



## COLLEGE of AMERICAN PATHOLOGISTS

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February 19, 2019

The Honorable Larry Bucshon, M.D.  
2313 Rayburn House Office Building  
Washington, DC 20515

The Honorable Charles Grassley  
135 Hart Senate office Building  
Washington, DC 20510

The Honorable Diana DeGette  
2111 Rayburn House Office Building  
Washington, DC 20515

The Honorable Michael Bennett  
261 Russell Senate Office Building  
Washington, DC 20510

Dear Representatives Bucshon and DeGette and Senators Grassley and Bennett:

The College of American Pathologists (CAP) appreciates the opportunity to comment on the Verifying Accurate Leading-edge IVCT Development (VALID) Act that provides regulatory oversight of in vitro clinical test (IVCT), which includes laboratory-developed tests (LDTs). As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

We commend your leadership to develop a regulatory approach that would encourage innovation while protecting patients. Given the large gaps that still exist in the draft, and our belief that there needs to be another discussion draft even before any legislation is introduced, our comments should be considered directional and broad.

The CAP believes a regulatory approach for the oversight of LDTs should be flexible and built on existing frameworks and institutional knowledge, while limiting intrusions and compliance burdens on laboratories. The CAP did not support the Diagnostic Accuracy and Innovation Act (DAIA) draft because we believe its regulatory structure is overly complex, and would subject clinical laboratories to regulations and scrutiny that would stifle innovation of tests including those of the lowest risk level. We support using the existing regulatory structures instead of creating new processes that would be costly and burdensome to laboratories, especially those with limited resources. After review, we believe there are some additional modifications in several areas that can help ensure regulatory pathways exists for quality clinical laboratory testing that is unimpeded and not overly burdensome to laboratories in the process.

Again, the CAP appreciates the opportunity to provide our views on the VALID Act. Please contact Michael Hurlbut, CAP Assistant Director, Legislation and Political Action at [mhurlbu@cap.org](mailto:mhurlbu@cap.org) if you have any questions on these comments.

Sincerely,  
The College of American Pathologists



### **Executive Summary**

Overall, the approach outlined by the VALID Act moves in a positive direction, away from the over-reach of the Diagnostic Accuracy and Innovation Act (DAIA), establishing a reasonable regulatory framework that ensures the quality of LDTs for patients and the public regarding while not stifling innovation. This summary will briefly outline our thoughts or concerns in the following pages.

While the jurisdiction of IVCTs is ultimately be up to Congress, we believe the VALID Act is moving in the right direction given its change in focus from DAIA. VALID is a better foundation for any future legislative proposal, since its focus remains on LDT oversight rather than extraneous CLIA modifications. We also appreciate that the VALID Act will not attempt to regulate the practice of medicine. The CAP cautions Congress on offering definitions regarding risk-classification that are too prescriptive in statute, and instead set up a public process to develop these criteria. Furthermore, the risk-based two-tier system needs extensive clarification of its categories. While we understand the concept of this framework, it has the potential to be a regulatory nightmare for laboratories.

The exempt categories within VALID are a crucial aspect of any agreement. They need precise setup. Exempting several categories of tests from some FDA regulatory requirements is the right idea. The approach to manual IVCTs is also a move in a positive direction, while we believe the threshold number for rare diseases should be based on prevalence or incidence of disease. The CAP looks forward to working with you to perfect this language as we move forward. Moreover, the CAP initially proposed stricter guidelines surrounding grandfathering; we believe that VALID appropriately addresses this class of tests.

We also look forward to working with Congress to fine-tune high-risk IVCTs and modifications. The draft's approach to high-risk IVCTs and modifications moves in the right direction, but needs to be further refined so as not to become a high-risk trap from which only a select few tests can escape. As with the definitions of risk-classification, there is a need for criteria, but we caution Congress on moving forward with prescriptive lists in legislation. These lists can make simple changes require new premarket applications, burdening not only laboratories but the FDA.

