U.S. FOOD & DRUG ADMINISTRATION

Oncology Center of Excellence

Clinical Trial Diversity -- Oncology Perspective and New FDA Policies

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Clinical Trial Diversity- Oncology Perspective

Diversity in clinical trials encompasses demographic characteristics and clinical characteristics:

- Ensures trial population is representative of population with disease/condition (e.g., based on distribution across various subgroups)

Medical products (i.e., drug, biological product, device) should be developed in a study population that is representative of the population for which the medical product is intended

- Trial population representativeness can be evaluated on the basis of clinical and other characteristics (e.g., race, ethnicity, sex, age group)

Scientific, regulatory, and ethical rationale for diversity and representativeness of the study population:

- Important to characterize drug effects in the context of diverse population benefits all;
- Disease presentation and drug response can vary within diverse populations;
- Facilitate generalizability of study results to the population affected by the disease;
- Generate evidence that is applicable to the U. S. population and U.S. medical practice;
- Provide equitable opportunities to contribute to science and to benefit from scientific advances.

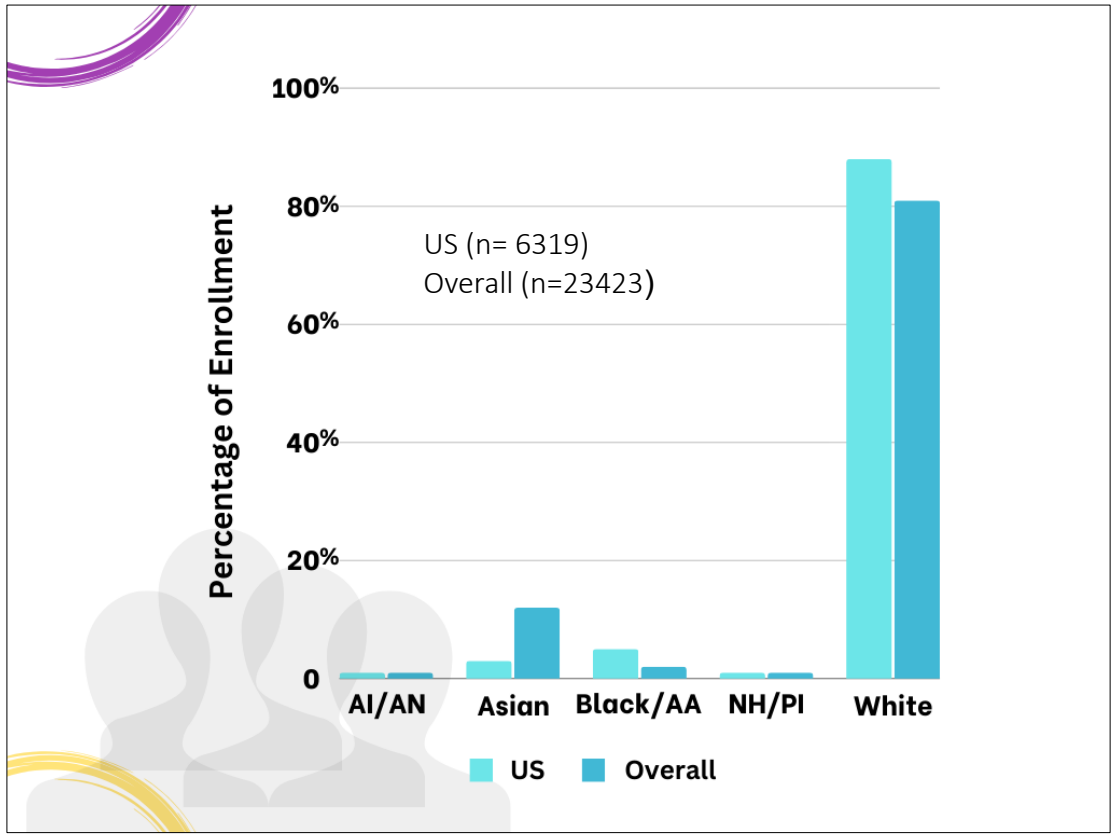
Fashoyin-Aje L, Beaver J, Pazdur R. Promoting Inclusion of Members of Racial and Ethnic Minority Groups in Cancer Drug Development. JAMA Oncol. 2021;7(10):1445-1446; Singh H et al. Enrollment of older adults on oncology trials: An FDA perspective. J Geriatric Oncology 2017 May;8(3):149-150; THE BELMONT REPORT- Ethical Principles and Guidelines for the Protection of Human Subjects of Research (April 18, 1979)

