

October 15, 2020

Representative Diana DeGette
Committee on Energy & Commerce
U.S. House of Representatives
2111 Rayburn HOB
Washington, DC 20515

Senator Richard Burr
Committee on Health, Education,
Labor and Pensions
217 Russell Senate Office Building
Washington, DC 20510

Representative Larry Bucshon, M.D.
Committee on Energy & Commerce
U.S. House of Representatives
1005 Longworth HOB
Washington, DC 20515

Senator Michael Bennet
Committee on Health, Education,
Labor and Pensions
261 Russell Senate Office Building
Washington, DC 20510

RE: Comments on the VALID Act of 2020

Dear Representatives DeGette and Bucshon, and Senators Burr and Bennet:

The American Clinical Laboratory Association (ACLA) is pleased to provide these initial comments on the Verifying Accurate Leading-Edge IVCT Development (VALID) Act of 2020 (hereinafter VALID Act or the Act). Also attached as Appendix 1, please find a redline of the VALID Act with proposed edits to effect the policies described in our comments.

As always, ACLA stands ready to answer any questions on our comments or otherwise collaborate with your staff on constructing a new framework for the regulation of diagnostic tests. ACLA appreciates your efforts in addressing this important topic and considering these comments.

I. Introduction and COVID-19 Lessons Learned

ACLA is a trade association representing the nation's leading providers of clinical laboratory services, including regional and national laboratories. Its diverse membership includes a broad array of clinical laboratories: large national independent labs, reference labs, esoteric labs, hospital labs, and nursing home labs. ACLA members both develop and perform laboratory developed test services (LDTs), in addition to purchasing and performing tests with in vitro diagnostic test kits (IVDs).

Over the past thirty years, the clinical laboratory industry has been at the forefront of significant advances in molecular and genetic diagnostics. These powerful tools have advanced medical knowledge through increasing levels of accuracy and precision in both screening and diagnostic tests never before contemplated or achievable, and, thereby, better guide diagnosis and prevention or treatment decisions. Through this innovation, clinical laboratories have played a critical role in reducing medical costs and increasing the quality of patient care.

Most recently, as part of the country's ongoing response to the COVID-19 pandemic, our members have taken unprecedented steps to rapidly scale testing capacity and provide a range of new tests to meet the pressing public health needs facing American families and workers.

Indeed, our members are uniquely qualified to rapidly develop, validate, and perform high-quality diagnostic tests that are necessary for managing a pandemic response. Our members are armed with the personnel, scientific expertise, and experience necessary to respond quickly and develop new tests. In the commercial sector, our members also have the most capacity, established supply chains, and operational systems to quickly and efficiently conduct large-scale testing of specimens from all over the country, 24 hours a day and 7 days a week.

As we continue to respond to the COVID-19 pandemic and safely reopen the economy, our members face a constantly shifting landscape on several fronts, including most recently an announcement by the Department of Health and Human Services (HHS) that the Food and Drug Administration (FDA) would no longer require premarket review for laboratory developed tests, unless FDA issues notice-and-comment rulemaking to effect such requirement.¹ ACLA appreciates that HHS recognizes the importance of flexibility to innovate for laboratories bringing quality testing services to the market, and this legal conclusion is consistent with one of ACLA's longstanding legal positions regarding the current framework of statutes and regulations. Nonetheless, we continue to believe it is appropriate for Congress to design a new oversight framework for diagnostic tests.² We therefore support the pursuit of appropriate comprehensive statutory reform for the oversight of LDTs and IVDs through a transparent process with Congress, the Administration, and other stakeholders.

In this pursuit, we urge Congress to consider the important lessons learned from the response to the COVID-19 pandemic and to ensure that any new statutory framework balances government oversight with the need for flexibility, innovation, and timely responses to emerging public health threats. Certainly, the COVID-19 pandemic demonstrates that robust provisions must be included that allow clinical laboratories to rapidly respond and scale up at the earliest possible time that a novel pathogen or public health threat emerges. More broadly, the COVID-19 pandemic illustrates the critical role played by laboratory diagnostics in our health care ecosystem. Any new regulatory framework must support the development of innovative diagnostics, maintain access to existing diagnostics, and not unduly impose regulatory burdens. Our comments below help to further these critical goals.

II. Key Principles for Legislative Reform

ACLA urges Congress to be guided by the following three key principles for legislative reform:

1. Legislation must recognize and take into account the differences between, on one hand, IVDs that are manufactured and distributed to third party labs and, on the other, tests that are developed and offered as services by laboratories.

¹ HHS, *Rescission of Guidances and Other Informal Issuances Concerning Premarket Review of Laboratory Developed Tests* (Aug. 19, 2020), available at <http://hhs.gov/coronavirus/testing/recission-guidances-informal-issuances-premarket-review-lab-tests/index.html>.

² See also *ACLA Comments on March 21, 2017 Discussion Draft of the Diagnostic Accuracy and Innovation Act*, ACLA.COM (Apr. 7, 2017), available at <https://www.acla.com/acla-comments-on-march-21-2017-discussion-draft-of-the-diagnostic-accuracy-and-innovation-act/>; *ACLA Comments on FDA Technical Assistance on the Diagnostic Accuracy and Innovation Act*, ACLA.COM (Aug. 21, 2018), available at <https://www.acla.com/acla-comments-on-fda-technical-assistance-on-the-diagnostic-accuracy-and-innovation-act/>; Appendix 2: *ACLA Comments on VALID Discussion Draft*.

2. IVCTs must be regulated according to a true risk-based framework.
3. The new framework must be implemented with transparency and accountability.

As we have learned from the COVID-19 pandemic, laboratory diagnostics are a critical part of our healthcare system. We must take care to ensure that legislative reform maintains the vibrancy of this part of our healthcare ecosystem. ACLA believes that these guiding principles are critical to protecting the progress made in diagnostic testing and to supporting further development and innovation.

