May 21, 2022

The Honorable Patty Murray
Chair
Committee on Health, Education, Labor & Pensions
U.S. Senate
Washington, DC 20510

The Honorable Richard Burr
Ranking Member
Committee on Health, Education, Labor & Pensions
U.S. Senate
Washington, DC 20510

Dear Chair Murray and Ranking Member Burr:

On behalf of the National Independent Laboratory Association (NILA), thank you for the opportunity to provide comments on the discussion draft of the Food and Drug Administration Safety and Landmark Advancements Act of 2022. Many NILA members use laboratory-developed tests to provide essential diagnostic services to physicians and patients in their communities. As it is currently written, NILA is concerned that the VALID Act of 2021, included in the FDASLA discussion draft, could slow down, or even prohibit, access to essential diagnostics.

NILA represents regional and community clinical laboratories across the United States that perform laboratory testing for physicians, hospitals, skilled nursing facilities, and other health care professionals. NILA members serve a wide variety of communities and patient populations, many of whom are inadequately served by the large national laboratories—including rural areas, underserved urban areas, mid- and small-sized cities and municipalities, congregate facilities, and critical access hospitals.

Laboratory-developed tests (LDTs) serve an irreplaceable role in patient care. Manufactured and commercialized in vitro diagnostic (IVD) test kits cover only a small fraction of clinically-ordered tests. Additionally, test kits can quickly become outdated. Unlike IVDs, LDTs can be developed rapidly in response to emerging public health threats. For example, LDTs continue to detect the rash of synthetic fentanyls and other drugs fueling the ongoing opioid epidemic. Without LDTs, public health officials and physicians would not have access to tests that can identify new, dangerous substances, identify emerging infectious agents, and provide other clinically important information, thus leaving the public at risk and slowing opportunities to save lives.

LDTs are frequently more accurate, reliable, and relevant to patient care than FDA-approved IVDs. IVD test manufacturers have a disincentive to improve or refine IVD tests because modifications to an existing IVD test may require additional regulatory review. Because LDTs are regulated by CLIA and do not require FDA approval, laboratories are able to modify existing LDTs safely and accurately to improve their performance, meet the needs of patients, and respond to emerging threats. Regulations that require LDTs to go through burdensome FDA approval processes will prevent patients from accessing accurate LDTs, harming or delaying patient care and limiting response to current and future public health threats.

Below are several proposed edits to the discussion draft that NILA members believe would significantly improve the legislation and mitigate some of its most potentially harmful effects within the proposed structure. Proposed additions are in bold and underlined typeface; proposed deletions are in strikethrough typeface. We appreciate your consideration of these proposed changes and would welcome the opportunity to discuss them further.

Registration and Listing

NILA appreciates that patients and practitioners want access to information about LDTs. For that reason, many independent laboratories maintain electronic, internet-based test menus that include much of the information sought for submission under Section 587J(b)(2). As proposed, the registration requirements imposed on community and regional laboratories by this section would be extremely burdensome, duplicative of existing laboratory resources, and of limited utility to both practitioners and patients. For that reason, **NILA recommends more limited registration requirements for grandfathered tests and permitting laboratories to meet the requirements of Section 587J(b)(2) by maintaining an electronic, internet-based test menu on the laboratory's website and submitting the link to that test menu to the FDA.** Rather than requiring laboratories to duplicate this information, FDA could access this information as needed on a given laboratory's website and maintain a less burdensome listing of test menu websites that patients could access, either through a laboratory's website or by accessing a link to the laboratory's website on the FDA's own website.

Consistent with this approach, NILA recommends the following modifications to Section 587J(b) on page 243 of the discussion draft:

> "(1) IN GENERAL.—Each person who—
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> (A) is a developer; and
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> (B) introduces or proposes to begin the introduction or delivery for introduction into interstate commerce through an exemption under subsection (a)(1), (a)(2), (a)(3), or (g) of section 587C or section 587G or through the filing of an application under section 587B or 587D,
>
> shall submit a listing to the Secretary containing the information described in paragraph (2), (4), or (5), as applicable, in accordance with the applicable schedule described under subsection (c) **or a link to a page on the entity's website that contains the same information**. Such listing shall be prepared in such form and manner as the Secretary may specify in guidance. Listing information shall be submitted through the comprehensive test information system in accordance with section 587U, as appropriate.

Definition of High-Risk

Because the VALID Act, as included with FDASLA, relies on risk stratification to assign obligations, the definition of "high risk" should be clear and narrow enough to avoid including tests that pose little risk of harm to patients or the general public. The risk of an inaccurate test is at its highest when a practicing clinician is entirely dependent on a test result for diagnosis or treatment planning. In most cases, however, diagnoses and treatment planning depend on test results, observation of clinical symptoms, and clinical decision making that assesses a patient's health and disease risk. For example, a clinician is likely to use a test result merely to confirm a patient's symptoms. In these cases, risk to patients is inherently low given that the review and assessment of test results relies upon the assessment and judgment of a trained clinician.

The definition of "high risk" and the associated requirements for "high risk tests" should be reserved only for the small subset of tests that supplant clinician decision making, are used in isolation to determine whether to undertake invasive or risky procedures or treatments or use clinical inputs and algorithms that are not readily available to the ordering clinician. In each of these circumstances, tests operate more as a clinical decision-making tool rather than a data point for clinicians to use when assessing a patient. For that reason, more scrutiny is warranted given the lack of opportunities for clinicians to intervene in case of a false positive or negative result.