Current Trends in Cancer Drug Development

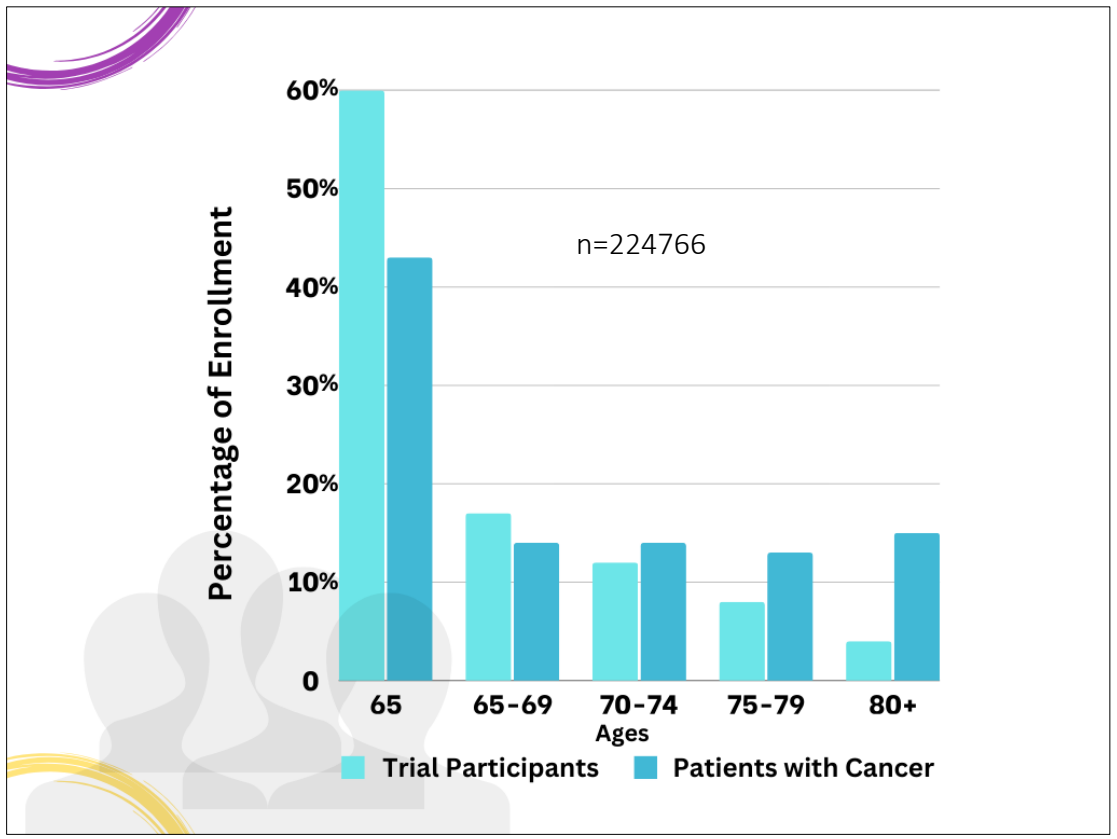
- **U.S. trial sites in large academic centers with limited community site participation**
- **Trial entry criteria not well-matched to real world population- significant trial enrollment barrier**
- **Expedited drug development timelines**
- **Approvals based on international clinical trials**
- **Limited planning to facilitate study population representativeness**

Participants in Oncology Clinical Trials
Race & Older Age

Racial Composition of Participants Enrolled in Trials of New Drugs Approved from 2011-2017[1]

