**ASSOCIATION FOR MOLECULAR PATHOLOGY**
*Education. Innovation & Improved Patient Care. Advocacy.*
6120 Executive Blvd., Suite 700, Rockville, MD 20852
Tel: 301-634-7939 | Fax: 301-634-7995 | amp@amp.org | www.amp.org

May 22, 2022

The Honorable Patty Murray
Chair, Senate Committee on
Health, Education, Labor and Pensions
154 Russell Senate Office Building
Washington, DC 20510

The Honorable Richard Burr
Ranking Member, Senate Committee on
Health, Education, Labor, and Pensions
217 Russell Senate Office Building
Washington, DC 20510

Delivered electronically to helpuserfeebill@help.senate.gov

Dear Chair Murray and Ranking Member Burr:

Thank you for the opportunity to comment on the discussion draft of the Food and Drug Administration Safety and Landmark Advancements (FDASLA) Act and in particular, Subtitle C of Title VIII which includes the Verifying Accurate Leading-edge IVCT Development (VALID) Act of 2022. As you know, the Association for Molecular Pathology (AMP) has actively engaged in the conversation on regulating laboratory developed testing procedures (LDPs) directly with the Food and Drug Administration (FDA) by responding to draft guidance and meeting with the agency, and also with Congress by providing written feedback on legislative text (often with redline edits), participating in roundtable discussions, providing experts in molecular pathology, and meeting with staff on numerous instances to inform your work to modernize federal laboratory test oversight for more than 10 years. Our feedback is based on the collective input of our organization's members – experts who have spent their entire professional lives dedicated to providing the highest quality care to patients, including during the COVID-19 pandemic. We are disappointed that few of our recommendations have been incorporated into the VALID Act of 2022. In the interest of patient care and protecting access to innovation, we provide the following comments and recommended edits to the VALID Act of 2022. While they do not reflect our full position on LDP oversight[1], we hope that Congress will move towards a more workable solution and avoid undue restrictions on the medical practice of molecular professionals.

**Health institution exemption**

AMP is greatly concerned that the proposed framework is excessively burdensome for the vast majority of clinical laboratories that offer molecular testing services, and as such, the VALID Act will drastically hinder the advancement of precision medicine, prevent local efforts to stem the spread of infectious diseases, disrupt localized care especially in underserved communities, and have additional unintended consequences. **AMP recommends that the Senate Health, Education, Labor, and Pensions Committee create an exemption in the VALID Act to allow academic medical, community hospital, and health system laboratories to offer laboratory developed testing services without premarket review.** The physicians making clinical management decisions based on LDP test reports within the above health institutions are in the same location as the molecular pathology professionals performing and interpreting tests in these settings. The close and frequent

[1] See here for information on AMP's positions: https://www.amp.org/advocacy/laboratory-developed-testing-procedures-ldps1/

consultations these professionals have, such as in tumor boards and in individual peer-to-peer conversation, are in themselves mitigating factors, that decrease the risk of testing performed in this setting. We believe that there are many inventive policy approaches that could be informed by currently existing programs, e.g. that of the New York State Department of Health, that would work to ensure that laboratory testing in these settings continues to be of high quality. In support of creating such an exemption, AMP is committed to working collaboratively with the Committee and other stakeholders to develop such language.

**Explicitly add the role of the health professional as a mitigating measure**

The VALID Act of 2022 continues to fail to take into account the integral role of the medical professional in the design, validation, performance, and interpretation of an LDP. These testing services are central parts of the practice of board-certified specialist physicians, geneticists, and other highly qualified doctoral-level laboratory professionals who apply their professional, scientific, and medical knowledge to optimize patient care. While developing and utilizing an LDP, there is constant attention to patient safety as a result of the professional judgment utilized at every stage of the testing process, and as such the role of these professionals greatly mitigates risk to the patient. The Food and Drug Administration (FDA) already acknowledges that genetic professionals serve an important role in mitigating risk for some kinds of testing and requires that over-the-counter 'genetic health risk assessment systems' provide information about how to obtain access to a genetic counselor, board-certified clinical molecular geneticist, or equivalent health care professional to interpret the results of a user's test as a special control.[2] AMP urges you to incorporate language in the VALID Act of 2022 that includes the involvement of the medical professional and the expertise and experience of the laboratory's personnel with testing methodology as a mitigating measure. **Specifically, AMP urges you to update the definition of mitigating measure to read as indicated (page 137):**

