

- Unexpected SADRs with unknown outcomes,
- Always expedited reports that contain a full data set,
- Actual and potential medication error reports that contain a full data set,
- 30-day followup reports, and
- 15-day followup reports.

These proposed revisions clarify the types of expedited reports that would be subject to the 15-day followup reporting requirements.

FDA notes that a 15-day followup report, rather than a serious and unexpected SADR report, should be submitted to FDA for an SADR that is initially reported to the agency as serious and expected or nonserious and unexpected, but is subsequently determined to be serious and unexpected. In these cases, manufacturers and applicants should include in the 15-day followup report a chronological history describing the events that transpired which resulted in determination of the serious and unexpected character of the SADR.

FDA is proposing to amend its postmarketing expedited safety reporting regulations at §§ 310.305(c)(2), 314.80(c)(1)(ii), and 600.80(c)(1)(ii) by removing the second sentence in these paragraphs regarding maintaining records if additional information is not obtainable for a serious and unexpected adverse drug experience. The agency is proposing this amendment because postmarketing safety reporting requirements for serious and unexpected SADR reports that do not contain a full data set are now prescribed under proposed §§ 310.305(c)(1)(iv) and (c)(2)(vi), 314.80(c)(1)(iv) and (c)(2)(vi), and 600.80(c)(1)(iv) and (c)(2)(vi).

III.D.7. Supporting Documentation

Proposed §§ 310.305(c)(2)(viii)(A), 314.80(c)(2)(viii)(A), and 600.80(c)(2)(viii)(A) would require that manufacturers and applicants submit to FDA, if available, a copy of the autopsy report if the patient dies. If an autopsy report is not available, the proposed rule would require that manufacturers and applicants submit a death certificate to FDA. If an autopsy report becomes available after the manufacturer or applicant has submitted a death certificate to the agency, the manufacturer or applicant must submit the autopsy report to FDA. If the patient was hospitalized, manufacturers and applicants would be required to submit to FDA, if available, a copy of the hospital discharge summary. If any of these documents is not in English, an English translation of the document would be required. FDA is proposing

that manufacturers and applicants submit these documents to provide the agency with complete information for SADRs that result in a death or hospitalization.

Proposed §§ 310.305(c)(2)(viii)(A), 314.80(c)(2)(viii)(A), and 600.80(c)(2)(viii)(A) would require that manufacturers and applicants use active query to obtain the documents required to be submitted to FDA under this paragraph. These documents would be required to be submitted to FDA as 15-day followup reports (see section III.D.6 of this document) within 15 calendar days of initial receipt of the document by the manufacturer or applicant. In instances when a document is not submitted to FDA in a 15-day followup report within 3 months after submission of the initial expedited report for the death or hospitalization, the agency would assume that active query by the manufacturer or applicant did not result in access to these documents. In this case, a record of the reason(s) for the lack of documentation and the effort that was made to obtain the documentation would be required to be maintained by the manufacturer and applicant.

Proposed §§ 310.305(c)(2)(viii)(B), 314.80(c)(2)(viii)(B), and 600.80(c)(2)(viii)(B) would require that each expedited report contain in the narrative a list of other relevant documents (e.g., medical records, laboratory results, data from studies) regarding the report that are maintained by manufacturers and applicants. FDA may require, when appropriate, that copies of one or more of these documents be submitted to the agency within 5 calendar days after receipt of the request. FDA would usually request such records in response to a suspected safety problem associated with the use of a drug or licensed biological product.

III.D.8. Scientific Literature

Current postmarketing expedited safety reporting regulations at §§ 314.80(d)(1) and 600.80(d)(1) require that expedited reports based on information from the scientific literature be accompanied by a copy of the published article. These regulations apply only to reports found in scientific and medical journals either as case reports or as the result of a formal clinical trial. Proposed §§ 314.80(c)(2)(ix) and 600.80(c)(2)(ix) would amend the current regulations by removing the phrase “either as case reports or as the result of a formal clinical trial” to clarify that all reports from the scientific literature, including case reports, and results of a formal clinical trial, epidemiological study, in

vitro study, or animal study, that qualify for expedited reporting under proposed §§ 314.80(c)(2) and 600.80(c)(2) would be required to be submitted to FDA.

The proposed rule would also remove §§ 314.80(d)(2) and 600.80(d)(2). These paragraphs provide that reports based on the scientific literature must be submitted on FDA Form 3500A or comparable format prescribed by the regulations and that, in cases where persons subject to the postmarketing safety reporting regulations believe that preparing the FDA Form 3500A constitutes an undue hardship, arrangements can be made with the agency for use of an acceptable alternative reporting format. FDA is proposing to remove these paragraphs because the reporting format for reports based on information in the scientific literature would be specified under proposed §§ 314.80(c)(4) and 600.80(c)(4) (see section III.F of this document).

For organizational purposes, FDA is proposing to move §§ 314.80(d) and 600.80(d), as revised by this proposed rule, to proposed §§ 314.80(c)(2)(ix) and 600.80(c)(2)(ix). Proposed § 310.305(c)(2)(ix) would amend § 310.305(c) by adding the paragraph:

Scientific literature. An expedited report based on information from the scientific literature applies only to reports found in scientific and medical journals. These expedited reports must be accompanied by a copy of the published article.

This proposed amendment would clarify for prescription drug products marketed for human use without an approved application the types of safety information found in scientific literature that would qualify for expedited reporting. The proposed amendment would also require that these reports include a copy of the published article that is the subject of the expedited report. The proposed amendment would provide the agency with more complete information for review of safety information from the scientific literature and would also provide uniformity between FDA's postmarketing expedited safety reporting requirements for prescription drugs marketed for human use without an approved application and marketed drugs with an approved application.

III.D.9. Contractors and Shared Manufacturers

Current regulations at §§ 310.305(c)(1)(i) and (c)(3), 314.80(c)(1)(iii), and 600.80(c)(1)(iii) require any person whose name appears on the label of a marketed drug product or licensed biological product as a packer or distributor to submit either