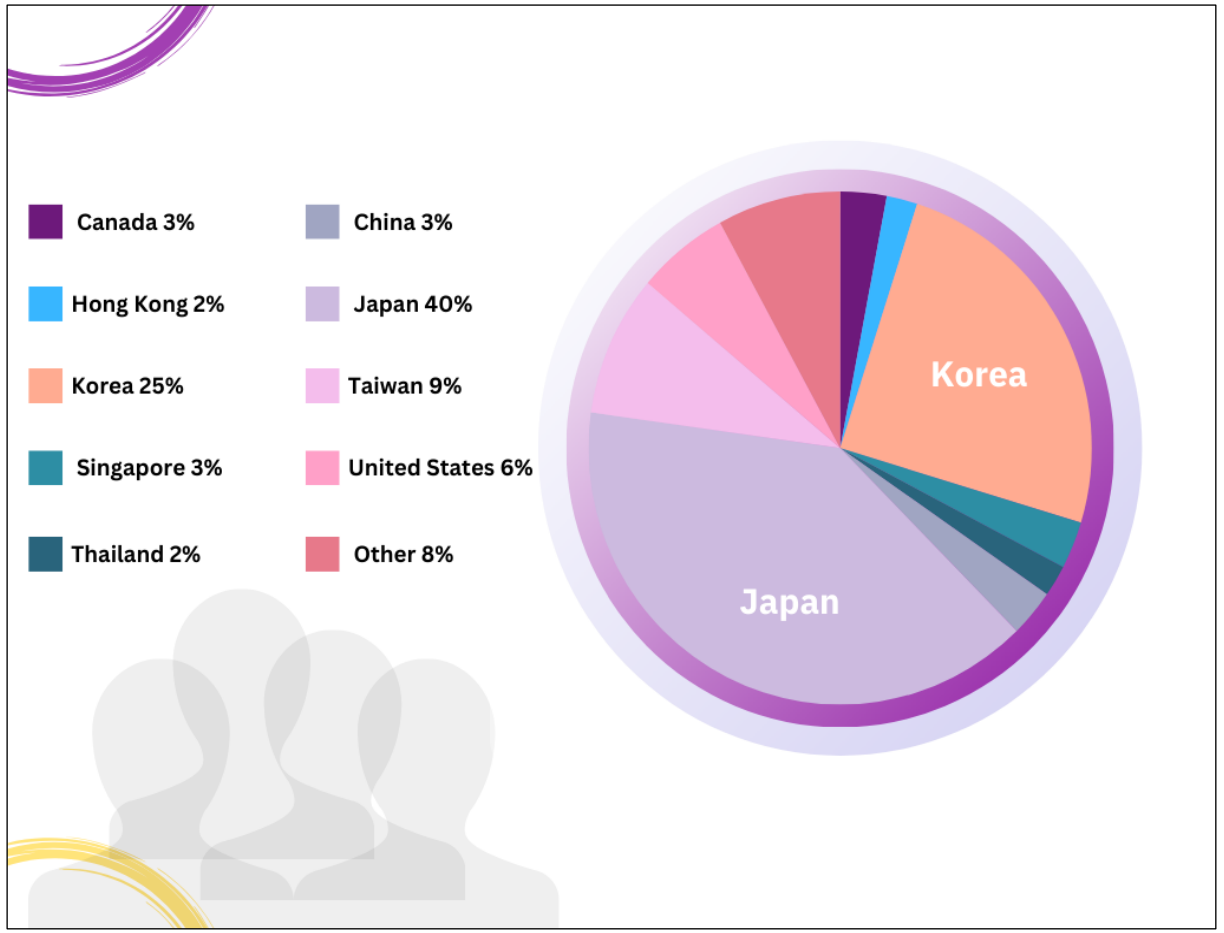


Older Adult Representation in Oncology Drug Trials[2]



1. Fashoyin-Aje et al. Unpublished FDA analysis of NME approved 2011- 2017
2. Singh et al, ASCO Annual Meeting, 2017

Asian Participants Enrolled in Trials of New Oncology Drugs Approved from 2011-2017[1]



Overall U.S. Asian Population[2]

Asian Subgroup	US Asian Population
Chinese	22%
Filipino	19%
Asian Indian	19%
Vietnamese	10%
Korean	9%
Japanese	7%
Others	14%

