



February 15, 2019

The Honorable Frank Pallone
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
2125 Rayburn Building
Washington, D.C. 20515

The Honorable Greg Walden
Ranking Member
Committee on Energy and Commerce
U.S. House of Representatives
2322 Rayburn Building
Washington, D.C. 20515

The Honorable Larry Bucshon
U.S. House of Representatives
1005 Longworth House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
U.S. House of Representatives
2111 Rayburn House Office Building
Washington, D.C. 20515

RE: Request for Comment on the “Verifying Accurate Leading-edge IVCT Development (VALID) Act of 2018”

Dear Chairman Pallone, Ranking Member Walden, and Representatives Bucshon and DeGette:

On behalf of the Personalized Medicine Coalition (PMC), which represents innovators, scientists, patients, providers, and payers to promote the understanding and adoption of personalized medicine concepts, services, and products for the benefit of patients and the health care system, I am writing to share PMC’s appreciation for the opportunity to comment on the “Verifying Accurate Leading-edge IVCT Development (VALID) Act of 2018.”

PMC defines personalized medicine as an emerging field that uses diagnostic tools to identify specific biological markers, often genetic, to help determine which medical treatments and procedures will be best for each patient. By combining this information with an individual’s medical history and other clinical information, personalized medicine allows doctors and patients to develop targeted prevention and treatment plans. The goal is to provide the right treatment in the right dose to the right patient at the right time. Our interest in the VALID Act pertains to how legislation can best support this emerging field.

We seek to ensure that the field can move forward in enhancing patient care and improving the quality, safety, accuracy, and effectiveness of treatments, with the acknowledgement that innovation and access should be balanced with patient protections. We encourage PMC’s members to present their own responses to the VALID Act and actively advocate for those positions. These comments are not intended to impact adversely in any way the ability of individual PMC members, alone or in combination, to pursue separate comments. Additionally, PMC does not hold a position on whether laboratory-developed tests (LDTs) should be regulated by

BOARD OF DIRECTORS

President
Edward Abrahams, Ph.D.

Chair
Stephen L. Eck, M.D., Ph.D.
Immatics Biotechnologies

Vice Chair
Jay G. Wohlgemuth, M.D.
Quest Diagnostics

Treasurer
Peter Maag, Ph.D.
CareDx

Amy P. Abernethy, M.D. Ph. D.
Flatiron Health

Bonnie J. Addario
Bonnie J. Addario Lung Cancer Foundation

Steven D. Averbuch, M.D.
Bristol-Myers Squibb Company

Paul R. Billings, M.D., Ph.D.
Natera

Randy Burkholder
PhRMA

William S. Dalton, Ph.D., M.D.
M2Gen

Tim Garnett, FRCOG, MFFP, FFPM
Eli Lilly and Company

Brad Gray
NanoString Technologies

Kris Joshi, Ph.D.
Change Healthcare

Anne-Marie Martin
Novartis

Susan McClure
Genome magazine

Howard McLeod, Pharm.D.
Moffitt Cancer Center

J. Brian Munroe
Bausch Health Companies

Lincoln Nadauld, M.D., Ph.D.
Intermountain Healthcare

Michael Pellini, M.D.
Section 32

Kimberly J. Popovits
Genomic Health

Hakan Sakul, Ph.D.
Pfizer, Inc.

Michael S. Sherman, M.D., M.B.A.
Harvard Pilgrim Health Care

Sean Tunis, M.D.
Center for Medical Technology Policy

Michael Vasconcelles, M.D.
Unum Therapeutics

Werner Verbiest
Janssen Diagnostics

the U.S. Food and Drug Administration (FDA) or by the Clinical Laboratory Improvement Amendments (CLIA) program at the Centers for Medicare and Medicaid Services (CMS). PMC's comments are focused exclusively on personalized medicine issues and are designed to communicate areas of consensus with regard to in vitro clinical tests (IVCTs).

