

E-ALERT | Food & Drug

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FDA ANNOUNCES PUBLIC MEETING TO DISCUSS PLANS TO REGULATE LABORATORY DEVELOPED TESTS AS MEDICAL DEVICES

AGENCY WILL IMPLEMENT A “RISK-BASED” REGULATORY APPROACH

On June 16, 2010, FDA announced that it will hold a public meeting on July 19 and 20, 2010 to discuss the agency’s intention to regulate laboratory developed tests (“LDTs”) as medical devices under the Federal Food, Drug, and Cosmetic Act (“FDCA”).¹ The purpose of the meeting is to allow for public input on this new initiative. In its meeting announcement, FDA stated that it intends to apply a risk-based approach to the regulation of LDTs, and following the meeting FDA “will move forward expeditiously to develop a draft oversight framework.”

While the agency has long asserted that it has jurisdiction over LDTs, it has not actively regulated most LDTs. FDA’s announcement, therefore, marks a significant policy shift. It is possible that certain stakeholders will seek to challenge FDA’s authority to regulate LDTs on the grounds that LDTs do not fit within the definition of a “device” under the FDCA.² Even putting aside jurisdictional questions, how FDA will apply its device authorities to LDTs raises numerous complex questions.

I. BACKGROUND

LDTs are diagnostic tests that are developed, validated, and performed by individual laboratories.³ These assays are developed for in-house use and are not commercially distributed to other laboratories. Every day, hundreds of laboratories use LDTs to test for a wide variety of diseases and conditions. LDTs can be distinguished from commercially available in vitro diagnostic (IVDs) test kits, which are developed by diagnostic manufacturers and sold to clinical laboratories. For many diseases or conditions, commercial test kits are not available, and development of an IVD kit may not be commercially feasible. In addition, LDTs have often been developed to respond to public health threats – such as AIDS, SARS, and H1N1 – where the delay inherent in obtaining FDA approval of a test could have had significant public health consequences.

Clinical laboratories that develop and use LDTs are currently subject to oversight and regulation under the Clinical Laboratories Improvement Amendments of 1988 (“CLIA”),⁴ which assigns primary responsibility for regulation of laboratories to the Centers for Medicare and Medicaid Services

¹ 75 Fed. Reg. 34463 (June 17, 2010);

<http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm212830.htm>.

² The FDCA defines a device (in relevant part) as “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is ... intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals ...” FDCA § 201(h); 21 U.S.C. § 321(h).

³ LDTs are sometimes referred to as “home brews.”

⁴ 42 U.S.C. § 263a; Pub. L. No. 100-578, 102 Stat. 2903 (1988).

("CMS").⁵ Under CLIA, laboratories that offer LDTs must be certified to perform high-complexity testing. To be certified, the laboratory must permit inspection by CMS, establish a quality assurance and proficiency testing program, and comply with other requirements. CLIA also requires that laboratories validate LDTs to ensure that the results are accurate and reproducible. In addition, some state laws impose additional requirements on clinical laboratories. New York, for example, requires that all LDTs be approved by state authorities before they may be used in testing specimens from state residents.

FDA's authority to regulate LDTs is less certain. Since at least the early 1990s, FDA asserted that LDTs were medical devices that were subject to regulation under the FDCA. However, the agency declined to implement a comprehensive regulatory scheme for LDTs and instead announced an enforcement discretion policy. In addition, rather than regulating LDTs themselves, FDA promulgated a regulation in 1997 under which it regulates analyte specific reagents ("ASRs"), which serve as the building blocks of LDTs.⁶ In recent years, however, the agency has begun to assert some regulatory oversight over certain types of LDTs. In 2006 and again in 2007, FDA issued draft guidance regarding in vitro diagnostic multivariate index assays ("IVDMIAs"), a subset of LDTs that diagnose high risk diseases or conditions and that use complex algorithms to combine multiple inputs. Consistent with that guidance document, FDA has cleared premarket notifications for several IVDMIAs. In addition, FDA has recently issued letters to several companies that offer genetic testing services directly to consumers, requesting that these companies submit premarket notifications or premarket approval applications for these tests.⁷

Despite the fact that FDA has asserted its regulatory authority over some types of LDTs, the vast majority of LDTs have continued to be offered without FDA oversight. FDA's announcement, therefore, represents a significant policy shift.

II. FDA'S ANNOUNCEMENT

In the announcement of its policy shift regarding LDTs, FDA cited the evolution of LDTs from well-understood pathology tests or tests for rare diseases and conditions to complex tests that "are playing an increasingly important role in clinical decisionmaking and disease management, particularly in the context of personalized medicine." In addition, FDA said, "even when FDA-approved tests are available for a disease or condition, laboratories often continue to use LDTs that have not been reviewed by the agency." FDA's concern is that "LDTs that have not been properly validated for their intended use put patients at risk," including "missed diagnosis, wrong diagnosis, and failure to receive appropriate treatment."