A. The differences between IVDs and laboratory diagnostics must be recognized.

Congress must ensure that the new IVCT framework recognizes and differentiates between LDTs, which are services, and IVDs, which are products. LDTs and IVDs are developed and commercialized differently, and although the new framework will result in a single regulatory system, that system must account for these differences. For example, LDTs are regulated by CMS under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), whereas IVDs are regulated by FDA under the Federal Food, Drug and Cosmetic Act (FDCA) as medical devices.³ Thus, with the passage of the VALID Act as part of the FDCA, laboratories developing and offering LDTs will be subject to regulation by *two* federal agencies under *two* different statutes, whereas IVDs will remain subject to regulation under the FDCA only. Therefore, the VALID Act must ensure that the boundaries of jurisdiction are clearly defined between CMS and FDA, and that the new regulatory framework under FDCA is not redundant, conflicting, or superfluous to the existing CLIA framework. For example, there should be meaningful differences in the quality requirements, labeling, and transition provisions for LDTs versus IVDs. Where VALID encroaches on areas that CLIA already regulates (e.g., results reporting, purchasing controls), conforming amendments to CLIA must be made.

Moreover, laboratory professionals performing LDTs provide a vital service as part of the practice of medicine, and this role in individualized patient care must be protected. As discussed further below, laboratory professionals are required to consult with healthcare providers and transparently discuss the results of the tests they perform. In contrast, IVDs are manufactured and distributed, and the manufacturers of such tests are under no such duty to consult with the healthcare providers relying on the results of their tests (and in many cases, such manufacturers are not qualified to do so). The new IVCT framework must acknowledge that LDTs are a service that is integral to patient care, and that service includes aspects of the practice of medicine.

B. IVCTs must be regulated according to a risk-based framework.

ACLA urges Congress to ensure that the new IVCT framework is risk-based, and that the level of regulatory oversight for an IVCT is commensurate and calibrated with the risk level that a test may provide. A risk-based framework enables the government to exercise appropriate oversight of test development and also provides the regulatory flexibility that is needed to facilitate development and innovation.

³ Note that some clinical laboratories have received FDA marketing authorization for LDTs. These are single-site IVDs and are therefore not distributed products. In these cases, the same entity is both the manufacturer and the laboratory service provider, regulated by both FDA and CMS-CLIA.

To ensure that the framework is risk-based, Congress must ensure that the framework includes a clearly defined moderate-risk category (in addition to the defined low-risk and high-risk categories), and that non-risk-based categories are omitted (i.e., cross-referenced and first-of-a-kind). Moreover, there must be meaningful differences in the regulatory requirements for low-, moderate-, and high-risk tests, especially with regard to premarket review. Specifically, there should be a defined special premarket pathway for moderate-risk tests that is meaningfully different from the general premarket pathway, and all moderate-risk tests should be eligible for introduction through technology certification. Additionally, for moderate-risk tests and breakthrough tests (i.e., high-potential tests), Congress should establish a premarket pathway that allows for postmarket confirmation of clinical validity when a test has established analytical validity.

C. The new framework must be implemented with transparency and accountability.

Implementing an entirely new framework for IVCTs is a significant undertaking, and it must be done thoughtfully and carefully. ACLA urges Congress to amend the VALID Act to ensure that substantive provisions of the Act are implemented through notice-and-comment rulemaking, not guidance documents. Although guidance may be useful for clarifying procedural points, substantive policy should be implemented with the input of stakeholders and the required accountability of the regulatory agency provided only through notice-and-comment rulemaking. Moreover, because rulemaking can be a lengthier process than issuing guidance documents, ACLA urges Congress to ensure the transition period between enactment and implementation of VALID is long enough to finish the rulemaking process and give regulated developers adequate time to come into compliance. ACLA has proposed a transition period of five years, or two years after the finalization of implementing regulations, whichever is longer.

ACLA also urges Congress to ensure that the VALID Act is not drafted in an overly ambiguous manner that grants FDA excessive discretion. Specifically, ACLA recommends striking several of the discretionary qualifiers in the VALID Act, such as “adequate,” “sufficient,” or “as the Secretary determines,” among others.

These three principles are further described and reflected in the comments that follow.

III. Comments

The following comments are the result of a review by ACLA and our member laboratories and do not encompass all policy issues within the VALID Act. As we continue to consider the VALID Act, ACLA would be pleased to provide additional comments.

A. Boundaries of Jurisdiction

ACLA continues to believe that a new framework for regulating IVCTs must recognize diagnostics as presenting unique opportunities and challenges for regulation. First and foremost, the framework must recognize the fundamental differences between LDTs—services regulated via CMS’s regulation of laboratory operations under CLIA, which would continue together with new authority for FDA regulation of certain activities under VALID, and IVDs—products historically regulated by FDA as devices, but able to be used within laboratories whose operations are regulated by CMS under CLIA. With a unique and extensive history, it is critical that the new regulatory framework clearly recognize that LDTs are not currently unregulated

and delineate the lines of jurisdiction between FDA and CMS for regulating IVCTs. Therefore, Congress must ensure that the bedrock of the new framework—the IVCT definition—recognizes the fundamental differences between LDTs and IVDs, and that the new framework does not permit jurisdictional creep, such that FDA—in addition to CMS—is regulating laboratory operations. Moreover, given the unique role that IVCTs play in individualized medical practice, Congress must ensure that the new framework does not encroach on the practice of medicine, which is the purview of the states.

1. *IVCT Definition*

The IVCT definition presently fails to recognize the fundamental differences between LDTs and IVDs. Specifically, it groups and treats as equal (1) test protocols, which include standardized and in-house proprietary methods for performing specific, complete laboratory tests, and (2) distinct articles, such as instruments, specimen receptacles, software, and components, all of which can be used interchangeably to support several different tests, but several of which alone are insufficient to yield a test result. This definition creates several problems.

First, this definition fails to recognize that LDTs (professional laboratory services) and IVDs (manufactured finished products) represent fundamentally different approaches to testing. Whereas an LDT is essentially a service, an IVD is a tangible product. As we have stated in prior comments,⁴ these different approaches require different treatment in several regards. For example, a label affixed to a test protocol used within a single laboratory organization would serve no meaningful purpose, and may not even be practicable given that a protocol consists of one or more documents, and is not a container, vial, ampule, or instrument to which a label may be attached. Likewise, application of certain quality requirements designed for commercial distribution of packaged products does not make sense for a laboratory test protocol used within a single laboratory organization that is neither packaged nor commercially distributed. Therefore, ACLA recommends that the definition of IVCT in VALID should be amended to separately define “laboratory test protocol” and other “finished product.” Using such terms would facilitate a framework that clearly distinguishes between these different approaches to testing, as appropriate.

