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. The speaker has no conflicts of interest to disclose.
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

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Non-demographic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Patients with comorbidities</td>
</tr>
<tr>
<td>Sex and Gender</td>
<td>Patients with disabilities</td>
</tr>
<tr>
<td>Race</td>
<td>Patients with rare diseases</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Patients at the extremes of BMI range</td>
</tr>
<tr>
<td>Geographic residence (rural, urban)</td>
<td>Patients with organ dysfunction</td>
</tr>
</tbody>
</table>
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
10903 New Hampshire Ave., Bldg. 38, 8th Floor
Silver Spring, MD 20903
Phone: 301-796-1490, Fax: 301-421-8403
Email: druginfo@fda.hhs.gov
https://www.fda.gov/about-fda/regulatory-information/treatment-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 3138
Silver Spring, MD 20993
Phone: 301-488-4709 or 301-488-4710
Email: ocod@fda.hhs.gov
http://www.fda.gov/about-fda/regulatory-information/treatment-drugs

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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