U.S. FOOD & DRUG ADMINISTRATION

ADEPT-9: Public Workshop on Enhancing Diversity in Therapeutics Development for Pediatric Patients

Overview of the Public Workshop to Enhance Clinical Study Diversity (November 2023)

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OMPI | OMP | CDER | FDA

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Disclaimer

The speaker has no conflicts of interest to disclose

Enhancing Diversity in Clinical Trials

- Clinical trials provide critical evidence regarding whether a medical product is safe and effective
- Clinical trials should, to the extent possible, enroll a population that is representative of the diversity of the population that will use the medical product, if approved
- FDA is committed to increasing the participation of underrepresented populations in clinical trials through:
  - Issuing guidance(s)
  - Encouraging the use of innovative trial designs and technologies (e.g., decentralized clinical trials, digital health technologies)

Public Workshop to Enhance Clinical Study Diversity

November 29 – 30, 2023 / 10 a.m. – 2:00 p.m. EST

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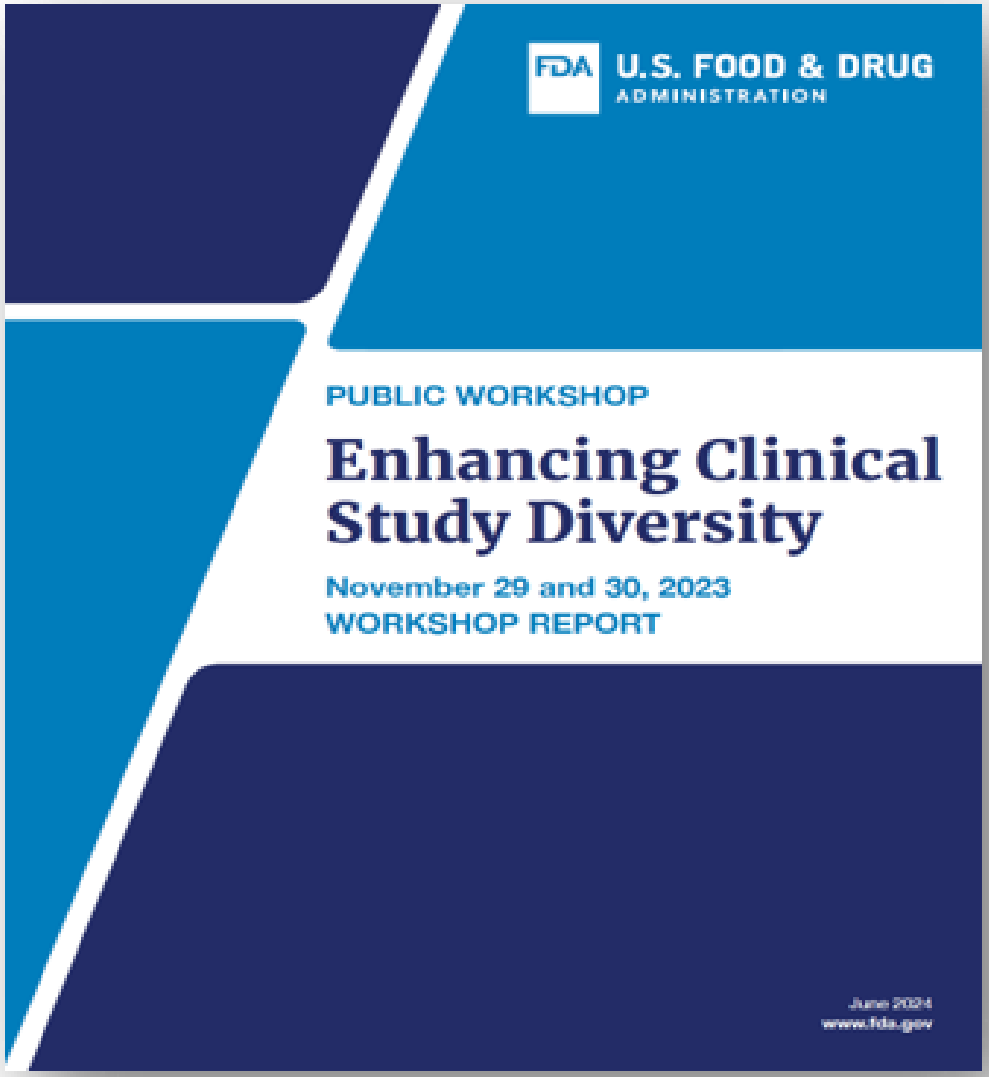
CLINICAL TRIALS TRANSFORMATION INITIATIVE

- Two-day virtual public workshop
- Fulfilled FDORA Section 3603 requirements
- Solicited input on increasing the enrollment of historically underrepresented populations in clinical studies

- Workshop Attendees
  - FDA and other federal agencies
  - Academia
  - Medical device and pharmaceutical sponsors
  - Patients and patient advocacy groups
  - Research study teams

