

of 1997 provides that summary tabulations of nonserious, expected adverse experiences be included in postmarketing periodic safety reports. If warranted, FDA could request submission of an individual case safety report for any nonserious, expected adverse experience. Thus, even if a waiver is granted, the agency will continue to receive sufficient information to monitor the safety of marketed drugs and licensed biological products. FDA is now proposing amendments to its postmarketing periodic safety reporting regulations that would require that nonserious, expected adverse experiences<sup>1</sup> be submitted to the agency in summary tabulations consistent with the clarification guidance of 1997. At this time, FDA is also proposing to codify the other recommendations in the clarification guidance of 1997 (*i.e.*, require a minimum data set for individual case safety reports, describe how solicited safety information from planned contacts with patients must be handled).

In the **Federal Register** of March 12, 2001 (66 FR 14391), FDA published a notice of availability of a draft guidance for industry entitled "Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines" (the draft guidance of 2001). The draft guidance of 2001 represents the agency's current thinking on reporting of postmarketing adverse drug experiences for human marketed drug and biological products including vaccines in accordance with FDA's postmarketing safety reporting regulations for these products in effect at the time the draft guidance of 2001 was issued. The draft guidance of 2001 consolidates the agency's existing guidances on this topic and revises them based on the October 1997 final rule and the increased frequency reports final rule. The draft guidance of 2001, once finalized, will replace FDA's

guidances entitled "Postmarketing Reporting of Adverse Drug Experiences" (57 FR 61437, December 24, 1992) (the guidance of 1992), "Adverse Experience Reporting for Licensed Biological Products" (the guidance of 1993), and the clarification guidance of 1997. The agency will issue a final guidance for industry on this topic after considering the comments received on the draft guidance of 2001.

FDA is now proposing to codify certain expectations described in the draft guidance of 2001 to improve the quality of postmarketing safety reports submitted to the agency for human marketed drug and biological products, and also to clarify certain postmarketing safety reporting requirements. Once this proposed rule is finalized, the draft guidance of 2001, as finalized, will be updated to provide industry with assistance in fulfilling the new safety reporting requirements for human marketed drug and biological products.

In June 2001, CIOMS issued a new report entitled "Current Challenges in Pharmacovigilance: Pragmatic Approaches" (CIOMS V report) (Ref. 29). This report provides recommendations for simplification, clarification, and harmonization of certain drug safety practices. Many of these recommendations serve to provide guidance for industry and would not be subject to requirements of individual regulatory authorities (*e.g.*, FDA). Those that are the subject of our proposed rule are essentially consistent with what we are proposing. However, in some cases, there may be differences (see section III.A.6 of this document for discussion of use of active query and written requests for acquisition of followup information).

In the **Federal Register** of November 5, 1998 (63 FR 59746), FDA published an advance notice of proposed rulemaking announcing that it is considering a proposal to require persons subject to the postmarketing

safety reporting regulations to submit postmarketing expedited individual case safety reports and individual case safety reports contained in postmarketing periodic safety reports to the agency electronically using a standardized medical terminology, standardized data elements, and electronic transmission standards recommended by the ICH. Under the auspices of ICH, standard medical terminology for regulatory purposes, MedDRA, the medical dictionary for regulatory activities (ICH M1), has been developed (63 FR 59746 at 59748). On November 24, 1998, an international maintenance and support services organization (MSSO) was established to maintain and update MedDRA in response to medical/scientific advances and regulatory changes and to serve as the licensing agent for distribution of MedDRA. This proposed rule on safety reporting would require that postmarketing individual case safety reports be coded using MedDRA prior to submission to the agency. In a separate rulemaking, FDA plans to propose that postmarketing individual case safety reports be submitted to the agency electronically using standardized data elements and electronic transmission standards. The proposed amendments for electronic submissions are beyond the scope of this proposed rule.

## II. Introduction

### II.A. Persons Subject to the Safety Reporting Regulations

#### II.A.1. Premarketing Expedited Safety Reporting Regulations

Section 312.32 (21 CFR 312.32), requires expedited reports of premarketing adverse experiences associated with the use of an investigational human drug or biological product (see table 1). Sponsors of INDs are subject to the premarketing expedited safety reporting regulations.

TABLE 1.—CURRENTLY REQUIRED PREMARKETING EXPEDITED SAFETY REPORTS

Safety report	Type of information	21 CFR section	Submission timeframe	Persons with reporting responsibility
Written IND safety report .....	<ul style="list-style-type: none"> <li>Serious and unexpected adverse experience associated with the use of the drug.</li> <li>Findings from tests in laboratory animals that suggest a significant risk for humans.</li> </ul>	312.32	15 calendar days ....	Sponsors.
Telephone and facsimile transmission safety report.	Unexpected fatal or life-threatening experience associated with the use of the drug.	312.32	7 calendar days .....	Sponsors.

<sup>1</sup> Adverse experiences are proposed to be called suspected adverse drug reactions (SADRs) in this proposed rule; see section III.A.1 of this document;

the term "adverse experiences" or "adverse drug experiences" will be used in this document when discussions pertain to FDA's current regulations

and the term "SADR" will be used in this document when discussions pertain to proposals in this rule.