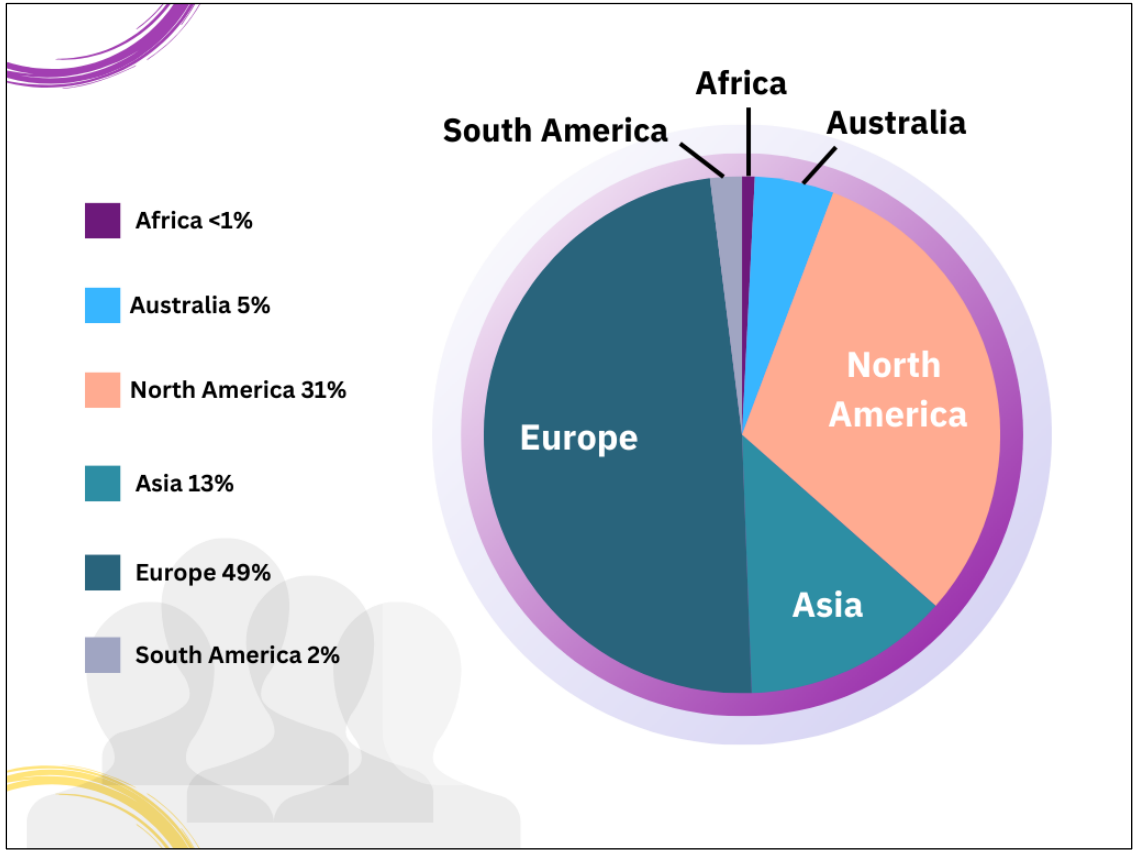
1. Fashoyin-Aje et al. Unpublished FDA analysis of NME approved 2011- 2017; 2. www.census.gov

Ethnic Composition of Participants Enrolled in Trials of New Oncology Drugs Approved from 2011-2017[1]

Ethnicity	Outside U.S. n= 17104	U.S. n= 6319
Hispanic	4%	4%
Not Hispanic	55%	59%
Not collected	20%	15%
Not reported	20%	20%
Other*	1%	2%

1. Fashoyin-Aje et al. Unpublished FDA analysis of NME approved 2011- 2017

Geographical Distribution of Participants Enrolled in Trials of New Oncology Drugs Approved from 2011-2017[1]



1. Fashoyin-Aje et al. Unpublished FDA analysis of NME approved 2011- 2017.

Select FDA Guidances[1]

Population	Related FDA Guidance
Age/Age group	▪ Pediatric Studies of Molecularly Targeted Oncology Drugs ▪ Considerations for the Inclusion of Adolescent Patients in Adult Oncology Clinical Trials ▪ Guideline for Industry- Studies in Support of Special Populations: Geriatrics ▪ Inclusion of Older Adults in Cancer Clinical Trials
Race/Ethnicity	▪ Collection of Race and Ethnicity Data in Clinical Trials ▪ Diversity Plans to Improve Enrollment of Participants From Underrepresented Racial & Ethnic Populations in Clinical Trials
Sex	▪ Evaluation of Gender Differences in Clinical Investigations ▪ Male Breast Cancer: Developing Drugs for Treatment
General	▪ Enhancing diversity in clinical trials

Clinical Characteristics	Related FDA Guidance (Oncology)
Brain metastases	▪ Cancer Clinical Trial Eligibility Criteria: Brain Metastases
HIV and Hepatitis	▪ Cancer Clinical Trial Eligibility Criteria: Patients with HIV, Hepatitis B Virus, or Hepatitis C Virus Infections
Organ dysfunction	▪ Cancer Clinical Trial Eligibility Criteria: Patients with Organ Dysfunction or Prior or Concurrent Malignancies

1. Applicable to drugs and biological products (i.e., does not include device-specific guidance documents)

Project Equity[1]- An FDA Oncology Center of Excellence Initiative

Aim: Ensure that data submitted for approval of oncology MPs is generated in a study population that is representative of the demographics[2] of patients for whom MPs are intended.

