MEDTECH INSIGHT
CITELINE COMMERCIAL

27 Oct 2022 | **News**

Diagnostics Have Evolved, So Too Has the VALID Act, Says FDA's Hillebrenner

by Brian Bossetta

As diagnostics have become more technologically advanced and are used more frequently in detecting diseases, uniform regulatory standards have become necessary, according to a panel of experts discussing testing reform at the MedTech Conference in Boston.

Lab results inform the majority of healthcare decisions, which is why patients relying on these tests need assurance that diagnostic outcomes are accurate.

At the same time, diagnostics are becoming ever more complex with the rapid advancement of technology. This is why a modern regulatory framework that sets a uniform standard for diagnostics is needed, according to Elizabeth Hillebrenner, associate director for scientific and regulatory programs at the FDA's Center for Devices and Radiological Health (CDRH). And the pending Verifying Accurate Leading-edge IVCT Development, or VALID, Act would do just that.

"I think it's a really good bill," Hillebrenner said during a panel discussion at the MedTech Conference in Boston. "We're hopeful to see it passed."

However, after the VALID Act was stripped from the Medical Device User Fee Amendments, or MDUFA V, in September, and with the midterms set to potentially shake up the balance of power in Congress, there's concern VALID will not be included in the omnibus spending bill lawmakers must pass in December to keep the government running. On top of that, Sen. Richard Burr, R-NC, who has been a staunch advocate of VALID, is retiring.

FDA Commissioner Robert Califf added to that concern with remarks at a MedTech Conference luncheon, when he said that if Congress fails to pass the diagnostic reforms laid out in VALID, the agency might resort to its rulemaking authority instead.

ELIZABETH HILLEBRENNER

But Califf's remarks, according to panel moderator Nathan Brown, a partner with Akin Gump Strauss Hauer and Feld, who addressed the comments during the panel discussion, were open to interpretation and more an expression of what the agency "could do, not what it planned on doing."

But panel member Carly McWilliams, head of regulatory policy, North America at Roche Diagnostics – and a former legislative staffer for the US House Energy and Commerce Committee – remains confident VALID will pass before the end of the year.

"I think lawmakers are waiting to see what happens with the election, and then I think they will finish hashing this out," she said, adding "I think that there is momentum with passing VALID at this point."

McWilliams also said Burr's retirement might end up only increasing the chances of the legislation passing before he leaves office. "You can never underestimate the passion and potential power that comes with a retiring member," she added.

> ***"These tests are sometimes the sole determinant of a patient's treatment. So all of these factors, these changes combined over the last 40 plus years, have really changed the landscape." – Elizabeth Hillebrenner***

A central component of VALID is that it would grant FDA oversight of lab-developed tests (LDTs), which are currently regulated by the Centers for Medicare and Medicaid Services (CMS) under the Clinical Laboratory Improvement Amendments (CLIA), federal standards regulating testing facilities enacted in 1988.

One issue with LDTs is that they are not centrally registered or tracked, which makes it difficult to know how many of them are currently on the market and how they perform in comparison to FDA-reviewed diagnostics.

MEDTECH INSIGHT
CITELINE COMMERCIAL

Speaking to reporters earlier this month, AdvaMed CEO Scott Whitaker said FDA oversight of LDTs is one of the trade group's top legislative priorities and will continue to push Congress to pass VALID in December. (Also see "*Bipartisan Support For AdvaMed's Legislative Priorities, Whitaker Says*" - Medtech Insight, 14 Oct, 2022.)

Carve-Outs

But not everyone thinks putting LDTs under the FDA's purview is a good idea. Medical and research centers argue it would weigh down their work with regulation and stifle innovation. These centers have pushed for carve-outs in the legislation that would exempt their labs from any future LDT oversight.

Health Industry Groups Press For Diagnostics Reform Bill

By Elizabeth Orr

21 Jul 2022

Almost 50 stakeholder groups have signed onto a letter to US Congressional leadership that asks lawmakers to pass the VALID Act, which would update the country's approach to diagnostic test regulation. Congress needs to pass a user fee package this month to ensure full FDA funding.

Read the full article here

These carve-outs are not completely off the table for AdvaMed, Whitaker said, though to support such exemptions he would need more specifics as to how they would work. In his view, consistency is paramount when it comes to diagnostics, which is why he favors the uniformity of regulatory standards as spelled out in VALID.

During the panel discussion, April Veoukas, director of regulatory affairs at Abbott, noted some exemptions already exist in VALID, such as manual tests and humanitarian assays for diseases aimed at treating less than 10,000 patients. These exemptions, she argued, could apply to the medical centers.

In defending VALID, Hillebrenner clarified that while the legislation allows tests to be "grandfathered, the agency would still be allowed to request information on those tests. She also tried to assuage concerns that once VALID is enacted the FDA is going to start calling in all CLIA-regulated tests for premarket review – concerns stemming from prior iterations of the legislation.

As she pointed out, VALID has evolved over the years since it was first proposed. Initially, a new center for the sole purpose of regulating in vitro clinical tests (IVCTs) was part of the mix. That center is no longer in the bill, and the language only gives FDA the authority to ask for information about a grandfathered test regarding specific areas of concern.

> *"It's very important for complex biomarkers to have some alignment to ensure that no matter where a patient receives genomic testing for their tumor that it be calibrated so the patient understands the results." – Jeff Allen*

But as VALID has evolved, so have LDTs, Hillebrenner added, noting that the tests have become highly complex, rather than the relatively simple tests they were in the 1970s when the medical device amendments gave the FDA premarket review authority. In their early stages, LDTs were often developed in local labs to meet a specific need with direct communication between the treating physician and the patient, she said.

"We have very sophisticated technologies today. And what these tests are being used for clinically is also more significant," Hillebrenner said. "These tests are sometimes the sole determinant of a patient's treatment. So all of these factors, these changes combined over the last 40 plus years, have really changed the landscape."

Hillebrenner also favors VALID because, in her view, its framework subjects all assays to the same rigors so that all developers have to back up their claims with science. Uniform standards will also spur innovation, she added, while providing clarity and predictability across the board.

Accuracy

In a pre-recorded message to the panel, Jeff Allen, president and CEO at Friends of Cancer Research, a Washington-based policy and advocacy organization, emphasized the complexities of diagnostics and – like Hillebrenner – noted how much they have evolved.

Diagnostics, he said, are central to his organization's goal of enacting policy that accelerates the pace of getting innovative treatments to patients. For example, his group participated in an oncology pilot that included experts from academia and government, as well as 17 test developers. The pilot examined tumor mutational burden (TMB), a biomarker from the field of immunology that estimates the mutational rates occurring in various types of cancer.

Most notably, he said, the pilot showed that multiple developers comparing their tests on a common set of samples often produced different measurements of TMB. This was an important revelation, Allen said, because differing values can result in different diagnoses for patients.

"So it's very important for complex biomarkers like TMB to have some alignment to ensure that

no matter where a patient receives genomic testing for their tumor that it be calibrated accurately so the patient understands the results," Allen said.

As he explained, variables in different tests do not mean that a particular test is wrong, but rather that a common set of standards is needed to compare the measurements of different mutational rates in order to improve the accuracy of the results.

Allen believes the modern regulatory framework as outlined in VALID will further the accuracy of many of the diagnostics that more and more patients are turning to for their healthcare decisions.

"Accuracy is imperative," he said, "because these complex biomarkers help us identify patients that could benefit from immunotherapy."