

FDA Takes a Bold Step Toward Laboratory Developed Test Regulation: How Labs and IVD Manufacturers Should Prepare for the Future

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On July 31, 2014, the U.S. Food and Drug Administration ("FDA") announced plans to regulate laboratory developed tests ("LDTs"). In this Client Alert, we explore FDA's proposed regulatory framework for LDTs and discuss some of the many issues that both laboratories and traditional *in vitro* diagnostic ("IVD") manufacturers should address in the months and years to come.

I. The Current State of Lab Diagnostic Regulation

Currently, diagnostic tests used by clinical laboratories in the United States are developed and introduced into the clinical environment in one of two ways:

1. The IVD Path. IVDs are medical devices (tests) that are intended to aid in diagnosing disease. These tests are designed, manufactured, and sold to clinical laboratories by FDA-regulated manufacturers. IVD manufacturers have been subject to extensive FDA requirements for—
 - a. product design and clinical testing to establish the safety and effectiveness of the tests;
 - b. premarket submissions, which FDA reviews to determine whether it will allow an IVD to be marketed in the United States;
 - c. registering manufacturing sites and listing IVDs manufactured at those sites with FDA;
 - d. "Quality Systems" to ensure that IVDs are manufactured properly;
 - e. post-market safety reporting in the form of medical device reports ("MDRs") to FDA disclosing serious injuries and malfunctions associated with the device;

- f. reporting voluntary removals and correction (e.g., letters informing physicians that test results were incorrect due to problems with the IVD);
 - g. labeling and promotional claims; and
 - h. inspections to ensure compliance with a. through g. above.
2. The LDT Path. An LDT is a test designed and manufactured by a single laboratory for in-house use. An LDT is functionally equivalent to an IVD—it provides diagnostic test results relied upon by physicians and patients. However, these tests are not subject to any of the above FDA requirements for IVDs; they are instead subject to less stringent requirements under the Clinical Laboratory Improvement Amendments of 1988 (“CLIA”) on self-validation of LDTs, and inspections for performance of laboratory services by the Centers for Medicare & Medicaid Services.

FDA long declared that it had jurisdiction to regulate LDTs,¹ but chose, as a matter of enforcement discretion, not to assert its authority over LDTs. On July 31, 2014, FDA announced its intent to change course when it submitted its draft framework for LDT regulation to Congress.² This procedural step toward regulating LDTs is required under Section 1143 of the Food and Drug Administration Safety and Innovation Act (“FDASIA”).³ Per FDASIA, FDA may now move forward with issuing its draft framework for public comment 60 days after the notification—September 30, 2014, or later.

II. FDA’s Proposed Framework for LDT Regulation

FDA has proposed a framework for LDT regulation that would require many LDTs to meet current IVD requirements. The system would be phased in over the course of several years,

¹ See, e.g., FDA Response to Citizen Petition Submitted by Hyman Phelps & McNamara, FDA Docket No. 92P-0405, PDN1 (Aug. 12, 1998) (stating that LDTs are medical devices but maintaining FDA’s enforcement discretion); U.S. FOOD & DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY, CLINICAL LABORATORIES, AND FDA CITIZEN PETITION RESPONSE, DOCKET NO. 92-P-0405 (“The Commissioner of Food and Drugs may regulate assays developed by clinical reference laboratories strictly for in-house use as medical devices.”) (August 12, 1998). This jurisdictional claim has not gone undisputed—clinical laboratories have long argued that LDTs are not products (articles) regulated under the Food, Drug, and Cosmetic Act, but are laboratory “services” regulated under the CLIA. Laboratories have also argued that LDTs are not in “commercial distribution.” For a discussion of these and other issues, see FDA Response to Citizen Petition Submitted by American Clinical Laboratory Association, Docket No. FDA-2013-P-0667-0008 (July 31, 2014), and Citizen Petition Submitted by American Clinical Laboratory Association, Docket No. FDA-2013-P-0667-0001 (June 4, 2013).

