



November 12, 2021

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

The Honorable Fred Upton
U.S. House of Representatives
2183 Rayburn House Office Building
Washington, D.C. 20515

RE: Cures 2.0 Act Draft Legislation

Dear Representatives DeGette and Upton,

On behalf of the LUNGevity Foundation, the nation's preeminent lung cancer nonprofit organization that funds research, provides education and support, and builds communities for the more than 230,000 Americans diagnosed with lung cancer each yearⁱ and the more than 600,000 Americans living with the disease,ⁱⁱ we appreciate the opportunity to submit our comments in response to the Cures 2.0 Act discussion draft. The draft includes provisions important to advancing our mission to improve lung cancer survivorship and quality of life for patients with the disease.

The 21st Century Cures Act aimed to bolster the research and development of diagnostic tools and treatments critical to advancing outcomes and quality of life for patients with life-threatening diseases like lung cancer. The bill's provisions establishing the Oncology Center of Excellence, the Breakthrough Devices Program, and others have accelerated the availability of revolutionary and life-saving therapies for patients with lung cancer. The legislation also laid the groundwork for evolving strategies to analyze and use real-world evidence in regulatory decision-making, which could lead to more efficient assessment of treatment safety and efficacy in more diverse patient populations.

Just as critical as the development of treatments for life-threatening diseases is the effective delivery of those treatments to patients. The Cures 2.0 Act discussion draft aims to build upon the 21st Century Cures Act, with a focus on improving patient access to life-saving diagnostics and therapies. On the whole, LUNGevity supports this important draft legislation, and we are grateful for the opportunity to offer comments from the perspective of the cancer patient. We acknowledge that our feedback likely aligns with other, but not necessarily all, patient advocacy groups.

Clinical Trial Diversity

LUNGevity is supportive of legislative action that will effectively improve representation of underrepresented subgroups in clinical trial participant populations, as evidenced by our work to address disparities and improve health equity in lung cancer care. **Sec. 203** of the draft legislation requires updates to the report mandated under section 907 of the Food and Drug Administration (FDA) Safety and Innovation Act, analyzing clinical trial participation and the relative inclusion of safety and effectiveness data across demographic subgroups in submitted applications to the FDA. The original report was issued in August of 2014, and since that time, the issue of poor diversity in clinical trial participant populations has become increasingly appreciated. As important as diversity, however, is the representativeness of trial populations according to disease prevalence, as disease burden varies across demographic subgroups. For example, Black men are 15% more likely to develop lung cancer than white men.ⁱⁱⁱ Representativeness in clinical trial populations ensures the applicability of a medical product's safety and efficacy data to its



ultimate end users in the postmarket setting. **We encourage the application of FDA resources specifically toward improving representativeness of clinical trial participant populations based on disease prevalence, which will also improve racial and ethnic diversity of clinical trial populations.**

Patient Experience Data

Patient Experience Data (PED) provide insight into patients' needs, priorities, and perspectives that only they can provide, and have the potential to serve as a valuable resource guiding the designs of pre- and post-market studies as well as regulatory decision-making. **Sec. 204** of the draft legislation mandates the inclusion of PED in marketing applications for consideration by the FDA. While LUNGEvity is supportive of the incorporation of PED into the regulatory decision-making process, important considerations must be made.

Outlining a clear research question to be answered that is important to patients, health care providers, and regulators is critical to directing appropriate PED collection. Relevant and valid questionnaires must be used, and, in the event the data will be included in statistical testing, the endpoint being assessed must not only be valid but also relevant. Requiring the collection of PED unrelated to meaningful research questions results in wasted resources and places an unnecessary burden on patients, particularly cancer patients who are often enrolled in clinical trials for an extended period of time. In addition to validity and relevance, PED must be appropriately applied in regulatory decision-making. A clear path for its utility in the FDA's medical product safety and efficacy assessments must be delineated.

LUNGEvity suggests that further efforts must be made to operationalize both the collection and assessment of PED before mandating its inclusion in marketing applications and its consideration by the FDA in regulatory decision-making, as provided by Sec. 204. Methods for the collection of valid and relevant PED must be further standardized, and the utility and assessment of such data by the FDA in its decision-making processes must become more fully evolved.

