# Guidance for Industry

## Collection of Race and Ethnicity Data in Clinical Trials

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**
**Center for Biologics Evaluation and Research (CBER)**
**Center for Devices and Radiologic Health (CDRH)**
**Office of the Commissioner (OC)**

**September 2005**
**Clinical Medical**

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*Contains Nonbinding Recommendations*

# Guidance for Industry[1]

# Collection of Race and Ethnicity Data in Clinical Trials

This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

## I. INTRODUCTION

This guidance recommends using a standardized approach for collecting and reporting race and ethnicity information in clinical trials conducted in the United States and abroad for certain FDA regulated products. The recommended standardized approach was developed by the Office of Management and Budget (OMB). The guidance lists the OMB categories for race and ethnicity and describes FDA's reasons for recommending the use of these categories. In addition, this guidance recommends a format for race and ethnicity data within study data that are submitted in standardized data sets such as the Study Data Tabulation Model[2] or in the electronic Common Technical Document (eCTD).[3]

This document is intended to provide guidance on meeting the requirements set forth in the 1998 final rule on investigational new drug (IND) applications and new drug applications (NDAs)[4] (Demographic Rule). The Demographic Rule requires IND holders to tabulate in their annual report the number of subjects enrolled in clinical studies of drugs and biologic products by age, race, and gender, and sponsors of NDAs to include summaries of effectiveness and safety data for important demographic subgroups, including racial subgroups.[5] This guidance is also intended to help applicants in preparing biologics license applications (BLAs).

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[1] This guidance has been developed by the Agency-wide Race and Ethnicity Working Group from the Office of the Commissioner (OC), the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA).

[2] See CDISC standardized Study Data Tabulation Model (SDTM), Analysis Data Model (ADaM), Operational Data Model (ODM) at http://www.cdisc.org.

[3] See FDA's guidance for industry titled *M4 Common Technical Document for the Registration of Pharmaceuticals for Human Use* (eCTD guidance) for the submission file location of the table format presented in section V of this guidance. Available at http://www.fda.gov/cder/regulatory/ersr/ectd.htm.

[4] 63 FR 6854 (February 11, 1998) (codified at 21 CFR 312.33(a)(2) and 21 CFR 314.50(d)(5)).

[5] 21 CFR 312.33(a)(2). See also 21 CFR 314.50(d)(5)(v) and (vi)(*a*) regarding demographic data submission in NDAs.

Although the regulations governing medical devices do not include requirements for the collection of demographic data comparable to those for INDs and NDAs, for those cases in which race and ethnicity data are relevant to determining the safety and effectiveness of a device, FDA encourages sponsors to collect the data in accordance with the OMB recommendations and the information collection standards discussed in this guidance document. Sponsors are also encouraged to discuss any race or ethnicity issues with the appropriate review division in the Office of Device Evaluation, Center for Devices and Radiological Health, when developing their study protocols.

This guidance does not address the level of participation of racial and ethnic groups in clinical trials. For questions related to the level of participation or the size of a study sponsors should consult with the review division prior to the start of a study.

FDA's guidance documents, including this guidance, 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.

## II. BACKGROUND

FDA regulations require sponsors of NDAs to present a summary of safety and effectiveness data by demographic subgroups (age, gender, race), as well as an analysis of whether modifications of dose or dosage intervals are needed for specific subgroups (21 CFR 314.50 (d)(5)(v) and (vi)(a)).[6] One consideration in such summaries is the identification of a subject's race or ethnicity.

In 1997, OMB issued its revised recommendations for the collection and use of race and ethnicity data by Federal agencies (Policy Directive 15).[7] FDA is now recommending the use of the standardized OMB race and ethnicity categories for data collection in clinical trials for two reasons. First, the use of the recommended OMB categories will help ensure consistency in demographic subset analyses in applications submitted to FDA (21 CFR 314.50(d)(5)(v) and (vi)(a), 312.120, 314.106(b), and 601.2) and in data collected by other government agencies. Second, consistency in these categories may make the demographic subset analysis more useful in evaluating potential differences in the safety and efficacy of pharmaceutical products among

[6] Under 21 CFR 314.101(d)(3), the Agency may refuse to file an NDA if it is incomplete because it does not contain information required by 21 CFR 314.50. Thus, if there is an inadequate evaluation for safety and/or effectiveness of the population intended to use the drug, including pertinent subsets, such as gender, age, and racial subsets the Agency may refuse to file the application. See FDA's guidance for industry titled *New Drug Evaluation Guidance Document: Refusal to File*, available on the Internet at http://www.fda.gov/cder/guidance/index.htm.

