July 1, 2023

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

Submitted electronically via http://www.regulations.gov

Dear Sir or Madam:

On behalf of 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 year[1] and the more than 400,000 Americans living with the disease[2], we appreciate the opportunity to submit comments on the draft guidance "Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints For Regulatory Decision-Making" (Docket No. FDA-2023-D-0026).

LUNGevity thanks the Food and Drug Administration (FDA) for its leadership in the area of patient-focused drug development (PFDD). For over a decade, FDA's PFDD initiative has worked to elevate the importance of the patient voice and experience in the drug development and approval process[3]. As one of the first diseases featured in a PFDD public meeting, in 2013, the lung cancer community has a long history working with FDA to characterize how patients feel, function, and survive while on treatment for the disease[4]. The PFDD guidance series, of which this draft guidance is the fourth and final installment, provides a road map for stakeholders regarding the collection and use of patient experience data for regulatory decision-making. LUNGevity is grateful for the thought and effort FDA has put into this series which we believe benefits the patient community; our comments on this fourth guidance are intended to highlight areas where we do not see added patient value and gaps to help sponsors navigate the comprehensive recommendations from the Agency.

Over the past decade, patient experience data in anti-cancer drug trials have started shifting from being used almost exclusively as exploratory endpoints to informing a few secondary endpoints that are included in the statistical hierarchy. As such, the rigor with which these data are collected has improved (i.e., PRO completion rates have improved, there was high quality data available to generate the FDA OCEs pilot Project Patient Voice) and this has translated into more interpretable results for clinicians and patients[5]. This trend has been, in our view, critical for the patient community. However, we are

[1] National Cancer Institute Surveillance, Epidemiology, and End Results Program, Cancer Stat Facts: Lung and Bronchus Cancer. https://seer.cancer.gov/statfacts/html.lungb.html. Accessed 9/26/2022.
[2] Centers for Disease Control and Prevention. United States Cancer Statistics. https://gis.cdc.gov/Cancer/USCS/#/NationalPrevalence/. Accessed 9/26/2022.
[3] Chalasani, M, Vaidya, P, & Mullin, T. Enhancing the incorporation of the patient's voice in drug development and evaluation. *Res Involv Engagem* **4**, 10 (2018). https://doi.org/10.1186/s40900-018-0093-3
[4] Fda.gov/Agenda for PFDD on Lung Cancer.pdf. Accessed 6/28/2023.
[5] Mercieca-Bebber R et al. The importance of patient-reported outcomes in clinical trials and strategies for future optimization. *Patient Relat Outcome Meas* **9,** 353-367 (2018). doi: 10.2147/PROM.S156279.

concerned that some of the language and recommendations in the draft guidance may temper sponsors' enthusiasm for continued inclusion of patient experience data in their trials' statistical hierarchies.

Specifically, LUNGevity is concerned that the addition of new terminology (i.e., meaningful score difference and region, page 20 line 776 and page 25 line 967, respectively) could sew confusion in a crowded field rather than provide clarity. Entering "minimal clinically important difference" into PubMed yields 3,331 results, while "minimal important difference" produces 572 results, and "minimally important change" another 107. All are commonly used to describe the concept referred to as *meaningful score difference* in the draft guidance and illustrate that there is already limited agreement around terminology in the field of measurement science. Unless there is uniform adoption of FDA's proposed language by **all** stakeholders, clinicians reading patient experience endpoints will likely encounter different terminology in industry-sponsored versus cooperative group trial results and may simply disregard those important data and not share them with their patients. We recommend that FDA encourage sponsors to explicitly describe their methods for assessing these important differences (e.g., between or within patient difference) in the study protocols, statistical analysis plans, and later trial publications so that readers can determine how the threshold/range was arrived at rather than adding to the lexicon in this space.

Additionally, the FDA acknowledges the reality that secondary endpoints may be "…relatively less critical, but still important, to patients and caregivers" (page 10 lines 349-352). LUNGevity agrees that these endpoints are relevant to patients and their families and would like to see this point discussed more explicitly. As written, it is unclear what the implications for work necessary to comply with the guidance may be for endpoints that are considered "less critical" by the FDA. Our concern is that for anti-cancer drug clinical trials, where patient experience data has not been used as the sole primary endpoint, this lack of clarity around when all the considerations outlined in the guidance are necessary may lead to patient experience data being relegated to exploratory endpoints once again if sponsors decide the net benefit of developing, evaluating, and implementing clinical outcome assessment-based endpoints is not worth the effort. Conversely, sponsors may feel the need to carry out all the outlined steps even for legacy measures being used for secondary endpoints, which will elevate patient burden (e.g., participation in extra stand-alone studies to determine the meaningful score range). This may be appropriate when endpoint results are critical for marketing authorization decision-making but may not be necessary for endpoints lower on the statistical hierarchy.

Thank you again for your dedication to pushing the drug development ecosystem to be more inclusive of the patient's voice. Please feel free to reach out to me at 240-454-3100 or aeferris@lungevity.org if you have any questions or would like to engage me or my staff in further dialogue.

Sincerely,

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 and Health Equity Council that guide the programs and initiatives of the organization.