

minimum information for actual medication errors that do not result in an SADR and potential medication errors (minimum information described below and at proposed

§§ 310.305(c)(1)(iii)(B) and (c)(1)(iii)(C), 314.80(c)(1)(iii)(B) and (c)(1)(iii)(C), and 600.80(c)(1)(iii)(B) and (c)(1)(iii)(C)). If the manufacturer or applicant is not able to immediately determine this information, active query would be required to be used by the manufacturer or applicant to obtain the information as soon as possible.

Proposed §§ 310.305(c)(1)(ii), 314.80(c)(1)(ii), and 600.80(c)(1)(ii) would require manufacturers and applicants who are unable to immediately determine the outcome of an SADR (whether the SADR is serious or nonserious) to continue to use active query to attempt to determine the outcome within 30 calendar days after initial receipt of the SADR report by the manufacturer or applicant. The proposed rule would require that manufacturers and applicants maintain records of their efforts to obtain this information. These proposed revisions clarify that due diligence must be used to obtain the outcome for SADRs. Unknown outcomes should not be classified arbitrarily as nonserious SADRs. Instead, each of the outcomes in the definition of serious SADR should be considered as a possibility.

Under proposed §§ 310.305(c)(1)(iii)(A), 314.80(c)(1)(iii)(A), and 600.80(c)(1)(iii)(A), individual case safety reports for SADRs that do not contain a minimum data set would not be submitted to the agency. Instead, the proposed rule would require that manufacturers and applicants maintain records of any information received or otherwise obtained for the SADR along with a record of their efforts to obtain a minimum data set for the individual case safety report. These proposed amendments are consistent with proposed revisions to the premarketing safety reporting regulations at proposed § 312.32(c) (see section III.B.2.a of this document). This change would clarify that, at a minimum, certain information must be submitted to FDA to provide the agency with enough information to allow an initial evaluation of the significance of an SADR.

Proposed §§ 310.305(c)(1)(iii)(B), 314.80(c)(1)(iii)(B), and 600.80(c)(1)(iii)(B) would require that reports of actual medication errors that do not result in an SADR be submitted to FDA even though the report does not contain a minimum data set (*i.e.*, does not have an SADR). In these cases, individual case safety reports would be

required to contain at least an identifiable patient, an identifiable reporter, and a suspect drug or biological product.

Proposed §§ 310.305(c)(1)(iii)(C), 314.80(c)(1)(iii)(C), and 600.80(c)(1)(iii)(C) would require that reports of potential medication errors 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). In these cases, individual case safety reports would be required to contain at least an identifiable reporter and a suspect drug or biological product.

FDA is requiring submission of individual case safety reports for actual medication errors that do not result in an SADR and potential medication errors because of their potential significance and the need for intervention to minimize future errors. For example, if an adult is given the wrong medication, no SADR may occur, but if the same error occurs with a child, an SADR may occur. Also, if an error is prevented prior to administration of a product, this information could be used to prevent the error from occurring in other situations. For example, the proprietary name, label, labeling or packaging of the product could be changed if sufficient evidence suggests such a change is warranted, or education announcements could be communicated to health care professionals and/or consumers.

Proposed §§ 310.305(c)(1)(iv), 314.80(c)(1)(iv), and 600.80(c)(1)(iv) state that, for reports of serious SADRs, always expedited reports, and medication error reports, manufacturers and applicants would be required to submit a full data set for the report (see section III.D.4 of this document for discussion of always expedited reports and section III.D.5 of this document for discussion of medication error reports). If a full data set is not available for the report, the manufacturer or applicant would be required to use active query to obtain this information. If a full data set is not available, after active query, the manufacturer or applicant would provide the following information:

- All safety information, received or otherwise obtained, for the report;
- The reason(s) for their inability to acquire a full data set; and
- Documentation of their efforts to obtain a full data set (*i.e.*, description of unsuccessful steps taken to obtain this information).

In some cases, the agency has received incomplete safety reports for serious SADRs, making interpretation of their significance difficult. This proposed

amendment would require submission of complete information for reports of serious SADRs, always expedited reports, and medication error reports, which would facilitate their expeditious review.

Proposed §§ 310.305(c)(1)(v), 314.80(c)(1)(v), and 600.80(c)(1)(v) state that:

For a serious SADR that was not initially reported to the manufacturer (applicant for proposed §§ 314.80(c)(1)(v) and 600.80(c)(1)(v)) by a health care professional (*e.g.*, report from a consumer), the manufacturer (applicant for proposed §§ 314.80(c)(1)(v) and 600.80(c)(1)(v)) 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 (applicant for proposed §§ 314.80(c)(1)(v) and 600.80(c)(1)(v)) 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.

The agency believes that contact with a health care professional is warranted for serious SADRs because of the critical nature of these reactions. However, in those situations in which a manufacturer or applicant is unable to contact the health care professional (*e.g.*, health care professional does not return phone calls, consumer does not permit manufacturer or applicant to contact its health care provider), it would include in its report to FDA the reason(s) for its inability to contact the health care professional and a description of its efforts to contact the health care professional.

For nonserious SADRs with a minimum data set, proposed §§ 314.80(c)(1)(vi) and 600.80(c)(1)(vi) would require applicants to submit to FDA all safety information received or otherwise obtained. Applicants would not be required to acquire information in addition to the minimum data set, except that reports of nonserious SADRs resulting from a medication error would require a full data set. Thus, followup would not be required for reports of nonserious SADRs that contain a minimum data set and do not occur because of a medication error.

III.C.6. Spontaneous Reports and Reports From Clinical Trials

Proposed §§ 310.305(c)(1)(i)(B), 314.80(c)(1)(i)(B), and 600.80(c)(1)(i)(B) would require that, for spontaneous reports, manufacturers and applicants must always assume, for safety reporting purposes only, that there is at least a reasonable possibility, in the opinion of the initial reporter, that the drug or