Decentralized Trials & Research Alliance

Response to Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies; Guidance for Industry

(Notice #FDA-2021-D-0789)
Submitted to the Food and Drug Administration (FDA)
Submitted on behalf of the Decentralized Trials & Research Alliance (DTRA)
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Background

The Decentralized Trials and Research Alliance (DTRA) is a non-profit collaboration with over 50 member organizations working together to ease the global adoption of decentralized research methods. DTRA members represent bio-pharmaceutical companies, technology and service providers, site networks and research centers, advocacy groups, and government agencies.

DTRA workstreams have produced a number of valuable resources which we encourage the FDA to leverage as they consider the implementation of DCTs. Examples include a glossary of DCT terms, best practices handbook, patient journey maps, and evidence of DCT impact. DTRA also remains actively engaged with interested parties who are seeking more information about decentralized clinical trials.

DTRA has engaged with multiple stakeholders to improve understanding and uptake of decentralized methods in clinical studies including:

- A Listening Session in 2023 for the NIH/NCATS RFI on Advancing Clinical and Translational Science through Accelerating the Decentralization of Clinical Trials. A recording of this listening session is available for review[1]. A copy of our response to the RFI is also available for review.[2]
- A listening session in 2023 for the FDA Decentralized Clinical Trials for Drugs, Biological Products, and Devices; Draft Guidance for Industry, Investigators, and Other Stakeholders; Availability and drafted a response of comments from our

[1] NIH/NCATS Listening Session - https://vimeo.com/820603329/6aa02fe714?share=copy

[2] Response to Advancing Clinical and Translational Science through Accelerating the Decentralization of Clinical Trials - https://shorturl.at/YCLP9

collective membership. A recording of this listening session is available for review.[3] A copy of our response to the RFI is available here.[4]

More broadly, DTRA welcomes the opportunity to share our membership's unique perspective and suggestions regarding federal initiatives to improve the decentralized trial research infrastructure and is pleased to provide our feedback and constructive suggestions to the Draft Guidance below.

The FDA Diversity Action Plan draft guidance (the DAP Draft Guidance) invites stakeholders throughout the scientific research, advocacy, clinical practice, industry, patient and lay communities, including the general public, to comment on recommendations for sponsors, investigators, and other stakeholders to meet requirements for submission of Diversity Action Plans as mandated by the US Congress via passage of the Food and Drug Omnibus Reform Act of 2022 (FDORA). These plans are intended to increase enrollment of participants who are members of historically underrepresented populations in clinical studies to help improve the strength and generalizability of the evidence for the intended use population.

Clinical trial participation can be a burden to patients and may disproportionately create barriers which may be mitigated through decentralized methods. As we modernize our clinical research enterprise to make it more patient-friendly, it will require reducing the exclusive reliance on hospitals and medical centers, and enabling broader access to patients, especially for participants from currently underserved or underrepresented communities, to trials. Utilizing decentralized trial elements and research methodologies offers significant potential to improve access to a greater segment of the population improving access to and diversity in clinical research participants. Investigational sites remain a cornerstone of our clinical research enterprise, but for a variety of reasons these institutions may sometimes fail to provide adequate access to traditionally underserved populations. A national plan for a modern clinical trial ecosystem meant to also support diversity and inclusion must include the thoughtful use of decentralized research methods.

General Comments

Importance of DCTs for Diversity Action Plans

Since its inception, DTRA's membership organizations have advocated that the use of decentralized clinical trial (DCT) elements can help reduce barriers to participation and enable greater and perhaps more diverse enrollment in clinical studies.

[3] DCT Draft Guidance Listening Session - https://vimeo.com/845089324/3ee09b1bfa?share=copy
[4] DCT Draft Guidance Response from DTRA Members - https://shorturl.at/TXCcj

DCT elements could enable reaching patients in their local communities rather than only at major research institutions. With that in mind, we believe there is a great opportunity to include community health care providers in the conduct of clinical research, either as investigators or in the conduct of standard of care assessments, with Investigator oversight.

