

physician or licensed physicians responsible for the content and medical interpretation of the data and information contained within the PSUR would be provided. The fax number and e-mail address of 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 PSUR. 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 PSUR.

The PSUR excluding appendices, as proposed in this rule, would represent a harmonized core document for worldwide postmarketing periodic safety reporting for marketed drugs and licensed biological products.

III.E.3. Interim Periodic Safety Reports (IPSRs)

Proposed §§ 314.80(c)(3)(iii) and 600.80(c)(3)(iii) would amend FDA's postmarketing periodic safety reporting regulations by adding another new type of postmarketing periodic safety report. FDA is proposing that this new report be identified as an "interim periodic safety report (IPSR)." An IPSR would contain the same information as a PSUR, except that the following information would not be provided:

- Summary tabulations for individual case safety reports, obtained or otherwise received during the reporting period and brief discussion of the data concerning these reports (*see* section III.E.2.f.ii of this document),
- Any important new information received after the data lock point (*e.g.*, significant new cases) (*see* section III.E.2.h of this document),
- Summary tabulations for spontaneous reports of SADR submitted to the applicant by an individual other than a health care professional (*see* section III.E.2.k.iii of this document),
- Summary tabulations for spontaneous reports of SADR with unknown outcome submitted to the applicant by health care professionals and other individuals (*see* section III.E.2.k.iv of this document),
- Summary tabulations for reports of SADR from class action lawsuits (*see* section III.E.2.k.v of this document),
- Summary tabulations of domestic reports of medication errors (*see* section III.E.2.k.viii of this document).

The IPSR would provide the agency with an overview of the safety profile of a drug product containing a drug substance or biological product without requiring summary information on individual case safety reports.

III.E.4. Semiannual Submission of Individual Case Safety Reports

Currently, postmarketing periodic safety reporting regulations (§§ 314.80(c)(2)(ii)(b) and 600.80(c)(2)(ii)(B)) require applicants to submit to FDA in periodic adverse drug experience reports an FDA Form 3500A (VAERS form for vaccines) for each spontaneously reported adverse drug experience occurring in the United States that has not been submitted to the agency as an expedited report (*i.e.*, serious, expected adverse drug experiences and all nonserious adverse drug experiences, whether unexpected or expected). FDA is proposing to remove this requirement (*see* section III.E.1.b of this document). Instead, under proposed §§ 314.80(c)(3)(v) and 600.80(c)(3)(v), the agency would require applicants to submit semiannually a separate report to FDA consisting of a compilation of FDA Form 3500As (VAERS forms for vaccines, CIOMS I forms, if desired, for foreign SADR) for certain spontaneously reported individual case safety reports as described in the following explanation. This report would be identified as "Individual Case Safety Reports—Semiannual Submission."

The semiannual submission from applicants that submit TPSRs for a drug or licensed biological product would include an individual case safety report for each serious, expected SADR, whether domestic or foreign, and each nonserious, unexpected SADR occurring in the United States that is submitted to the applicant during the reporting period from all spontaneous sources (*i.e.*, health care professionals and other individuals). The semiannual submission for vaccines would also include an individual case safety report for each nonserious, expected SADR and each expected SADR with unknown outcome occurring in the United States that is submitted to the applicant during the reporting period from all spontaneous sources. For drugs and licensed biological products that are not vaccines, nonserious, expected SADR and expected SADR with an unknown outcome would not be submitted as individual case safety reports in a semiannual submission. Instead, they would be reported as part of a summary tabulation in a TPSR (*see* section III.E.1.e of this document).

The semiannual submission from applicants that submit PSURs for a drug product containing a drug substance or licensed biological product would include an individual case safety report for each serious, listed SADR, whether

domestic or foreign, and each nonserious, unlisted SADR occurring in the United States that is submitted to the applicant during the reporting period from all spontaneous sources. The semiannual submission for vaccines would also include an individual case safety report for each nonserious, listed SADR and each listed SADR with unknown outcome occurring in the United States that is submitted to the applicant during the reporting period from all spontaneous sources. For drugs and licensed biological products that are not vaccines, nonserious, listed SADR and listed SADR with an unknown outcome would not be submitted as individual case safety reports in a semiannual submission. Instead, they would be reported as part of a summary tabulation in a PSUR (*see* sections III.E.2.f.ii and III.E.2.k.iii of this document). The semiannual submission should not include individual case safety reports for serious, listed SADR that were previously submitted to FDA as a serious, unexpected SADR in an expedited report (*i.e.*, the agency does not want to receive duplicative reports for the same SADR).

FDA needs to continue to receive information on serious, expected/listed SADR and nonserious SADR, whether unexpected/unlisted or expected/listed, to monitor the safety profile of marketed products to determine if studies need to be undertaken to evaluate a particular issue and/or to take appropriate regulatory action (*e.g.*, labeling change, distribution of Dear Healthcare Professional letter, restriction on distribution of product, withdrawal of product from the market). Reports of serious, expected/listed SADR are used to monitor changes in the frequency of occurrence or severity of a serious, expected/listed SADR (*e.g.*, frequency of serious, expected/listed SADR increases because product interacts with a new approved product that is frequently used concomitantly with the product). The agency's proposal to require submission of spontaneously reported serious, expected/listed SADR from foreign sources would provide FDA with important information that the agency currently does not receive (*e.g.*, reports from foreign countries in which the product is approved for more indications than in the United States or the product results in exposure to certain populations that are limited in the United States).

Reports of nonserious, unexpected/unlisted SADR are used to identify new nonserious SADR that are associated with the use of a product (*e.g.*, sedation, sexual dysfunction, gastrointestinal distress). This information is valuable