FORCE
Facing Hereditary Cancer EMPOWERED

August 23, 2021

The Honorable Richard Burr
U.S. Senate
217 Russell Senate Office Building
Washington, DC 20510

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

The Honorable Michael Bennet
U.S. Senate
261 Russell Senate Office Building
Washington, DC 20510

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

Re: VALID Act (H.R.4128 / S.2209) Feedback

Dear Senators Bennet and Burr, and Representatives Bucshon and DeGette:

Thank you for the opportunity to provide input on the Verifying Accurate Leading-edge IVCT Development (VALID) Act. FORCE is a national nonprofit organization that represents the millions of Americans with or at increased risk of hereditary cancers. Our community relies on laboratory developed tests and *in vitro* diagnostics to identify those with an inherited predisposition to cancer and to guide treatment of those diagnosed with the disease.

Below, we have detailed our top 3 areas of concern and feedback:

1. Current High/Low risk categories - inadequately reflect test impact on patients
2. Grandfathering of currently marketed tests - is not acceptable in perpetuity
3. Technical certification - places undue emphasis on test accuracy without incorporating interpretation of results and therefore, impact on patient risk

1. Risk categories

Current risk categories inadequately address risk of tests. The High risk and Low risk categories present a false dichotomy. There is need for a Moderate risk category to encompass tests that if inaccurate do not lead to immediate harm or death but are either irreversible (e.g. surgical procedures) or lead to delay or alteration in care that is life-sustaining (e.g. cancer treatment).

The **High-risk category** applies to test which "presents unreasonable risk for serious or irreversible harm or death to a patient or patients, or would otherwise cause serious harm to the public health" or "is potentially likely to result in the absence, significant delay, or discontinuation of life-supporting or life-sustaining medical treatment."

In contrast, the **Low-risk category** applies to tests that either:

A. “would cause minimal or no harm, or minimal or no disability, or immediately reversible harm, or would lead to only a remote risk of adverse patient impact or adverse public health impact, taking into

account the degree to which the technology for the intended use of an in vitro clinical test or category of tests is well characterized and the criteria for performance of the test or category of tests are well-established for the intended use, the clinical circumstances under which the in vitro clinical test or category of tests is used, and the availability of other tests (such as confirmatory or adjunctive tests)"

-OR-

B. "would cause a serious adverse health consequence, harm that is reversible, a delay in necessary treatment that is not life-supporting or life-sustaining, or would lead to a serious risk of adverse patient experience or adverse public health impact, but applied mitigating measures have the capacity to ensure the test meets the standard described in subparagraph (A)"

For patients undergoing genetic testing that impacts decision-making about cancer treatment or prophylactic surgery, risk is not Immediate, non-life supporting—but it is irreversible and of significant life-altering consequence. For example, national medical guidelines recommend that women with BRCA genetic mutations undergo risk-reducing, bilateral salpingo-oophorectomy (removal of ovaries and fallopian tubes) and consider risk-reducing mastectomy to mitigate their significant cancer risk. An inaccurate test result could lead to an unnecessary, life- and body-altering surgery.

Tests impacting this situation are not adequately categorized as High-risk or Low-risk. A Moderate-risk category is needed for tests that are not immediately life-threatening if inaccurate, but have the potential for substantial harmful impact over a patient's lifetime (e.g. due to irreversible decisions such as surgery or modification of treatment). Tests deemed "Moderate-risk" should be subject to oversight and evaluation by the FDA for test accuracy and whether potential harm can be adequately mitigated.

2. Grandfathering

Grandfathering all currently extant tests will result in inadequate protection for consumers. This legislation is proposed exactly because there are tests currently marketed that are of concern to consumers. While we recognize that the numerous currently marketed tests would require time for FDA review should this legislation become law, we propose that tests currently on the market not be grandfathered in perpetuity but rather have required review within a reasonable time (5-7 years) after enactment of this legislation.

3. Technical certification

The VALID Act provision for technical certification is too broad. As written, laboratories that do multiple tests may choose a technology certification which allows the laboratory to submit one test as proof of its proficiency. A laboratory may submit a representative test for technology certification. Approval of a technology certification application would allow a laboratory to market tests with similar clinical and analytical validity within the scope of the order - a single technology. A premarket application can serve as a representative test for technology certification.

While some tests may be sufficiently similar to a reviewed and approved test, others using the same or comparable platforms may have varying diagnostic accuracy or different clinical accuracy impacting interpretation and intended use of the test. As depicted, technical certification places an undue emphasis on diagnostic accuracy and similarity of tests; insufficient weight is placed on clinical accuracy or similarity of tests. Because the evaluation of tests is driven by the risk to patients, there is a need to adequately incorporate whether interpretation of test results (clinical accuracy) is sufficiently similar to an approved test, or not.

A single test example cannot adequately convey the clinical accuracy for a range of tests. For example, next generation sequencing (NGS) as a platform may have a verifiable accuracy of sequence results, however interpretation of that result and its bearing on patient health differs dramatically in different regions of the genome with different genes or mutations. The proposed technical certification places unwarranted emphasis on analytical test evaluation and insufficient weight on the clinical accuracy or interpretability of the results for diagnostic decision-making. This process for certifying an entire class of tests based on the diagnostic accuracy of the test bypasses review of key information that impacts patient risk.

Additional concerns include:

- Exemptions are too wide-ranging and include cross referenced tests.
- Expiration of technology certification does not negate the certification.
- Lab errors are not included as adverse events.
- The bill includes a provision that exempt tests can also be subject to post-market approval; it is unclear how that would take place.
- There are inadequate provisions to ensure that the FDA can request data about a test as needed.

We would greatly appreciate the opportunity to engage and further discuss our feedback and concerns at your convenience. If you have any questions or would like to schedule a meeting, please contact me.

Sincerely,

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