DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2021–D–0368]

Investigator Responsibilities—Safety Reporting for Investigational Drugs and Devices; Guidance for Investigators, Industry, and Institutional Review Boards; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the availability of a final guidance for investigators, industry, and institutional review boards (IRBs) entitled ''Investigator Responsibilities—Safety Reporting for Investigational Drugs and Devices.'' The guidance is intended to help clinical investigators comply with the safety reporting requirements for investigational new drug application (IND) studies and investigational device exemption (IDE) studies. As such, recommendations are provided in this guidance to help investigators identify safety information that needs to be reported to sponsors and IRBs. This guidance finalizes the draft guidance of the same title issued on September 30, 2021.

DATES: The announcement of the guidance is published in the **Federal Register** on December 16, 2025.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2021–D–0368 for ''Investigator Responsibilities—Safety Reporting for Investigational Drugs and Devices.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002; or to the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 800–835–4709 or 240–402–8010, *industry.biologics@fda.hhs.gov.* Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT: Juanita Marner, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993–0002, 301–796–2500, *cderomp@fda.hhs.gov*; Phillip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240–402–7911; or Soma Kalb, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. G318, Silver Spring, MD 20993–0002, 301–796–6359.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for investigators, industry, and IRBs entitled ''Investigator Responsibilities—Safety Reporting for Investigational Drugs and Devices.'' This guidance is intended to help clinical investigators comply with the safety reporting requirements for IND studies under 21 CFR 312.64(b) and 21 CFR 312.66 and for IDE studies under 21 CFR 812.150. This guidance also provides relevant information for persons reporting serious adverse events (SAEs) for bioavailability (BA) and

bioequivalence (BE) studies that meet conditions for IND-exemption under 21 CFR 320.31(d)(3) (IND-exempt BA/BE studies).

In January 2009, FDA issued the final guidance entitled ''Adverse Event Reporting to IRBs—Improving Human Subject Protection'' (the 2009 procedural final guidance). In the **Federal Register** of September 29, 2010 (75 FR 59935), FDA published a final rule amending the IND safety reporting requirements under 21 CFR 312.32 and adding safety reporting requirements for persons conducting BA and BE studies under § 320.31(d). Subsequently, in December 2012, FDA issued the final guidance entitled ''Safety Reporting Requirements for INDs and BA/BE Studies'' (the 2012 final guidance) to help sponsors and investigators comply with safety reporting requirements for INDs and for IND-exempt BA/BE studies.

To further improve the overall quality of safety reporting, this guidance builds upon the concepts in FDA's previously published guidance documents and provides additional recommendations. This guidance provides information on safety reporting requirements for investigators of investigational drugs and investigational devices.

Elsewhere in this issue of the **Federal Register**, FDA also is announcing the availability of a guidance entitled ''Sponsor Responsibilities—Safety Reporting Requirements and Safety Assessment for IND and Bioavailability/Bioequivalence Studies.'' These two guidances being announced replace the 2012 final guidance and the 2009 procedural final guidance. Accordingly, FDA is withdrawing the 2012 final guidance and the 2009 procedural final guidance at this time.

This guidance finalizes the draft guidance of the same title issued on September 30, 2021 (86 FR 54208). FDA considered comments received on the draft guidance as the guidance was finalized. Changes from the draft guidance to the final guidance include editorial changes for clarity, based on public comments.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on ''Investigator Responsibilities—Safety Reporting for Investigational Drugs and Devices.'' It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

FDA considered the applicability of Executive Order 14192, per Office of Management and Budget (OMB) guidance in M–25–20, and finds this action to be deregulatory in nature.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. The previously approved collections of information are subject to review by the OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521). The collections of information in 21 CFR part 50 and part 56 pertaining to the protection of human subjects and IRBs, respectively, have been approved under OMB control number 0910–0130. The collections of information in 21 CFR part 312 pertaining to the content and format of IND applications and the collections of information in § 320.31 pertaining to IND-exempt BA and BE studies have been approved under OMB control number 0910–0014. The collections of information in 21 CFR part 812 pertaining to IDEs have been approved under OMB control number 0910–0078.

III. Electronic Access

Persons with access to the internet may obtain the guidance at *https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs*, *https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances*, *https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products*, *https://www.fda.gov/regulatory-information/search-fda-guidance-documents*, or *https://www.regulations.gov*.

Lowell M. Zeta,

Acting Deputy Commissioner for Policy, Legislation, and International Affairs.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2020–D–2099]

Sponsor Responsibilities—Safety Reporting Requirements and Safety Assessment for Investigational New Drug Application and Bioavailability/Bioequivalence Studies; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the availability of a final guidance for industry entitled ''Sponsor Responsibilities—Safety Reporting Requirements and Safety Assessment for Investigational New Drug Application and Bioavailability/Bioequivalence Studies.'' The guidance provides recommendations for sponsors and sponsor-investigators to comply with the requirements of investigational new drug application (IND) safety reporting and safety reporting for bioavailability (BA) and bioequivalence (BE) studies. This guidance finalizes the draft guidance of the same title issued on June 28, 2021.

DATES: The announcement of the guidance is published in the **Federal Register** on December 16, 2025.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

Electronic Submissions

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- If you want to submit a comment with confidential information that you