² U.S. FOOD & DRUG ADMIN., ANTICIPATED DETAILS OF THE DRAFT GUIDANCE FOR INDUSTRY, FOOD AND DRUG ADMINISTRATION STAFF, AND CLINICAL LABORATORIES: FRAMEWORK FOR REGULATORY OVERSIGHT OF LABORATORY DEVELOPED TESTS (LDTs) (2014) (hereinafter “LDT FRAMEWORK”), *available at* <http://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/UCM407409.pdf>; U.S. FOOD & DRUG ADMIN., ANTICIPATED DETAILS OF THE DRAFT GUIDANCE FOR INDUSTRY, FOOD AND DRUG ADMINISTRATION STAFF, AND CLINICAL LABORATORIES: FDA NOTIFICATION AND MEDICAL DEVICE REPORTING FOR LABORATORY DEVELOPED TESTS (LDTs) (2014) (hereinafter “LDT REPORTING GUIDANCE”), *available at* <http://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/UCM407409.pdf>.

³ Food and Drug Administration Safety and Innovation Act of 2012 § 1143, Pub. L. No. 112-144, 126 Stat. 993, 1130.

during which time laboratories would continue to enjoy enforcement discretion, provided that they take action in accordance with FDA timelines. The different elements of the regulatory rollout are provided below. Also, keep in mind, the framework could change significantly from the proposed version to the final version based on comments that FDA receives from stakeholders, so none of the following is “written in stone.”

A. Notifications

LDT regulation would start with a requirement that laboratories notify FDA of the LDTs that they perform within six months of the guidance’s finalization.⁴ The notification must include the information described in Table 1.

1. Laboratory name and contact e-mail address	8. Indicated patient population
2. Test name	9. Statement of whether the patient population includes pediatric patients (<21 years old)
3. Monthly test volume	10. Sample type (e.g., serum, saliva)
4. Intended use	11. Test method(s) (e.g., mass spectrometry, immunoassay)
5. Category of use (e.g., screening, diagnosis)	12. Statement of whether the test is a modification of an FDA cleared/approved IVD, and summary of modifications
6. Means of measurement or detection (i.e., analyte, biomarker)	
7. Disease/Condition for which the diagnostic device is indicated (i.e., cardiovascular disease, diabetes, breast cancer, etc.)	

After the final guidance has been published for six months, and during the enforcement discretion phase, laboratories would be required to notify FDA *prior* to offering a new LDT.⁶ Notification is expected to occur once for each LDT, although if significant changes are made to an LDT, additional notification should be provided.⁷ In addition, when a laboratory makes a significant change to the marketed intended use of an LDT for which it has previously provided notification, the LDT will be considered a “new” LDT.⁸

The notification process may be used in lieu of registration and listing requirements until the applicant submits a premarket application (“PMA”) or receives a 510(k) clearance for an LDT.⁹ Prior to listing the device, it would continue to be exempt from the medical device excise tax, a 2.3 percent tax that applies to all medical device sales, including diagnostics.¹⁰ Once the LDT is listed, it may become subject to the tax, though the exact method for applying the tax to LDTs that are used solely at the originating laboratory remains unclear.

⁴ See LDT FRAMEWORK, *supra* note 2, at 16.

⁵ The reporting elements in Table 1 are set forth in LDT REPORTING GUIDANCE, *supra* note 2, app. A, at 21.

⁶ See LDT FRAMEWORK, *supra* note 2, at 16-17.

⁷ *Id.* at 17.

⁸ *Id.* at 16-17.

⁹ *Id.* at 17.

¹⁰ Patient Protection and Affordable Care Act of 2010 § 9009, Pub. L. No. 111-148, 124 Stat. 119, 862 (codified at 26 U.S.C. § 4191 (2012)).

B. MDR Reporting

Also, six months after the finalization of guidance, laboratories must begin to submit MDRs for their LDTs.¹¹ An MDR must be submitted to FDA no later than 30 calendar days after the day that the lab receives or otherwise becomes aware of information that reasonably suggests that the LDT:

- (1) may have caused or contributed to a death or serious injury; or
- (2) has malfunctioned and this device or a similar device that the lab markets would likely cause or contribute to a death or serious injury, if the malfunction were to recur.¹²

FDA interprets the reporting standards very liberally and has a “when in doubt, report” philosophy. For diagnostics, FDA has frequently said that most events where a product problem has led to a treatment change must be reported.¹³ Many companies also report if additional testing or retesting is needed. In addition, where an event has potentially affected multiple patients, investigations of each potentially inaccurate result and reports for each patient may be required.¹⁴

MDR reporting can also require considerable resources. For example, companies often have dedicated employees or centers that investigate complaints to determine reportability. Often, input from medical professionals may be needed to assess the potential for a malfunction event to cause or contribute to a serious injury.

