AMERICAN CLINICAL LABORATORY ASSOCIATION

May 22, 2022

Chair Patty Murray
154 Russel Senate Office Building
Washington, DC 20510

Ranking Member Richard Burr
217 Russell Senate Office Building
Washington, DC 20510

***Via E-mail**: helpuserfeebill@help.senate.gov*

RE: ACLA Comments on the VALID Act of 2022

Dear Chair Murray and Ranking Member Burr:

The American Clinical Laboratory Association (ACLA) appreciates the opportunity to provide initial comments on the discussion draft of the Verifying Accurate Leading-Edge IVCT Development (VALID) Act of 2022 (hereinafter VALID 2022 or the Act). ACLA is the national trade association representing leading laboratories delivering essential diagnostic health information to patients and providers every day. ACLA appreciates the ongoing bipartisan work the HELP Committee has undertaken, including engaging with stakeholders on the important matter of diagnostics regulatory reform.

In consideration of the window of time for review of the Act, these comments are intended to focus your attention on key issues that ACLA feels must be addressed in the Act before a novel framework for the regulation of diagnostic products is enacted. These comments are not comprehensive and should not be viewed as such. As always, ACLA stands ready to answer any questions on our comments or otherwise collaborate with your staff. Thank you for your consideration of these comments.

I. Grandfathered Tests

ACLA supports strong grandfathering provisions in VALID 2022, but changes are necessary to avoid interruption in test availability for patients and clinicians, including:

(1) changes to the "special rule" to ensure a predictable and evidence-based process that applies when there is a legitimate risk of patient harm; and

(2) limiting the types of modifications that cause a test to require premarket review to those modifications that meaningfully impact performance or use of the test.

For many diseases and conditions, the standard of care in clinical practice relies on laboratory-developed tests (LDTs) that were developed in compliance with existing laws, regulations and policies. Many of these important tests have been on the market for years or even decades, and they are used every day by clinicians across the healthcare continuum.

Clinicians must be confident that tests on which they rely will remain available, and that enactment of a new regulatory framework for diagnostics does not cause gaps in test availability. Thus, ACLA supports strong grandfathering provisions in VALID 2022 that ensure the Act is

prospectively applied and does not subject existing LDTs to novel regulatory requirements retroactively. ACLA particularly appreciates the improvements that have been made to avoid undercutting the grandfathering provisions through overly burdensome registration and listing requirements.

However, as drafted, VALID 2022 risks interrupting test availability in two key ways. First, as drafted, the "special rule" under section 587G(c) would subject grandfathered tests to premarket review if FDA makes a determination that "there is insufficient valid scientific evidence to support" that the test is analytically or clinically valid. Moreover, FDA may make this determination after reviewing limited information submitted by the developer within 30 days of a request from FDA, with no opportunity for clarification or discussion between FDA and the developer. ACLA has several concerns with this approach, which essentially requires developers to establish that a grandfathered test meets the new applicable standard—which is yet to be interpreted or applied—on an expedited timeline of 30 days. This type of retroactive application of new requirements could result in frequent interruption in the availability of important tests for patients and clinicians.

ACLA believes it is appropriate to provide FDA with authority to request information about a grandfathered test when it has scientific concerns that indicate a risk of patient harm. However, to ensure predictable application of this authority, VALID 2022 must (1) enumerate specific, clear grounds for FDA to initiate a process to examine a grandfathered test, and (2) provide appropriate due process protections before such a test can be subject to additional regulation. Under ACLA's proposal, attached in **Exhibit A**:

- FDA can initiate a process by detailing scientific concerns, based on credible information, indicating that the test (1) lacks sufficient valid scientific evidence of analytical or clinical validity; (2) is offered with false or misleading claims; or (3) is likely to cause serious adverse health consequences;

- Following a request for information, there is a clear, predictable, and timely process through which the developer can submit information to address FDA's scientific concerns, including opportunities for the developer and FDA to meet and clarify information, as appropriate; and

- Only if FDA and the developer cannot find a way to resolve FDA's concerns, FDA may require that the test be taken off the market until it is approved under the new framework.

Second, as drafted, routine modifications with no meaningful impact on performance or use of the test could cause a test to lose its grandfathered status. As drafted, a grandfathered test is required to undergo premarket review if a modification "affects" analytical or clinical validity or "changes" performance or performance claims, among other things. ACLA has several concerns with this approach as described below.