In light of these concerns, the agency determined that now is the time to reconsider its policy of enforcement discretion over LDTs. But the agency also referred to issues "unique to the laboratory community" that would have to be taken into account in its regulatory framework for LDTs. In

⁵ Pursuant to CLIA, FDA has been assigned responsibility for complexity categorization determinations for IVD devices. 42 C.F.R. § 493.17(c)(1)(i).

⁶ 62 Fed. Reg. 62243 (November 21, 1997). In promulgating the ASR rule, FDA reiterated its view that FDA clinical laboratories that develop LDTs are "acting as manufacturers of medical devices and are subject to FDA jurisdiction under the act." *Id.* at 62249. FDA declined again to regulate LDTs, reiterating its enforcement discretion policy. *Id.* The regulations governing ASRs are promulgated at 21 C.F.R. §§ 809.10(e), 809.30, and 864.4020.

⁷ Various stakeholders disagree as to whether FDA has statutory authority to regulate LDTs. Several comments and citizen petitions have been submitted to FDA arguing that FDA lacks statutory authority to regulate LDTs as medical devices. See, e.g., Docket No. 2006-P-0402, Petition of Washington Legal Foundation. Others, however, have encouraged FDA to actively regulate all LDTs, or at least certain types of high-risk LDTs. See, e.g., Docket No. 2008-P-0638, Petition of Genentech, Inc.

particular, FDA noted that “the field of genomics and genetic testing has the potential to revolutionize patient care,” and its hope was to foster innovation in this area while assuring such tests are safe and effective. FDA also noted the need to foster innovation in tests for rare diseases and conditions. FDA stated its intent to “provide a reasonable, predictable, and consistent regulatory policy for ensuring the safety and effectiveness of LDTs and provide sufficient time for implementation.”

While the agency did not set forth a specific proposal, it did state that “[a]t this time, FDA believes that a risk-based application of oversight to LDTs is the appropriate approach to achieve the desired public health goals.” No further discussion was provided regarding this risk-based approach. The upcoming public meeting and docket are intended to permit interested persons to provide input to FDA.

FDA did not set forth a specific timetable for implementing a new LDT policy. Following the public meeting and the close of the public docket, “FDA will move forward expeditiously to develop a draft oversight framework for public comment to provide predictability as quickly as possible.” FDA also intends to phase in such a framework over time based on the level of risk of the test, and has asked for public comment on “the issues that pose the greatest concern to the public health.” The agency did not indicate whether its LDT policy would be implemented by regulation or guidance documents. The comment period for this public meeting closes on August 15, 2010.

III. QUESTIONS RAISED BY FDA’S ANNOUNCEMENT

As an initial matter, there is significant chance that FDA’s policy will be challenged by stakeholders. In addition to the potential jurisdictional challenges, FDA’s announcement raises numerous questions, including (but not limited to) the following:

1. Will the agency seek to promulgate device classification regulations for LDTs?
2. Will the agency exempt certain categories of LDTs from premarket notification? If so, what criteria will FDA use to make such determinations?
3. Does the agency expect that every laboratory provider will submit a 510(k) or PMA for each LDT offered? How will FDA apply its usual safety and effectiveness approach of evaluating one analyte and one disease/condition in the context of the multiple analytes often involved in complex LDTs?
4. How will FDA regulation be reconciled with regulation under CLIA? Will laboratories be subject to dual regulation under both CLIA and the FDCA? Will separate proficiency testing and validation under CLIA still be required?
5. How will FDA implement quality system regulation (“QSR”) and good manufacturing practice (“GMP”) requirements for a clinical laboratory?
6. What is the status of FDA’s IVDMA guidance document as a result of this announcement? How will FDA reconcile its initial steps to regulate LDTs that are IVDMA with its just-announced intentions to “provide sufficient time for implementation” and to “phase in” a regulatory framework over time for LDTs?⁸

⁸ The Director of the FDA’s Center for Devices and Radiological Health (“CDRH”), was quoted as saying that the agency no longer intends to develop a final IVDMA guidance in light of this new regulatory initiative. See “FDA to drop IVDMA policy,” *BioCentury Extra*, Vol. 118 No. 114 (June 16, 2010).

7. What is the status of FDA's recent actions regarding DTC genetic testing? Will these and other DTC LDTs be incorporated into the regulatory framework under this announcement, or regulated under a separate and distinct framework?
8. Will FDA continue to regulate analyte specific reagents? By directly regulating the finished devices (i.e., the LDTs), will regulation of ASRs become no longer necessary?

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The public meeting will be held July 19 and 20, 2010, from 8 a.m. to 5 p.m. Persons interested in presenting must submit a request and, if granted, will be given 10 minutes to present. FDA's docket in connection with the public meeting (Docket No. FDA-2010-N-0274) will remain open for written comments until August 15, 2010.

If you are interesting in discussing this new regulatory initiative, please feel free to contact any of the attorneys listed below.

Ellen Flannery	202.662.5484	eflannery@cov.com
Richard Kingham	202.662.5268	rkingham@cov.com
Scott Danzis	202.662.5209	sdanzis@cov.com

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