

determined that the center had failed to establish a lower limit for blood pressure measurements for donors as required by 21 CFR 640.3. Had these serious adverse events been required to be reported to FDA, immediate analysis of them is likely to have identified the problem sooner.

Thus, required reporting of all serious SADRs related to blood collection and transfusion would enhance FDA's ability to take appropriate action to protect the blood supply more consistently. Currently, there is no assurance that FDA will receive reports of serious SADRs that have the potential to adversely affect both the donors and recipients of the nation's blood supply. Such information is essential for evaluating the agency's scientific and regulatory policies and for monitoring industry practices and their implications on blood safety.

#### II.B.4. Bioavailability and Bioequivalence Studies Not Subject to an Investigational New Drug Application (IND).

FDA is also proposing to amend its bioavailability and bioequivalence regulations under part 320 (21 CFR part 320) (see section III.K of this document). Under the existing regulations at § 320.31, persons conducting a bioavailability or bioequivalence study in humans are only required to comply with the IND requirements of part 312 (21 CFR part 312) for certain products or for certain types of studies. This proposed rule would require submission of expedited safety reports for serious, unexpected adverse experiences (adverse experiences proposed to be called SADRs in this proposed rule; see section III.A.1 of this document) as prescribed under § 312.32 for human bioavailability and bioequivalence studies that are not being conducted

under an IND. FDA believes that bioavailability and bioequivalence studies that are not being conducted under an IND are, in general, safe. However, the agency is occasionally made aware of safety-related information associated with these types of studies. This information could either reflect a problem with the drug product being evaluated or with the study design being used. Timely review of serious, unexpected SADRs from these studies is critical to ensure the safety of study subjects. FDA would use this information to determine if the study design needs to be altered or if the study needs to be stopped.

#### II.C. New Safety Reporting Abbreviations

Table 3 provides a list of new safety reporting abbreviations that are used in this document.

TABLE 3.—NEW SAFETY REPORTING ABBREVIATIONS

Phrase	Abbreviation	Reference in section III of this document
Company core safety information .....	CCSI .....	A.9
Interim periodic safety report .....	IPSR .....	E.3
Medical dictionary for regulatory activities .....	MedDRA .....	F.2
Periodic safety update report .....	PSUR .....	E.2
Suspected adverse drug reaction .....	SADR .....	A.1
Traditional periodic safety report .....	TPSR .....	E.1

#### II.D. Highlights of Proposed Changes to FDA's Safety Reporting Regulations

this proposed rule, are identified in table 4.

Specific changes to FDA's safety reporting requirements, as described in

TABLE 4.—HIGHLIGHTS OF PROPOSED CHANGES TO FDA'S SAFETY REPORTING REQUIREMENTS

21 CFR Section	Proposed Change (reference in section III of this document)	Is the change based on ICH (ICH guidance)?
Changes apply to: 310.305, 312.32, 314.80, 314.98, and 600.80. <sup>1</sup>	<ul style="list-style-type: none"> <li>• "Associated with the use of the drug" and "adverse drug experience" changed to "suspected adverse drug reaction (SADR)" and "adverse experience" changed to "suspected adverse reaction (SAR)" (A.1).</li> <li>• Minimum data set required for all individual case safety reports of SADRs (A.5, B.2.a, C.5, E.4).</li> <li>• Reporting requirements for lack of efficacy reports revised (B.2.c, C.7, D.2, E.1.c, E.2.h, E.2.k.vi).</li> <li>• Sources of safety information revised (B.1, C.2, D.8) .....</li> <li>• Individual case safety reports from clinical trials based on opinion of either the sponsor/applicant or investigator (B.2.b, B.3, C.6).</li> <li>• Narrative format required for safety reports of overall findings or data in the aggregate (B.2.d, F.1).</li> </ul>	<p>Yes (E2A)</p> <p>Yes (E2A)</p> <p>Yes (E2A and E2C)</p> <p>No</p> <p>Yes (E2A)</p> <p>No</p>
Changes only apply to 312.32 .....	<ul style="list-style-type: none"> <li>• Determination of a life-threatening SADR based on opinion of either sponsor or investigator (A.2).</li> <li>• Expedited reports of findings from tests in laboratory animals revised to include other information sufficient to consider product administration changes (B.2.c).</li> </ul>	<p>Yes (E2A)</p> <p>Yes (E2A)</p>
Changes only apply to 310.305, 314.80, 314.98, 600.80.	<p><i>New Safety Reports</i> .....</p> <ul style="list-style-type: none"> <li>• Expedited report for information sufficient to consider product administration changes (D.2).</li> <li>• Expedited report for unexpected SADRs with unknown outcome (A.3, D.3).</li> </ul>	<p>Yes (E2A)</p> <p>No</p>