Importantly, high quality, clinical laboratory science often requires routine modifications to ensure the quality and continued availability of tests. Such modifications include changes to address interruptions in supply of reagents—such as occurred during the COVID-19 pandemic—as well as changes to address specimen stability. As VALID 2022 is drafted, however, premarket review would be required before these changes could be implemented. This would severely undermine the grandfathering exemption and require submission of enormous numbers of premarket review applications under a variety of circumstances, even though these modifications are unlikely to

have any meaningful impact on the performance or use of the test. This overly narrow approach to exempting modifications is not in the interest of FDA or developers, who would both be overburdened by submission and review requirements, and certainly not in the interest of clinicians and patients, who would lose access to high quality tests.

In ACLA's proposal within **Exhibit A**, we have proposed additional changes to limit the types of modifications that could cause a test to lose its grandfathered status. As proposed, the test would lose such status only if a modification significantly changes the indications for use, significantly and adversely changes performance, or adversely changes performance claims. **Exhibit A** also includes additional edits that are necessary to ensure the grandfathering provision is not undermined by other provisions of the Act.

II. Transition

As part of a robust transition period that requires rulemaking and guidance to be finalized far in advance of the effective date, ACLA believes VALID must explicitly state that CLIA applies to LDTs until the effective date of the legislation. ACLA also views as essential a staged approach to requiring premarket review for LDTs introduced during the transition period, where such tests have been reviewed and approved by a third party.

VALID 2022 represents a fundamental overhaul of the regulation of the diagnostics industry in the United States. Implementation of this entirely new framework would be both an enormously significant undertaking for FDA and a transformative reconstruction of the regulation of laboratory diagnostics, which are relied upon each day by patients and providers across the health care continuum in the service of informed clinical decision-making. The nation's clinical laboratory industry has grown and evolved to an industry that employs hundreds of thousands of professionals across the country and serves millions of patients and physicians with critical diagnostic testing. Successful implementation of the VALID framework would require transparency and accountability by the implementing agency and predictability for regulated industry. Thus, ACLA supports at least a five-year transition timeline for FDA and stakeholders to complete notice-and-comment rulemaking for important topics, with additional time for stakeholders to come into compliance with the requirements described in such rules.

ACLA also appreciates that LDTs could be offered subject to existing requirements during the transition period, as well as after the effective date until FDA completes its review of a premarket or technology certification application. ACLA has long held that the existing requirements for LDTs are limited to those imposed under the Clinical Laboratory Improvement Amendments (CLIA), and we recommend that the transition provisions make this explicit.

However, ACLA is concerned that a significant influx of LDT applications would significantly outpace FDA resources. This would first occur shortly before the effective date, when applications for transitional in vitro clinical tests (IVCTs) would be required to be submitted, and it would likely be an ongoing challenge for FDA as the 11,000+ clinical laboratories that develop LDTs submit applications in the following weeks, months and years. Indeed, FDA has repeatedly stated that it is insufficiently resourced to handle existing workload, which does not account for future LDT submissions. To avoid overwhelming FDA with an avalanche of applications, we believe it is appropriate to extend the deadline for submission of an application for transitional IVCTs that are approved by well-known and experienced third-party reviewers during the transition period.

In the attached **Exhibit B**, we have proposed that transitional IVCTs approved by New York State's Wadsworth Center would have an additional two years (for non-molecular tests) and an additional five years (for molecular tests) after the effective date before a premarket or technology certification application is required to be submitted. New York's Wadsworth Center already reviews LDTs before they can be offered in New York and is accredited by FDA to review *in vitro* diagnostic devices. Thus, an approval from New York provides assurance that the transitional IVCT is analytically and clinically valid, and there is no pressing public health need for an additional review by FDA on the effective date.

Reliance on review by accredited third-party organizations is far from a new concept. Indeed, there are numerous examples of programs administered by FDA or HHS that rely extensively on third-party review. For example:

- ***COVID diagnostics.*** During the COVID-19 public health emergency, FDA permitted state health authorities to review and authorize LDTs for COVID-19, without further review by FDA.
- ***Mammography facilities.*** Under the Mammography Quality Standards Act, mammography facilities are accredited by FDA-approved entities, which are private nonprofit organizations or State agencies.
- ***Third party laboratories.*** Beginning in 2017, FDA piloted a program in which FDA relied on third-party laboratories to perform testing for premarket submissions of medical devices. The Food and Drug Amendments of 2022, introduced earlier this month by the House of Representatives Energy & Commerce Committee, proposes to make this program permanent.
- ***Laboratory Accreditation.*** Pursuant to CLIA, CMS authorizes third parties to issue a certificate of accreditation that allows a laboratory to develop LDTs and perform the most complex tests. Accreditation by certain third-party organizations is considered the "gold standard" for clinical laboratories.

