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PROTECTING RESEARCH SUBJECTS AND RESEARCHERS

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IRBs and Including More Older Adults as Research Subjects (#5)

We return now to this concluding article on a topic that we have been addressing; namely, the ongoing underrepresentation of older adults in many types of critical clinical trials.

As we have described, a few months ago the FDA issued the final version of a guidance that it originally proposed in March of 2020, when the pandemic was beginning in earnest in the US.

This guidance contains numerous recommendations for researchers on how to increase the participation of older research subjects in experiments. Its focus, however, is on cancer rather than COVID.

The guidance also contains related cautions and areas of particular concern for IRBs. The reality is that older populations pose a different range of risk factors, in contrast to younger participants, that can affect the protection of human research subjects.

Special Subject Recruitment Factors

We resume our coverage of this timely guidance with its recommendation that researchers should:

"• *Develop recruitment strategies targeted to older adults*

Clinical trials do not have an upper age limit for exclusion, however adults 75 years of age and older, continue to be underrepresented [sic]. FDA encourages sponsors and clinical trial cooperative groups to develop strategies to recruit patients that are reflective of the intended population.

Possible challenges with recruiting older adults that could be mitigated, particularly among patients 75 years of age and older, include: location of clinical trial sites (e.g., sites in community-based settings may be more accessible to older adults than sites located in urban academic centers), format (e.g. digital) and content of informational material for the trial, caregiver support, accommodations needed for impairment (e.g., visual, mobility, etc.), and travel and other logistics. Where feasible, remote monitoring approaches should be considered.

Sponsors should discuss specific goals for enrollment of older adults with clinical in-

NOTE #1: Quoted materials in this newsletter appear exactly as originally published in source documents, including any misspellings, grammatical errors, or missing words. However, we will on occasion insert words or edit text and/or formating in brackets [ ] to make the material easier to read.

NOTE #2: Emphases are added to articles by HRR by underlining or adding ***bold/italics*** to selected text, unless stated otherwise.

NOTE #3: Articles **T**o **B**e **C**ontinued in subsequent issues are marked at the end of the article with **{TBC}**.

Also In This Issue

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vestigators and keep the clinical trial sites updated on the progress of enrolling older adults in the trial ....

In addition, sponsors should consider getting input on trial design, trial conduct[,] and recruitement [sic] strategies from geriatricians, geriatric oncologists, [and] social and behavioral scientists with expertise in treating older adults. Additional input from patient advocates/navigators should also be sought" ("Inclusion of Older Adults in Cancer Clinical Trials," March; on the Web at https://www.fda.gov/media/135804/download, p. 5).

Different Kinds of Subject Information

"• *Consider collecting additional information for older adults*

Sponsors should prospectively consider information that should be collected for older adults that will be clinically informative and will provide an understanding of clinical outcomes in older adults.

For example, in addition to collection of age and performance status, elements from geriatric assessment tools (e.g. functional status, cognitive function), and a comprehensive assessment of comorbidities should be considered during trial design ...." (supra at p. 16).

Subjects' Own Perspective Is Important

"Incorporating a patient reported outcome instrument(s) in cancer trials may encourage older adults to participate in clinical trials and the information obtained may inform future research ....

• *Consider additional strategies in adverse event monitoring and management*

Older adult patients' experience with adverse events may differ from younger patients. Developing strategies to capture and manage adverse events in older patients (e.g., supportive care measures, involvement of geriatric oncologists and other health care professionals with expertise in treating older adults) may facilitate older patients completing the trial.

• *Report more discrete age subgroups*

Because outcomes may differ by increasing age group in patients 65 years of age and older, sponsors should identify further age subgroups to understand the drug's benefits and risks.[18]

[FN #18: See the guidance for industry *E7 Studies in Support of Special Populations: Geriatrics Questions and Answers* (March 2012).]" (ibid).

Subjects Over Age 75 Especially Scarce

"For example, subgroups such as age 65 years to 74 years of age and 75 years of age and older may be relevant. A particular need exists for information in patients 75 years of age and older. Sponsors may consider combining data across trials of similar design to ensure adequate representation of older adults across discrete age subgroups ....

FDA's guidance for industry *Integrated Summary of Effectiveness* (October 2015) includes recommendations regarding subpopulation assessment and reporting in the NDA or BLA that are applicable to subgroups of older adults in cancer trials (see section III.D of that guidance)" (ibid).

Possible Role of Postmarket Studies

"**C. Postmarket**

• Ideally, adequate information on older adults should be captured in the premarket clinical trials. However, if older adults are not adequately represented in pre-market clinical trials, it may be appropriate to develop a plan to collect data on older adults in the postmarket setting.

This could be accomplished with postmarketing trials examining a broader population, or through collection of real world data in an observational study or registry. In certain situations, FDA may require postmarket studies and clinical trials.[20]

[FN #20: See *Postmarketing Studies and Clinical Trials - Implementation of 505(o)(3) of the Federal Food, Drug and Cosmetic Act* (Oct. 2019) ….]" (p.7). ©