Second, the IVCT definition is incompatible with a risk-based framework for regulation of IVCTs because it includes standalone instruments, collection articles, and other components that do not render test results. As proposed in VALID, whether a test is “low-risk” or “high-risk” depends on the consequences of an undetected inaccurate result from the test, but instruments, collection articles and other components (historically regulated as medical devices) do not render results on their own, and therefore cannot be classified according to risk (as defined in VALID). For example, a genetic sequencing instrument may be low-risk when it is used as part of a test to detect a non-life-threatening mutation, but high-risk when used as part of another test, such as a test to detect SARS-CoV-2. Thus, IVCTs that are not specific to a particular test cannot fit within a risk-based framework. As described further below, ACLA urges Congress to ensure that any enacted framework is risk-based.

Third, this definition of IVCT expands FDA’s jurisdiction beyond what is necessary to regulate diagnostic tests. As proposed, the definition of IVCT encompasses laboratory equipment that currently is not regulated by FDA. For example, “instruments,” as defined in the bill, could include laboratory equipment such as test tubes, microscopes, mass spectrometers, and

⁴ See Appendix 2: *ACLA Comments on VALID Discussion Draft* at 2–3.

sequencers, all of which would become regulated IVCTs by virtue of the IVCT definition including “instruments.” Similarly, although “manual tests” are purported to be exempt from VALID under proposed section 587A(f), it is not clear what Congress intends by this exemption. It seems to apply to items like microscopes, which should not be regulated as IVCTs in the first place (or at least should be exempt already as general laboratory equipment).

Finally, the definition also creates confusion and could result in duplicative regulation of the same item. The word “test” is used interchangeably with “in vitro clinical test,” but several of the articles encompassed by the IVCT definition are not “tests.” For example, specimen collection articles, microscopes, and test tubes are not “tests.” Further, components regulated independently as IVCTs would be regulated again when included in one or more IVCTs that are capable of generating a result.

2. *Laboratory Operations*

As described in our prior comments, the new diagnostic framework must account for the distinct role that CMS plays in the regulation of laboratory operations and must avoid redundant and contradicting regulation by both FDA and CMS.⁵ ACLA appreciates improvements in the VALID Act to strengthen boundaries of jurisdiction between FDA and CMS with regard to the laboratory industry, but several ambiguities remain in the bill. For example, although the VALID Act requires the Secretary to “avoid issuing or enforcing regulations that are duplicative of regulations” under CLIA, it says nothing about duplicative guidance documents, nor about regulations or guidance that are additive or otherwise different from regulations and interpretive guidelines under CLIA. Additional and potentially contradictory FDA regulation of already-regulated services and activities would be unnecessarily burdensome for laboratories and could hamper both innovation and ongoing performance of current testing services.

An example of additional and potentially contradictory FDA regulation is in the proposed quality requirements. As proposed, the full scope of FDA quality requirements would apply to non-high-complexity laboratories, but such application is unnecessary because these laboratories do not develop and perform their own tests – they are performing tests developed or manufactured by others. CLIA-certified high-complexity laboratories should be subject only to a small subset of FDA quality requirements for test development activities that are not duplicative of existing CLIA requirements. Therefore, the full scope of FDA quality requirements should not apply to laboratories at all, but only to finished product manufacturers.

Additionally, application of FDA purchasing control quality requirements to laboratories—high-complexity or otherwise—overlaps with existing CLIA regulations pertaining to test systems, equipment, instruments, reagents, materials and supplies.⁶ As evidenced by the COVID-19 response, such duplicative restrictions can result in mini-monopolies for certain materials suppliers and create bottlenecks for test development. Specifically, in the early days of the COVID-19 response, laboratories were unable to perform authorized COVID-19 tests, in part, because the specific transport reagents authorized as part of those tests were unavailable. Even now, FDA has loosened restrictions related to viral transport media for use with COVID-19 tests, but FDA’s policy still states that “if a laboratory modifies a test by using unauthorized, alternative components (e.g., alternative transport media), the modified test may no longer be

⁵ See Appendix 2: *ACLA Comments on VALID Discussion Draft* at 3–4.

⁶ See 42 CFR § 1252(c).

authorized under the EUA.”⁷ Thus, although CLIA permits laboratories to validate alternative materials for use with laboratory tests, FDA regulations restrict this flexibility and, ultimately, the availability of tests.

Finally, we recommend that Congress consider conforming amendments to CLIA, which are needed to ensure there is no jurisdictional overlap. Currently, CLIA includes oversight of certain test development activities for which FDA would also become responsible under VALID. With regard to analytical validity, the CLIA regulations require laboratories to establish test performance characteristics prior to reporting patient test results based on modified FDA--cleared or -approved tests, LDTs, or tests that use test systems for which the manufacturers do not provide performance specifications. Specifically, laboratories must establish performance characteristics for: accuracy; precision; analytical sensitivity; analytical specificity to include interfering substances; reportable range of test results for the test system; reference intervals (normal values); and any other performance characteristic required for test performance.⁸ With regard to clinical validity, CLIA regulations currently require laboratory directors to ensure that “[t]he test methodologies selected have the capability of providing the quality of results required for patient care.”⁹ Tests can have such capability only if they are clinically relevant for the patient populations being tested, i.e., are clinically valid.

3. *Practice of Medicine*

The practice of medicine is not adequately protected under VALID, and as a result, VALID directly conflicts with CLIA. Unlike IVD manufacturers, clinical laboratories have a unique role – acting both as the developer of tests and as health care providers. CLIA requires that clinical laboratories be staffed by licensed health care professionals, including pathologists that are engaged in the practice of medicine. However, this unique role is not recognized or appropriately protected by VALID. For example, under proposed section 587A(a)(3), the Act protects a health care practitioner’s authority “to prescribe or administer any legally marketed [IVCT] for any condition or disease within a health care practitioner-patient relationship.” However, this protection does not “alter any prohibition on the promotion of unapproved uses of legally marketed [IVCTs].” Thus, as proposed under VALID, a developer must not discuss off-label uses of the test with physicians. This runs in direct contradiction to the requirements under CLIA and the ability of a laboratory medical director to practice medicine.