Staging FDA review of premarket and technology certification applications for transitional IVCTs would allow FDA to prioritize its resources on tests that have not been scrutinized and reviewed by a trusted third party. We strongly believe that such an approach is in the best interest of developers, FDA, and the public health.

III. Meaningful Third-Party Review

A meaningful third-party review program will be a critical part of the implementation plan for a new diagnostics framework.

As noted above, ACLA is concerned that the number of IVCT applications—which would encompass both IVD applications and LDT applications—submitted under the new framework is likely to significantly outpace FDA's capabilities, even assuming the Agency ramps up its resources over time. This could lead to delays in approval of important tests, such as occurred during the COVID-19 pandemic when FDA struggled to keep pace with the large number of EUA submissions from clinical laboratories. Thus, to maximize the successful implementation of VALID 2022, ACLA urges Congress to ensure that the framework includes a meaningful third-party review program that would complement FDA's resources.

Third party review of diagnostic tests is not new, and ACLA's proposal would build upon already-successful models. As noted above, FDA already relies upon New York's Wadsworth Center to

review *in vitro* diagnostic devices and to review COVID-19 LDTs. FDA also relies upon accredited laboratories to perform testing of medical devices for premarket submissions and to oversee the quality of mammography facilities. Likewise, CLIA has "deemed" third party accreditation organizations—such as the College of American Pathologists (CAP)—to have authority to certify that clinical laboratories meet the requirements established by CLIA. Wadsworth, CAP and other qualified entities can serve as the backbone of a new program for IVCTs.

In addition, for such a program to reduce the burden on FDA, it must be attractive to developers. It is widely accepted that FDA's third-party review program for medical devices is not used extensively because FDA routinely conducts a duplicative review of the 510(k) submission, meaning it can take *longer* for a device to be cleared through the third-party review program. Learning from this history, ACLA's proposal, attached in **Exhibit C**, would minimize duplicative reviews in several ways:

- Within 30 days of receiving a recommendation for approval of a premarket application from a third-party reviewer, FDA would be required to (1) approve the application, (2) deny approval of the application and provide to the applicant a written explanation of the scientific basis for the denial, or (3) initiate a process with the applicant to resolve any outstanding issues.

- FDA must post on its website an annual report detailing metrics associated with its implementation of this program and describing its progress in minimizing duplicative reviews of applications.

This proposal would build upon successful precedents and known third parties with experience reviewing diagnostic tests, while preserving FDA authority.

IV. Risk-Based Classifications and Marketing Pathways

ACLA supports the risk-based framework that clearly defines tests as low-, moderate-, or high-risk and permits moderate-risk tests—including first-of-a-kind tests and combination products—to be marketed pursuant to an abbreviated pathway or technology certification. However, changes are necessary to:

(1) Meaningfully distinguish between the abbreviated premarket review pathway for moderate-risk tests and the standard premarket review pathway for high-risk tests; and

(2) Ensure the technology certification pathway will be used by expert test developers.

A new diagnostics framework should be risk-based, and the level of regulatory oversight for an IVCT must be commensurate and calibrated with the risk level of the test. A risk-based framework enables the government to exercise appropriate oversight of test development and provides the regulatory flexibility that is needed to facilitate development and innovation. Thus, ACLA supports the inclusion of a defined "moderate-risk" category that enables clear delineation of which tests are eligible for the different premarket review pathways. Likewise, ACLA agrees that non-risk-based categories—such as first-of-a-kind tests, tests that utilize home specimen collection, and tests that reference other medical products in labeling—should not be categorically excluded from abbreviated premarket review or technology certification.

However, ACLA sees several opportunities to improve the premarket review pathways for IVCTs that is consistent with this risk-based approach. First, the abbreviated premarket review pathway, which would be available for moderate-risk tests, must be meaningfully different from the standard premarket review pathway, which is required for high-risk tests. Currently in VALID 2022, FDA could request the submission of raw data for these applications and conduct preapproval inspections, meaning the only real difference between an abbreviated premarket application and a regular premarket application is that abbreviated premarket applications would not require submission of information related to test design and quality requirements. ACLA recommends clarifying that raw data and preapproval inspections are *never* required for abbreviated premarket review.

