



August 1, 2023

Robert M. Califf, M.D.  
Commissioner  
U.S. Food and Drug Administration  
Docket No. FDA-2022-D-2870  
5360 Fishers Lane  
Room 1061  
Rockville, MD 20852

**Re: FDA-2022-D-2870: Decentralized Clinical Trials for Drugs, Biological Products, and Devices; Draft Guidance for Industry, Investigators, and Other Stakeholders; Availability (May 3, 2023)**

Dear Commissioner Califf:

The American Cancer Society Cancer Action Network (ACS CAN) advocates for evidence-based public policies to reduce the cancer burden for everyone. As the American Cancer Society's nonprofit, nonpartisan advocacy affiliate, ACS CAN is making cancer a top priority for public officials and candidates at the federal, state, and local levels. By engaging advocates across the country to make their voices heard, ACS CAN influences legislative and regulatory solutions that will end cancer as we know it. ACS CAN appreciates the opportunity to comment on Decentralized Clinical Trials for Drugs, Biological Products, and Devices; Draft Guidance for Industry, Investigators, and Other Stakeholders (Draft Guidance).

**Willingness to Participate in Cancer Clinical Trials**

When eligible and offered, over half of all cancer patients participate in a cancer clinical trial.<sup>1</sup> However, only a minority of eligible patients have access to a trial at their treatment location<sup>2</sup> which means patients are often required to travel farther than they do for regular care to participate in a trial. Willingness to participate in cancer trials requiring additional travel time and longer distances compared to a patient's regular site of care varies by income and age — those who are lower-income or older are less likely to travel farther or attend more frequent trial-related visits.<sup>3</sup> The added cost burden (e.g., fuel cost, lodging, airfare, meals, time away from work) associated with increased travel time and distance to trial sites is commonly cited as a barrier to patient enrollment.<sup>4,5,6</sup> These barriers can ultimately limit enrollment of a diverse population (e.g., race ethnicity, age, sex, geographic location, and income) of participants. We commend the Administration for recognizing the role that decentralized clinical trials (DCTs) can play in expanding access to more diverse patient populations.

In addition to potentially increasing the number of trials available for patients to participate via removal of site restrictions, DCTs may also increase the likelihood that patients, particularly those facing logistical challenges, agree to participate.<sup>3</sup> The majority (60%–85%) of cancer patients and cancer survivors report an increased likelihood to enroll in cancer clinical trials that leverage remote technology (e.g., wearable technology to capture trial data) and decentralization tools (e.g., trial activities completed at local facility)

that reduce time and travel burdens associated with participating in trials.<sup>3</sup>

### **Decentralized Clinical Trials**

During the federal Coronavirus Disease 2019 Public Health Emergency (PHE), FDA issued guidance on the *Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency*. This guidance (in effect until November 7, 2023) expanded opportunities for the use of DCT practices and allowed research to continue while reducing the risk of SARS-CoV-2 transmission among patients and research staff. Outside of a pandemic setting or PHE, DCT designs that enable the use of virtual study visits (e.g., telehealth), use of local health care providers and facilities, digital health technologies (DHTs), and delivery of investigational products to patients' homes can help to alleviate enrollment barriers.

ACS CAN has supported provisions, such as those included in the *Diversifying Investigations Via Equitable Research Studies for Everyone (DIVERSE) Trials Act (H.R. 5030/S.2706)* and the *Food and Drug Omnibus Reform Act (FDORA) of 2022* that call for permanent FDA guidance on the conduct of DCTs to improve the diversity of clinical trials. Demographically diverse clinical trials advance both scientific and ethical goals of research by helping to ensure broad applicability of study results and equal access to advances in treatment. Permanent guidance on DCTs will continue to allow sponsors and investigators to take advantage of innovative technology and trial design to reach more diverse populations.

### **Decentralized Tools and Diversity**

While DCTs hold the potential to reduce trial access disparities, care must be taken to ensure that they do not create new disparities. Of particular concern is any potential “digital divide” separating individuals with the equipment and knowledge to use options like telehealth visits or logging symptom in virtual diaries. The guidance for sponsors to provide DHTs to participants who do not otherwise have their own, is key to addressing the potential disparities in technology ownership. However, current anti-kickback restrictions place the provision of DHTs in an uncertain legal domain, making some sponsors hesitant to provide these to participants. We urge the Department of Health and Human Services to clarify that the provision of DHTs to trial participants is not a violation of the Anti-Kickback Statute.<sup>7</sup>

### **Clarity on Provider Roles and Registration**

One common source of frustration in executing DCTs has been ambiguity regarding which providers need to register on Form 1572 for a particular study. This draft guidance provides helpful clarity that providers administering routine care in which a detailed understanding of the trial protocol is not needed do not have to be listed on Form 1572.

