February 28, 2022

Dockets Management Staff
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Dear Sir or Madam:

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 year[i] and the more than 600,000 Americans living with the disease,[ii] we appreciate the opportunity to submit comments on the draft guidance "Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products" (Docket No. FDA-2021-D-1146). Our mission is to improve lung cancer survivorship and quality of life for patients living with the disease, and it is with those patients in mind that we submit the following comments.

LUNGevity thanks the U.S. Food and Drug Administration (FDA) for drafting the entire set of real-world data (RWD)-related guidance documents as part of its Real-World Evidence (RWE) Program. We applaud data-driven efforts like FDA's RWE Program that aim to increase and speed access to safe, effective treatments for a broader range of patients.

LUNGevity is particularly interested in the potential of RWD sources to support external control arms for interventional clinical trials, recognizing the particular opportunities for this use in lung cancer drug development. As one of the most common types of cancer, the natural history of lung cancer is well established.[iii] Many subtypes of lung cancer are rare, affecting fewer than 200,000 people in the United States, including small cell lung cancer (SCLC) and certain non-small cell lung cancer (NSCLC) subtypes.[iv] Some, but not all, lung cancer subtypes harbor specific driver mutations for which effective targeted therapies have been developed. However, tumors frequently develop resistance to these treatments and patients whose disease progresses after treatment often have limited therapeutic alternatives. Further development of precision medicine for these patients is hindered by small numbers of eligible participants for enrollment in randomized, controlled clinical trials. Furthermore, as additional driver mutations are discovered and corresponding targeted therapies are developed, the pools of available clinical trial participants will continue to shrink.

While the draft guidance provides general considerations for using registry data as a potential source of RWE to support regulatory decisions, additional details would be helpful. For example, the draft guidance outlines high-level considerations for assessing whether a registry is fit for use, including whether the data are of sufficient quality to support the intended use. According to the guidance, "the minimum set of data elements in a registry may need to be more comprehensive if the sponsor intends to use the registry data for an external control arm in an

externally controlled trial, compared to if the sponsor intends to use the registry to enroll participants in an interventional study." More clarity on the data elements required to support various intended uses of registry data—particularly external control arms—would be appreciated. Explicit differentiation of requirements for prospective versus retrospective controls would also be helpful.

The draft guidance also highlights but does not provide sufficient detail on the role of data accrual in assessing the reliability of registry data. The acceptability of different data accrual methods (e.g., clinician-reported, patient-reported, sourced from electronic health records, etc.) may change depending on the intended use of the data. Further details on the relationship between the methods of data accrual of a registry and its utility for specific uses are warranted.

Clarifying the points outlined above would benefit stakeholders designing and developing registries with the intent that they will support regulatory decision-making. For example, LUNGevity has developed a registry that meets criteria for ensuring data relevance and reliability outlined in the draft guidance, including conformance with 21 CFR part 11 and application of defined processes and procedures for data collection and management.[v] However, given that the data are patient-reported (and not verified), and do not include precise treatment history and start/end dates, our registry would likely not be fit for use to support an external control arm or natural history study. Further defining the requirements around registry data utility for various purposes is necessary to avoid confusion and wasting of resources.

In addition to providing more detail around data elements and accrual, LUNGevity recommends the inclusion of worked examples applicable across disease types to illustrate how stakeholders can design new registries or use existing ones for specific purposes. For example, the final guidance should detail the specific characteristics, including necessary data elements, data sources, data linkage plans, etc. of registries that either have been or could be used to support an externally-controlled interventional trial. Most published examples of the successful use of RWE in regulatory decision-making involve a dramatic improvement in outcomes for patients in the experimental arm. Such cases demonstrate substantial evidence of effectiveness of the medical product under study and/or address an unmet medical need. Providing examples of FDA approvals supported by registry data in which neither a dramatic effect was observed nor was an unmet medical need addressed would be helpful to advance the appropriate use of such data in support of regulatory decision-making.

LUNGevity thanks the FDA for the thoughtfulness that went into drafting "Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products." By outlining important considerations around the use of registries as a source of RWD, the FDA has taken an important step toward improving access to safe and effective treatments for a broader range of patients.

LUNGevity looks forward to RWD and RWE reaching their optimal utility in supporting regulatory decision-making to advance the understanding of medical product safety and effectiveness in more real-world patient populations. We support the draft guidance in addition

to the FDA's other ongoing efforts to optimize the quality and advance the application of RWD/RWE in ways that will ultimately benefit patients.

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.

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[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/.
[iii] Popper HH. Progression and Metastasis of Lung Cancer. *Cancer Metastasis Reviews* 2016; 35:75-91.
[iv] LUNGevity Foundation. Types of Lung Cancer. Available at https://www.lungevity.org/for-patients-caregivers/lung-cancer-101/types-of-lung-cancer.
[v] LUNGevity Foundation. Project Peer. Available at https://www.lungevity.org/research/patient-focused-research-center-patient-force/patient-preferences-and-patient-experience-5.