

submitted either on an FDA Form 3500A or, if preferred, on a Council for International Organizations of Medical Sciences (CIOMS) I form. Reports of overall findings or data in the aggregate from published and unpublished in vitro, animal, epidemiological, or clinical studies must be submitted in a narrative format. Each written notice must bear prominent identification of its contents, *i.e.*, "IND safety report." Each written notification to FDA must be transmitted to the FDA review division that has responsibility for the review of the IND. If FDA determines that additional data are needed, the agency may require further data to be submitted.

(2) *Telephone and facsimile transmission safety reports.* The sponsor must also notify FDA by telephone or by facsimile transmission of any unexpected fatal or life-threatening SADR based on the opinion of the investigator or sponsor as soon as possible but in no case later than 7 calendar days after receipt by the sponsor of the minimum data set for the unexpected fatal or life-threatening SADR. * * *

(4) *Investigations of marketed drugs.* A sponsor of a clinical study under an IND for a drug marketed in the United States is only required to submit IND safety reports to FDA (review division that has responsibility for the IND) for SADRs from the clinical study itself, whether from domestic or foreign study sites of the IND. The sponsor must also submit to FDA safety information from these clinical studies as prescribed by the postmarketing safety reporting requirements under §§ 310.305, 314.80, and 600.80 of this chapter. * * *

5. Section 312.64 is amended by revising paragraph (b) to read as follows:

§ 312.64 Investigator reports.

(b) *Safety reports.* An investigator must report to the sponsor any serious SADR (as defined in § 312.32(a)) immediately and any other SADR (as defined in § 312.32(a)) promptly unless the protocol or investigator's brochure specifies a different timetable for reporting the SADR. * * *

PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

6. The authority citation for 21 CFR part 314 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 355a, 356, 356a, 356b, 356c, 371, 374, 379e.

7. Section 314.80 is revised to read as follows:

§ 314.80 Postmarketing safety reporting and recordkeeping.

(a) *Definitions.* The following definitions of terms apply to this section:

Active query means direct verbal contact (*i.e.*, in person or by telephone or other interactive means such as a video conference) with the initial reporter of a suspected adverse drug reaction (SADR) or medication error by a health care professional (*e.g.*, physician, physician assistant, pharmacist, dentist, nurse, any individual with some form of health care training) representing the applicant. For SADRs, active query entails, at a minimum, a focused line of questioning designed to capture clinically relevant information associated with the drug product and the SADR, including, but not limited to, information such as baseline data, patient history, physical exam, diagnostic results, and supportive lab results.

Actual medication error means a medication error that involves an identifiable patient whether the error was prevented prior to administration of the product or, if the product was administered, whether the error results in a serious SADR, nonserious SADR, or no SADR.

Company core data sheet means a document prepared by the applicant containing, in addition to safety information, material relating to indications, dosing, pharmacology, and other information concerning the drug substance. The only purpose of this document is to provide the company core safety information (CCSI) for periodic safety update reports (PSURs), interim periodic safety reports (IPSRs), and certain individual case safety reports—semiannual submissions (*i.e.*, if PSURs are submitted for the product).

Company core safety information (CCSI) means all relevant safety information contained in the company core data sheet that the applicant proposes to include in the approved product labeling in all countries where the applicant markets the drug substance. It is the reference information by which an SADR is determined to be "listed" or "unlisted" for PSURs, IPSRs, and certain individual case safety reports—semiannual submissions (*i.e.*, if PSURs are submitted for the product).

Contractor means any person (*e.g.*, manufacturer, packer or distributor) whether its name appears on the label of the product; licensee; contract

research organization) that has entered into a contract with the applicant to manufacture, pack, sell, distribute, or develop the drug or to maintain, create, or submit records regarding SADRs or medication errors.

Data lock point means the date designated as the cut-off date for data to be included in a postmarketing periodic safety report.

Disability means a substantial disruption of a person's ability to conduct normal life functions.

Full data set means completion of all the applicable elements on FDA Form 3500A (or on a Council for International Organizations of Medical Sciences (CIOMS) I form for reports of foreign SADRs), including a concise medical narrative of the case (*i.e.*, an accurate summary of the relevant data and information pertaining to an SADR or medication error).

International birth date means the date the first regulatory authority in the world approved the first marketing application for a human drug product containing the drug substance.

Life-threatening SADR means any SADR that, in the view of the initial reporter, places the patient at immediate risk of death from the SADR as it occurred. It does not include an SADR that, had it occurred in a more severe form, might have caused death.

Listed SADR means an SADR whose nature, specificity, severity, and outcome are consistent with the information in the CCSI.

Medication error means any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the health care professional, patient or consumer. Such events may be related to professional practice, health care products, procedures, and systems including: Prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.

Minimum data set means the report includes an identifiable patient, an identifiable reporter, a suspect drug product, and an SADR.

Nonserious SADR means any SADR that is determined not to be a serious SADR.

Potential medication error means an individual case safety report of information or complaint about product name, labeling, or packaging similarities that does not involve a patient.

SADR with unknown outcome means an SADR that cannot be classified, after active query, as either serious or nonserious.