Furthermore, rather than awarding grants for novel trial designs incorporating PED, as provided in **Sec. 302, we encourage the awarding of grants for the development and validation of relevant clinical outcome assessment (COA) questionnaires/tools where there are gaps, as well as development and validation of COA-related endpoints.** Optimizing COA measures will improve the utility of PED in marketing applications with the FDA to aid the Agency in regulatory decision-making.

Real-World Evidence

Real-world evidence (RWE) provides important information regarding the safety and efficacy of medical products outside of the traditional randomized controlled trial (RCT), and LUNGEvity looks forward to RWE reaching its optimal utility in supporting regulatory decision-making. Some real-world studies examining large cohorts of patients through national cancer registries have demonstrated trends in patient outcomes similar to those seen in corresponding RCTs. However, a systematic assessment of real-world data (RWD) studies for cancer drugs approved by the FDA and European Medicines Agency (EMA) over the course of five years revealed that only two percent of the reviewed studies used data from national cancer registries, which tend to represent larger cohorts and more heterogeneous samples. The same systematic study revealed that 80 percent of the real-world studies exhibited poor methodological quality. These lower quality studies were more likely to demonstrate better survival outcomes compared to clinical trial data.^{iv} Low quality real-world studies therefore may overstate the benefits of new cancer therapies.



The methodologies used to conduct real-world studies must be improved and made more transparent and consistent. The FDA just published two draft guidance documents in September and October 2021 on assessing the use of electronic health care data in regulatory decision-making, and data standards for real-world data-containing submissions, respectively.^{v.vi} Further guidance documents on the use of RWE are forthcoming, including one on the appropriate use of registry data. The agency is also planning a pilot program to assist drug developers in identifying types of RWE that could be utilized to support approval, while also developing internal methods to improve consistency in RWE decision-making. The program will likely be implemented by the end of 2022, as part of the forthcoming reauthorization of the Prescription Drug User Fee Act (PDUFA).^{vii}

LUNGEvity is hopeful that RWE can be reliably incorporated into regulatory decision-making in the near future, which could substantially shift the burden off of patients in evaluating medical product safety and efficacy. However, the use of RWE in drug development and regulatory decision-making should be implemented carefully, as the regulatory science around its utilization continues to develop and RWE applications require further standardization. LUNGEvity supports **Sec. 302**, which prioritizes the incorporation of RWE in drug development among applicants for grants awarded for novel trial designs, and **Sec. 309**, which would provide for the acceptance of RWE to support confirmation of clinical benefit of a medical product under accelerated approval. **However, we recommend waiting to implement these provisions until such time that the FDA has sufficiently collected and considered community feedback on its new and forthcoming RWE guidance documents. Furthermore, we suggest awarding grants for studies aimed at standardizing the conduct of RWD studies and the use of RWE in regulatory decision-making.**

FDA-CMS Communication

Breakthrough therapy drugs provide transformative solutions for patients with limited treatment options, including patients with lung cancer. The breakthrough therapy sotorasib, for example, was approved by the FDA in June 2021 for the treatment of adults with non-small cell lung cancer harboring a specific mutation in the KRAS gene, which for decades had been considered an “undruggable” target.^{viii} Breakthrough therapies have the potential to drastically improve patient outcomes, and barriers to coverage for these therapies must be minimized to ensure appropriate patient access. We support **Sec. 305** of the draft legislation establishing a system of communication between the FDA and the Centers for Medicare and Medicaid Services (CMS), regarding approval and coverage decisions for a therapy once it receives breakthrough designation. As breakthrough devices are also critical for the diagnosis or treatment of patients with life-threatening diseases, **we also encourage the establishment of a communication system between FDA and CMS upon breakthrough designation of medical devices.**

Telehealth

Disruptions in care for patients with cancer, even for short amounts of time, can have significant impacts on patient outcomes. The COVID-19 public health emergency necessitated a dramatic uptake of virtual methods of healthcare delivery in oncology. National Cancer Institute (NCI)-designated cancer centers across the country reported significant increases in utilization of telehealth services over the course of the COVID-19 pandemic, and telehealth has become a vital tool in facilitating continuity of care and improving outcomes for patients with cancer.^{ix} Postoperative telehealth visits were recently shown to prevent emergency room visits and readmissions for patients undergoing thoracic surgery, with a high degree of patient satisfaction.^x