> ***''(B) may include, as required by the Secretary, as appropriate, applicable requirements regarding labeling, conformance to performance standards and consensus standards, performance testing, submission of clinical data, advertising, website posting of information, clinical studies, postmarket surveillance, user comprehension studies, involvement of qualified health professionals in the design and testing process, training, and confirmatory laboratory, clinical findings, or testing.***

**Remove duplication with CLIA**

The VALID framework as a whole duplicates many aspects of the Clinical Laboratory Improvement Amendments (CLIA) program within the Centers for Medicare and Medicaid Services (CMS), creating extensive and burdensome overlapping requirements. AMP recommends laboratories and their testing services be exclusively regulated at the federal level by a modernized CLIA program. However, if the Committee continues to pursue advancing an FDA-centric framework, we reiterate the following comments, with additional recommendations for edits to the language included in the VALID Act of 2022.

**Sec 587K. Test design and quality requirements**

As written, Section 587K is unnecessarily burdensome and does not translate well to laboratories using LDPs. Our members report that they would likely have to redirect resources to additional staff to demonstrate compliance with regulations, especially those associated with design controls, design transfer, design history file,

[2] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr=866.5950

and purchasing controls. Regarding design transfer, one member with expertise in this area expects that laboratories will need to institute a completely separate department employing dozens of medical laboratory scientists and masters-level employees to fulfill this function. Further, AMP members find that the regulations for purchasing controls will shift the burden of ensuring supply quality from suppliers to laboratories. We appreciate that there are sometimes issues with reagents obtained from suppliers, but these issues are currently successfully addressed under current regulation. For example, suppliers sometimes change reagent composition and laboratories are not always notified, but standard quality control practices identify and mitigate potential issues.

Laboratories already comply with quality system regulations under 42 CFR Subpart K Part 493. It is not sufficient to simply instruct FDA to promulgate regulations that avoid duplication with CLIA as FDA is instructed in other parts of the VALID Act of 2022 to issue regulations on aspects of laboratory testing covered by CLIA regulations. **In other words, if the VALID Act of 2022 does not also modernize CLIA, then FDA requirements will be duplicative**. As such, edits should be made to allow FDA to rely upon information indicating compliance with CLIA requirements to meet most, if not all, of FDA's test design and quality requirements.

Additionally, we appreciate that the co-sponsors recognize that not all quality system requirements should apply to LDPs, however, the terms listed at Section 587K(b)(1)(C) is terminology pulled from existing medical device regulations. We believe all of these terms should be removed to provide FDA with the flexibility to develop regulations that are most appropriate for laboratory tests.

**The following language edits should be made (page 254-255):**

***"(b) QUALITY REQUIREMENTS.—***
***"(1) IN GENERAL.—The quality requirements applicable under this section shall—***
***"(A) avoid duplication of regulations under section 353 of the Public Health Service Act;***
***"(B) except as set forth in subsection (a)(5), apply to developers of finished products, related to the design and associated manufacture and distribution of an in vitro clinical test offered under this Act; and***
***"(C) sufficiently ensure that a developer meeting the requirements has established, and maintains, a quality management system appropriate for any in vitro clinical test developed and offered by the developer. ~~include the following, as applicable, subject to subparagraph (D) and paragraphs (2) and (3)—~~***
***~~"(i) management responsibilities;~~***
***~~"(ii) quality audits;~~***
***~~"(iii) personnel;~~***
***~~"(iv) design controls;~~***
***~~"(v) document controls;~~***
***~~"(vi) purchasing controls;~~***
***~~"(vii) identification and traceability;~~***
***~~"(viii) production and process controls;~~***
***~~"(ix) acceptance activities;~~***
***~~"(x) nonconforming in vitro clinical tests;~~***
***~~"(xi) corrective and preventive action;~~***
***~~"(xii) labeling and packaging controls;~~***
***~~"(xiii) handling, storage, distribution, and installation;~~***
***~~"(xiv) complaints and records;~~***
***~~"(xv) servicing; and~~***

~~*"(xvi) statistical techniques.*~~

***"(2) QUALITY REQUIREMENTS FOR LABORATORY TEST PROTOCOLS.—Quality requirements applicable to the in vitro clinical tests and developers described in subsections (a)(2) and (a)(5), as applicable, shall—***
***"(A) be met by a developer demonstrating compliance with*** ~~*avoid duplication of*~~ ***regulations*** ~~*for performing laboratory examinations and other procedures*~~ ***under section 353 of the Public Health Service Act; and***
***"(B) not apply to laboratory operations.***
~~*"(3) EXCEPTION FOR LABORATORY TEST PROTOCOLS.—Developers that are developing test protocols for use as described in subsection (a)(2)(A) are exempt from the requirements under paragraph (1)(C) except for the requirements described in clauses (iv), (vi), (ix), (xi), and (xiv) of such paragraph.*~~

