

Breaking: FDA Moves to Broadly Regulate LDTs

by Dan Vorhaus

Earlier today, the U.S. Food and Drug Administration (FDA) [announced](#) that it will hold a public meeting July 19-20 to "discuss how the agency will oversee laboratory-developed tests (LDTs)." The FDA has made several high-profile announcements over the past month - particularly in the area of direct-to-consumer (DTC) genetic testing - but today's development, despite its not receiving the same degree of media attention, is likely the most significant development to date.

Why? Until today, the FDA's recent announcements have involved a series of letters to DTC genetic testing companies, [beginning last month with Pathway Genomics](#) and continuing last week with [letters to five other prominent DTC companies](#). Despite all of the attention paid to these letters, the sum total of the FDA's regulatory focus amounted to only a handful of products. Today's announcement, on the other hand, declares the FDA's intent to much more aggressively regulate the entire field of LDTs. While an exact count of the number of LDTs available is impossible, [GeneTests.org lists more than 2,000 genetic tests from nearly 600 laboratories](#), numbers which do not even include genetic tests and other diagnostic products offered DTC. After having been criticized for a policy of case-by-case regulation, the FDA has answered with a move to regulate the entire field of laboratory-based testing.

Why the FDA is Regulating LDTs. The FDA's [notice of public meeting and request for comments](#) (pdf) provides a roadmap for how the agency came to the conclusion that it must begin to more actively regulate LDTs. (For more on the FDA's current regulation of LDTs see [here](#) and [here](#).) [According to the agency](#) (pdf), LDTs were initially "relatively simple, well-understood" diagnostic tests "intended to be used by physicians and pathologists within a single institution in which both were actively part of patient care." Components of the test were generally regulated by the FDA, either as analyte specific reagents or as general reagents, and the tests were performed in CLIA laboratories certified to perform high-complexity testing.

While most LDTs are still performed in high-complexity CLIA laboratories, according to the FDA, over the past two decades the other characteristic elements of LDTs have all changed. Today's tests are "often used to assess high-risk but relatively common diseases...and to inform critical treatment decisions" and are "often performed in geographically distant commercial laboratories instead of within the patient's health care setting under the supervision of a patient's pathologist and treating physician, or may be marketed directly to consumers."

Furthermore, the FDA alleges that LDTs are now manufactured increasingly by "corporations rather than hospitals or public health laboratories, which represent a significant shift in the types of tests developed and the business model for developing them." In language reminiscent of [Genentech's 2008 petition urging the FDA to regulate LDTs](#), the FDA also points out that the agency's regulation of genetic test kits, but not LDTs, has produced an uneven playing field and created "a competitive disadvantage and potential disincentive to innovation" by test kit manufacturers.

In addition to the changes in the complexity, development and usage of LDTs, the FDA notes that "diagnostic tests are playing an increasingly important role in clinical decisionmaking and disease management, particularly in the context of personalized medicine." The increased prominence of LDTs has increased the risks associated with tests "that have not been properly validated for their intended use." These risks include "missed diagnosis, wrong diagnosis, and failure to receive appropriate treatment." Ultimately, the FDA believes that "the public must be assured that the tests used in the provision of health care, whether developed by a laboratory or other manufacturer, are safe and effective." Clearly, the FDA does not think the current regulatory regime accomplishes this goal.

How the FDA Intends to Regulate LDTs. In light of these concerns, the FDA "believes it is time to reconsider its policy of enforcement discretion over LDTs." (For more on the agency's "enforcement discretion" policy see [here](#) and [here](#).) To ensure the safety and efficacy of LDTs, the FDA "believes that a risk-based application of oversight to LDTs is the appropriate approach."

Just what, exactly, a "risk-based application of oversight" entails is unclear. The agency still needs to develop those details and, indeed, the primary purpose of the FDA's notice is to solicit public comment from stakeholders interested in assisting the FDA in devising its LDT regulatory policy. (A secondary purpose, no doubt, is to avoid challenges to the FDA's regulatory overhaul based on the Administrative Procedure Act (APA), an issue I [discussed yesterday](#).)

It will be months before the details become clear, but the FDA's top priority appears to be ensuring the safety and efficacy of LDTs. However, regulated parties will be relieved to note that the FDA has acknowledged its responsibility to "provide a reasonable, predictable, and consistent regulatory policy" that will "encourage innovation, improve patient outcomes, strengthen patient confidence in the reliability of [LDTs], and help reduce health care costs." The agency has also indicated that it "intends to phase in [its LDT regulatory] framework over time based on the level of risk of the test."

After [failing to reach a decision on the regulation of IVDMIAs in 2007](#), and after [delivering a series of regulatory letters aimed at individual DTC companies over the past several weeks](#), the FDA now appears to be gearing up for its most ambitious regulatory move yet within the burgeoning field of diagnostic testing. In the abstract, at least, the agency has presented a balanced understanding of the benefits and costs of LDT regulation, acknowledging explicitly that regulations meant to ensure safety and efficacy can threaten the innovation and commercialization of diagnostic tests essential to improving health care in the United States.

The devil, however, remains in the details. At next month's meeting in Rockville, MD, the FDA will begin the process of balancing these competing considerations. Whether the agency will ultimately do so in a way that satisfies its safety and efficacy concerns, while simultaneously addressing the competing concerns of a diverse array of healthcare providers, patients and consumers, and companies and investors, all of whom have a significant stake in the future regulation and development of LDTs, remains to be seen.

[Update 6/17]. Turna Ray of *Pharmacogenomics Reporter* has confirmed that the FDA [intends to shelve its IVDMA initiative in favor of its new and much broader proposal to regulate all LDTs](#). "It's possible that we will issue [an] IVDMA guidance in the future but with this public meeting [scheduled for July], we are addressing LDTs at once in a public dialogue, instead of dealing with [them] subset by subset," FDA spokesperson Erica Jefferson said. No surprises here. **[End Update 6/17]**