Workshop Report: Enhancing Clinical Study Diversity



[Workshop Report: Enhancing Clinical Study Diversity]

Overview of Workshop Topics

- Clinical Study Diversity – A Brief Overview: Where Are We Now?
- Establishment of Clinical Study Enrollment Goals and Use of Disease Prevalence or Incidence Data
- Approaches to Support the Inclusion of Underrepresented Populations and to Encourage Clinical Study Participation
- Appropriate Use of Decentralized Studies, Digital Health Tools, and Other Trial Elements to Support the Inclusion of Underrepresented Populations in Clinical Studies
- Post-Approval Dissemination of Clinical Study Enrollment Demographic Data to the Public
- Community Engagement
- Moving Forward

Introduction: Where Are We Now

- Certain populations continue to experience barriers to accessing innovative treatments in clinical trials following approval, which can result in adverse health outcomes
- Barriers that are common across several historically underrepresented groups
  - distrust in the research enterprise;
  - not being referred to clinical studies;
  - restrictive eligibility criteria;
  - transportation problems;
  - inflexible trial visit and procedure windows;
  - receipt of clinical trial materials that are not appropriate to a participant's language, reading level, or knowledge capacity; and
  - lack of community engagement that can foster enrollment of populations that typically do not enroll
- Efforts to address common barriers (in addition to barriers specific to a demographic group) can help achieve a trial population that is more reflective of the population that will use the medical product, if approved

Strategies to Overcome Barriers to Diverse Trial Enrollment

- Diversify trial investigators, staff, and sites
  - Better engagement and successful recruitment of a diverse population;
- Provide language-appropriate cultural literacy and sensitivity training for trial staff
- Be mindful of underlying lack of information about, interest in, or trust in clinical trials
  - Especially in those who have been historically excluded
- Demonstrate trustworthiness and in turn earn their trust
- Understand the demographic, political, social, cultural, and health care environments in which populations affected by a given disease exist
- Engage a diverse patient population in the process before the clinical study protocol is drafted
- Simplify informed consent forms

Strategies to Overcome Barriers to Diverse Trial Enrollment (cont)

- Employ targeted patient engagement plans
- Utilize enhanced site selection and inclusive patient educational materials
- Use decentralized trial tools and digital technologies
- Choose sites located in diverse areas
- Utilize protocol optimization with inclusive study design elements
- Use patient concierges to help with scheduling and reimbursement for travel and transportation

Establishment of Clinical Study Enrollment Goals

- Establish goals based on the three stages of clinical trial participation and the challenges of each stage - Initial approach, recruitment, and retention
- For device trials, consider relevant characteristics of various populations with the disease early in device design. Meet with engineers, physicians, and patients in the initial planning stages to understand implantation constraints and long-term patient concerns
    - Historically, women have been excluded from some medical device trials because the sizes of the devices limited enrollment of participants with smaller body sizes
- Leverage available data sources to derive disease prevalence, such as registries and national or global health care databases

Other Approaches to Support the Inclusion of Underrepresented Populations

- Collect and track relevant demographic data in real time and conduct ongoing data-driven assessments of diversity and representativeness
- Dispel the myths, misconceptions, and fear about including certain populations such as pregnant persons and persons with disabilities and complex health conditions in clinical trials
- Shift the paradigm of protecting vulnerable populations ***from*** research to protecting complex populations ***with*** research
- Change the clinical trial ecosystem from the status quo of default exclusion of people with disabilities. Investigators and sponsors must make a case for exclusion based on a clear scientific or ethical rationale
- Provide better education about mental illness to address stereotypes
  - Mental illness does not necessarily make a patient less likely to adhere to the requirements for participation in the trial, either due to hospitalizations or being more likely to drop out of the trial

Use of Decentralized Studies (DCTs) and Digital Health Tools To Support the Inclusion of Underrepresented Populations

- Use of DCTs to improve participant experience and access, particularly for those living in rural or underserved areas and patients with disability
- Leverage DCTs to maintain trials in an unpredictable environment
  - For example, a pandemic or severe weather conditions when participants cannot travel to trial sites
- Incorporate DCT elements in trials conducted at the point of care to help increase opportunities for participation in research
- Evaluate appropriateness of DCTs and digital health technologies
  - Consider availability of broadband or smartphone access and digital literacy
- Build a human connection with participants and communities

Post-Approval Dissemination of Clinical Study Enrollment Demographic Data to the Public

- Develop communications that are patient-centric, reflect an understanding of the patient community's needs, and address the trustworthiness of researchers and their investment in helping the community
- Protect the privacy of participants and clearly explain the broader context of the study's purpose and outcomes
- Transparently and accurately portray the study results and share demographic information to highlight the importance of representative clinical research
- Use plain language with visual aids to make study results more understandable
- Put procedures in place to guarantee that the information being communicated is accurate

Community Engagement

- Work collaboratively with community- and faith-based organizations to speak to communities through a voice of trust
- Convey information about how participating in research can benefit their community and the wider patient community
- Build capacity, competence, and resources within these communities as part of the overall strategy to overcome distrust and improve clinical trial diversity
- Implement proactive, collaborative, and sustainable community-based investments with a bidirectional relationship between the researchers and the communities being engaged

To Achieve Meaningful Representation in Clinical Trials

- Responsive guidelines that are informed by the community
- Engagement and communication
  - Sharing ideas
  - Sharing experiences
  - Sharing best practices
- Implementation of innovative approaches
- **"What got us here won't get us there"**

It Takes a Village!

