

III.E.2.k.i. *Company core data sheet.* A copy of the company core data sheet covered by the PSUR (*i.e.*, in effect at the beginning of the period covered by the PSUR) would be provided. The company core data sheet would be numbered and dated and include the date of last revision. In addition, a copy of the company core data sheet for the next reporting period would be provided.

III.E.2.k.ii. *U.S. labeling.* A copy of the current approved U.S. labeling would be provided. Any safety information that is included in the CCSI but not in the U.S. labeling would be identified and an explanation for the discrepancy provided. Any safety-related changes or proposed changes to the U.S. labeling made during the reporting period would be described, including the supplement numbers and dates of submission for the supplements. Any suggested change or changes in the U.S. labeling that should be considered based on the safety analysis in the PSUR would also be described. (If appropriate, a supplemental application would be filed with FDA concerning those changes as prescribed under §§ 314.70 or 601.12.)

III.E.2.k.iii. *Spontaneous reports submitted to the applicant by an individual other than a health care professional.* This appendix would contain summary tabulations (*e.g.*, serious unlisted SADR, serious listed SADR, nonserious unlisted SADR, nonserious listed SADR) for all spontaneously reported serious SADRs, whether domestic or foreign, and all spontaneously reported nonserious 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.*, SADR reports from consumers). These summary tabulations would consist of lists by body system or by standard organ system classification scheme (*e.g.*, cardiovascular, central nervous system, endocrine, renal) of all SADR terms and counts of occurrences. For those SADRs that are determined to be both serious and unlisted, cumulative data (*i.e.*, all cases reported to date by individuals other than a health care professional) would also be provided. The impact of these spontaneous reports on the overall safety evaluation would be discussed briefly. FDA may require applicants to submit to the agency, when appropriate, SADR reports (*e.g.*, FDA Form 3500As), within 5 calendar days after receipt of the request, for any or all of the SADRs contained within this appendix (*see* section III.H of this document).

III.E.2.k.iv. *SADRs with unknown outcome.* This appendix would contain 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 would consist of lists by body system or by standard organ system classification scheme of all SADR terms and counts of occurrences. The impact of these spontaneous reports on the overall safety evaluation would be discussed briefly. FDA may require applicants to submit to the agency, when appropriate, individual case safety reports (*e.g.*, FDA Form 3500As), within 5 calendar days after receipt of the request, for any or all of the listed SADRs with unknown outcome contained within this appendix (*see* section III.H of this document).

III.E.2.k.v. *Class action lawsuits.* This appendix would contain summary tabulations (*e.g.*, serious unlisted SADR, serious listed SADR, nonserious unlisted SADR, nonserious listed SADR) for all SADRs obtained or otherwise received during the reporting period by the applicant from class action lawsuits. These summary tabulations would consist of lists by body system or by standard organ system classification scheme of all SADR terms and counts of occurrences. For SADRs that are both serious and unlisted, cumulative data would also be provided. The impact of these reports on the overall safety evaluation would be discussed briefly. FDA may require applicants to submit to the agency, when appropriate, individual case safety reports (*e.g.*, FDA Form 3500As), within 5 calendar days after receipt of the request, for any or all of the SADRs contained within this appendix (*see* section III.H of this document).

III.E.2.k.vi. *Lack of efficacy reports.* This appendix would contain 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 results from a lack of efficacy of the product.

III.E.2.k.vii. *Information on resistance to antimicrobial drug products.* This appendix would contain information, received or otherwise obtained by the applicant, on resistance to antimicrobial drug products intended to treat infectious diseases. Information would include:

- 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 the report.

III.E.2.k.viii. *Medication errors.* This appendix would contain summary tabulations for all domestic reports of medication errors submitted during the reporting period as an expedited report. For actual medication errors, summary tabulations would be provided for serious SADRs, nonserious SADRs, and no SADRs. For serious SADRs, cumulative data (*i.e.*, all cases reported to date) would also be provided. For potential medication errors, the number of reports for specific errors would be provided. If an SADR occurs, the summary tabulations would consist of lists by body system or by standard organ system classification scheme of all SADR terms and counts of occurrences. The impact of these reports on the overall safety evaluation would be discussed briefly.

III.E.2.k.ix. *U.S. patient exposure.* This appendix would contain, for the reporting period, an estimate of the U.S. patient exposure to the drug product(s) or 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 would always be described. If the patient exposure is impossible to estimate or is meaningless, an explanation of and justification for such conclusions would 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.

III.E.2.k.x. *Location of safety records.* This appendix 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. The list of addresses would provide rapid access to safety-related records for FDA inspections and for requests by FDA for additional information concerning safety issues.

III.E.2.k.xi. *Contact person.* The name and telephone number of the licensed