



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Requirements and Safety Assessment for Investigational New Drug Application and Bioavailability/Bioequivalence Studies; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Sponsor Responsibilities--Safety Reporting Requirements and Safety Assessment for Investigational New Drug Application and Bioavailability/Bioequivalence Studies.” The draft guidance provides recommendations for sponsors and sponsor-investigators to comply with the requirements of investigational new drug application (IND) safety reporting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. In doing so, the guidance provides recommendations related to the two IND safety reporting provisions that require assessment of aggregate data to facilitate appropriate IND safety reporting practices. An earlier draft guidance for industry entitled “Safety Assessment for IND Safety Reporting” (December 2015) (the 2015 draft guidance) has been incorporated into this draft guidance. However, this content was revised to address feedback from stakeholders and comments received on the 2015 draft guidance. Concurrent with the publication of this draft guidance, we are withdrawing the 2015 draft guidance. Additionally, this draft guidance incorporates content from the final guidance for industry and investigators entitled “Safety Reporting Requirements for INDs and BA/BE Studies” (December 2012) (the 2012 final guidance). This incorporated content remains largely unchanged in this draft guidance.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance 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-2020-D-2099 for “Sponsor Responsibilities--Safety Reporting Requirements and Safety Assessment for Investigational New Drug Application and Bioavailability/Bioequivalence Studies.” 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 the draft 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. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Paul Gouge, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6328, Silver Spring, MD 20993-0002, CDEROMP@fda.hhs.gov; or Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Sponsor Responsibilities--Safety Reporting Requirements and Safety Assessment for Investigational New Drug Application and Bioavailability/Bioequivalence Studies.” The draft guidance provides recommendations for sponsors and sponsor-investigators to facilitate compliance with the requirements of IND safety reporting and safety reporting for BA and BE studies under §§ 312.32 and 320.31(d)(3) (21 CFR 312.32 and 320.31(d)(3)). In doing so, the draft guidance provides recommendations for sponsors related to the two IND safety reporting provisions

(§ 312.32(c)(1)(i)(C) and (iv)) that require assessment of aggregate data to facilitate appropriate IND safety reporting practices. More generally, it provides sponsors and sponsor-investigators recommendations regarding expedited safety reporting requirements for human drug and biological products that are being investigated under an IND and for drugs that are the subject of BA and BE studies that are exempt from the IND requirements.

In the *Federal Register* of December 17, 2015 (80 FR 78743), FDA announced the availability of the 2015 draft guidance entitled “Safety Assessment for IND Safety Reporting.” FDA received numerous comments on the 2015 draft guidance, and these comments were carefully considered and addressed by FDA in this draft guidance. Noteworthy changes include revised recommendations on the following: (1) planned unblinding of safety data and implications for trial integrity, (2) increased flexibility regarding the party reviewing safety information across a development program for IND safety reporting purposes, (3) clarification regarding the scope and methodology for aggregate analyses, and (4) clarification regarding the plan for safety surveillance, including what elements should be included in the plan. Accordingly, concurrent with the publication of this draft guidance, we are withdrawing the 2015 draft guidance.

Further, this draft guidance incorporates content from the 2012 final guidance entitled “Safety Reporting Requirements for INDs and BA/BE Studies”. The content from the 2012 final guidance remains largely unchanged in this draft guidance; however, this draft guidance does not incorporate the investigator provisions of the 2012 final guidance. FDA intends to publish a separate draft guidance on investigator’s responsibilities for safety reporting for human drug and biological products that are being investigated under an IND.

When this draft guidance and the draft guidance on investigator’s responsibilities for IND safety reporting are finalized, FDA plans to withdraw the 2012 final guidance. However, until FDA finalizes these two draft guidances, the 2012 final guidance remains in effect and represents FDA’s current thinking.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on “Sponsor Responsibilities--Safety Reporting Requirements and Safety Assessment for Investigational New Drug Application and Bioavailability/Bioequivalence Studies.” 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.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR parts 312 and 320 have been approved under OMB control number 0910-0014.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>, <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: June 22, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

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