



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2024-D-2754]

M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of Medicines; International Council for Harmonisation; Draft Guidance for Industry; Availability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SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of Medicines.” The draft guidance was prepared under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The draft guidance outlines general principles on planning, designing, and analyzing observational (noninterventional) pharmacoepidemiological studies that utilize fit-for-purpose data for safety assessment of medicines (drugs, vaccines, and other biological products). The draft guidance includes recommendations and high-level best practices for the conduct of these studies. The draft guidance is intended to streamline the development and regulatory assessment of postmarketing pharmacoepidemiological safety studies that include Real-World Data. This guidance also seeks to improve the ability of the study protocol and/or results to be accepted across health authorities and support decision making in response to study results.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.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-2024-D-2754 for "M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiological Studies

That Utilize Real-World Data for Safety Assessment of Medicines.” 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 the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), 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. The guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: *Regarding the guidance:* Wei Hua, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave. Bldg. 22, Rm. 2414, Silver Spring, MD 20993-0002, 240-402-8658, OSE.PMKTREGS@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.

Regarding the ICH: Jill Adleberg, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6364, Silver Spring, MD 20993-0002, 301-796-5259, Jill.Adleberg@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of Medicines.” The draft guidance was prepared under the auspices of ICH. ICH seeks to achieve greater regulatory harmonization worldwide to

ensure that safe, effective, high-quality medicines are developed, registered, and maintained in the most resource-efficient manner.

By harmonizing the regulatory requirements in regions around the world, ICH guidelines enhance global drug development, improve manufacturing standards, and increase the availability of medications. For example, ICH guidelines have substantially reduced duplicative clinical studies, prevented unnecessary animal studies, standardized the reporting of important safety information, and standardized marketing application submissions.

The six Founding Members of the ICH are FDA; the Pharmaceutical Research and Manufacturers of America; the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; and the Japanese Pharmaceutical Manufacturers Association. The Standing Members of the ICH Association include Health Canada and Swissmedic. ICH membership continues to expand to include other regulatory authorities and industry associations from around the world (refer to <https://www.ich.org/>).

ICH works by engaging global regulatory and industry experts in a detailed, science-based, and consensus-driven process that results in the development of ICH guidelines. The regulators around the world are committed to consistently adopting these consensus-based guidelines, realizing the benefits for patients and for industry.

As a Founding Regulatory Member of ICH, FDA plays a major role in the development of each of the ICH guidelines, which FDA then adopts and issues as guidance for industry. FDA's guidance documents do not establish legally enforceable responsibilities. Instead, they describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.

In May 2024, the ICH Assembly endorsed the draft guideline entitled "M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiological Studies That Utilize Real-World Data for Safety Assessment of Medicines" and agreed that the guideline should be made

available for public comment. The draft guideline is the product of the Quality Expert Working Group of the ICH. Comments about this draft will be considered by FDA and the Quality Expert Working Group.

This draft guidance provides general considerations and recommendations for use of real-world data for drug, vaccine, and other biologic product safety assessments. The draft guidance seeks to harmonize regional recommendations for the design, analysis, and reporting of postmarketing pharmacoepidemiologic studies that use real-world data as the number of pharmacoepidemiological studies utilizing real-world data in a regulatory context have increased globally.

This draft guidance has been left in the original ICH format. The final guidance will be reformatted and edited to conform with FDA's good guidance practices regulation (21 CFR 10.115) and style before publication. The draft guidance, when finalized, will represent the current thinking of FDA on "M14 General Principles on Plan, Design, and Analysis of Pharmacoepidemiologic Studies That Utilize Real-World Data for Safety Assessment of Medicines." 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 (44 U.S.C. 3501-3521). The collections of information supporting investigational new drug regulations in 21 CFR part 312 have been approved under OMB control number 0910-0014. The collections of information supporting FDA approval of new drugs in part 314 (21 CFR part 314) have been approved under OMB control number 0910-0001. The collections of information supporting general licensing provisions of biological products in 21

CFR part 601 have been approved under OMB control number 0910-0338. The collections of information supporting adverse experience reporting in 21 CFR 310.305 and 329.100, and §§ 314.80, 314.81, and 314.98, have been approved under OMB control number 0910-0230. The collections of information supporting MedWatch safety and adverse event reporting have been approved under OMB control number 0910-0291. The collections of information supporting biological products postmarket adverse experience reporting in 21 CFR part 600 have been approved under OMB control number 0910-0308 and the collections of information supporting medical device reporting have been approved under OMB control number 0910-0437.

III. Electronic Access

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

Dated: July 1, 2024.

Lauren K. Roth,

Associate Commissioner for Policy.

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