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Dockets Management Staff (HFA-305)
Food and Drug Administration 5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Submitted via Regulations.gov

Re: Docket No. FDA-202 1-D-0789 for Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies

The Association of American Medical Colleges (AAMC) appreciates the opportunity to comment on the Food and Drug Administration's (FDA) draft guidance regarding the format and content of Diversity Action Plans to improve the enrollment of participants from populations underrepresented in certain clinical studies involving drugs, biological products, and devices. We appreciate the FDA's interest in the development of a Diversity Action Plan "to increase enrollment of participants who are members of populations historically underrepresented populations in clinical studies to help improve the strength and generalizability of the evidence of the intended use population."[1]

The AAMC is a nonprofit association dedicated to improving the health of people everywhere through medical education, health care, medical research, and community collaborations. Its members are all 158 U.S. medical schools accredited by the Liaison Committee on Medical Education; 13 accredited Canadian medical schools; approximately 400 academic health systems and teaching hospitals, including Department of Veterans Affairs medical centers; and more than 70 academic societies. Through these institutions and organizations, the AAMC leads and serves America's medical schools, academic health systems and teaching hospitals, and the millions of individuals across academic medicine, including more than 193,000 full-time faculty members, 96,000 medical students, 153,000 resident physicians, and 60,000 graduate students and postdoctoral researchers in the biomedical sciences. Following a 2022 merger, the Alliance of Academic Health Centers and the Alliance of Academic Health Centers International broadened participation in the AAMC by U.S. and international academic health centers.

The goal of the AAMC's Center for Health Justice (Center), founded in 2021, is for all communities to have an equal opportunity to thrive — a goal that reaches well beyond medical care. Achieving health equity means addressing the common roots of health, social, and economic injustices and implementing policies and practices that are explicitly oriented toward equal opportunity. The Center partners with public health and community-based organizations, government and health care entities, the private sector, community leaders, and community members to build a case for health justice through research, analysis, and expertise. For more information, visit www.aamchealthjustice.org.

It is both a critical and opportune time for the FDA to address the underrepresentation of minoritized racial and ethnic populations in clinical trials, especially as agencies are implementing policies and programs that promote racial justice, civil rights, and equal opportunity pursuant to the Administration's comprehensive approach to advancing equity across the federal government. The AAMC has expressed

[1] Diversity Action Plans To Improve Enrollment of Participants From Underrepresented Populations in Clinical Studies; Draft Guidance for Industry (June 28, 2024).

strong support for these initiatives,[2] including the Department of Health and Human Services' (HHS) *Equity Action Plan,* which includes recommended actions for increasing the diversity of research and clinical trials as one of the plan's five priority areas.[3] This aligns with broader initiatives across other HHS agencies, including prior FDA guidance on patient-focused drug development and the collection of race and ethnicity data in FDA clinical trials. These efforts have directly influenced the recommended actions in this draft guidance

In the comments below, we offer recommendations on two main aspects of the draft guidance—the collection of demographic characteristics and the content of a Diversity Action Plan—and we request that the FDA provide additional clarity and/or more concrete strategies to improve sponsors' ability to successfully implement comprehensive plans.

I. Race, Ethnicity, Sex, and Age Group in Diversity Action Plans

The draft guidance instructs sponsors on how to address race, ethnicity, sex and age group demographic characteristics of clinically relevant populations within a Diversity Action Plan. One notable recommendation is the disaggregation or tabulation of these characteristics to better understand population representation.

We are pleased to review the FDA's emphasis on the importance of disaggregation to increase meaningful enrollment for certain groups. We also appreciate the suggestion that sponsors consider additional factors, such as the inclusion of pregnant and lactating individuals, to support more detailed subgroup analyses. However, we note that this section is not as comprehensive nor detailed as other sections in the draft guidance. Given the significance of the topic, we believe the document would benefit from additional guidance on how to enhance inclusivity and ensure alignment with broader government initiatives for the collection of race and ethnicity data.

