



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2023-D-5470]

Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products.” FDA is issuing this draft guidance as part of a series of guidance documents under its Real-World Evidence (RWE) Program and to satisfy, in part, a mandate under the Federal Food, Drug, and Cosmetic Act (FD&C Act) to issue guidance about the use of RWE in regulatory decision-making. The draft guidance provides recommendations to sponsors who are considering submitting a non-interventional study, also referred to as an observational study, to FDA to contribute to a demonstration of substantial evidence of effectiveness and/or evidence of safety of a drug. This draft guidance was developed in response to stakeholders’ growing interest in the potential use of non-interventional studies to contribute to a demonstration of the effectiveness or safety of a drug.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 90 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2023-D-5470 for "Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products." 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; or to the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, 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: Dianne Paraoan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 3326, Silver Spring, MD 20993-0002, 301-796-3161, dianne.paraoan@fda.hhs.gov; or James Myers, 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 “Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products.” This draft guidance discusses attributes regarding the design and analysis of a non-interventional study that sponsors should consider when proposing such a study to contribute to a demonstration of substantial evidence of effectiveness and/or evidence of safety of a product. Examples of non-interventional study designs for evaluating the effectiveness and/or safety of a drug include, but are not limited to, cohort studies, case-control studies, and self-controlled studies.

Identifying and addressing the presence of confounding and other forms of bias is critical when planning and conducting non-interventional studies. Before choosing a non-interventional study design for a study intended to support regulatory decisions regarding the safety and effectiveness of a drug, sponsors should consider how likely it is that such a study design and its conduct will be able to distinguish a true treatment effect from other influences. The draft

guidance assists sponsors in identifying and addressing commonly encountered challenges when considering the use of a non-interventional study to contribute to a demonstration of substantial evidence of effectiveness and/or evidence of safety of a drug, including topics sponsors should consider before developing a prespecified protocol and statistical analysis plan. This draft guidance discusses the following major topics: (1) summary of the proposed approach, (2) study design, (3) data sources, and (4) analytical approach. The topics in this draft guidance should be considered in conjunction with the recommendations in other published guidances under the RWE Program.

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 "Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products." 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. The previously approved collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521). The collections of information in 21 CFR part 312 (investigational new drug applications) have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 314 (new drug marketing applications) have been approved under OMB control number 0910-0001; and the collections of information in 21 CFR part 601 (biologic license applications) have been approved under OMB control number 0910-0338. The collections of information in 21 CFR part 11 (electronic records and signatures) have been approved under OMB control number 0910-0303. The collections of

information in 21 CFR parts 50 and 56 (protection of human subjects and institutional review boards) have been approved under OMB control number 0910-0130.

III. Electronic Access

Persons with access to the internet may obtain the draft 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/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: March 15, 2024.

Lauren K. Roth,

Associate Commissioner for Policy.

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