C. Premarket Submissions, Quality Systems, and Registration and Listing

After notification and MDR requirements have come into effect, additional regulations will be phased in, starting with the highest-risk (Class III) tests and followed by moderate-risk (Class II) tests,¹⁵ as described in Table 2 below.¹⁶ Most of these tests will eventually require premarket submissions, as well as manufacturing procedures that comply with FDA’s

¹¹ See LDT FRAMEWORK, *supra* note 2, at 18.

¹² See LDT REPORTING GUIDANCE, *supra* note 2, at 9.

¹³ See U.S. FOOD & DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY AND FOOD AND DRUG ADMINISTRATION STAFF: MEDICAL DEVICE REPORTING FOR MANUFACTURERS §§ 2.14, 4.4 (2013), *available at* <http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm359130.htm#s4-4> (stating that a malfunction is reportable if “[t]he malfunction results in the failure of the device to perform its essential function and *compromises the device’s therapeutic, monitoring or diagnostic effectiveness*, which could cause or contribute to a death or serious injury or other significant adverse device experiences required by regulation. (The essential function of a device refers not only to the device’s labeled use, but also to any use widely prescribed within the practice of medicine.)” (emphasis added)).

¹⁴ See Instructions for Completing Form FDA 3500A at iii (2013), *available at* <http://www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM387002.pdf>.

¹⁵ See LDT FRAMEWORK, *supra* note 2, at 22-25. Examples of Class III diagnostics include bladder cancer detection and monitoring using fluorescence in situ hybridization reagents, a HPV assay using DNA detection, and a hepatitis B test using antibody immunoglobulin M detection. Examples of Class II diagnostics include over-the-counter glucose monitoring systems, influenza A and B nucleic acid assays, and vitamin D tests.

¹⁶ Low-risk devices will not be required to make premarket submissions or, apparently, come into compliance with other regulatory requirements, such as quality systems or registration and listing.

Quality System requirements. For LDTs that have the same intended use as IVDs, the risk classification can be determined by FDA precedents and existing classification regulations.¹⁷ To handle classification of novel tests, FDA plans to develop guidance that outlines its thinking, presumably based, in large part, on the notifications and MDR reports that it receives during the initial phase.¹⁸

A PMA submission or 510(k) clearance also triggers additional requirements for LDTs. Once a laboratory submits its first PMA or 510(k) for an LDT, it will become subject to registration and listing requirements.¹⁹ In addition, once a laboratory submits a PMA, or receives a clearance for a 510(k), it must come into compliance with Quality System requirements.²⁰

Date	Phase of Regulatory Rollout
On or after Sept. 30, 2014	FDA may issue a draft guidance for public comment
TBD	After considering comments, FDA will issue a final guidance
Within 6 months of final guidance	<ul style="list-style-type: none"> • Each clinical laboratory must notify FDA of LDTs being used at the facility • Laboratories must start submitting medical device reports (“MDRs”); these are reports of certain injuries and malfunctions associated with diagnostics
Within 12 months	<p>A laboratory must submit a premarket submission for any:</p> <ul style="list-style-type: none"> • LDTs with the same intended use as cleared/approved companion diagnostics • LDTs with the same intended use as a Class III device • Certain LDTs used to determine the safety/efficacy of blood or blood products <p>Quality System requirements must be met at the time of premarket application (“PMA”) submission or at the time of 510(k) clearance, depending on the applicable premarket submission</p>
Within 18 months	FDA will release a draft guidance describing its thinking on LDTs that do not fall within existing IVD classifications
Within 2 years	FDA will develop a priority list for regulating the remaining high-risk devices
Within 4 years	FDA will develop its thinking on priorities for moderate-risk devices
Within 5 years	<p>All labs must have submitted applications for remaining high-risk (Class III) diagnostics</p> <p>Quality System requirements must be met at the time of PMA submissions</p>

¹⁷ See LDT FRAMEWORK, *supra* note 2, at 25.

¹⁸ See *id.*

¹⁹ See *id.* at 17.

²⁰ See *id.* at 28.

