August 21, 2023

Dear Tribal Leader:

The U.S. Food and Drug Administration (FDA) wishes to inform federally recognized American Indian and Alaska Native Tribes of the opportunity to review and provide comment on the draft guidance "Postmarketing Approaches to Obtain Data on Populations Underrepresented in Clinical Trials for Drugs and Biological Products,"issued by FDA's Onocology Center of Excellence.[1] On August 11, 2023, FDA announced the availability of this draft guidance in the *Federal Register* (88 FR 54624)(Docket Number FDA-2022-D-2629). This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. FDA welcomes input from Tribes and encourages the submission of comments concerning any potential implications this draft guidance mayhave for tribal communities.

FDA regulations require sponsors to present information from premarket clinical trials on the safety and effectiveness of drugs[2] in terms of gender, age, and racial subgroups.[3,4] These clinical trials should include patient populations that are historically underrepresented in clinical research (e.g., populations based on race, ethnicity, sex, or age.)[5] However, if, despite the sponsor's best efforts, these populations are not adequately represented in premarket clinical trials, it may be appropriate to collect such data in the postmarketing setting. The purpose of this draft guidance is to describe FDA requirements and provide recommendations for obtaining safety and effectiveness information on drugs, when appropriate, in the postmarketing setting in historically underrepresented patient populations in clinical trials.

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[1] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/postmarketing-approaches-obtain-data-populations-underrepresented-clinical-trials-drugs-and

[2] This guidance applies to drugs, including biological products. For the purposes of this guidance, drug or drug product is used to refer to human drugs and human biological products that are regulated as drugs.

[3] See 21 CFR 314.50(d)(5)(v)-(vi); 21 CFR 312.33(a)(2).

[4] See also section 505(z) of the FD&C Act, which would require sponsors to submit a diversity action plan for a phase 3 study or other pivotal study of a drug. This requirement will apply with respect to clinical investigations for which enrollment commences 180 days after the publication of a final guidance on diversity action plans. FDA will also hold a public workshop to solicit input on increasing the enrollment of historically underrepresented populations in clinical studies and encouraging clinical study participation that reflects the prevalence of the disease or condition among demographic subgroups, as required under section 3603 of the Food and Drug Omnibus Reform Act of 2022.

[5] This list is not all inclusive. Efforts should be made, whether in the premarket or postmarketing setting, to include other underrepresented populations including but not limited to, geographic location, gender identity, socioeconomic status, disability, pregnancy status, lactation status, and co-morbidity.

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Specifically, this draft guidance discusses:

- Mechanisms by which FDA can require or request information on safety and effectiveness be collected in the postmarketing setting
- Design and statistical considerations for subpopulation analyses
- Postmarketing approaches to obtain information on the benefit-risk profile in underrepresented clinical trial populations

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

All written comments on this draft guidance submitted in the docket by October 10, 2023, will be considered before the final guidance is published. Comments must be submitted to FDA using any of the following methods:

- Electronic Submissions: Please follow the instructions for submitting comments on the Federal eRulmaking Portal at: http://www.regulations.gov.
- Written submissions via Mail/Hand delivery/Courier: Division fo Docket Management (HFA-305) Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

All comments must include the docket number for the draft guidance (FDA-2022-D-2629). Received comments will be placed in the docket and publicly viewable at http://www.regulations.gov or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

For Tribes seeking further information on the process to submit comments on the draft guidance or needing assistance with another FDA-related issue, please contact the FDA Intergovernmental Affairs (IGA) team at IGA@fda.hhs.gov.

Sincerely,

Paul Kluetz, M.D.
Deputy Center Director
Oncology Center of Excellence