Biotechnology Industry Organization
1225 Eye Street NW, Suite 400
Washington, DC 20006

February 6, 2004

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

Re: Docket No. 2003N-0529, Federal Register: December 8, 2003 (Volume 68, Number 235, Page 68402-68403)

Dear Sir/Madam:

The following comments are provided by the Biotechnology Industry Organization (BIO). BIO represents more than 1,000 biotechnology companies, academic institutions, state biotechnology centers and related organizations in all 50 U.S. states and 33 other nations. BIO members are involved in the research and development of health-care, agricultural, industrial and environmental biotechnology products. BIO appreciates the opportunity to comment on the Food and Drug Administration's (FDA) request for comments on Amending the MedWatch Forms to Collect Postmarketing Adverse Event Data Relating to Race and Ethnicity.

As a general matter, for the reasons set forth in BIO's March 28, 2003, comments on the FDA Draft Guidance for Industry on the Collection of Race and Ethnicity Data in Clinical trials, BIO does not support the collection of data based on the race and ethnicity criteria proposed. As described in our March 28, 2003, comments, BIO believes the proposed categories represent social, not scientific information and that such data will have limited scientific value.[1] We are also concerned that the proposed race and ethnicity categories appear "U.S.-centric" and would not be considered appropriate for the purpose of reporting in other

[1] The designation of persons as "Native Hawaiian or Other Pacific Islander" is illustrative of the poor correlation between "race" or "ethnicity" and any biological basis for an adverse drug event. As is more fully described in Chapter 13 "The End of Race, *Hawaii and the Mixing of* People" in Mapping Human History by Steve Olson (Mariner Books 2002), scientists cannot ascertain scientifically who is a Native Hawaiian, and most Native Hawaiians are not "pure" descendants of the Polynesians who first occupied the Hawaiian islands. Moreover, in Hawaii there is a very loose correlation between ethnicity and biology, in part because persons self-identify themselves ethnically not only based on who their ancestors were but on the basis of groups to which they would like to belong prospectively. Thus, use of the term "Native Hawaiian or other Pacific Islander" is of particularly limited scientific value.

countries. A copy of BIO's March 28, 2003 submission is attached and ask that you consider all of the arguments made there as part of this submission.

General Comments

While BIO does not support the use of race and ethnicity categories, at the least we recommend that expansion, if any, into these categories not be undertaken until completion and finalization of the Draft Guidance Collection of Race and Ethnicity Data in Clinical Trials, initially published in January 2003.

BIO is also concerned that this effort is not consistent with FDA's goals, which we share, of harmonization with regulatory bodies in other countries, to the extent such harmonization is feasible and advances the public health. We believe that expanding the use of racial and ethnicity data is contrary in particular to the goals of ICH. As noted above, the categories proposed appear related only to the United States; we are concerned that collection of such data would not be required by other countries and that the data would not be usable in other countries if collected according to the proposed categories.

Additionally, we are concerned about the cost of these proposed data collection requirements. Currently, company data collection systems are not set up to collect information according to these criteria. Thus, the proposed requirements will require companies to revise their data collection systems – an expensive and time-consuming prospect -- and to have separate data collection and adverse event reporting systems for regulatory agencies in different countries. This last would, again, be contrary to the goals of the ICH.

Lastly, the advantage gained by any post-marketing adverse event system is the generation of scientifically valid hypotheses that can be used either to develop additional studies of a product or to change the product labeling. BIO believes that racial and ethnic categories will be of little, if any, value in generating valid and scientifically defensible hypotheses and, thus, that there is no apparent advantage to collecting and/or reporting such data. We are concerned, however, that there are economic, informational, and personal privacy disadvantages to such data collection that argue against its implementation.

Specific Comments

1) *Should the MedWatch forms (Forms FDA 3500A) and 3500) be amended with a special field or fields to capture adverse event data on race and ethnicity?*

For the reasons set out above, BIO does not believe that the MedWatch forms should be amended to capture data on race and ethnicity. In addition, a change in these forms to capture new information would require either (a) reduction of space on the form for valuable information currently sought and already used, or (b) the addition of a second page on the form. Neither approach seems efficient or appropriate.

First, the information currently sought on the MedWatch form is demonstrated to be valuable and useful, unlike the proposed race and ethnicity data, which we believe will have limited utility. Second, the contents of the MedWatch form, as well as its length, readability, and ease of use were carefully analyzed by FDA before the form was issued. (*See*, Form for

Reporting Serious Adverse Events and Product Problems with Human Drug and Biological Products and Devices, Notice of Availability, 58 Federal Register 31596, 31596-99 (June 3, 1999)). At that time, FDA carefully considered whether race and ethnicity data should be collected, and properly concluded that they should not.

