

An “actual medication error” would be defined as:

A medication error that involves an identifiable patient whether the error was prevented prior to administration of the product or, if the product was administered, whether the error results in a serious SADR, nonserious SADR, or no SADR.

A “potential medication error” would be defined as:

An individual case safety report of information or complaint about product name, labeling, or packaging similarities that does not involve a patient.

The proposed rule would define these terms to clarify what would be considered a medication error. The proposed definition for “medication error” was developed by the National Coordinating Council for Medication Error Reporting and Prevention, of which FDA is a member. FDA would not consider a case in which a patient deliberately took an overdose of a drug to be a “medication error” because the agency does not believe that this type of situation is “preventable.” Instead, it would be considered a “non-accidental overdose.”

The proposed definitions for actual and potential medication errors were developed by FDA. Actual medication errors involve an identifiable patient whether or not the product is administered and, if the product is administered, whether or not an SADR occurs. Potential medication errors do not involve a patient, but rather describe information or complaint about product name, labeling, or packaging similarities that could result in a medication error in the future.

III.A.9. Company Core Data Sheet, Company Core Safety Information (CCSI), Listed SADR, Unlisted SADR, and Unexpected SADR

Proposed §§ 314.80(a) and 600.80(a) would amend FDA’s postmarketing safety reporting regulations to define the terms “company core data sheet,” “company core safety information (CCSI),” “listed SADR,” and “unlisted SADR.” The “company core data sheet” would be defined as:

A document prepared by the applicant containing, in addition to safety information, material relating to indications, dosing, pharmacology, and other information concerning the drug substance (biological product for proposed § 600.80(a)). The only purpose of this document is to provide the company core safety information (CCSI) for periodic safety update reports (PSURs), interim periodic safety reports (IPSRs), and certain individual case safety reports—semiannual submissions (*i.e.*, if PSURs are submitted for the product).

The “CCSI” would be defined as:

All relevant safety information contained in the company core data sheet that the applicant proposes to include in the approved product labeling in all countries where the applicant markets the drug substance (biological product for proposed § 600.80(a)). It is the reference information by which an SADR is determined to be “listed” or “unlisted” for PSURs, IPSRs, and certain individual case safety reports—semiannual submissions (*i.e.*, if PSURs are submitted for the product).

A “listed SADR” would be defined as: “an SADR whose nature, specificity, severity, and outcome are consistent with the information in the CCSI.”

An “unlisted SADR” would be defined as: “an SADR whose nature, specificity, severity, or outcome is not consistent with the information included in the CCSI.”

The proposed rule would define these terms to help applicants determine which SADRs must be reported in PSURs, IPSRs, and certain individual case safety reports—semiannual submissions (*i.e.*, if PSURs are submitted for the product) (see sections III.E.2, III.E.3, and III.E.4 of this document). For this purpose, the CCSI would be used as the reference document by which an SADR would be judged as “listed” or “unlisted.”

Company core data sheets would usually be prepared by applicants for a drug substance rather than a drug product because postmarketing PSURs and IPSRs would be based on a drug substance. Under the existing regulations at § 314.3(b) (21 CFR 314.3(b)), a drug substance is defined as:

An active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body, but does not include intermediates use[d] in the synthesis of such ingredient.

Under these same regulations, a drug product is defined as:

a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.

Thus, drug substances refer to active moieties of drug products.

In the United States, the company core data sheet would be used only to provide the CCSI for a drug or biological product to determine whether an SADR is listed or unlisted. Company core data sheets would not require approval from FDA, unlike the U.S. labeling for a marketed drug or licensed biological product which does require approval from FDA. Company core data sheets would not be used in the United States

as the labeling for an approved drug or licensed biological product. FDA believes that preparation of a company core data sheet would not impose a new burden on most applicants because it codifies a common practice in the pharmaceutical industry (see the ICH E2C guidance, 62 FR 27470 at 27472).

Postmarketing PSURs may be submitted by applicants to multiple countries, and the drug or licensed biological product may have different approved labeling in the different countries. The CCSI for the product should not be a compilation of all the safety information contained in the various approved labelings for the product. Instead, the CCSI should contain the critical safety information for the product that would be relevant in all countries where the product is approved for marketing. In some cases, the CCSI and an approved labeling for the product would contain the same safety information (*i.e.*, all the safety information in an approved labeling for the product is relevant in all countries where the product is approved for marketing or the product is only approved for marketing in one country). In other cases, an approved labeling for a product may contain more safety information than the CCSI for the product because the labeling may contain safety information specific to the country in which the product is approved for marketing (*e.g.*, safety information regarding a specific indication for which the product is approved for marketing in one country but not other countries). In these cases, the use of the CCSI as the reference document for determining whether an SADR is listed or unlisted for the postmarketing PSURs may result in overreporting of some SADRs to FDA as “unlisted” when they actually are “expected” by the approved U.S. labeling.

This proposal would not affect the reference document used to determine expectedness (*i.e.*, unexpected or expected SADR) for SADRs reported in premarketing IND safety reports, postmarketing expedited reports, postmarketing TPSRs, and certain postmarketing individual case safety reports—semiannual submissions (*i.e.*, if TPSRs are submitted for the product) (see table 5 and sections III.B, III.D, III.E.1, and III.E.4 of this document). Under the existing regulations at §§ 310.305(b), 314.80(a), and 600.80(a), the definition of “unexpected adverse drug experience” designates the current approved labeling for the drug or licensed biological product as the reference document to be used to determine what would be considered