In 2016, PMC moderated a series of discussions on potential legislative solutions with representatives from the diagnostics community, including but not limited to those with an interest in personalized medicine. Six consensus principles emerged from those conversations, which we highlighted in comments submitted to Congress on the Diagnostic Accuracy and Innovation Act (DAIA) in July of 2017 and again in response to calls for feedback on the FDA's technical assistance provided to congressional leaders in August of 2018. We will reiterate these principles because we believe they are critical for you to consider as you revise the VALID Act. Where possible, we have provided preliminary redline edits and comments on the VALID Act bill text to reflect changes that we believe are consistent with PMC's consensus principles. In addition, we have included comments and outstanding questions on the bill text that reflect some areas of concern among PMC's members. This is not a comprehensive statement of PMC's position on the bill, but it is an attempt to highlight certain issues we would urge you to address this year as you pursue additional legislative activity.

1. Protect public health labs.

Public health labs should be protected by any regulatory paradigm, which means that sentinel, infectious disease, and public health labs must be able to design, deploy, and use rapidly developed diagnostics to address critical public health needs. The VALID Act indicates that any FDA review requirements should not apply to tests intended to be used solely for public health surveillance. We appreciated the inclusion of this language in the VALID Act and we urge you to retain these provisions in any future versions of the legislation.

2. Allow flexibility and efficiency when managing modifications.

As test developers have long argued, the way test modifications are managed by a regulatory system should be flexible and efficient to allow diagnostic tests to evolve with the clinical science that underpins them. We believe modifications that do not have a meaningful clinical impact or result in a meaningful change in the intended use should not be subject to review. A change in specimen type or collection method are examples of common modifications that can be verified or validated to determine whether they have a meaningful clinical impact or meaningfully change the intended use. We are concerned that under the VALID Act, a test is considered a new or "first-of-a-kind" IVCT (and is therefore subject to review) if it changes any element of the test group, such as a specimen, a disease or condition, or the intended patient population. The VALID Act also details several common modifications that would potentially trigger the need for premarket submission to the FDA. This broad view of modifications subject to premarket submission would undermine a test's grandfather status and in some cases it may disrupt patient access to currently-available laboratory tests and service.

Modifications need to be made frequently to improve test performance and address quickly evolving clinical needs, like those described above. It is important that a regulatory scheme does not unduly limit modifications. The definition for test group and first-of-a-kind should be revised to more appropriately

focus review on modifications that have the highest risk to patients. Future versions of the VALID Act should provide more flexibility in managing modifications so that improvements like these can be made without causing unnecessary regulatory burdens or delaying patient access.

3. Mitigate regulatory burdens for government and industry.

To reduce burdens on government and industry, we believe regulatory agencies should recognize when certain safeguards are already in place. These mitigation strategies can help regulators keep pace with the rapidly evolving science of personalized medicine diagnostic testing. The VALID Act attempts to delineate between FDA- and CLIA-associated activities, but like FDA's technical assistance on DAIA, definitions in the VALID Act would give FDA jurisdiction over many aspects of laboratory operations and overlap with CMS activities under CLIA. We appreciate where the VALID Act has attempted to reduce regulatory burdens, but PMC asks that you more clearly identify how successful programs and systems that have resulted from CLIA will be protected under a new legislative framework. In addition, we encourage you to further explore with the community how reporting systems should be harmonized to prevent unnecessary administrative burdens on what types of information should be reported to whom.

4. Design grandfathering provisions for tests already on the market along with a risk classification system for novel tests.

As of March 2018, there were nearly 75,000 personalized medicine diagnostics offered by labs, with another fourteen coming to market each day.¹ To manage such an enormous workload, the VALID Act must implement a grandfathering system that will allow most tests to remain on the market unless there is a compelling reason to remove them. PMC is concerned that the VALID Act does not fully address issues previously raised by stakeholders regarding grandfathering and transitioning policies. We believe the VALID Act could negatively impact patient access to valuable tests already in routine use by retroactively increasing regulatory burden for tests when they lose grandfathered status through modification. As stated previously, modifications to grandfathered tests should only require notification if they have a meaningful clinical impact or a meaningful change in intended use. In addition, by placing tests evaluated shortly after the bill's enactment under existing device regulations until the VALID Act goes into effect, the Act would force developers to transition through two regulatory frameworks. To minimize disruption, developers should be permitted to continue operating under CLIA until a new framework is effective.