For those reasons, NILA proposes the following modifications to the definition of "high risk" at Section 587(9):

> (9) HIGH-RISK.— ~~the term 'high risk', with respect to~~ An in vitro clinical test or category of in vitro clinical tests **is considered 'high risk' if,** ~~(i) means that,~~ an undetected inaccurate result from such test or category of tests when used as intended, **taking into account the degree to which the technology is well-characterized and the criteria for performance of the test is well-established for the intended use, the clinical circumstances under which the in vitro clinical test is used, and the availability of other tests (such as confirmatory or adjunctive tests):**
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> (A)(i) has the substantial likelihood for serious or irreversible harm or death to a patient or patients, or would otherwise cause serious harm to the public health; or
>
> (ii) is ~~potentially~~ reasonably likely to result in the absence, significant delay, or discontinuation of life-supporting or life-sustaining medical treatment; and **the test or category of tests is intended to act as a substitute for a health care practitioner's clinical judgment;**
>
> **(iv) the test is used in isolation to inform a decision to undertake an invasive, harmful, or risky intervention or procedure; or**
>
> **(v) the test or category of test utilizes a proprietary algorithm that is not made available to the ordering health care practitioner.**

Preserving Access to LDTs

Laboratory tests differ from manufactured in vitro diagnostic test kits in several respects. LDTs are faster to deploy and help community and regional independent laboratories respond quickly to the needs of patients and practitioners. To preserve this important patient service, it is important that the VALID Act recognize the inherent differences between LDTs and in vitro diagnostic test kits. For that reason, NILA recommends creating a definition for LDT within the VALID Act for tests that are developed in a single, CLIA-certified high-complexity laboratory and performed only within the laboratory that developed the test. Once defined, LDTs can then be exempted from requirements, such as labeling, that are unnecessary for tests used within a single laboratory.

For these reasons, NILA recommends the insertion of a new provision (21) in Section 587 to read as follows:

> **(21) Laboratory-Developed Test. – The term "laboratory-developed test" means an in vitro clinical test that:**
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> **(i) is developed by a CLIA-certified high-complexity laboratory and;**
>
> **(ii) is performed only within the laboratory that developed the test.**

With "laboratory-developed test" defined, NILA recommends that laboratory-developed tests be exempted from labeling requirements (Section 587L) as follows:

SEC. 587L. LABELING REQUIREMENTS.

(a) In General.—An in vitro clinical test **that is not a laboratory-developed test** shall bear or be accompanied by labeling, and a label as applicable, that meet the requirements set forth in subsections (b) and (c), unless such test is exempt as specified in subsection (d) or (e).

Differentiating the Role of Laboratories and Clinicians

LDTs serve many purposes in clinical care. The majority of LDTs are relatively simple tests that provide information on biomarkers that are well-established and well-understood to be associated with disease risk or status by ordering clinicians. Independent laboratories frequently offer LDTs that quantify allergen responses, presence of a specific substance, drug, or infectious agent. As written, the VALID Act would require laboratories to justify the clinical validity of simple and widely used clinical information. For example, a laboratory that creates an A1C or HbA1c LDT would be required to provide the clinical justification for using the output of that test for monitoring a patient for diabetes, despite the association of A1C and diabetes being well-understood and widely accepted by clinicians. Requiring laboratories to justify the measurement of A1C for diabetes management, the presence of opiates in urine for monitoring opioid use disorder care, or feline dander IgE level for allergy testing, derives no public health benefit and puts laboratories in the position of needing to validate clinician decision-making. The following suggested modifications to the VALID Act are intended to better differentiate the role between laboratory and ordering clinician and focus regulatory oversight on LDTs where clinical validity is not well-established or widely understood.

At 587B(a)(3), insert the following and renumber the following provisions as necessary:

(4) PREMARKET REVIEW INAPPLICABLE. – Not later than 2 years after the date of enactment of the Verifying Accurate Leading-edge IVCT Development Act of 2021 and annually thereafter, the Secretary shall develop and issue a list of clinical tests and categories of clinical tests that, for the purposes of the Act have a rebuttable presumption of clinical validity.

Protecting Competition

As written, the VALID Act will erect higher barriers to entry and is likely to accelerate the existing trend towards consolidation in the independent laboratory market. To preserve competition, it is imperative that community and regional, independent laboratories have a seat at the table. To preserve competition in the laboratory market, NILA recommends modifying the structure of advisory committees to require the inclusion of small business considerations and creating a sliding scale for fees based on revenue.

NILA recommends that Section 587H(b)(2) be modified as follows:

(2) NONVOTING MEMBERS.—In addition to the individuals appointed pursuant to paragraph (1), the Secretary shall appoint to each committee established under subsection (a), as nonvoting members—

(A) **two** representative**s** of consumer interests; and

(B) ~~a~~ **two** representativ**es** of interests of in vitro clinical test developers not directly affected by the matter to be brought before the committee~~.~~**, wherein at least one is a representative of community and regional independent laboratories**.

NILA additionally recommends that Section 9(b)(1)(E)(ii), regarding user fee recommendation requirements, be modified by including a new provision V as follows:

> **(V) provide that the fees assessed on in vitro clinical test developers operate on a sliding scale based on developer revenue.**

Thank you for the opportunity to provide these proposed edits to this discussion draft.

Sincerely yours,

Mark S. Birenbaum, Ph.D.
Executive Director
National Independent Laboratory Association