Specifically, we recommend the following:

1) **Align Draft Guidance with Existing FDA Guidance:** In lines 202-204, the draft guidance references other FDA guidance documents and encourages sponsors to review them for relevant information. While cross referencing and footnoting relevant guidance documents is important, it would be beneficial to include a statement to underscore what the agency believes to be the most pertinent recommendations from those guidance documents directly within Section IV. This approach would better ensure this draft guidance is consistent with other FDA guidance and minimize the potential burdens on sponsors, who would otherwise need to navigate multiple guidance documents to inform their Diversity Action Plans.

2) **Ensure Consistency with OMB Statistical Policy Directive:** We urge the FDA ensure that its ongoing data collection initiatives, as well as this draft guidance, reflect the recent changes to the Office of Management and Budget Statistical Policy Directive 15 (SPD 15).[4] The January 2024 draft guidance, *Collection of Race and Ethnicity Data in FDA Clinical Trials* and the 2022 guidance *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and*

[2] AAMC Comments on Methods and Leading Practices for Advancing Equity and Support for Underserved Communities Through Government, OMB 2021-0005 (July 2, 2021); https://www.aamc.org/media/55326/download?attachment. Also see, Biden-Harris Administration Releases Agency Equity Action Plans to Advance Equity and Racial Justice Across the Federal Government (April 14, 2022).
[3] U.S. Department of Health Human Services Agency Equity Action Plan, https://www.hhs.gov/sites/default/files/hhs-equity-action-plan.pdf
[4] AAMC Comments to the Office of Management and Budget, Re: Initial Proposals for Updating OMB's Race and Ethnicity Statistical Standards, Docket No. OMB – 2023 – 0001https://www.aamc.org/media/66246/download?attachment (April 2023).

Ethnic Populations in Clinical Trials, reference the now outdated OMB standards which were substantially revised in March 2024.[5] The FDA should revise this draft guidance to reflect the OMB's changes. For example, the updated SPD 15 introduces a new reporting category, Middle Eastern and North African ("MENA"), which is distinct from the white category. Additionally, the updated SPD 15 requires the collection of detailed data beyond the minimum categories to increase consistency and comparability of federal data. Incorporating these updates would help the FDA achieves its goal of ensuring a more accurate representation of diverse populations in certain clinical studies.

3) **Broaden the Scope of Diversity Action Plans to Include Social Drivers of Health (SDOH):** We are pleased to see the FDA's acknowledgment that "other factors" (lines 128-132) should be considered when developing Diversity Action Plans. However, we recommend that the guidance explicitly state that sponsors should broaden the scope of demographic characteristics beyond race, ethnicity, sex, and age to include social drivers of health such as socioeconomic status, geographic location, education level, transportation, and access to healthcare. Additionally, we believe this recommendation should be included in Section V, Content of the Diversity Action Plan (Subsection A. Enrollment Goals), rather than being understated or implied in other sections, such as the Background. Given the potentially profound impact of this draft guidance on enhancing clinical trial diversity and reducing disparities, it important that the FDA adopt a comprehensive approach to diversity.

4) **Incorporate Sexual Orientation and Gender Identity Data In Diversity Action Plans:** Building on the recommendation immediately above (subsection 3), we would like to underscore the ongoing efforts across the Federal government to improve the collection and analysis of sexual orientation and gender identity (SOGI) data. Recently, the AAMC submitted a letter to the NIH in response to their request for information (RFI) on the NIH-Wide Strategic Plan for sexual and gender minority health research.[6] In the RFI, the NIH acknowledges that while progress has been made, "challenges remain in the collection and analysis of sexual orientation and gender identity (SOGI) data."[7] We concur, and in our comments we emphasized the work of the AAMC Center for Health Justice (the Center).[8] The Center is committed to building evidence that supports policy changes which benefit communities that are underrepresented in health research— both as researchers and study participants— including Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual and other sexual and/or gender minority (LGBTQIA+) populations.