Similarly, CLIA requires that laboratories report “[t]he test result and, if applicable, ... interpretation”¹⁰ and “information that may affect the interpretation of test results.”¹¹ To the extent that such required contextual information is outside of the FDA approval of a particular IVCT, a laboratory medical director could be faced with the unavoidable situation of being squeezed between two conflicting regulatory requirements. Moreover, the VALID Act requires test reports to contain an entire set of information that is not relevant to the medical needs of the doctor and patient, and which would render the report difficult to read, lengthy and

⁷ FDA Guidance, Enforcement Policy for Viral Transport Media During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency at 4 (July 2020).

⁸ 42 C.F.R. § 493.1253(b)(2).

⁹ 42 C.F.R. §§ 493.1407(e)(3)(i), 493.1445(e)(3)(i).

¹⁰ *Id.* at 493.1291(c)(1).

¹¹ *Id.* at 493.1291(e),

burdensome.¹² Instead, ACLA recommends that laboratory test results reporting—a key component of individualized patient medical care—should remain governed by CLIA. Additionally, the VALID Act should explicitly protect the ability of laboratories to consult with clients regarding the interpretation of IVCT results and to share new information that affects interpretation of test results, as labs are *required* to do under CLIA.

B. Ambiguity and Discretion

ACLA continues to support an oversight framework that avoids both unnecessary ambiguity and the granting of unfettered discretion to regulatory agencies. We appreciate the improvements made to the VALID Act compared to earlier drafts of legislation. Nevertheless, several ambiguous provisions remain. For example, the VALID Act states that a premarket application must include “[s]uch other data or information as the Secretary may require in accordance with the least burdensome requirements....”¹³ The data requirements for a premarket application already are extensive, and developers need to know with certainty what data they need to support an application. Moreover, although ACLA agrees with incorporation of the least burdensome principle, it is inherently contradictory to couple the least burdensome principle with this open-ended requirement for “[s]uch other data or information as the Secretary may require.”

ACLA also continues to object to broad discretion granted to FDA to create substantive regulatory policy through guidance. Throughout the VALID Discussion Draft, FDA is granted authority to issue guidance that amounts to substantive regulatory policy regarding IVCTs. For example, the VALID Act calls for guidance on the applicability of exemptions under section 587A¹⁴, information requirements for premarket and special premarket applications under section 587B¹⁵, criteria for designation as a breakthrough IVCT under section 587C¹⁶, criteria relating to technology review and lists of applicable technologies under section 587D¹⁷, among other requirements. As a general rule, the Act should require FDA to issue regulations where FDA is establishing substantive policy, such as the above listed topics. In contrast, guidance may be acceptable where FDA is clarifying procedural points and the substantive requirements already have been established.

Finally, ACLA also continues to object to the Act’s provision that permits the Secretary to “exempt a class of persons from any section under this subchapter upon a finding that such exemption is appropriate for the protection of the public health and other relevant considerations.”¹⁸ Such authority poses a real potential for abuse and could result in unfair competitive advantages.

C. Transition Provisions

¹² See VALID Act § 587K(c)(2)(A).

¹³ See VALID Act § 587B(c)(2)(K).

¹⁴ See *id.* Sec. 5(a)(2)(C).

¹⁵ See *id.* § 587B(c)(3) and Sec. 5(a)(2)(C).

¹⁶ See *id.* § 587C(f)(1)(C).

¹⁷ See *id.* § 587D(d).

¹⁸ See *id.* § 587A(q).

ACLA appreciates the improvements to the transition provisions that have been made to the VALID Act compared to the VALID Discussion Draft, but we continue to have several concerns. First and foremost, although the VALID Act proposes an effective date for the statute, the date is uncertain and too short. ACLA urges Congress to establish a clear, fixed transition of at least five years, wherein FDA has three years to finalize implementing regulations, and regulated developers would have two years from the date of issuance of final rules to come into compliance. Thus, the effective date would be the longer of (1) five years from enactment, or (2) two years from the finalization of implementing regulations. As described above, much of the VALID Act defers substantive policymaking to FDA through guidance and rulemaking. ACLA strongly believes that substantive policymaking should be conducted through careful notice-and-comment rulemaking, which requires time. As we have seen in the response to the COVID-19 pandemic, rushed regulation can have detrimental effects for patients. ACLA's proposed transition framework enables FDA to thoughtfully craft implementing regulations with the input of public comments.

Second, ACLA agrees with the changes to the transition section that seek to ensure only CLIA and the claw-back provisions apply to grandfathered tests during the transition period. We continue to object, however, to granting FDA enforcement authority over transitional LDTs under the device laws during the transition, and there is some ambiguity regarding potential application of these provisions to grandfathered tests as well.¹⁹ ACLA agrees that appropriate oversight should be applied to transitional LDTs, but application of device laws to LDTs is not appropriate.

Third, ACLA appreciates the attempt to provide for separate treatment of what are essentially transitional LDTs and transitional IVDs,²⁰ but we believe the distinction needs to be made more clear, as proposed in the attached redline. Contingent on clarifying this distinction, ACLA is open to the application of an earlier effective date for the VALID Act's requirements for registration and listing of transitional IVCTs, but not application of device law.

Finally, ACLA continues to object to the requirement that instruments used for IVCT development comply with the VALID Act within five years of enactment.²¹ Such a requirement inappropriately conceptualizes that FDA must approve components of a test, which limits the available resources for developers to innovate and develop new tests. Moreover, this imposes on laboratories costly burdens to update instruments before such updates may otherwise be required to ensure continued analytical and clinical validity. To the extent that Congress insists on FDA regulating as IVCTs instruments that are components of a test, ACLA seeks clarification on the concept of an "instrument family," including whether an "instrument family" is confined to instruments from a single manufacturer—which could create monopolies and result in

¹⁹ See VALID Act Sec. 5(c)(2) (granting the Secretary "authority to enforce the device provisions of the [FDCA] and the [PHSA] for any specific transitional in vitro clinical test, or any type of transitional in vitro clinical test, as the Secretary determines necessary to protect the public from a serious risk to health"). The title of subsection 5(c) includes a reference to grandfathered IVCTs, even though the text of the subsection appears to apply solely to transitional LDT IVCTs.

