MEDTECH INSIGHT
CITELINE COMMERCIAL

25 Mar 2024 | **News**

Congress Revives Talks On LDTs With Clock Ticking On FDA Rule

While lawmakers continue to debate how LDTs should be regulated, the FDA's proposed rule is fast approaching

by Brian Bossetta

During a recent hearing of the US House Energy and Commerce Health Subcommittee, lawmakers discussed the best approach to regulating laboratory developed tests (LDTs) with a panel of experts representing clinical labs. At issue was the FDA's proposed rule that places LDTs under the same regulatory purview as other in vitro diagnostics, which would require medical facilities to receive agency approval for the LDTs they develop in their own labs.

Creating a regulatory framework for laboratory-developed tests shouldn't be as complicated as the tests themselves.

But months after Congress failed to advance legislation that would have established that framework — and with the FDA's final rule on LDT regulation set to drop — lawmakers on the Hill continue to debate the issue, with many arguing that the agency has stepped out of regulatory bounds.

During a House Subcommittee on Health hearing on 21 March, members on both sides of the aisle generally agreed LDTs require additional oversight but disagreed on the how.

Most Republican committee members, such as Rep. Cathy McMorris Rodgers, R-WA, felt the FDA draft rule amounts to regulatory overkill.

The proposal, which the FDA said was necessary after Congress failed to pass the VALID

(Verifying Accurate Leading-edge IVCT Development) Act in December 2022, classifies LDTs as medical devices. The FDA plans to roll out the new regulations over a four-year period after publication of the final rule, which could come as early as April.

“Instead of focusing on advancements in precision medicine and genetic technologies to help patients, the FDA is dramatically increasing the regulatory burden on LDTs,” Rodgers said. "These regulations extend far beyond any of the legislative proposals that Congress has considered.”

Rodgers added the FDA’s proposed rule would also mean increased costs for facilities, which already operate with limited resources. She further criticized the rule’s requirement that labs submit test samples for “proof of proficiency” as impractical both for the labs as well as for the FDA to review in a timely manner.

“Given that the FDA is already struggling to keep up with innovation and what it currently regulates, this undertaking would mean fewer diagnostics, higher costs, and delays in care for patients who can't afford to wait for the FDA to approve a test,” Rodgers said.

But the problem, as Rep. Anna Eshoo, D-CA, pointed out, is that despite broad bipartisan support for legislation to address the LDT quandary — as well as the FDA’s preference for a legislative solution as expressed on several occasions by agency commissioner Robert Califf — Congress has failed to act, even though it has had many chances to do so.

“This is the sixth year for Congress to be grappling with the VALID Act. And we have not acted,” Eshoo said. “We have to accept that.”

FDA Receives Thousands Of Opinions On Proposal To Regulate LDTs As Comment Period Comes To A Close

By Brian Bossetta

01 Dec 2023
As the US FDA works to finalize new regulation of lab-developed tests, it must consider more than two thousand comments that have poured into the agency since the proposed rule was published in October. The comment period closes Monday.

Read the full article here

Had Congress passed the VALID Act, the FDA more than likely would not have gone down the rulemaking path. In the absence of legislation, however, the FDA has maintained it was compelled to act because LDTs have become more complex over the decades and the public needs assurance that such tests – which often diagnose life-threatening diseases – are safe and reliable.

The agency also has also argued that because LDTs are not centrally registered or tracked, it is

difficult to know how many of them are currently on the market and how they perform in comparison to other FDA-reviewed diagnostics.

> *"New technologies can improve the lives of patients and laboratory developed tests, LDTs, are no exception. But for them to make a difference for patients they must be accurate and reliable." — Frank Pallone*

It's estimated that 70% of medical decisions are based on laboratory test results, with more than 14 billion lab tests ordered on an annual basis. Increasingly, diagnostics and precision medicine are critical for patient care.

But concerns about quality, traceability, and accountability have intensified as LDTs are produced in higher volumes for larger and more diverse populations.

Pro-Rule

During the hearing, ranking committee member Frank Pallone, D-NJ, voiced his support of the rule.

