

The proposed rule would also require that this section of the TPSR include an assessment of whether it is believed that the frequency of lack of efficacy reports, obtained or otherwise received during the reporting period, is greater than would be predicted by the premarketing clinical trials for the drug or biological product. This assessment would be provided whether a serious SADR, nonserious SADR, or no SADR occurs as a result of a lack of efficacy of the product.

III.E.1.d. *Safety-related actions to be taken.* Proposed §§ 314.80(c)(3)(i)(A)(4) and 600.80(c)(3)(i)(A)(4) would require applicants to include in TPSRs the applicant's conclusion as to what, if any, safety-related actions should be taken based on the analysis of the safety data in the TPSR (e.g., labeling changes, studies initiated). FDA is proposing this amendment to highlight safety-related actions that may be necessary.

III.E.1.e. *Summary tabulations.* Proposed §§ 314.80(c)(3)(i)(B), and 600.80(c)(3)(i)(B) would require that a new section of summary tabulations (i.e., lists of all SADR terms and counts of occurrences) be included in TPSRs for all serious, expected SADRs; nonserious, unexpected SADRs; nonserious, expected SADRs; and expected SADRs with unknown outcome occurring in the United States that are submitted to the applicant during the reporting period from all spontaneous sources (i.e., health care professionals and other individuals). These tabulations would include SADRs that were previously submitted to FDA in an expedited report (i.e., serious, unexpected SADRs, unexpected SADRs with unknown outcome, and always

expedited reports) and reports of SADRs not previously submitted to FDA by applicants (e.g., reports submitted to applicants by FDA; reports obtained from FDA from freedom of information requests at the discretion of applicants; reports from class action lawsuits). The proposed rule would require that cumulative data be provided for SADRs that are determined to be both serious and unexpected (i.e., all cases reported to date). These summary tabulations would be presented by body system or standard organ system classification scheme (e.g., cardiovascular, central nervous system, endocrine, renal). The proposed rule would also require summary tabulations for all domestic reports of actual medication errors (i.e., serious SADRs, nonserious SADRs, no SADRs) and potential medication errors (i.e., number of reports for specific errors) that were previously submitted to the agency as an expedited report.

In the guidance of 1992, FDA advises applicants to include in their postmarketing periodic safety reports a listing by body system of all adverse drug experience terms and counts of occurrences submitted during the reporting period. FDA is now proposing to clarify and codify this expectation.

III.E.1.f. *History of safety-related actions taken.* Proposed §§ 314.80(c)(3)(i)(C), and 600.80(c)(3)(i)(C) would amend §§ 314.80(c)(2)(ii)(c) and 600.80(c)(2)(ii)(C) by adding the phrase "safety-related" before the word "actions" and by removing the phrase "because of adverse drug experiences." FDA is proposing these changes because actions may be taken for safety-related reasons other than SADRs. The

proposed rule would also amend these regulations by adding the phrase "periodic safety" before the word "report" for clarification.

III.E.1.g. *Location of safety records.* Proposed §§ 314.80(c)(3)(i)(D) and 600.80(c)(3)(i)(D) would require another new section in TPSRs that would contain a list of the current address(es) where all safety reports and other safety-related records for the drug product or licensed biological product are maintained. FDA is proposing to require a list of these addresses to provide rapid access to safety-related records for FDA inspections and for requests by FDA for additional information concerning safety issues.

III.E.1.h. *Contact person.* Proposed §§ 314.80(c)(3)(i)(E) and 600.80(c)(3)(i)(E) would require another new section in TPSRs that would contain the name and telephone number of the licensed physician or licensed physicians responsible for the content and medical interpretation of the data and information contained within the TPSR. The fax number and e-mail address for the licensed physician would also be included, if available. This proposal would provide the agency with someone to contact with any questions that may arise during review of a TPSR. FDA is proposing that the contact persons be licensed physicians because of their crucial knowledge of the medical significance of the information provided in a TPSR.

Table 10 highlights the differences in content between the currently required postmarketing periodic adverse drug experience reports and proposed TPSRs.

TABLE 10.—DIFFERENCES BETWEEN THE CURRENT REQUIREMENT FOR THE CONTENT OF POSTMARKETING PERIODIC ADVERSE DRUG EXPERIENCE REPORTS AND THE PROPOSED CONTENT OF TPSRS.

Content of periodic adverse drug experience report	Proposed revisions to content of periodic adverse drug experience report (proposed TPSRs)
Narrative summary and analysis of the information contained in the report.	Excludes nonserious expected SADRs. Includes discussion of increased frequency of serious expected SADRs and lack of efficacy reports. Includes applicant's recommendations for safety-related actions to be taken.
Analysis of expedited reports submitted to FDA during the reporting interval.	Not revised.
FDA Form 3500A (VAERS form for vaccines) for each adverse drug experience not submitted to FDA as an expedited report.	Revoked requirement. ¹
Index consisting of a line listing of the applicant's patient identification number and adverse reaction term(s).	Not revised.
History of actions taken since the last report because of adverse drug experiences.	Not revised. Require submission summary tabulations. ² New section added for location of safety records. New section added for contact information for licensed physician responsible for information in TPSR.

¹ Individual case safety reports would be submitted to FDA separately on a semiannual basis (see section III.E.4 of this document).

² Summary tabulations are currently requested (see the guidance of 1992) but not required for postmarketing periodic adverse drug experience reports.