April 1, 2024

The Honorable Bill Cassidy, MD
Ranking Member
U.S. Senate Committee on Health, Education,
Labor, and Pensions
428 Dirksen Senate Office Building
Washington, DC 20510

RE: Request for Information from Stakeholders on Regulation of Clinical Tests

Dear Ranking Member Cassidy,

On behalf of the LUNGevity Foundation, the nation's preeminent lung cancer nonprofit that funds research, provides education and support, and builds communities for the more than 230,000 Americans diagnosed with lung cancer each year[i] and over 600,000 Americans living with the disease,[ii] we appreciate the opportunity to submit these comments in response to your request for information from stakeholders on the regulation of clinical tests. LUNGevity submits these comments specifically from the perspective of patients with lung cancer, for whom the accuracy and reliability of diagnostic tests used to direct their treatment is of paramount importance.

How well is FDA's medical device framework working for the regulation of diagnostic products? Are there improvements that should be made? Of these specific changes, which would require Congressional action, and which can be effectuated by FDA alone?

Currently, FDA's medical device framework applies specifically to in vitro diagnostics (IVDs) manufactured and sold as kits. FDA-regulated IVDs include companion diagnostics (CDx) used to identify patients most likely to benefit from a particular treatment. In lung cancer, CDx are typically developed to detect specific biomarkers and paired with corresponding targeted therapies.

Biomarker testing is necessary for determining the most appropriate treatment option for patients with lung cancer. However, the one-drug-one-test paradigm is not reflective of real-world clinical practice, where treatment decisions are frequently made based on laboratory-developed tests (LDTs): in-house IVDs designed, manufactured, and used within a single clinical laboratory.

Since the FDA's medical device regulatory framework was established under the Medical Device Amendments of 1976, the Agency has exercised enforcement discretion regarding LDTs. Instead, LDTs are regulated by CMS under CLIA, which primarily focuses on laboratory operations rather than assessing the clinical validity of individual diagnostic tests.

These differing forms of oversight between FDA-regulated IVD test kits and LDTs result in variable levels of test validation, potentially impacting the consistency of results across tests used for the same clinical purpose. All IVDs used for the same purpose should be subject to consistent validation standards regardless of where they are made and used, to improve consistency in performance of all tests used for the same purposes, increase transparency, and better ensure patients and physicians can trust the accuracy of test results.

We understand that FDA has moved forward with rulemaking to end enforcement discretion for LDTs and begin regulating them under the medical device regulatory framework. **However, we are concerned that this framework is ill suited to ensure LDTs receive appropriate oversight without stifling innovation or hindering patient access.**

LDTs often require modifications to improve test efficiency and address changing clinical needs. Existing regulatory requirements for device modifications are unnecessarily restrictive for low-risk changes that do not alter the analytical validity, clinical validity, or intended use of an LDT. If the FDA proceeds with regulating LDTs as proposed, the medical device regulatory framework must change to better facilitate the incorporation of low-risk modifications by removing burdensome and time-consuming review processes that could unnecessarily delay patient access to these tests.

In contrast to utilizing an existing regulatory pathway, **legislation is necessary to create a new, fit-for-purpose regulatory framework specifically tailored for IVDs. Moreover, legislation could clarify and codify that FDA has both the authorities and resources necessary to effectively oversee the development and marketing of all IVDs.**

Do the proposed reforms to FDA's device framework warrant the establishment of a new regulatory pathway specific to diagnostics? If yes, what are the principles that should guide such a new framework, as it would be applied to diagnostics currently subject to FDA premarket review?

The establishment of a new regulatory pathway specific to IVDs would be preferable to reforming FDA's medical device framework. The proposed rule would bring all IVDs under a single mechanism of oversight, regardless of where they are made or used. As mentioned above, subjecting all IVDs used for making critical treatment decisions to FDA oversight would improve consistency in test performance and increase trust in the validity of diagnostic test results for the patients who rely on them. However, a new IVD-specific regulatory framework, unlike the proposed reforms, could appropriately balance the assurance of test accuracy and reliability with other important priorities, including innovation in test development and patient access.

One key principle that should guide the development of a regulatory framework specific to IVDs is the need for flexibility in innovation. The Verifying Accurate, Leading-edge IVCT Development (VALID) Act of 2022 proposed a fit-for-purpose regulatory framework for all IVDs, including LDTs, which serves as a good example of this principle. In addition to providing flexibilities for test developers to make modifications, this proposed framework included flexible pathways for marketing them, such as technology certification, to accelerate the delivery of innovative diagnostics to patients without unnecessary regulatory hurdles. Incorporating these kinds of provisions would improve the ability of test developers to keep pace with scientific advancements and help ensure patients can benefit from those advancements without unnecessary delays.

Another key principle is the importance of patient access to accurate, reliable biomarker tests. Given the high volume of LDTs currently in clinical use, the FDA may lack adequate capacity to review the number of premarket applications it expects to receive in a timely manner, should the Agency proceed with LDT regulation as proposed. A process by which the Agency accredits third parties to review applications and make recommendations regarding approval, such as the one outlined in the VALID Act, could be used to ease the FDA's workload and prevent delays in regulatory decision making and patient

access. An IVD-specific regulatory framework should also include exemptions from premarket review, when appropriate, to remove unnecessary roadblocks to patient access to accurate IVDs critical to their care. For example, the framework put forward in the VALID Act included exemptions via grandfathering, through which tests currently in use would remain on the market and accessible to the patients who rely on them.

Such exemptions, however, must be appropriately balanced with **the provision of adequate FDA post-market authorities - a third principle that must guide the development of an IVD-specific regulatory framework.** The grandfathering of existing tests under the framework put forth under the VALID Act, for instance, would have been balanced by the bill's "Special Rule," which gave the FDA the authority to investigate and take necessary action on concerns regarding analytical or clinical validity or health risks potentially attributable to grandfathered tests.

The Special Rule is just one example of the ability of a new regulatory framework, established through legislation, to clarify and codify FDA's authorities to effectively oversee the development and marketing of all IVDs. Because it was drafted specifically with IVDs in mind with input from across the spectrum of stakeholders, the VALID Act contained a number of innovative provisions that better suited the iterative, evolving nature of IVDs.

We appreciate the opportunity to respond to your request for information on the regulation of clinical tests. Please feel free to reach me at aeferris@lungevity.org or at 240-454-3103 with any questions.

Sincerely,

Andrea Stern Ferris
President and Chief Executive Officer
LUNGevity Foundation

[i] Howlader N, Noone AM, Krapcho M, et al. (eds). SEER Cancer Statistics Review, 1975-2018, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2018/, based on November 2020 SEER data submission, posted to the SEER web site, April 2021.
[ii] Centers for Disease Control and Prevention. United States Cancer Statistics. Available at https://gis.cdc.gov/Cancer/USCS/#/Prevalence/.