Likewise, it is critical that a consistent and transparent risk classification system be agreed to and described before enactment of new legislation governing the oversight of IVCTs. The VALID Act defines two risk categories, high-risk and low-risk, and provides the FDA broad discretion regarding when tests should be classified as high- or low-risk. For a risk-based classification system to be meaningful, the risk levels must be adequately defined, and it must be clear how that system will be applied. We propose a risk-based approach to when an IVCT requires review. No IVCT should automatically be deemed as requiring review. Such an approach does not incorporate an actual risk evaluation of these IVCTs. IVCTs that do not meet the definition of high-risk should be designated as low-risk and should be exempt from premarket review.

The VALID Act proposes a voluntary precertification program, which is a concept that was cautiously received by many PMC members when it was initially proposed as part of FDA’s August 2018 technical assistance on DAIA. It was initially described as a way for tests that might not be considered high-risk (requiring premarket approval) or low-risk (exempt from premarket review) to benefit from a more streamlined pathway after an IVCT developer was pre-certified. While this section remains under development, we urge you to consider that precertification should be more accessible, which may require revising the scope and eligibility, assessment process and criteria, and utilization of a risk-based approach using quality systems. Requiring a renewal of precertification after two years could impose an unnecessary regulatory burden on developers. At a minimum, policymakers should describe the rationale for requiring precertification renewal.

The bracketed precertification provisions exclude a large number of tests from precertification. After their technical assistance on DAIA was released, FDA publicly stated that they envisioned precertification expanding to include some of these categories once they gained experience with the program. IVCTs that meet the definition of high-risk but can have that risk reduced through mitigating measures, by being well-characterized, or through other confirmatory tests, should have the option of undergoing precertification or an individual streamlined premarket review. All IVCT categories that meet the definition of high-risk with risk reducing factors should be eligible for this pathway. We also disagree with categorical exemption of IVCTs, such as those for home use, from precertification, which is not a risk-based approach.

5. Ensure regulatory burdens reflect testing volumes.

Regulatory burden must reflect testing volume. For example, diagnostics designed for rare and unmet needs should be given careful and different consideration to ensure that tests are developed for micromarkets. PMC appreciates that the VALID Act designs a special pathway for tests that fill unmet needs and provides carve-outs for custom IVCTs and tests for rare diseases. The definitions for these tests, however, are overly restrictive. PMC believes that the definitions should be based not on the number of individuals who would be subject to testing, which may not be knowable, but rather on disease prevalence. As a starting point, we have proposed that the rare disease language reflect exemptions for tests that are intended to identify, measure, detect, predict, monitor, or assist in selecting treatment for a disease or condition with a prevalence of 50,000 or fewer in the United States. PMC urges you to work with stakeholders to find a reasonable solution to this issue.

6. Accept valid scientific evidence for regulatory purposes — even if that evidence does not include data from a randomized, controlled trial.

Personalized medicine challenges how health care products and services are conceived, developed, regulated, covered, paid for, and used by physicians. Evidentiary requirements for regulatory review must also evolve. The community agrees that, regarding diagnostics, valid scientific evidence should be acceptable for regulatory review even when that evidence does not include data from randomized, controlled trials. The VALID Act outlines various types of evidence to demonstrate if a test is well-characterized, including peer-reviewed literature, clinical guidelines, case studies or histories, consensus standards, reference standards, and real-world data. We urge you to retain this language in future

versions of the legislation but add the availability of proficiency testing as evidence that a test is well-established and recognized by the scientific or clinical community.

Thank you for the opportunity to provide preliminary feedback and for carefully considering our comments on the bill text that follows. PMC is committed to working with you and your colleagues to advance these principles and find additional areas of consensus. We welcome the opportunity to provide ongoing input to you as you work to strike the appropriate balance between regulation, innovation, and access to personalized medicine diagnostic tests. If you have any questions about the content of this letter, please contact me at cbens@personalizedmedicinecoalition.org or 202-589-1769.

Sincerely,



Cynthia A. Bens
Senior Vice President, Public Policy

ⁱ Concert Genetics. *The Current Landscape of Genetic Testing: 2018 Edition*. Accessed; February 11, 2019. http://www.concertgenetics.com/wp-content/uploads/2018/04/12_ConcertGenetics_CurrentLandscapeOfGeneticTesting2018.pdf