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February 15, 2019

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

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

The Honorable Diana DeGette
U.S. House of Representatives
211 Rayburn House Office Building
Washington, DC 20515

The Honorable Larry Bucshon
U.S. House of Representatives
2313 Rayburn House Office Building
Washington, DC 20515

Re: Comments on Verifying Accurate Leading-edge IVCT Development Act of 2018 or the "VALID Act of 2018."

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

On behalf of the American Cancer Society Cancer Action Network (ACS CAN), the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, thank you for the opportunity to provide feedback on the discussion draft for the "Verifying Accurate Leading-edge IVCT Development Act of 2018" or "VALID Act of 2018." Cancer patients rely on accurate and clinically valid diagnostic tests to optimize their treatment options. We are committed to working with Congress to craft legislation that meets the needs of patients.

ACS CAN's overarching goal for diagnostic reform legislation is to ensure that patients have confidence in the results of diagnostic tests, which have become increasingly critical in the management of cancer. Currently, diagnostic tests undergo widely different levels of oversight depending on whether they are submitted to the FDA for review or are offered as laboratory developed tests (LDTs). This difference opens the door to the possibility that test results may vary depending on where the test is conducted, potentially leading to incorrect treatment decisions and patient harm if a test result is not valid. Cancer patients and their physicians should be able to trust the information produced by a diagnostic test regardless of where that test is conducted.

The VALID Act proposes to create harmonized oversight for all diagnostics with tiered requirements tied to the risk posed by a given diagnostic test, with rigorous review of high-risk tests, while providing flexibility to accommodate innovation and simplified requirements for low-risk tests. Overall, we are pleased with the legislation, but have comments on specific aspects contained within the proposal which are outlined below and in the attached redline copy of the legislation. We have focused our comments on areas of the legislation that are of the most importance to our organization.

Risk Classification

We support the concept of a risk-based oversight framework, which focuses oversight proportionally on tests based on risk to a patient if a test result is incorrect. The difference in oversight proposed by this legislation between high-and low-risk tests is significant, therefore it is critical that tests be appropriately classified.

Risk classification in this legislation is a combination of risk to a patient's health posed by an inaccurate test result and a test's risk of being inaccurate. We believe that risk should be based on risk to a patient's health and have concerns about the legislation's provisions to downgrade risk classification based on factors other than risk to a patient's health. Specifically, the legislation introduces the idea of mitigating measures along with other factors like the availability of confirmatory tests.

We believe that using the "availability" of confirmatory tests to reduce risk classification, and associated review scrutiny, is inappropriate. The premise behind this modification of an IVCT's risk classification is that if other tests exist, an erroneous test result is more likely to be caught before it is acted on clinically. Simply having another test "available" does not mean that it will be used. Standard medical practice, recognized practice guidelines, or even insurance coverage may discourage the use of confirmatory or adjunctive tests that could catch an error. In fact, a recent Centers for Medicare and Medicaid Services (CMS) national coverage determination (NCD) related to next-generation sequencing tests for cancer specifically limit coverage of such testing to once per cancer per lifetime, meaning formal Medicare policy is single diagnostic testing. It is not appropriate, therefore, in life and death situations like cancer to categorically downgrade a test's risks based upon the mere existence of a confirmatory test, since the use of such tests cannot be assured by FDA. In cases were confirmatory testing is standard, for example in screening asymptomatic adults, confirmatory tests could potentially be considered as a risk-reducing factor.

Further, the legislation proposes to rely on how well-established a technology is to determine level of oversight. Examples of relatively well-established technologies still yielding discordant

results are not uncommon in cancer and provide caution in relying on pervasiveness of use as a proxy for low-risk [1,2].

The legislation indicates that requirements on labeling, posting of website information, and advertising as well as the use of post-market surveillance could be considered mitigating measures. While these activities may provide important guidance or instill caution regarding the reliability or applicability of a test result, this type of protection is not as robust as instituting measures that ensure the reliable function of the test or prevent misapplication of the test. We are concerned about the reliance on communications tools such as these as the basis of down classification of an otherwise high-risk test given that communications efforts, especially with non-medical personnel, are challenging given varying levels of medical literacy and the multiplicity of languages used in the U.S.

