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Diversity Action Plans Should Be Brief And Waiver Requests Filed Early, US FDA Says

by Sue Sutter

In what could amount to a de facto enforcement mechanism, the new draft guidance also “strongly encourages” sponsors to share details about their diversity action plan and enrollment goals with the public.

The US Food and Drug Administration wants new clinical trial diversity action plans to be short and waiver requests filed early, albeit with little expectation that they will be granted.

In addition, the agency’s push for sponsors to publicly disclose details about their diversity action plan (DAP) and enrollment goals may be the only enforcement mechanism established.

The recommendations come in a much anticipated draft *guidance* on the diversity action plans required under the 2022 Food and Drug Omnibus Reform Act.

The guidance describes the format and content of DAPs pertaining to clinical study enrollment goals disaggregated by age group, sex, and racial and ethnic demographic characteristics, as well as explains the timelines and process for submitting the plans. The draft guidance also includes recommendations for setting enrollment goals and measures to meet them. *(See sidebar for related story.)*

Key Takeaways

- Diversity action plans should be succinct, running no more than 10 pages.
- Waiver requests need to be filed early so there is time to submit a DAP if the waiver is denied.
- The FDA 'strongly encourages' sponsors to publicly disclose details about their enrollment goals.

Under FDORA, the FDA was required to issue guidance by the end of December 2023. The draft

document, released on 26 June, was six months overdue. The public comment period is open for 90 days following publication in the *Federal Register*.

Agency Feedback Not Automatic

DAP plans should be succinct, generally not to exceed 10 pages excluding references, the guidance states.

To ensure the FDA can conduct a timely and efficient review, "sponsors should describe the required elements of the diversity action plan clearly and concisely, with limited cross-referencing to previously submitted documents," the guidance states.

For drugs and biologics, the requirement for DAP submission applies to Phase III or other pivotal clinical trials where enrollment begins 180 days after publication of the final guidance.

The agency exempted trials with protocols submitted within 180 days after the final guidance's publication, but where enrollment is scheduled to begin 180 days after the final guidance is released, from the DAP submission requirement, citing the time needed for planning and implementation activities necessary for clinical trials.

Sponsors must submit the required DAP to their investigational new drug application as soon as practicable, but no later than the date the protocol for the Phase III trial or other pivotal study is submitted.

Diversity Enrichment: US FDA Guidance Suggests Sponsors May Need To Overenroll Key Groups

By Sarah Karlin-Smith

26 Jun 2024
New draft guidance on clinical trial diversity action plans pushes for disproportionately high enrollment of traditionally underrepresented groups, while also asking companies to tailor global programs to US populations and consider diversity aspects that Congress did not outline.

Read the full article here

Because the agency's DAP review and feedback is most efficient in the context of discussions on trial design, study population selection, and other study characteristics, the FDA recommended the DAP be submitted when a sponsor is seeking feedback on the applicable clinical trial, typically at the end-of-Phase II meeting.

However, there is no guarantee that a sponsor will hear feedback from the agency on its plan.

Depending on the specifics for each clinical development program, the relevant division in the Center for Drug Evaluation and Research or Center for Biologics Evaluation and Research may or

may not provide feedback on the DAP, the guidance states.

"FDA feedback on a new or revised diversity action plan may be at FDA's initiative or per the sponsor's specific request for feedback," the guidance states. "Sponsors with specific questions regarding a planned or submitted diversity action plan may include them as a topic for discussion in meetings with FDA."

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An Oncology Center of Excellence review of the first year of diversity plans submitted under an April 2022 draft guidance found that feedback was provided on 41% of plans submitted to CDER's oncology divisions. Enrollment goals were the most common feedback topic, followed by trial enrollment monitoring and accrual enhancement strategies to meet goals. (Also see "*Clinical Trial Diversity Plans: Early Oncology Experience Shows More Work Needed, US FDA Says*" - Pink Sheet, 2 Dec, 2023.)

Sponsors should provide an update in IND annual reports on their progress toward meeting DAP enrollment goals.

"If such goals are not on track for being met at the conclusion of the study, the status report should include a description of the reason(s) the sponsor is not currently meeting or does not expect to meet enrollment goals and the sponsor's plan to mitigate such an outcome," the guidance states.

In marketing applications, sponsors should provide a brief overview of the DAP for the Phase III or other pivotal trial, an assessment of whether the plan's enrollment goals were met in the context of the specific study or the overall Phase III development program, and an explanation of what factors may have contributed to the observed DAP outcomes.