[7] Statistical Policy Directive No. 15, Race and Ethnic Standards for Federal Statistics and Administrative Reporting, 1997 (reprinted in Appendix 2). See also the OMB guidance entitled *Provisional Guidance on the Implementation of the 1997 Standards for Federal Data on Race and Ethnicity* (2000), available at http://www.whitehouse.gov/omb/bulletins/b00-02.html.

population subgroups. To assess potential subgroup differences in a meaningful way, it is important to use uniform, standard methods of defining racial and ethnic subgroups.

## A. Relevance of Population Subgroup Studies

Differences in response to medical products have already been observed in racially and ethnically distinct subgroups of the U.S. population.[8] These differences may be attributable to intrinsic factors (e.g., genetics, metabolism, elimination), extrinsic factors (e.g., diet, environmental exposure, sociocultural issues), or interactions between these factors. For example, in the United States, Whites[9] are more likely than persons of Asian and African heritage to have abnormally low levels of an important enzyme (CYP2D6) that metabolizes drugs belonging to a variety of therapeutic areas, such as antidepressants, antipsychotics, and beta blockers (Xie 2001). Other studies have shown that Blacks respond poorly to several classes of antihypertensive agents (beta blockers and angiotensin converting enzyme (ACE) inhibitors) (Exner 2001 and Yancy 2001). Racial differences in skin structure and physiology that can affect response to dermatologic and topically applied products have been noted (Taylor 2002). Clinical trials have demonstrated lower responses to interferon-alpha used in the treatment of hepatitis C among Blacks when compared with other racial subgroups (McHutchison 2000 and Reddy 1999).

## B. FDA Decision to Recommend Use of the OMB Categories

The OMB stated that its race and ethnicity categories were not anthropologic or scientifically based designations, but instead were categories that described the sociocultural construct of our society. The Department of Health and Human Services (HHS) chose to adopt these standardized categories for its agencies that report statistics because the categories are relevant to assessing various health related data, including public health surveillance and research. FDA believes that the use of the current OMB categories and any future revisions will facilitate comparisons across clinical studies analyzed by FDA and data collected by other agencies. Collection of data using standard categories can enhance patient safety by helping FDA evaluate potential differences in drug response among subpopulations. Using standard categories may also facilitate analyses seeking to identify differences in response.

Although FDA has long requested race and ethnicity data on subjects in certain clinical trials, the Agency has not previously made explicit recommendations on the categories to use when collecting and reporting the data. In 1998, the Agency issued the Demographic Rule, which reflected growing recognition within the Agency and the health community that (1) different subgroups of the population may respond differently to specific drug products, and (2) although an effort should be made to look for differences in effectiveness and adverse reactions among such subgroups, that effort is not being made consistently.[10] In the Demographic Rule, FDA

[8] In fact, in June of 2005, FDA approved BiDil, the first drug approved by the Agency to treat a disease in patients identified by race. The drug was approved for the treatment of heart failure in black patients. The company conducted two trials in the general population that failed to show a benefit, but suggested a benefit of BiDil in black patients. The company then studied the drug in 1,050 self-identified black patients and it was shown to be safe and effective.

[9] The terms used in this guidance to describe the various racial and ethnic groups are those used by OMB.

[10] 63 FR 6854 at 6855, February 11, 1998.

discussed the importance of collecting data in clinical trials (and of presenting those data in applications to the Agency) on population subgroups organized by gender, race, age, and other relevant categories. The Agency recommended that sponsors ask subjects in certain clinical trials to identify their racial group and, if desired, that sponsors use OMB categories when collecting race and ethnicity data.[11]

During the past two decades, efforts have been under way in a number of Federal organizations to collect race and ethnicity data in Federal programs in a standardized way. (See Appendix 1 for a summary of those efforts). In 1997, HHS issued a document entitled *Policy Statement on Inclusion of Race and Ethnicity in DHHS Data Collection Activities.*[12] In this policy statement, HHS adopted the revised OMB categories for including race and ethnicity in HHS funded and sponsored data collection and reporting systems. The HHS policy states that the categories described in revised OMB Directive 15 and its future revisions should be used when collecting and reporting data in HHS data systems or reporting HHS funded statistics.[13]

The Agency recommends that sponsors use the categories outlined in this guidance when collecting race and ethnicity data in clinical studies for FDA-regulated products conducted in United States and abroad. More detailed race and ethnicity data can be collected when appropriate to the study or locale, but we recommend that these more detailed race and ethnicity data be related to the identified OMB categories of all clinical trial participants when submitting such data to the Agency.

