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January 21, 2003

MERCK
Research Laboratories

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

RE: [Docket No. 96D-0041: International Conference on Harmonisation; Draft Guidance on Addendum to E2C Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs; Availability]

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 has participated with health authorities from around the globe in the harmonization of regulatory standards under the auspices of the International Conference on Harmonization (ICH). The objectives of ICH have been to identify and correct unnecessary redundancies and time-consuming inefficiencies in development of pharmaceutical products caused by incompatible regulatory schemes. We continue to monitor the equitable and consistent application of these harmonized standards to product development in order to ensure that *new* or *improved* therapies reach patients as swiftly as possible and to help ensure consistent evaluation of post-marketing adverse experience report data across all ICH regions.

Accordingly, we are very interested and well qualified to comment on the September 12, 2002 draft addendum to the ICH E2C guideline announced in the Federal Register notice dated January 2, 2003.

We commend the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) for providing additional information on the content and format of periodic safety update reports (PSURs), including clarification of the objectives, general principles, and model for PSURs provided in the May 19, 1997 ICH E2C guidance.

Comment
Section 1.1 (Objectives of the Guideline) includes the following paragraph:

> If, in addition to the usual safety analysis done in the PSUR, a more comprehensive safety or risk-benefit analysis (e.g., all indications reviewed) is considered appropriate this more comprehensive analysis should be prepared and submitted as a "stand alone" document. The results of this analysis should be included in the next PSUR.

In light of the inclusion of risk management activities within the meaning of the term, "process for the review of human drug applications" in the reauthorization of the Prescription Drug User Fee Act (PDUFA III), and the subsequent inclusion of voluntary risk management planning in the PDUFA III performance goals and procedures, it would be helpful to further clarify the statement in Section 1.1 that, "The results of this analysis should be included in the next PSUR".

We recognize that a number of aspects from specific risk management programs can be routinely incorporated into existing sections of a PSUR, for example, information on patient exposure, special population exposure, additional Phase IV safety studies, program effectiveness. However, since some risk management programs may have regionally specific aspects, the results of a comprehensive analysis are less amenable for seamless inclusion in the PSUR. Guidance on where the results of the comprehensive analyses should be presented in the PSUR is needed.

Recommendation

With the evolution of risk management , Merck recommends the inclusion of more specific discussion in this ICH document concerning the presentation of comprehensive analyses for products with specific risk management plans. We welcome the opportunity to comment on this document.

Sincerely,

for David W. Blois, Ph.D.
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