- FDA
- Industry
- Academic Institutions
- Institutional Review Boards
- Clinical Investigators
- Trial personnel
- Clinicians
- Participants
- Patient Advocacy Groups
- Health care systems
- Other members of the diversity community

Training and Education are Critical

Diversity Action Plans

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

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (OCE) Lola Fashoyin-Aje, 240-402-0205, (CDER) Tamy Kim 301-796-1125, (CBER) Office of Communication, Outreach, and Development, 800-835-4709, or 240-402-8010, or (CDRH), CDRH Clinical Evidence Mailbox, CDRHClinicalEvidence@fda.hhs.gov.

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June 2024
Clinical/Medical

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Diversity Action Plans

- In June of 2024, FDA issued a draft guidance, Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies
- Guidance replaces draft guidance for industry titled Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials (April 2022).
- Public comments can be submitted through September 26, 2024 - Docket Number FDA-2021-D-0789
- The statutory requirement for submitting Diversity Action Plans applies to clinical studies for which enrollment commences after 180 days from the publication of the final guidance

Purpose of Diversity Action Plans

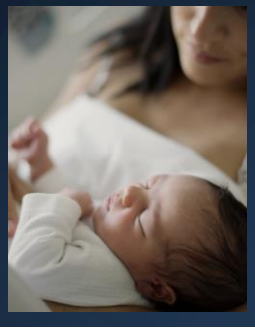
- Satisfies section 3602 of FDORA which requires that FDA update or issue guidance relating to the format and content of Diversity Action Plans (DAPs)
  - DAPs required by sections 505(z) and 520(g)(9) of the FD&C Act
- DAPs are intended to increase enrollment of participants who are members of historically underrepresented populations in clinical studies
  - helps improve generalizability of the results to the intended use population
- Assist sponsors in meeting the requirements for the submission of Diversity Action Plans
  - describes format and content of DAP (timing & process for submitting DAPs)
  - describes criteria & process for evaluating sponsors' requests for waivers from section 505(z) or 520(g)(9) of the FD&C Act
  - provides general recommendations for sponsors to publicly post key information regarding DAPs

Clinical Studies Requiring DAPs

- **Drugs** – A clinical investigation that is a phase 3 study (as defined in 21 CFR 312.21), or as appropriate, another pivotal clinical study of a drug (other than a bioavailability or bioequivalence study)
- **Devices -**
  - DAP must be included in IDE application to FDA
  - For studies not requiring an IDE application to FDA, DAP must be included in:
    - premarket notification (i.e., 510(k) submission)
    - request for classification (i.e., De Novo classification request)
    - application for premarket approval (i.e., PMA application)
- FDA strongly recommends that sponsors develop and implement a comprehensive diversity strategy across the entire clinical development program, including in early studies, when possible

Content of DAPs

- Under sections 505(z) and 520(g)(9) of the FD&C Act, a DAP must include:
  - goals for enrollment in the clinical study, disaggregated by race, ethnicity, sex, and age group of clinically relevant study populations
  - rationale for such goals
  - explanation of how the sponsor intends to meet such goals
- Guidance describes the form & content of a DAP and provides recommendations to help ensure that the requirements of a DAP are met



Selected FDA Guidances for Industry

- *Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies (Draft Guidance, June 2024)*
- *Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for FDA-Regulated Medical Products* (Draft Guidance, January 2024)
- Decentralized Clinical Trials for Drugs, Biological Products, and Devices (Draft Guidance, May 2023)
- *Digital Health Technologies for Remote Data Acquisition in Clinical Investigations* (Final Guidance, December 2023)
- *Inclusion of Older Adults in Cancer Clinical Trials* (Final Guidance, March 2022)
- *Enhancing the Diversity of Clinical Trial Populations—Eligibility Criteria, Enrollment Practices, and Trial Designs* (Final Guidance, November 2020)
- *Clinical Lactation Studies: Considerations for Study Design* (Draft Guidance, May 2019)
- *Postapproval Pregnancy Safety Studies* (Draft Guidance, May 2019)
- *Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials* (Draft Guidance, April 2018)
- *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies* (Final Guidance, September 2017)
- Evaluation of Sex-Specific Data in Medical Device Clinical Studies (Final Guidance, August 2014)
- *E7 Studies in Support of Special Populations: Geriatrics* (Final Guidance, August 1994)

Acknowledgements

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