Enhancing the Diversity of Clinical Trial Populations: An Overview of FDA's Guidance on Clinical Trial Diversity

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Disclaimer: The views expressed are those of the speaker and should not be construed to represent FDA's views or policies.
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Learning Objectives

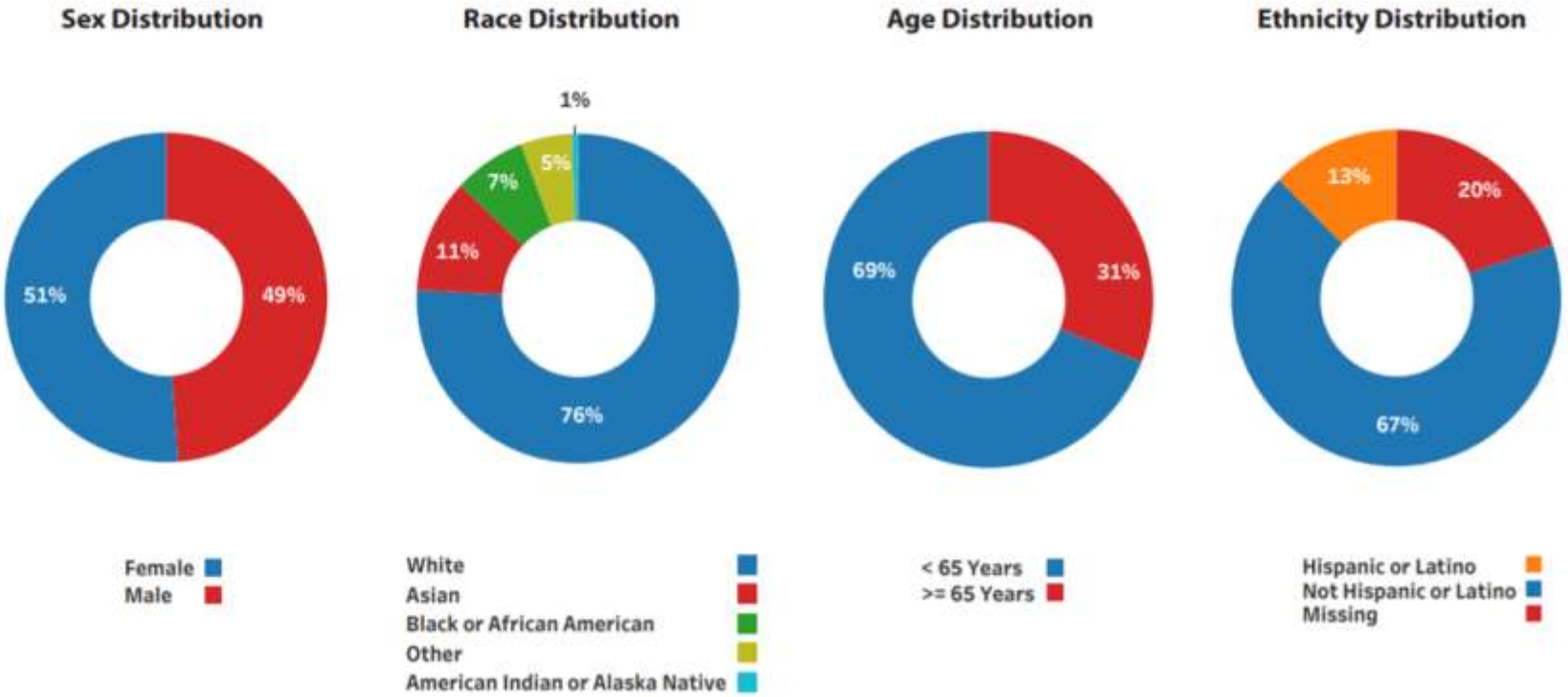
- Discuss FDA's final guidance *Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs*
- Review FDA's recommendations on achieving a clinical trial population that represents the population of patients that will use the drug, if approved, through:
  - Trial practices and designs to improve clinical trial diversity
  - Enrollment, recruitment, and retention practices to promote inclusivity
  - Recruitment and retention practices specific to trials for drugs intended to treat rare diseases

