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4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2026-N- 10742]

Patient-Level Data for Drugs and Biological Products Submissions Containing Real-World Data and Real-World Evidence; Request for Information

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; Request for Information.

SUMMARY: The Food and Drug Administration (FDA or Agency), is announcing a request for information (RFI) from interested parties to share perspectives on patient-level data access related to the use of real-world evidence (RWE) in regulatory decision-making for drugs and biological product submissions. The purpose of this RFI is to solicit input from interested parties on innovative solutions to address the challenges in submitting patient-level data for real-world data (RWD) analyzed in clinical studies included in a marketing application. Interested parties may include regulated industry, health information technology (HIT) vendors, academic medical centers, electronic data capture vendors, patient advocates, and other interested parties.

DATES: Either electronic or written comments on the notice must be submitted by **[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The https://www.regulations.gov electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of **[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

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-2026-N-10742 for "Patient-level data for drugs and biological products submissions containing real-world data and real-world evidence; Request for Information." Received comments, those filed in a timely manner (see ADDRESSES), 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.

FOR FURTHER INFORMATION CONTACT: Marie Bradley, Office of Medical Policy, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Room 6360, Silver Spring, MD 20993, 301-796-2500, email: cder-rwe@fda.hhs.gov, or

Philip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240-402-7911, email: industry.biologics@fda.hhs.gov with the subject line "Patient-level data for drugs and biologics submissions containing real-world data and real-world evidence."

SUPPLEMENTARY INFORMATION:

I. Background

The rapid advancement of technologies and innovative methods (e.g., super intelligence, digital health technologies, and RWD) in drug development presents both opportunities and challenges for regulatory decision-making. Aligned with the U.S. Department of Health and Human Services (HHS) priorities, the FDA is committed to realizing the full potential of fit-for-use RWD to generate RWE that advances the development and safety of regulated products. RWD are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. RWE is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD. Despite increasing submissions to the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) that include RWD and RWE for consideration in regulatory decision-making for drug and biological products, challenges persist with submission of patient-level data to allow FDA review and verification of study results during the regulatory review process.

For clinical trials, patient-level data are routinely submitted to CDER and CBER to conduct independent analyses and assess the adequacy of study results as part of the regulatory review process for drug and biological products. Sponsors must ensure they are able to submit patient-level data for any RWD that have been analyzed as part of clinical studies included in a marketing application, when required under 21 CFR 314.50 and 21 CFR 601.2.[1] Frequently, sponsors do not own the RWD used in studies submitted to FDA and, therefore, lack

[1] *See* FDA Guidance for Industry, Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products, August 2023, *available at* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/considerations-use-real-world-data-and-real-world-evidence-support-regulatory-decision-making-drug.

authorization to submit patient-level information to the Agency. When certain RWD are owned and controlled by entities other than the sponsor, sponsors should establish agreements with those entities to ensure that relevant patient-level data can be provided to FDA and that source data[2] necessary to verify the RWD are made available for inspection, as applicable.

In the United States, where privacy protections including the Health Insurance Portability and Accountability Act (HIPAA) Security Rule exist[3] and public scrutiny of digital privacy continues to intensify, the sharing of clinical data presents significant challenges. These challenges are further compounded by patient privacy considerations related to data sharing and the transfer of data across multiple jurisdictions, particularly from the European Union due to the General Data Protection Regulation (GDPR).[4]

When an appropriate justification exists for a sponsor's inability to directly submit patient-level data to FDA in support of a marketing application, regulatory pathways are available for third parties to provide this data to FDA in support of a sponsor's marketing application. For example, third-party data providers, including other federal agencies, may currently elect to open either a pre-investigational new drug application (pre-IND), or FDA may receive the information through a Type V drug master file (DMF).[5] In such cases the sponsor provides to FDA a letter of authorization from the third-party data provider permitting FDA to reference the data contained in the third party's DMF or pre-IND for the purpose of reviewing their application.[6] FDA does not currently accept links to external databases for such data submissions.

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[2] For the purposes of this RFI, source data include all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation used for reconstructing and evaluating the investigation.

[3] For further information on the HIPPA Security Rule *see* 45 CFR Part 160 and Part 164, Subparts A and C.

[4] For further information on General Data Protection Regulations *see* https://gdpr-info.eu/.

[5] *See* 21 C.F.R. 314.420(a)(5), describing Type V DMF's.

[6] *See* 21 C.F.R. 314.420(b), referencing the need for a written authorization from the DMF holder prior to the incorporation by reference of the DMF into any particular IND or application for marketing.

Even when a sponsor or third party is authorized to submit patient-level RWD to the Agency, real-world datasets are often substantially larger than typical clinical trial datasets, particularly when they include longitudinal data, imaging, or multi-omics information, and submission via traditional channels is often difficult – creating significant technical challenges for data transfer, storage, and processing within FDA's existing infrastructure.

When a sponsor or third party seeks to submit patient-level RWD to the Agency as part of an NDA or BLA submission (or in a DMF or pre-IND), they often encounter challenges because FDA cannot sign a data-use agreement that potentially conflicts with existing legal obligations of the Agency. The agency's ability to commit to the agreements that are often required by third party data vendors is frequently limited because they contain terms that do not align with the agency's legal obligations (e.g., data destruction requirements that may conflict with the agency's federal record keeping obligations; data ownership or access terms that may conflict with the agency's obligation to preserve data informing a regulatory decision as part of an administrative record; limitations on sharing that conflict with FDA's obligations under the Freedom of Information Act).

FDA is exploring potential solutions to address these challenges while ensuring alignment with existing agency policies regarding RWD and applicable legal requirements. The purpose of this RFI is to solicit input from interested parties on innovative solutions to address the challenges FDA encounters in accessing patient-level data for submissions containing RWD and RWE. FDA aims to develop a comprehensive understanding of the current landscape of available solutions and emerging approaches, while gathering insights regarding potential barriers and facilitators to implementation. Information obtained through this RFI will inform the Agency's strategic planning and policy development concerning RWD/RWE utilization, assist in identifying opportunities for any potential collaborative frameworks, and support FDA's ongoing efforts to modernize its information technology capabilities while maintaining the highest standards of patient privacy protection and data stewardship.

II. Request for Information

FDA is requesting public comments on the questions below.

A. Patient-level Data Access

1. CDER and CBER are committed to ensuring patient-level data is available for regulatory submissions using RWE. What opportunities and/or challenges do you see for the pharmaceutical industry regarding the current requirement to submit patient-level data collected from RWD sources to FDA for submissions proposing the use of RWE?
2. When a sponsor or third party submits patient-level RWD to the Agency as part of an NDA, BLA, DMF, or pre-IND submission, they often encounter challenges because FDA cannot sign a data-use agreement that potentially conflicts with existing legal obligations of the FDA. What potential solutions exist to address current industry practices around data-use agreements that would allow for more efficient sharing of patient-level RWD with FDA?
3. What solutions could assist FDA in addressing current challenges associated with receiving and retaining patient-level data, technical interoperability, and conducting independent reviews of submissions that include RWD?
4. How might FDA work with external parties to develop solutions to the challenges associated with patient level data submission for regulatory submissions proposing the use of RWE?

To help FDA review comments efficiently, please identify the question to which you are responding by its associated category and number. If you are responding to more than one question, please identify each question to which you are responding, and categorize each response by question. FDA is issuing this request for information pursuant to its authority at 21 U.S.C. § 393(b).

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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