Rare Disease Exemption

We believe that it is appropriate to exempt truly rare tests from full review requirements. The risk of an inaccurate result is based on the number of individuals subject to a test rather than the number of individuals with a positive result; therefore, we support this legislation's definition of rare based on tests performed rather than disease incidence.

Grandfathering

Under the VALID Act, grandfathered tests along with those enjoying other premarket exemptions including rare and low-risk tests, may be required to provide additional data to demonstrate analytical and clinical validity if their performance is suspect, claims are misleading, or if they pose a risk to public health. Further, grandfathered tests which are modified are likewise subject to additional review by FDA. We support this ability for FDA to exercise oversight over suspect or altered grandfathered tests.

Grandfathered tests have not undergone the same level of review as those fully reviewed by FDA, therefore we also support the FDA recommendation requiring grandfathered tests to include a disclaimer that they have not been reviewed by FDA within their report template.

Clinical and analytical validity requirements for approval

The VALID Act provides a clear standard that a "reasonable assurance of adequate analytical and clinical validity..." is required for approval and differentiates these standards by category (e.g. IVCT, platform, or articles). The use of "adequate" is an important qualifier; however, that qualifier is not used consistently throughout the legislation. We encourage adding "adequate" in instances where the approval standard is invoked (e.g. precertification elements on page 48 or standards on page 84).

Patient awareness issues

Patients are neither typically well versed in concepts like analytical and clinical validity or in regulatory procedures, nor should they be in order to trust the results of their diagnostic tests. Nonetheless, it is important to provide patients and practitioners with useful information to make sense of their test results, and to empower them to report incorrect results and adverse events. We support the test report template requirements within this legislation that provide performance information, intended use, warnings, limitations, and the process for reporting adverse events. These requirements recognize the importance of providing context to results for end users. Similarly, we support the adverse event reporting requirements that ensure any known harms caused by a diagnostic test are promptly reported to the FDA and these, along with less serious reports, are made publicly available. Lastly, as mentioned above, we support the disclaimer required on grandfathered test result templates.

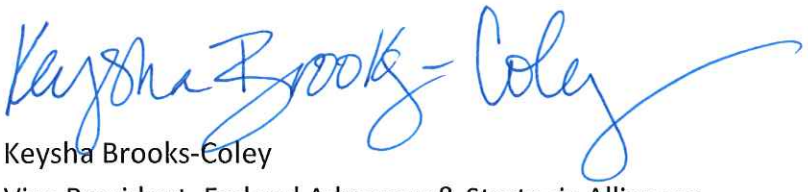
Additional Regulatory Pathways

In addition to high-and low-risk tests, the VALID Act includes additional regulatory concepts such as the use of change protocols, test groups, and precertification, all of which are relatively new concepts. Further clarification would also be helpful on the role of these tools, which diagnostics they apply to, and how they interact with each other. Example applications for these provisions would better enable stakeholders to understand and evaluate their potential use.

Summary

We applaud your leadership in updating and harmonizing the oversight framework for molecular diagnostic tests and appreciate the opportunity to represent patient perspectives as you shape this legislation. We encourage you to move forward with finalizing legislation for introduction, and we look forward to continuing to work with you to enact meaningful diagnostic test reform. If you have any questions regarding our comments, please contact Phylicia L. Woods (Phylicia.woods@cancer.org).

Sincerely,



Keysha Brooks-Coley
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American Cancer Society Cancer Action Network

References

1. "HER2 Testing by Local, Central, and Reference Laboratories in Specimens From the North Central Cancer Treatment Group N9831 Intergroup Adjuvant Trial," Perez E, Suman V, et al., Journal of Clinical Oncology, 24(19), 2006.
2. "Conflicting Interpretation of Genetic Variants and Cancer Risk by Commercial Laboratories as Assessed by the Prospective Registry of Multiplex Testing," Blman J, Digiovanni L, et al., Journal of Clinical Oncology, 34(34), 2016.