"New technologies can improve the lives of patients and laboratory developed tests, LDTs, are no exception. But for them to make a difference for patients they must be accurate and reliable," Pallone said, noting risks including patients undergoing unnecessary treatments or delaying or foregoing treatment that is necessary as a result of bad information.

"Physicians have years of training and the best interests of their patients in mind, but by not providing oversight of LDTs we're failing them by not ensuring they can trust the tools that they have to guide their patient counseling and develop effective interventions," Pallone argued. "So the proposal is, in my opinion, an important step to help ensure that healthcare decisions are made based on test results that providers and patients can reliably trust."

Panelist Zach Rothstein, executive director of AdvaMedDx, the division of AdvaMed that represents IVD manufactures, agreed more regulation was needed and that the FDA initiated its rule to close the oversight gap that continues to widen as LDTs become more varied and sophisticated.

"The vast majority of us do not know where the test that might diagnose a life-threatening

disease or infection is made. But we should have the confidence that whatever test we use, and wherever it is made, that it has met the same standard and is subject to the same oversight as any other test," he said. "For high stakes tests such as for cancer diagnosis, or to guide important treatment decisions, we believe that those standards should involve a premarket review of analytical and clinical validity."

Notwithstanding his more favorable view of the FDA rule compared with others, Rothstein reiterated AdvaMed's support for the VALID Act, maintaining it provides the necessary reforms to ensure regulatory certainty while allowing for innovation. He further emphasized the importance of technology certification, which VALID includes.

"We continue to support comprehensive legislative reform that results in a modernized regulatory framework that spurs innovation and access to testing and is applied to all diagnostic tests based on their level of risk," he said.

Citing the vital role tests play in determining treatment, Eshoo said better processes to validate tests are needed, whether those tests are to detect COVID or cancer. "Certainty is sorely needed," she said. "We should ensure test results are accurate and do not contribute to worsening health outcomes or higher costs for patients."

However, Eshoo also made clear her support of the VALID Act and expressed her hope that the FDA's action would reinvigorate the legislative process and "call all stakeholders back to the table to earnestly negotiate a framework."

> ***"The first test to detect the BRCA gene mutation, which revolutionized breast cancer care, was offered by an ACLA member laboratory." — Susan Van Meter***

Panelist Jeff Allen, president and CEO at Friends of Cancer Research, said without FDA oversight there's no way to know how many LDTs are being offered — or how they perform.

"This is not the reliable path to precision medicine," Allen said. "The reality is some patients may be making major medical decisions based on potentially discrepant test results."

Allen too supported the VALID Act, stating it would provide the framework for the future by establishing a quality assurance floor for the performance of all tests while ensuring an open

ceiling to foster future innovations in diagnostic testing. Without VALID, Allen said the FDA must move forward to clarify uniform policies for diagnostic tests.

He stressed, however, that the FDA's pending rule doesn't tie lawmakers' hands.

"It should be noted that nothing precludes Congress from continuing to work on a legislative approach as FDA continues working on its proposed rule," he said. "No matter the path forward, action to ensure high-quality test performance is needed. And progress to that end can no longer be stalled. The future of precision medicine and the health and lives of patients depends on the accuracy of these tests."

Innovation and Patient Access

Panelist Susan Van Meter, president of the American Clinical Laboratory Association (ACLA), was clear in her opposition to the FDA rule and sided with those who believe it will stifle innovation. To illustrate her point, Van Meter noted decades of groundbreaking tests, such as the BRCA gene test, which labs have produced.

"The first test to detect the BRCA gene mutation, which revolutionized breast cancer care, was offered by an ACLA member laboratory," she said.

Van Meter also pointed out that labs are frequently the first to respond to emerging public health threats with products to address unmet patient needs.

"But today, the FDA is poised to reshape the industry by bypassing Congress and unilaterally imposing medical device regulation," she said. "Device regulation is inappropriate when applied to laboratories and raises profound concerns."

> *"I've trusted my own care to LDTs even when FDA-approved choices are available for the same clinical question." — Dara Aisner*

Van Meter based her argument on three areas: patient access, innovation, and legal concerns.

