



August 23, 2020

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Reauthorization of the Prescription Drug User Fee Act (Docket No. FDA-2010-N-0128)

Dear Sir or Madam:

On behalf of LUNGevity Foundation, the nation's preeminent lung cancer nonprofit that funds research, provides education and support, and builds communities for the approximately 230,000 Americans diagnosed with lung cancer each year and the 538,243 Americans living with the disease,¹ we appreciate the opportunity to submit comments on the reauthorization of the Prescription Drug User Fee Act (PDUFA) (Docket No. FDA-2010-N-0128). As the leading patient advocacy group representing the voice and interest of the national lung cancer survivor community we are well positioned to provide input from the perspective of those most impacted by the drug development and approval process: patients, survivors, and caregivers.

LUNGevity applauds the U.S. Food and Drug Administration (FDA) for the strides it has made under PDUFA V and VI to incorporate the patient voice into the drug development process and we look forward to working with the agency and sponsors to build on that progress through PDUFA VII. The best way to ensure that drug development is truly patient focused is by including and consulting patients and survivors throughout the entire process. To that end, we would like to see the following priorities included in the upcoming PDUFA reauthorization.

Enhance current efforts to make clinical trials more inclusive.

Increases in our understanding of the underlying biology of disease combined with new therapeutic modalities have ushered in an age of precision medicine. Patients suffering from what were long considered incurable diseases are now living longer, healthier lives. Unfortunately, these advances have not benefitted everyone equally. In lung cancer, where clinical trials are more often considered means of accessing the next treatment than an effort of last resort, there are often significant barriers to participation. For lung cancer and many other diseases, these barriers have contributed to the current undesirable situation in which the clinical trial population differs considerably from real-world patients and limits the generalizability of trial results. In order to ameliorate this situation, steps must be taken to ensure that patients who receive investigational drugs through clinical trials resemble end users in terms of race/ethnicity, age, and biological and socioeconomic characteristics. LUNGevity advocates the following steps:

- 1. Modernize eligibility requirements.** The FDA recently finalized guidance documents regarding the expansion of eligibility criteria for cancer clinical trials. Specifically, sponsors of cancer clinical trials should consider strategies for including patients with: brain metastases; kidney, liver, or heart dysfunction; prior or concurrent malignancies; and/or hepatitis or HIV. Additionally, a working group of the LUNGevity Scientific and Clinical Research Roundtable identified 14 eligibility criteria that *might* not be necessary in every lung cancer trial. The working group concluded that trial developers (sponsors) should give serious thought to which eligibility criteria will meet the needs of each individual trial based on the pharmacokinetics, pharmacodynamics, and expected adverse events of the molecule/compound under investigation, and also be mindful that the elimination of some commonly used criteria might have minimal effect on patient safety and would expand opportunities for trial participation.² The approach employed by the expert working group to identify and justify the 14 criteria could easily be adapted for other cancers and diseases. The FDA and sponsors should work together with the advocacy community to work towards implementation of these and other recommendations that will expand the eligible clinical trial participant pool.
- 2. Ensure diversity and representativeness in clinical trial populations.** Disparities and inequalities in clinical research are well documented and represent a real problem for sponsors in terms of establishing the generalizability of clinical trial results. In cancer clinical trials, for example, racial and ethnic minority groups have low rates of inclusion relative to the representation of the burden of disease in the U.S. population. Increasing clinical trial diversity has been a priority of the FDA for years, although it is limited in what it can require of sponsors in terms of including specific demographic subgroups. Many sponsors have now instituted diversity and inclusion programs to increase enrollment and accrual of racial and ethnic minorities to their trials. In addition, having an institutional presence in the community has emerged as a fundamental requirement for increasing visibility and developing trustful relationships with potential research partners. Cancer Centers of Excellence have noted the need to invest time and effort with key community representatives to learn about the community, its needs, and potential facilitators and barriers to research participation before approaching communities about research.^{3,4} The insights gained help research partners to deliver impactful and logistically sensitive research that meets the needs of the community along with the justification to add capacity. Similar to the National Cancer Institute, which requires principal investigators to provide plans for the recruitment and retention of minority populations in all clinical trials it funds, the FDA could require that sponsors develop, report, and execute recruitment plans that include community engagement at sites in high risk geographies. LUNGevity supports these efforts and hopes they will extend to all medically underserved populations, including older patients, those in rural areas, and those with low socioeconomic status, with the ultimate goal of clinical trial populations being representative of the disease under investigation.

- 3. Increase utilization of decentralized clinical trials and their components.** Clinical trial-associated travel was one of the primary burdens of trial participation identified in a LUNGevity study of lung cancer patients and caregivers.⁵ Having to complete the informed consent process in-person and travel for routine bloodwork, laboratory tests, and follow-up visits were all noted as areas in which virtual and/or local alternatives could suffice without sacrificing patient safety. “Experiments” with decentralized clinical trials due to the COVID-19 pandemic will provide insights to instruct future trial design. Effects on trial participation, patient safety, and trial completion of allowances by the FDA for clinical trial protocol modifications including home delivery of trial drugs, use of virtual visits and/or local labs for safety assessments, alternative drug doses/schedules, and alternative study visit schedules should be studied post-COVID. Based on the results, the FDA should prepare guidance on modifications that can be made permanent.