	Registration and listing requirements become applicable with the <i>first</i> PMA submission
Within 9 years	All labs must be in compliance for moderate-risk (Class II) diagnostics Quality System requirements must be met at the time of 510(k) clearance Registration and listing requirements become applicable with the <i>first</i> 510(k) submission

D. Continued Enforcement Discretion

Although IVD requirements will eventually apply to the majority of LDTs, certain types of LDTs will continue to enjoy some level of enforcement discretion after the phase-in period of FDA regulation is complete. For example, LDTs used solely for law enforcement and certain transplantation tests will be exempt from all FDA requirements.²¹ LDTs for rare diseases that are used on fewer than 4,000 patients per year will be exempt from premarket submission requirements.²² Also, traditional LDTs (the kinds of lower-tech tests that would have existed when FDA first developed its LDT enforcement discretion policy in the 1970s)²³ and LDTs for unmet medical needs²⁴ will continue to be exempt from premarket submission requirements depending on their alignment with certain factors outlined in the guidance and summarized in Table 3, below.

Type of LDT	Enforcement Discretion
LDTs used solely for forensic (law enforcement) purposes	Exempt from all FDA requirements (including notifications and MDRs)
LDTs used in CLIA-certified high-complexity histocompatibility labs for transplantation	Exempt from all FDA requirements (including notifications and MDRs)
LDTs for rare diseases	If tests would be used on fewer than 4,000 patients per year, such tests would be exempt from premarket clearance or approval
Traditional LDTs	Premarket clearance or approval is not required for traditional LDTs. To determine if a test is a traditional LDT, FDA will consider the following factors that weigh <i>in favor</i> of continued enforcement discretion: (1) whether the device meets the definition of an “LDT” in the LDT framework guidance (i.e., a device designed, manufactured, and used by a single laboratory);

²¹ *Id.* at 15-16.

²² *Id.* at 19-20.

²³ *Id.* at 20-21.

²⁴ *Id.* at 21-22.

	<p>(2) whether the LDT is both manufactured and used by a health care facility laboratory (e.g., a hospital or clinic laboratory) for a patient who is being diagnosed and/or treated at that same health care facility or within the facility's health care system;</p> <p>(3) whether the LDT is comprised of only components and instruments that are FDA-authorized for clinical use (e.g., analyte-specific reagents); and</p> <p>(4) whether the LDT is interpreted by qualified laboratory professionals, without the use of automated instrumentation or software for interpretation</p>
LDTs for an unmet clinical need	<p>Premarket clearance or approval is not required for tests that serve unmet medical needs. To determine if a test is for an unmet clinical need, FDA will consider the following factors:</p> <p>(1) whether the device meets the definition of an "LDT" in this guidance (i.e., a device designed, manufactured, and used by a single laboratory);</p> <p>(2) whether there is no FDA-cleared or approved IVD available for that specific intended use; and</p> <p>(3) whether the LDT is both manufactured and used by a health care facility laboratory (e.g., a hospital or clinic laboratory) for a patient who is being diagnosed and/or treated at that same health care facility or within that facility's health care system</p>

Since premarket submission or clearance makes the LDT developer subject to registration and listing requirements and Quality System requirements, laboratories that *exclusively* make tests subject to enforcement discretion (i.e., "low risk" tests) can potentially avoid considerable regulatory burdens, annual FDA registration fees, and the 2.3 percent medical device excise tax. This consequence could, potentially, have a huge impact on laboratory business models.

In addition, FDA's continued use of enforcement discretion provides opportunities for IVD manufacturers to press for reforms to liberalize the standards for IVDs. For example, the development of diagnostics for rare devices has been stifled by the many requirements imposed by humanitarian use device ("HUD") requirements. HUDs are subject to cost recovery provisions that prevent profit on the sale of rare disease diagnostics,²⁵ continued institutional review board ("IRB") oversight,²⁶ the medical device tax (as listed devices),²⁷ premarket submission requirements,²⁸ registration and listing requirements,²⁹ and Quality System requirements. In addition, IVD manufacturers often need to navigate a difficult

²⁵ 21 C.F.R. § 814.104(b)(5) (2014).

²⁶ *Id.* § 814.124.

²⁷ See Patient Protection and Affordable Care Act of 2010 § 9009, Pub. L. No. 111-148, 124 Stat. 119, 862 (codified at 26 U.S.C. § 4191 (2012)); see also T.D. 9604, I.R.B.-2012-52 (Dec. 27, 2012).

²⁸ 21 C.F.R. §§ 814.104, .108, .114, .116.

