Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for FDA-Regulated Medical Products

Guidance for Industry

DRAFT GUIDANCE

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January 2024
Clinical/Medical
Revision 1

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Collection of Race and Ethnicity Data in Clinical Trials and Clinical Studies for FDA-Regulated Medical Products Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

The purpose of this guidance is to provide FDA's expectations for, and recommendations on, use of a standardized approach for collecting and reporting race and ethnicity data in submissions including information collected and reported from clinical trials and clinical studies[2] for FDA-regulated medical products.[3,4] Using standard terminology for race and ethnicity helps ensure that data are collected and reported consistently in submissions to FDA. FDA's recommended approach is based on the Office of Management and Budget (OMB) Statistical Policy Directive No. 15 (Policy Directive 15)[5] and was developed in accordance with section 4302 of the Affordable Care Act;[6] the Health and Human Services (HHS) Implementation Guidance on Data

[1]This guidance has been developed by the Office of the Commissioner, the Office of Minority Heath and Health Equity, the Office of Women's Health, the Office of Clinical Policy, the Office of Pediatric Therapeutics, the Center for Biologics Evaluation and Research, the Center for Drug Evaluation and Research, the Center for Devices and Radiological Health, and the Oncology Center of Excellence at the Food and Drug Administration.

[2] Going forward in this guidance, we use the term *clinical studies* to refer broadly to research that evaluates human health outcomes associated with the use of medical products. We use the term clinical studies to include interventional (clinical trial) and non-interventional (observational) designs. Some recommendations in this guidance are specific to clinical trials and are identified as such when relevant.

[3] See the guidance for industry *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies* (September 2017). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[4] For the purposes of this guidance, the term *medical products* refers to drugs, including biological products, and devices as defined by the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301–392) unless otherwise specified.

[5] OMB Statistical Policy Directive No. 15, Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity (Policy Directive 15) (October 30, 1997), available at https://obamawhitehouse.archives.gov/omb/fedreg_1997standards.

[6] Patient Protection and Affordable Care Act, Public Law 111–148, section 4302 (42 U.S.C. 300kk) (March 23, 2010), available at https://www.gpo.gov/fdsys/pkg/CREC-2009-11-19/pdf/CREC-2009-11-19-pt1-PgS11607-3.pdf#page=127.

Collection Standards for Race, Ethnicity, Sex, Primary Language, and Disability Status;[7] and the Food and Drug Administration Safety and Innovation Act (FDASIA) Section 907 Action Plan.[8] This guidance revises the guidance for industry and FDA staff *Collection of Race and Ethnicity Data in Clinical Trials* issued in October 2016. When finalized, this guidance will replace the October 2016 guidance.

Current OMB standards for the classification of Federal data on race and ethnicity were developed to provide a common framework for uniformity and consistency in the collection and use of data on race and ethnicity by Federal Agencies.

On January 27, 2023, OMB announced a formal review of OMB Policy Directive 15 and requested public comments on initial proposals to revise the directive to account for large societal, political, and economic demographic shifts in the United States over the 25 years since its publication.[9] FDA began the process to update this guidance before the OMB announcement. FDA continued the process to update this guidance, including updating references and contact information for FDA and revising the title, to ensure the appropriate collection and reporting of race and ethnicity data in submissions from clinical studies and clinical trials for FDA-regulated medical products. FDA will update this guidance as appropriate if OMB revises Policy Directive 15.

This guidance provides recommendations on:

1. Meeting the requirements set forth in the 1998 final rule[10] regarding presentation of demographic data in investigational new drug applications (INDs) and new drug applications (NDAs) (known as the Demographic Rule)

2. Collection of race and ethnicity data in biologics license applications (BLAs) and medical device applications[11]

3. Addressing the FDASIA Section 907 Action Plan to improve the completeness and quality of demographic data collection and reporting

[7] HHS Implementation Guidance on Data Collection Standards for Race, Ethnicity, Sex, Primary Language, and Disability Status (October 31, 2011), available at https://aspe.hhs.gov/reports/hhs-implementation-guidance-data-collection-standards-race-ethnicity-sex-primary-language-disability-0.

[8] See the FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data (FDASIA Section 907 Action Plan), August 2014, available at https://www.fda.gov/media/89307/download.

[9] See OMB *Federal Register* notice (88 FR 5375), https://www.federalregister.gov/documents/2023/01/27/2023-01635/initial-proposals-for-updating-ombs-race-and-ethnicity-statistical-standards.

