American Cancer Society
Cancer Action Network
555 11th Street, NW
Suite 300
Washington, DC 20004
202.661.5700
www.acscan.org

August 20, 2020

The Honorable Stephen M. Hahn, MD
Commissioner
Food and Drug Administration
Dockets Management Staff (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: FDA-2010-N-0128 for Reauthorization of the Prescription Drug User Fee Act; Public Meeting; Request for Comments

Dear Commissioner Hahn,

The American Cancer Society Cancer Action Network (ACS CAN) appreciates the opportunity to comment on our proposed priorities for the seventh Prescription Drug User Fee program (PDUFA VII). ACS CAN is the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, supporting evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem.

Our primary focus within the agreement is a drug development and approval process that is responsive to, and focused on, patient needs. Specifically, we are recommending 1) increased resources for the patient representative program; 2) the development of additional guidance promoting decentralized trials that remove barriers to patient participation in clinical research; and 3) development of the science and guidance informing evaluation of differential therapeutic outcomes for subgroups.

Patient Representative Program

Section 1137 of the Food and Drug Administration Safety and Innovation Act (FDASIA) codified a patient representative program at FDA, intended to provide patients a seat at the discussions being held between sponsors and FDA. These patient representatives are most frequently used as members of a formal advisory committee but can also be given divisional assignments to serve as advisors to reviewers on proprietary aspects of therapeutic development and review.

As special government employees (SGEs), patient representatives must submit to a conflict of interest (COI) review process to determine eligibility prior to taking part in sponsor-FDA meetings.

With a growing emphasis on the importance of patient-focused drug development, the Patient Representative Program remains a critical program at FDA. However, the Patient Representative Program is currently staffed by only one FTE. While the program continues to provide patients for advisory committees and some divisional assignments, there are concerns that its potential for growth - either in terms of the number of representatives utilized or the disease areas in which they are utilized – is limited. Growth would require internal outreach to collaborate with review divisions not currently using patient representatives and external outreach to patient organizations to recruit additional patients with relevant experience. Growing the program is critical for ensuring patient input and advice on proprietary aspects of FDA's regulatory responsibilities currently left without such patient expertise.

- We request additional staff resources for the Patient Representative Program to further increase the strength and reach of the program, recognizing that utilization of the program requires not only patient representatives, but also awareness and demand from review divisions.

- We further request regular reporting on the utilization of the Patient Representative Program and other programs soliciting patient engagement throughout the drug review divisions. Reporting should also capture efforts to ensure diverse and representative makeup of participating patients.

- We encourage consideration of additional engagement models for soliciting patient input that can inform review staff, yet not require product-specific information be shared. Such a model may reduce the conflict of interest burdens involved for engagement on product specific issues.

Decentralized Trials Guidance

While most cancer patients express a willingness to participate in clinical research, only a small fraction ultimately end up enrolling in a cancer clinical trial due to barriers that make participation difficult or even impossible. A recent meta-analysis showed that, on average, roughly one in four patients will be eligible for a trial offered at their institution, making local

trial availability by far the largest barrier, and pointing to the critical role that reducing location-based restrictions can have for patient access to cancer clinical trials.

During the current pandemic FDA allowed increased flexibility for practices and procedures that reduce travel for clinical trial participants. These flexibilities include using local providers for some care, delivery of drugs to a patient's home, and use of telemedicine. These flexibilities are slated to expire once the coronavirus public health emergency is over, yet the need will continue for clinical trial designs tailored to reducing participant burden. We suggest that the PDUFA VII agreement should include resources and provisions to create permanent guidance promoting decentralized trial design. This process should include gathering public input to inform the guidance design.

Identification of Factors Known to Impact Drug Metabolism, Safety or Efficacy

By design, clinical trials conducted to collect data leading to new drug approval exclude many patients to protect the safety of participants and minimize confounding factors that may affect patient outcomes. The result is a trial population that does not necessarily reflect the intended population for the treatment, with the trial participants generally skewing younger, healthier and less diverse. When drugs are approved and move into broader use, the real-world patient outcomes often do not match those observed in clinical trials due to these differences in patient characteristics. While minor differences in trial and real-world outcomes are not unusual, large overall differences, or large subgroup differences are concerning, especially since the latter can lead to disparities in outcomes.

While registrational trials are not generally required to be designed to be able to conduct subgroup analyses that could detect racial or ethnic outcome differences, evidence has nonetheless been generated in certain cases demonstrating differential responses to certain drugs or drug classes. FDA is well-poised to lead an effort to catalog drugs and drug classes where known racial differences in response or metabolism exist and identify evidence gaps on this issue that would require further research. We would like to see resources within PDUFA VII dedicated to performing this research, as well as the development of guidance that would ensure appropriately powered trials for subgroup analyses for drugs or drug classes where past evidence has suggested differential outcomes are likely to occur.

For further information on our recommendations to FDA for addressing disparities, please refer to our February 28th comment letter to FDA's Office of Minority Health and Health Equity

(Docket FDA-2019-N-4824) located at:
https://www.fightcancer.org/sites/default/files/ACS_CAN_OMHHE_Comments_28Feb2020.pdf

Thank you again for the opportunity to provide comments, and we look forward to working with all stakeholders during the PDUFA VII reauthorization process. If you have any questions, please do not hesitate to contact Mark Fleury, PhD (mark.fleury@cancer.org), Principal, Policy Development - Emerging Science, and Phylicia Woods (phylicia.woods@cancer.org), Director of Federal Relations.

Sincerely,

Lisa Lacasse
President
American Cancer Society Cancer Action Network