Background - Clinical Trial Diversity

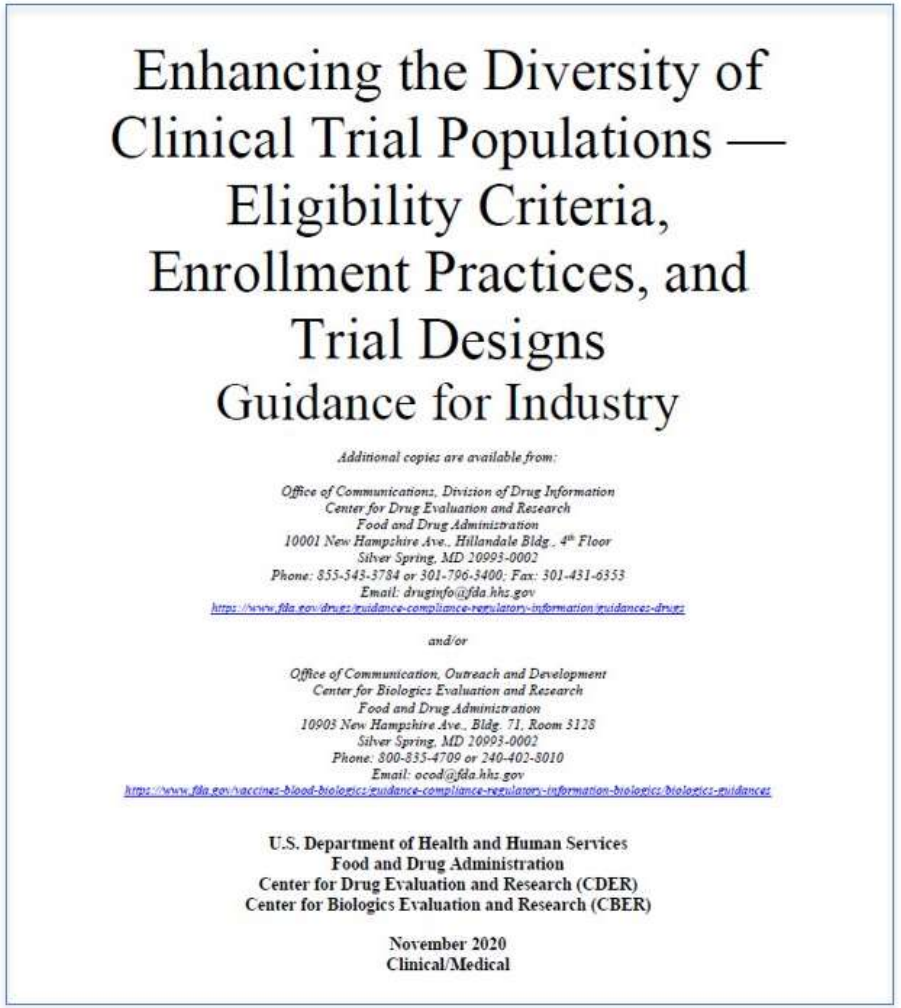
Diversity Landscape

Demographic	Non-demographic
Age	Patients with comorbidities
Sex and Gender	Patients with disabilities
Race	Patients with rare diseases
Ethnicity	Patients at the extremes of BMI range
Geographic residence (rural, urban)	Patients with organ dysfunction

Current State of Trial Diversity



*2015-2019 DRUG TRIALS SNAPSHOTS SUMMARY REPORT



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

Guidance for Industry

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

and/or

Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010
Email: ocod@fda.hhs.gov
https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 2020
Clinical/Medical

Background- *Enhancing the Diversity of Clinical Trial Populations*

- FDA Reauthorization Act of 2017 required a public meeting and publication of a draft and final guidance on improving clinical trial diversity
- Public Meeting held April 16, 2018
- Draft Guidance *Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs* published June 2019
  - FDA received approximately 90 public comments in response to the guidance
- Final guidance published November 2020

