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Dockets Management Staff (HFA-305)
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On behalf of the Cancer Support Community (CSC), an international nonprofit organization that provides support, education, and hope to cancer patients, survivors, and their loved ones, we appreciate the opportunity to comment on the FDA’s Draft Guidance, Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry (Draft Guidance). Clinical trials provide individuals with cancer and other serious medical conditions the opportunity to participate in ground-breaking research that may bring about treatments that improve quality of life, extend survival, and even prove life-saving. CSC applauds the FDA’s ongoing efforts to have clinical trial participants better reflect the population of people likely to use a drug post approval and appreciates its Draft Guidance on new approaches that sponsors of clinical trials can take to broaden eligibility criteria, when scientifically and clinically appropriate, and increase enrollment of underrepresented populations.

As the largest direct provider of social and emotional support services for people impacted by cancer, and the largest nonprofit employer of psychosocial oncology 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 over 45 licensed affiliates, more than 170 satellite locations, and a dynamic online community of individuals receiving social support services. Overall, we deliver more than $50 million in free, personalized services each year to individuals and families affected by cancer nationwide and internationally.

Additionally, CSC is home to the Research and Training Institute (RTI)—the only entity of its kind focused solely on the experiences of cancer patients and their loved ones. The RTI has contributed to the evidence base regarding the cancer patient experience through its Cancer Experience Registry (with over 14,000 participants), various publications and peer-reviewed studies on the psychosocial impact of cancer and cancer survivorship. This combination of direct services and research uniquely positions CSC to gather and provide valuable patient feedback.
While most cancer patients express a willingness to participate in clinical trials, numerous barriers to enrollment drastically reduce the number of adult cancer patients in clinical trials to about 1 in 20, or 5%.\(^1\) With data being consistent with the idea that higher rates of patients enrolled in clinical trials produce faster rates of treatment advances, and concurrent survival increases and mortality reductions,\(^2\) CSC shares the commitment, need, and urgency to ensure the broadest and most inclusive patient participation possible in clinical trials while maintaining safety and efficacy standards. Approximately 20% of cancer clinical trials fail due to insufficient patient enrollment.\(^3\) Barriers to clinical trial participation, whether resulting from restrictive eligibility criteria, patient burdens, social determinants, or patient mistrust, are thwarting potential treatment advances, survival increases, and reduction in mortality.

**Eligibility Criteria**

CSC supports broadening eligibility criteria to increase diversity in enrollment. Safety rightfully maintains the top priority position in connection with patient participation in clinical trials. However, as acknowledged in the Draft Guidance, certain populations are often excluded from trials without strong clinical or scientific justification. The Belmont Report recognizes this fine balance in what it terms the obligation of “beneficence” or “[t]wo general rules … formulated as complementary expressions of beneficent actions … (1) do no harm and (2) maximize possible benefits and minimize possible harms.”\(^4\) With a recent meta-analysis finding that eligibility criteria on average keeps 21.5 percent of cancer patients from enrolling in clinical trials,\(^5\) it is imperative that the second of the two rules, (i.e. maximizing possible benefits) is also given its rightful consideration and not discounted or diminished in its importance due to outdated and/or unnecessary eligibility criteria. In 2018, CSC joined sixteen other stakeholders endorsing a set of recommendations aimed at reducing barriers to patient enrollment to clinical trials, with one of those recommendations addressing eligibility criteria.\(^6\) Specifically, that recommendation reads:


\(^2\) Unger, Cook, Tai, Bleyer, Role of Clinical Trial Participation in Cancer Research: Barriers, Evidence, and Strategies, 185.

\(^3\) Overcoming Barriers to Patient Enrollment in Therapeutic Clinical Trials for Cancer, Recommendations, American Cancer Society Cancer Action Network (April 11, 2018), available at https://www.fightcancer.org/policy-resources/clinical-trial-barriers


\(^6\) Overcoming Barriers to Patient Enrollment in Therapeutic Clinical Trials. (April, 2018): https://www.fightcancer.org/policy-resources/clinical-trial-barriers
Modernize eligibility/inclusion/exclusion criteria to achieve the most relevant parameters that will ensure scientific integrity without unnecessarily excluding patients.

a) Ensure eligibility criteria do not preferentially exclude a racial or demographic group, e.g. upper age limits, or excluding comorbidities more highly associated with demographic or socioeconomic subgroup unless specific rationale for exclusion exists.

Applying the above expressed need to modernize eligibility/inclusion/exclusion criteria to this Draft Guidance, CSC agrees with both the specific recommendations set forth in Section II(B)(1) and II(B)(2) of the Draft Guidance and supports FDA’s written statement that “encourages the use of others (broadened eligibility criteria) as appropriate.” Approving (or disapproving) drugs without regard or applicability to real world patients who would potentially receive the medication following the clinical trial satisfies neither the first (do no harm) nor second (maximize possible benefits and minimize possible harms) general rule of the Belmont Report.

