May 22, 2022

The Honorable Patty Murray
Chair, Health, Education,
Labor & Pensions Committee
US Senate
Washington, DC 20510

The Honorable Richard Burr
Ranking Member, Health, Education,
Labor & Pensions Committee
US Senate
Washington, DC 20510

Dear Chair Murray and Ranking Member Burr,

The American Association for Clinical Chemistry (AACC) appreciates the opportunity to provide feedback on the draft Food and Drug Administration (FDA) Safety and Landmark Advancements (FDASLA) Act, which reauthorizes agency-industry user fee agreements. While we are supportive of the user fee agreements, we strongly object to the inclusion of the *Verifying, Accurate, Leading-edge IVCT Development (VALID) Act* in the bill.

We strongly urge the Committee to remove VALID from the user fee package and initiate a thorough, public examination of this measure and its potential impact on patient care. This legislation would radically change the face of clinical testing. Getting the bill right is more important than swift passage of a work in progress.

VALID would create a new, duplicative regulatory structure for laboratory developed tests (LDTs) that would have far-reaching consequences on patient access to quality, cutting-edge testing. AACC and many others have worked with the committee in good faith to correct the serious problems in the measure. This version of the bill does not address those concerns. In fact, some of the changes we have identified in this iteration raise even more questions about the efficacy of the bill. The administrative, regulatory, and financial investments required under VALID make developing LDTs cost prohibitive for all but the wealthiest laboratories. If VALID is allowed to put hospital labs out of the test-developing business, the market will see significant concentration that would be bad for patients and the economy alike.

AACC is deeply concerned with the exceedingly short time period for review and assessment of this legislation, given the length of the draft bill; the drastic changes it would introduce to the regulation of both *in vitro* diagnostic devices (IVDs) and laboratory developed testing procedures; and the far-reaching and unexamined consequences it would have on patient care. While AACC supports modernizing both the IVD and LDT regulatory processes, these are two distinct arms of the clinical testing enterprise and should be treated as such. **Five days is**

grossly insufficient to review a bill that would create a single regulatory pathway to govern both the manufacture of products and the delivery of medical services.

Nonetheless, AACC offers insights into the flaws of this legislation in the hope that the committee will take note and remove VALID from MDUFA so that all stakeholders can provide meaningful contributions to the process of modernizing our country's clinical testing enterprise.

Current Regulatory System

AACC has stated previously that while we agree that increases in the number and complexity of LDTs may necessitate a review of the regulations governing these critically important clinical testing services, we believe the process for carrying out these reviews already exists within the Clinical Laboratory Improvement Amendments (CLIA) regulations.

Administered by the Centers for Medicare and Medicaid Services (CMS), CLIA provides a robust framework within which the agency oversees laboratory testing. CMS, with public input, created stringent federal standards that regulate laboratory testing, including LDTs. These standards include rigorous personnel, quality control and proficiency testing requirements; regular inspections; and required corrective actions, if necessary.

In addition, many of the testing facilities that perform LDTs actively participate in the New York State, Joint Commission, College of American Pathologists (CAP) or other oversight programs, where they must meet requirements even more stringent than CLIA. AACC is concerned that expanding oversight to include the FDA will divert limited laboratory resources from the provision of care to new, duplicative administrative requirements.

It is important to understand the differences in the roles of medical device manufacturers and clinical laboratories in providing testing services. Manufacturers develop the IVD instruments and test kits sold to and used by a laboratory; laboratories create LDTs to help physicians diagnose and treat patients when no comprehensive IVD product is available for a particular condition or purpose.

While VALID identifies many proposals that may improve the effectiveness and efficiency of the IVD review process, the same proposals will cause irreparable damage if applied to LDTs. AACC urges that any refinements to the regulation of LDTs be acted upon within the Clinical Laboratory Improvement Advisory Committee (CLIAC), which is the federal advisory body that guides CMS, FDA, and the Centers for Disease Control and Prevention (CDC) on changes to the CLIA policy. This view is shared by the American Medical Association, the American Hospital Association, and many other medical and professional societies.[1]

[1] November 5, 2021 joint letter from healthcare groups to the Clinical Laboratory Improvement Advisory Committee urging it to take up the LDT issue as part of CLIA modernization.