In Van Meter's view, regulating LDTs as medical devices would reduce patient access to critical diagnostic testing services.

"Laboratory developed testing services would be removed from testing menus, not because they

don't yield reliable and accurate results, but because seeking FDA approval can be prohibitively expensive," she said. "We are acutely concerned that patients will lose access to essential testing services, especially those that serve pediatric patients, small patient populations, and patients with rare diseases cases."

Further, innovation and diagnostic testing would suffer because the device framework is wrong for laboratories, according to Van Meter.

"Device regulation is rigid and cannot account for the rapid evolution that occurs in diagnostics," she said. "The device approval standard and numerous other aspects of device law do not work when applied to professional services."

And lastly, regulating LDT services, in her view, is beyond the agency's jurisdiction.

"Congress has always been clear the FDA regulates medical products but not healthcare services," she said. "Laboratory developed testing services are not products but professional services that leverage a variety of tools to derive a test result for a patient."

After the hearing, Van Meter told *Medtech Insight* that while ACLA has not endorsed the VALID Act, she believes it has many positive attributes. "We've got a lot of groundwork that's already been covered, and we'd really like the opportunity to robustly re-engage on that legislation as quickly as possible," she said.

Allen expressed a similar view.

"I think that today's hearing demonstrated the extensive considerations, thoughtfulness, and input that has gone into the VALID Act, resulting in its broad support," Allen told *Medtech Insight*.

"Hopefully the key takeaways will make it over to the other side of the Hill and the Senate will see the consensus, both in terms of the need for action, as well as the fact that there is a pretty good solution in the works with the VALID Act."

Panelist Donald Karcher, president of the College of American Pathologists, opposes the FDA rule, agreeing with Allen that the VALID Act outlined a regulatory framework that ensures quality and reliable testing results for patients while not bogging down labs in endless red tape.

He also agreed the FDA rule would reduce the number of highly accurate LDTs available to patients and would constrain medical innovation and timely patient care.

"Instead, the FDA should be focused mostly on tests that pose the highest risk to patients," he

said.

Time, however, remains a factor, and while Congress delays, the FDA proceeds.

Van Meter said ACLA members are operating under the assumption the FDA rule takes effect.

“We are working with our member laboratories on implementation. And that's very important. It's not theoretical,” she said. “Once a final rule comes out, clinical labs across the country have to implement it.”

On 1 March, the FDA sent a draft of the final rule to the White House, signaling the likelihood of an April publication. (Also see "*FDA Set To Drop Final Rule On LDTs, Sends Draft To White House*" - Medtech Insight, 5 Mar, 2024.)

A Patient Perspective

But of all the panelists, Dara Aisner, medical director at the Colorado Molecular Correlates Laboratory and representative of the Academic Coalition for Effective Laboratory Developed Tests, was least receptive to further regulation under either the FDA’s rule or the VALID Act.

Aisner, who is also a professor of pathology at the University of Colorado, said there was a middle ground, which can be found through the “pathway that asks laboratories to undergo proficiency testing” prior to launching a new test.

But the most compelling aspect of Aisner’s testimony came from her perspective as a cancer patient.

“I've trusted my own care to LDTs even when FDA approved choices are available for the same clinical question,” she said. “I find the FDA’s proposal to be misguided, and I worry for the future of American medicine. LDTs are not devices. They are processes performed with expertise knowledge of all the steps combined with an understanding of the scientific and clinical data that allows for nuanced care that simply cannot come from an assay kit. The use of FDA’s device infrastructure is quite simply forcing a square peg into a round hole.”

Aisner concurred that the rule would be an anchor for innovation while slowing down needed tests getting to patients. She cited the example of targeted therapy for lung cancer, which is one of the most effective forms of precision medicine based on a mutation first reported in 2004.

“Labs started offering LDTs for that mutation that very same year,” Aisner said, adding it took nine years for the FDA to approve a test kit for the same mutation. “In that interval, roughly 2 million Americans were diagnosed with lung cancer.”