The FDA's Diversity Action Plan guidance establishes clear new requirements for sponsors to proactively develop diversity action plans thus improving the possibility of enrolling such a patient population, and DCTs are a meaningful tool that could aid sponsors in reaching these goals. We commend the FDA for drafting this guidance and are supportive of its aim to improve diverse clinical trial participation.

FDA Transparency & Clarity for DCT Expectations

Recognizing the potential for DCT methodologies to support trial diversity goals, FDA should continue to prioritize transparency and clear expectations for sponsors leveraging decentralized methodologies in trials. This could include noting in approval documents, or other public-facing materials, when decentralized methodologies have supported diversity strategies (while preserving existing commercially confidential sponsor information).

We note the efforts already started through C3TI and are supportive of the center or other FDA groups closely involved with clinical innovation continuing them– whereby case studies and FDA-perspectives on innovative trial methodologies are shared with the public. Ultimately, FDA perspectives on how trials using DCT elements can be designed in a manner that ensures high-quality and acceptable data will help drive risk-averse sponsors to adopt more innovative and patient-friendly decentralized methodologies. Greater sponsor acceptance of patient-centric and decentralized methodologies should help drive greater reach of trials to previously underrepresented populations.

Annual Congressional DAP Progress Reports

Pursuant to Section 3604 of the 2022 Food and Drug Omnibus Reform Act (FDORA), FDA is required to submit annual reports summarizing the status of sponsor DAP submissions. Within these reports, we recommend including any available aggregated data which describes if any DCT methodologies have been used and if so, if they have had a notable impact on meeting sponsor DAP goals. This ensures that successful practices are shared broadly alongside any limitations to particular methodologies. Since measures to meet enrollment goals (see Lines 385-421) are a critical component of a DAP submission, it will be important to have regular and consistent readouts of which methodologies have proven effective in advancing these research objectives. These reports can also highlight any barriers that sponsors and FDA face as they look to

implement decentralized and other innovative trial methodologies. In addition to submitting the reports to Congress, FDA should make the report available to the public. Since multiple methods might be used by sponsors to meet their DAP goals, making the report searchable by methodology might be a functionality that FDA might consider building e.g. use of wearables, use of local labs etc.
As always, DTRA would be happy to partner in collating some of these cross-industry use cases.

Support for Diversity Enrollment Goals through DCTs
If the FDA is able to share their willingness to accept DCT elements in studies, we believe this will encourage sponsors to include them in their study design, thereby improving access to studies and improving diversity.

1. Role of DCTs in Enhancing Diversity
   - FDA's guidance emphasizes the need for diversity action plans that are tailored to the demographic characteristics of the intended use population.
   - DCTs can reduce geographic and socioeconomic barriers faced by patient groups who are typically underrepresented in trials by providing options such as use of remote monitoring, teleconsults, local labs etc.

2. Leveraging DCTs Effectively Requires Consistent Reinforcement of Acceptability

   The FDA can help sponsors to adopt DCT methods through consistent receptivity to accepting those approaches. Maintaining trial integrity and data reliability are key points reinforced in the final Conducting Clinical Trials With Decentralized Elements Guidance[5] and are consistent expectations for all trials. We acknowledge that it will take time for trials using DCT methods to be conducted and analyzed. In the meantime, FDA can and must showcase successful approaches taken by sponsors to integrate any aspect of decentralization into studies to support diversity action plan objectives and successful trial conduct as a whole.

   By explicitly noting willingness to accept DCT elements in studies, FDA will encourage sponsors to include them in study design. This can improve access to studies, and diversity in participation. By being transparent in supporting the use of these DCT elements, the FDA can help create a virtuous cycle to improve access to and diversity in trials.