### **Optionality**

The guidance states that sponsors should implement a Safety Monitoring Plan to ensure the “*safety and welfare*” of trial participants in a DCT, including enabling participants “*to arrange for an unscheduled visit using telehealth or an in-person visit, as appropriate.*” As stated in the definition, DCTs allow for some or all trial-related activities to occur at locations other than traditional clinical trial sites. However, we recognize that DCTs may not be the appropriate or preferred option for a patient to participate in clinical research and a

patient may not become aware of this until after already enrolled. For example, a minority (4%-20%) of cancer patients and survivors report that some DCT modifications would decrease their willingness to participate.<sup>3</sup> Therefore, we believe that patient preference is appropriate grounds for an unscheduled or *scheduled* in-person visit.

If enrolled in a trial in which all trial-related activities could be done in their home, the option for in-person visits when desired is an important factor for nearly 90 percent of cancer patients and survivors.<sup>3</sup> We recommend FDA include “*patient preference*” as an example of an appropriate reason for an unscheduled visit and add the words “*or scheduled*” after “*unscheduled*” in line 464.

## Conclusion

This draft guidance builds on previous FDA recommendations issued in 2022 to provide greater clarity for regulatory approval based on data collected using DHTs. How a trial is designed and where it is conducted plays the biggest role in facilitating enrollment and this draft guidance has the opportunity to expand access to more diverse patient populations and reduce the burden of participation. We appreciate the opportunity to provide comments and look forward to working with you to ensure clinical trials are more open and accessible to all patients with cancer. If you have any questions, please do not hesitate to contact Mark Fleury, PhD ([mark.fleury@cancer.org](mailto:mark.fleury@cancer.org)), Principal, Policy Development - Emerging Science.

Sincerely,



Lisa A. Lacasse, MBA  
President  
American Cancer Society Cancer Action Network

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<sup>1</sup> Unger, J. M., Hershman, D. L., Till, C., Minasian, L. M., Osarogigbon, R. U., Fleury, M. E., & Vaidya, R. (2021). “When Offered to Participate”: A Systematic Review and Meta-Analysis of Patient Agreement to Participate in Cancer Clinical Trials. *JNCI: Journal of the National Cancer Institute*, 113(3), 244–257. <https://doi.org/10.1093/jnci/djaa155>

<sup>2</sup> Barriers to Patient Enrollment in Therapeutic Clinical Trials. American Cancer Society Cancer Action Network. (2019) Retrieved July 10, 2023, from <https://www.fightcancer.org/sites/default/files/National%20Documents/Clinical-Trials-Landscape-Report.pdf>

<sup>3</sup> Adams, D. V., Long, S., & Fleury, M. E. (2022). Association of Remote Technology Use and Other Decentralization Tools With Patient Likelihood to Enroll in Cancer Clinical Trials. *JAMA network open*, 5(7), e2220053. <https://doi.org/10.1001/jamanetworkopen.2022.20053>

<sup>4</sup> Meropol NJ, Buzaglo JS, Millard J, et al. Barriers to clinical trial participation as perceived by oncologists and patients. *J Natl Compr Canc Netw*. 2007;5(8):655-664. doi:10.6004/jnccn.2007.0067

<sup>5</sup> Javid SH, Unger JM, Gralow JR, et al. A prospective analysis of the influence of older age on physician and patient decision-making when considering enrollment in breast cancer clinical trials (SWOG S0316). *Oncologist*. 2012;17(9):1180-1190. doi:10.1634/theoncologist.2011-0384

<sup>6</sup> Nipp RD, Powell E, Chabner B, Moy B. Recognizing the financial burden of cancer patients in clinical trials. *Oncologist*. 2015;20(6):572-575. doi:10.1634/theoncologist.2015-0068

<sup>7</sup> ACS CAN Comments to HHS Supporting Regulatory Safe Harbor For Ancillary Costs. Solicitation of Proposals for New and Modified Safe Harbors and Special Fraud Alerts OIG-1122-N, 87 Fed. Reg. 72953 (Nov. 28, 2022) (“Annual Solicitation”) Retrieved July 31, 2023, from: [https://www.fightcancer.org/sites/default/files/acs-can\\_proposed\\_safe\\_harbor\\_27jan23finalv.pdf](https://www.fightcancer.org/sites/default/files/acs-can_proposed_safe_harbor_27jan23finalv.pdf)