



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2019-D-1264]

Enhancing the Diversity of Clinical Trial Populations--Eligibility Criteria, Enrollment Practices, and Trial Designs; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled "Enhancing the Diversity of Clinical Trial Populations--Eligibility Criteria, Enrollment Practices, and Trial Designs." This guidance recommends approaches that sponsors of clinical trials intended to support a new drug application or a biologics license application can take to increase enrollment of underrepresented populations in their clinical trials. This guidance is being issued, in part, to satisfy the mandates of the FDA Reauthorization Act of 2017 (FDARA). This guidance finalizes the draft guidance of the same title issued on June 7, 2019.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment

does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.

- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2019-D-1264 for "Enhancing the Diversity of Clinical Trial Populations--Eligibility Criteria, Enrollment Practices, and Trial Designs." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information

you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at:

<https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in

processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Dat Doan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3334, Silver Spring, MD 20993, 240-402-8926, Dat.Doan@fda.hhs.gov; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled "Enhancing the Diversity of Clinical Trial Populations--Eligibility Criteria, Enrollment Practices, and Trial Designs." In issuing this guidance, FDA is satisfying the mandates under section 610(a)(3) of FDARA (Pub. L. 115-52).

One objective of eligibility criteria is to help protect participants by excluding people for whom the risk of an adverse event from participation is not likely to be reasonable in relation to any potential benefit and the importance of the knowledge that may be expected to result. FDA recognizes that certain exclusions are appropriate when necessary to help protect these individuals. For example, patients with varying degrees of kidney or liver impairment are often excluded early in drug development programs because adequate information is not available on how to adjust doses for such patients or whether these patients could be more vulnerable to certain risks. Medically complex patients with certain concomitant illnesses or those taking particular drugs may also be excluded from drug development programs. As data on excretory and metabolic pathways and drug-drug interactions become available during the drug development program, allowing appropriate dose adjustments, exclusions related to concomitant medications or comorbidities should be narrowed. Similarly, as the safety experience with a product increases, eligibility criteria should be broadened to include more medically complex

participants; any remaining exclusions should be justified. This guidance provides recommendations on broadening eligibility criteria in clinical trials through inclusive trial practices, trial designs, and methodological approaches.

Beyond the limitations in participation imposed by narrow eligibility criteria, potential participants may face additional challenges to enrolling in clinical trials. A trial requiring participants to make frequent visits to specific sites may result in an added burden for participants, especially the elderly, children, disabled, and cognitively impaired individuals who require transportation or caregiver assistance, or participants who live far from research facilities, such as those in rural or remote locations. Financial costs (e.g., travel, missing work, dependent care) may also impede participation, and study visits may interfere with jobs and/or family and community obligations. Moreover, for individuals under current clinical care on a regularly scheduled basis (e.g., individuals with multiple chronic conditions), additional clinical trial study visits may be psychologically, physically, and financially burdensome and a disincentive for enrollment. This guidance provides recommendations on how sponsors can improve the diversity of enrolled participants by accounting for logistical and other participant-related factors that could limit participation in clinical trials.

Clinical trials of investigational drugs intended to treat rare diseases or conditions present a unique set of challenges. Because of the limited numbers of patients, maximum participation in clinical trials is essential for successful trial completion and interpretation. Rare diseases often affect small, geographically dispersed patient populations with disease-related travel limitations, so special efforts may be necessary to enroll and retain these participants to ensure that a broad spectrum of the patient population is represented. This guidance provides recommendations on broadening clinical trial eligibility criteria for clinical trials of investigational drugs intended to treat rare diseases and recommendations on improving the enrollment and retention of participants with rare diseases.

This guidance finalizes the draft guidance of the same title issued on June 7, 2019 (84 FR 26687). FDA considered comments received on the draft guidance as the guidance was finalized. Changes to the guidance include additional recommendations on broadening eligibility criteria, such as the use of real-world data to find trial participants and the use of mobile medical professionals to visit participants at their locations instead of requiring participants to visit distant clinical trial sites. FDA added information on the inclusion of racial and ethnic minorities, with recommendations included from FDA's draft guidance entitled "Collection of Race and Ethnicity Data in Clinical Trials." FDA also added recommendations on fostering community engagement and making recruitment events more accessible as well as information on how to reach participants with little or no internet access. In addition, editorial changes were made to improve clarity.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on "Enhancing the Diversity of Clinical Trial Populations--Eligibility Criteria, Enrollment Practices, and Trial Designs." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014.

III. Electronic Access

Persons with access to the internet may obtain the guidance at

<https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>,

[https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-](https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances)

[biologics/biologics-guidances](https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances), or <https://www.regulations.gov>.

Dated: November 4, 2020.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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