

SADRs occurring in the United States, obtained or otherwise received during the reporting period by the applicant from an individual other than a health care professional (e.g., reports from consumers). These summary tabulations must consist of lists by body system or by standard organ system classification scheme of all SADR terms and counts of occurrences. For those SADRs that are determined to be both serious and unlisted, include cumulative data (i.e., all cases reported to date by individuals other than a health care professional). Include a brief discussion of the impact of the spontaneous reports described in this appendix on the overall safety evaluation.

(4) *SADRs with unknown outcome.* Provide summary tabulations for unlisted and listed SADRs with unknown outcome from all spontaneous sources (i.e., health care professionals and other individuals), obtained or otherwise received by the applicant during the reporting period. These summary tabulations must consist of lists by body system or by standard organ system classification scheme of all SADR terms and counts of occurrences. Include a brief discussion of the impact of the spontaneous reports described in this appendix on the overall safety evaluation.

(5) *Class action lawsuits.* Provide summary tabulations (e.g., serious unlisted SADRs, serious listed SADRs, nonserious unlisted SADRs, nonserious listed SADRs) for all SADRs obtained or otherwise received during the reporting period by the applicant from class action lawsuits. These summary tabulations must consist of lists by body system or by standard organ system classification scheme of all SADR terms and counts of occurrences. For those SADRs that are determined to be both serious and unlisted, include cumulative data. Include a brief discussion of the impact of the reports described in this appendix on the overall safety evaluation.

(6) *Lack of efficacy reports.* Provide 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 product.

(7) *Information on resistance to antimicrobial drug products.* Provide information, received or otherwise obtained by the applicant, on resistance to antimicrobial drug products intended to treat infectious diseases. Include information on changes in U.S. microbial in vitro susceptibility, the relationship of changes in U.S. microbial in vitro susceptibility and

clinical outcomes, therapeutic failure that may possibly be due to resistance to the antimicrobial drug product, and whether the U.S. labeling should be revised because of the information on antimicrobial resistance learned during the period covered by this PSUR.

(8) *Medication errors.* Provide summary tabulations of all domestic reports of medication errors submitted during the reporting period under paragraph (c)(2)(v) of this section. For actual medication errors, provide summary tabulations for serious SADRs, nonserious SADRs, and no SADRs (for serious SADRs include cumulative data, i.e., all cases reported to date). For potential medication errors, provide the number of reports for specific errors. If an SADR occurs, the summary tabulations must consist of lists by body system or by standard organ system classification scheme of all SADR terms and counts of occurrences. Include a brief discussion of the impact on the overall safety evaluation of these reports.

(9) *U.S. patient exposure.* Provide, for the reporting period, an estimate of the U.S. patient exposure to the drug product(s) covered by the PSUR (i.e., number of patients, average or median dose received, and average or median length of treatment). The method used to estimate patient exposure must always be described. If the patient exposure is impossible to estimate or is meaningless, an explanation of and justification for such conclusions must be provided. If patient exposure is impossible to estimate, other measures of exposure, such as patient-days, number of prescriptions, or number of dosage units, may be used. If these or other more precise measures are not available and an adequate explanation for the lack of such information is provided, bulk sales may be used.

(10) *Location of safety records.* Provide a list of the current address(es) where all safety reports and other safety-related records for the drug product(s) are maintained.

(11) *Contact person.* Provide the name and telephone number of the licensed physician(s) responsible for the content and medical interpretation of the data and information contained within the PSUR. Include, if available, the fax number and e-mail address of the licensed physician(s).

(iii) *Interim periodic safety report (IPSR).* An applicant holding an application for a human drug product approved under section 505(c) of the act on or after January 1, 1998, must submit an IPSR to FDA 7.5 years and 12.5 years after U.S. approval of the application. The data lock point for the IPSR is the

month and day of the international birth date of the drug substance or any other month and day agreed on by the applicant and FDA. The reporting period for the IPSR covers the period between the last PSUR or TPSR and the data lock point for the IPSR (e.g., between years 5 and 7.5 for an IPSR with a data lock point 7.5 years after U.S. approval of the application). Each IPSR must contain:

(A) *Title page, table of contents, and introduction.* (1) The title page includes, at a minimum, the following information:

(i) Name and international birth date of the drug substance that is the subject of the IPSR,

(ii) Various dosage forms and formulations of the drug substance covered by the IPSR,

(iii) Name and address of the applicant,

(iv) Reporting period covered by the IPSR, and

(v) Date of the IPSR.

(2) The introduction:

(i) Provides a brief description of how the IPSR relates to previous reports and circumstances,

(ii) References relevant drug products or substances reported in other periodic safety reports (e.g., a combination product reported in a separate IPSR), and

(iii) Indicates any data duplication with other IPSRs.

(B) *Worldwide marketing status.* This section of the IPSR contains a table of the chronological history of the worldwide marketing status of the drug product(s) covered by the IPSR from the date the product(s) was first approved (i.e., the international birth date) through its current status (i.e., cumulative information). The table consists of:

(1) Dates of drug approval and renewal;

(2) Safety-related restrictions on product use;

(3) Indications for use and special populations covered by the drug approval;

(4) Lack of approval of the drug substance in any dosage form or for any indication for use by any regulatory authority(ies);

(5) Withdrawal of a pending marketing application for a drug product by the applicant for safety or efficacy related reasons;

(6) Dates of market launches; and

(7) Trade name(s).

(C) *Actions taken for safety reasons.*

(1) This section of the IPSR includes details on the following types of regulatory authority-initiated (e.g., by FDA) and/or applicant-initiated actions