## III. COLLECTING RACE AND ETHNICITY DATA IN CLINICAL TRIALS

The recommendations in this section reflect the Agency's interest in more consistent data collection. For studies conducted in the United States, the Agency recommends that a two-question format be used, and that trial participants self-report their racial and ethnic ancestral origins. Based on the current OMB Directive, the Agency provides the following recommendations for the collection of the data:

1. We recommend using the two-question format for requesting race and ethnicity information, with the ethnicity question preceding the question about race.

[11] In the preamble to the final rule, FDA stated that it did not believe it was necessary to define specific racial categories in the rule itself because drug sponsors have been successful in identifying the relevant racial categories to examine safety and efficacy profiles of drugs (63 FR 6854 at 6859). However, FDA now believes that using uniform categories will enhance the consistency and comparability of data across studies submitted in marketing applications and other government reported statistics.

[12] Memorandum issued by HHS Sec. Donna Shalala on October 24, 1997 reaffirming HHS' commitment to the inclusion of data on minority groups in research, services and related activities. Effective as of November 1,1997. Available at http://aspe.hhs.gov/datacncl/inclusn.htm.

[13] OMB directed these activities to begin by January 1, 2003, in all Federal programs, including HHS. Although in the past FDA sought and received a variance from OMB exempting the Agency from reporting data using the Directive 15 categories, FDA now recommends the use of the categories to enhance data consistency. To view the policy memorandum see: http://www.hhs.gov/oirm/infocollect/nclusion.html

2. We recommend that study participants self-report race and ethnicity information whenever feasible, and that individuals be permitted to designate a multiracial identity. When the collection of self-reported designations is not feasible (e.g., because of the subject's inability to respond), we recommend that the information be requested from a first-degree relative or other knowledgeable source.

3. For ethnicity, we recommend the following minimum choices be offered:
    - Hispanic or Latino
    - Not Hispanic or Latino

4. When race and ethnicity information is collected separately, we recommend the following minimum choices be offered for race:[14]
    - American Indian or Alaska Native
    - Asian
    - Black or African American
    - Native Hawaiian or Other Pacific Islander
    - White

5. In certain situations, as recommended in OMB Directive 15, more detailed race and ethnicity information may be desired (e.g., *White* can reflect origins in Europe, the Middle East, or North Africa; *Asian* can reflect origins from areas ranging from India to Japan). If more detailed characterizations of race or ethnicity are collected to enhance data consistency, we recommend these characterizations be traceable to the five minimum designations for race and two designations for ethnicity (five and two) listed in numbers 3 and 4. When more detailed characterizations are desired, the use of Race and Ethnicity vocabulary tables located within Health Level Seven's[15] Reference Information Model Structural Vocabulary Tables is recommended. These tables provide the OMB characterizations traceable to more detailed characterizations and concept ID code sets to help ensure that traceability is consistent. Where gaps exist in the representation of race or ethnicity categories, sponsors are encouraged to discuss the race or ethnicity issue with the appropriate review division.

## IV. CLINICAL TRIALS CONDUCTED OUTSIDE OF THE UNITED STATES

To assist in assessing the relevance of foreign study population data to U.S. populations, we recommend that sponsors use the OMB standardized categories when collecting data from study participants in clinical trials conducted outside of the United States. However, 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 foreign countries. Therefore, for studies conducted outside the United States, we recommend using more detailed categories to provide sponsors the flexibility to adequately characterize race and ethnicity. If

[14] To identify ancestral origins for each of the named categories see OMB Directive 15 (Appendix 2).

[15] Health Level Seven (HL7), an American National Standards Institute (ANSI) accredited organization, has been designated by the Department as a Standards Development Organization for the development of interoperability standards for health care and health related information, and is available at http://hl7.org.

sponsors choose to use more detailed characterizations of race and ethnicity, it is important for analytical purposes that the data can be traced back to the recommended categories described below. When more detailed characterizations are desired, the use of the Race and Ethnicity vocabulary tables located within Health Level Seven's Reference Information Model Structural Vocabulary Tables is recommended[16]. These tables provide the five and two OMB characterizations traceable to more detailed characterizations and concept ID code sets and their use will help ensure that traceability is consistent. Where gaps exist in the representation of race or ethnicity categories, sponsors are encouraged to discuss the issue with the appropriate review division.