Too Much Paperwork

Another criticism of the rule is that the already swamped FDA would be flooded with new tests to review. As Van Meter noted, the proposed rule does not include a grandfathering provision, which means the FDA would have to review tens of thousands of tests that already exist.

"The FDA lacks the resources to deal effectively with that certain workload," Van Meter said.

To illustrate her point, Van Meter cited an ACLA member lab which obtained the first FDA authorization for a genetic test to identify patients at higher risk for developing cancer. However, she added, it took the lab more than a year — and seven figures — to prepare the submission.

Further, the FDA spent more than two years to review and finally authorize the test. In the meantime, the laboratory performed the test for more than 230,000 patients, according to Van Meter, of which more than 22,000 tested positive.

"Had FDA's rule been in place, those 22,000 patients would not have learned about their risk of cancer or had their cancer care informed by their genetics," she said.

Not the Wild West

Van Meter also stressed to *Medtech Insight* the importance of clearing up any misconceptions that LDTs are unregulated with nothing in place to provide patients with confidence in their quality and reliability.

"That's simply not the case," she said, adding all ACLA member labs are certified under the Clinical Laboratory Improvement Amendments, or CLIA, federal standards regulating testing facilities enacted in 1988. "All of our labs are accredited to do high complexity testing."

> ***"While the VALID Act, like the LDT rule, assumes that diagnostic regulation is in need of change, it takes a much different approach." — Larry Bucshon***

Currently, LDTs are regulated by the Centers for Medicare and Medicaid Services (CMS) as part of CLIA, which requires test developers to substantiate their work.

During the hearing, Karcher also noted that while LDTs represent innovations in patient care, most utilize well-established laboratory methods and that the clinical validity of the majority of

LDTs is already well documented in medical literature.

Back in the House

Last March, representatives Larry Bucshon, R-IN, and Diana DeGette, D-CO, reintroduced the VALID Act. (Also see "*Diagnostics Reform Reintroduced in House*" - Medtech Insight, 31 Mar, 2023.)

The bill, according to the sponsors, would create a comprehensive framework for oversight of a new category of in vitro clinical tests (IVCTs), which include LDTs, and would move LDT oversight from CMS to the FDA. The framework is intended to be better tailored to diagnostic tests than existing medical device authorities.

Specifically, the VALID Act would establish a risk-based mechanism for the FDA to prioritize applicable regulatory requirements based on levels of risk and benefits to patients, with exemptions for certain lower-risk and low-volume tests.

"While the VALID Act, like the LDT rule, assumes that diagnostic regulation is in need of change, it takes a much different approach," said Bucshon, noting in particular its grandfather clause.

He also pointed to VALID's framework that categorizes LDTs as low, medium, or high risk and addresses each according to that level of risk. Low risks tests, Bucshon said, could bypass the agency's pre-market approval altogether while most medium-risk tests could obtain a technology certification that would allow them to immediately enter the market. On the other hand, most high-risk tests — "while generally subject to FDA approval" — would be exempted if developed for specific individuals or small groups of people.

"This would allow, for example, a hospital to offer a highly sensitive toxicology test to a toddler presenting with seizures and an altered mental state to accurately identify potential substances consumed," he said.

Bucshon affirmed his view that the VALID Act is the right approach, but said the legislation requires further work and asked the panelists if they would be willing to continue to work with Congress and the committee to find the best legislative solution to LDT regulation.

They all agreed.

Yet, if past is prologue — and based on the current dysfunction of Congress and the FDA's clear willingness to act unilaterally — it is doubtful the VALID Act will land on the president's desk before the FDA publishes its final rule.

Regardless of how it shakes out, Aisner said whatever regulatory system is put in place should

hold everyone to the same standard. “That means working to ensure outcomes are similarly safe and effective, not that regulations are similarly burdensome. There are other approaches for an outcomes-based paradigm instead of a one-size-fits-all approach.”

What matters most for Aisner, though, is that patients facing an uphill battle have all the tools modern medicine can offer.

“I never once questioned the use of LDTs in my cancer care, not once, not even a little,” she said. “I know that as the FDA moves forward patients will suffer.”