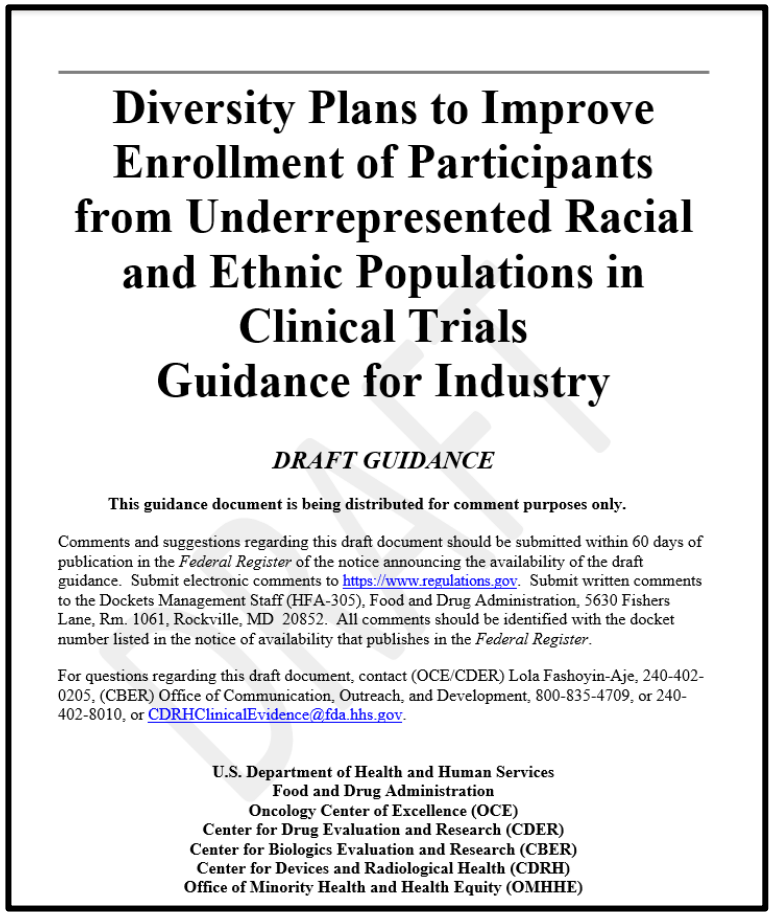
OUTREACH/ ENGAGEMENT

POLICY[3] DEVELOPMENT

RESEARCH[4]

1. https://www.fda.gov/about-fda/oncology-center-excellence/project-equity
2. *See also OCE Project ASIATICA (https://www.fda.gov/about-fda/oncology-center-excellence/project-asiatica) and Project Silver (https://www.fda.gov/about-fda/oncology-center-excellence/project-silver).*
3. *Fashoyin-Aje L et al. Promoting Inclusion of Members of Racial and Ethnic Minority Groups in Cancer Drug Development. JAMA Oncol. 2021;7(10):1445-1446; Diversity plans guidance- https://www.fda.gov/media/157635/download*
4. *OCE Scientific Collaborative https://www.fda.gov/about-fda/oncology-center-excellence/oce-scientific-collaborative*

FDA Guidance- Diversity Plans in Clinical Trials[1]



Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials
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 60 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/CDER) Lola Fashoyin-Aje, 240-402-0205, (CBER) Office of Communication, Outreach, and Development, 800-835-4709, or 240-402-8010, or CDRHClinicalEvidence@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Minority Health and Health Equity (OMHHE)