1. For ethnicity, we recommend the following categories or the use of categories that are mappable to the two categories listed below:
    - Hispanic or Latino
    - Not Hispanic or Latino

2. When race is collected separately in clinical studies conducted in foreign countries, we recommend that the categories be modified to reflect the following, as appropriate:
    - American Indian or Alaska Native
    - Asian
    - Black
    - Native Hawaiian or Other Pacific Islander
    - White

    Note that the ethnic and racial categories for studies inside and outside the United States are the same, except for one racial designation: the racial designation is African American in the United States, whereas it is Black for studies conducted in foreign countries.

## V. PRESENTATION OF DEMOGRAPHIC TABULATIONS IN THE eCTD

For INDs, NDAs, BLAs and relevant device submissions we recommend the submission of tabulated demographic data based on the Demographic Rule for all clinical studies using the characterizations of race and ethnicity described in this guidance.

For submitting an electronic application not in FDA's typical application format (i.e., when using the ICH document for submitting a marketing application to FDA and regulatory agencies in Japan and Europe, the eCTD) presentation of demographic data is described in ICH M4E eCTD Guidance (section 2.7.4.1.3 and table 2.7.4.2), which suggests a tabular display of demographic characteristics (e.g., age, gender, race) by treatment group (e.g., active drug, placebo). The document suggests specific kinds of demographic information to be collected as a part of a clinical trial, but does not provide rigid specifications on how the data should be presented, noting, for example, that "if relative exposure of demographic groups in the controlled trials differ from the overall exposure, it may be useful to provide separate tables." Choices of how

[16] These tables are located at http://hl7.org. To locate the tables from HL7's home page click on HL7 Standards under Resources, then RIMS, HL7 Reference Model Structured Vocabulary Tables in HTML, 2.1 HL7 Vocabulary Domain Values and select either the Race or Ethnicity table from the list.

best to summarize demographic data depend on the nature of the data to be conveyed. For some trials, it may be useful to show the distribution of one demographic characteristic within a second demographic (e.g., the age distribution of men and women enrolled in a set of controlled trials).

With regard to the description of race and ethnicity, the categories that are suggested previously in this document (sections III and IV) are preferable to those suggested in ICH M4E eCTD guidance.

# APPENDIX 1

# HISTORY OF FEDERAL EFFORTS IN DATA COLLECTION ON RACE AND ETHNICITY AND OTHER SUBPOPULATIONS

For more than 20 years, a number of U.S. Government initiatives have tried to address questions related to whether to and how to collect race and ethnicity data. Major initiatives are reviewed briefly here.

## Office of Management and Budget (OMB) Initiatives

In May 1977, OMB issued "Statistical Policy Directive No. 15, Race and Ethnic Standards for Federal Statistics and Administrative Reporting." The standards were developed in response to the need to enforce civil rights laws in education. These classifications were not to be interpreted as being scientific or anthropological in nature, or to be viewed as determinants of eligibility for participation in any Federal program. They were developed in response to needs expressed by both the Executive Branch and the Congress to provide for the collection and use of compatible, nonduplicated, exchangeable race and ethnicity data by Federal agencies. This Directive specified four categories for race:

- American Indian or Alaskan Native
- Asian or Pacific Islander
- Black
- White

And two categories for ethnicity:

- Hispanic
- Not of Hispanic origin

The OMB Directive specified two questionnaire formats for data collection: (1) a format combining race and ethnicity, and (2) a preferred format with two separate questions for race and ethnicity.

Since 1993, efforts have been under way to standardize the collection of race and ethnicity data to foster comparability across data collection and reporting systems. In 1997, OMB published Directive 15, "Revisions to the Standards for the Classification of Federal Data on Race and Ethnicity" (see Appendix 2). These revisions specified the minimum racial and ethnic diversity categories to be used when race and ethnicity are included in data collection and reporting for Federal programs. The Directive does not require that race and ethnicity be included in data collection and reporting; rather, it specifies what formats and categories to use when collecting this kind of data.

The revised OMB standards made the following changes:

- Introduced the option of reporting more than one race for multiracial persons
- Divided the Asian or Pacific Islander category into two — one labeled Asian, the other Native Hawaiian or Other Pacific Islander
- Changed Hispanic to Hispanic or Latino
- Changed Black to Black or African-American
- Strongly encouraged the use of self-identification
- Maintained the two-question format for race and Hispanic ethnicity when self-identification is used (the Hispanic origin question should precede the race question)

The revised categories were described in an OMB guidance entitled *Implementation of the 1997 Standards for Federal Data on Race and Ethnicity* (2000) as sociopolitical and intended for use in the collection of health data, among other types of statistics.