**Sec. 587M. Adverse Event Reporting**

CLIA already requires laboratories to report errors in test results to ordering physicians. Additionally, CMS-approved accrediting organizations must notify CMS within 10 days of any deficiency identified in an accredited or CLIA-exempt laboratory if the deficiency poses an immediate jeopardy to the patient or hazard to the general public. AMP agrees that adverse event reporting requirements should be modernized -- albeit within CLIA -- to mandate ready mechanisms for reporting, promote transparency, and avoid duplication of these requirements. However, if the VALID Act continues to be FDA-centric, then FDA should be required to work with CMS to create a single, national adverse event reporting system for developers offering LDPs.

Additionally, the VALID Act requires reporting within five calendar days for certain adverse events which is not enough time to gather the necessary information that should be included in a report. Laboratories will need to take time to determine the cause of the event and whether it was due to laboratory operations, test design/development, or unrelated to the test itself and due to treating provider error. This will involve reviewing reports, patient records, reagents/supplies, and possible failures in development, validation, or verification of the test or in the transfer of the specimen to the laboratory.

Further, the legislation should clarify that laboratories are not responsible for further gathering information outside of its health care system to provide information in an adverse event report.

**To mitigate our concerns, the language should be amended as follows (page 265):**

***"(b) ADVERSE EVENT REPORTS.—If a developer receives or otherwise becomes aware of information that reasonably suggests that the developer's in vitro clinical test may have caused or contributed to an adverse event, the developer shall submit an adverse event report with such information to the Secretary, in accordance with subsections (c) and (d).***
***"(1) A developer is not required to obtain any further information not immediately available within its own healthcare or records system for the purposes of submitting an adverse event report.***
***"(c) SUBMISSION OF INDIVIDUAL REPORTS.—A developer shall submit an individual adverse event not later than 10 calendar days after the developer receives or becomes aware of an adverse event that reasonably suggests that an in vitro clinical test may—***
***"(1) have caused or contributed to a patient or user death; or***
***"(2) present an imminent threat to public health.***

***"(d) SUBMISSION OF QUARTERLY REPORTS.—As applicable, a developer shall submit quarterly reports that include any in vitro clinical test errors related to the design or analytical performance and serious injuries that occurred during the applicable quarter. Such quarterly reports shall be submitted not later than the end of the quarter following the quarter in which the developer receives or becomes aware of such adverse events.***
***"(e) The Secretary shall establish a single, national adverse event reporting system to allow developers of test protocols to meet the requirements of this Act and section 353 of the Public Health Service Act.***
***"(f) DEFINITIONS.—For the purposes of this section—***

**Sec. 587N. Corrections and removals.**

The terms used in Section 587N do not translate well to LDPs and we believe it is highly likely that FDA regulations will duplicate CLIA based on our reading of part 806 of title 21 of the Code of Federal Regulations. **Developers offering LDPs should be exempt from meeting these requirements if they demonstrate compliance with 42 CFR Subpart K Part 493.**

**Clarify the risk classification definitions**

Overall, AMP finds the definitions of risk to be ambiguous and additional clarity is needed. We are concerned that provisions in the legislation indicate that extensive and time-consuming discussions with the FDA will be required to establish or resolve classification differences for many tests, further exacerbating the administrative burden of this approach. AMP appreciates that the VALID Act of 2022 includes a definition for moderate risk; however, as currently written, it overlaps with the definition of high risk. Instead, AMP recommends that the risk definitions be modified to factor in transparency of the test methodology. **Specifically, only tests that (1) use methodologies, procedures, techniques, or proprietary algorithms and/or computations such that the test results cannot be tied to the methods used or (2) inter-laboratory comparisons cannot be performed should be considered high risk. All other tests should be considered either moderate or low risk based on risk to the patient or public health.**

**Expand the scope of a technology certification**

Based on the success of the New York State Department of Health (NYSDOH) Clinical Laboratory Evaluation Program (CLEP), AMP believes that laboratories with demonstrated experience with similar technologies and/or methodologies can successfully offer other accurate and precise LDPs, including high risk LDPs. **Thus, we urge you to make the following language edits (page 187):**

~~***"(E) high-risk;***~~
***"(E) a combination product unless such test has been determined to be eligible to be introduced into interstate commerce under a technology certification order pursuant to the regulatory pathway designation process described in section 587F, or as described in subsection (k); or***
***"(F) a first-of-a-kind in vitro clinical test, unless such test has been determined to be eligible to be introduced into interstate commerce under a technology certification order pursuant to the regulatory pathway designation process described in section 587F, or as described in subsection (k).***

