The Regulation of Laboratory-Developed Tests

Background

In October 2014, the U.S. Food and Drug Administration (FDA) released draft guidance on its proposed oversight of laboratory-developed tests (LDTs), and in vitro diagnostic (IVD) tests, both of which are both designed and used by a single laboratory. The LDTs offered by clinical labs at academic health centers are not currently regulated by the FDA through the current device regulations, but many would be subject to this regulatory oversight under the proposed guidance. According to the FDA, the purpose of the revised framework is to give the FDA oversight of LDTs "based on risk to patients rather than whether they were made by a conventional manufacturer or a single laboratory." In this new structure, LDTs designated as higher-risk, including companion diagnostics and LDTs used to inform treatment decisions, would be reviewed by the FDA through the existing pre-market review process. The FDA proposes to use its enforcement discretion and not require the same process for certain LDTs, including those deemed to be low-risk and those used for rare diseases.

Community Response

Immediately after the release of the proposed guidance, academic institutions and other entities raised concerns that the proposed framework would slow down innovation, create a burdensome and expensive process, and potentially jeopardize patient care and advances in personalized medicine. In addition to submitting comments to the FDA on the guidance, several interest groups including physician and other health care provider associations, academic entities, and industry each developed alternative proposals to the FDA draft guidance. The alternative proposals address whether the FDA or the Centers for Medicare and Medicaid Services (CMS) should bear primary responsibility for LDT oversight and include different approaches to classifying tests based on risk. Those alternative frameworks that propose an expanded role for CMS note that LDTs, while currently not regulated by the FDA, are subject to some level of oversight through the Clinical Laboratory Improvement Amendments (CLIA). More "CLIA-centric" proposals suggest that CMS' role should be expanded by investing additional federal resources in CMS and modernizing CLIA to give greater oversight responsibility and enforcement authority over LDTs. Some have suggested a blended approach, where certain tests, such as those deemed very high risk or containing proprietary information are automatically or voluntarily submitted to the FDA for approval, while the vast majority of LDTs would either be regulated through CLIA or not subject to additional regulation.

Agency and Congressional Action

To date, the FDA has not finalized the draft guidance, and has been engaged with stakeholder groups and in discussions with members of Congress regarding the impact of implementation of its proposed oversight framework. Of note, in public hearings and discussions with various stakeholders, both the FDA and CMS have asserted that the regulation of LDTs should be under the jurisdiction of the FDA, and not with CMS through the modification or application of CLIA.

As part of the 21st Century Cures initiative, the House Energy and Commerce Committee looked at the regulation of diagnostic tests and laboratory operations through a series of hearings and requests for information. Additionally, the House Appropriations Committee has included report language in the FY 2017 Department of Agriculture appropriations legislation directing the FDA to "suspend further efforts to finalize the LDT guidance and continue working with Congress to pass legislation that addresses a new pathway for regulation of LDTs in a transparent manner."

AAMC Position

The AAMC agrees that LDTs used for diagnostic and treatment decisions should have clinical validity and accuracy. **However, we share our members' concerns that the FDA's regulation of LDTs as proposed would interfere with delivering innovative, cutting-edge medical care, negatively impact patients, or mire the development of critical new tests in a costly and laborious process.**

As the AAMC wrote in its comment letter to the FDA, academic medical centers and teaching hospitals that are performing LDTs every day are "on the front line of patient care and are best able to define the impact on their own institutions and their ability to treat patients with important information gleaned from clinically validated, well-proven, and carefully tailored diagnostic tests. In light of the President's initiative on precision medicine, the FDA should be working in concert with academic medicine to encourage innovation in patient care, not stifle it."

As the LDT issue is debated in Congress and as the FDA considers whether to finalize its guidance, AAMC is engaged with many stakeholders and continues to advocate regarding the importance of the LDT issue. With the input of many AAMC-member institutions who are deeply engaged in the provision of LDTs for use with patients across the nation, the AAMC has identified key issues that must be considered and addressed in any implemented oversight of LDTs.

Key Considerations in the Regulation of LDTs

- Any revised regulatory framework must include as one goal a recognition that an overly burdensome system to review LDTs could greatly slow the rate of clinical innovation that is critical to keeping our healthcare system vital, providing care to patients, and responding quickly to emerging public health risks.
- There is no current understanding of the number of tests that would be affected by a proposed revision to the current framework, both for existing tests that would be impacted and for tests that are yet to be developed. Before a new approach is finalized, it must take into account the frequency of modification to new and existing tests, which modifications would require a new approval process, and the rate at which new tests are being developed. This information is critical to accurately estimate the federal and institutional resources needed to implement the revision without negatively impacting patient care.
- LDTs are often innovative or low-volume tests whose speed of adoption has out-paced the ability of commercial IVD manufacturers to plan and submit formal clinical trials that would be required for the FDA approval for marketing.
- A system that recognizes the proven success and validity of certain tests or categories of LDTs is essential in ensuring that the nation's resources are targeted to the review of the subsection of diagnostic tests that present the most potential risk to patients. Any regulation of LDTs should include a wide range of situations under which enforcement jurisdiction or grandfathering is applied to facilitate the continued use of current well-known and well-developed tests without undue burden on the system as a whole.
- The economic impact of institutional compliance with the proposed new regulatory framework for currently administered and newly developed LDTs could be untenable, given the cost of guiding even a single test through the FDA premarket approval process. This cost would necessarily lead to institutional decisions that could limit patient access to innovative and targeted diagnostic tests.

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