**Department of Health and Human Services Initiatives**

In 1999, the Department of Health and Human Services (HHS) issued a report, *Improving the Collection and Use of Racial and Ethnic Data in HHS*. The report describes HHS policy on collecting and reporting data on race and ethnicity for HHS programs. The report asks for the inclusion of race and ethnicity categories in HHS funded and sponsored data collection and reporting systems in all HHS programs, including in both health and human services. This policy clearly states that the minimum standard categories in OMB Directive 15 and revisions should be used when collecting and reporting data in HHS data systems or reporting HHS funded statistics. The policy was developed 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.

**National Institutes of Health Initiatives**

In 1993, the National Institutes of Health (NIH) Revitalization Act directed NIH to establish guidelines for including women and minorities in NIH-sponsored clinical research. NIH was directed to ensure that women and minorities were included as subjects, unless their exclusion was justified due to circumstances specified by NIH guidelines. Furthermore, clinical trials were to be designed and carried out in a manner that would elicit information about individuals of both genders and diverse racial and ethnic groups to examine differential effects on such groups. NIH guidelines stipulate that when proposing a Phase 3 clinical trial, evidence must be reviewed to establish whether or not there are potentially clinically important gender- and minority-based differences in the anticipated effects of the intervention. If previous studies support the existence of significant differences, the primary questions and design of the study must specifically accommodate this. For example, if men and women are thought to respond differently to an intervention, then the Phase 3 clinical trial must be designed to answer two separate primary questions, one for men, and the other for women. When prior studies support no significant differences for either gender or minorities with a given intervention, then gender and minority status will not be required as subject selection criteria, although the inclusion and analysis of both genders and minorities is strongly encouraged. When prior studies neither support nor negate significant differences, then the design of the Phase 3 clinical trial will be required to support

sufficient representation of both genders and minorities to allow for valid analysis of the intervention effects across all groups. However, the trial will not be required to provide high statistical power for these comparisons.

**Food and Drug Administration Initiatives**

Beginning in the 1980s, FDA grew concerned about possible differences in drug safety and efficacy among different population subgroups. Because the origins of subpopulation issues stem from the identification of differences in response in women and geriatric populations, references to those initiatives are included below. In 1983, the Agency initiated development of guidance on the study of drugs to be used in geriatric patients. FDA's *Guideline for the Study of Drugs Likely to be Used in the Elderly* was issued in 1989.

The first regulation specifying the analysis of population subsets appeared in 1985 in 21 CFR 314.50, which called for evidence to support the "dosage and administration section of the labeling, including support for the dosage and dose interval recommended," and modifications for specific subgroups (e.g., pediatrics, geriatrics, patients with renal failure) (21 CFR 314.50(d)(5)(v)).

In 1988, the Agency issued guidance describing elements of a new drug application's analysis of clinical study data. *Guideline for the Format and Content of the Clinical and Statistical Sections of New Drug Applications* emphasized the importance of conducting subset analyses on data from clinical studies submitted in new drug applications (NDAs). This guidance specified race and ethnicity as types of population subsets for which separate analyses of data from clinical studies should be conducted for assessments of product safety and effectiveness.

In July 1993, FDA published a guidance on the study of drugs in both genders entitled *Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs*. The guidance specifically called for analyzing trials by gender and for evaluating pharmacokinetics in women. In the *Federal Register* notice announcing the guidance, FDA also abandoned the policy explained in a 1977 guidance, excluding women of childbearing potential from participation in the earliest phases of clinical trials.

In 1993, FDA also published *New Drug Evaluation Guidance Document: Refusal to File*, on the Agency's use of the refusal-to-file (RTF) option if certain analyses were not performed. The guidance states that the Agency can exercise its RTF authority under 21 CFR 314.101(d)(3) if there is "inadequate evaluation for safety and/or effectiveness of the population intended to use the drug, including pertinent subsets, such as gender, age, and racial subsets."

In the Food and Drug Administration Modernization Act of 1997 (the Modernization Act), Congress directed FDA to examine issues related to the inclusion of racial and ethnic groups in clinical trials of new drugs. Section 115(b) of the Modernization Act required the Secretary, "in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, [to] review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials. . . ." (codified at 21 U.S.C. 355(b)(1)). In response, FDA established the Women and Minorities Working Group to review and implement this

section of the Modernization Act. In a report issued on July 20, 1998, the Working Group concluded that the Agency would implement procedures to enhance its ability to gather and evaluate demographic data, and then decide whether additional guidance should be developed in the future.

