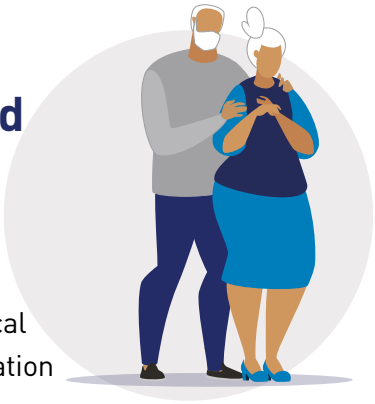
U.S. FOOD & DRUG ADMINISTRATION

Guidance Snapshot

Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs

Final Guidance



What is recommended in the guidance?

This guidance discusses approaches that sponsors can take to increase enrollment of underrepresented populations in clinical trials that are intended to support a new drug application or a biologics license application. It also discusses representing demographic and non-demographic characteristics[1] in study populations. This guidance provides recommendations on the following:

1. Broadening eligibility criteria and avoiding unnecessary exclusions in clinical trials to increase diversity in enrollment
2. Designing trials that are accessible
3. Adopting enrichment strategies
4. Applying the recommendations for broadening eligibility criteria to clinical trials of drugs intended to treat rare diseases or conditions

Why is clinical trial diversity important?

Enrolling participants with a wide range of baseline characteristics may create a study population that more accurately reflects the patients likely to take the drug, if approved. It also may uncover differences by demographic and non-demographic characteristics that maybe important for safe and effective use of the investigational drug.

[1]Demographic characteristics are considered characteristics such as sex, race, ethnicity, age, location of residency, while non-demographic characteristics are considered patients with organ dysfunction, comorbid conditions, disabilities, those at the extremes of the weight range, and populations with diseases or conditions with low prevalence.

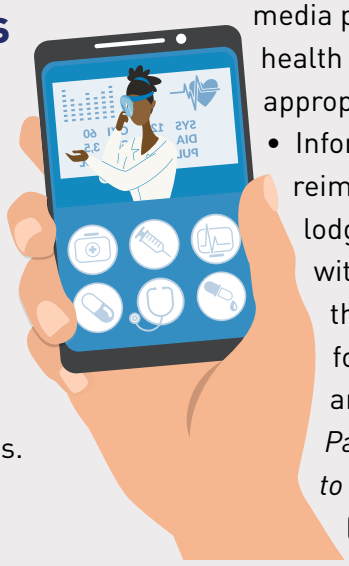
Broadening Eligbility Criteria to Increase Diversity in Enrollment

How can sponsors make their clinical trials more inclusive?

- Ensure, when developing clinical trial protocols, that eligibility criteria are representative of the population for whom the drug has been developed.
- Examine each exclusion criterion and determine whether it is necessary to help assure the safety of trial participants or to achieve the study objectives. If it is not necessary, consider eliminating or modifying the criterion to expand the study population.
- Consider whether exclusion criteria from phase 2 studies can be eliminated or modified for phase 3.
- Consider characterizing the drug metabolism and clearance across populations that may metabolize or clear the drug differently early in clinical development.
- Consider using an adaptive clinical trial design[2] that would allow for pre-specified trial design changes during the trial when data become available, including altering the trial population.
- Consider creating a broader pediatric development program that does not arbitrarily limit the study population and unnecessarily delay development of medicines for children. including pharmacokinetic sampling to establish dosing in individuals who become pregnant during a trial.
- Consider including a reasonable sample of marker-negative participants who have the disease but do not meet the enrichment criteria.

How can sponsors make clinical trials less burdensome for participants?

- Reduce the frequency of in-person study visits and consider flexibilities in visit times.
- Enlist mobile medical professionals, such as nurses and phlebotomists, to visit participants instead of requiring participants to visit distant clinical trial sites.
- Replace visits to clinical trial sites with electronic communication tools and devices, such as telephones/mobile phones, secured email, social media platforms, or digital health technologies, where appropriate.



