September 26, 2024

Dr. Robert McKinnon Califf
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Docket No. FDA-2021-D-0789

RE: FDA Guidance for Industry: Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies

Commissioner Califf,

The Infectious Diseases Society of America (IDSA) and the HIV Medicine Association (HIVMA) appreciate the opportunity to comment on the Food and Drug Administration's (FDA) Draft Guidance: Diversity Action Plans to Improve Enrollment of Participants from Underrepresented Populations in Clinical Studies.

IDSA and HIVMA represent more than 12,000 infectious disease physicians, scientists, public health practitioners and other health care professionals specializing in infectious diseases. IDSA and HIVMA members focus on investigating, diagnosing, preventing and treating infectious diseases, and are involved in both patient care and clinical research. We are pleased to offer recommendations to the FDA that will help increase participation in clinical studies from underrepresented populations.

We strongly commend the FDA for its updated guidance to ensure diverse clinical study participation and improve the data the agency receives for the population for which medical products are being developed. We applaud the FDA for employing clinical study decentralization when appropriate. Leveraging remote technology to facilitate participation and data collection outside of traditional clinical trial sites allows for more flexible trial designs, where participants can engage from their homes rather than traveling to distant locations. By removing barriers to participation, decentralized trials can help ensure that a wide range of participants are engaged.

These measures are essential for addressing historical disparities in clinical research and ensuring trial outcomes reflect the diverse population that may be impacted by the study. However, while we celebrate these advancements, it is crucial to identify specific areas for further improvement to maximize the effectiveness of these guidelines and ensure equitable access for all populations in clinical trials. We hope to see additional progress as outlined in our recommendations below:

Sex and Gender Identity Data Collection

- Clarifying and differentiating between sex assigned at birth and gender is essential when collecting data for clinical trials, as it ensures that research accurately reflects the diverse

experiences and needs of participants. Sex, which refers to differences in chromosomes and reproductive organs, and gender, encompassing the social, psychological and behavioral roles and identities shaped by society, can significantly influence health outcomes and responses to treatment. By recognizing these distinctions, researchers can strengthen the validity of their findings, tailor interventions effectively, and improve patient care. This nuanced approach contributes to more inclusive research and promotes a deeper understanding of how various factors affect health across different populations.

- FDA should always include sex as a demographic data point and clearly define sex as assigned at birth. We encourage the FDA to consider collecting data for gender identity and gender-diverse individuals as well as adding a clarifying statement to any study where gender data is being collected, especially in products involving hormones and/or in studies focusing on relevant populations, such as people with HIV or for HIV prevention strategies.

Addressing Race, Ethnicity, Sex, and Age Group in Diversity Action Plans

- Researchers must exercise caution in the language used to describe how different racial and ethnic groups may respond to various medical products. While it is essential to acknowledge and track racial and ethnic diversity in clinical research, any guidance must refrain from implying that treatment responses are inherently different based on socially constructed racial categories.

- Clarify that specific predictors of treatment response are related to genetic traits often associated with geographic origin and not racial/ethnic categories and provide examples that contrast with racial/ethnic identity. Common traits misidentified with race include G6PD deficiency and sickle cell trait/disease, which are united by ancestry from malarial regions, and not a particular group identity.

- Geographic diversity in clinical studies is crucial for ensuring that medical research reflects the varied populations that will ultimately use the treatments developed. It is equally important that when clinical trials conclude in a specific area, a tailored treatment implementation plan is developed for that region. Ideally - the implementation plan should be developed in advance of conducting the clinical trial to ensure the research findings benefit the geographic areas that made the clinical trial possible. In addition, we must emphasize that using race as a proxy for health data across different geographic populations can lead to misinterpretations. For instance, populations in Africa should not be considered substitutes for African Americans, as these groups may have distinct environmental and social conditions that have a significant impact on people's health.