3. Emphasis on DCTs Without Specific Methodology

[5] Conducting Clinical Trials With Decentralized Elements Guidance for Industry, Investigators, and Other Interested Parties - https://www.fda.gov/media/167696/download

- DTRA recognizes that the FDA DAP draft guidance acknowledges the potential of innovative methodologies, such as DCTs, to increase diversity in clinical trials, especially from underrepresented populations.
- The draft guidance does not provide a detailed framework for applying DCTs in achieving diversity objectives; however, it does broadly encourage innovation in trial design. We would respectfully suggest that FDA highlight successful DCT approaches in its annual report to Congress.

Transparency and Communication with Sites

Transparency and clear communication between sponsors and clinical trial sites regarding diversity goals and expectations is essential early in the trial design and conduct stages Continued engagement is important to ensure sites are partners in helping reach enrollment goals.

Sites often lack visibility into sponsors' diversity targets and how they are performing against those goals. In fact, we suggest that the ability for sites to support diversity action plan objectives becomes a key consideration in site selection for trials. Sites can help sponsors understand and evaluate which approaches are or are not scalable, successful and practical.

More transparency and collaboration between sponsors and sites would help drive accountability and engagement, enabling sites to better support diversity efforts. The draft guidance section on “Measures to Meet Enrollment Goals” (starting on line 385) would be appropriate for stating that sponsors should communicate enrollment targets and strategies for achieving targets with clinical investigators (e.g. during an investigator meeting). Furthermore, it would be helpful for the final guidance to provide examples of what supportive measures sponsors can offer to sites to help them achieve diversity objectives, and which are not appropriate (e.g. financial, legal or oversight limitations) We also encourage FDA to hold listening sessions with representatives of sites so the agency can hear directly from the frontlines of clinical trials. DTRA would be happy to facilitate such discussions as we believe deeply in the power of stakeholders working together to resolve challenges.

Defining and Standardizing Diversity Metrics

Clinical trials are multi-regional and global in scope. Thus, varying definitions and classifications of terms such as ‘race’ and ‘ethnicity’ across countries and regions create challenges in understanding, interpreting, adopting and applying diversity metrics. Current differences in how race and ethnicity are understood and recorded between regions risks undermining the comparability and generalizability of trial results across diverse populations. The lack of alignment can lead to discrepancies in trial design, recruitment efforts, and the analysis of safety and efficacy data.

We recommend that the FDA consider partnering with other regulatory agencies to establish globally harmonized definitions of the terms 'race' and 'ethnicity'. This would constitute a significant and influential change to ensure the data from global trials are meaningful to the intent-to-treat population in multiple regions. Aligning on these definitions will allow for better cross-trial data comparison and integration and will enhance the robustness of diversity efforts across global drug development programs. Additionally, global alignment on these definitions is essential to clearer data reporting, resulting in more comprehensive and accurate reports. DTRA encourages the FDA to continue fostering and engaging in international dialogue on this issue and to work toward a unified framework that accounts for the complexities of race and ethnicity across different societies.

Applying Diversity Action Plans Globally

DTRA requests FDA consider clarifying how the Diversity Action Plan guidance applies to global clinical trials. Specifically, is it acceptable for sponsors to set diversity objectives based on US incidence and prevalence data, while still leveraging data from ex-US sites to support those goals. Disease epidemiology may differ from region to region but may be helpful to achieve overall diversity participation objectives in trials conducted multi-regionally.

Guidance is needed on the appropriate use of global data to meet US-focused diversity requirements. This would include the level of justification a sponsor would have to provide to demonstrate the applicability of global data to the intended-use US patient population.

Summary

DTRA thanks the FDA for issuing the draft Diversity Action Plan guidance to support the need for diverse clinical trial participation. We wholly endorse the need for representative participation to ensure the collection and analysis of the most robust and applicable safety and efficacy data as new treatments are developed. We believe that the use of DCT elements can be a foundational part of achieving diverse patient participation both within the US and globally. We welcome the opportunity to clarify any comments or to partner on developing additional supportive materials aligned to DAP guidance and its application.

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