In 1998, the Agency published the Demographic Rule, which amended the language in 21 CFR 312.33(a)(2) and 314.50(d)(5), requiring sponsors to (1) tabulate the numbers of participants in clinical trials by age group, gender, and race in investigational new drug application (IND) annual reports, (2) characterize the data in NDAs according to these same subgroups, and (3) when appropriate, present safety data from other subgroups of the population of patients, such as for patients with hepatic or renal failure or patients with different levels of severity of the disease.

In 1999, a guidance for industry entitled *Population Pharmacokinetics* made recommendations on the use of population pharmacokinetics in the drug development process to help identify differences in drug safety and efficacy among population subgroups, including race and ethnicity. This guidance recommended that industry conduct clinical studies in subjects representative of the population to be treated with the drug.

In 2002, the Best Pharmaceuticals for Children Act (Public Law 107-109, January 4, 2002) directed FDA to monitor the racial and ethnic designations of children participating in clinical studies for pharmaceutical products.

**ICH E5 - Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data**

In 1999, as part of an international effort by Japan, the European Union, and the United States to harmonize technical requirements for pharmaceutical drug development and regulation (the International Conference on Harmonization (ICH)), the FDA published a guidance entitled *E5 Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data* (63 FR 31790, June 10, 1999), to permit the clinical data collected in one region to be used in the registration or approval of a drug or biological product in another region, while allowing for the influence of ethnic factors. The *E5* guidance defines ethnic factors that affect response in terms of both intrinsic and extrinsic issues. Because differences in ethnic factors have the potential to affect responses in some subpopulations, the *E5* guidance provides a general framework for evaluating medicines with regard to their sensitivity to ethnic factors.

**APPENDIX 2**

**REVISED DIRECTIVE 15**

# OMB Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity

*(Adopted on October 30, 1997)*

This classification provides a minimum standard for maintaining, collecting, and presenting data on race and ethnicity for all Federal reporting purposes. The categories in this classification are social-political constructs and should not be interpreted as being scientific or anthropological in nature. They are not to be used as determinants of eligibility for participation in any Federal program. The standards have been developed to provide a common language for uniformity and comparability in the collection and use of data on race and ethnicity by Federal agencies.

The standards have five categories for data on race: American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, and White. There are two categories for data on ethnicity: Hispanic or Latino, and Not Hispanic or Latino.

## 1. Categories and Definitions

The minimum categories for data on race and ethnicity for Federal statistics, program administrative reporting, and civil rights compliance reporting are defined as follows:

**American Indian or Alaska Native.** A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment.

**Asian.** A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent, including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.

**Black or African American.** A person having origins in any of the black racial groups of Africa. Terms such as “Haitian” or “Negro” can be used in addition to “Black or African American.”

**Hispanic or Latino.** A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race. The term, “Spanish origin,” can be used in addition to “Hispanic or Latino.”

**Native Hawaiian or Other Pacific Islander.** A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.

**White.** A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.

Respondents shall be offered the option of selecting one or more racial designations. Recommended forms for the instruction accompanying the multiple response question are "Mark one or more" and "Select one or more."

## 2. Data Formats

The standards provide two formats that may be used for data on race and ethnicity. Self-reporting or self-identification using two separate questions is the preferred method for collecting data on race and ethnicity. In situations where self-reporting is not practicable or feasible, the combined format may be used.

In no case shall the provisions of the standards be construed to limit the collection of data to the categories described above. The collection of greater detail is encouraged; however, any collection that uses more detail shall be organized in such a way that the additional categories can be aggregated into these minimum categories for data on race and ethnicity.

With respect to tabulation, the procedures used by Federal agencies shall result in the production of as much detailed information on race and ethnicity as possible. However, Federal agencies shall not present data on detailed categories if doing so would compromise data quality or confidentiality standards.

### a. Two-question format

To provide flexibility and ensure data quality, separate questions shall be used wherever feasible for reporting race and ethnicity. When race and ethnicity are collected separately, ethnicity shall be collected first. If race and ethnicity are collected separately, the minimum designations are:

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

**Ethnicity**:
Hispanic or Latino
Not Hispanic or Latino

When data on race and ethnicity are collected separately, provision shall be made to report the number of respondents in each racial category who are Hispanic or Latino. When aggregate data are presented, data producers shall 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, data producers are strongly encouraged to provide the detailed distributions, including all possible combinations of multiple responses to the race question. If data on multiple responses are collapsed, at a minimum the total number of respondents reporting "more than one race" shall be made available.

