

submit their postmarketing safety reports to FDA coded using MedDRA.

Even though FDA is proposing to use MedDRA as the standard medical terminology for reporting purposes under this rule, the agency recognizes that alternative standard classification systems for clinical information exist in the United States and supports the national health data standardization initiatives underway in the United States under the Health Insurance Portability and Accountability Act.

Although this proposed rule does not impose reporting requirements on health care providers, the agency recognizes that clinicians, medical centers, hospitals and others may report safety information to pharmaceutical companies. These third parties may employ clinical terminology standards that differ from those proposed here. Therefore, the agency invites comment on the unintended potential impact of this proposed rule on those parties not subject to FDA's safety reporting requirements. The agency also invites comment on the potential strategies and approaches for facilitating seamless cross-standard communications, such as mapping between alternative terminologies and MedDRA.

II.B.2. Quality of Postmarketing Safety Reports

In light of the recommendations of ICH and CIOMS, FDA has reviewed its postmarketing safety reporting regulations for human drugs and licensed biological products and identified additional changes that the agency believes would further enhance surveillance of marketed products. Many of the postmarketing safety reports that FDA receives are complete and of very high quality. Others are incomplete, of mediocre or poor quality or both, making it difficult to ascertain the significance of these reports. In the latter cases, FDA is unnecessarily spending considerable amounts of time trying to collect additional information for the reports.

To address this problem, FDA is proposing amendments to its postmarketing safety reporting requirements. For most of these amendments, a risk-based approach is being proposed (*i.e.*, greater emphasis and effort would be required for reports of serious adverse drug experiences while less information would be required for nonserious adverse drug experiences (adverse drug experiences proposed to be called SADRs in this proposed rule; see section III.A.1 of this document)). For example, FDA is proposing that complete information be submitted for reports of serious SADRs

(see section III.C.5 of this document). If complete information is not available, in some cases, a followup report would be required (*e.g.*, for serious, unexpected SADRs) (see section III.D.6 of this document). On the other hand, for SADRs that are determined to be nonserious, not as much information would need to be acquired (see section III.C.5 of this document).

Another amendment would require direct contact with the initial reporter of an SADR by a health care professional at the company for collection of certain postmarketing safety information (*e.g.*, collection of followup information for a serious SADR) (see section III.A.6 of this document). Currently, some companies use this approach for collecting information, whereas others send the initial reporter a letter. The latter case is a passive approach which, in FDA's experience, results in limited acquisition of new information. In most cases, the initial reporter simply does not respond to the letter. Instead, using an active approach, as proposed by FDA, companies would more likely obtain the additional information needed for an SADR. Thus, use of this approach should result in submission of higher quality reports to FDA for review.

Another amendment would require that a licensed physician at the company be responsible for the content of postmarketing safety reports submitted to FDA (see sections III.E.1.h, III.E.2.k.xi, and II.F.4 of this document). As in the previous examples, some companies currently use licensed physicians for this purpose, whereas others have their postmarketing safety reports prepared and submitted by clerical personnel with no health care training. The medical significance of postmarketing safety reports warrants review by a licensed physician. The agency believes that licensed physicians would ensure submission of high quality reports to FDA that articulately conveys all clinically relevant information associated with an SADR.

II.B.3. New Postmarketing Expedited Safety Reports

FDA currently requires postmarketing expedited safety reports for serious and unexpected adverse drug experiences (adverse drug experiences proposed to be called SADRs in this proposed rule; see section III.A.1 of this document). To facilitate identification of significant safety problems, FDA is proposing that additional safety information be submitted expeditiously to the agency for marketed drugs and biological products. Some of this information is currently submitted to the agency but

not in an expedited manner. In other cases, the information is not currently required to be submitted to the agency.

II.B.3.a. *Medication errors.* In 1999, the Institute of Medicine (IOM) issued a report, "To Err is Human: Building a Safer Health System," that cited studies and articles estimating the number of Americans dying each year as a result of medical mistakes to be between 44,000 and 98,000 (Ref. 10). The IOM report concluded that preventable adverse drug events impose significant medical, personal, and economic costs to the United States.

Requiring medication errors to be reported in an expedited manner to a centralized location would provide a systematic approach for collecting comprehensive information on these errors and result in timely assessment of the information. Various organizations and health care professional associations, including the 1999 IOM report, have advocated mandatory medication error reporting efforts, as well as encouragement of voluntary efforts, aimed at making sure the system continues to be made safer for patients. Such a system would provide the public with a higher level of protection by assuring that the most serious errors are investigated and reported, and that appropriate followup action is taken both by FDA and the company whose product is associated with the error. Second, it would provide companies with an incentive to improve patient safety regarding medication errors associated with their products. Finally, it would require that FDA and the pharmaceutical industry make some level of investment in preventing medication errors and improving patient safety. In some instances, information gathered through this type of a reporting system and analyzed for root causes can lead to various changes within the health care system to prevent or minimize recurrence.

Currently, FDA maintains both a voluntary adverse event reporting system for health care professionals, through MedWatch (the Medical Products Reporting Program), and a mandatory adverse event reporting system for companies subject to the agency's postmarketing safety reporting regulations. Through these systems, FDA receives only about 3,000 reports of medication errors annually. FDA believes that these safety reporting systems do not adequately address the nature and extent of problems caused by medication errors. In most cases, safety reports associated with a medication error are not identified in the report as being associated with an error. Instead, the report only highlights the effect of