How FDA Differs From CMS In Clinical Lab Test Oversight

Law360, New York (March 14, 2013, 12:36 PM ET) -- The U.S. Food and Drug Administration has previously announced an interest in regulating diagnostic tests used in providing personalized medicine clinical care. Interested stakeholders such as the American Clinical Laboratory Association, the College of American Pathologists and the Association for Molecular Pathology, have weighed in on whether the FDA can and should expand its jurisdiction to laboratory-developed tests (LDTs) performed by clinical laboratories.

To the end of understanding the issues and concerns of stakeholders and the public, the Personalized Medicine Coalition (PMC) recently issued a white paper reporting on the regulatory landscape for personalized medicine tests and services in U.S. clinical practice. The report “Personalized Medicine Regulation: Pathways for Oversight of Diagnostics” (available here) explains the current regulatory oversight of diagnostic tests and, in particular, LDTs, and contrasts their regulation with regulation of certain diagnostic tests by the FDA.

Current Regulatory Framework

Personalized medicine relies on the accurate analysis of a patient’s clinical symptoms and/or genome. Diagnostic medicine is integral to the basic tenet of personalized medicine — finding the right treatment for the right patient at the right time. Thus, the safe and appropriate use of reliable and valid diagnostic tests is central to the successful adoption of personalized medicine.

The report notes that two separate agencies in the U.S. Department of Health and Human Services oversee personalized medicine products and services in the United States. The FDA regulates pharmaceutical products, biological products and medical devices used in patient care, including care that is considered personalized medicine.

Clinical laboratories that perform diagnostic medicine such as genetic analysis (typically called LDTs) are under the jurisdiction of the Centers for Medicare and Medicaid Services, pursuant to the Clinical Laboratory Improvement Amendments (CLIA). CMS certification currently is required before clinical laboratories can generally perform diagnostic tests and interpret and report results to health care providers.

Comparison of FDA and CMS Regulation of Diagnostic Tests

The PMC report reviews in detail the structure of the FDA and the CMS and the current oversight of LDTs by each agency. The PMC report notes five key ways the FDA’s approach to regulating the manufacture and distribution of diagnostic medical devices differs from the CMS’ approach to regulating diagnostic test services performed by laboratories:

Requirements for Evidence of Analytical and Clinical Validity

The PMC report notes that the FDA regulated tests (termed “in vitro diagnostics” or "IVDs") require clinical evidence to support the intended use and indications for the test (i.e., the test’s ability to identify or predict the disorder of interest) and require review of analytical performance.

CLIA regulations for LDTs require a demonstration of laboratory performance and that the test methodologies selected have the capability of providing quality results. However, this information generally does not require review by an external body prior to the lab offering the test unless required by state law.

Time to Market

Because the FDA requires detailed clinical review of IVDs prior to market, the premarket review process for tests regulated by the FDA can take several months to years. The FDA can also require approval or

clearance of new premarket submissions if changes are made to diagnostic tests after FDA approval or clearance. Laboratories using FDA-approved tests must also comply with CLIA quality controls.

In contrast, LDTs do not require review or approval from an outside body prior to clinical use, again unless required by state law.

Labeling and Promotion

The FDA permits the promotion of regulated IVDs only in accordance with their cleared or approved intended uses. The CMS, in contrast, does not restrict the clinical claims for LDTs developed by CLIA labs. However, advertisement of clinical claims for LDTs is subject to oversight by a separate federal agency — the Federal Trade Commission and applicable state laws — and must carry a disclaimer that the test has not been cleared or approved by the FDA.

Quality Programs and Post-Market Capabilities

The quality programs for FDA-regulated IVDs and LDTs have different elements that may or may not overlap. In brief, FDA-regulated tests must utilized design controls for development and validation of diagnostic assays and other process controls, which are not required for LDTs.

LDTs, in contrast, need only to follow good laboratory practice standards and process requirements. Also, manufacturers of IVDs are subject to periodic FDA inspection while CLIA laboratories generally are subject only to their own quality control inspections for compliance with CLIA regulations.

FDA regulations also require reporting of adverse events associated with a product, and the manufacturer must have a process for implementing a product recall. CLIA regulations, in contrast, simply require policies and procedures to monitor, access and correct problems uncovered during use of the tests.

Financial Consequences

CLIA laboratories pay a user fee for initial laboratory certification and biennial recertification based on the volume of clinical testing. Manufacturers of IVDs pay fees for diagnostic premarket submissions and pay an annual establishment registration fee.

As of Jan. 1, of 2013, FDA-regulated tests (with a few exceptions) are subject to a 2.3-percent federal excise tax pursuant to the Patient Protection and Affordable Care Act. If LDTs were to be regulated by the FDA, LDTs would likely be subject to the FDA fees and excise tax in addition to CLIA fees.

Recommendations and Conclusion

The PMC report indicates that there are significant differences of opinion among stakeholders on the optimal level of regulation and oversight of LDTs, especially when the outcome of an LDT impacts pharmacological intervention.

Some stakeholders view FDA regulation of LDTs, in addition to CMS regulation, as creating a disproportionate burden on laboratories that would slow innovation to the detriment of physicians and patients and would unnecessarily increase the cost of providing laboratory services.

Other stakeholders opine that the current regulatory oversight of LDTs is insufficient in view of the increased complexity of the tests. They argue that a risk-based FDA approach can sustain and promote innovation, while benefiting patient safety.

The PMC report closes by noting, “[w]hether the various stakeholders working with Congress, the interested government agencies, and other authoritative bodies can reach an understanding on the optimal path forward remains to be seen.”

Those institutions or individuals involved in LDTs would be well advised to closely monitor ongoing discussions of this topic in the coming months and provide their feedback during the public comment period for any proposed regulations governing LDTs.

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