

February 22, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857



RE: Docket No. 2004N-0535 Agency Information Collection Activities; Proposed Collection; Comment Request; MedWatch: Food and Drug Administration Medical Products Reporting Program

Merck & Co., Inc. is a leading worldwide human health product company. Merck Research Laboratories (MRL), Merck's research division, is one of the leading U.S. biomedical research organizations. Merck's R&D pipeline has produced many of the important pharmaceutical products on the market today.

Merck supports regulatory oversight of pharmaceutical products throughout their life cycle and welcomes regulatory revisions that are based on sound scientific principles and good judgment. As a leading pharmaceutical company, Merck has extensive experience in thoroughly evaluating our products from discovery to approval and throughout their marketing life to assure that they continue to provide health benefits with minimum risk. Safety reporting to regulatory agencies is an integral part of the process. Therefore, we are well qualified to comment on the proposed revisions to Form FDA 3500 and Form FDA 3500A (also known as MedWatch reporting forms).

Below, please find Merck's comments regarding the recently published draft guidance entitled, "*MedWatch: Food and Drug Administration Medical Products Reporting Program*". Please note that our comments focus on the mandatory reporting form as it is relevant to our business practices. We have provided general comments followed by specific comments related to particular sections or fields in MedWatch Form 3500A.

Throughout the modified version of 3500A, several of the proposed new fields are not consistent with international standards, as specified in International Conference on Harmonisation (ICH) E2B (Data Elements for Transmission of Individual Case Safety Reports) and E2D (Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting). The ICH guidances impact mandatory reporting and play a major role in ensuring accurate and consistent exchange of safety data worldwide. Additionally, the proposed changes to Form 3500A would require significant effort and resources in programming, validation, and documentation, without much value added, as approximately 50% of the post-marketing expedited reports submitted by pharmaceutical companies to the FDA use the electronic ICH E2B format. Therefore, Merck

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recommends that FDA consider the ICH and Council for International Organizations of Medical Sciences (CIOMS) guidances when the Agency finalizes the MedWatch Mandatory Form 3500A to ensure continued international harmonization of adverse event reporting.

Additionally, to facilitate mandatory reporting for reports that do not concern medical devices, FDA currently accepts from pharmaceutical manufacturers a modified version of the Form 3500A in which the boxes that apply to drug products are located on the first page. This format makes the form easier to read and results in fewer pages per report. Therefore, Merck recommends that FDA arrange the boxes so that the first page applies to drugs, and the second page to devices.

We also believe that the 6-month timeframe provided for companies to update databases to accommodate the new MedWatch forms should be adjusted. We estimate that it will take approximately 9 months to 1 year for most companies to make these changes, especially if a vendor is involved.

Lastly, we recommend that the Agency provide guidance when the final changes to the MedWatch forms are issued. As detailed below, the FDA has added several new fields to the MedWatch forms without corresponding text describing the definition and content requirements of the fields. Merck recommends that FDA provide a guidance document that provides an explanation of each new field on the proposed form.

Specific Comments

B.1. Product Use Error / Product Switch

The new classifications of “product use error” and “product switch” are not consistent with ICH E2B. As a result, these data would not be available in ICH E2B submissions sent to regulatory agencies. There will be little benefit to FDA in adding these fields to the form without a change in the ICH E2B standard.

Recommendation: FDA should continue discussions with the Medical Dictionary for Regulatory Activities (MedDRA) Maintenance and Support Services Organization (MSSO) to ensure that the standard MedDRA vocabulary has adequate terminology to classify product problems, and to then require the use of those terms, when applicable, in Box G.8 - Adverse Event Term(s).

B.2. Outcomes

The definitions of the new outcomes “not serious” and “no harm” are not defined. If “not serious” is defined as “not meeting any of the serious criteria”, and if “no harm” is defined as “no adverse event occurred”, then this information could be derived from section G.8.-Adverse Event Term(s). Having additional check boxes would lead to

potential data discrepancies. In addition, a new checkbox is being proposed for “important medical events”.

Recommendation: Since “required intervention” is part of the definition of “medically important event” in ICH E2D, we request that FDA provide clarification through guidance for the use of these two fields. Further, the terms required for use in the outcome boxes should be reflective of ICH E2A and E2D definitions.

B.5. Describe Event, Problem, or Product Use Error

The new fields “Product Used During Pregnancy” and “Product Used During Breast Feeding” are not consistent with ICH E2B. As a result, these data would not be available in ICH E2B submissions sent to regulatory agencies. MedDRA currently captures these concepts with the terms “drug exposure during pregnancy” and “drug exposure via breast milk”

Recommendation: Since there are currently terms in MedDRA to capture these concepts, FDA should use the above referenced MedDRA terms in section G.8. - Adverse Event Term(s), when applicable. If the terms are coded, a separate box would not be needed.

C. Product Availability

The value of the proposed new Section C. “Product Availability” is not clear, as manufacturers have no control over how a product is handled once it reaches the patient. In addition, this field is not consistent with applicable ICH guidances.

Recommendation: The Agency should remove this section from the form. Alternatively, if the FDA requires the inclusion of this section in the revised Form 3500A for medical device AE reports, we recommend that the section be moved to the second page in order to better organize the document, with the first page applicable to drugs and the second page applicable to devices.

D.1,6,7 Suspect Product(s)

The strength, manufacturer, lot number and expiration date fields under the “Suspect Product(s)” section of the form no longer contain the text “(if known).” The reason for this change is not clear, but it could be inferred that this means those fields are now required.

Recommendation: The text should remain as worded on the current form.

D.9 NDC # or Unique ID

A new term, “Unique ID” has been added to the form without clarification or a definition.

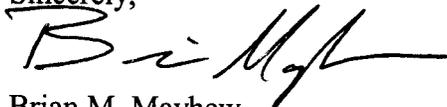
Recommendation: We request that FDA provide a definition of the term “Unique ID.” Additionally, we encourage the FDA to maintain consistency with ICH E2B and ICH M5 fields when considering unique identification numbers.

Conclusions

In conclusion, Merck supports the effort to modify the voluntary reporting form to better characterize the suspected adverse experience, product problem or error, and provide better quality safety-related data for Agency evaluation. While we support the FDA's efforts to modify the MedWatch reporting forms, we recommend that actions to improve the collection of mandatory reporting data be conducted through current ICH initiatives, to ensure continued international harmonization of adverse event reporting.

We appreciate this opportunity to work with the FDA on this important initiative. If you have questions about our comments, or would like to meet with us to discuss them further, please call me at (301) 941-1402.

Sincerely,

A handwritten signature in black ink, appearing to read "Brian M. Mayhew". The signature is fluid and cursive, with the first name "Brian" being the most prominent part.

Brian M. Mayhew
U.S. Regulatory Policy