²⁹ *Id.* § 814.126.

process to demonstrate to FDA's satisfaction that a test is only intended for use in populations of less than 4,000 patients prior to submitting an application. Given that IVD manufacturers have the expertise for developing tests for rare diseases that is at least on par with laboratories, there is no strong reason to impose continued restrictions on IVD development. However, some language in the draft framework suggests that IVD reform along these lines might not be part of FDA's plans.³⁰

E. Current Enforcement

FDA also reminds the regulated community that (1) direct-to-consumer ("DTC") tests,³¹ and (2) "LDTs for Infectious Agents (donor screening tests) used in blood and blood components and HCT/Ps" are currently regulated by FDA and, thus, are not subject to enforcement discretion, even if they otherwise meet the definition of an "LDT."³²

F. Misbranding, Adulteration, and Other Requirements

Although left primarily to a footnote, FDA indicates that it will apply "general controls" not specifically accounted for in the proposed guidance documents to all LDTs.³³ Important general controls not covered by enforcement discretion include misbranding provisions (which give FDA its authority over device "labeling," including promotion), adulteration provisions (to ensure quality), and records and reports (e.g., recordkeeping, reports of recalls conducted to reduce risk to health).³⁴ These requirements could have impacts on all LDTs, although when they will begin to apply is unclear.

III. Preparing for FDA Regulation

Clinical laboratories that are currently using LDTs should take the following actions now to better position themselves for the upcoming LDT regulations:

1. Get familiar with the concept of "intended use." Under the Food, Drug, and Cosmetic Act, an LDT is defined by its *intended use*. In general, labs can expect intended use will be determined primarily by statements (e.g., promotion) describing what the test is meant for, as well as the circumstances surrounding the product's marketing. However, navigating the intricacies of intended use can be a complicated legal exercise.

Understanding this concept is important not only to complying with FDA requirements, but also to avoiding "off-label" promotion (promotion of tests for

³⁰ See, e.g., LDT FRAMEWORK, *supra* note 2, at 20. The cited note states that FDA will consider whether an LDT is manufactured and used by a health care facility laboratory for a patient diagnosed in that facility and that such combined manufacture and use "ensures common responsibility for patient outcomes that may result from the clinical decisions informed by those device results." The focus on health care facilities suggests that reforms for IVD manufacturers are not in the works, though the argument for restricting reforms is not a strong one—manufacturers of diagnostics, whether a health care facility or a traditional IVD manufacturer, may bear legal responsibility for results that inform clinical decisions.

³¹ See *id.* at 4 n.4.

³² See *id.* at 29, Appendix A.

³³ See *id.* at 11 n.14.

³⁴ *Id.*

unapproved/uncleared uses) that can lead to misbranding enforcement and False Claims Act (“FCA”) violations with significant penalties.

2. Inventory current tests based on their intended use(s), and assess both the revenue that they generate (to help assess their value to your business) and how they may be regulated under the proposed FDA framework. Are they likely to be high-, moderate-, or low-risk devices? Are they tests for rare diseases or unmet medical needs that would continue to be subject to FDA enforcement discretion on premarket submissions? Are there ways to modify the product’s intended use to keep it on one side of regulation or the other? These are all important, and potentially complex, legal analyses that can take time to work through, so it is crucial to start sooner rather than later.

Also, as discussed above, under the proposed regulatory framework, a laboratory might be able to avoid premarket submissions, Quality System requirements, registration and listing, and the 2.3 percent medical device tax, if it exclusively produces tests that are either low risk or remain subject to enforcement discretion. Thus, a laboratory should consider what proportion of its business is derived for those kinds of tests and evaluate the value of a shift of its current business model to minimize regulatory disruption and costs.

3. Conduct a gap assessment to determine what would be required to bring LDTs and your laboratory into compliance with FDA regulations. What is required to develop an MDR system and an FDA-compliant quality system? What are likely requirements for premarket submissions? How much will it cost to create a system to manage product advertising and promotion in alignment with FDA expectations? How long will it take to come into compliance? Understanding the upfront and on-going expenses of operating in the FDA-regulated environment, and the time to come into compliance, is crucial to grasping how regulation may affect your business.
4. Prepare comments on FDA’s proposed framework. On or after September 30, 2014, FDA will begin to solicit comments on its LDT framework from the public. Comment periods often last a minimum of 60 days but could last significantly longer. FDA has a history of being very responsive to comments that offer reasonable changes to its proposed guidance and regulation, especially where a good case for the public health is made, and they are based in solid law, policy, and science.