The precertification program is likely the most discussed aspect of the VALID Act. The CAP is open to this concept, but we need more clarification on regulatory categories and the role of accreditors within the program. This will require extensive input from the stakeholder community to ensure it performs as intended. Finally, the CAP is pleased with the use of accredited persons to perform as an agent of the FDA, and we suggest that CMS and the FDA collaborate on collecting any reporting requirements.

We appreciate the opportunity to comment on this complex legislation and look forward to working with Congress to refine language that will work for all stakeholders.



**CAP Specific Comments  
on the  
VALID ACT**

**1. Sec. 587 A. Definitions p. 6 - High-risk IVCT**

The CAP appreciates the direction in which this provision is moving since it exempts the categories as from some or all FDA regulatory requirements. High-risk is an IVCT that will likely cause serious or irreversible harm or death to a patient or patients or would otherwise cause serious harm to the public health; and would impose a likelihood of adverse patient impact or adverse public health impact cause by such an inaccurate result that is not remote. However, an IVCT is not high-risk if it meets such mitigating factors like being well characterized, well-established technology and the availability of other tests (ie, confirmatory or adjunctive tests) or relevant materials standards, it is unclear the premarket requirements for these tests. Are they exempt for pre-market review? Is there a streamlined process? Are they eligible for third-party review or precertification?

**2. Sec. 587. Definitions. p. 8 - Test group**

The CAP acknowledges the need for criteria but caution congress on moving forward with such a prescriptive list in legislation. This is a new concept which would have significant ramifications on risk-classification, grandfathering eligibility, and modifications submissions. The criteria included specimen types, test methodology, patient population are narrowly focused and would increase the number of test subject to premarket review. The CAP agreed that the Secretary should develop this criteria through a public process and include risk as a part of the criteria for making such determinations.

**3. Sec. 587A. Applicability. p. 11 - Practice of medicine**

The CAP supports this provisions that does not codify the practice of medicine.

**4. Sec. 587A. Applicability. p.19 and 20 - Exempt categories**

The CAP believes the inclusion of exempt categories in the discussion draft is crucial to ensuring a balance regulatory system. VALID exempts several categories of tests from some FDA regulatory requirements. These categories of tests include manual IVCT, custom and low volume tests, rare diseases, and low-risk tests. We agree that these categories should be exempt from premarket requirements only. In addition, manual tests and custom/low volume IVCTs, which are developed or modified in order to comply with an order of an individual physician, dentist, or other health care professional (or any other specially qualified person), should be exempted from notification, premarket review, QS requirements, adverse event reporting, and labeling requirements.

**5. Sec. 587A. Applicability. p. 21 - Manual IVCT**



The CAP appreciates the direction in which this provision is moving since it exempts the categories as from some or all FDA regulatory requirements. VALID defines a manual test as one where the result of manual interpretation (meaning direct observation) by a qualified laboratory professional, without the use of automated instrumentation or software for intermediate or final interpretation and is either is not a high-risk test; or a high-risk test that is not used for interstate commerce. These tests are exempt from notification, premarket review, adverse event reporting, QS elements, and FDA labeling requirements. Pathologists use manual methods to diagnosis cancer which under VALID could potentially be classified as high-risk once a therapeutic is introduced. We believe these tests should be not be considered high-risk if used directly by pathologists in manual interpretation.

**6. Sec. 587A. Applicability. p. 17 - Grandfathering**

The VALID draft would apply to any IVCT first offered for clinical use in the period that is within the 90 days preceding the enactment date and up to the effective date of this Act. The CAP included a grandfathering provision that was more stringent than VALID because we allowed for any tests developed prior to April 23, 2003 to be grandfathered. In 2009, our approach focused the review on novel technology and higher-risk tests. While we support grandfathering, we believe VALID should allow FDA to review grandfathered tests if they pose a significant patient safety risk. These tests are exempt from premarket review, QS elements, and FDA labeling requirements. We also believe lower risk LDTs should be exempt for notification and registration requirements under the grandfathering provision.

