Alliance FOR AGING RESEARCH
Catalyzing Innovation for Healthy Aging

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Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

**Re: Docket No. FDA-2019-D-5572 for "Inclusion of Older Adults in Cancer Clinical Trials"**

Dear U.S. Food and Drug Administration's Oncology Center of Excellence, Center for Drug Evaluation and Research, and Center for Biologics Evaluation and Research,

As the leading nonprofit organization dedicated to accelerating research to enhance aging and health through public policy and education, the Alliance for Aging Research also serves as the voice of older Americans. We are grateful for the opportunity to comment on this draft guidance and help ensure the voice and needs of adults are incorporated.

We are encouraged the U.S. Food and Drug Administration (FDA) continues to urge industry and other stakeholders to enroll diverse populations in their clinical trials, especially older adults. The Alliance recognizes and appreciates the ongoing efforts from the FDA to encourage the medical product research communities to recruit and enroll older adults in clinical studies, including numerous draft guidances, public awareness campaigns, fact sheets, personalized consultation with researchers, and more.

This draft guidance is another important step in addressing the underrepresentation of older adults in cancer clinical trials. It sends a strong message to oncology clinical development programs that they should be deliberate in their recruitment efforts to enlist a group of older adults that reflects the intended population for the treatment being studied and evaluated. As the FDA itself states, "To make sure that the FDA has a full picture of the risk or benefit of a medical product, patients enrolled in a trial should be representative of the types of patients who are likely to use the medical product if it is approved or cleared by the FDA."[i] The guidance also recognizes that effective solutions to underrepresentation must also include a strategy to include older adults throughout the trial process—from early clinical development to postmarket data collection. The Alliance strongly supports this broad vision for inclusion.

Below are our detailed comments on the draft guidance that we hope the FDA will take into consideration before finalizing.

**Early Clinical Development**

The Alliance appreciates that the FDA recommends including older adults in all stages of clinical development, including in its earliest phases. With nearly 9 in 10 adults ages 65 and older taking at least one prescription medication, and more than half taking four or more,[ii] inclusion in early clinical development is imperative in

learning more about potential drug-drug interactions and ensuring the inclusion of older adults with concomitant medication use. Inclusion in early clinical development will better inform which older adults can tolerate and benefit from treatments.

Additionally, strategies to include more older adults in early phase trials should include recruitment efforts to community oncologists and their patients. The majority of older adults receive their cancer care in the community and the data collected from this patient population would likely be more generalizable than data collected from strictly university-based cancer centers. The FDA and other stakeholders need to be thoughtful about decentralizing the clinical trial process to include more older adults.

**Clinical Trial Design and Analysis**

A flexible approach to trial design and analysis, as suggested by the guidance, is critical for the recruitment and retention of older adults. Consideration and incorporation of patient and caregiver perspectives help anticipate needs, make accommodations when needed, and keep participants happy and willing to return.

Encouraging innovative trial designs that best answer particular research questions would improve the evidence base in general, and specifically for older adults. A statement from the American Society of Clinical Oncology (ASCO) on improving the evidence base calls for innovative trial designs such as extended design trials, which allow the trial to reopen to accrue a sufficient number of older adults to match the age distribution of the at-risk population.[iii]

The FDA's own 2019 draft guidance, "Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry," urges industry to design trials in a manner which reduces the barriers to entry and overall burden on participants, including older adults, therefore encouraging diversity in enrollment and study. This includes broadening eligibility requirements to include older adults, which "…maximizes the generalizability of trial results and the ability to understand the therapy's benefit-risk profile across the patient population likely to use the drug in clinical practice, without jeopardizing patient safety."[iv] This also includes designing trials so that the criteria for various phases can be modified to reduce limitations on specific participants.[v] **This oncology-focused draft guidance should include and encourage the full range of research designs outlined in the FDA's broader "Enhancing the Diversity of Clinical Trial Populations" guidance.**