### b. Combined format

The combined format may be used, if necessary, for observer-collected data on race and ethnicity. Both race (including multiple responses) and ethnicity shall be collected when appropriate and feasible, although the selection of one category in the combined format is acceptable. If a combined format is used, there are six minimum categories:

American Indian or Alaska Native
Asian
Black or African American
Hispanic or Latino
Native Hawaiian or Other Pacific Islander
White

When aggregate data are presented, data producers shall provide the number of respondents who marked (or selected) only one category, separately for each of the six categories. In addition to these numbers, data producers are strongly encouraged to provide the detailed distributions, including all possible combinations of multiple responses. In cases where data on multiple responses are collapsed, the total number of respondents reporting "Hispanic or Latino and one or more races" and the total number of respondents reporting "more than one race" (regardless of ethnicity) shall be provided.

## 3. Use of the Standards for Record Keeping and Reporting

The minimum standard categories shall be used for reporting as follows:

### a. Statistical reporting

These standards shall be used at a minimum for all federally sponsored statistical data collections that include data on race and/or ethnicity, except when the collection involves a sample of such size that the data on the smaller categories would be unreliable, or when the collection effort focuses on a specific racial or ethnic group. Any other variation will have to be specifically authorized by the OMB through the information collection clearance process. In those cases where the data collection is not subject to the information collection clearance process, a direct request for a variance shall be made to OMB.

### b. General program administrative and grant reporting

These standards shall be used for all Federal administrative reporting or record keeping requirements that include data on race and ethnicity. Agencies that cannot follow these standards must request a variance from OMB. Variances will be considered if the agency can demonstrate that it is not reasonable for the primary reporter to determine racial or ethnic background in terms of the specified categories, that determination of racial or ethnic background is not critical to the administration of the program in question, or that the specific program is directed to only one or a limited number of racial or ethnic groups.

### c. Civil rights and other compliance reporting

These standards shall be used by all Federal agencies in either the separate or combined format for civil rights and other compliance reporting from the public and private sectors and all levels of government. Any variation requiring less detailed data or data which cannot be aggregated into the basic categories must be specifically approved by OMB for executive agencies. More detailed reporting which can be aggregated to the basic categories may be used at the agencies' discretion.

## 4. Presentation of Data on Race and Ethnicity

Displays of statistical, administrative, and compliance data on race and ethnicity shall use the categories listed above. The term "nonwhite" is not acceptable for use in the presentation of Federal Government data. It shall not be used in any publication or in the text of any report. In cases where the standard categories are considered inappropriate for presentation of data on particular programs or for particular regional areas, the sponsoring agency may use:

**a.** The designations "Black or African American and Other Races" or "All Other Races" as collective descriptions of minority races when the most summary distinction between the majority and minority races is appropriate;

**b.** The designations "White," "Black or African American," and "All Other Races" when the distinction among the majority race, the principal minority race, and other races is appropriate; or

**c.** The designation of a particular minority race or races, and the inclusion of "Whites" with "All Other Races" when such a collective description is appropriate. In displaying detailed information that represents a combination of race and ethnicity, the description of the data being displayed shall clearly indicate that both bases of classification are being used.

When the primary focus of a report is on two or more specific identifiable groups in the population, one or more of which is racial or ethnic, it is acceptable to display data for each of the particular groups separately and to describe data relating to the remainder of the population by an appropriate collective description.

## 5. Effective Date

The provisions of these standards are effective immediately for all new and revised record keeping or reporting requirements that include racial and/or ethnic information. All existing record keeping or reporting requirements shall be made consistent with these standards at the time they are submitted for extension, or not later than January 1, 2003.

## REFERENCES

Exner, D., D. Dries, M. Donamski, and J. Cohn, 2001, "Lesser Response to Angiotensin-Converting-Enzyme Inhibitor Therapy in Black as Compared with White Patients With Left Ventricular Dysfunction," *N Engl J Med*, 344: 1351-1357.

Freedman, L.S., R.M. Simon, M.A. Foulkes, L.M. Freedman, N.L. Gordon, et al., 1995, "Inclusion of Women and Minorities in Clinical Trials and the NIH Revitalization Act — the Perspective of NIH Clinical Trialists," *Control Clin Trials*, 16(5):277-285, 310-312.

