David W. Blois, Ph.D.
Senior Vice President
Global Regulatory Policy

Merck & Co., Inc.
West Point PA 19486
E-Mail: david_blois@merck.com
Tel 484 344 2304
215 652 5000
Fax 484 344 2335

August 21, 2003

Division of Dockets Management (HFD-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: [Docket No. 2003D-0231; Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format -- Postmarketing Periodic Adverse Drug Experience Reports]

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. In the course of developing and marketing pharmaceuticals, Merck has extensive experience in electronic submissions of a variety of regulatory documents as well as experience submitting traditional postmarketing periodic adverse drug experience reports. For these reasons, we are interested and well qualified to comment on the "Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format - Postmarketing Periodic Adverse Drug Experience Reports."

General Comments

In the introduction to this draft guidance, the history of FDA's issuance of guidance for industry related to the electronic submission of safety reports is briefly described. To summarize, with the issuance of this draft guidance, the agency has issued the following documents:

1. Guidance for Industry: Providing Regulatory Submissions in Electronic Format -- General Considerations (January 1999);

2. Draft Guidance for Industry -- Providing Regulatory Submissions in Electronic Format -- Postmarketing Expedited Safety Reports (May, 2001);

3. Draft Guidance for Industry -- Providing Regulatory Submissions in Electronic Format -- Postmarketing Periodic Adverse Drug Experience Reports (June, 2003);

Although the "General Considerations" guidance is final, the agency notes that it is in the process of revising that document and has plans to issue a draft guidance for public comment[1].

In addition to these guidances, the Agency has recently released its draft revision of the safety reporting rules[2] which proposes significant revisions to the safety reporting regulations.

Given the fact that the Agency is (1) revising the general considerations, (2) still finalizing the guidance on electronic submission of post-marketing expedited reports, (3) collecting comments on this latest draft guidance on electronic postmarketing periodic adverse experience reporting, and (4) still collecting comments on the Proposed Rule, "Safety Reporting Requirements for Human and Biological Products," which will introduce changes in safety reporting requirements, we strongly recommend that FDA postpone finalizing either of the draft guidances on electronic format for safety reports until the new safety reporting rule is finalized.

There are several indications that it is premature to issue the guidance on electronic safety reporting at this time because the agency is still developing systems and processes to accommodate it. These include:

- the fact that the previously issued draft on electronic submission of postmarketing expedited reports has not been finalized and certain information therein is superseded by the draft guidance on electronic postmarketing periodic adverse event reporting (lines 44-48);
- the notation on lines 86 - 89 that descriptive information cannot be submitted electronically until the agency announces that capability in public docket 92S-0251;
- the discussion on lines 130-133 and in footnote 10 regarding submission of descriptive information for postmarketing periodic adverse drug experience reports on physical media as described in the *General Considerations Guidance*, but that guidance is being revised and will be re-issued in draft for public comment; and
- FDA is in the process of developing a system for accepting PDF files through the EDI gateway - a capability not now available.

The issuance of official guidance at a time when the Agency clearly is still in the process of developing systems creates unnecessary confusion. Further, it seems likely that information in the draft guidances on which comment is being solicited will change

[1] See Footnote 5, Draft Guidance for Industry -- Providing Regulatory Submissions in Electronic Format -- Postmarketing Periodic Adverse Drug Experience Reports (June, 2003)

[2] 68 FR 12406, March 14, 2003; "21 CFR Parts 310, 312, et al., 'Safety Reporting Requirements for Human Drug and Biological Products; Proposed Rule'"

before the final guidance is available simply because of advances and revisions in process being made by the agency to handle these documents electronically. This may trigger the need for the reissue of a revised draft and an additional public comment period as is the case with the *General Considerations Guidance.* Furthermore, the fragmentation of guidance on electronic safety reporting across a number of separate draft guidances introduces further confusion. Accordingly, we recommend that, prior to finalizing separately the electronic postmarketing expedited and periodic safety reporting guidances, the agency consider combining them into a single, comprehensive document.

We welcome the opportunity to comment on this draft guidance and, if appropriate, to meet with you to discuss these issues.

Sincerely,

for David W. Blois, Ph.D.
Senior Vice President
Global Regulatory Policy