August 22, 2016

Robert M. Califf, MD, MACC
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Submitted electronically

RE: Prescription Drug User Fee Act; Public Meeting; Request for Comments
[FDA-2016-N-1895]

Dear Dr. Califf:

On behalf of the Cancer Support Community (CSC) and the patients we represent, we thank you for the opportunity to submit these comments to the United States Food and Drug Administration (FDA or Agency). We submit this letter in response to the Agency’s proposed recommendations for the reauthorization of the Prescription Drug User Fee Act (PDUFA) for Fiscal Years 2018 through 2022 as published in the Federal Register on July 19, 2016.

As the largest direct provider of social and emotional support services for people impacted by cancer, and the largest nonprofit employer of psychosocial oncology mental health professionals in the United States, CSC has a unique understanding of the cancer patient experience. Each year, CSC serves more than one million people affected by cancer through its network of 170 locations, telephone helpline, and a vibrant online community and delivers more than $40 million in free, personalized services each year to those impacted by cancer.

Additionally, CSC is home to the Research and Training Institute— the only entity of its kind — focusing solely on the cancer patient experience. The Research and Training Institute has contributed to the evidence base regarding the cancer patient experience through its Cancer Experience Registry®, publications and peer-reviewed studies on distress screening, the psychosocial impact of cancer and cancer survivorship, to name a few.¹ This combination of direct services and cutting edge research uniquely positions CSC to provide policymakers and regulators with feedback based on evidence as well as our views on the real world impact.

¹ To see more information, please visit: http://www.cancersupportcommunity.org/publications-presentations
CSC is pleased that the PDUFA VI commitment letter acknowledges the benefit and importance of patient input in drug development, clinical trial design, and the generation of real world evidence. CSC is also encouraged about plans to expand the patient engagement opportunities which were established in PDUFA V. In particular and in accordance with conversations we have had with FDA, CSC looks forward to advancing the current standard of patient feedback, which primarily consists of physical measures recorded as a part of the clinical trial. The reality is that real-time feedback should be collected throughout the clinical trial process and should include more than simply the physical burdens of disease (i.e. disease symptoms, treatment side effects, and functional status). In fact, the current clinical trial process and the patient reported outcome (PRO) structure should seamlessly incorporate psychosocial measures in the same way physical measures (i.e. blood pressure, hemoglobin, etc.) are measured, addressed and recorded. It is our view that such measures are relevant to FDA’s determination of the safety and efficacy of a drug product.

In today’s dynamic environment where the patient’s comprehensive burden of disease (i.e. physical, financial, and functional) continues to grow, the regulatory process must ensure that all elements of the experience are considered. The Belmont Report\(^2\), which is referenced in the World Health Organization Good Clinical Practices (WHO-GCPs) documents states, “[m]any kinds of possible harms and benefits need to be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.”\(^3\) In the modern research industry environment, the recommendations of the Belmont Report could be operationalized with significant relevance by simply measuring the impact of each arm of a clinical trial to a person’s work/home life. This one variable has been demonstrated to predict, with 92 percent probability, a person’s risk for a clinical diagnosis of depression.\(^4\) Other studies demonstrate the cost and health consequences associated with the failure to adequately screen for and treat depression and distress. Depression is associated with significantly higher annual health care utilization costs\(^5\) while distressed patients who participate in psychotherapeutic interventions have been shown to experience a decrease in hospitalization frequency, length of stay, number of physician office and emergency room visits.\(^6\) Furthermore, if a therapeutic regimen or

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diagnostic test demonstrated a statistically meaningful benefit or risk against this attribute, it would be a significant finding that should be included in FDA’s approved physician labeling and would be information relevant to patients, caregivers and clinicians.

CSC would like to comment specifically on the following sections of the PDUFA VI goals letter:

1) **Enhancing Use of Real World Evidence for Use in Regulatory Decision-Making** (pp 26-27)

In response to the provisions on enhancing the use of real world evidence for use in regulatory decision-making, CSC encourages FDA to consider using the data collected through validated tools to gather real feedback from patients in real time on measures that truly represent the patient experience and impact on quality of life. As FDA begins to plan the stakeholder meetings on real-world evidence we ask FDA to include psychosocial and behavioral health experts to ensure that data sources under consideration are actually capturing values that matter to patients and accurately reflect the true and comprehensive impact of an investigational drug product on an individual.

