



February 15, 2019

The Honorable Frank Pallone
Chairman, House Committee on
Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Greg Walden
Ranking Member, House Committee on
Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Larry Bucshon
House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Re: Request for Feedback, The Verifying Accurate Leading-Edge IVCT Development Act
House Discussion Draft

Dear Representatives Pallone, Walden, DeGette, and Bucshon:

On behalf of AdvaMedDx, a Division of the Advanced Medical Technology Association, we applaud your leadership in efforts to seek comprehensive reform to modernize the regulatory framework for *in vitro* clinical tests (IVCTs) through development of the Verifying Accurate Leading-Edge IVCT Development (VALID) Act discussion draft. A modern framework is critical to Food and Drug Administration (FDA or Agency) regulatory oversight over all diagnostics, including laboratory-developed tests (LDTs) and *in vitro* diagnostics (IVDs), in a risk-based manner that provides vital assurances to the public health for accurate and high-quality testing, keeps pace with scientific progress in the field, and fosters overall innovation. A modern risk-based framework bringing together essential reforms for all diagnostics is vitally important to ensure a consistent and predictable pathway for developers as well as timely patient access to cutting-edge diagnostic technologies.

AdvaMedDx member companies produce advanced, *in vitro* diagnostic tests that facilitate evidence-based medicine, improve quality of patient care, enable early detection of disease and, in many cases, reduce overall health care costs. Functioning as an association within AdvaMed, AdvaMedDx is the only multi-faceted, policy organization that deals exclusively with issues facing *in vitro* diagnostic companies in the United States and abroad. Our membership includes manufacturers engaged in the development of innovative diagnostic tests supporting patient care and the advancement of precision medicine.

Thank you for the opportunity to provide our comments on the VALID draft, released December 6, 2018. AdvaMedDx strongly supports FDA oversight of diagnostics under a rational risk-based approach that promotes the public health and diagnostic innovation. Notably, we appreciate Congressional commitment to advance a framework that is tailored for diagnostics with reforms reflective of the unique way diagnostics are used in healthcare today and that regulates all clinical diagnostic tests under a unified approach, regardless of where a test is developed. We are also pleased to see explicit integration of near-patient (or point-of-care) technologies to help address outdated categorical limitations on exemptions established in regulation over 20 years ago to

support access to timely point-of-care diagnostics. Additionally, we also note the incorporation of harmonization provisions in VALID to support international harmonization of quality system standards, which can leverage current audit programs, such as the Medical Device Single Audit Program, as well as use of international consensus standards to promote global regulatory harmonization. Further, we appreciate inclusion of longstanding and critically important de-identified specimen policy to support diagnostic research and development.

Our comments are provided to recommend clarity in several fundamentally important areas for consistency in and transparency of expectations as part of a risk-based regulatory framework for diagnostics. We appreciate the extensive undertaking in development of the discussion draft and believe these suggested revisions will support robust public health protections, appropriate public input under the new framework, and a comprehensive legislative framework that is adaptable and can withstand and foster advancements in technology and science and meet current and future patient needs.

Based on your request for specific redline feedback on the “Verifying Accurate Leading-Edge IVCT Development Act” (or “VALID” Act) discussion draft, our comments address the following key areas:

- (1) clarifications to key terms and definitions;
- (2) refinements to ensure a risk-based framework to IVCT oversight and review;
- (3) adoption of appropriate flexibility for the precertification program, particularly scope; and
- (4) other enhancements, such as assurances of public input and public process and recognition of real-world evidence.

The bulk of our comments relate to the definitions, framework, and overall premarket regulatory approach generally tied to these thematic areas. We have provided an overview of our feedback below and redline in the attached document. While we have strived to provide detailed feedback on these priority areas, we would welcome the opportunity to provide additional comments, such as with respect to the postmarket provisions as well as further fine-tuning of the premarket system and overall framework. We sincerely appreciate the efforts of Congress and the draft bill sponsors to advance the public health through modernizing the regulatory framework for diagnostics.