Expanded FDA Responsibilities
AACC does not believe the FDA should be assigned additional duties. The agency has admitted to having problems hiring the necessary staff to carry out its current responsibilities. To add to this burden would harm both the agency and patient health. This problem was evident during the COVID pandemic when the FDA had to limit its review of COVID Emergency Use Authorization tests to those with a volume greater than 500,000 per week. The inability of the agency to review new COVID-19 tests raised legitimate concerns about whether the agency has the bandwidth to handle LDT oversight.

Risk-Based Classification Process
In the last iteration of VALID there were only high and low risk categories, which raised concerns about how the agency would categorize the tests. That concern remains with the current version. The draft bill provides the FDA with wide discretion in how it interprets such phrases as "substantial likelihood" and "reasonably likely" when determining high-risk. In addition, mitigating phrases such as "well characterized" and "well established" that could be used to down classify tests have been removed. This broad authority gives the agency too much latitude in determining the placement of tests.

The new bill also includes a moderate risk category. While conceptually we think this makes sense, we have questions about the definition and how the FDA would utilize the category. The legislative language does not make a clear distinction between high and moderate risk. Greater clarity is essential, since a test's categorization determines the regulatory pathway a lab must follow for introducing a test.

Tests for Rare Diseases
There are many medical conditions for which it is not cost-effective for an IVD manufacturer to develop a commercial assay. Clinical laboratories have traditionally filled this void through LDTs. The draft bill identifies several testing categories that would be exempt from pre-market review, such as low-risk, rare disease, and public health surveillance testing, amongst others, if they meet certain criteria. We agree that these LDTs should not be subject to additional FDA oversight. AACC has real concerns about how the FDA, if it were given authority over this testing, would implement the provisions.

The revised measure does not exempt newborn screening from FDA oversight. A separate section on Public Health Testing that specifically exempts newborn screening is needed.

The draft proposal also defines a rare disease as testing "for use for a diagnostic purpose for a disease or condition that affects not more than 10,000" individuals per year. This is a seemingly arbitrary number that is exceedingly low. The 2002 Rare Disease Act (Public Law 107-280) specifies that a rare disease is "any disease or condition that affects less than 200,000 persons in the United States." This provision needs significant clarification.

Technology Certification
VALID proposes a technology certification provision that would allow an individual, if they meet certain criteria, to introduce tests without going through the premarket review process. The technology certification process is as cumbersome and costly, from a clinical laboratory perspective, as the existing 510(k) review process. Few, if any hospital laboratories, would be able to comply with this requirement.

This section reenforces the fact that clinical laboratories are not medical device manufacturers. Modifications pertaining to regulatory oversight of clinical laboratories should take place within CLIA, which already requires significant information.

There also remains a lack of clarity within the measure. VALID states that a technology certificate should be no broader than a "single technology type." It is not clear whether this phrase applies solely to the methodological platform, the assays used on the platform, or each individual analyte.

Depending on the definition, one example of a single technology that encompasses multiple types of testing could be mass spectrometry. Clinical laboratories use this technology to perform a wide variety of testing, such as: drugs of abuse – (e.g., antifungals, cannabinoids, opioids, immunosuppressants, etc.); newborn screening; testing for inborn errors of metabolism (i.e., acylcarnitine's); thyroid hormones (TSH, T4); blood lead testing (i.e., ICP-MS), microbial identification (MALDI-TOF), and more.

Using this example, the VALID Act gives no indication as to whether the single technology type would be a single version of mass spectrometry (e.g., triple quadrupole) or each individual test (e.g., opioids by mass spectrometry). If each person files for each application of the technology, then this provision is wildly prohibitive for nearly all LDT-certified laboratories. This issue, among others, need to be addressed before VALID moves forward.

Grandfathering of LDTs and Maintaining Innovative LDTs
One of the strengths of the current regulatory process is that it encourages healthcare providers to continually update and improve the LDTs they perform. We support the continuation of this practice as permitted under CLIA. VALID proposes to grandfather LDTs that are performed prior to a certain date from having to comply with premarket review requirements. While we appreciate the intent of the provision to permit continued access, we are concerned that if enacted, it may have unintended consequences, such as stifling innovation.

