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Diversity Action Plans: regulatory requirements and clinical trial enrollment goals

Contributors

Beatriz Rocha, MD, PhD, Chief Regulatory Liaison Officer, Fortrea

Alicia Baker McDowell, DRSc, MS, EMBA, Head of Regulatory Strategy and Product Development Consulting, Fortrea

The U.S. FDA's Omnibus Reform Act of 2022 (FDORA) was enacted in December 2022 and included provisions to promote diversity and inclusion in clinical trials. To help sponsors reach their diversity goals throughout the regulatory process and trial execution, this white paper discusses the FDA's requirement for a Diversity Action Plan. Learn what to expect and how you can best support your Phase III or pivotal study equivalent clinical trials of new drugs or devices with registrational intent.

Understanding the importance of diversity in clinical trials

In an ideal world, the participants in a clinical trial would reflect the race and ethnicity of those who will use the medication in the real world. Reaching a broad study population helps understand how a medical product affects people of different races and ethnicities, yet the past and even current disparities in clinical trial populations are well known.

Consider the example of the inclusion of Black Americans with cancer in clinical trials. Black Americans constitute at least 13% of the general population in the U.S.[1] Even though the death rate from cancer is higher in this population, Black Americans are still underrepresented in cancer clinical trials.[2]

Researchers have examined the barriers for inclusion of Black Americans in clinical trials. Some barriers are related to the clinical trial itself, such as the design, eligibility, sites and long enrollment periods. Other factors are directly related to patients and the health system. Of relevance is the limited access to healthcare that is prevalent in this population, a lack of trust in healthcare systems[3] as well as the lack of incentive to participating hospitals.[1]

While the FDA has previously encouraged sponsors to include traditionally underrepresented demographic subgroups, the new law gives the FDA authority to require and enforce diversity in clinical trials.

Following the progression of U.S. legislation leading to Diversity Action Plans

The FDA first published draft guidance in April 2022, which recommended that sponsors develop Diversity Action Plans.[4] On December 29, 2022, legislation was passed, which contained several provisions to promote diversity in clinical trials and to support the FDA's evaluation of safety and efficacy. This included requirements for the FDA to finalize guidance on clinical trial Diversity Action Plans.

The U.S. FDA continues to intensify its focus on improving diversity in clinical trials, and in November 2023, it published information about clinical trial participation that highlights the importance of the inclusion of a diverse population in clinical trials and provides resources to potential participants.[5]

On June 26, 2024, another draft guidance was published: *Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies*.[6] This draft guidance is now open for comments through September 26, 2024. Until the final version is published, it replaces the FDA's previous guidance published in April 2022. Once the guidance document is finalized, 180 days after its publication, an FDA-agreed upon Diversity Action Plan will be required for Phase III enrollment, or any pivotal study in the U.S., of new drugs or medical devices and diagnostics that use the 510(k), premarket approval (PMA), *de novo* and investigational device exemption (IDE).

Aligning with the FDA's current request for data pertaining to underrepresented populations

Since 2022, the FDA has asked sponsors to discuss their plans to ensure diversity and inclusion of underrepresented populations in pivotal clinical trials.[4] Even though ongoing Phase III studies and those starting in 2023 and 2024 have been grandfathered in, sponsors have been preparing Diversity Action Plans and submitting them to the FDA. They are actively gathering the agency's feedback to better prepare for studies that will start once approval of a Diversity Action Plan is mandated. The FDA has also been enforcing diversity in the post-approval space. Even though a Diversity Action Plan is not mandated, the lack of diversity in a clinical trial population can still result in a post-marketing commitment study.

As mentioned earlier, a Diversity Action Plan for all Phase III/pivotal studies applies to any investigational drug/biologic or medical device studies that will support a marketing application. This requirement applies to pediatric and rare diseases, but not to expanded access programs.

The Diversity Action Plan should be submitted to the FDA before the protocol is submitted for a Phase III or other pivotal study and can be modified after submission. The FDA *may* consider one Diversity Action Plan for an indication covering multiple studies. Finally, if the inclusion of a certain population is impractical or unreasonable, the sponsor can submit an official waiver request and FDA will review it within 60 days.

At a high level, a Diversity Action Plan includes a sponsor's goals for enrollment, the rationale for the goals and an explanation of the plans to meet the goals. Even though enrollment targets are determined with basis in the U.S. population data, they will apply to global research programs.

At a more detailed level, the Diversity Action Plan includes four main sections:

1. **Title page**
   - Product name
   - IND/IDE number, or other relevant submission information
   - Proposed indication(s) for use statement and intended use
   - Clinical study identification information
   - Diversity Action Plan version number and date

2. **Goals for enrollment**
   - State enrollment goals, disaggregated by race, ethnicity, sex and age group (following relevant FDA guidance categories/definitions) of the clinically relevant study population

3. **Rationale for enrollment goals**
   - Describe rationale for enrollment goals, including methodology used to derive target enrollment goals
   - Describe how an individual clinical study contributes to overall enrollment goals for the clinical development program (even though an individual study may not have proportionate representation)
   - Rationale should also include:
     - Data and information that describe the potential for differential safety and effectiveness (e.g., differences in pharmacokinetics/pharmacodyamics (PK/PD)
     - Data regarding genetic differences in PK, PD, safety or effectiveness (e.g., sex, age or genetic variations that may impact drug metabolism or susceptibility to adverse reactions)
     - Relevance of other population-level or individual characteristics which available data suggest may impact clinical outcomes (geographic location, socioeconomic status [SES] or comorbidities)
   - Include citations for sources of data and information for which enrollment goals are based

4. **Measures to meet enrollment goals**
   - Describe enrollment and retention strategies for the study population that support diversity and representativeness (such as community engagement, cultural competency and proficiency training for trial staff, participant awareness and knowledge of study, participant experience [reduction of burden], site location and access, and study decentralization [where appropriate])
   - Describe plan to monitor enrollment goals and actions to meet targets or mitigations to overcome barriers

Our role in promoting diversity in clinical trials

At Fortrea, we're committed to helping sponsors increase diverse representation of populations in their clinical trials and have implemented a complete and integrated solution across our Consulting and Clinical Operations services. We can provide an appropriate framework for success based on our:

- Diversity in Clinical Trials Multifunctional Workstream and Advisory Board
- Methodology for writing a Diversity Action Plan, including real-world data (RWD) and literature to identify the targets and propose the goals
- Innovative analytical dashboard that tracks real-time progress of enrollment in the different populations
- Final Diversity Action Plan report writing and submission to regulators
- An Integrated Research Organization (IRO) strategy

From protocol development to study close, we have been providing innovative diversity solutions to support sponsors with establishing, monitoring and reporting on Diversity Action Plan metrics in their clinical trials. Our comprehensive solution helps:

- Inform and develop targeted recruitment strategies for specific populations, including patient advocacy groups
- Write, submit and engage with regulators and support the final report writing and submission
- Incorporate the Voice of Patient to understand patients' needs and support protocol optimization and capture feedback at the close of the study to continually improve the Diversity Action Plan design
- Assess the impact and track progress toward study enrollment goals (and potentially identify safety signals) with a real-time dashboard
- Perform corrective actions and adjust enrollment and retention strategies based on findings presented in the dashboard

Together with our sponsors, learn how we're advancing our shared goals to bring clinical research closer to all.

Diversity and Inclusion in Clinical Trials

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