²⁰ Compare VALID Act Sec. 5(b)(2) (apparently intended to refer to transitional IVDs, but applicable to all transitional IVCTs) and Sec. 5(c) (transitional LDTs). Sec. 5(b)(2) should be clarified to apply solely to transitional IVDs (finished products, not laboratory test protocols).

²¹ See *id.* Sec. 5(e).

increased health care costs—or whether it spans instruments from different manufacturers that otherwise meet the definition for “instrument family.”

D. Grandfathered Tests

ACLA continues to believe that strong grandfathering policies are critical to ensure that patients do not lose access to valuable tests, many of which are the gold standard in clinical practice and have been relied upon by clinicians (in some cases, for decades).²² ACLA’s position remains that any new regulatory framework affecting IVCTs should be a *prospective* framework that does not *retroactively* increase regulatory burden and harm patient access.

ACLA agrees with many aspects of the grandfathering provisions in the VALID Act, and appreciates the improvements in these provisions compared to the VALID Discussion Draft. For example, ACLA agrees that the grandfathering provisions should apply to eligible tests introduced prior to enactment, including those introduced within the 90 days prior to enactment.²³ We also agree that the Secretary should be required to have “valid scientific evidence” indicating that the claw-back provisions should apply.²⁴ Nonetheless, ACLA continues to have concerns with aspects of the grandfathering policy, as described below.

1. Claw-Back

As stated above, ACLA supports the change requiring FDA to have “valid scientific evidence” to begin the claw-back process. However, requiring only that FDA *has* such evidence without requiring FDA to *demonstrate* or *share* that evidence with the developer still places the initial burden on developers to establish that a grandfathered test should retain its grandfathered status. Therefore, ACLA urges Congress to require FDA to demonstrate that it has valid scientific evidence that the criteria for initiating the claw-back process exist, e.g., by sharing such information with the developer, when it initiates the claw-back process.

Additionally, ACLA objects to the language permitting FDA to claw back a test because it is “reasonably possible” that an IVCT will cause serious adverse health consequences.”²⁵ FDA should not be able to claw back a grandfathered test on the basis of a *possibility* that an IVCT will cause serious adverse health consequences. This creates too much regulatory uncertainty and establishes an unreasonably low bar for FDA to regulate an otherwise grandfathered test. Even tests meeting the approval standard of “reasonable assurance of analytical and clinical validity” could be associated with a “reasonabl[e] possib[ility]” of causing serious adverse health consequences. Thus, ACLA recommends that this language should be revised from “reasonably possible” to “reasonably probable.” This strikes the appropriate balance between patient protection and regulatory consistency for maintaining access to grandfathered tests.

2. Modifications

As ACLA has commented previously, a grandfathered test should require a premarket submission only if it is modified in a way that would have a meaningful clinical impact or

²² See Appendix 2: *ACLA Comments on VALID Discussion Draft* at 5–7.

²³ See VALID Act § 587A(c).

²⁴ See *id.* § 587A(a)(4)(B)(1).

²⁵ See *id.* 587A(a)(4)(A)(ii).

significantly modify the test's intended use.²⁶ Under the VALID Act, however, a test would lose its grandfathered status if it is modified even in an insignificant way. Indeed, under proposed section 587A(l), a modification requires a new premarket submission if it "affects" analytical or clinical validity. For the reasons described in the modifications section below, requiring premarket submissions for such modifications would result in unnecessary burdens on laboratories and FDA, could threaten continued access to existing tests, and would slow the pace of innovation to the detriment of patients relying on the highest quality tests.

3. Registration and Listing

As stated in our prior comments, ACLA's position continues to be that it is unnecessary to include *any* listing requirements for grandfathered tests.²⁷ Clinical laboratories currently offer tens of thousands of tests that would qualify for grandfather status, and submitting listing data for these tests would require devotion of tens of thousands of hours. FDA review of such listing submissions also would be burdensome for the Agency. To the extent Congress insists that some listing process is necessary for grandfathered tests, such requirements should be narrowly tailored. Specifically, the narrative description of the IVCT, the summary of analytical and clinical performance, and the description of conformance with mitigating measures should not be required listing information for grandfathered tests. Additionally, an alternative listing mechanism should be made available for registered developers of grandfathered tests, such as providing a link to the laboratory's online directory. This would reduce the burden for such developers of having to redundantly supply information that is already publicly available. Finally, the Act must be clear that developers are not required to list their tests until the Comprehensive Test Information System (CTIS) is operational.

E. Modifications

As described in our prior comments, a premarket submission should be required for a test only when the modification would have a meaningful clinical impact or significantly modify the test's intended use. Requiring premarket submissions for other modifications would be unnecessarily burdensome for both the developer and FDA. It would also slow the availability of improved versions of tests that could provide higher quality care to patients.²⁸

ACLA appreciates improvements to the VALID Act that exempt from premarket review modifications made pursuant to methods or criteria in an approved premarket submission, specimen-related modifications made solely for the purpose of extending specimen stability, and certain software modifications.²⁹ These types of modifications are extraordinarily common for developers, and requiring a premarket submission for each one would grind the pace of innovation to a crawl. Because such changes are validated under CLIA prior to implementation, and because the risk of adversely affecting analytical or clinical validity in a clinically meaningful way is small, it is not necessary to require a premarket submission and approval prior to implementing each one.

ACLA recommends that modifications also should be exempt from premarket review if they

²⁶ See Appendix 2: *ACLA Comments on VALID Discussion Draft* at 6.

²⁷ See *id.*

²⁸ See *id.* at 7–8.

²⁹ See VALID Act § 587A(l)(2).

satisfy a standard recognized by, or contained in a regulation or guidance issued by, the Secretary. For example, FDA has recognized more than 100 Clinical & Laboratory Standards Institute (CLSI) consensus standards. If a modification satisfies a recognized consensus standard (e.g., CLSI standard C62-A for Liquid Chromatography-Mass Spectrometry Methods), the modification should not require FDA review.