The clinical laboratory community has historically been quick to respond to changing clinical and service demands, such as meeting the need for more sensitive and specific tests and filling the gaps when FDA-cleared or approved commercial tests are unavailable or inappropriate for a specific clinical indication. AACC is concerned that the grandfathering provision as written may discourage labs from modifying their LDTs or introducing new and better testing services to replace grandfathered tests, since they would then be subject to additional oversight.

Interestingly, VALID limits the value of the grandfathering provision by specifying that a modification to a test, even if it improves tests performance, makes it subject to premarket review. This provision once more demonstrates the internal contradictions that exist within the bill that should be addressed before moving it forward.

Custom Tests and Low Volume Tests
VALID states that a laboratory that performs an LDT on no more than five patients per year is exempt from pre-market review for that test. We think this provision will deter laboratories from developing custom/low volume tests. To perform the test on a sixth patient would subject the lab to detailed submission requirements. Further, the lab would be prohibited from listing the test on its test menu, when other patients with the unidentified rare condition would benefit from the test.

AACC is also very concerned about potential unintended consequences that could result from this provision. We believe establishing an arbitrary and excessively low limit on the number of patients who can receive care puts clinicians in a difficult position of being forced to choose which patients receive the care they need. Physicians might be forced to offer different levels of care to different patients based on when they are seen during a calendar year and not on their medical needs.

Adverse Event Reporting
The FDA document states that test developers shall "establish and maintain" a reporting system that notifies the agency of adverse events quarterly. AACC does not believe the adverse event framework, which was developed for reporting problems involving medical devices, is appropriate for services provided by clinical laboratories. Results from LDTs do not generally result or contribute to the death or severe injury of a patient. During a January 2015 FDA Public Workshop on LDTs, the Mayo Clinic reported that over the previous five years it had conducted more than 2.5 million LDT-based tests without a single sentinel event (The Joint Commission defines a sentinel event as a safety event that results in death or permanent harm to the patient).

One reason for the overall safety of LDTs is that laboratories implement internal quality controls that detect many analytical and pre-analytical errors and prevent inaccurate results from being reported. The current CLIA regulatory framework also requires laboratories to identify, document and perform corrective measures for any laboratory errors, and this would include errors resulting in patient harm if they were to occur. This documentation is reviewed on a regular basis by a CLIA inspector or its accrediting bodies. The current CLIA process could be modified to recommend that when a laboratory identifies a testing error it should report that mistake to the appropriate oversight body. This does not require legislative action.

User Fees
The bill would create a new user fee program that would be applied to laboratories performing LDTs. Reimbursement for clinical laboratories is being cut dramatically under the Protecting

Access to Medicare Act, while at the same time, testing facilities must pay registration and accreditation fees under CLIA, as well as incur the costs of on-site inspections and frequent proficiency testing to demonstrate performance. The regulatory requirements outlined in this measure, along with the additional costs, would assure that only a few laboratories would continue to offer LDTs. Unfortunately, this outcome would stifle innovation and harm patient care. While we support your efforts to reform the broader medical device review process, AACC believes that LDTs should remain under CLIA and that improvements should occur within the existing process established by Congress.

We remain willing to work with the committee to develop language that will ensure patients and physicians continue to have access to vital LDTs.

AACC is a global scientific and medical professional organization dedicated to clinical laboratory science and its application to healthcare. AACC brings together more than 50,000 clinical laboratory professionals, physicians, research scientists, and business leaders from around the world focused on clinical chemistry, molecular diagnostics, mass spectrometry, translational medicine, lab management, and other areas of laboratory science to advance healthcare collaboration, knowledge, expertise, and innovation.

On behalf of AACC, I would like to thank you for the opportunity to provide comments on this legislation. If you have any questions, please email Vince Stine, PhD, AACC's Senior Director of Government and Global Affairs, at vstine@aacc.org.

Sincerely,

Stephen R. Master, MD, PhD
President, AACC