August 9, 2021

Janet Woodcock, MD
Acting Commissioner
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Via Electronic Submission: https://www.regulations.gov

Re: Docket No. FDA-2020-D-2303, "Core Patient-Reported Outcomes in Cancer Clinical Trials.; Draft Guidance for Industry; Availability."

Dear Acting Commissioner Woodcock,

The Cancer Support Community (CSC), an international nonprofit organization that provides support, education, and hope to cancer patients, survivors, and their loved ones, applauds the Food and Drug Administration's continuing efforts to incorporate the patient and caregiver voice in the drug development process. As the largest provider of social and emotional support services for people impacted by cancer, CSC has a unique understanding of the cancer patient experience. In addition to our direct services, our Research and Training Institute and Cancer Policy Institute are industry leaders in advancing the evidence base and promoting patient-centered public policies. We appreciate the opportunity to comment on the draft guidance entitled "Core Patient-Reported Outcomes in Cancer Clinical Trials" which will provide sponsors with recommendations on the collection of a core set of patient-reported clinical outcomes in cancer.

Background

Passage of 21st Century Cures in 2016 and the Food and Drug Administration Reauthorization Act (FDARA) in 2017 heightened the importance of collecting patient experience data (PED). PED includes not only the physical impacts of a condition, therapy, or clinical investigation/trial but also the psychosocial impacts. The FDA's leadership in providing guidance to sponsors on the collection of patient-reported outcome (PRO) measures will help achieve the goals of 21st Century Cures and FDARA. A PRO is a type of clinical outcome assessment based on a report that comes directly from the patient about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else (FDA, 2021). Recognizing that PROs represent only one form of PED, we appreciate and agree with the FDA that some of the recommendations in this draft guidance may be relevant to other clinical outcome assessments (i.e., clinician-reported outcome, observer-reported outcome, performance outcome) that make up PED.

Need for Consistency in Collection

The FDA currently requires clinical trial sponsors to report what (if any) patient experience data were collected during the trial. To date, there has not been clear and uniform guidance on how patient experience data could and should be captured and communicated to patients and providers to benefit

the shared decision-making process. Congress' well-established and strong support for inclusion of PED in clinical trials per 21st Century Cures and FDARA empowers the FDA to take steps to standardize and formalize the methodology of collecting and using PED. We cannot make progress until stakeholders—regulators, insurers, industry, clinicians, and patients—have the clarity needed, and the data are being collected, reported on, and made available to the public in a meaningful manner. This guidance may help provide that clarity with regard to PROs and serve as a model toward achieving consistency in not only the collection, but also the reporting of all PED.

Breadth of Patient Experience Data Addressed in the Draft Guidance

Meaningful PED, including but not limited to PROs, not only provide sponsors with a better understanding of patient needs and concerns related to their experiences while receiving the drug during the development process, but also give patients and providers important data and learnings as they determine treatment pathways that best meet a patient's unique needs. Understanding a patient's social and emotional well-being is so fundamental to care that it is a required patient-centered standard in the accreditation process for the American College of Surgeons' Commission on Cancer. Further, in oncology, the Institute of Medicine concluded "it is not possible to deliver good quality cancer care without using existing approaches, tools, and resources to address patients' psychosocial health needs (Adler et al., 2008)." For manufacturers, tracking patient experience and offering interventions throughout the trial would provide vital information that could benefit patients and may also allow for more efficient trials by improving a patient's compliance and retention.

Trial sponsors increasingly recognize their responsibility to measure and record the full patient experience - both physical and psychosocial. In fact, a 2019 study found 48 of the 59 drug and biologics applications to the FDA in 2018, voluntarily included a table summarizing PED (Kieffer et al., 2019). Of note, seven of the 11 products that did not include a PED table were submitted before Section 3001 of the 21st Century Cures Law went into effect. Approximately 71% of the drugs approved by the FDA voluntarily reported using PED in the review, with patient-reported outcomes (PROs) the most significant source of PED. While PROs are important, it is critical that FDA help researchers fully understand and navigate the difference in, and importance of, collecting the full breadth of PED. This study revealed that other sources of patient experience data such as studies designed to gather patient input around disease or treatment burden, experiences during or after a clinical trial, patient preference, or other information gleaned from meetings with patient groups such as PFDD meetings and/or summary reports, are considered less frequently by the FDA in the context of drug application review. As such, we welcome the FDA's acknowledgement in this guidance that while a core PRO set can provide a minimum expectation for patient experience data across cancer settings, it may not include all important patient experience outcomes to measure in specific disease contexts.