McHutchison, J., T. Poynard, S. Pianko, S. Gordon, A. Reid, et al., 2000, "The Impact of Interferon Alpha Plus Ribavirin on Response to Therapy in Black Patients with Chronic Hepatitis C. The International Hepatitis Interventional Therapy Group," *Gastroenterology*, 119: 1317-23.

Reddy, K. R., J. Hoofnagle, M. Tong, W. Lee, P. Pockros, et al., 1999, "Racial Differences in Responses to Therapy with Interferon in Chronic Hepatitis C. Consensus Interferon Study Group," *Hepatology*, 30: 787-93.

Taylor, S., 2002, "Skin of Color: Biology, Structure, Function, and Implications for Dermatologic Disease," *Journal of American Academy of Dermatology*, 46:S41-62.

Xie, H., R. Kim, A. Wood, and C. Stein, 2001, "Molecular Basis of Ethnic Differences in Drug Disposition and Response," *Annu Rev Pharmacol Toxicol*, 41:815-50.

Yancy, C., M. Fowler, W. Colucci, E. Gilbert, M. Bristow, et al., 2001, "Race and the Response to Adrenergic Blockade with Carvedilol in Patients with Chronic Heart Failure," *N Engl J Med*, 344: 1358-1365.

## BIBLIOGRAPHY


### DHHS Policy and Reports

Department of Health and Human Services (DHHS), 1997, *Policy For Improving Race and Ethnicity Data, October 24, 1997*, http://www.hhs.gov/oirm/infocollect/nclusion.html.

DHHS, 1999, *Improving the Collection and Use of Racial and Ethnic Data in HHS*, joint report of the HHS Data Council Working Group on Racial and Ethnic Data and the Data Work Group of the HHS Initiative to Eliminate Racial and Ethnic Disparities in Health, December 1999, http://aspe.hhs.gov/datacncl/racerpt/index.htm.

### FDA Regulations

Food and Drug Administration (FDA), 1998, "Investigational New Drug Applications and New Drug Applications," Final Rule, *Federal Register* (63 FR 6854, February 11, 1998).

FDA, *Content and Format for Human Prescription Drugs; Addition of "Geriatric Use" Subsection in the Labeling*, Final Rule, *Federal Register* (62 FR 45313, August 27, 1997).

### FDA Guidance for Industry

*Clinical Studies Section of Labeling for Prescription Drugs and Biologics* (Draft)[17]

*Content and Format for Geriatric Labeling*

*Content and Format of the Adverse Reactions Section of Labeling for Human Prescription Drugs and Biologics* (Draft)

*General Considerations for Pediatric Pharmacokinetic Studies for Drugs and Biological Products* (Draft)

*General Considerations for the Clinical Evaluation of Drugs*

*Format and Content of the Clinical and Statistical Sections of an Application*

*Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs*

*Study of Drugs Likely to be Used in the Elderly*

*In Vivo Drug Metabolism/Drug Interaction Studies — Study Design, Data Analysis, and Recommendations for Dosing and Labeling*

*Pharmacokinetics in Patients with Impaired Hepatic Function: Study Design, Data Analysis, and Impact on Dosing and Labeling*

*Pharmacokinetics in Patients with Impaired Renal Function: Study Design, Data Analysis and Impact on Dosing and Labeling*

*Population Pharmacokinetics*

*Refusal to File*


[17] Draft guidances are included for completeness only. As draft documents, they are not intended to be implemented until published in final form.

**ICH Guidances**

ICH, *E4 Dose Response Information to Support Drug Registration*

ICH, *E5 Ethnic Factors in the Acceptability Of Foreign Data*

ICH, *E7 Studies in Support of Special Populations: Geriatrics*

ICH, *E11 Clinical Investigation of Medicinal Products in the Pediatric Population*

ICH, *M4 Common Technical Document for the Registration of Pharmaceuticals for Human Use*

**Other Sources**

Office of Management and Budget, 1994, Standards for the Classification of Federal Data on Race and Ethnicity, http://www.whitehouse.gov/omb/fedreg/notice_15.html.

General Accounting Office, *FDA Needs to Ensure More Study of Gender Differences in Prescription Drug Testing*, GAO/HFD-93-17.

NIH Revitalization Act of 1993, (PL 103-43).

NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research-Updated August 1, 2000. Available at http://grants.nih.gov/grants/funding/women_min/women_min.htm.

Food and Drug Administration Modernization Act of 1997 (Public Law 105-115).

Best Pharmaceuticals Act for Children of 2002 (Public Law 107-109).