[10] 1998 final rule, "Investigational New Drug Applications and New Drug Applications" (the Demographic Rule), see 63 FR 6854 (February 11, 1998) (codified at 21 CFR 312.33(a)(2) and 21 CFR 314.50(d)(5)), available at https://www.gpo.gov/fdsys/pkg/FR-1998-02-11/pdf/98-3422.pdf.

[11] For medical devices, see also the guidance for industry and FDA staff *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies*.

For drugs, the Demographic Rule requires the sponsor of an IND to tabulate in an IND annual report the number of participants enrolled in the clinical trial by certain demographic subgroups including race and requires NDA submissions to include summaries of effectiveness and safety data for demographic subgroups, including racial subgroups.[12] FDA also strongly recommends the collection and reporting of ethnicity data (Hispanic or Latino or not Hispanic or Latino) consistent with OMB standards.[13]

This guidance is also intended to help an applicant preparing a BLA or a device premarket submission, which should be done in accordance with the OMB standards regarding collection and reporting of race and ethnicity data described herein.[14]

This guidance also recommends the use of the OMB race and ethnicity categories in proposed medical product labeling.

Sponsors of investigational new drugs and investigational devices should enroll participants who reflect the population that will use the medical product if approved.[15] Sections 505(z) and 520(g) of the Federal Food, Drug, and Cosmetic Act, as amended by section 3601 of the Food and Drug Omnibus Reform Act of 2022 (FDORA) require that such sponsors submit a diversity action plan outlining (1) the sponsor's goals for enrollment in the clinical trial, (2) the sponsor's rationale for such goals, and (3) an explanation of how the sponsor intends to meet such goals. As described in section 3602 of FDORA, this requirement will apply with respect to clinical trials for medical products for which enrollment commences 180 days after the publication of a final guidance on diversity action plans.[16] This guidance does not address diversity action plans or the appropriate population for a clinical study. For questions related to enrollment of clinically relevant demographic subpopulations in clinical trials, sponsors should consult with the review division of the appropriate centers and offices.[17]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

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[12] See footnote 10.

[13] See footnote 5.

[14] Ibid.

[15] See also the guidance for industry *Enhancing the Diversity of Clinical Trial Populations – Eligibility Criteria, Enrollment Practices, and Trial Designs* (November 2020).

[16] See Food and Drug Omnibus Reform Act of 2022 (FDORA) available at https://www.congress.gov/117/bills/hr2617/BILLS-117hr2617enr.pdf.

[17] See also the draft guidance for industry *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials* (April 2022). When final, this guidance will represent FDA's current thinking on this topic.

II. BACKGROUND

Although uncommon, differences in response to medical products have been observed in racially and ethnically distinct populations in the United States.[18] In some cases, differences in the pharmacokinetics, efficacy, or safety of medical products that lead to these different responses may be attributable to intrinsic factors (e.g., genetics, metabolism, elimination, skin pigmentation), extrinsic factors (e.g., diet, environmental exposure, socioeconomic status, culture), or interactions between these factors.[19] Collecting data on race and ethnicity is critical to identifying population-specific signals.

In 1997, OMB issued its revised recommendations for the collection and use of race and ethnicity data by Federal Agencies (Policy Directive 15).[20] OMB stated that the recommended race and ethnicity categories were not anthropologically or scientifically based designations, but instead are categories that describe the sociocultural construct of our society.

In 1999, HHS issued the report *Improving the Collection and Use of Racial and Ethnic Data in HHS*.[21] The report describes HHS policy on collecting and reporting data on race and ethnicity for HHS programs. The report recommends inclusion of race and ethnicity categories in HHS-funded and sponsored data collection and reporting systems in all HHS programs to (1) help monitor HHS programs, (2) determine whether Federal funds are being used in a nondiscriminatory manner, and (3) promote the availability of standard race and ethnicity data across various agencies to facilitate HHS responses to major health and human services issues. This policy, updated in 2011,[22] states that the minimum standard categories in OMB Policy Directive 15 should be used when collecting and reporting data in HHS data systems or when reporting HHS-funded statistics. On September 21, 2016, HHS issued the final rule, "Clinical Trials Registration and Results Information Submission" (81 FR 64982) (42 CFR part 11). The final rule requires the submission of race and ethnicity information with summary results information if it is collected during the trial.