Continue to explore ways to incorporate the use of real-world data in the drug development process.

As the FDA and sponsors continue to explore the opportunities and challenges associated with the use of real-world data (RWD) and real-world evidence (RWE) for regulatory purposes, LUNGevity requests that special attention be paid to the collection and use of patient experience data from digital sources to complement and round out data collected in clinical trials. Online forums and platforms are being increasingly used by patients not only to develop communities but also share their experience as they go through their disease journey. At LUNGevity Foundation, we have a very active social media community and currently moderate 14 lung cancer-specific Facebook groups. Members of these groups candidly share their experience on clinical trials, their current medications and associated quality-of-life issues, and side effect management. This suggests that online platforms can be valuable sources for capturing exploratory and hypothesis-generating data. Failure to use such data, which can be extremely informative in understanding the true patient journey, would be a missed opportunity especially for patients who do not participate in formal research studies. We encourage the Agency to provide a clear categorization of purpose of patient- and community-level experience data and the level of rigor required for them. In our opinion, patient- and community-level data that are not meant to accompany an investigational new drug submission may be collected through informal platforms as long as the objectives of the data gathering are clearly stated. We also see this as an opportunity for the FDA to provide guidance on data benchmarks required for RWE and RWD, online platforms being one source of RWD, since these terms are often used interchangeably but have different levels of rigor in terms of data collection and quality.

We also reiterate the Personalized Medicine Coalition’s request for the FDA to share learnings from real-world data submissions. One approach that has been helpful is the presentation of use cases, where the submitting party lays out their rationale and methods for using RWD and



review staff from the FDA walk through the pros and cons of the submission and their thought process in either approving or rejecting it. Such insights are informative for all stakeholders and will improve the quality and utility of future real-world data submissions.

Ensure adequate resources for FDA staffing needs.

Previous PDUFA agreements as well as the 21st Century Cures Act have worked to provide increases and flexibility in resources for the FDA to recruit and retain qualified, well-trained staff. Continuing this trend through PDUFA VII is imperative with the increased demands being placed on staff related to COVID-19 reviews, the increasing complexity of clinical trial designs, and the expected surge of gene and cell-based therapies in the next few years.

LUNGEvity is thankful for the opportunity to submit the above comments on the reauthorization of the Prescription Drug User Fee Act (Docket No. FDA-2010-N-0128). The comments outlined above can be discussed with me, my staff, and LUNGEvity's Scientific Advisory Board, which is made up of some of the world's leading experts in lung cancer biology, practice management, access to innovative medicines, and overall patient care. I can be reached at 240-454-3100 or aeferris@lungevity.org if you have any questions or would like to engage in further dialogue.

Sincerely,

A handwritten signature in black ink, appearing to read "Andrea Stern Ferris".

Andrea Stern Ferris
President and Chief Executive Officer
LUNGEvity Foundation

ABOUT LUNGEVITY:

LUNGEvity's mission is to improve outcomes for people diagnosed with lung cancer. Our goals are three-fold: (1) to accelerate research to patients that is meaningful to them; (2) to empower patients to be active participants in their care and care decisions; and (3) to help remove barriers to access to high quality care. We have the largest lung cancer survivor network in the country and actively engage with them to identify, understand, and address unmet patient needs. We also have a world class Scientific Advisory Board that guides the programs and initiatives of the organization. Additionally, we collaborate with other lung cancer patient advocacy groups and organizations, such as the American Lung Association and CHEST, who serve the lung cancer community.



REFERENCES:

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2. Forde PM, Bonomi P, Shaw A, et al. Expanding Access to Lung Cancer Clinical Trials by Reducing the Use of Restrictive Exclusion Criteria: Perspectives of Multistakeholder Working Group. *Clinical Lung Cancer* 2020; 21:P295-307. <https://doi.org/10.1016/j.clc.2020.02.008>
3. Regnante JM, Richie NA, Fashoyin-Aje L, et al. US Cancer Centers of Excellence Strategies for Increased Inclusion of Racial and Ethnic Minorities in Clinical Trials. *Journal of Oncology Practice* 2020;15:e289-299. <https://doi.org/10.1200/JOP.18.00638>
4. Regnante JM, Richie NA, Fashoyin-Aje, et al. Operational Strategies in US Cancer Centers of Excellence that Support the Successful Accrual of Racial and Ethnic Minorities in Clinical Trials. *Contemporary Clinical Trials Communications* 2020;17:100532. <https://doi.org/10.1016/j.conctc.2020.100532>
5. LUNGevity Barriers to Clinical Trial Participation *as perceived by Lung cancer patients and caregivers*. Available at https://lungevity.org/sites/default/files/file-uploads/Barriers-to-Clinical-Trial-Participation-Study_0.pdf