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PhRMA

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

Re: Docket No. 2003N-0529 – Proposal to Amend the MedWatch Forms to Collect Post-marketing Adverse Event Data Relating to Race and Ethnicity; 68 Federal Register 68402; December 8, 2003

Dear Sir or Madam:

The following comments on the above notice are submitted on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA). PhRMA represents the country's leading research-based pharmaceutical and biotechnology companies. Our member companies are devoted to inventing medicines that allow patients to lead longer, happier, healthier, and more productive lives. In 2003, our members invested over $33 billion in the discovery and development of new medicines.

PhRMA member companies support the Food and Drug Administration's (FDA) interest in and attempts to collect and analyze post-marketing adverse event data for patterns related to race and ethnicity. However, we do not support revision of the MedWatch forms (specifically the FDA 3500A form) to collect race and ethnicity data as outlined in the Federal Register notice.

Our major concerns with the proposal are as follows:

- such a change will create discrepancies between reports submitted via Medwatch forms and those submitted electronically or via CIOMS I forms;
- fields for race and ethnicity are not part of internationally accepted data standards for post-marketing reports;
- US Office of Management and Budget (OMB) categories for classifying race and ethnicity data are not internationally applicable; and
- It is unclear how such data might be analyzed, interpreted, and used in evaluation of patterns of adverse events.

PhRMA recommends that FDA pursue this matter within the International Conference on Harmonization forum, and develop internationally agreed categories and definitions for race and ethnicity data, and that any attempts to modify the MedWatch forms be postponed until agreement is reached. We also recommend that FDA work with ICH to include internationally agreed race and ethnicity categories in the ICH E2B data standards for electronic submissions.

Comments

FDA is seeking comment on the following questions:

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Pharmaceutical Research and Manufacturers of America

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- What are the advantages and disadvantages of systematically collecting race and ethnicity data in post-marketing adverse event reports?
- Should FDA's MedWatch forms (Forms FDA 3500 and 3500A) be amended to collect race and ethnicity data based on the standardized OMB categories?
- Should the MedWatch forms be amended with a special field or fields to capture race and ethnicity data?
- Should the MedWatch race and ethnicity data distinguish between self-reported and observer-reported designations? If so, how should the designations be captured?
- Would collection of race and ethnicity data on MedWatch forms have an impact on the ICH E2B guidance related to electronic submission of adverse event reports?
- What is the financial impact associated with adding a special field or fields to the MedWatch forms to collect data on race and ethnicity?

Our comments are organized as responses to each of these questions.

- **What are the advantages and disadvantages of systematically collecting race and ethnicity data in post-marketing adverse event reports?**

Ideally, systematically collecting race and ethnicity data for post-marketing adverse event reports would enable both the Agency and manufacturers to better understand the role that race and ethnicity play in the development of adverse events. This would enable pharmaceutical companies to provide patients and prescribers information about potential race and ethnicity risk factors so that drug and biologic products can be used as safely as possible. Capturing these data in specific fields would allow analysis of the information much more easily than if the information was reported in narrative fields, as is the current situation.

However, there are considerable limitations inherent in the spontaneous adverse reporting system that must be taken into account in evaluating how useful and valid race and ethnicity data from these reports will be in identifying any patterns of adverse events. Spontaneous reports are intended to be a signaling system; they are not intended to provide the complete information necessary for a detailed analysis. Because of the voluntary nature of spontaneous reports, they are not an optimal mechanism for systematic data collection. Unlike clinical trials where the sponsor and FDA can dictate the data collected from study participants, spontaneous reporters provide only the information they are willing and able to provide. In addition, accurate denominators for race and ethnicity cannot be established for spontaneous reports as they can be in controlled clinical trials. There may be a difference in the propensity to report adverse events among different racial and ethnic groups; thus, a difference in the reporting rate of a specific event among these groups may reflect this difference, rather than a true difference in a group's inherent susceptibility to develop certain adverse events. Therefore, PhRMA does not agree with the Agency's premise that because companies seek to collect race and ethnicity data in clinical trials, the same level of detail can or should be collected for spontaneous reports. The two data collection systems are different, serve different purposes, and hence, yield different data. In the experience of PhRMA member companies, reporters often decline to provide racial and ethnic data, and may find probing for this information to be offensive. We would certainly not want to "turn off" reporters from providing information about post-marketing adverse events because they are offended by our efforts to collect race and ethnicity data. It is

also important to ensure that companies do not inadvertently violate patient privacy regulations in other parts of the world in our efforts to collect race and ethnicity information.

In addition, any analysis of race and ethnicity data would require standardized categories for these data fields. Although FDA proposes to use the OMB standard categories for race and ethnicity, there are significant drawbacks to using these US-centric classifications for worldwide post-marketing adverse events. Please refer to our detailed comments on use of the OMB categories below.

- **Should FDA's MedWatch forms (Forms FDA3500 and 3500A) be amended to collect race and ethnicity data based on the standardized OMB categories?**

PhRMA strongly discourages adoption of the OMB categories for race and ethnicity for post-marketing adverse event reports, primarily because these categories are not suitable for use for worldwide reporting, and are not consistent with the current ICH-agreed racial categories. The OMB categories were developed for use specifically within the US, are based on US social-political constructs, and may not be applicable or understood outside the US. For instance, the minimum choices for ethnicity are designated as "Hispanic or Latino" or "not Hispanic or Latino". The meaning of these terms even within the US may vary; it is unreasonable to expect that individuals residing in Spain, Mexico, Central America or Brazil will answer this question consistently. While addition of definitions to the form may enhance consistency, this would take a considerable amount of space on an already crowded form.