[18] For example, in 2005, FDA approved BiDil (isosorbide dinitrate and hydralazine hydrochloride tablets), the first drug approved by the Agency to treat a disease only in patients who identified by a specific racial subgroup. BiDil is approved for the treatment of heart failure as an adjunct to standard therapy in self-identified Black patients to improve survival, to prolong time to hospitalization for heart failure, and to improve patient-reported functional status. Although the sponsor's initial two trials in certain patients with heart failure failed to show a benefit in the overall population (sum of all racial groups), there was a suggestion of benefit of BiDil in one racial subgroup (i.e., Black patients). In a subsequent study in 1,050 self-identified Black patients with a certain type of heart failure, BiDil was shown to be safe and effective for the treatment of heart failure as an adjunct to standard therapy.

[19] Ramamoorthy A, MA Pacanowski, J Bull, L Zhang, 2015, Racial/Ethnic Differences in Drug Disposition and Response: Review of Recently Approved Drugs, Clin Pharmacol Ther, Mar;97(3):263–273.

[20] See footnote 5.

[21] Improving the Collection and Use of Racial and Ethnic Data in HHS (December 1, 1999), available at https://aspe.hhs.gov/report/improving-collection-and-use-racial-and-ethnic-data-hhs.

[22] See footnote 7.

III. COLLECTING RACE AND ETHNICITY DATA IN CLINICAL TRIALS AND CLINICAL STUDIES[23]

OMB Policy Directive 15 provides a minimum standard for maintaining, collecting, and presenting data on race and ethnicity for Federal reporting purposes. As previously stated, the categories in this classification are social-political constructs and should not be interpreted as being scientific or anthropological in nature. OMB recommends a two-question format to provide flexibility and ensure data quality for reporting race and ethnicity as described below.

A. Two-Question Format

To remain consistent with OMB Policy Directive 15, FDA recommends using the two-question format for requesting race and ethnicity information, with the ethnicity question preceding the question about race.[24] For example:

Question 1 (answer first): Are you Hispanic/Latino or not Hispanic/Latino?

Question 2 (answer second): What is your race?[25] More than one choice is acceptable.

B. Self-Reporting

Consistent with best practices, FDA recommends that trial participants self-report race and ethnicity information and that those individuals be permitted to designate a multiracial identity. When the collection of self-reported designations is not feasible (e.g., because of the participant's inability to respond), FDA recommends requesting information from a first-degree relative or other knowledgeable representative. Race and ethnicity should not be assigned by the study team conducting the trial. While data on race and ethnicity may be available in a patient's medical record, FDA recommends that investigators and/or other clinical study staff verify the accuracy of the information provided in the medical record with the study participant.

C. Ethnicity

For ethnicity, we recommend the following minimum choices be offered:

- **Hispanic or Latino**
- **Not Hispanic or Latino**

[23] FDA recognizes that the collection of race and ethnicity data in clinical practice may vary considerably and impact demographic data available for analysis in non-interventional studies. Sponsors seeking to conduct non-interventional studies to support regulatory decision-making should discuss the availability of race and ethnicity data with the relevant review division.

[24] For more information on the basic racial and ethnic categories for Federal statistics and program reporting, see OMB Policy Directive 15, described in footnote 5.

[25] Note: Please see racial designations in section III.D of this guidance.

D. Race

For race, we recommend the following minimum choices[26] be offered:

- **American Indian or Alaska Native**
- **Asian**
- **Black or African American**
- **Native Hawaiian or Other Pacific Islander**
- **White**

FDA recommends offering an option of selecting one or more racial designations or additional subgroup designations. Recommended forms for the instruction accompanying the multiple response questions are "Mark one or more" and "Select one or more."

Sponsors should report the number of respondents in each racial category who self-reported as Hispanic or Latino. When aggregate data are presented, data producers should provide the number of respondents who marked (or selected) only one category, separately for each of the five racial categories. In addition to these numbers, sponsors are encouraged to provide the detailed distributions, including all possible combinations of multiple responses to the race question. If data on multiple responses are condensed, at a minimum the total number of respondents reporting "more than one race" should be reported.

E. Use of More-Detailed Racial and Ethnic Categories

In certain situations, as recommended in OMB Policy Directive 15, more-detailed race and/or ethnicity information may be desired. For example, for clinical trials enrolling participants outside the United States, FDA recognizes that the recommended categories for race and ethnicity were developed in the United States and that these categories may not adequately describe racial and ethnic groups in other countries.