Additionally, language should be flexible and allow developers to propose a scope for a technology certification that is appropriate for their laboratory. **As such, we recommend that the language read as follows on page 190-191:**

> ***"(A) IN GENERAL.—A developer shall propose a description of the scope of techniques, technologies, and test types that would fall under the developer's certification order. ~~Subject to subparagraph (B), the scope of a technology certification order issued under this section shall be no broader than—~~***
> ***~~"(i) a single technology type; or~~***
> ***~~"(ii) a fixed combination of technologies where multiple in vitro clinical tests utilizing the technology do not significantly differ in control mechanisms, energy sources, or operating principles and for which development, including design, and analytical and clinical validation, of the in vitro clinical tests would be addressed through similar procedures.~~***
> ***~~"(B) INCLUSIONS.—Notwithstanding subparagraph (A), the scope of a technology certification order issued under this section may be for one fixed combination of technology types if the Secretary determines appropriate and promulgates regulations establishing criteria and procedures for a technology certification order for a fixed combination of technology types.~~***
> ***~~"(C) TECHNOLOGY TYPE.—A technology type described in this paragraph may include clot detection, colorimetric (non-immunoassay), electrochemical (non-immunoassay), enzymatic (non-immunoassay), flow cytometry, fluorometry (non-immunoassay), immunoassay, mass spectrometry or chromatography, microbial culture, next generation sequencing, nephlometric or turbidimetric (nonimmunoassay), singleplex or multiplex non-NGS nucleic acid analysis, signal based technology, spectroscopy, and any other technology, as the Secretary determines appropriate.~~***

**<u>Establish a predictable regulatory framework</u>**

Throughout the legislation, the text grants discretion to the Secretary, potentially creating an unpredictable regulatory process and ambiguities in the significance of the policy. This is especially problematic as stakeholders try to understand the implications for their laboratories and practices. For example:

(1) In the section on an abbreviated premarket review, the legislation says that developers will not need to provide raw data as part of their submission unless requested by the FDA. The requirement of providing raw data is a meaningful distinction between full premarket review and abbreviated premarket review, and yet the Secretary has the discretion in any instance to require that data. This potential unpredictability drastically reduces the appeal of this abbreviated process.
(2) Additionally, in the grandfathering provision, the Secretary has the discretion to direct any grandfathered test for premarket review. This further creates confusion as laboratories determine which of their tests will be subject to review.
(3) The proposed language under Section 587F. Regulatory pathway designation gives wide discretion to the Secretary, which creates even more uncertainty and raises concerns that a reasonable proposal may become overly restrictive and burdensome if interpreted in a more limiting sense.

There are dozens of instances in the legislation similar to these examples. Given that the bill's sponsors intended to provide regulatory certainty, **we strongly urge the Committee to narrow the discretion so that stakeholders may better evaluate and understand the implications of this legislation.**

**Include preemption language that is meaningful**

AMP believes that the process to review analytical and clinical validity utilized by state programs such as NYSDOH has been a successful effort and represents a balanced approach to oversight that does not duplicate federal regulatory efforts and has resulted in a harmonious and effective approach to regulating laboratory practice. As such, stakeholders have encouraged the Committee to recognize the value of such programs, prevent duplication with state efforts, and apply lessons learned. The VALID Act of 2022 fails to incorporate any of these recommendations and instead allows states with programs in place prior to 2022 to continue their programs only if their requirements match those of the FDA. Further, as developers will still need to comply with both the FDA requirements and those state requirements, this will further create unavoidable duplication as regulatory oversight. AMP requests that the Committee clarify the preemption language to allow review by existing state programs to be sufficient in meeting the requirements of premarket review under the VALID Act. It would be reasonable for those regulated under the existing state programs to also complete the registration and listing requirements under VALID Act.

**Establish EUA policy to enhance the United States' pandemic preparedness**

Early in the pandemic, FDA made the decision to require laboratories to obtain an emergency use authorization (EUA) regardless of whether a test was a boxed-and-shipped as an in vitro diagnostic test kit or a LDP. This drastic change in review requirements for laboratories using LDPs created a barrier for professionals to institute testing services in the early days of the pandemic, greatly hampering the country's collective ability to stem the spread of SARS-CoV-2 in spring 2020.