Moreover, the size, format, and design of the MedWatch form were studied and reviewed specifically with health care professionals before the form was adopted. If FDA decides to amend the form, we believe the agency should both provide information about how it would amend the form to include race and ethnicity data and make a proposed amended form available for review prior to adopting it. BIO believes that one way to do this would be for FDA to publish a copy of the proposed revised form in the Federal Register and permit interested persons, including other users of the form (e.g., medical device firms) and health-care professionals who likely would be intimately involved in the collection of the proposed additional data, to comment. This was the process employed by FDA when it first established the MedWatch form (in the February 26, 1993 Federal Register).

2. *Should MedWatch race and ethnicity data distinguish between self-reported and observer-reported designations? If so, how should the designations be captured?*

The other data collected on the MedWatch form are observer-reported, though the reporter is permitted to obtain information from others. In its explanation of a related area on the MedWatch reports 3500A and 3500, FDA stated:

> FDA believes that health professionals will generally know the patient's gender, and FDA encourages whoever has the first direct contact with the patient or knowledge of the event to provide as much information as possible. As with all the fields in the report, if information is not known, the field can be marked as unknown (58 Federal Register at 31599.)

BIO believes that race/ethnicity history in post-marketing spontaneous reports is likely to be either 1) not reported (e.g., due to inconvenience) or worse, 2) reported inaccurately (e.g., due to difficulty in race/ethnicity determinations by reporters, awkwardness in questioning patients or patients' family for confirmation). The consequence could be faulty conclusions about drug/race or drug/ethnicity relationships with resultant faulty labeling.

Since FDA does not distinguish between observer-reported and self-reported data for any other part of the MedWatch form, BIO believes that it should not do so for any required race or ethnicity information. To use different reporting requirements for different types of data could not only complicate the reporting and make it more time-consuming, but also have potential implications for patient privacy rights.

While BIO recommends the self- or observer-reported designations not be reported, if FDA proceeds with these revisions to the MedWatch forms, we suggest the agency make certain that there is space for the reporter to mark that the race/ethnicity are "unknown" or "mixed."

3. Would collection of race and ethnicity data on the MedWatch forms have an impact on the ICH E2B guidance relating to the electronic submission of adverse event reports ("E2B Data Elements for Transmission of Individual Case Safety Reports" (63 FR 2396 at 2397, January 15, 1998))?

Race and ethnicity are not currently captured in any field according to ICH E2B guidelines; therefore, including that data on MedWatch forms would be an additional data field difference between a MedWatch form and an E2B file. Considering the intended global use of E2B, we believe that various regional interpretations of race and ethnicity may make it difficult to find a common description or code list for the data that would be acceptable to all.

BIO also believes that collection of race and ethnicity data on the MedWatch forms would have a negative impact on the electronic submission of adverse event reports. Companies will need to re-write the computer programs used to collect and transmit individual case safety reports. Further, as noted above, since the data collected are not likely to be either required by or useful in other countries, companies may need to have two sets of data on individual case safety reports – one for submission to the FDA and one for submission to all other regulatory authorities.

4. What is the financial impact associated with adding a special field or fields to the MedWatch forms to collect data on race and ethnicity?

BIO does not believe that there is sufficient information in the proposal to assess fully the financial impacts of this proposal. For example, if the MedWatch form is expanded to two pages, then non-electronic submission of the form (e.g., by facsimile or on paper) will double. There also will be substantial costs associated with the collection, storage, and transmission of these additional data. As stated above, computer systems and other corporate and health care data systems will need to be revised. Data already collected will need to be transferred to the new systems so that later patients with the required data on race or ethnicity can be added to the systems. Training regarding the new requirements also will be needed for corporate and health care personnel worldwide.

If the newly required information captured were to trigger requirements for additional data collection or studies on already approved medicines, costs would be significant, though not calculable at this point. Further, if other countries were to develop their own race and ethnicity categories and require additional data submission, costs will rise further.

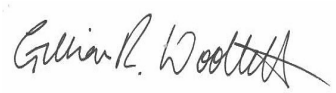
There is no doubt that more information on what causes adverse events would be very useful not only to biotechnology companies but also to health care providers and patients. BIO supports that evolving science. However, we do not believe that the classification of persons according to the proposed racial and ethnic categories will achieve that goal. BIO believes that if and when scientifically valid and reliable genetic markers are developed and found highly correlative with adverse events, the issue can be revisited, including collection and reporting of such data in the future.

BIO respectfully requests that the proposed changes to the adverse events reporting systems and to the MedWatch forms be withdrawn. We remain committed to improving the identification and reporting of adverse events, with the goal of science-based improvements in

the safety and effectiveness of medications. We look forward to continuing to work with the agency toward that end.

Thank you for your consideration of these comments. Please do not hesitate to contact me should you have any questions.

Sincerely,



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