

registries, or any organized data collection scheme. It also does not include information compiled in support of class action lawsuits.

Suspected adverse drug reaction (SADR) means a noxious and unintended response to any dose of a drug 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.

Unexpected SADR means any SADR that is not included in the current U.S. labeling for the drug product. Reactions that may be symptomatically and pathophysiologically related to a reaction included in the U.S. labeling, but differ from the labeled reaction because of greater severity or specificity, would be unexpected. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the U.S. labeling only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the U.S. labeling only included cerebral vascular accidents. "Unexpected," as used in this definition, refers to an SADR that has not been previously observed (*i.e.*, included in the U.S. labeling); it does not refer to an SADR that might be anticipated from the pharmacological properties of the drug product. SADRs that are mentioned in the U.S. labeling as occurring with a class of drugs but not specifically mentioned as occurring with the particular drug are considered unexpected.

(b) **Review of safety information.** (1) Each manufacturer of a prescription drug product marketed for human use without an approved application must promptly review all safety information pertaining to its product obtained or otherwise received by the manufacturer from any source, foreign or domestic, including information derived from commercial marketing experience, postmarketing clinical investigations, postmarketing epidemiology/surveillance studies, animal or in vitro studies, electronic communications with manufacturers via the Internet (*e.g.*, e-mail), reports in the scientific literature, and unpublished scientific papers, as well as reports from foreign regulatory authorities that have not been previously reported to the Food and Drug Administration (FDA) by the manufacturer.

(2) Individual case safety reports that are forwarded to the manufacturer by FDA must not be resubmitted to the agency by the manufacturer; however,

manufacturers must submit to FDA all followup information for these reports.

(c) **Reporting requirements.** The manufacturer must submit to FDA one copy of each expedited report (described under paragraphs (c)(2)(i) through (c)(2)(vii) of this section) pertaining to its drug product. Upon written notice, FDA may require, when appropriate, that the manufacturer submit reports under this section to FDA at times other than those stated.

(1) **Determination of outcome, minimum data set, and full data set—**(i)(A) **Initial determinations.** Upon initial receipt of an SADR report, the manufacturer must immediately determine the outcome for the SADR (whether the SADR is serious or nonserious) and at least the minimum data set for the individual case safety report. For reports of actual medication errors that do not result in an SADR and potential medication errors, the manufacturer must immediately determine the minimum information for the individual case safety report (minimum information described under paragraphs (c)(1)(iii)(B) and (c)(1)(iii)(C) of this section). If the manufacturer is not able to immediately determine the information in this paragraph, active query must be used to obtain it as soon as possible.

(B) **Spontaneous reports.** For spontaneous reports, the manufacturer must always assume, for safety reporting purposes under this section, that there is at least a reasonable possibility, in the opinion of the initial reporter, that the drug product caused the spontaneously reported event.

(C) **Clinical trials.** For a clinical trial, the possibility that the drug product caused the SADR or that a medication error has occurred must be assumed if either the investigator or the manufacturer believes that such a reasonable possibility exists.

(ii) **SADRs with unknown outcome.** For an SADR with unknown outcome that cannot be immediately determined, the manufacturer must continue to use active query to attempt to determine the outcome of the SADR within 30 calendar days after initial receipt of the SADR report by the manufacturer. The manufacturer must maintain a record of its efforts to determine the outcome for an SADR with unknown outcome.

(iii)(A) **Minimum data set for SADR reports.** The manufacturer must not submit an individual case safety report for an SADR to FDA if the report does not contain a minimum data set; instead, the manufacturer must maintain records of any information received or otherwise obtained for the

SADR along with a record of its efforts to obtain a minimum data set.

(B) **Minimum information for reports of actual medication errors that do not result in an SADR.** For reports of actual medication errors that do not result in an SADR, an individual case safety report must be submitted to FDA even though the report does not contain a minimum data set (*i.e.*, does not have an SADR). These reports must contain at least an identifiable patient, an identifiable reporter, and a suspect drug product.

(C) **Minimum information for potential medication error reports.** For reports of potential medication errors, an individual case safety report must be submitted to FDA even though the report does not contain a minimum data set (*i.e.*, does not have an identifiable patient or an SADR). These reports must contain at least an identifiable reporter and a suspect drug product.

(iv) **Full data set.** For reports of serious SADRs, always expedited reports (see paragraph (c)(2)(iv) of this section), and medication error reports (see paragraph (c)(2)(v) of this section), the manufacturer must submit a full data set. If a full data set is not available for the report, the manufacturer must use active query to obtain this information. If a full data set is not obtainable, after active query, the manufacturer must:

(A) Submit all safety information, received or otherwise obtained, for the report;

(B) Indicate the reason(s) for its inability to acquire a full data set; and

(C) Document its efforts to obtain a full data set (*i.e.*, description of unsuccessful steps taken to obtain this information).

(v) **Serious SADRs not initially reported by health care professional.** For a serious SADR that was not initially reported to the manufacturer by a health care professional (*e.g.*, report from a consumer), the manufacturer must contact the health care professional associated with the care of the patient using active query to gather further medical perspective on the case and to acquire a full data set for the report. If the manufacturer is unable to contact the health care professional, it must include in the report for the serious SADR:

(A) The reason(s) for its inability to contact the health care professional; and

(B) A description of its efforts to contact the health care professional.

(2) **Postmarketing "expedited reports"—**(i) **Serious and unexpected SADR.** The manufacturer must report to FDA each SADR, received or otherwise obtained, that is both serious and