Second, the scope of a technology certification should not be limited to a "single technology" or only a "fixed combination" of technologies that are specified in regulation. Limiting the scope of a technology certification order in this way is not based on the risk presented by in-scope IVCTs that would be introduced under an order. Rather, this limited scope would only serve to increase the burden on FDA and developers by requiring the submission of multiple applications for individual technologies, as well as rulemaking to establish limited fixed combinations of technologies that are highly unlikely to encompass the full scope of combinations that may be used by innovative test developers. Instead, ACLA continues to recommend that the scope of a technology certification order may include "one or more technologies" or a "fixed combination" of technologies that is not limited by FDA rulemaking. If the developer can meet the requirements for certification for more than one technology, we are aware of no basis for denying the request or requiring multiple applications to achieve the same result.

Additionally, the notification procedure for introduction of moderate-risk first-of-a-kind tests and combination products must be revised to ensure predictable application. Currently, it is unclear whether FDA could issue a notice to stop the introduction of such a test *after* it already has been introduced, which would create confusion for clinicians and patients, and it is unclear on what grounds such a notice may be issued. ACLA proposes that FDA would have to issue such a notice prior to introduction of the test under the technology certification and that such notice cannot be based on the fact that the test is first-of-a-kind or a combination product, alone.

Finally, tests introduced pursuant to a technology certification order must be "deemed approved," rather than exempt from premarket review. This is important to ensure such tests receive equal treatment under other provisions of law, such as related to reimbursement, and to promote international harmonization. ACLA has proposed these changes to premarket review and technology certification as described above, within the attached **Exhibit D**.

V. Additional Comments and Redline

In addition to the attached exhibits that propose legislative language to address key policies as described above, ACLA is submitting with these narrative comments a redline of the Act with additional comments. As noted above, these comments—as well as the redline—are not comprehensive given the window for comment. However, all the proposals and comments reflect key issues that we strongly believe should be addressed before any diagnostic reform is enacted. Proposals and comments address topics such as, but not limited to:

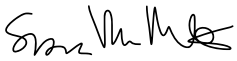
- ***Preserving access to accurate and reliable tests.*** ACLA strongly supports the registration and listing provisions in VALID 2022 that do not require developers of grandfathered tests to prepare and submit summaries of analytical and clinical

performance for the thousands of tests that they already offer. A change in this policy would impose an exceedingly burdensome requirement on clinical laboratories and divert important resources away from patient care and development of novel tests.

- ***Encouraging innovation and addressing unmet needs.*** The new framework must also encourage innovation and facilitate test development to address unmet needs. Thus, ACLA supports establishment of a humanitarian test designation, in addition to the humanitarian test exemption, that enables tests for unmet needs to be offered if they have a reasonable probability of demonstrating clinical validity, on the condition that they are offered for a limited time during which developers collect data to demonstrate that the applicable standard is met.
- ***Ensuring clear jurisdictional boundaries between FDA under the new framework and CMS under CLIA***. The applicability section of VALID 2022 should be amended to state explicitly that laboratory operations (which are properly under the sole jurisdiction of CMS under CLIA) shall not be subject to the requirements of VALID. For example, new labeling requirements imposed under VALID must not overlap or interfere with existing CLIA requirements for test results reports. Additionally, laboratories should not be required to submit adverse event reports for in vitro clinical test errors are that are due to laboratory operations regulated under CLIA.
- ***Transparency in implementation.*** FDA should not be given unfettered authority to exempt any "class of persons" from complying with the Act, nor to request "such other data or information as the Secretary may require" for IVCT submissions. Additionally, ACLA continues to recommend that implementation of the Act must be contingent on the promulgation of final rules, which should be required for any substantive requirement under the Act. Developers must have a clear sense of what is required of them, and the due process protections of rulemaking are essential for ensuring proper implementation of substantive requirements. Guidance should be reserved solely for non-substantive procedural matters.
- ***Accountability in implementation.*** ACLA has significant concerns with inclusion of the preemption savings clause in section 587V(c). If enacted, VALID 2022 would establish a national, uniform standard for the development and commercialization of IVCTs. As such, lawsuits under state legal requirements could create a patchwork of inconsistent requirements that would undermine this effort.
- ***Resources.*** As reflected in these comments, if enacted, implementation of the Act would require appropriate resources. Accordingly, and given the potential for an extended transition period, FDA should be provided with adequate funding by Congress, which may be augmented after the effective date by authorized user fees that are negotiated with industry through a transparent and thoughtful process.

Again, we thank you for the opportunity to submit these comments, which we believe would improve VALID 2022 and its prospects for successful implementation. We would be pleased to answer any questions you or your staff may have on our comments and recommendations. Please feel free to direct those inquires to Tom Sparkman at tsparkman@acla.com.

Sincerely yours,



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