The pandemic also forced a shift toward more decentralized methods of clinical trial conduct, allowing participants to engage in remote monitoring for safety and clinical outcome assessments. Telehealth has been vital in expanding access to trial participation for remote participants and fostering a shift toward a more patient-centric paradigm of clinical trial conduct.^{xi}

It is critical that patients with cancer have continued access to telehealth services beyond the COVID-19 public health emergency. LUNGEvity supports **Sec. 403** of the draft legislation, which would extend access to telehealth services regardless of geographic location, expand the types of healthcare providers eligible to furnish telehealth services, and broaden the list of telehealth services eligible for coverage for Medicare beneficiaries. We also support the provisions outlined in **Sec. 402** geared toward better understanding the impacts of telehealth utilization on healthcare access, health outcomes, etc., and facilitating the integration of telehealth services into states' Medicaid programs.

A critical barrier to telehealth access not addressed in the draft legislation is the requirement for healthcare providers furnishing such services to be licensed in the state in which a patient is cared for. State licensure laws are particularly burdensome to patients with many types of cancer, including lung cancer, for which the number of specialists across the United States is limited. These patients face hurdles in consulting experts for remote second opinions (RSOs) critical to the development of effective treatment plans. Licensure requirements also pose hurdles to participation in decentralized clinical trials.^{xii}

In response to the COVID-19 pandemic, individual states instituted policies waiving certain licensure requirements and facilitating access to telehealth across state lines. However, these flexibilities have either expired or are set to expire by the official end of the COVID-19 public health emergency. Many patients who have received remote care via telehealth during the height of the COVID-19 pandemic are now having to travel extensive distances to continue seeing their specialists and/or participating in clinical trials.

To furnish services via telehealth to out-of-state patients, healthcare providers may be licensed in the states wherein their patients receive care. However, the interstate licensure process is laborious and may hinder eligible candidates from applying. The Interstate Medical Licensure Compact (IMLC) was developed by the Federation for State Medical Boards to streamline the interstate licensure process for providers in states that opt into it via enactment of legislation. However, not all states have joined IMLC.^{xiii}

LUNGEvity encourages the development of provisions that would ease interstate licensure requirements regarding care administered via telehealth across state lines. Such provisions may include providing incentives for states to join the IMLC and/or to adopt special registration procedures to more easily allow out-of-state providers to furnish care via telehealth. Prospective provisions may also include exemptions from licensure requirements under certain circumstances like RSOs and remote care for clinical trial participants.

Genomic Precision Medicine Consultations

We are pleased to see **Sec. 408** of the discussion draft mandating Medicare coverage for genomic precision medicine consultations. Genomic testing, which in cancer refers to the use of sequencing technology to identify acquired genetic mutations responsible for driving tumor growth, is a critical tool for improving outcomes for patients with lung cancer through precision medicine. However, it is unclear whether the term “genetic or genomic test” within the bill’s definition of “precision genomic medicine consultations” in this section truly includes genomic testing as described above, particularly in the context



of the language used throughout other parts of the bill. The language in **Sec. 407** appears to treat the terms “genetic and genomic testing services” and “DNA sequencing clinical services,” the latter apparently referring to specifically genetic testing for inherited rather than acquired mutations, as interchangeable.

LUNGevity founded and led the Consistent Testing Terminology Working Group, which is composed of over forty patient advocacy organizations, professional societies, diagnostics companies, testing laboratories, and other stakeholders committed to promoting clear and consistent use of common terms for biomarker and germline genetic testing.^{xiv} Genetic testing refers to the use of sequencing technology to identify germline mutations responsible for inherited risk for disease, whereas genomic testing refers to the use of sequencing technology to identify acquired mutations in diseases including cancer, and serves as a form of biomarker testing.

LUNGevity recommends that the sponsors clearly define the testing terminology used in the bill.