**7. Sec. 587A. Applicability p. 22 - Rare diseases**

The CAP believes the definition of rare diseases should be based on incidence or prevalence of a disease rather than number of tests performed. VALID allows IVCT performed on fewer than 8,000 individuals per year in the United States would be subject to testing using such in vitro clinical test and not a cross-referenced test (ie, companion diagnostic). The CAP proposal based it rare disease definition on incidence or prevalence of disease not test because it would be easier for laboratories to determine applicable regulatory requirements.

**8. Sec. 587A. Applicability p.25 - Modifications**

The CAP appreciates the criteria listed in VALID but caution congress on moving forward with such a prescriptive list in legislation. VALID leverages the premarket review process for any tests that make modifications that impact any test group criteria, change test performance or safety, were omitted from the original application change protocol, meet the mitigating factors. As a result, many minor modifications would require a new premarket application. The CAP 2009 Policy stipulated that reporting would be required for any modification to a Moderate Risk LDT or Low Risk LDT that results in a change to the intended use and has a meaningful clinical impact. Meaningful clinical impact means with respect to a modification of an LDT, the potential to result in a change to the patient's diagnosis or the therapy delivered to the patient. We believe the criteria should be changed to subjecting only those modifications that result in a change in intended use and has a meaningful clinical impact.

**9. Sec. 587D. Precertification. p. 44**

The CAP is receptive to the precertification paradigm to the but will seek clarification on the regulatory categories and the role of accreditors in the program. The Precertification



program as described in the legislative draft is narrowly focused on low-risk tests therefore applying to a small number of tests. This would result in numerous submissions to the agency. The CAP believes the program should be applicable to a larger number of tests and used as a pathway to reduce the amount of regulatory burden. As currently drafted, the prescriptive language may result in greater regulatory burden for laboratories.

**10. SEC. 587F. Regulatory Pathway Designation. p. 59 - Risk-based model: Two-tier system**

The CAP appreciates the two-tiered system but would like to better understand the regulatory requirements for the high-risk and high-risk with mitigating factors. As currently drafted, the two-tiered system provide regulatory uncertainty for laboratories about premarket submission and precertification. Currently, any tests defined as high-risk would be excluded from precertification and potentially expedited reviews.

**11. SEC. 587I. Registration and notification p. 62 and Sec. 587L. Adverse event reporting. P.72**

The CAP supports the inclusion of reporting elements but encourage the Secretary to ensure collaboration among the sister agencies to reduce the regulatory burden on laboratories. These reporting requirements would include notification, registration and listing, and adverse event reporting. We would encourage inclusion of language that would direct the Secretary to ensure collaboration among the sister agencies to adapt existing processes for reducing the regulatory burden on laboratories.

**12. SEC. 587 J. Quality System Requirements p. 67**

Despite the VALID ACT limiting QSR requirements for laboratories to design controls, purchasing controls, including supplier controls, acceptance activities, corrective and preventative action, and records, the CAP is concerned about requiring laboratories to comply with the QSR would be duplicative, costly, and burdensome because laboratories would need to implement new processes and procedures as well as hire additional staff in order to comply. We would encourage inclusion of language that would direct the Secretary to ensure collaboration among the sister agencies to adapt existing processes for reducing the regulatory burden on laboratories.

**13. SEC. 587 P. Accredited Person p. 79**

The CAP supports the use of accredited person to perform all activities as an agent of the FDA. Accredited Person should be allowed review applications for precertification and applications for premarket approval of an IVCT and making recommendations to the FDA with respect to adherence to FDA requirements. In addition, accredited persons can perform inspections.

**14. SEC. 587Q. Standards p. 84**

The CAP believes analytical and clinical validity are critical additions to any LDT oversight scheme; however, we believe development and implementation of such requirements must be carefully considered. Demonstrating these performance standards can be a



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labor-intensive process that can be costly and time consuming. We believe the Secretary should take into consideration various methods on demonstrating performance standards such as either summary of comparative studies or peer-reviewed literature. We support the development of these standards should be through a public transparent process.