the first compliance date. Additionally, there are a number of important non-FDA federal and state requirements applicable to medical device manufacturers that now could be applied to, and enforced against, LDT manufacturers, some of which start immediately. For example, as a general matter, manufacturers of Medicare-covered medical devices are subject to the Sunshine Act and similar state compliance and transparency laws.

OVERVIEW OF LDT FINAL RULE AND PHASE-OUT POLICY

The LDT Final Rule revises the definition of "in vitro diagnostic products" at 21 C.F.R. § 809.3(a) to mean, "devices as defined in section 201(h)(1) of the Federal Food, Drug, and Cosmetic Act . . . including when the manufacturer of these products is a laboratory" (new language underlined). This revision has the effect of ending a long-standing policy of "enforcement discretion" for LDTs, in which FDA contends that it opted not to apply the Federal Food, Drug, and Cosmetic Act ("FDCA") and implementing device regulations to laboratory tests designed, manufactured, and used within a single laboratory.

The LDT Final Rule includes the following "phase-out" policy, in which FDA will gradually apply the statutory and regulatory device pre-market and post-market requirements to LDTs over a period of four years:

- **Stage 1:** Beginning May 6, 2025, FDA will enforce compliance with Medical Device Reporting ("MDR") requirements under 21 C.F.R. Part 803, correction and removal reporting requirements under 21 C.F.R. Part 806, and complaint handling requirements under 21 C.F.R. § 820.198.
- **Stage 2:** Beginning May 6, 2026, FDA will enforce compliance with requirements not covered during other stages of the phase-out policy, including registration and listing requirements under 21 C.F.R. Parts 607 and 807, labeling requirements under 21 C.F.R. Parts 801 and 809, and investigational use requirements under 21 C.F.R. Part 812.
- **Stage 3:** Beginning May 6, 2027, FDA will enforce compliance with 21 C.F.R. Part 820 (currently, the Quality System Regulation ("QSR"), but the Quality Management System Regulation ("QMSR") by the time Stage 3 begins), except for complaint handling (required in Stage 1).
- **Stage 4:** Beginning November 6, 2027, FDA will enforce compliance with pre-market review requirements for high-risk in vitro diagnostics ("IVDs") offered as LDTs (i.e., Class III devices).
- **Stage 5:** Beginning May 6, 2028, FDA will enforce compliance with pre-market review requirements for moderate-risk and low-risk IVDs offered as LDTs that require pre-market submissions (i.e., non-510(k)-exempt Class I and II devices).

The LDT Final Rule includes several significant carve-outs. FDA has stated that it intends to exercise partial enforcement discretion, and not enforce pre-market review and QSR/QMSR compliance (except for recordkeeping requirements under 21 C.F.R. Part 820, Subpart M), for currently marketed LDTs that were first marketed prior to issuance of the LDT Final Rule. These "grandfathered" LDTs still will be required to comply with MDR requirements, reports of corrections and removals, registration and listing requirements, and labeling requirements. In other words, FDA takes the position that the "grandfathered" tests still will need to comply with Stage 1 and Stage 2.

FDA has indicated that it intends to exercise partial enforcement discretion for "grandfathered" tests unless and until certain significant modifications are made to the LDTs. If a modification changes the indications for use, alters the operating principle, includes significantly different technology, or adversely changes the performance or safety specifications, then FDA has stated that it intends to require pre-market review and QSR/QMSR compliance for the modified test in accordance with the requirements in Stage 3, Stage 4, and Stage 5.

Further, the following categories of tests will be carved out from both pre-market review and compliance with the QSR/QMSR, except for records requirements under 21 C.F.R. Part 820, Subpart M:

- Tests 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.
- Non-molecular antisera LDTs for rare red blood cell antigens, when such tests are manufactured and performed by blood establishments, including transfusion services and immunohematology laboratories, and when there is no alternative IVD available to meet the patient's need for a compatible blood transfusion.

FDA has indicated that, like the "grandfathered" tests, these tests also will be subject to the requirements in Stage 1 and Stage 2.