   Given the interest across agencies to incorporate SDOH and SOGI data collection into their programs and processes,[9] we urge the FDA to ensure that sponsors collect both SDOH and SOGI data as part of the Diversity Action Plan. This would align with HHS' *SOGI Data Action Plan* and support broader efforts to create a more inclusive research environment.

[5] Office of Management and Budget's Statistical Policy Directive No. 15, https://spd15revision.gov/ (accessed September 20, 2024).
[6] AAMC letter to NIH, Re: The National Institutes of Health Request for Information on NIH-Wide Strategic Plan for Sexual and Gender Minority Health Research [NOT-OD-24-122] (July 2024)
[7] I*d*.
[8] AAMC Center for Health Justice, https://www.aamchealthjustice.org/.
[9] See, HHS-wide SOGI Data Action Plan, https://www.hhs.gov/sites/default/files/hhs-sogi-data-action-plan.pdf and HHS Secretary's Advisory Committee for Human Research Protections Recommendations for the Ethical Review and Inclusion of LGBTQI+ Participants in Human Subjects Research, https://www.hhs.gov/ohrp/sachrp-committee/recommendations/ethical-review-inclusion-lgbtqi-participants-human-subjects-research/index.html (accessed September 20, 2024).

II. Content of the Diversity Action Plan and Enrollment Goals

Section V describes the form and content of the Diversity Action Plan and provides recommendations on the enrollment goals and measures to meet those goals.

Considerations for Global Clinical Trials

Section A contains a paragraph (lines 295-311) on global clinical trials and global medical product development, noting that "lack of uniformity across the globe in the use of population descriptors such as race and ethnicity may pose challenges when setting enrollment goals for international sites." Given the growing trend of clinical trials conducted on a global level, we appreciate that the FDA has attempted to address multi-national clinical trials and the potential issues which arise when setting enrollment goals for international sites. However, while the FDA makes the recommendation that clinical trial enrollment "should not be limited to U.S. enrolled participants," it falls short of offering guidance on the potentially significant challenges associated with global trials. These challenges include how the FDA will review Diversity Action Plans from international regulatory agencies, how sponsors should approach cultural sensitivities in diverse populations, as well as racial, ethnic, sociocultural complexities related to participant recruitment, enrollment, and retention.

Finally, the FDA advises sponsors refer to its January 2024 draft guidance on the collection of race and ethnicity data[10] if they encounter challenges setting enrollment goals. Consistent with our recommendations in Section I, we urge the FDA to take swift action to promptly finalize the January draft guidance since it contains clarifications and recommendations that would help sponsors identify and define populations when setting enrollment goals for multi-national clinical trials.

Community Engagement and Trustworthiness

Subsection C (Measures to Meet Enrollment Goals) outlines how sponsors should achieve the specified enrollment goals, emphasizing the importance of retention and engagement strategies. It also highlights the need for the implementation of "sustained community engagement" with trusted partners, as well as "cultural competency and proficiency training for investigators and research staff."

In the AAMC's previous comments to the HHS and FDA on issues related to clinical trials, patient participation in FDA decision-making, and the protection of human subjects in research,[11] we have consistently highlighted the need for HHS and FDA to prioritize meaningful, robust, bi-directional community and patient engagement throughout the entire clinical trial cycle, including recruitment, enrollment, clinical design, implementation, analysis, dissemination of research findings and beyond. We also believe that this type of engagement is essential for building and maintaining public trust, transparency in communication, and sustained community partnerships.

We appreciate the inclusion of explicit, community-engaged strategies for enrollment and retention and would like to bring to the FDA's attention a resource that the Center co-created with community

[10] Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for FDA-Regulated Medical Products, https://www.fda.gov/media/175746/download (January 2024), see also AAMC Comments, https://www.aamc.org/media/75891/download?attachment (April 2024).

