

conclusion by the applicant or FDA that the report or information constitutes an admission that the drug caused or contributed to an adverse effect. An applicant need not admit, and may deny, that the report or information submitted under this section constitutes an admission that the drug caused or contributed to an adverse effect.

Additionally, a “disclaimer” is included on the first page of the voluntary reporting form used by health care professionals and consumers, FDA Form 3500, stating “Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.” A similar disclaimer is included on the mandatory reporting form used by manufacturers and applicants, FDA Form 3500A. In its notice of availability announcing FDA Form 3500 and 3500A, the agency reiterated that “Although the underlying information may be relevant to product liability issues, submitting the form itself, as is clearly stated on the form, does not constitute an admission that the product caused the adverse event” (58 FR 31596 at 31600, June 3, 1993).

FDA seeks comment as to whether these “disclaimers” are sufficient to protect manufacturers, applicants, and sponsors, from the use of SADR reports in product liability actions. For instance, perhaps the agency should consider also prohibiting use of SADR reports the agency receives in product liability actions. Accordingly, FDA seeks comment on the need for any further action to promote submission of SADR reports to the agency and guard against their misuse, as well as FDA’s legal authority to take any such action.

FDA is proposing to remove the current provisions in §§ 310.305(c)(1)(ii), 314.80(e)(1), and 600.80(e)(1). The agency is proposing this amendment because the information contained in these paragraphs is included in the proposed definition of SADR.

III.A.2. A Life-Threatening SADR

FDA’s existing premarketing safety reporting regulations at § 312.32(a) define a life-threatening adverse drug experience as:

Any adverse drug experience that places the patient or subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, *i.e.*, it does not include a reaction that, had it occurred in a more severe form, might have caused death.

FDA is proposing to amend this definition by adding the phrase “or sponsor” after the word “investigator.” Thus, reports of life-threatening SADRs would be based on the opinion of either

the investigator or sponsor. In some cases, the opinions of the investigator and sponsor may be discordant. In these situations, the sponsor would submit an IND safety report to FDA for the life-threatening SADR and include in the report the reason(s) for any differences in opinions. This proposed revision is consistent with the ICH E2A guidance (60 FR 11286): “Causality assessment is required for clinical investigation cases. All cases judged by either the reporting health care professional or the sponsor as having a reasonable suspected causal relationship to the medicinal product qualify as ADR’s [adverse drug reactions].”

FDA’s existing postmarketing safety reporting regulations at §§ 310.305(b), 314.80(a), and 600.80(a) define a “life-threatening adverse drug experience” as:

Any adverse [drug] experience that places the patient, in the view of the initial reporter, at immediate risk of death from the adverse [drug] experience as it occurred, *i.e.*, it does not include an adverse [drug] experience that, had it occurred in a more severe form, might have caused death.

Proposed §§ 310.305(a), 312.32(a), 314.80(a), and 600.80(a) would amend the premarketing and postmarketing definition of life-threatening adverse drug experience by making minor revisions. FDA is proposing to move the phrase “places the patient” (“patient or subject” for proposed § 312.32(a)) before the phrase “at immediate risk of death” and also to replace the phrase “adverse drug experience” with the abbreviation “SADR.”

III.A.3. Serious SADR, Nonserious SADR, and SADR With Unknown Outcome

FDA’s existing premarketing and postmarketing safety reporting regulations at §§ 310.305(b), 312.32(a), 314.80(a), and 600.80(a) define a serious adverse drug experience as:

Any adverse [drug] experience occurring at any dose that results in any of the following outcomes: Death, a life-threatening adverse [drug] experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. * * *

Proposed §§ 310.305(a), 312.32(a), 314.80(a), and 600.80(a) would amend this definition by removing the phrase “occurring at any dose,” because the proposed definition of SADR includes the phrase “response to any dose of a drug (“biological” for proposed § 600.80(a)) product” and it is unnecessary to refer to “any dose” in both definitions. FDA is also proposing

to amend this definition by replacing the phrase “adverse drug experience” with the abbreviation “SADR” for consistency as proposed previously.

Under proposed §§ 310.305(a), 314.80(a), and 600.80(a), FDA would amend its postmarketing safety reporting regulations to define the term “nonserious SADR” to mean: “Any SADR that is determined not to be a serious SADR.” FDA is proposing to add this definition to clarify what constitutes a nonserious SADR. SADRs would only be classified as “nonserious” if manufacturers and applicants have determined that the reaction does not meet the definition of a serious SADR. If the outcome for an SADR is not known, a determination of seriousness cannot be made; the SADR would not default to a “nonserious” designation, but would rather be classified as an “SADR with unknown outcome” as described below.

Under proposed §§ 310.305(a), 314.80(a), and 600.80(a), FDA would amend its postmarketing safety reporting regulations to define the term “SADR with unknown outcome” to mean: “An SADR that cannot be classified, after active query, as either serious or nonserious.” FDA is proposing to define this term to describe those SADRs for which an outcome (*i.e.*, classification as either serious or nonserious) cannot be determined. FDA believes that, in most cases, manufacturers and applicants are usually able to determine the outcome of an SADR. However, in a few cases, this may not be possible, even after active query, and these SADRs would be designated as “SADR with unknown outcome” (see section III.A.6 of this document for proposed definition of active query).

III.A.4. Contractor

Under proposed § 310.305(a), FDA would amend its postmarketing safety reporting regulations to define the term “contractor” to mean:

Any person (*e.g.*, packer or distributor whether or not its name appears on the label of the product; licensee; contract research organization) that has entered into a contract with the manufacturer to manufacture, pack, sell, distribute, or develop the drug or to maintain, create, or submit records regarding SADRs or medication errors.

Under proposed § 314.80(a), the term “contractor” is defined as persons (*e.g.*, manufacturer, packer, or distributor whether or not its name appears on the label of the product; licensee; contract research organization) that have entered into a contract with the applicant. Under proposed § 600.80(a), the term “contractor” is defined as persons (*e.g.*,