The Alliance supports the recommendation to use geriatric assessment tools within trials which will not only encourage participation but will provide important data to the current and future trials. A 2015 Institute of Medicine quality report recommended that a common set of data elements be developed and collected in all trials.[vi] The report recommends that this data set includes geriatric assessment domains such as functional status, comorbid medical conditions, nutritional status, cognition, psychological state and social support, and polypharmacy.[vii] Additionally, tumors are often biologically different in people of different ages, so specimens can offer important clues as to how aging affects cancer biology. Collectively, these data sets will "help identify which older adults are most likely to benefit or not from treatment, because factors other than age are crucial to making these assessments."[viii] **The final guidance should ensure the collection of this critical geriatric and aging biology data.**

**Also, we support the recommendation to develop and report on age sub-groups. However, we encourage the FDA to provide more detail in the final guidance.** Metabolism and immune system responses change with age, the rate of decline and the appearance of physiological changes due to aging vary from person to person, and functional status differences may warrant further sub-grouping in cancer trials. Measures that can gauge

biological age are likely more useful than chronologic age since they more accurately account for genetics, lifestyle, and other environmental factors that impact overall health status.

**Postmarket Data**

We support the recommendation to collect data on older adults in the postmarket setting. **The agency should require the publication of postmarket studies on older adult patients, so that clinicians and the public—in addition to the sponsor and agency—may benefit from this additional knowledge.** Postmarket data may enhance clinical guidelines, including information on dosing, side effects, and treatment response; as well as patient decision-making regarding risk-benefit and shared decision-making with providers on treatment choice.

**Expanding to All Clinical Trials**

We applaud the FDA's ongoing efforts to reinforce the importance of including older adults in oncology clinical trials**. The Alliance urges the FDA to formalize this guidance and issue similar agency-wide guidance for all medical products meant to treat conditions that primarily impact older adults.**

**Additional Considerations**

The Alliance agrees with a key recommendation made by ASCO: the FDA should enhance the aging expertise on its advisory boards.[ix] As part of the draft guidance in consideration**, the FDA should add specialists in geriatrics, and if possible, geriatric oncology, to provide oversight and input into oncology clinical trials submitted to the FDA Oncology Center for Excellence.** This position can ensure the unique clinical considerations of the older adult trial participant are taken into consideration throughout the study period.

**Conclusion**

This guidance sends a clear signal to research sponsors that the FDA values inclusion of older adults in cancer research, therefore reiterating previous FDA guidance for industry emphasizing the importance of diversity in clinical trial participation. The guidance identifies important considerations for recruitment, retention, and data collection that will hopefully increase older adult enrollment by reducing the burden on participants and enhance research findings. The FDA should take this to the next level and issue this guidance for all clinical research.

We appreciate this opportunity to provide feedback and would be happy to serve as an ongoing resource to the agency on this issue. Please do not hesitate to contact us at lclarke@agingresearch.org and lsmith@agingresearch.org.

Sincerely,

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[i] U.S. Food and Drug Administration. *FDA Encourages More Participation, Diversity in Clinical Trials.* Available at https://www.fda.gov/consumers/consumer-updates/fda-encourages-more-participation-diversity-clinical-trials. Last updated on 1/16/18.

[ii] Kirzinger, Neuman, Cubanski, and Brodie. 2019. Data Note: Prescription drugs and older adults. *Health Reform.* Available at https://www.kff.org/health-reform/issue-brief/data-note-prescription-drugs-and-older-adults/.

[iii] Hurria, Levit, Dale, Mohile, Muss, et al. 2015. Improving the Evidence Base for Treating Older Adults With Cancer: American Society of Clinical Oncology Statement. *J Clin Onc* 33(32):3826-33.

[iv] Center for Drug Evaluation and Research. June 2019. *Guidance Document: Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry*. Rockville, MD: U.S. Food and Drug Administration.

[v] Ibid.

[vi] Institute of Medicine 2013. Delivering High-Quality Cancer Care: Charting a new course for a system in crisis. Washington, DC: National Academies Press.

[vii] Ibid.

[viii] Hurria, Levit, Dale, Mohile, Muss, et al. 2015. Improving the Evidence Base for Treating Older Adults With Cancer: American Society of Clinical Oncology Statement. *J Clin Onc* 33(32):3826-33.

[ix] Ibid.