

manufacturers and applicants with adequate safety information and could eliminate or decrease followup time expended by manufacturers, applicants, and the agency. The agency does not believe that it is sufficient for manufacturers and applicants just to send a letter to reporters of SADRs and medication errors requesting further information. These reporters could, however, submit written materials to manufacturers and applicants to clarify or provide support for verbal discussions.

Even though the agency is not proposing that manufacturers and applicants request followup information for SADR and medication error reports in writing, the CIOMS V report describes instances when it might be appropriate to do so. FDA seeks comment as to whether the agency should permit written requests for followup information and, if so, in which situations should these requests be permitted.

Active query would be conducted by a health care professional, such as a physician, physician's assistant, pharmacist, dentist, nurse, or any individual with some form of health care training. The agency believes that a health care professional would be able to understand better the medical consequences of a case and ask reporters of SADRs and medication errors appropriate questions to acquire more complete safety information effectively and rapidly.

The proposed definition of active query would provide that, at a minimum, a focused line of questioning be used to acquire further information on SADRs. For this purpose, questions would be designed to capture clinically relevant information associated with the drug or licensed biological product and the SADR. This information would include, but would not be limited to, baseline data, patient history, physical exam, diagnostic results, and supportive lab results.

### III.A.7. Spontaneous Report

Under proposed §§ 310.305(a), 314.80(a), and 600.80(a), FDA would amend its postmarketing safety reporting regulations to define the term "spontaneous report" to mean:

A communication from an individual (*e.g.*, health care professional, consumer) to a company or regulatory authority that describes an SADR or medication error. It does not include cases identified from information solicited by the manufacturer or contractor (applicant or contractor for proposed § 314.80(a); applicant, shared manufacturer, or contractor for proposed § 600.80(a)), such as individual case safety

reports or findings derived from a study, company-sponsored patient support program, disease management program, patient registry, including pregnancy registries, or any organized data collection scheme. It also does not include information compiled in support of class action lawsuits.

The agency would define this term to clarify which reports would be considered "spontaneous." Over the years, changes in marketing practices in the United States have led to expanded contacts between consumers and manufacturers, applicants, contractors, and shared manufacturers. This has resulted in the acquisition of new types of solicited safety information. Under the proposed rule, only unsolicited safety information from an individual, such as a health care professional or consumer, to a company or regulatory authority would be considered a "spontaneous report."

Cases identified from information solicited by companies, such as individual case safety reports or findings obtained from a study, company-sponsored patient support program, disease management program, patient registry, including pregnancy registries, or any organized data collection scheme would not be considered spontaneous. Instead, safety information from these sources would be considered "study" information and would be handled according to the postmarketing safety reporting requirements for a "study." As proposed, study information would be subject to reporting as discussed below:

- Expedited reports for serious and unexpected SADRs from a study (see section III.D.1 of this document),
- Expedited reports for information from a study that would be sufficient to consider product administration changes (see section III.D.2 of this document),
- Expedited reports for an unexpected SADR with unknown outcome from a study (see section III.D.3 of this document),
- Always expedited reports from a study (see section III.D.4 of this document),
- Medication error reports from a study (see section III.D.5 of this document),
- Summary tabulations of all serious SADRs from studies or individual patient INDs in PSURs (see section III.E.2.f.ii of this document), and
- Discussion of important safety information from studies in PSURs and IPSRs (see sections III.E.2.g and III.E.3 of this document).

The proposed rule would consider SADR information compiled in support of class action lawsuits to be neither

spontaneous nor "study" information. FDA believes that the vast majority of SADR information from class action lawsuits is duplicative (*i.e.*, the same SADR information is reported by multiple individuals). In many cases, information in addition to the minimum data set is not available for these SADR reports and followup is unlikely to result in acquisition of new information. For these reasons, the agency is proposing to require in TPSRs, PSURs and IPSRs summary information for SADRs from class action lawsuits (see sections III.E.1.e, III.E.2.k.v, and III.E.3 of this document).

Any safety information obtained from an individual (*e.g.*, health care professional, consumer) who has initiated contact with a company or regulatory authority would be considered spontaneous. For example, if an individual calls a company and asks if a particular SADR has been observed with one of the company's drug or licensed biological products because the individual or someone the individual knows has experienced such an SADR, the call would be considered spontaneous. The agency would consider these calls spontaneous because the individual making the call has a belief or suspicion that the drug or licensed biological product may have caused the SADR.

The proposed definition for spontaneous report is consistent with the definition of "spontaneous report or spontaneous notification" in the ICH E2C guidance (62 FR 27475):

An unsolicited communication to a company, regulatory authority, or other organization that describes an adverse reaction in a patient given one or more medicinal products and which does not derive from a study or any organized data collection scheme.

### III.A.8. Medication Error

Proposed §§ 310.305(a), 314.80(a), and 600.80(a) would amend FDA's postmarketing safety reporting regulations to define the terms "medication error," "actual medication error," and "potential medication error." A "medication error" would be defined as:

Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems including: Prescribing; order communication; product labeling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use.