Although the Federal Register notice refers to the previously issued draft guidance for industry entitled "Collection of Race and Ethnicity Data in Clinical Trials", which recommended use of standardized OMB race and ethnicity categories, no mention is made of the considerable feedback FDA received concerning applicability of these categories internationally. These same comments regarding the international utility of the OMB categories would continue to apply to post-marketing reports. In fact, using the US-centric OMB categories is even more problematic for post-marketing adverse event reporting than for clinical trials, since post-marketing reports emanate from a wide variety of sources in potentially all countries, rather than the limited number of relatively knowledgeable investigators and subjects participating in clinical trials.

The notice recommends that clinical trial participants be able to designate a multiracial identity. If this is also considered for post-marketing adverse event reporting, we recommend that this information also be collected in a structured manner, with relevant choices available on the form (i.e., not just "multiracial"). One accurate method to collect this information, which is currently used in genetics research studies, is to request information on the patient's parents' race, country of origin, and native language. Unfortunately, this will also add to the complexity of the form, and since requesting this information may hinder our ability to collect information about the adverse event itself, it is of questionable value in the post-marketing arena.

- **Should the MedWatch forms be amended with a special field or fields to capture race and ethnicity data?**

PhRMA does not support amending the MedWatch forms, specifically the FDA 3500A mandatory form, to include specific fields to capture race and ethnicity data as outlined in the

proposal at this time. Although analysis of race and ethnicity data would be easier if the information was contained in structured fields rather than in text fields, race and ethnicity fields are not consistent with internationally agreed data elements for post-marketing reporting, and they are not part of either the CIOMS I form or the ICH E2B data elements for electronic submission of adverse event reports. Amending the FDA 3500A form to include these fields will introduce discrepancies between the information an applicant reports to FDA for US cases (via FDA 3500A) and foreign cases (via CIOMS I form), as well as differences between the information reported to FDA and other regulatory authorities for US cases.

At FDA's urging, many PhRMA member companies have been working with the Agency to convert from paper submissions to electronic submission of post-marketing adverse event reports, and we find it odd that FDA is proposing to amend a form that will soon become obsolete. According to a presentation by an FDA representative at a recent Drug Information Association meeting, it is FDA's goal to have 80% of adverse event reports submitted electronically by the end of 2004. We suggest that the Agency's and industry's resources would be more effectively utilized if they were directed toward enhancing electronic submissions, and/or amending the ICH E2B data fields, rather than revising the Form FDA 3500A.

The Form FDA 3500 (the "voluntary" form) is used by individuals within the US to submit reports to FDA, and will probably make up the vast majority of the 20% of reports received on paper in the future. An alternate suggestion would be for FDA to add fields for race and ethnicity to only the FDA 3500 paper form, and to leave the mandatory FDA 3500A paper form in its current format for the few mandatory reports expected to be submitted in paper format in the future.

PhRMA also urges FDA to finalize the draft guidance for industry on "Collection of Race and Ethnicity Data in Clinical Trials" before amending the MedWatch forms, so that post-marketing and pre-marketing guidance on this topic are consistent.

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

PhRMA member companies do not think it is necessary to distinguish between self-reported and observer-reported race and ethnicity designations on the MedWatch form. This would add unnecessary clutter to the form, without adding any additional value or validity to the information. The issue of self- versus observer-reported designations raises a question regarding the situation where a patient reports one racial/ethnic category and their health care provider reports a different category. PhRMA requests FDA provide guidance regarding which designation would take precedence in such a situation.

- **Would collection of race and ethnicity data on MedWatch forms have an impact on the ICH E2B guidance related to electronic submission of adverse event reports?**

As noted above, there would definitely be an impact on the ICH E2B guidance if FDA were to move forward with collection of race and ethnicity data on MedWatch forms. These fields are not included in the ICH E2B data standards for electronic submission of adverse event reports, and there would be discrepancies in the information applicants report to FDA depending on whether they used paper or electronic submissions.

PhRMA agrees that there is value in capturing race and ethnicity data in structured fields, and in using internationally accepted categories and definitions. Therefore, we urge FDA to work within the ICH framework to develop standardized categories for race and ethnicity, and to add these fields to the E2B data standards and the CIOMS I form, in conjunction with adding them to the MedWatch forms.

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

There could be considerable financial impact on pharmaceutical companies if these fields are added to the MedWatch form. These costs would arise from the requirement to reprogram and revalidate computer systems to add these fields if they don't currently exist in company databases, to reprogram and revalidate the output of computer-generated FDA 3500A forms, and to revise company post-marketing data collection forms to include these fields. Depending on the company, this could extend to revising local data collection forms and computer systems in affiliate companies around the world. Lists of valid entries for these fields would need to be developed and incorporated into databases, and any existing data values would need to be mapped to the new ones. Additional training of safety staff worldwide would also be required, particularly with regard to consistent interpretation and application of the race and ethnicity categories and definitions.

It is not clear whether FDA would consider race and ethnicity data to be part of the "full data set" described in the March 2003 proposed rules on safety reporting requirements for human drug and biologic products. If FDA does include these fields in the full data set, applicants would be required to conduct extensive follow-up efforts to obtain this information, which would add to the costs of post-marketing pharmacovigilance, with little or no benefit to the public health. If the Agency proceeds with amending the MedWatch forms to include fields for race and ethnicity data, we strongly urge that this not be considered mandatory information, and that the Agency specifically exclude it from the full data set.

Sincerely,