Unfortunately, even after the FDA modified its guidance to simplify the EUA process later in 2020 in an attempt to mitigate testing delays, approximately 35% of the laboratory professionals surveyed by AMP[3] noted that it took more than a month for their laboratory to receive an EUA. Several individuals reported that their laboratory submitted their application and even after four months, had yet to receive authorization. One individual reported that FDA did not respond to their application for six weeks, and then when the agency finally did answer, staff asked questions that could have easily been answered up front. In fact, 32% of the respondents in one of our 2020 surveys said that they encountered hurdles in completing the EUA process. Laboratory professionals that participated in the survey noted FDA's lack of experience with certain kinds of technology and, combined with inefficiencies in the submission and review process, led to unnecessary delays implementing tests for clinical care in the midst of a incredibly fast-moving pandemic. AMP's survey revealed that the FDA's inability to efficiently and expertly review EUA submissions for COVID-19 tests delayed the ability of laboratories to offer testing during times when the country was far below meeting test capacity needs. This not only delayed patient care but potentially compromised the ability to utilize contact tracing and other measures in the effort to stem the spread of COVID-19. **For these reasons, we strongly urge you to include language similar to the legislative language under Section 587A(a)(5) on emergency use laboratory tests in the VALID Act of 2021 (S. 2209) as introduced.**

Moreover, we should consider testing policy as a case study for how well FDA might perform during non-pandemic times if the VALID Act of 2022 were to become law. Public reports indicate that as of October 2020, there were over 160,000 genetic tests being used for clinical care in the United States.[4] This is just a sliver of the

[3] https://www.amp.org/advocacy/sars-cov-2-survey/

[4] Concert Genetics, "The Genetic Test Unit (GTU) - A unique identifier for every genetic test,

laboratory testing services that would be within FDA's purview if the VALID Act were to become law. According to an independent review, FDA reviewed and closed out 1,294 molecular EUA submissions, including 83 submissions FDA declined to review, between the start of the public health emergency and April 2021.[5] Even if we considered the total number of EUA requests for all COVID-19 tests, 2,133, this does not likely come close to representing the number of tests that FDA would likely have to review on an annual basis under the VALID framework. Our members directly experienced the devastating consequences stemming from a situation in which FDA was crippled by the volume of its work -- we hope you seriously weigh this impact on patient and public health as you continue your work on this legislation.

**Future commitment to modernize CLIA**

AMP is disappointed by your commitment to move forward with this flawed legislation that does not take advantage of knowledge gleaned from currently operating oversight systems. Current oversight mechanisms ensure that the laboratory test, the laboratory, and its personnel are intrinsically linked and cannot be reasonably decoupled for oversight purposes. If you opt to continue to advance this legislation, AMP also calls upon you to commit to working to modernize CLIA as well. Only minor updates to the program have been made since the final federal regulations implementing the CLIA program were promulgated in 1992, and thus the regulations do not fully reflect the advances that have been made in the science and application of laboratory medicine over the past three decades. The Clinical Laboratory Improvement Advisory Committee (CLIAC) provides scientific and technical advice to the Department of Health and Human Services (HHS) regarding CLIA. CLIAC also recognizes the need for the program to be modernized and recently recommended to HHS that the regulations be updated. A workgroup has already been formed to provide specific recommendations for doing so. This work is an opportunity for a full discussion on how best to ensure that laboratory testing services are high quality and clinically appropriate. AMP also recommends that Congress mandate that CMS hold a public meeting to solicit recommendations from the greater public on ways to update CLIA regulations. AMP believes that additional congressional action is required to appropriately update the CLIA program, as we have outlined in our CLIA modernization proposal[6]; starting with a public meeting is needed to ensure that various stakeholder perspectives are factored in.

These comments in no way serve as endorsement for the VALID Act of 2022. However, we hope that ultimately these comments will be used to develop legislation that best serves the medical practice of molecular professionals and their patients. Should you have any questions or wish to discuss these issues further, please don't hesitate to Sarah Thibault-Sennett at SThibaultSennett@amp.org.

Sincerely,

Daniel E. Sabath, MD PhD
President, Association for Molecular Pathology

accessible royalty-free by all." 2021. http://www.concertgenetics.com/wp-content/uploads/2021/06/Concert-Genetic-Testing-Unit-GTU-Unique-Test-Identifier-Whitepaper-June-2021.pdf Accessed November 8, 2021

[5] https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/emergency-use-authorization-covid-19-tests-independent-assessment-fdas-response?utm_medium=email&utm_source=govdelivery

[6] http://www.amp.org/AMP/assets/File/advocacy/AMPCLIAmodernizationproposalFINAL8_14_15.pdf