

expedited reports which are subject to the 30-day followup reporting requirement under proposed §§ 310.305(c)(2)(vi), 314.80(c)(2)(vi), and 600.80(c)(2)(vi). Proposed §§ 310.305(b)(2), 314.80(b)(2), and 600.80(b)(2) would also require manufacturers and applicants to submit 15-day followup reports to FDA with any new information concerning an individual case safety report forwarded to the manufacturer or applicant by FDA. Proposed §§ 310.305(c)(2)(viii)(A), 314.80(c)(2)(viii)(A), and 600.80(c)(2)(viii)(A) would also require manufacturers and applicants to submit to FDA as 15-day followup reports any documents required under these paragraphs that become available after submission of an expedited report. These 15-day followup reports would be submitted within 15 calendar days of initial receipt of the new information by the manufacturer or applicant. Based on data concerning the number of followup reports currently received by the agency, FDA estimates that approximately 55 15-day followup reports will be submitted annually under proposed § 310.305(b)(2), (c)(2)(vii), and (c)(2)(viii)(A); approximately 10,000 15-day followup reports will be submitted annually under proposed § 314.80(b)(2), (c)(2)(vii), and (c)(2)(viii)(A); and approximately 1,000 15-day followup reports will be submitted annually under proposed § 600.80(b)(2), (c)(2)(vii), and (c)(2)(viii)(A). FDA estimates that approximately 10 manufacturers under proposed § 310.305 will submit 15-day followup reports; approximately 184 applicants under proposed § 314.80 will submit 15-day followup reports; and approximately 69 applicants under proposed § 600.80 will submit 15-day followup reports. Based on the agency's familiarity with the content of followup reports for serious and unexpected SADRs, FDA estimates that it will take an average of 4 hours for manufacturers and applicants to prepare and submit a 15-day followup report to FDA. Preparation of 15-day followup reports would include gathering information (proposed §§ 310.305(b) and (c)(1), 314.80(b) and (c)(1), and 600.80(b) and (c)(1)), providing attachments, if applicable (proposed §§ 310.305(c)(2)(ix) and (c)(2)(x), 314.80(c)(2)(ix), and 600.80(c)(2)(ix)), and formatting information (proposed §§ 310.305(c)(2)(xii), (d), and (e), 314.80(c)(2)(xi), (c)(4), and (e), and 600.80(c)(2)(xi), (c)(4), and (e)).

Proposed §§ 310.305(c)(2)(xi), 314.80(c)(2)(x), and 600.80(c)(2)(x)

would require contractors and shared manufacturers to submit safety reports of any SADRs or medication errors for the product to the manufacturer (proposed §§ 310.305(c)(2)(xi) or applicant (proposed §§ 314.80(c)(2)(x) and 600.80(c)(2)(x)) within 5 calendar days of its receipt by the contractor or shared manufacturer. Based on information included in individual case safety reports currently submitted to the agency, FDA estimates that approximately 10 safety reports will be submitted to manufacturers annually under proposed § 310.305(c)(2)(xi); approximately 11,370 safety reports will be submitted to applicants annually under proposed § 314.80(c)(2)(x); and approximately 250 safety reports will be submitted to applicants annually under proposed § 600.80(c)(2)(x). FDA estimates that approximately 5 contractors under proposed § 310.305 will submit safety reports to the manufacturer; approximately 100 contractors under proposed § 314.80 will submit safety reports to the applicant; and approximately 20 contractors and shared manufacturers under proposed § 600.80 will submit safety reports to the applicant. Based on the agency's familiarity with the content of individual case safety reports, FDA estimates that it will take an average of 2 hours for contractors and shared manufacturers to prepare and submit a safety report to a manufacturer or applicant.

Proposed § 312.32(c)(1)(i) would require sponsors to notify FDA and all participating investigators in a written IND safety report of any SADR, based on the opinion of the investigator or sponsor, that is both serious and unexpected, as soon as possible, but in no case later than 15 calendar days after receipt by the sponsor of the minimum data set for the serious, unexpected SADR. The sponsor would identify all safety reports previously filed with the IND concerning a similar SADR and would analyze the significance of the SADR in light of previous, similar reports. Based on data concerning the number of written IND safety reports currently received by the agency, FDA estimates that approximately 4,860 written IND safety reports of serious and unexpected SADRs will be submitted annually under proposed § 312.32(c)(1)(i) for human drugs, and approximately 2,980 written IND safety reports will be submitted annually under proposed § 312.32(c)(1)(i) for human biological products. FDA estimates that approximately 457 sponsors will submit written IND safety reports for human drugs, and

approximately 602 sponsors will submit written IND safety reports for human biological products. Based on the agency's familiarity with the content of written IND safety reports for serious and unexpected SADRs, FDA estimates that it will take an average of 16 hours for sponsors to prepare and submit one of these reports to FDA. Preparation of a written IND safety report for a serious and unexpected SADR would include gathering information (proposed § 312.32(b)) and formatting information (proposed § 312.32(c)(1)(iii)).

Proposed § 312.32(c)(1)(ii) would require sponsors to notify FDA and all participating investigators in a written IND safety report of information, based on appropriate medical judgment, that might materially influence the benefit-risk assessment of an investigational drug, or would be sufficient to consider changes in either product administration or in the overall conduct of a clinical investigation (e.g., any significant unanticipated safety finding or data in the aggregate from an in vitro, animal, epidemiological, or clinical study, whether or not conducted under an IND, that suggests a significant human risk, such as reports of mutagenicity, teratogenicity, or carcinogenicity, or reports of a lack of efficacy with a drug or biological product used in treating a life-threatening or serious disease). This information would be submitted as soon as possible, but in no case later than 15 calendar days after determination by the sponsor that the information qualifies for expedited reporting. Based on information contained in written IND safety reports that the agency has received in the past, FDA estimates that approximately 300 written IND safety reports concerning information that might materially influence the benefit-risk assessment of an investigational drug, or that would be sufficient to consider changes in either product administration or in the overall conduct of a clinical investigation will be submitted annually under proposed § 312.32(c)(1)(ii) for human drugs, and approximately 300 reports will be submitted annually under proposed § 312.32(c)(1)(ii) for human biological products. FDA estimates that approximately 100 sponsors will submit these written IND safety reports for human drugs, and approximately 100 sponsors will submit these reports for human biological products. Based on the agency's familiarity with the content of written IND safety reports, FDA estimates that it will take an average of 8 hours for sponsors to prepare and submit this type of written IND safety