Finally, ACLA is concerned by the change that requires a premarket submission for any modification that “affects” analytical or clinical validity.³⁰ Requiring a premarket review for all such changes—capturing even very slight increases and decreases in sensitivity or specificity—is too broad and excessively burdensome for developers and FDA. Instead, premarket review should be required for any modification that “affects the analytical or clinical validity of such test such that there is a meaningful clinical impact.” Using the “meaningful clinical impact” standard, FDA would review significant changes to tests before the modified tests are marketed, and developers would have a workable standard for use in their quality programs when determining when to seek FDA review.

F. Risk-Based Framework

Consistent with our previous comments, ACLA continues to strongly believe in a risk-based regulatory framework for IVCTs.³¹ For the risk-based framework to be meaningful, the risk levels must be adequately defined and consistently applied. There also must be a clear and meaningful difference in the regulatory gatekeeping requirements for tests with different risk levels.

1. Test Categorization

To ensure consistent application of risk levels, ACLA again is calling for inclusion of a moderate-risk category of tests. Without such a defined category, there is too much discretion for FDA to up-classify non-low-risk tests as high-risk tests. There should be sufficient differentiation of oversight to ensure that differently profiled tests (e.g., moderate-risk profile and high-risk profile) are not treated in the same manner (i.e., as high-risk tests). For this same reason, we also strongly recommend striking the words “potential” and “potentially” from the definition for “high-risk.”³² These words create too much discretion for the Agency to up-regulate tests as high-risk when the real risk-profile is more moderate.

We also continue to call for the removal of the “first-of-a-kind” and “cross-referenced” test categories, which are not risk-based, and thus are inconsistent with a risk-based framework. Under the VALID Act, such tests are regulated as high-risk (e.g., presumptively ineligible for technology certification), but in actuality, such tests may be low- or moderate-risk. Separately classifying tests as cross-referenced or first-of-a-kind—and subjecting such tests to greater regulatory scrutiny regardless of the actual risk presented by the particular IVCT—is not consistent with a risk-based approach. Nonetheless, ACLA believes that it may be appropriate for a developer and FDA to consider whether a test is cross-referenced or first-of-a-kind in relation to the data needed to support approval of a particular IVCT. Accordingly, contingent on striking use of these classifications elsewhere in the statute, ACLA has proposed incorporating

³⁰ See *id.* at § 587A(D)(1)(A).

³¹ See Appendix 2: *ACLA Comments on VALID Discussion Draft* at 8–9.

³² See VALID Act § 587(9).

these concepts into the definition of “reasonable assurance.”

2. *Approval Pathways*

Generally, the VALID Act is not clear regarding which IVCTs are eligible for regular premarket review versus special premarket review versus technology certification. ACLA recommends that, rather than defining which tests are *not* eligible for special premarket review and technology certification, the VALID Act should explicitly define which tests *are* eligible for different review pathways. Moreover, eligibility for the different pathways should *not* turn on non-risk-based classifications of tests (e.g., first-of-a-kind, cross-referenced, direct-to-consumer (DTC), home use). Eligibility should turn only on a test’s risk-classification: high-risk tests generally should be required to pursue regular premarket review; moderate-risk tests should be eligible for special premarket review and technology certification; and low-risk tests should be exempt from premarket review. This makes a defined moderate-risk classification necessary.

ACLA also urges Congress to ensure that the different pathways are meaningfully different. Presently, the only meaningful difference between the regular and special premarket review pathways is that the special premarket review pathway does not require demonstration of compliance with quality requirements or, *as long as it is not requested by the Secretary*, raw data.³³ These differences are not sufficiently meaningful, particularly when the Secretary can request raw data for tests for any reason. Rather VALID should create a clear rule that certain information is not required for the special premarket pathway, including the requirements for submission of raw data, a risk-assessment, and a bibliography and discussion of known, published reports. These data elements are not necessary to facilitate the review of moderate risk tests.

3. *Approval Standards*

As stated in our previous comments, ACLA agrees that, generally, “reasonable assurance of analytical and clinical validity” is an appropriate standard of approval for IVCTs.³⁴ However, by defining analytical validity as the ability of an IVCT to “sufficiently” identify, measure, detect, calculate, or analyze a target³⁵, Congress inserts ambiguity into the approval standard by granting FDA vast discretion to determine whether such ability is “sufficient.” Thus, the term “sufficiently” should be stricken from the definition for “analytical validity,” and “reasonable assurance” should be defined.

ACLA also proposes inclusion of a pathway that permits “approval with confirmatory postmarket obligations.” Under such pathway, eligible tests for which clinical validity evidence is promising but still under development may be approved upon demonstration of (1) reasonable assurance of analytical validity and (2) probable clinical validity. Reasonable assurance of clinical validity would then be demonstrated through postmarket evidence. ACLA recommends incorporating this concept into the VALID Act in two places: (1) special premarket review, enabling all moderate-risk tests to be eligible for approval through such pathway, and (2) breakthrough IVCT pathway, enabling eligible breakthrough tests, including high-risk tests, to have an expedited path to market.

³³ Compare VALID Act § 587B(c) and VALID Act § 587B(d).

³⁴ See Appendix 2: *ACLA Comments on VALID Discussion Draft* at 9–10.

³⁵ See VALID Act § 587(1)(A)(i).

Moderate-risk tests should be eligible for approval on the basis of a reasonable assurance of analytical validity and probable clinical validity, with postmarket demonstration of reasonable assurance of clinical validity. Under VALID (and as proposed to be explicitly defined by ACLA), a moderate-risk test is a test for which the risk of serious harm or absence/delay in life-supporting treatment are found to be mitigated, after consideration of, among other things, the clinical circumstances in which the IVCT is used.³⁶ Because the clinical risks associated with an undetected inaccurate result are mitigated, it makes sense to permit initial approval of such tests with probable clinical validity, with continued approval contingent on demonstrating reasonable assurance of clinical validity.

Additionally, breakthrough IVCTs should be eligible for approval with probable clinical validity, subject to confirmatory postmarket studies, independent of the risk level of such tests. Congress and FDA have recognized in the context of other medical products that an appropriately structured modified pathway coupled with postmarket commitments is appropriate to encourage rapid innovation and introduction of new therapies for serious and life-threatening diseases and conditions.³⁷ Likewise, ACLA believes this pathway is critical to ensuring rapid patient access to cutting edge IVCTs.