IV. Issues for Both Laboratories and IVD Manufacturers to Consider

Laboratories will clearly be impacted by FDA’s regulation of LDTs, but so will IVD manufacturers that sell instrumentation and reagents to labs, along with manufacturers that compete against LDTs. The proposed guidance raises a number of issues on which labs and manufacturers may want to comment during the comment period. Note that FDA values specific comments from individually affected stakeholders in addition to comments from trade associations. Plan to submit your own comments to ensure that the particular issues applicable to your business—whether they are concerns about certain LDTs or other aspects of the guidance—get specific attention. Such issues concern the following:

- Contract manufacturing. The proposed FDA framework states that LDTs do not include tests that are manufactured using contract manufactured components.³⁵ Although FDA has stated this position in recent years, it was not always the case. Indeed, the use of contract manufacturing in making LDTs has historically served an important function in helping ensure the quality of LDTs. The FDA framework document alternately says that new enforcement policies would generally apply to tests even if they use contract manufacturing (to FDA's mind, not "true" LDTs), but it later states that manufacturing outside of a single lab will weigh *against* extending enforcement discretion to traditional LDTs and LDTs for unmet medical needs.³⁶
- The Fate of Analyte Specific Reagents (and Other Tools). In an effort to manage the growth of LDTs while improving their quality, FDA created a class of products called "analyte specific reagents" ("ASRs"). These products are the building blocks of LDTs and serve an important function. However, FDA has prohibited scientific communication between ASR manufacturers and their laboratory clients, requiring ASR manufacturers to sell reagents to labs with little information and no discussion about their potential uses. Similarly, FDA has taken a similar approach with general purpose equipment and instrumentation, which limits possible claims that could be made. Now that laboratories will be treated as manufacturers—and will have responsibility for ensuring compliance of any test they develop with FDA regulation—will FDA remove the communication restrictions and facilitate scientific exchanges that could enhance LDT development and quality?
- Clinical Validity. Per FDA, the clinical validity of an LDT is "the accuracy with which the test identifies, measures, or predicts the presence or absence of a clinical condition or predisposition in a patient."³⁷ Many LDTs collect immense amounts of information from the human genome, and several segments of the genome that may have unknown relevance today might be discovered to have special significance tomorrow. Will FDA approve or clear tests that detect markers for which clinical validity data is limited, or will it limit release of these results? Such a determination may well turn on FDA's consideration of what is in the best interest of the public health.
- Predictive Tests. Many LDTs to assess an individual's genetics and (possibly) help that individual understand his or her chance of developing a particular disease, even if he or she does not currently suffer from that disease. How will FDA classify the risk level of these tests?
- Software LDTs. Many LDTs rely on software that analyzes information from a patient's genetics to help guide decision-making with respect to medical management. How will FDA manage regulation of these tools that help guide clinical decision-making? Will FDA's work in the area of clinical decision support software—particularly, the anticipated guidance in this area—address the LDT issue?

³⁵ *Id.* at 4 ("The following are some examples of devices that FDA does not consider to meet the definition of an LDT: A laboratory contracts with a third party manufacturer to produce a key component (e.g., a coated microtiter plate, specialized specimen collection kit) used in its device.").

³⁶ See *id.* at 21 (listing "[w]hether the device meets the definition of LDT" as a factor that FDA will consider to determine whether an LDT is for an unmet need).

³⁷ *Id.* at 6.

- Tests for Rare Diseases. FDA notes that tests for rare diseases are defined by regulation as those meeting the definition of a “humanitarian use device”: used on 4,000 patients or fewer per year. Will FDA independently assess whether tests meet this standard without input from laboratories?
- Enforcement Discretion. How long will enforcement discretion remain in place after a laboratory submits a PMA or 510(k)? For example, if an application takes multiple review cycles, spanning years, or requires internal appeals to FDA of a decision to deny clearance or approval of a test, will enforcement discretion remain in place until a final decision is reached, or could such discretion terminate at some prior point?
- CLIA Requirements That Satisfy FDA Requirements. On a July 31, 2013, stakeholder call, FDA mentioned that compliance with CLIA requirements might be able to satisfy FDA requirements. What will those FDA requirements be?
- Staffing Concerns. How can FDA manage to regulate LDTs effectively with its current staffing? How much can it rely on third-party reviewers and inspectors? There are thousands of laboratories using LDTs, each with a potentially large suite of tests. Will Congress allocate the necessary budget to fully implement the system?

This is really just the tip of the iceberg with respect to the issues raised by FDA’s proposed regulatory framework for LDTs. How these, and many other issues, will be handled could have a huge impact on the world of diagnostics, making stakeholder engagement with FDA crucial. It is time to start planning and getting involved.

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