

expedited reports of serious and unexpected adverse drug experiences directly to FDA or reports of all serious adverse drug experiences to the manufacturer (§ 310.305(c)(3) or applicant (§§ 314.80(c)(1)(iii) and 600.80(c)(1)(iii)) instead of FDA in 5 calendar days. This provision also applies to manufacturers for §§ 314.80(c)(1)(iii) and 600.80(c)(1)(iii) and to shared manufacturers, joint manufacturers, and any participants involved in divided manufacturing for § 600.80(c)(1)(iii). Proposed §§ 310.305(c)(2)(xi)(A), 314.80(c)(2)(x)(A), and 600.80(c)(2)(x)(A) would amend these regulations to require contractors, as defined in proposed §§ 310.305(a), 314.80(a) and 600.80(a) (see section III.A.4 of this document), to submit to the manufacturer (proposed § 310.305(c)(2)(xi)(A)) or applicant (proposed §§ 314.80(c)(2)(x)(A) and 600.80(c)(2)(x)(A)) safety reports of all SADR (serious and nonserious) and medication errors for the manufacturer's (proposed § 310.305(c)(2)(xi)) or applicant's (proposed §§ 314.80(c)(2)(x) and 600.80(c)(2)(x)) drug or biological product, obtained or otherwise received, within 5 calendar days of initial receipt of the report by the contractor. This provision would also apply to shared manufacturers of licensed biological products for proposed § 600.80(c)(2)(x)(A) (*i.e.*, all SARs and medication errors would be required to be submitted to the applicant within 5 calendar days). The contractor would be required to submit a report of an SADR to the manufacturer (proposed § 310.305(c)(2)(xi)(A)) or applicant (proposed §§ 314.80(c)(2)(x)(A) and 600.80(c)(2)(x)(A)) even if the report does not contain a minimum data set. Contractors and shared manufacturers would only be required to convey to manufacturers (proposed § 310.305(c)(2)(xi)(A)) or applicants (proposed §§ 314.80(c)(2)(x)(A) and 600.80(c)(2)(x)(A)) whatever safety information was obtained or otherwise received. They would not be required to use active query to acquire safety information, to conduct followup, or to submit postmarketing safety reports to FDA. Upon receipt of a safety report from a contractor or shared manufacturer, the manufacturer (proposed § 310.305(c)(2)(xi)(A)) or applicant (proposed §§ 314.80(c)(2)(x)(A) and 600.80(c)(2)(x)(A)) would be required to comply with the postmarketing safety reporting requirements under proposed §§ 310.305, 314.80 and 600.80 (*e.g.*, use active query, if necessary, to acquire

safety information, conduct followup, submit postmarketing safety reports to FDA). These proposed amendments would provide manufacturers and applicants with complete safety information regarding its products.

Proposed §§ 310.305(c)(2)(xi)(B), 314.80(c)(2)(x)(B), and 600.80(c)(2)(x)(B) would require that contracts between manufacturers and contractors (§ 310.305(c)(2)(xi)(B)) and applicants and contractors (§§ 314.80(c)(2)(x)(B) and 600.80(c)(2)(x)(B)) specify the postmarketing safety reporting responsibilities of the contractor. Although contractors and shared manufacturers have postmarketing safety reporting responsibilities, the manufacturer (proposed § 310.305(c)(2)(xi)(B)) or applicant (proposed §§ 314.80(c)(2)(x)(B) and 600.80(c)(2)(x)(B)) would be responsible for ensuring that the contractors and shared manufacturers of its products comply with these postmarketing safety reporting responsibilities. FDA believes that, in general, this proposal represents a practice that is already customary and usual in the pharmaceutical industry because contractors are typically considered agents of the manufacturer or applicant.

Proposed §§ 310.305(c)(2)(xi)(C), 314.80(c)(2)(x)(C), and 600.80(c)(2)(x)(C) would require that contractors and shared manufacturers maintain records of SADR reports and medication errors. This proposal is consistent with current postmarketing safety reporting requirements.

Proposed §§ 310.305(c)(2)(xi)(D), 314.80(c)(2)(x)(D), and 600.80(c)(2)(x)(D) state that the recordkeeping, written procedures, and disclaimer provisions under proposed §§ 310.305, 314.80 and 600.80 would apply to contractors and shared manufacturers. This proposal clarifies for contractors and shared manufacturers which of the postmarketing safety reporting provisions would apply to them.

#### III.D.10. Prescription Drugs Marketed for Human Use Without an Approved Application

Proposed § 310.305(c)(2)(x) would amend § 310.305(c)(1)(i) to require that expedited reports for prescription drugs marketed for human use without an approved application be accompanied by a list of the current addresses where all safety reports and other safety-related records for the drug product are maintained by manufacturers and contractors. In the October 1994 proposal, FDA proposed to include, under §§ 314.80(c)(2) and 600.80(c)(2), a section in its postmarketing periodic safety reports on location of adverse

drug experience records (59 FR 54046 at 54061). FDA is now reproposing this amendment for its postmarketing periodic safety reports (see sections III.E.1.g, III.E.2.k.x, and III.E.3 of this document). The agency is also proposing to require the list of addresses in expedited reports for drugs covered under § 310.305 because manufacturers of these drugs are not required to submit postmarketing periodic safety reports to FDA. The list of addresses would provide rapid access to safety-related records for FDA inspections and for requests by FDA for additional information concerning safety issues.

#### III.D.11. Class Action Lawsuits

Manufacturers and applicants should not submit SADR from class action lawsuits to FDA in an expedited report. The agency believes that SADRs from class action lawsuits would be submitted to FDA from other sources (*e.g.*, spontaneous reports) prior to initiation of the class action lawsuit. Summary tabulations of SADRs from class action lawsuits would be required in postmarketing periodic safety reports (see sections III.E.1.e and III.E.2.k.v of this document).

#### III.D.12. Blood and Blood Component Safety Reports

Current § 606.170(a) requires a blood establishment to thoroughly investigate any complaint of an adverse reaction arising as a result of blood collection or transfusion and to prepare and maintain a written report of the investigation, including followup and conclusions, as part of the record for that lot or unit of final product. If appropriate, the report must be forwarded to the manufacturer of the blood or blood component or the collection facility. Under § 606.170(b), a complication of a blood collection or blood transfusion resulting in a fatality must be reported to FDA as soon as possible by telephone or other rapid means of communication, and a written report of the investigation must be submitted to FDA within 7 days of the fatality. Each year, in accordance with § 606.170(b), FDA receives between 50 and 80 reports of fatalities.

Current § 606.171 requires licensed manufacturers of blood and blood components, unlicensed registered blood establishments and transfusion services to report biological product deviations. A biological product deviation is an event that represents either: (1) A deviation from current good manufacturing practices, applicable regulations, applicable standards, or established specifications that may affect the safety, purity, or potency of a product; or (2) an unexpected or