Enrollment
CSC also recognizes the importance of Section III of the Draft Guidance, Other Study Design and Conduct Consideration for Improving Enrollment. As noted in the Draft Guidance, narrow eligibility criteria is just one potential barrier to participants enrolling in clinical trials. CSC agrees that additional barriers have resulted in the underrepresentation of particular demographic (e.g., sex, race, ethnicity, age) and non-demographic (e.g., patients with organ dysfunction, comorbid conditions, and those at the extremes of the weight range) populations in the clinical trial process. Specifically referenced in Section III are current and previous clinical trial requirements/designs that impose disproportionate burdens on certain populations, thereby preventing these individuals from participating in a clinical trial and gaining/contributing potentially valuable information, individually and collectively, to the study.

Through our direct services with cancer patients, CSC is able to confirm the often overwhelming challenges presented by the requirement of frequent visits to a particular site and the burdensome financial costs connected with participation in a clinical trial. Frequent travel to a clinical trial site is difficult for older patients, children, people living with disabilities and cognitive impairments, and those living a far distance from a research facility, including, but not limited to, those living in rural geographic locations. The issue of age, for both children and older adults, not only adds logistical hardships, but often raises the automatic disqualifier of an arbitrary minimum or maximum age. The urgency to eliminate all unnecessary barriers to clinical trial enrollment is accentuated by the growing aging population and the increased prevalence of cancer and other serious medical conditions that is and will continue to accompany this population.

The financial burden associated with participation in a clinical trial referenced in Section III has been a leading barrier to ensuring a diverse and representative patient sampling in clinical trials. The cost of travel, missed work, and dependent care represent just a few of the financial
challenges of enrolling in a clinical trial. While recent FDA guidance\(^7\) has clarified that financial reimbursement for expenses associated with travel and lodging costs incurred by participation in clinical trials is permissible and not considered undue influence, the additional financial costs of participating in a clinical trial have, historically, been a major barrier for many people of limited financial means. There must be flexibility in terms of allowable reimbursement for patient travel and logistical costs, particularly for those who have historically been underserved or those who face significant hurdles such as patients living in rural areas. For these reasons, CSC supports the approaches suggested in Section III(A) of the Draft Guidance, including reduced frequency of required study visits, increased use of alternate means of communication (such as the use of telemedicine), and the explanation of permissible reimbursable expenses during the recruitment process. However, CSC also encourages the development of additional approaches, as permitted in the Draft Guidance, to further expand access such as members of the health care team traveling to patients. Increased enrollment of underrepresented populations in clinical trials will only fully be accomplished if sponsors of clinical trials, and all other stakeholders across disciplines and from all vantage points, actively embrace inclusiveness as a defining measure of clinical trial success.

CSC applauds the measures outlined in Section III(B) of the Draft Guidance titled, Adopt Enrollment and Retention Practices That Enhance Inclusiveness. As mentioned above, CSC is dedicated to ensuring that all people impacted by cancer are empowered by knowledge, strengthened by action, and sustained by community. Section III(B) of the Draft Guidance recognizes and gives credence to CSC’s long held belief in the power and importance of community for those confronting serious health issues. As the majority of patients receive their cancer care within their communities, CSC commends the recommendation to work directly with communities to address participant needs and to involve patients, patient advocates, and caregivers in the design of clinical trial protocols contained in the first bullet point of Section III(B). By ensuring clinical trials are conducted in geographic areas with a higher concentration of racial and ethnic minority, including rural locations, patients will not only increase diverse participation, but also lessen the increased financial barrier imposed by having to travel far distances to clinical trial sites. CSC is encouraged by FDA’s recognition of the importance to reach out to people where they live, work, go to school, and play by holding recruitment events often, including during evening and weekend hours, and in trusted locations outside of the medical setting.

As recognized in Section IV of the Draft Guidance, patients diagnosed with a rare disease confront all of the challenges of access to clinical trials discussed above and more. CSC supports increased engagement of patients, patient advocacy organizations, and sponsors as set forth in Section IV to meet the needs of this unique population.

**Patient Experience Measures**
When considering diversity in clinical trials, CSC also encourages the FDA to use this opportunity to consistently and meaningfully seek robust patient feedback and patient experience

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data at all points along the research continuum. As amended by the Food and Drug Reauthorization Act of 2017, patient experience data now includes both “physical and psychosocial impacts of a disease or condition, or related therapy or clinical investigation.” Clinical trial design, trial endpoint selection, and regulatory reviews should all include meaningful patient feedback and patient experience data. Clinical trials that incorporate patient experience data allow us to better understand and address patient needs and concerns. Such information should be collected, reported on, and used as a part of a shared decision making process both for the benefit of the patient and their loved ones but also for future trial design and intervention. Ultimately, this information can be used to enhance trial recruitment and ensure retention. It can also be incorporated into drug labeling to better inform decisions by patients, their loved ones, and their health care team.

In summary, CSC is pleased to support the FDA’s Draft Guidance to broaden the eligibility criteria and enhance the diversity (and subsequent number) of individuals enrolled in clinical trials. We urge the FDA to look to sponsors to not only implement the recommendations and approaches specifically outlined in the Draft Guidance, but to go beyond these recommendations and approaches as encouraged and requested by the FDA. CSC would be happy to schedule a meeting to share additional concerns and challenges which factor into a patient’s ability and ultimate decision whether or not to enter into a clinical trial. Feel free to contact me at efranklin@cancersupportcommunity.org.

Sincerely,

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Cancer Support Community