

discrepancy. Describe any safety-related changes or proposed changes to the U.S. labeling made during the reporting period (include the supplement number(s) and date(s) of submission for the supplement(s)) and any suggested change(s) that should be considered based on the safety analysis in this PSUR.

(3) *Spontaneous reports submitted to the applicant by an individual other than a health care professional.* Provide summary tabulations (e.g., serious unlisted SARs, serious listed SARs, nonserious unlisted SARs, nonserious listed SARs) for all spontaneously reported serious SARs, whether domestic or foreign, and all spontaneously reported nonserious SARs 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 SAR terms and counts of occurrences. For those SARs 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) *SARs with unknown outcome.* Provide summary tabulations for unlisted and listed SARs 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 SAR 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 SARs, serious listed SARs, nonserious unlisted SARs, nonserious listed SARs) for all SARs 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 SAR terms and counts of occurrences. For those SARs 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 biological product.

(7) *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 of serious SARs, nonserious SARs, and no SARs (for serious SARs, include cumulative data, i.e., all cases reported to date). For potential medication errors, provide the number of reports for specific errors. If an SAR occurs, the summary tabulations must consist of lists by body system or by standard organ system classification scheme of all SAR terms and counts of occurrences. Include a brief discussion of the impact on the overall safety evaluation of these reports.

(8) *U.S. patient exposure.* Provide, for the reporting period, an estimate of the U.S. patient exposure to the biological 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.

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

(10) *Contact person.* Provide the name and telephone number for 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 for the licensed physician(s).

(iii) *Interim periodic safety report (IPSR).* An applicant holding a biologics license under § 601.20 of this chapter for a human biological product approved 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 licensed biological product 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 licensed biological product(s) that is the subject of the IPSR,

(ii) Various dosage forms and formulations of the biological product(s) 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 biological products 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 biological 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). This table consists of:

(1) Dates of biological product approval and renewal;

(2) Safety-related restrictions on product use;

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

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

(5) Withdrawal of a pending marketing application for the biological 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