G. Technology Certification

ACLA continues to believe that a well-structured and thoughtful technology certification program has the potential to expedite patient access to innovative tests from qualified laboratories, while still providing a reasonable assurance of the analytical and clinical validity of those tests. As stated in our prior comments,³⁸ the key to a successful technology certification program is striking the correct balance between the benefits to laboratories of a valid technology certification order and the burden associated with applying for and maintaining the certified status. Therefore, ACLA urges Congress to make the following improvements to the proposed technology certification program.

First, the scope of eligibility for technology certification is too narrow.³⁹ Consistent with our comments above on the need for a risk-based framework, ACLA believes that all moderate-risk IVCTs should be eligible for technology certification. A test should not be excluded from this marketing pathway simply because it is “first-of-a-kind,” “cross-referenced,” DTC, or fits within some other non-risk-based category.

Second, the potential scope of a technology certification should be broader than a single

³⁶ See *id.* § 587(9) (definition of high-risk) and Appendix 1: ACLA Redline at proposed § 587(17).

³⁷ See FDCA § 506(c) (accelerated approval of drug products for serious or life-threatening diseases or conditions based on intermediate or surrogate endpoints with confirmatory postmarket studies); *id.* § 515B(e)(2)(C) (permitting “expedited and efficient development and review of [a breakthrough] device through utilization of timely postmarket data collection”).

³⁸ See Appendix 2: *ACLA Comments on VALID Discussion Draft* at 10–11.

³⁹ See VALID Act § 587D(b)(2) (excluding components and parts, instruments, specimen receptacles, donor tests, and, subject to specific permission, high-risk, first-of-a-kind, cross-referenced, home-use and DTC tests).

technology.⁴⁰ Under the current proposal, a developer would have to submit multiple applications to become certified in more than a single technology. This is unnecessarily burdensome for developers and FDA, particularly when much of the information in these applications will overlap. There should be a mechanism that enables developers to submit a single application that supports certification across multiple technologies, if the developer so chooses. In such cases, if the submitted data supported certification of some but not all of the technologies for which the application was submitted, FDA would only certify the technologies supported by the submitted data.

Third, the data requirements to support technology certification are overly burdensome. Specifically, raw data should not be required to support an application for technology certification. If raw data is not required for other moderate-risk IVCTs under the special premarket review pathway, then raw data should not be required for the same moderate-risk test deemed approved as part of a technology certification application. Nor should developers be required to provide a notification for each IVCT that the developer “plans to offer” upon receiving a technology certification order.⁴¹ Listing for such tests already is required under proposed section 587I prior to such tests being offered⁴², so this notification is redundant and unnecessarily intrusive into the developer’s business. ACLA also objects to the “catch-all” provision permitting the Secretary to require “[s]uch other information” as it may require in an application for technology certification.⁴³ The data requirements already are extensive, and developers need to know with certainty what data is needed to support an application.

Fourth, ACLA recommends amending the requirements for the technology certification application so that the representative IVCT need not be a *new* IVCT. Currently, the application requires submission of information to support an IVCT “that would be introduced or delivered for introduction into interstate commerce upon the issuance of the technology certification order to serve as the representative test.”⁴⁴ A developer may have already sought premarket approval for the test with the greatest analytical complexity within the proposed scope of the technology certification order, however, and such test should be permitted to serve as the “representative test.”

Fifth, ACLA recommends that the technology certification renewal process be streamlined for developers who allowed an otherwise valid technology certification to lapse. Currently, only developers with a technology certification order “in effect” may seek renewal of the order.⁴⁵ Developers may allow an otherwise valid technology certification order to lapse, however, if they do not have immediate plans for introduction of new, eligible tests. Thus, such developers cannot “renew” a technology certification order, but rather must assemble and submit an entirely new application. Technology certification renewal should focus on whether the

⁴⁰ See *id.* § 587D(e)(2)(A) (stating the scope of a proposed technology certification “shall be no broader than a single technology”).

⁴¹ See *id.* § 587D(e)(2)(F).

⁴² See *id.* § 587I(c)(1)(C)(ii) (requiring listing information to be submitted “prior to offering, introducing, or marketing the [IVCT]” and “at least 30 business days after receiving such technology certification order”).

⁴³ See *id.* § 587D(e)(2)(H).

⁴⁴ See *id.* § 587D(e)(2)(G)(i).

⁴⁵ See *id.* § 587D(g)(3).

developer remains in compliance with the requirements for certification. Therefore, developers should be permitted to certify that relevant application information has not changed, and to submit information for a different representative test, much like developers renewing an active order.⁴⁶

Finally, there are several clarifications that should be made to the technology certification program. For example, the Act should more clearly define the term of a technology certification, i.e., “four years,” rather than “up to 4 years” unless the Secretary specifies an earlier date.⁴⁷ Additionally, the Act should clarify that if a technology certification order expires, any IVCTs introduced pursuant to a then-valid order may continue to be lawfully marketed without a premarket application. Without such clarification, FDA could assert that tests may only be offered under an existing technology certification order, rendering such order nothing more than a temporary authorization for such tests. The result is harm to patients and uncertainty for healthcare providers, who could see tests they have grown to depend upon disappear overnight, until developers can assemble, submit, and receive approval for each of the tests that were lawfully introduced.

H. Emergency Use Provisions

Last, ACLA Congress must enact emergency use provisions that reflect the lessons learned from the COVID-19 response. Currently, the proposed VALID Act emergency use provisions mirror the policy set forth in section IV.A of FDA’s Immediately in Effect Guidance for the Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (“COVID-19 Testing Policy”).⁴⁸ Under this policy, CLIA-certified high-complexity laboratories may introduce IVCTs without premarket review, following validation of the test and notification to the FDA, as long as an EUA is submitted within a short period of time. While ACLA supports this increased flexibility to streamline introduction of urgently needed tests by experienced developers, ACLA urges Congress to strengthen the emergency use provisions in the following ways.