- Inform participants of possible reimbursements for travel, lodging, and costs associated with participation in trials. See the information sheet guidance for institutional review boards and clinical investigators *Payment and Reimbursement to Research Subjects* (January 2018).[3]

[2]See the guidance for industry *Adaptive Design Clinical Trials for Drugs and Biologics* (November 2019). For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[3]For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

How can sponsors improve their clinical trial enrollment and retention practices to enhance inclusiveness?

ENROLLMENT

- Enroll participants who reflect the characteristics of clinically relevant populations regarding age, sex, race, and ethnicity. Consider having a diverse clinical trial staff to facilitate enrollment and retention of diverse participants.

GENERAL ENGAGEMENT

- Educate participants about clinical trial participation. Industry, patient advocacy groups, medical associations, and other stakeholders can consider collaborating to educate participants about clinical trial participation.
- Ask for patient feedback. For more information, see the guidance for industry, FDA staff, and other stakeholders *Patient-Focused Drug Development: Collective Comprehensive and Representative Input* (June 2020).[4]
- Engage medical societies, focus groups, community advisory boards, and disease registries to meet the needs of potential participants. More information is available at the National Institute on Minority Health and Health Disparities' *Community-Based Participatory Research Program* website.
- Hold recruitment events frequently and offer them during evenings and weekends.
- Consider holding the events in nonclinical but trusted locations, such as places of worship or community centers; social places of business, such as barbershops and beauty salons; and public events, such as cultural festivals, carnivals, and parades.
- Use online/social media recruitment strategies to identify participants for whom traditional referral centers are not accessible.

CULTURAL COMPETENCY

- Provide research staff with cultural competency and proficiency training to facilitate building of trust with participants.
  - Avoid the use of cultural generalizations and stereotypes.
  - Share trial resources and documents in multiple languages and use multilingual research staff and/or interpreters.
  - Remain engaged with communities after the clinical research ends and share trial updates to continue strengthening relationships with communities.

GEOGRAPHY

- Ensure that clinical trial sites include geographic locations with a higher concentration of racial and ethnic minority patients and indigenous populations, as well as locations within the neighborhoods where these populations receive their health care.

TRIAL EFFICIENCY

- Consider using real-world data to promote more efficient recruitment of a diverse population by using, for example, claims data and electronic health records to identify potential sites and participants.
- Consider using "electronic informed consent" to allow participants to read and sign necessary forms remotely instead of traveling to a clinical trial site, while ensuring that all potential participants, including those with literacy issues, understand all necessary information.

How can sponsors improve diversity in clinical trials for rare diseases?

- Early in the drug or biologic development process, engage with patient advocacy groups, experts in the rare disease, and patients with the rare disease; ask for their suggestions on the design of trials, including trial procedures.
- Re-enroll participants from the early-phase trials into later-phase trials when medically appropriate and scientifically sound to ensure that participants continue to have access to the investigational drug or biologic based on tolerability and benefit.
- Refer to the following guidance: *Rare Diseases: Common Issues in Drug Development* (January 2019).[4]

As a sponsor, where can I obtain more information?

- Clinically Relevant Population - FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data
- Older Adult Populations
- Pregnant Women - Task Force on Research Specific to Pregnant Women and Lactating Women
- Participants with Rare Diseases - Rare Diseases: Common Issues in Drug Development Guidance
- FDA's Office of Women's Health web page
- Oncology Center of Excellence's Project Equity
- FDA's Consumer Updates web page
- FDA's Office of Minority Health and Health Equity web page
- Office for Human Research Protections (OHRP) web page
- NIH Clinical Research Trials and You web page
- Clinicaltrials.gov web page, a database of privately and publicly funded clinical studies conducted around the world
- ResearchMatch, which connects researchers with people who are interested in participating in clinical trials

[4]For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

Guidance Recap Podcast - Hear Highlights Straight from FDA Staff

Speakers: **Jamie Gamerman, JD, Regulatory Counsel, Office of Medical Policy**

Click here to listen **Click here to read transcript**

Guidance Snapshots are a communication tool and are not a substitute for the guidance document. To learn more about enhancing the diversity of clinical trials, read the guidance.

To see additional Guidance Snapshots, check out the pilot program.