Content of Diversity Action Plan: Enrollment Goals

- Safeguards are needed against over-representation or experimentation on historically marginalized populations. Enrollment goals should describe the need and justification for the percentage of participants in each trial phase to ensure that no underrepresented population is disproportionately investigated. Underrepresented communities have faced over-experimentation and unethical research practices rooted in a legacy of historical trauma. We must acknowledge this history, and the FDA must prioritize ethical standards that protect vulnerable clinical research populations.

- We also encourage the FDA to allow for better categorization of how individuals self-identify their race and ethnicity. A growing number of people identify as mixed-race or mixed ethnicity, yet many find themselves forced into categories that do not represent their identities accurately. For example, including the Middle Eastern and North African (MENA) category in the U.S. Census is a significant step towards more nuanced racial categorization. Similarly, Latinx and Hispanic individuals often face challenges in adequately expressing their multifaceted identities within traditional racial categories. We encourage the FDA to allow for better categorization that reflects how people self-identify when collecting population data, including options to identify with mixed/multiple race/identity and/or mestizo.

- We recommend prioritizing the population that would benefit most from the intervention and take into account the social determinants of health that hinder access for certain groups, including socioeconomic status and geography, e.g., urban and rural areas. This focus should ensure that clinical trial participants represent those who face significant barriers to participation while also balancing diversity across other demographic metrics.

Content of Diversity Action Plan: Rational for Enrollment Goals

- Any rationale used to describe data regarding differences attributed to genetic variations must be clearly defined. A "genetic variation" definition must be established to avoid the misleading implication that certain races and ethnicities are inherently "genetically different." Such assumptions can perpetuate stereotypes. As the Diversity Action Plan is formulated, we encourage the inclusion of clear definitions and relevant examples of genetic variation to avoid misrepresentation, as noted in our comments on addressing race, ethnicity, sex, and age group in Diversity Action Plans.

Content of Diversity Action Plan: Measures to Meet Enrollment Goals

- Addressing the financial barriers participants face, such as unstable housing and transportation challenges, is essential to increase the participation of individuals from lower socioeconomic backgrounds in clinical research. Current reimbursement practices often fail to adequately compensate participants for their time and effort, particularly for those who may have to miss hourly work or incur travel expenses to attend study sites. It is equally important to strike a balance to avoid perceptions of coercion that can arise from offering excessive compensation. We support equitable reimbursement that reflects the actual costs and lost wages associated with participation, which acknowledges the value of participants' time and contributions.

- Support revision of informed consent language and the informed consent process with a focus on clarity and approachability. The consent process and language in consent forms are designed to address historical abuses of research populations. The balance has shifted too far in the opposite direction, in which the degree of legal language, length, and complexity serve as a deterrent to populations with rightful skepticism of medicine and medical research. The process of reconsent should also be revisited to evaluate the balance between providing appropriately updated risk/benefit information and increasing the opacity of the research process when meaningful changes to the individual are not present.

Elements of a Diversity Action Plan Summary

- It is essential to clarify the inclusion criteria for pregnant and lactating individuals in clinical trials, as the current default practice often excludes these populations unless a clear justification

for their inclusion is provided. This exclusion limits the understanding of how treatments may affect pregnant and lactating individuals and delays innovations and advancements that could significantly benefit these populations.

- Diversity Action Plans should include explicit language that addresses the rationale for including or excluding pregnant and lactating people from clinical trials. The FDA should advocate for the inclusion of these populations, including people who use drugs, as well as minors and children, provided they meet the eligibility requirements for the study unless there is a compelling reason to exclude them. Such justifications should be clearly documented.

- It is imperative to consistently use the term "participant" instead of "subject" in the Diversity Action Plans. The continued use of outdated terminology fails to honor the principles of individual autonomy and voluntary participation that we strive for.

Thank you for considering these comments. IDSA and HIVMA look forward to working on many of the FDA's ongoing efforts to improve the enrollment of participants from underrepresented populations in clinical studies. Please contact HIVMA's Associate Director of Public Policy and Advocacy, Jose Rodriguez, at JRodriguez@hivma.org or IDSA's Director of Public Policy, Eli Briggs, at EBriggs@idsociety.org for additional information or with any questions.

Sincerely,

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