CSC encourages FDA to operationalize the commitment in the letter to pilot a study which captures psychosocial measures as a part of the clinical trial. Further, FDA should use the data from the pilot to establish a functional workflow which will allow industry and FDA to scale the process to all diagnostic and therapeutic trials over time. Ideally, such data points would be obtained during the conduct of all clinical trials and then included in FDA-approved drug labeling where appropriate.

CSC again extends its sincere commitment to collaborate with FDA to structure a pilot program and to assist in the development of draft guidance on how real-world evidence such as data derived from psychosocial measures can contribute to the assessment of risk/benefit scenarios in regulatory submissions.

2) **Enhancing Regulatory Decision Tools to Support Drug Development and Review** (pp 27-29)

CSC applauds FDA for strengthening and expanding staff capacity to facilitate development and use of patient-focused methods to inform drug development and regulatory decisions, and we are very pleased to see the psychometric expertise specifically mentioned; however, we encourage FDA to also include staff with expertise in clinical psychology. It is essential that individuals with knowledge of patient care are able to
provide input as to how data submitted will actually translate to clinical utility, and what data elements are important to and impact the patient experience.

When developing the sequential series of guidances to gather stakeholder feedback on approaches to collecting meaningful patient and caregiver input for use in regulatory decision-making and labeling, CSC asks that FDA honor the principles of the Belmont Report and the WHO-GCPs to expand the definition of PROs beyond the physical burdens of disease to include psychosocial measures. CSC would like to offer its expertise in the drafting of the proposed guidance documents to ensure that the proposed measures and datasets account for the psychosocial needs of patients.

As FDA creates the repository of publically available tools, CSC asks that FDA only include validated tools to maintain a high level of integrity for the repository and the science of patient-experience data.

3) Enhancing Capacity to Review Complex Innovative Designs (pp 31-33)

With the addition of new types of real world data, it is essential that FDA has the appropriately skilled staff to review the data. CSC encourages FDA to include staff with clinical psychology and behavioral research backgrounds to ensure that trials are designed to best capture the true patient experience, and that those trials use social and emotional measures such as the elements of distress screening captured through use of a validated tool. As part of the proposed voluntary program for innovative clinical trial designs, CSC requests FDA to use its existing regulatory authority to create incentives for sponsors to include psychosocial measures as a clinical measure in the clinical trial protocol as a novel trial design that will inform the dataset in a more comprehensive way and also improve the patient experience.

4) Advancing Postmarketing Drug Safety Evaluation Through Expansion of the Sentinel System and Integration into FDA Pharmacovigilance Activities (p 35)

When evaluating the Sentinel System’s data collection, CSC asks FDA to include psychosocial measures captured by validated tools, such as distress screening. CSC feels strongly that this will enhance the system’s ability to collect, analyze and report data that is meaningful to patients. CSC also asks FDA to include psychometric and clinical psychosocial and behavioral health researchers in the proposed public meeting, engaging stakeholders.

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5) **Improving FDA Hiring and Retention of Review Staff (pp 39-41)**

CSC strongly supports expanding FDA’s capacity to improve and modernize its hiring system infrastructure. As part of these much-needed updates, CSC asks that FDA address the lack of robust psychosocial expertise in its workforce, particularly among staff who will be involved in trial design and review of products.

In closing, CSC would like to thank FDA for acknowledging the value of patient input in drug development and scientific discovery. In addition to collecting data that are relevant to FDA and the research industry, collecting data that matters to patients, such as measures of distress and psychosocial wellbeing must become a standard in clinical studies, just as it is a standard for accreditation by the Commission on Cancer. CSC urges FDA to use its leadership and regulatory authority to make progress in this area by looking beyond traditional burdens of disease to include psychosocial measures. PDUFA VI provides the perfect opportunity to advance and improve upon the current standard of patient feedback by including psychosocial measures as part of the required dataset used in determining safety and efficacy of drug products.

Sincerely,

Linda House
President, Cancer Support Community

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