First, Congress must ensure that laboratories are involved in developing and offering tests *before* the threat of an epidemic or pandemic reaches our nation’s shores. As we saw with the COVID-19 response, testing is the first critical steps in stemming a public health emergency: once the emergency exists within our borders, we are already steps behind. Therefore, an exemption from premarket review should extend to apply *prior* to declaration of a public health emergency. Specifically, ACLA recommends that the exemption should apply upon FDA recognition of an “emerging pathogen,” which would be defined as “a pathogen that causes a contagious disease or condition with the potential to result in serious or irreversible harm or death to a patient or patients, or could otherwise cause serious harm to the public health.” The Secretary should be granted authority to recognize such “emerging pathogens,” and limitations

⁴⁶ As ACLA has proposed for new technology certification applications, a developer seeking renewal of its technology certification order should be permitted to provide information for an already-introduced test, i.e., the developer should not be required to submit information for a new test that “would be” introduced upon renewal. The developer should not be restricted from applying for renewal simply because the developer has no plans for introducing a new test within scope.

⁴⁷ See VALID Act § 587D(g)(2).

⁴⁸ See FDA Immediately in Effect Guidance, *Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (Revised)* at 8–10 (May 11, 2020), available at <https://www.fda.gov/media/135659/download> (hereinafter “FDA COVID-19 Testing Policy”).

on use of IVCTs for emerging pathogens would be appropriate. ACLA has proposed a framework for such emergency use of IVCTs for emerging pathogens in the attached redline, at new section 587A(a)(6).

Second, Congress must ensure that the emergency response leverages the capacity of the entire in vitro clinical testing industry. Over the course of the pandemic, FDA updated its COVID-19 Testing Policy to extend its policy for pre-authorization testing to commercial manufacturers of COVID-19 diagnostic tests, subject to the same conditions as CLIA-certified high-complexity labs offering COVID-19 diagnostic tests.⁴⁹ ACLA recommends that Congress likewise expand the exemption for emergency use during a declared public health emergency to commercial manufacturers of diagnostic tests, as long as such tests are validated, FDA is notified, and an EUA submission is forthcoming.

Third, Congress must ensure that FDA's limited resources are prioritized during an emergency, and that the Agency does not get bogged down in the review of applications for lower-risk tests when such review is not necessary to address particular issues or risks. During the COVID-19 pandemic, FDA has been flooded with applications for diagnostic and serological tests. By early August, FDA reported having hundreds of applications pending review.⁵⁰ This is despite the fact that, in May, the Agency revised its COVID-19 testing policy to permit CLIA-certified high-complexity laboratories to offer serological tests following validation of such tests, without notification to FDA or submission of an EUA. ACLA agrees with this approach for lower-risk tests, like serology tests which do not provide results regarding active infection. Therefore, ACLA recommends that Congress revise the emergency use provisions of VALID so that notification and EUA submission is required for CLIA-certified high-complexity laboratories only when such laboratories intend to offer a high-risk test (i.e., moderate-risk tests would not require notification or an EUA). ACLA does not recommend that this change apply to commercial manufacturers of IVCTs, for the reasons espoused by FDA in its revised policy.⁵¹ Unlike LDTs, which are still regulated under CLIA if no FDA regulation applies, IVDs that are not subject to FDA regulation are unregulated; therefore, different considerations are warranted for each.

Fourth, at the conclusion of an emergency justifying use of an IVCT prior to authorization, developers must be given a reasonable amount of time to submit a marketing application for a test offered under either of the exemptions for emergency use or emerging pathogens. Although FDCA section 564(b)(3) requires the Secretary to give "advance notice that a declaration [for emergency use] will be terminated," in practice such advance notice has been unreasonably short and does not provide sufficient time for sponsors to shift resources from emergency use operations to assembly and submission of a marketing application. Indeed, when the emergency use declaration for H1N1 diagnostic tests was terminated in 2010, notice was

⁴⁹ *Id.* at 12–14 (Section IV.C).

⁵⁰ See Transcript of FDA Virtual Town Hall Series – Immediately in Effect Guidance on Coronavirus (COVID-19) Diagnostic Tests at 2 (Aug. 5, 2020) (statement of Dr. Timothy Stenzel, "We have hundreds of EUA applications in house."), *available at* <https://www.fda.gov/media/140975/download>.

⁵¹ See FDA COVID-19 Testing Policy at 7 ("FDA has become aware that a concerning number of commercial serology tests are being promoted inappropriately, including for diagnostic use, or are performing poorly based on an independent evaluation by the NIH, indicating that greater FDA oversight of commercial serology tests is important to protect the public health.") (citations and footnotes omitted).

provided to EUA requesters only two days prior to termination of the declaration.⁵² Therefore, ACLA urges Congress to ensure that the emergency use provisions for IVCTs provide that IVCTs marketed for emergency use, or for an emerging pathogen, may continue to be marketed for a reasonable amount of time after termination of the relevant declaration, during which time a developer may submit a premarket application, and that the test may also continue to be marketed during the pendency of that application.

Finally, Congress must ensure that the new framework for diagnostic tests does not block laboratories from conducting important public health surveillance work that is key to detecting emerging pathogens that threaten the public health. Currently, the VALID Act exemption for public health surveillance activities applies only if such activities are “conducted, supported, requested, ordered, required, or authorized by a public health authority,” and the activities “allow a public health authority” to conduct public health surveillance work. These conditions limit the ability of laboratories to conduct important public health surveillance work, and the second condition in particular—requiring private activities to “allow a public health authority” to conduct public health surveillance work”—fails to recognize the independent value of laboratories conducting surveillance work. Moreover, such conditions run contrary to FDA’s stated policies that it generally does not regulate surveillance testing.⁵³

IV. Concluding Comments

Thank you for the opportunity to submit these comments. If you have any questions, please do not hesitate to contact Tom Sparkman at tsparkman@acla.com.

Sincerely yours,



Julie Khani
President

⁵² See FDA, *Notice of Termination of Declarations Justifying Emergency Use Authorizations of Certain In Vitro Diagnostic Devices, Antiviral Drugs, and Personal Respiratory Protection Devices*, 75 Fed. Reg. 36432 (June 25, 2010) (stating that letters were sent to EUA requesters on June 21, 2010 and that the EUA declaration would expire on June 23, 2010, after which date EUAs issued under the declaration would no longer be effective).

⁵³ See FDA, FAQs on Testing for SARS-CoV-2, available at <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/faqs-testing-sars-cov-2> (last visited Aug. 25, 2020) (“The FDA does not generally regulate the use of a test for surveillance purposes, such as determining the prevalence of acute infections in a population.”).