Clarification of Key IVCT Terms

Based on the experience of AdvaMedDx member companies, we have provided suggested revisions in the accompanying redline document to several terms in the definitions section, in order to avoid confusion and ensure that the legislation can be implemented in a manner that tailors appropriate oversight to various test technologies based on their level of risk and potential impact on public health. We offer changes to the definitions including:

- Suggesting a simplified definition of *test group* and notification elements that leverage the well-established concept of intended use in place of several new concepts that are potentially confusing, incorporating the well-understood context of professional versus lay use, and ensuring that test groups are sufficiently flexible to accommodate a range of IVCT submissions;

- Integrating more common IVCT-specific industry terminology such as *companion diagnostic* and *specimen receptacle* in place of not well-understood, vague terms such as *cross-referenced test* and *specimen collection article*;
- Ensuring definition of IVCTs for *rare disease* is consistent with 21st Century Cures Act;
- Expanding the context for *mitigating measures* to incorporate the clinical circumstances of the IVCT's intended use and the extent to which it is well-characterized along with improved focus on FDA recognized sources of risk mitigation in the form of special controls where applicable, including performance standards and postmarket surveillance rather than ill-defined categories such as *website limitations* and the like that are also already covered by the concept of labeling;
- Providing additional specification to *first-of-a-kind* tests to reflect differences in both technology and intended use from other legally marketed tests;
- Removing the term *manual tests* to avoid potential ambiguity absent better understanding of intent and types of IVCTs that might be appropriately encompassed; and
- Clarifying exclusion of employment and insurance testing in addition to law enforcement testing, when intended solely for non-clinical use.

Ensuring a Risk-Based Approach to IVCTs and IVCT Submissions

Consistent with shared objectives of a risk-based approach that serves the public health by applying calibrated oversight to IVCTs based on their level of risk, our suggested revisions seek to further advance a stratified, risk-based approach by providing a consistent application of these principles. This will ensure focus of FDA's review resources on higher risk tests, risk-based regulatory requirements are outlined more clearly for moderate risk (or what appears referenced in the draft as "high risk mitigated") tests, and the nature of premarket review is more clearly tailored based on whether an IVCT is high-risk, or not.

Importantly, our recommended updates are consistent with Congressional efforts in the 21st Century Cures Act and historical regulatory treatment of diagnostics. We believe the following changes would achieve a more consistent, fundamentally risk-based approach and continuity in availability of generally well-established, lower risk diagnostics:

- Providing technical change to the *low-risk* criteria to confirm that a test can be low-risk through satisfying mitigating measures, which appears consistent with intent;
- Providing technical change to the *high-risk* criteria to connect the two subprongs to the nature of the risk;
- Clarifying that *regulation is grounded on intrinsic risk* based on the sponsor's intended uses of the product, subjecting IVCT test components and parts, and instruments (platforms), to the same risk-based framework and subjecting those that further develop an IVCT using a component, part, or platform to regulatory oversight based on the risk level of their IVCT;

- Carrying over continuation of exemption for *currently-exempt test platforms*, to the extent that they remain low-risk (and subject to review when incorporated into another IVCT), and taking care not to subject legally marketed lower risk products to new requirements under a duplicative systems-based approach irrespective of their actual risk level;
- Assuring that *custom and low-volume IVCTs* are listed with FDA for purposes of transparency (i.e., notification);
- Aligning of the provisions on *modifications* and refinement to ensure that appropriate modifications are submitted under risk-based analysis for supplemental review while permitting use of change protocols (consistent with Agency efforts to support flexible timely updates for the public health) and clarifying appropriately scoped approvals;
- Streamlining of submission elements for those IVCTs that, under the current draft, are *neither high-risk nor low-risk* (generally referred to as Class II or “moderate” risk under current classification) and are recognized to be well-characterized, qualify for precertification, and/or apply mitigating measures;
- Affirming a *least burdensome approach* to submissions, including during the transitional period until FDA promulgates specific application elements for IVCTs;
- Providing technical change to carry over exemption for *platforms* and *collection articles* from providing clinical validity data into the submission elements;
- Applying *Quality System* demonstration during premarket review to high-risk tests, akin to PMA submissions for high-risk tests; and
- Ensuring *public transparency* by providing for FDA to maintain a public list of low-risk tests that are subject to premarket review consistent with our support of a publicly accessible listing of comprehensive test information.