Need to Expand Core PROs to Include Psychosocial Function and Cognitive Function

This draft guidance recommends collecting and analyzing the following core PROs to maximize the utility of the information collected:

- Disease-related symptoms
- Symptomatic adverse events
- Overall side effect impact summary measure
- Physical function

- Role function

It also provides that additional PROs important to patients, but outside of these the core concepts, could be prospectively specified and collected in clinical studies based on the context of a given clinical trial. CSC agrees that the core PROs listed above help incorporate the patient perspective and provide information critical to the development and approval of cancer therapies. We also support the flexibility of allowing for the prospective identification and collection of additional PROs dependent upon the clinical trial.

However, equally essential to maximizing the utility of cancer clinical trials as the five PROs currently enumerated in the draft guidance is the identification and collection of psychosocial function and cognitive function. The five listed PROs speak overwhelmingly to "physical" symptom burden (with the partial exception of role function discussed below), which does not fully illustrate cancer patients' experiences. The social and emotional impact of cancer is undeniable, leading to FDARA's expanded definition of PED to include both physical and psychosocial impacts of a disease or condition, or related therapy or clinical investigation. Nor are psychosocial and physical well-being mutually exclusive, as evidenced by psychosocial factors such as depression being predictive of recovery and health-status after surgery (Addario et al., 2019). Failing to recognize and include psychosocial function as a core PRO is contrary to both well-established scientific findings and practices (Adler et al., 2008; McNiff, 2009; CoC, 2012; Ganz & IOM, 2013), as well as the goals of 21st Century Cures and FDARA.

We commend the FDA for including role function in the current five core PROs and for specifically recognizing the importance of evaluating a treatment's impact on patients' ability to work and carry out daily activities. However, while the draft guidance provides that role function may also help inform other functional abilities such as *cognitive function*, we urge the FDA to include cognitive function, and psychosocial function, as additional core PROs. While not unrelated, the ability to physically work and carry out activities does not necessarily or satisfactorily measure a treatment's impact on a patient's cognitive or psychosocial ability to work or physically carry out activities as desired or required to remain employed or fully care for one's family.

Offering Free Text in PROs

Notwithstanding the development of meaningful core PROs and the flexibility to prospectively specify and collect additional PROs, CSC appreciates and supports the consideration for sponsors to include a free text option in PROs as mentioned in connection with the symptomatic adverse events core PRO with one important caveat – we support the use of a free-text option in connection with each of the core PROs, as well as a free text option separate and apart from the core PRO categories. This will ensure that patients have the opportunity to share issues or major concerns that fail to be captured in the standardized process. Sponsors should incorporate strong qualitative data analysis in connection with use of free text options.

Including the Patient Voice in the Drafting of PROs

In addition to including *categories* of PROs that reflect patient priorities and preferences as well as maximize the utility of the information collected in the clinical trial, it is equally important to incorporate the patient voice at the outset to ensure that the language and references used in the questionnaires/forms are understandable, relatable, and culturally appropriate. Doing so will not only

help ease the patient burden in completing PROs, but also help facilitate wide geographical and cultural usefulness of standardized PROs, enabling broader comparison and application of research findings (Addario et al., 2019).

Incorporation of PROs and Broader PED in the Label

The identification and collection of core PROs (and broader PED) is only beneficial when such information is meaningfully communicated to patients and providers to better inform the shared decision-making process. Standardizing the identification and collection without simultaneously developing a consistent method of reporting that information will not maximize the utility of the data – thus severely limiting, if not defeating, the intended goal.

Conclusion

The Cancer Support Community appreciates the opportunity to share these comments and we look forward to working with the FDA, sponsors, and other stakeholders to ensure that clinical trials consistently identify, collect, and communicate the full breadth of patient experience data to better inform the drug development process as Congress intended. Should you have any questions or would like to discuss these comments in more detail, please reach out to Kim Czubaruk at kczubaruk@cancersupportcommunity.org.

Sincerely,

Kim Czubaruk, Esq.
Senior Director, Policy and Advocacy
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Cancer Support Community Headquarters

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