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VICE PRESIDENT
SCIENCE POLICY AND TECHNICAL AFFAIRS

PhRMA

March 28, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Draft Guidance for Industry on the Collection of Race and Ethnicity Data in Clinical Trials for FDA Regulated Products [Docket No. 02D-0018, 68 *Federal Register*, 4788, January 30, 2003]

Dear Sir/Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer and more productive lives. Investing more than $30 billion annually in discovering and developing new medicines, PhRMA companies are leading the way in the search for cures.

We welcome the opportunity to comment on the draft guidance on the collection of race and ethnicity data in clinical trials for FDA regulated products. We trust that you will give careful consideration to our attached comments as you finalize the guidance.

Please feel free to contact me if you have any questions.

Sincerely,

Alice E. Till

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Att.

02D-0018

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PhRMA Comments/Recommendation

Docket No. 02D-0018: FDA Draft GUIDANCE

"Guidance for Industry Collection of Race and Ethnicity Data in Clinical Trials"

Summary Key Issue and Recommendation: For these categories to be valuable globally and to permit identification of ethnic differences, there should be only one set of agreed ethnic/racial categories. These should be defined to permit evaluation of differential ethnic responses to drugs globally, not only among socio/cultural groups within the U.S. It is recommended that this subject be brought to the next ICH meeting for discussion recommending standardized racial/ethnic categories.

Content for Comments

The relevant material for clinical trials in this draft guidance document is assumed to be in pages one to six. The Appendices bulleted below are considered to serve as background information.

- Appendix 1: History of Federal Efforts in Data Collection on Race and Ethnicity and Other Subpopulations, and
- Appendix 2: Revised Directive 15 OMB Standards for Maintaining, Collecting, and Presenting Federal Data on Race and Ethnicity
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Collection of Racial/Ethnic Data

Given that sponsors currently are required to collect data on race and to summarize it in our analyses, there is minimal additional burden from the guidance. We agree with the 3rd paragraph on page 3 -- having standardized categories allows easier and more valid comparisons between races (pooling data across trials). However, as detailed below the nature of the data requested, its definitions, and its ultimate use may be problematic.

In (Line 38-40) In Section I. INTRODUCTION, it is stated that the paragraph "does not discuss increasing the number of studies ... total number of participants ... "
Although the guidance does not consider these issues, the mention of them in the introduction invites the suggestion that increasing the number of studies and subjects may be a consequence of collecting this information. This paragraph should be removed; it adds no value and raises a potentially problematic issue.

Basis for Choice of Racial Categories

The evaluation of the safety and effectiveness of FDA-regulated products requires a science-based data analysis.
In Section II. A. Relevance of Population Subgroup Studies (Lines 69-95), it is stated that the OMB race and ethnicity categories were not scientifically based designations but instead, were categories describing the sociocultural construct of society in the USA. In the next paragraph, the OMB categories are proposed as appropriate for evaluation of the influence of intrinsic factors such as genetic factors.

Without a scientific basis for examining the effects (either positive or negative) in these groups, differences may be found where none exist or not found where real differences are present. It is recommended that, if the goal includes gaining scientific information, the race and ethnicity categories should be scientifically based.

Lack of Definitions

No clear definition of race and ethnicity is given to meet the need to identify potential issues around drug efficacy and/or safety.
To ensure consistent data collection, the guidance should be very specific on the questions to be asked and the definitions of all terms.
We suggest that FDA confirm that the race categories are and will remain consistent with the most recent US census guidelines.

Consistency with ICH E5 Guidance

Since a large proportion of sponsor trials are now done outside of the US, the Guidance should be consistent with ICH standards. According to the "ICH E5 Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data," the assessment of potential differences between populations should be based on the evaluation of extrinsic and intrinsic factors. It is not clear from the Guidance how the recommended categories for race and ethnicity are to be translated into these factors.

Applicability of Data from Other Countries to USA Population

In Section II. BACKGROUND (Line 58), it is mentioned that one of the reasons in recommending the use of the OMB race and ethnicity categories is to help ensure consistency in demographic analysis across data collected by other government agencies in the US as well as ICH countries in accordance with the E5 Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data.

The OMB race and ethnicity categories can be used only in the US, but not in EU and Japan, especially the ethnicity question (Hispanic/Latino vs. Not Hispanic/Latino). The definition of ethnicity varies among the ICH countries as well as non-ICH countries. There is likely to be more opportunity in the future for the US to utilize foreign clinical data in evaluating safety and efficacy of new drugs. Therefore, it is recommended that the race and ethnicity categories should be defined so as to allow application outside of the USA.

Applicability of Data from USA to Other Countries

In Section B (Line 129-133), FDA Decision to Recommend Use of the OMB Categories, FDA states that it has decided to recommend use of the OMB categories in clinical studies for FDA–regulated products conducted in the US and abroad. The OMB categories are designated as describing a sociocultural construct of the US society, and these categories are not necessarily appropriate for application to other countries. We suggest that the race and ethnicity categories be defined so as to allow application outside of the USA.

Number of Racial Categories

The ICH agreed to three major race categories ("White", "Black"," Asian"). We believe that this should be the minimum race information requested depending on the patient population being studied. The draft guidance document itself provides the support for limiting the number of racial categories (page 3 - lines 80-95). Several examples were given to support capturing just these 3 major categories and of the differences between them.
To convince our non-US colleagues to expand the categories we need to ensure clear delineation of how the proposed OMB categories will correspond to the ICH categories.

Recommended choices for race and ethnic category

In Section III, Lines 140-176, COLLECTING RACE AND ETHNICITY DATA IN CLINICAL TRIALS, there are five and two choices in selecting race and ethnicity, respectively. Since the OMB categories were originally issued in 1977, US society has changed dramatically. We recommend that FDA add multi-racial

categories to the list so that an individual volunteer would not be forced to choose a single category, and the data collected can be used scientifically.

Collecting the information is straightforward, but its accuracy may be questionable, particularly in studies conducted outside the United States. In particular, the terms Hispanic and Latino will not have the same meaning outside the USA as they do within the USA. According to the definition, Spaniards are considered Hispanic, but they are both culturally and racially more similar to French than Mexicans.

Asking subjects about their race/ethnicity may be very sensitive in many circumstances and could be viewed as a bureaucratic burden. Conducting a study in Japan, for example, and asking a subject whether they are Hispanic may result in patients' taking questionnaires less seriously and may compromise other data being collected.

The difference between "Black or African American" and "Black, of African heritage" appears to be semantic. By contrast, the guidance makes no distinction among the Asian group, which may be more genetically variable. There should be consistency among the classifications that would permit a scientific determination of any ethnic/racial differences.

There are some other racial groups that do not fit clearly into this guidance. For example Australian Aborigines are black in skin color but are not directly of African Ancestry. Likewise, native New Zealanders (Maori) and Laplanders are not clearly covered by any of the available categories. Finally, the Asian racial group might be very wide and could really be subdivided among those peoples derived from the Indian sub-continent and those from Southeast Asia.

There is a conflict between the definitions used in the document for "white" and the commonly used "Caucasian". The latter includes the peoples of northern India who would presumably be lumped in with "Asian". To this extent the guideline is very US-centric and does not fully reflect international usage.

Relation to Pharmacogenetic Data

The paragraph in lines 80-89 promotes the perspective that pharmacogenetic data substantiate the OMB categorizations. This may be true in some cases, but it fails to account for more recent research showing a markedly different situation in other cases. The possibility of genetic-based tests should be mentioned and allowed as part of a more extensive demographic characterization of study participants, where appropriate.