EMD

October 7, 2003

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

Re: Docket No. 00N-1484 (Safety Reporting Requirements for Human Drugs and Biological Products)

Reference is made to the Federal Register Notice of March 14, 2003, which included a proposed rule for Safety Reporting Requirements for Human Drug and Biological Products. EMD Pharmaceuticals has reviewed the proposed regulation and wishes to make the following comments.

Section III.A.1. Definition of Suspected Adverse Drug Reaction (SADR)

In this section of the proposed rule the definition of an SADR is described as:

> A noxious and unintended response to any drug (biological) product for which there is a reasonable possibility that the product caused the response. In this definition, the phrase "a reasonable possibility" means that the relationship cannot be ruled out.

This definition is not consistent with ICH Guideline E2A in which the term reasonable causal relationship 'is meant to convey in general that there are facts (evidence) or arguments to suggest a causal relationship.'

These two definitions clearly have different meanings and will result in different interpretation by sponsors leading to different reporting decisions. We strongly urge the Agency to adopt the ICH definition allowing a uniform interpretation of the definition of SADR worldwide.

Furthermore, the proposed definition will result in the submission to FDA of large numbers of reports that will ultimately not be related to therapy. A comment by the agency in the proposed rule highlights the risks created by the excessive reporting that would result from the adoption of this "relationship cannot be ruled out" standard. The following comment should be retracted or modified since it appears to be a baseless and dangerous assertion.

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> The proposed definition of SADR may result in submission to FDA of some reports from clinical studies and the scientific literature in which the reported SADR is suspected to be associated with the product, but in fact it is ultimately demonstrated not to be due to the product. (68 Fed. Reg. 12418 (2003))
> (Emphasis added)

With a standard of "relationship cannot be ruled out," it is an understatement to say "may result" in "some" reports that may ultimately not be associated. Rather it seems more likely that many, if not most, of the additional ADRs required to be reported under this excessive revised standard would ultimately be determined to be unrelated. The agency's comment would encourage plaintiff's attorneys to contend that SADR reports are usually signals of real association and failure to include every serious adverse event reported to FDA in the labeling is clear evidence of negligence. This will contribute to more product liability defensive labeling rather than useful information for prescribers.

Section III.A.2 Definition of a Life-Threatening SADR

We concur with the Agency's proposal to add the term 'or sponsor' to the definition of a Life-Threatening SADR.

Section III.A.5 Minimum Data Set and Full Data Set for an Individual Case Safety Report

The requirement for collection of a full data set for 'postmarketing' individual case safety reports of serious SADRs, always expedited reports and medication errors' is a lofty goal, but totally unrealistic. Sponsors should be encouraged to exercise diligence in obtaining as much information as possible for these types of reports. However, the agency needs to develop practical requirements for sponsors.

Section III.A.10 Data Lock Point and International Birth Date

We congratulate the agency for aligning postmarketing periodic report dates with the ICH process.

Section III.C.3 Reporting Requirements

We believe that the information presented in Table 6 – Proposed Postmarketing Expedited Safety Reports is somewhat confusing and should be simplified

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In Table 7, we do not understand the rationale for the PSURs at 7.5 and 12.5 years for applications approved before January 1, 1998 and believe this request is excessive.

Section III E.2 b Worldwide Marketing Status

We question the value of providing the agency with dates of Market Launch and Trade names for every country worldwide. Rather, we recommend that the agency develop a list of key countries for which launch and trade name information would be of some benefit, e.g., ICH countries and affiliated countries.

Section III.F.4 Contact Person

Section III.F.4 calls for each Form 3500A or CIOMS form to include 'the name and telephone number (and fax number and e-mail address, if available) for the licensed physician responsible for the content and medical interpretation of the data contained within the form.' We request that the agency clarify the use of the term 'licensed physician' as many companies have qualified medical staff outside the US who are responsible for safety reports but are not necessarily 'licensed' by their government. We assume that the agency did not mean to exclude these qualified professionals from serving as the medical officers for safety reports and request that the requirements be so modified.

We trust that the agency will find these comments useful and appreciate the opportunity to offer them for consideration.

Sincerely yours,

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