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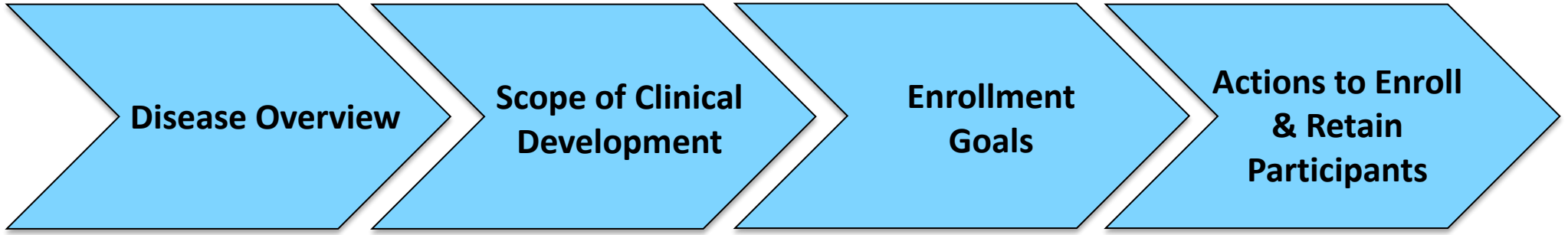
1. https://www.fda.gov/media/157635/download

Elements of a Diversity Plan



- Disease prevalence
- Distribution across subgroups

- Studies in clinical development program

- Planned enrollment across relevant groups

- Measures to enroll & retain relevant population

Snapshot of Food and Drug Omnibus Reform Act[1] (FDORA) Clinical Trial Diversity Provisions

- **What is FDORA and how does it relate to diversity in clinical trials?**

  The Food and Drug Omnibus Reform Act (FDORA) was signed into law by President Biden as part of the Consolidated Appropriations Act of 2023, in December 2022. This law includes provisions for clinical trial diversity and modernization. These provisions amend the Food, Drug, and Cosmetic Act to require that sponsors of certain clinical studies submit Diversity Action Plans to the FDA.

- **What is the purpose of FDORA as it relates to clinical trial diversity and Diversity Action Plans?**

The purpose is to improve the enrollment of populations that have historically been underrepresented in clinical studies of drugs, biological products and devices. This law gives FDA the authority to require that sponsors submit Diversity Action Plans that specify their enrollment goals disaggregated **by race, ethnicity, sex, and age group** and provide the rationale for such goals, and that these Diversity Action Plans also specify the measures that Sponsors will implement to achieve the stated enrollment goals.

- **Which clinical studies are subject to the requirement for submitting DAPs?**

The requirement to submit Diversity Action Plans applies to phase 3 clinical studies or other pivotal clinical studies of drugs, biological products, and devices, for which enrollment commences 180 days after publication of final guidance on Diversity Action Plans.

1. See Consolidated Appropriations Act, 2023, FDORA Section 3601 through 3604 (December 2022) (P.L. 117-328).

Snapshot of Food and Drug Omnibus Reform Act[1] (FDORA) Clinical Trial Diversity Provisions

- **When does the FDORA requirement to submit Diversity Action Plans go into effect?**

The requirement to submit Diversity Action Plans will apply to clinical studies that commence after the date that is 180 days after the publication of the final guidance on Diversity Action Plans- this guidance must describe the form and content of Diversity Action Plans.

- **How does FDA's current draft guidance on Diversity Plans (*https://www.fda.gov/media/157635/download*) fit into these new requirements related to Diversity Action Plans?**

FDA's existing draft guidance provides recommendations for sponsors to develop and submit Diversity Plans that specify enrollment goals for racial and ethnic populations in clinical trials of drugs, biological products, and devices. The recommendations in the draft guidance are not binding and emphasize enrollment goals by race and ethnicity. FDORA authorizes FDA to update existing guidance or issue new guidance according to the provisions in FDORA and, requires that FDA issues such guidance no later than 12 months from when FDORA was signed into law.

1. See Consolidated Appropriations Act, 2023, FDORA Section 3601 through 3604 (December 2022) (P.L. 117-328).

FDORA Clinical Trial Diversity and Modernization- Summary of Statutory Deliverables

- **Draft guidance on Diversity Action Plans** (no later than 12 months after enactment of FDORA)
- **Final guidance on Diversity Action Plans** (no later than 9 months after closing the public comment period on the draft guidance on Diversity Action Plans)
- **Conduct one or more Public Workshops** (no later than 1 year after enactment of FDORA)
- **Public Workshop Public Docket** (open for 60 days after public workshop(s))
- **Workshop Report(s)** (no later than 180 days from close of the public comment period for workshop(s))
- **Diversity Action Plans Annual Summary Report to Congress** (no later than 2 years after enactment of FDORA and annually thereafter)

1. See Consolidated Appropriations Act, 2023, FDORA Section 3601 through 3604 (December 2022) (P.L. 117-328).

Slide Deck Credit

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https://www.fda.gov/about-fda/oncology-center-excellence/project-equity