

11. Section 320.31 is amended by revising paragraph (d) to read as follows:

**§ 320.31 Applicability of requirements regarding an "Investigational New Drug Application."**

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(d) A bioavailability or bioequivalence study in humans other than one described in paragraphs (a) through (c) of this section is exempt from the requirements of part 312 of this chapter, except for the safety reporting requirements under § 312.32 of this chapter, if the following conditions are satisfied:

(1) If the study is one described under § 320.38(b) or § 320.63, the person conducting the study, including any contract research organization, must retain reserve samples of any test article and reference standard used in the study and release the reserve samples to FDA upon request in accordance with and for the period specified in § 320.38;

(2) An in vivo bioavailability or bioequivalence study in humans must be conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter and informed consent set forth in part 50 of this chapter; and

(3) Safety reports as prescribed under § 312.32 of this chapter must be transmitted to all participating investigators and the appropriate FDA division in the Center for Drug Evaluation and Research (*i.e.*, safety reports for the reference listed drug must be sent to the new drug review division that has responsibility for that drug, safety reports for the investigational drug product must be sent to the Director, Division of Bioequivalence, Office of Generic Drugs). Each written notification under this paragraph must bear prominent identification of its contents, *i.e.*, "bioavailability/bioequivalence safety report." For reporting purposes under this paragraph, an unexpected suspected adverse drug reaction (SADR) is any SADR, the specificity or severity of which is not consistent with the U.S. labeling for the reference listed drug.

**PART 600—BIOLOGICAL PRODUCTS: GENERAL**

12. The authority citation for 21 CFR part 600 continues to read as follows:

**Authority:** 21 U.S.C. 321, 351, 352, 353, 355, 360, 360i, 371, 374; 42 U.S.C. 216, 262, 263, 263a, 264, 300aa–25.

13. Section 600.80 is revised to read as follows:

**§ 600.80 Postmarketing reporting of suspected adverse reactions.**

(a) *Definitions.* The following definitions of terms apply to this section:

*Active query* means direct verbal contact (*i.e.*, in person or by telephone or other interactive means such as a video conference) with the initial reporter of a suspected adverse reaction (SAR) or medication error by a health care professional (*e.g.*, physician, physician assistant, pharmacist, dentist, nurse, any individual with some form of health care training) representing the applicant. For SARs, active query entails, at a minimum, a focused line of questioning designed to capture clinically relevant information associated with the licensed biological product and the SAR, including, but not limited to, information such as baseline data, patient history, physical exam, diagnostic results, and supportive lab results.

*Actual medication error* means 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 SAR, nonserious SAR, or no SAR.

*Blood component* means as defined in § 606.3(c) of this chapter.

*Company core data sheet* means a document prepared by the applicant containing, in addition to safety information, material relating to indications, dosing, pharmacology, and other information concerning the biological product. 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).

*Company core safety information (CCSI)* means 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 biological product. It is the reference information by which an SAR 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).

*Contractor* means any person (*e.g.*, manufacturer, joint manufacturer, 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 applicant (includes participants involved in divided manufacturing) to manufacture, pack, sell, distribute, or develop the licensed biological product or to maintain, create, or submit records regarding SARs or medication errors.

*Data lock point* means the date designated as the cut-off date for data to be included in a postmarketing periodic safety report.

*Disability* means a substantial disruption of a person's ability to conduct normal life functions.

*Full data set* means completion of all the applicable elements on FDA Form 3500A or the vaccine adverse event reporting system (VAERS) form (or on a Council for International Organizations of Medical Sciences (CIOMS) I form for reports of foreign SARs), including a concise medical narrative of the case (*i.e.*, an accurate summary of the relevant data and information pertaining to an SAR or medication error).

*International birth date* means the date the first regulatory authority in the world approved the first marketing application for a human biological product.

*Life-threatening SAR* means any SAR that, in the view of the initial reporter, places the patient at *immediate* risk of death from the SAR as it occurred. It does not include an SAR that, had it occurred in a more severe form, might have caused death.

*Listed SAR* means an SAR whose nature, specificity, severity, and outcome are consistent with the information in the CCSI.

*Medication error* means 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.

*Minimum data set* means the report includes an identifiable patient, an identifiable reporter, a suspect biological product, and an SAR.

*Nonserious SAR* means any SAR that is determined not to be a serious SAR.

*Potential medication error* means an individual case safety report of information or complaint about product name, labeling, or packaging similarities that does not involve a patient.

*SAR with unknown outcome* means an SAR that cannot be classified, after