In addition, FDA has taken the position that it will not enforce pre-market review requirements for LDTs that have been approved by New York State's Clinical Laboratory Evaluation Program. For these LDTs, all other applicable requirements under the FDCA and device regulations will apply. In other words, these tests will have to comply with the requirements in Stage 1, Stage 2, and Stage 3.

Finally, FDA has indicated that it will continue its general enforcement discretion policy, and will not enforce pre-market or post-market regulatory requirements, for the following categories of LDTs:

- "1976-Type LDTs," which are tests that share the following characteristics with the tests offered in 1976 (at the time of enactment of the Medical Device Amendments of 1976): (1) use of manual techniques, without automation, performed by laboratory personnel with specialized expertise; (2) use of components legally marketed for clinical use; and (3) design, manufacture, and use within a single laboratory certified in accordance with the Clinical Laboratory Improvement Amendments ("CLIA") for high-complexity testing.
- Human leukocyte antigen tests for organ, stem cell, and tissue transplantation that are designed, manufactured, and used within a single CLIA-certified laboratory that meets requirements to perform high-complexity histocompatibility testing.
- Tests intended solely for forensic (i.e., law enforcement) purposes.
- Tests manufactured and performed within the Department of Defense or Veterans Health Administration.

Notably, FDA has suggested that these tests will not have to comply with the requirements in Stage 1, Stage 2, Stage 3, Stage 4, or Stage 5.

The phase-out policy, compliance dates, and carve-outs are all outlined in a Small Entity Compliance Guide published by FDA on June 25, 2024.

WHAT SHOULD LABORATORIES DO STARTING TODAY TO PREPARE FOR FDCA COMPLIANCE?

Due to FDA's planned phase-out policy, FDA has indicated that it intends to enforce its new device requirements gradually over a four-year period. Additionally, there are several categories of LDTs that are exempt, in full or in part, from pre-market and/or post-market device requirements. We recommend that, even though the first compliance date is not until 2025, laboratories should promptly undertake an assessment of all LDTs designed and run at the laboratory and create a matrix of LDTs that are subject to the LDT Final Rule, the FDA requirements that will apply, and when compliance is phased in.

This assessment process could consist of the following steps:

1. **Create a complete list of all LDTs designed and run at the laboratory.** Individual LDTs should be identified, not only by the test methodology and analyte, but also the clinical application. From an FDA regulatory perspective, medical devices are identified by their intended use (e.g., the disease or condition that is diagnosed with the test) *and* by the technological features of the device (e.g., principles of operation, reagents, analytes, and instruments).
2. **For each test, determine whether it is within the scope of the LDT Final Rule.** As outlined above, FDA has incorporated a number of carve-outs to the LDT Final Rule (e.g., non-molecular antisera LDTs for rare red blood cell antigens). Identify whether any of the laboratory's LDTs fall into one of these categories. If so, determine the scope of the enforcement discretion that applies, and which aspects of pre-market and post-market requirements are still required (i.e., which stages of requirements will apply to the test).

3. **Determine the compliance schedule for each LDT subject to the LDT Final Rule.** Stages 1-3 are the same for all LDTs subject to the rule. However, the compliance dates for pre-market review requirements (i.e., Stages 4 and 5) vary depending on whether the LDT is considered a Class I, II, or III device. To determine the classification of each LDT, laboratories should review FDA classification regulations and existing FDA-cleared and approved devices to determine how FDA classifies that type of laboratory test. Laboratories should also monitor FDA's planned down-classification of most Class III diagnostic tests into Class II, as announced by FDA on January 31, 2024.
4. **For currently marketed LDTs, create a process for tracking modifications to the test.** LDTs first marketed before the LDT Final Rule was issued (May 6, 2024) are exempt from pre-market review and QSR/QMSR compliance (except for recordkeeping requirements under 21 C.F.R. Part 820, Subpart M), *only until* a significant modification is made to the test. A significant modification is a change to the indications for use, a change to the operating principle, inclusion of a significantly different technology, or an adverse change to the performance or safety specifications. Laboratories should have a process in place for tracking modifications to determine when a significant modification triggers pre-market review and QSR/QMSR compliance.

