4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2023-D-4395]

Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices; Guidance for Industry and Food and Drug Administration Staff; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is announcing the availability of a final guidance entitled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices." FDA is issuing this guidance to clarify how FDA evaluates real-world data (RWD) to determine whether they are of sufficient quality for generating real-world evidence (RWE) that can be used in FDA regulatory decision-making for medical devices. This final guidance supersedes the final guidance, "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices," issued August 31, 2017, and provides expanded and updated recommendations.

DATES: The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

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-2023-D-4395 for "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical 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)).

An electronic copy of the guidance document is available for download from the internet. See the **SUPPLEMENTARY INFORMATION** section for information on electronic access to the guidance. Submit written requests for a single hard copy of the guidance document entitled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" to the Office of Policy, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5441, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your request.

FOR FURTHER INFORMATION CONTACT: Soma Kalb, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 318, Silver Spring, MD 20993-0002, 301-796-6359; or Phillip Kurs, Center for Biologics Evaluation and Research, Food and Drug Administration, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is issuing this guidance to clarify how FDA evaluates RWD to determine whether they are of sufficient quality for generating RWE that can be used in FDA regulatory decision-making for medical devices. This guidance provides expanded and updated recommendations to the 2017 guidance, "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" (the 2017 RWE Guidance) and supersedes the 2017 RWE Guidance. On December 29, 2022, the Food and Drug Omnibus Reform Act of 2022 (FDORA) was signed into law as part of the Consolidated Appropriations Act, 2023, Pub. L. 117-328. Section 3629 of FDORA "Facilitating the Use of Real World Evidence" directs FDA to issue or revise existing guidance on considerations for the use of RWD and RWE to support regulatory decision-making. FDA issued the draft guidance on December 19, 2023, to propose revisions to the 2017 RWE Guidance to satisfy the requirement under section 3629(a)(2), and is finalizing this guidance to fulfill a commitment in section V.F. of the Medical Device User Fee Amendments Performance Goals and Procedures, Fiscal Years 2023 Through 2027 (MDUFA V).

This guidance includes FDA's recommendations and considerations on the factors that sponsors should assess to demonstrate whether the RWD are relevant and reliable for a particular regulatory decision relating to medical devices. These recommendations and considerations apply regardless of the RWD source and encompass processes for conducting studies to generate RWE. FDA recognizes that there may be other approaches to address the considerations identified in this guidance. We encourage sponsors to discuss their approach with FDA, especially if the approach diverges from the recommendations in this guidance.

The topics covered within this guidance are framed specifically for the use of RWD/RWE in regulatory submissions. This guidance includes additional clarity regarding the recommended methodologies for collection and analysis of RWD to generate RWE, and provides updated examples on previously used and accepted methodologies. This guidance also provides additional clarity regarding the use of clinical data collected from the use of a device authorized under an Emergency Use Authorization (EUA) and describes the type of information that could be applicable to support a determination under the Clinical Laboratory Improvement Amendments (CLIA) (e.g., Waiver by Application).

FDA recognizes and anticipates that the Agency and industry may need up to 60 days to perform activities to operationalize the recommendations within this final guidance. For regulatory submissions that will be currently pending with FDA after publication of this final guidance, as well as those submissions received within 60 days following publication of this final guidance, FDA generally does not anticipate that sponsors will be ready to include the newly recommended information outlined in this final guidance in their submission. FDA, however, intends to review any such information if submitted at any time.

A notice of availability of the draft guidance appeared in the *Federal Register* of December 19, 2023 (88 FR 87782). FDA considered comments received and revised the guidance as appropriate in response to the comments, including clarifying the recommendations in the guidance. This included clarifications on the relevance and reliability assessment, updating examples of how RWE is used in regulatory decision-making for medical devices, and how the relevance and reliability assessment fits into existing benefit/risk frameworks.

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 "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical 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 OMB guidance in M-25-20, and finds this action to be deregulatory in nature.

II. Electronic Access

Persons interested in obtaining a copy of the guidance may do so by downloading an electronic copy from the internet. A search capability for all Center for Devices and Radiological Health guidance documents is available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products. This guidance document is also available at https://www.regulations.gov, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics. Persons unable to download an electronic copy of "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" may send an email request to CDRH-Guidance@fda.hhs.gov to receive an electronic copy of the document. Please use the document number GUI01500012 and complete title to identify the guidance you are requesting.

III. Paperwork Reduction Act of 1995

While this guidance contains no new 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 the following table have been approved by OMB:

21 CFR Part or Guidance	Topic	OMB Control No.
807, subpart E	Premarket notification	0910-0120
814, subparts A through E	Premarket approval	0910-0231
814, subpart H	Humanitarian Use Devices; Humanitarian Device Exemption	0910-0332
812	Investigational Device Exemption	0910-0078
860, subpart D	De Novo classification process	0910-0844
822	Postmarket Surveillance of Medical Devices	0910-0449

"Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program"	Q-submissions and Early Payor Feedback Request Programs for Medical Devices	0910-0756
"Administrative Procedures for CLIA Categorization" and "Recommendations: Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices"	CLIA Administrative Procedures; CLIA Waivers	0910-0607
800, 801, 809, and 830	Medical Device Labeling Regulations; Unique Device Identification	0910-0485
803	Medical Device Reporting	0910-0437
50, 56	Protection of Human Subjects and Institutional Review Boards	0910-0130
601	Biologics License Application	0910-0338
860	Reclassification Petition for Medical Devices	0910-0138
"Emergency Use Authorization of Medical Products and Related Authorities"	EUA	0910-0595

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