The term “genetic testing” should have a clear definition that indicates its application in identifying inherited mutations in patients for the purposes of either determining the risk of disease development, or the cause of disease in those already diagnosed. Regarding “genomic testing,” we recommend the inclusion of a broader term to also include testing for non-genomic biomarkers, which is also important in guiding a patient’s treatment. For example, testing for the presence of protein biomarkers involved in cancer immune evasion is critical to predict a patient’s response to immunotherapy. For this reason, LUNGevity urges the authors to adopt the term “biomarker testing,” as opposed to “genomic testing,” which is more inclusive of all biomarkers and serves as an evergreen term capable of adapting to new scientific developments and diagnostic advancements.

The interpretation of genetic or genomic tests requires specialized training and may be performed by medical professionals including those with either a medical degree (MD), such as a pathologist, or a scientific degree (PhD). However, PhD scientists are not directly reimbursed by Medicare for interpretive services provided for beneficiaries. **We recommend that the sponsors engage with the appropriate stakeholders to draft language allowing qualified doctoral scientists the ability to bill Medicare directly for their work in performing and interpreting test results.** Doing so would further facilitate the practice of precision medicine among the Medicare population.

ARPA-H

Decades of basic discoveries serve as the foundation for today’s medical advances that improve outcomes for patients with cancer. By supporting high-risk, high-reward research projects, the proposed Advanced Research Projects Agency for Health (ARPA-H) would hasten the discovery of transformative approaches to how diseases like cancer are diagnosed, treated, and prevented. However, it is important that funding for ARPA-H not reduce appropriations for the National Institutes of Health (NIH) or the National Cancer Institute (NCI), which have received sustained funding increases over the past decade. While LUNGevity supports the proposed establishment of ARPA-H in **Sec. 501**, **we encourage the development of ARPA-H priorities distinct from those of NIH’s centers and institutes to avoid reductions in NIH/NCI funding and duplication of efforts.**



In closing, LUNGevity is, by-and-large, supportive of the Cures 2.0 discussion draft, and we appreciate the opportunity to provide comments as well as the sponsors' consideration of the feedback we have provided. This draft legislation builds on the important work initiated through the 21st Century Cures Act by improving access to life-saving treatments for patients. We would like to offer ourselves as a resource to represent the patient perspective as this legislative draft moves forward. Please feel free to reach me at aeferris@lungevity.org or at 240-454-3103, or you may contact Kristen Santiago, Senior Director of Public Policy Initiatives at ksantiago@lungevity.org or 240-454-3105.

Sincerely,

Andrea Stern Ferris
President and Chief Executive Officer
LUNGevity Foundation

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ⁱⁱ Centers for Disease Control and Prevention. United States Cancer Statistics. Available at <https://gis.cdc.gov/Cancer/USCS/#/Prevalence/>.

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^{vii} U.S. Food and Drug Administration. PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 through 2027. 2021 Aug; Available at www.fda.gov/media/151712/download.

^{viii} U.S. Food and Drug Administration. FDA Grants Accelerated Approval to Sotorasib for KRAS G12C Mutated NSCLC. 2021 May 28; Available at <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-sotorasib-kras-g12c-mutated-nsclc>.

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^x Tham E, Nandra K, Whang SE, et al. Postoperative telehealth visits reduce emergency department visits and 30-day readmissions in elective thoracic surgery patients. *Journal for Healthcare Quality* 2021; 43(4):204-213.

^{xi} Flaherty KT, Doroshow JH, Galbraith S, et al. Rethinking cancer clinical trial conduct induced by COVID-19: An academic center, industry, government, and regulatory agency perspective. *Cancer Discovery* 2021; 11(8):1881-1885.

^{xii} Faget KY. The role of telehealth in decentralized clinical trials. *Journal of Health Care Compliance* 2021; 23(2):11-14, 43-44.

^{xiii} Adashi EY, Cohen IG, McCormick WL. The Interstate Medical Licensure Compact: Attending to the Underserved. *JAMA* 2021; 325(16):1607-1608.

^{xiv} Martin NA, Tepper JE, Giri VN, et al. Adopting Consensus Terms for Testing in Precision Medicine. *JCO Precision Oncology* 2021; 5:1563-1567.