April 24, 2024

Robert M. Califf, M.D.
Commissioner
U.S. Food and Drug Administration
Docket No. FDA–2019–N–5959
5360 Fishers Lane
Room 1061
Rockville, MD 20852

Re: FDA–2016–D–3561: Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for Food and Drug Administration-Regulated Medical Products; Draft Guidance for Industry; Availability (January 30, 2024)

Dear Commissioner Califf:

The American Cancer Society Cancer Action Network (ACS CAN) advocates for evidence-based public policies to reduce the cancer burden for everyone. As the American Cancer Society's nonprofit, nonpartisan advocacy affiliate, ACS CAN is making cancer a top priority for public officials and candidates at the federal, state, and local levels. By engaging advocates across the country to make their voices heard, ACS CAN influences legislative and regulatory solutions that will end cancer as we know it, for everyone. We appreciate the opportunity to comment on the Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for Food and Drug Administration Regulated Medical Products; Draft Guidance for Industry (Draft Guidance).

ACS CAN commends FDA for this draft guidance, which revises previous guidance issued in October 2016. **We agree that using standardized terminology for race and ethnicity helps to ensure that data are collected and reported consistently in submissions to FDA.** While race and ethnicity are sociopolitical concepts that are not based on biology, and genetic ancestry is often a better predictor of pharmacogenomic variability, different racial and ethnic groups have at times been shown to have disparate responses to drug therapies. Additionally, compared to their cancer burden, some racial and ethnic minority populations in the U.S. are vastly underrepresented in cancer clinical trials that support new drug approvals. Standardized terminology for race and ethnicity can facilitate the characterization of any disparate response to therapies and help identify and address underrepresentation in clinical trials.

The draft guidance defines the term *clinical studies* to include interventional (clinical trial) and non-interventional (observational) designs. **ACS CAN supports this definition because it includes the totality of data that support application requirements.** Standardized terminology for race and ethnicity is important to enable review of any disparities between pre-approval racial and ethnic groupings and post-marketing real-world use and associated outcomes.

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Benefits of Data Disaggregation

There are widely documented disparities in cancer incidence, prevalence, survivorship, and mortality among certain racial and ethnic groups in the U.S. Addressing these disparities so that individuals within these groups have the best opportunity to prevent, treat, and survive cancer starts with ensuring the collection of detailed, accurate, and disaggregated racial and ethnic data. However, the populations that would nominally be covered in the minimal set of categories for race and ethnicity set forth in the Office of Management and Budget's (OMB) Statistical Policy Directive No. 15 (SPD 15), which was developed to provide consistent data on race and ethnicity throughout the Federal Government, still contain significant differences in ancestry.

FDA acknowledges that the recommended categories for race and ethnicity were developed in the U.S. and that these categories may not adequately describe racial and ethnic groups in other countries. **ACS CAN supports FDA's recommendation that applicants use more detailed categories by geographic region to provide sponsors flexibility in characterizing race and ethnicity.** In previous comments to FDA on *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Draft Guidance for Industry* (FDA-2021-D-0789), we recommended that FDA encourage sponsors to provide more detailed race and ethnicity data in Diversity Plans beyond the minimum OMB categories for race and ethnicity. Aggregating heterogenous racial and ethnic subpopulations in the collection of public health data can obscure health disparities and, in the context of clinical studies, pharmacogenomic-linked variability. Disaggregated racial and ethnic data allows for description of specific cancer disparities within subpopulations that can be addressed through targeted interventions.

ACS CAN is also supportive of the recommendation that applicants include race and ethnicity information in their proposed product labeling in the Clinical Studies and Adverse Reactions sections. This information is essential to communicate if there is data to suggest a signal of a serious risk to members of a population or subgroup.

Clinical trials used to gather data for submission to FDA are not required to be conducted in the U.S. and, in oncology, trials are increasingly global.[1] Clinical trial participants of the same self-selected race and ethnicity category may nonetheless have dissimilar geographic origins. For example, two individuals participating in the same clinical trial who identify as Asian and Chinese could reside in two different countries (e.g. U.S. vs China). These individuals would be influenced by different extrinsic factors which could impact drug response. **We ask that FDA go further and recommend that in addition to the inclusion of race and ethnicity information in product labeling, applicants also include the geographic origin of trial participants in the Clinical Studies and Adverse Reactions sections.**

[1] Oladimeji Akinboro et al., Trends in U.S and global patient enrollment from 2014 to 2022 in lung cancer clinical trials supporting marketing applications: An FDA analysis. JCO 41, 1576-1576(2023). DOI: 10.1200/JCO.2023.41.16_suppl.1576

Statistical Policy Directive No. 15

The recommended approach for the collection and reporting of race and ethnicity collected for submissions to FDA outlined in the draft guidance is based on OMB SPD 15. In January 2023, OMB announced a formal review of SPD 15 to account for demographic shifts in the U.S. over the last 25 years. FDA acknowledges that the development of its draft guidance began before OMB announced the formal review and states that the draft guidance will be updated if OMB revises SPD 15. Since the publication of the draft guidance, OMB has published final revisions to SPD 15. These revisions are significant and should be considered for the draft guidance. For example, the revised SPD 15:

- Combines the separate questions on race and ethnicity into a single race and ethnicity question and includes modifications to encourage respondents to select all categories that reflect their identity;
- Adds Middle Eastern or North African (MENA) as a minimum reporting category separate and distinct from the White category; and
- Requires collection of more detail beyond the minimum race and ethnicity reporting categories unless an agency requests and receives an exemption.

ACS CAN appreciates the work OMB has done to improve upon the Federal data standards. We are particularly supportive of the addition of MENA as a new minimum reporting category and the explicit requirement to collect more detail beyond the minimum reporting categories.

The draft guidance also coincides with several legislative and regulatory efforts to improve clinical trial diversity. Standardizing terminology for race and ethnicity helps ensure that data are collected and reported consistently in submissions to FDA. Since FDA's recommended approach to standardizing terminology for race and ethnicity is based on SPD 15 and given the recent update to SPD 15, we encourage FDA to revise and replace the draft guidance to reflect these important changes. If you have any questions, please feel free to contact me or have your staff contact Mark Fleury, PhD (mark.fleury@cancer.org), Principal, Policy Development - Emerging Science.

Sincerely,

Lisa A. Lacasse, MBA
President
American Cancer Society Cancer Action Network