Definition: Eligibility Criteria

- Guidelines for entry into a clinical trial, i.e., the characteristics the participants must or must not have to be able to participate in the study (often referred to as inclusion and exclusion criteria)
- Include evidence that a participant has the disease or condition under consideration, at times for a defined minimum duration, defined severity, and with particular symptoms or signs
- May also include characteristics such as age, sex, medical history, current health status, presence or absence of certain genotypes, blood pressure or other physiologic parameter, and absence of certain diseases
- For more information on clinical trials, see FDA's Basics About Clinical Trials

Recommendations on Improving Clinical Trial Diversity

Inclusive Trial Practices

- Develop specific eligibility criteria for each trial - avoid templates
- Ensure eligibility criteria are representative of diverse participants when developing clinical trial protocols
- Eliminate restrictive criteria, e.g., when moving from Phase 2 to Phase 3 trials

Inclusive Trial Practices (Continued)

- Enroll participants from clinically relevant populations
  - Include both sexes in clinical trials to allow detection of clinically significant sex-related differences when appropriate
  - Justify age restrictions - include pediatric and geriatric patients when appropriate
  - Include race and ethnic minorities in trials and analysis to identify differences in responses to medical products in distinct population subgroups; include a plan for inclusion of relevant populations by end of Phase 2 meeting

Trial Designs

- In early clinical development, characterize drug metabolism and clearance across populations that may metabolize or clear the drug differently
- Use adaptive clinical trial designs (e.g., start with a narrow population and later expand to a broader population)
- Consider a broader pediatric development program early - justify age-based enrollment staggering

Trial Designs (Continued)

- Consider including pharmacokinetic sampling to establish dosing in individuals who become pregnant during a trial*
- Consider including a broader participant group even in enriched clinical trials

*For more information on including pregnant individuals in clinical trials, see the draft guidance for industry Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials

Study Conduct

- Make trials less burdensome:
  - Use mobile medical professionals (e.g., nurses, phlebotomists, mobile clinical trial units, mobile health clinics)
  - Reduce the frequency of in-person visits and consider electronic communication (e.g., email, social media, telephone)
  - Consider digital health technology tools
- Make participants aware of financial reimbursements

Recruitment

- Hold recruitment events on nights and weekends and in non-clinical locations (e.g., places of worship, social commercial venues, public events)
- Recruit using real-world data (e.g., claims data, electronic health records) and social media
- More inclusive strategies for public outreach and education (e.g., patient-focused research)
  - Consult patient advocacy groups and medical associations to educate patients about potential trials
  - Engage communities through focus groups, medical societies, and disease registries*

*For more information, see Integrating Research into Community Practice — Toward Increased Diversity in Clinical Trials

Retention

- Provide trial documents in multiple languages and at a literacy level appropriate for all patients
- Design clinical trial protocols along with patients, patient advocates, and caregivers
- Hold clinical trials in locations with higher concentrations of racial and ethnic minorities
- Use electronic informed consent, while considering the needs of patients without internet access
- Explore agreements to facilitate the exchange of medical records between clinical trial sites

Rare Diseases

- Engage with rare disease patients and their advocates early in the trial design process
- Re-enroll patients from early-phase trials into later-phase trials
- Use open-label extension studies

Available FDA Resources

- Beyond guidance documents, FDA promotes the following tools to encourage clinical trial diversity:
  - Drug Trials Snapshots: publishes demographic data on clinical trials
  - Consumer Update webpage: provides general information on clinical trials for consumers
  - Many Clinical trial resources: published by FDA's Office of Minority Health and Health Equity

Challenge Questions

1. All of the following are examples of demographic characteristics of patient populations except:

   a) Age

   b) Sex

   c) Comorbidity

   d) Race

Challenge Questions

2. In what year did FDA finalize its guidance *Enhancing the Diversity of Clinical Trial Populations*?

a) 2019

b) 2020

c) 2021

d) 2022

Challenge Questions

3. When does FDA recommend sponsors include a plan for inclusion of relevant populations?

a) End of Phase 2

b) End of Phase 3

c) End of Phase 1

d) Pre-IND

Summary

- Clinical trial populations should reflect the population of patients that will use the drug, if approved
- FDA's *Enhancing the Diversity of Clinical Trial Populations* guidance is one of many FDA resources for clinical trial sponsors supporting the diverse trial practices

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Questions?

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