Waivers Granted 'In Rare Instances'

FDORA allows the FDA to waive the requirement for submission of a DAP, or any part of the plan, on the agency's initiative or at the sponsor's request if any of three criteria are met:

- A waiver is necessary based on what is known or can be determined about the prevalence or incidence of the disease or condition in the US.
- Conducting a clinical investigation in accordance with a DAP would be impracticable.
- A waiver is necessary to protect public health during a public health emergency.

Before releasing the draft guidance, an OCE official made clear that waivers would be "very rare." (Also see "*Clinical Trial Diversity Action Plan Waivers Will Be 'Very Rare,' US FDA Official Says*" - Pink Sheet, 19 Jun, 2024.)

In the guidance, the FDA said it anticipates DAP submission "will be possible in most cases."

"Given the importance of increasing enrollment of historically underrepresented populations in clinical research, including in clinical studies of drugs and devices, in order to detect potential differences in product performance and improve the generalizability of the results, full or partial waivers from the requirements around the submission of a diversity action plan will only be granted in rare instances," the guidance states.

If the FDA determines that the statutory criteria for a waiver are met and that granting one on the agency's initiative is appropriate, "such as the need to protect public health during a public health emergency, FDA will notify interested parties through appropriate channels. For example, to the extent permitted under applicable disclosure law, FDA may consider public communications and/or post relevant information on FDA's website regarding the decision to issue the waiver."

The guidance lists several considerations for sponsors when deciding whether to request a waiver. For instance, the agency generally does not intend to waive the DAP requirement even if the disease or condition is relatively homogenous in race, ethnicity, sex or age group.

> ***"Sponsors should request a waiver early enough to allow sufficient time for preparation and submission of the diversity action plan as required, should FDA deny the waiver request."***

Waiver requests also must be filed early and should not be viewed as a last-minute option for skirting the DAP submission requirement.

The agency must act on a waiver request within 60 days of receipt. Sponsors should submit requests as early as feasible, but no later than 60 days before the DAP submission would be required, the guidance states.

"FDA strongly encourages sponsors to discuss plans to request a waiver early in the planning stages of the clinical study or clinical development program," the guidance states. "Sponsors should request a waiver early enough to allow sufficient time for preparation and submission of the diversity action plan as required, should FDA deny the waiver request."

Since sponsors may include different enrollment goals across multiple planned Phase III or other pivotal studies, the targets for each individual study may not be fully reflective of the goals across all studies, the agency said.

"In these cases, sponsors should not seek a waiver for each study," the guidance states. "Rather, in their diversity action plans, sponsors should specify how the enrollment goals are expected to be met across the development program and provide a rationale for the enrollment goals for a specific study."

Public Disclosure As An Enforcement Mechanism?

The guidance also provides general recommendations for sponsors who may wish to publicly release key information on their DAPs.

The FDA "strongly encourages" sponsors to share strategies for meeting DAP enrollment goals with the public, the guidance states.

"To further promote transparency, sponsors may consider publicly posting on their website key information from their diversity action plans, namely their clinical study enrollment goals disaggregated by race, ethnicity, sex, and age group, and a brief description of the measures taken to achieve the stated goals."

Public interest groups and patient advocates, among others, could pressure sponsors to publicly disclose their DAP enrollment goals in the name of transparency and health equity.

"For medical products or uses that are not approved, licensed, cleared, or classified, such key information should be available in the same location as other content regarding such products

(e.g., on the ‘pipeline’ page of a sponsor’s website),” the guidance states.

Sponsors can post such key information at any time, while the study is open for recruitment, but may wish to consider disclosure strategies, including linking a posting to a trial recruitment website or a commonly used repository for clinical trials information, such as ClinicalTrials.gov.

“FDA recommends the use of consumer-friendly language when sharing key information from diversity action plans,” the guidance states.

The statute and guidance do not address potential enforcement for failure to meet DAP enrollment goals. The strong encouragement for public disclosure by sponsors could be a hands-off way for the agency to flex its statutory authority.

Public interest groups and patient advocates, among others, could pressure sponsors to publicly disclose their DAP enrollment goals in the name of transparency and health equity. Failure to disclose the goals, or subsequent evidence that the goals were missed, could lead to public naming and shaming that sponsors would prefer to avoid.

An OCE official previously has suggested that when trials fall well short of their diversity enrollment goals, the matter could go to an advisory committee, or a sponsor could be required to do additional studies after approval. But some in industry have suggested the FDA should exercise a heavier hand by declining to approve a drug if trials are not sufficiently diverse. (Also see "*‘Do It Or We’re Not Going To Approve Your Drug:’ Industry Reps Ask FDA For Trial Diversity Sticks*" - Pink Sheet, 13 May, 2024.)