

on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

**Title:** Safety Reporting Requirements for Human Drug and Biological Products

**Description:** The proposed rule would amend FDA's safety reporting regulations for human drug and biological products to implement definitions, and reporting formats and standards as recommended by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and by the World Health Organization's Council for International Organizations of Medical Sciences (CIOMS); codify the agency's expectations for timely acquisition, evaluation, and submission of relevant safety information for marketed drugs and licensed biological products; require that certain information, such as domestic reports of medication errors, be submitted to the agency in an expedited manner; clarify certain safety reporting requirements; and make other minor revisions. The proposed rule would also amend FDA's postmarketing annual reports regulations for human drugs and licensed biological products by revising the content for these reports. These changes would further worldwide consistency in the collection of safety information and submission of safety reports, increase the quality of safety reports, expedite FDA's review of critical safety information, and enable the agency to protect and promote public health. The estimates provided in this section are not only attributed to the new proposed requirements in this rulemaking but also include burdens associated with our current safety reporting requirements.

**VI.A. Expedited Safety Reporting**

Proposed §§ 310.305(c)(2)(i), 314.80(c)(2)(i), and 600.80(c)(2)(i) would require manufacturers and applicants to submit a report to FDA for each SADR, received or otherwise obtained, that is both serious and unexpected, whether foreign or domestic, as soon as possible, but in no case later than 15 calendar days after receipt by the manufacturer or applicant of the minimum data set for the serious, unexpected SADR. Based on data concerning the number of expedited reports currently received by the agency, FDA estimates that approximately 350 expedited reports of serious and unexpected SADRs will be submitted annually under proposed § 310.305(c)(2)(i); approximately 50,000 reports will be submitted annually under proposed § 314.80(c)(2)(i); and

approximately 3,000 reports will be submitted annually under proposed § 600.80(c)(2)(i). FDA estimates that approximately 14 manufacturers under proposed § 310.305(c)(2)(i) will submit these reports; approximately 282 applicants under proposed § 314.80(c)(2)(i) will submit these reports; and approximately 69 applicants under proposed § 600.80(c)(2)(i) will submit these 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 for manufacturers and applicants to prepare and submit one of these reports to FDA. Preparation of an expedited report for a serious and unexpected SADR 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)(ii), 314.80(c)(2)(ii), and 600.80(c)(2)(ii) would require manufacturers and applicants to submit a report to FDA concerning information, received or otherwise obtained, whether foreign or domestic, that would be sufficient, based upon appropriate medical judgment, to consider product administration changes (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). Manufacturers and applicants would be required to submit this information to FDA as soon as possible, but in no case later than 15 calendar days after determination by the manufacturer or applicant that the information qualifies for expedited reporting. Expedited reports containing information that would be sufficient to consider changes in product administration are a new type of safety report. Based on data concerning voluntary reporting of this type of information to the agency, FDA estimates that approximately 5 expedited reports concerning information sufficient to consider

product administration changes will be submitted annually under proposed § 310.305(c)(2)(ii); approximately 300 reports will be submitted annually under proposed § 314.80(c)(2)(ii); and approximately 4 reports will be submitted annually under proposed § 600.80(c)(2)(ii). FDA estimates that approximately 5 manufacturers under proposed § 310.305(c)(2)(ii) will submit these expedited reports; approximately 50 applicants under proposed § 314.80(c)(2)(ii) will submit these expedited reports; and approximately 4 applicants under proposed § 600.80(c)(2)(ii) will submit these expedited reports. Based on the content of the voluntary reports submitted to the agency, FDA estimates that it will take an average of 8 hours for manufacturers and applicants to prepare and submit an expedited report to FDA concerning information sufficient to consider product administration changes. Preparation of these expedited 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)(iii), 314.80(c)(2)(iii), and 600.80(c)(2)(iii) would require manufacturers and applicants to submit a report to FDA for each SADR that is unexpected and for which the determination of an outcome is unattainable (i.e., SADR with unknown outcome) within 45 calendar days after initial receipt by the manufacturer or applicant of the minimum data set for an unexpected SADR. Expedited reports of unexpected SADRs with an unknown outcome are a new type of safety report. Based on data concerning the number of unexpected SADR reports with an unknown outcome currently received by the agency, FDA estimates that approximately 46 expedited reports of an unexpected SADR with an unknown outcome will be submitted annually under proposed § 310.305(c)(2)(iii); approximately 912 reports will be submitted annually under proposed § 314.80(c)(2)(iii); and approximately 25 reports will be submitted annually under proposed § 600.80(c)(2)(iii). FDA estimates that approximately 10 manufacturers under proposed § 310.305(c)(2)(iii) will submit these expedited reports; approximately 109 applicants under proposed