Ensuring a Meaningful and Sustainable Precertification Program

AdvaMedDx supports the concept of precertification for diagnostics as part of a diagnostics reform framework and believes there is tremendous promise in a well-designed, appropriately implemented program for all developers that can demonstrate high quality while advancing a least burdensome approach to support accurate high-quality, cutting-edge diagnostics for patients and public health. Through leveraging the regulatory apparatus to keep the pace with and accommodate future scientific advancement, a precertification program for diagnostics can both promote excellence in quality while maintaining the highest standard for ensuring analytical and clinically valid tests for patients.

As demonstrated in FDA’s provision of technical assistance on a prior discussion draft, the Agency views precertification as a critical element in achieving successful oversight of the diagnostics industry. We commend the sponsors for including and refining the precertification program in this legislation. However, we believe it can be further improved upon by thoughtfully expanding its scope to ensure it is not overly rigid and will withstand the test of time as technologies continue to evolve and our understanding of innovative test types and how they can be used effectively matures.

Our suggested revisions aim to ensure that entity precertification can be available, when appropriate, to include a scope that might encompass multiple technologies or medical specialties in a reasonable manner. We believe this is of critical importance for success of and participation in the program. Therefore, we have suggested use of well recognized clinical testing specialty areas in the IVCT community for purposes of scope of the precertification under the program. Finally, we believe it is important that certain test types not be preemptively excluded from eligibility under the law, and that there are appropriate opportunities for public participation in decisions concerning test eligibility and ineligibility, as well as in implementing the program overall. Our suggested changes detailed in our redline include the following, all of which we view as essential for a meaningful and sustainable precertification program for all interested developers:

- Eliminating the *default statutory disqualification* from precertification, including for test platforms, first-of-a-kind IVCTs, home use IVCTs and DTC IVCTs, such that FDA retains discretion to determine particular types of such tests are not appropriate for precertification;
- Ensuring that the *scope* of a developer's precertification approval is sufficiently flexible that it can include multiple test elements and multiple technologies; and
- *Enhancing of procedures* surrounding a withdrawal of approval, providing for a *periodic reassessment* of any categorical determinations of ineligible test types, and providing for *public input and the development of guidance* concerning the program.

Other Comments

Finally, we have offered other technical suggestions, clarifications, and potential enhancements to the legislation in our redline, including the following:

- Ensuring appropriate *appeals procedures* consistent with appeals of significant decisions for medical devices;
- Suggesting that various FDA actions not be removed from *Administrative Procedure Act* protections;
- Providing assurances of transparency and opportunity for engagement and feedback of interested stakeholders in *collaborative communities* when FDA intends to obtain advice or recommendations;
- Improving the process for time-sensitive labeling changes resulting from newly identified *interferences*; and
- Acknowledging the potential application of *real world data* as a source of valid scientific evidence, when otherwise appropriate, and for supplemental applications/modifications as part of a modern regulatory system.

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AdvaMedDx appreciates this opportunity to provide our feedback as you update and refine the VALID Act. We view this effort as vital and look forward to working with you and other stakeholders to advance diagnostic reform. Thank you for your leadership.

Sincerely,

A handwritten signature in blue ink that reads "Susan Van Meter". The signature is fluid and cursive, with a horizontal line extending from the end of the name.

Susan Van Meter
Executive Director, AdvaMedDx

Attachment