[11] AAMC Comments, Re: Diversity Plans to Improve Enrollment of Participants From Underrepresented Racial and Ethnic Populations in Clinical Trials; Draft Guidance for Industry [Docket No. FDA – 2021 – D – 0789], https://www.aamc.org/media/61296/download?attachment (June 2022); AAMC Comments, Re: Docket No. FDA-2018-D-1893 for "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input; Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders; Availability" (September 2018).

members—the Principles of Trustworthiness.[12] This resource provides guidance on how to build authentic, long-term community partnerships. Incorporating the Center's Principles and corresponding toolkit will equip sponsors with guidance and practical tools on how to strengthen and build new partnerships with individuals, communities, and community-based organizations.

Historical and Current Mistrust in Clinical Research and Burden of Participation
In the Background section of the draft guidance, the FDA appropriately conveys the urgent need to improve representation in clinical studies. However, this section overlooks the important acknowledgment of the historical and ongoing distrust in clinical research and the healthcare system, particularly among marginalized communities. However, missing from this section is the important acknowledgment continued distrust in clinical research and the health care system, particularly among of the historical and currently marginalized communities..

This mistrust is rooted in documented exploitation and abuses such as the *US Public Health Service Study of Untreated Syphilis in the Negro Male*.[13] or other unethical practices that hinder or prevent participation in clinical research by underrepresented individuals or populations. We recommend the FDA prominently position this issue in the Background section, prior to outlining the purpose and goals of the draft guidance. Further, in Section C, we also recommend an elaboration on the potential barriers and/or burdens associated with clinical trial participation to include potential issues related to decentralized clinical trials,[14] compensation to research participants, language and literacy barriers, web literacy, access to telecommunication services, and considerations for individuals with disabilities.[15]

We sincerely appreciate the opportunity to comment on such an important endeavor, particularly at a time when there is extraordinary interest in the promotion of health equity and justice across the Federal government and beyond. The AAMC and the AAMC Center for Health Justice have extensive, multi-sector relationships with organizations and community leaders, many of whom would be eager to assist the FDA with these efforts. We would be happy to work with the FDA in furtherance of any of the recommendations discussed in this letter, including bridging connections with our multi-sector partners. Please do not hesitate to reach out to me or my colleagues Daria Grayer, MA, JD (dgrayer@aamc.org) or Heather Pierce, JD, MPH (hpierce@aamc.org).

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cc. David J. Skorton, MD, President and Chief Executive Officer

[12] AAMC Center for Health Justice, https://www.aamc.org/healthjustice; See also, AAMC Principles of Trustworthiness, https://www.aamc.org/trustworthiness, Principles of Trustworthiness Toolkit, https://www.aamc.org/trustworthiness#toolkit. See also, From the National to the Local: Issues of Trust and a Model for Community-Academic-Engagement, https://www.frontiersin.org/articles/10.3389/fpubh.2023.1068425/full.
[13] The Milbank Memorial Fund and the US Public Health Service Study of Untreated Syphilis in Tuskegee: A Short Historical Reassessment, https://www.milbank.org/quarterly/articles/the-milbank-memorial-fund-and-the-us-public-health-service-study-of-untreated-syphilis-in-tuskegee-a-short-historical-reassessment/ (accessed September 20, 2024).
[14] AAMC Comments on Accelerating the Decentralization of Clinical Trials, https://www.aamc.org/advocacy-policy/washington-highlights/aamc-comments-accelerating-decentralization-clinical-trials (May 2023).
[15] AAMC Joins Letter in Support of Inclusion of People with Disabilities, https://www.aamchealthjustice.org/news/testimony-and-correspondence/aamc-joins-letter-support-inclusion-people-disabilities (September 2023), see also, AAMC Center for Health Justice Comments to HHS on Proposed Rule Updating Section 504, https://www.aamc.org/advocacy-policy/washington-highlights/aamc-center-health-justice-comments-hhs-proposed-rule-updating-section-504 (November 2023).