Where appropriate, FDA recommends using more-detailed categories by geographic region to provide sponsors flexibility in characterizing race and ethnicity. FDA recommends that these characterizations be aligned with the five minimum designations for race and the two designations for ethnicity listed previously in subsections D and C, respectively. If additional granularity or more-detailed characterizations of race or ethnicity are collected to enhance understanding of the trial participants, FDA recommends following the 2011 HHS Implementation Guidance on Data Collection Standards for Race, Ethnicity, Sex, Primary Language, and Disability Status,[27] as described below.

[26] As explained in the next section of this guidance (section III.E), sponsors may include more-detailed categories, and doing so is recommended where appropriate.

[27] See footnote 7.

Ethnicity Data Standard

Are you Hispanic or Latino? (One or more categories may be selected.)

a. No, not Hispanic or Latino
b. Yes, Mexican, Mexican American, Chicano
c. Yes, Puerto Rican
d. Yes, Cuban
e. Yes, Other Hispanic or Latino

These categories are part of the Hispanic or Latino category of the OMB standard

Race Data Standard

What is your race? (One or more categories may be selected.)

a. White
b. Black or African American
c. American Indian or Alaska Native

These categories are part of the OMB standard

d. Asian Indian
e. Chinese
f. Filipino
g. Japanese
h. Korean
i. Vietnamese
j. Other Asian

These categories are part of the Asian category of the OMB standard

k. Native Hawaiian
l. Guamanian or Chamorro
m. Samoan
n. Other Pacific Islander

These categories are part of the Native Hawaiian or Other Pacific Islander category of the OMB standard

OMB Policy Directive 15 states that the term *nonwhite* is not acceptable for use in the presentation of Federal Government data. It should not be used in publication or text of any report. If there are questions or concerns regarding the collection of race or ethnicity categories, sponsors are encouraged to discuss the matter with the appropriate review division.

IV. PRESENTATION OF RACE AND ETHNICITY DATA IN CLINICAL TRIALS AND CLINICAL STUDIES

For INDs, NDAs, and BLAs, we recommend that the submission of demographic data for all new clinical trials and clinical studies be tabulated using the characterizations of race and ethnicity described in this guidance. For medical device submissions, see also the guidance for industry *Evaluation and Reporting of Age-, Race-, and Ethnicity-Specific Data in Medical Device Clinical Studies* (September 2017)

The Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) require marketing applications to be submitted electronically.[28] CDER and CBER use the electronic common technical document (eCTD) as the standard for their electronic applications. When submitting an electronic application, presentation of demographic data is described in the ICH guidance for industry *M4E(R2): The CTD – Efficacy* (July 2017), which suggests a tabular display of demographic characteristics, including race, by treatment group (e.g., active drug, placebo).[29]

FDA recommends that applicants include race and ethnicity information (using the categories described in section III of this guidance) in their proposed product labeling. For example, the CLINICAL STUDIES section of drug and biological product labeling should include the baseline demographics (including racial and ethnic characteristics) of the studied population.[30] The ADVERSE REACTIONS section of drug and biological product labeling should include the baseline demographics of the safety population.[31] If the baseline demographics in the safety and efficacy populations are generally the same and the description of the baseline demographics are included in the CLINICAL STUDIES section, instead of repeating the same baseline demographics in the ADVERSE REACTIONS section, the ADVERSE REACTIONS section can cross-reference the CLINICAL STUDIES section. OMB Policy Directive 15 states that the term *nonwhite* is not acceptable for use in the presentation of Federal Government data. It should not be used in publication or text of any report. If there are questions or concerns regarding the collection of race or ethnicity categories, sponsors are encouraged to discuss the matter with the appropriate review division.[32]

[28] See the guidance for industry *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (February 2020).

[29] See the revision of M4E Guideline on Enhancing the Format and Structure of Benefit-Risk Information in the International Council for Harmonisation (ICH) guidance for industry *M4E(R2): The CTD – Efficacy* (July 2017).

[30] See section III.B.4 in the guidance for industry *Clinical Studies Section of Labeling for Human Prescription Drug and Biological Products – Content and Format* (January 2006).

[31] See the guidance for industry *Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products – Content and Format* (January 2006).

[32] See section III.E of this guidance.