

report to FDA. Preparation of these written IND safety reports would include gathering information (proposed § 312.32(b)) and formatting information (proposed § 312.32(c)(1)(iii)).

Proposed § 312.32(c)(2) would require sponsors to 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 an unexpected fatal or life-threatening SADR. Based on data concerning the number of telephone IND safety reports currently received by the agency, FDA estimates that approximately 490 telephone and facsimile IND safety reports will be submitted annually under proposed § 312.32(c)(2) for human drugs, and approximately 290 reports will be submitted annually under proposed § 312.32(c)(2) for human biological products. FDA estimates that approximately 135 sponsors will submit these reports for human drugs, and approximately 180 sponsors will submit these reports for human biological products. Based on the agency's familiarity with telephone and facsimile IND safety reports, FDA estimates that it will take an average of 4 hours for sponsors to prepare and submit one of these reports to FDA. Preparation of a telephone or facsimile IND safety report would include gathering information (proposed § 312.32(b)).

Proposed § 312.64(b) would require an investigator to notify the sponsor of any serious SADR immediately and any other SADR promptly unless the protocol or investigator's brochure specifies a different timetable for reporting the SADR. Based on data concerning the number of sponsors currently conducting clinical investigations under an IND and the number of written IND safety reports currently received by the agency, FDA estimates that approximately 100,000 investigator safety reports will be submitted to sponsors annually under proposed § 312.64(b) for human drugs, and approximately 60,000 investigator safety reports will be submitted to sponsors annually under proposed § 312.64(b) for human biological products. FDA estimates that approximately 10,000 investigators will submit safety reports to sponsors for human drugs, and approximately 6,000 investigators will submit safety reports to sponsors for human biological products. Based on the agency's familiarity with the content of IND safety reports, FDA estimates that it will

take an average of 2 hours for an investigator to prepare and submit one of these reports to the sponsor.

Proposed § 320.31(d)(3) would require persons conducting human bioavailability and bioequivalence studies that are not subject to an IND to submit to FDA written safety reports as prescribed under proposed § 312.32(c)(1) and telephone and facsimile safety reports as prescribed under proposed § 312.32(c)(2). These persons would submit these safety reports to all participating investigators and the appropriate FDA division in the Center for Drug Evaluation and Research (*i.e.*, safety reports for the reference listed drug would be forwarded to the new drug review division that has responsibility for that drug; safety reports for the investigational drug product would be forwarded to the Director, Division of Bioequivalence, Office of Generic Drugs). These persons would be required to identify all safety reports previously filed for the bioavailability or bioequivalence study concerning a similar SADR, and analyze the SADR in light of previous similar reports, as required under proposed § 312.32(c)(1)(i). Written, telephone, and facsimile safety reports for bioavailability and bioequivalence studies not subject to an IND are a new type of safety report. Based on data concerning voluntary reporting to the agency of safety information for these bioavailability and bioequivalence studies, FDA estimates that approximately 200 safety reports will be submitted annually under proposed § 320.31(d)(3). FDA estimates that approximately 10 sponsors will submit these safety reports. Based on the agency's familiarity with the content of IND safety reports, FDA estimates that it will take an average of 14 hours for sponsors to prepare and submit a safety report to FDA.

Proposed § 606.170(b) would require blood establishments to notify FDA in a written report of any serious SAR, except a fatality, within 45 calendar days after determination of a serious SAR. These written reports would be submitted to FDA using the reporting format provided in proposed § 600.80(c)(4). Based on data from the scientific literature and reports voluntarily received by the agency, FDA estimates that approximately 7,000 written reports will be submitted annually under proposed § 606.170(b). FDA estimates that approximately 3,062 blood establishments will submit these written reports. Based on the agency's familiarity with the content of expedited reports for serious and unexpected SADRs, FDA estimates that it will take

an average of 16 hours to prepare and submit each of these written reports to FDA.

Proposed § 606.170(c) would require blood establishments to notify FDA by telephone, facsimile, express mail, or electronically transmitted mail as soon as possible of an SAR that results in a fatality. Proposed § 606.170(c) would also require these facilities to submit a written report to FDA within 7 calendar days after the fatality. The written reports would be submitted using the reporting format provided in proposed § 600.80(c)(4). Based on data concerning the number of reports for fatalities associated with blood collection and transfusion currently received by the agency, FDA estimates that approximately 75 reports will be submitted annually under proposed § 606.170(c). FDA estimates that approximately 75 blood establishments will submit these reports. Based on the agency's familiarity with the content of written reports for a fatality, FDA estimates that it will take an average of 20 hours to prepare and submit each of these reports to FDA.

#### *VI.B. Periodic Safety Reports*

Proposed §§ 314.80(c)(3)(i) and 600.80(c)(3)(i) would require persons holding an application (*i.e.*, NDA, ANDA, BLA) approved before January 1, 1998, to submit a TPSR every 5 years after U.S. approval of the application. These persons would also be required to submit a TPSR at 7.5 and 12.5 years after U.S. approval of the application. Based on data concerning postmarketing periodic safety reports currently received by the agency, FDA estimates that approximately 1,400 TPSRs will be submitted annually under proposed § 314.80(c)(3)(i); approximately 35 TPSRs will be submitted annually under proposed § 600.80(c)(3)(i). FDA estimates that approximately 80 applicants under proposed § 314.80(c)(3)(i) will submit TPSRs, and approximately 20 applicants under proposed § 600.80(c)(3)(i) will submit TPSRs. Based on the agency's familiarity with the content of postmarketing periodic safety reports, FDA estimates that it will take an average of 20 hours for applicants to prepare and submit a TPSR to FDA. Preparation of a TPSR would include gathering information (proposed §§ 314.80(b) and 600.80(b)), and providing attachments (proposed §§ 314.80(c)(3) and 600.80(c)(3)).

Proposed §§ 314.80(c)(3)(ii) and 600.80(c)(3)(ii) would require persons holding an application (*i.e.*, NDA, ANDA, BLA) approved on or after January 1, 1998, to submit a PSUR to