LDT MANUFACTURERS MAY NOW BE SUBJECT TO OTHER FEDERAL AND STATE REQUIREMENTS APPLICABLE TO DEVICE MANUFACTURERS

Though there is a gradual phase-in of FDA compliance, laboratories (including hospital and physician-office labs) should not be under the misimpression that the same necessarily is true for all federal and state requirements. As of today, FDA considers LDTs to be FDA-regulated medical devices, even though FDA will not enforce all pre-market and post-market requirements right away. FDA's position implies that non-FDA federal and state regulatory requirements applicable to medical device manufacturers may apply to laboratories starting today and could be soon enforced. Laboratories should assess the scope of their obligations under these requirements based on this change in FDA's treatment of LDTs. Many of these requirements also have exceptions and carve-outs that laboratories should consider in analyzing the impact on their activities and operations.

Specifically, many medical device manufacturers are generally subject to federal and state transparency, compliance, and licensing laws and regulations. The Physician Payments Sunshine Act ("Sunshine Act"), which was signed into law in 2010 as part of the Affordable Care Act, requires manufacturers or medical devices that are covered by federal health care programs and require FDA premarket notification or approval to comply with specific transparency requirements with respect to payments and transfers of value to licensed prescribers and teaching hospitals. See, https://www.cms.gov/priorities/key-initiatives/open-payments. Certain entities, such as hospitals, hospital-based pharmacies, and laboratories are exempt from the Sunshine Act's requirements if they "manufacture a covered product solely for use by or within the entity itself or by an entity's own patients," but that carve-out may likely not apply to most LDT manufacturers. Applicable manufacturers subject to the Sunshine Act that derive less than ten percent (10%) of their revenues from covered medical devices (e.g., LDTs) do not need to report all payments or transfers of value, but only those that related to the covered medical devices. In addition, Connecticut, Massachusetts, and Vermont have similar reporting requirements for payments or transfers of value made to recipients licensed by their states (even if the payment occurs outside of the state), and not all of the federal exemptions under the Sunshine Act apply.

Further, California, Connecticut, Massachusetts, and Nevada require most medical device manufacturers to establish and maintain compliance programs. Some of these laws specifically require that those programs be consistent with the PhRMA Code or AdvaMed Code, or and the Department of Health and Human Services Office of the Inspector General ("HHS-OIG") Compliance Program Guidelines. Vermont also requires medical device manufacturers to comply with a

stringent ban on gifts or other items of value provided to Vermont healthcare providers. Additionally, California requires medical device manufacturers to set an annual spending limit on transfers of value to licensed California prescribers. All of these laws have exclusions, exceptions, and threshold applicability requirements that laboratories should assess to determine the potential scale and scope of the impact they could have on their activities.

Many states also have unique licensing requirements applicable to medical devices, which require manufacturers and/or distributors to obtain licenses for the manufacturing and/or distribution of devices to patients in the state, including when a medical device is transported from one state to another. In some states, these licensing requirements only apply to in-state facilities, but some states require out-of-state facilities to obtain licenses. Determining which state licensing requirements apply and completing applications (and sometimes state inspections) to obtain and maintain state licenses can be a time-consuming and resource-intensive process. Further, given the uniqueness of LDTs as medical devices, state licensing authorities may be uncertain as to how their rules will apply.

CONCLUSION: PREPARATION IS KEY

Today's effective date of the LDT Final Rule impacts the legal analysis as to the applicability of many federal and state requirements for laboratories. To avoid compliance issues, with either federal or state regulators, laboratories should act now to determine what requirements may apply to their LDTs, the applicable compliance dates, and the modifications to devices that could trigger different requirements. In addition, laboratories should understand that FDA considers their LDTs to be FDA-regulated medical devices today, even if FDA is not yet enforcing pre-market and/or post-market requirements. In the case of the Sunshine Act and the many potentially applicable state laws, manufacturers of LDTs, which are now considered by FDA to be medical devices, will have to conduct a careful analysis to understand whether any or all of these laws and regulations may now apply. The analysis may depend on the specific structure and location of the LDT provider, among other key facts. King & Spalding has deep expertise in FDA regulatory and federal and state healthcare compliance and is glad to assist clients with assessing any issues.