



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-D-2153]

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 or Agency) is announcing the availability of the guidance entitled "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices." FDA is issuing this guidance to clarify how we evaluate real-world data to determine whether it may be sufficiently relevant and reliable to generate the types of real-world evidence that can be used in FDA regulatory decision-making for medical devices. The guidance describes the circumstances when real-world evidence can be used, and the scientific criteria that must be fulfilled in order to have confidence in the data. Finally, the guidance describes some examples of actual uses of real-world evidence that have already led to FDA decisions.

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-2016-D-2153 for "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices;

Guidance for Industry and Food and Drug Administration Staff." 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 office between 9 a.m. and 4 p.m., Monday through Friday.

- 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 docket, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/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.

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 the Center Director, Guidance and Policy Development, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5431, Silver Spring, MD 20993-0002; or 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 request.

FOR FURTHER INFORMATION CONTACT: Benjamin Eloff, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 2254, Silver Spring, MD 20993-0002, 301-796-8528; and 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

To protect and promote public health, FDA needs to understand and evaluate the available evidence related to regulated products. For medical devices, available evidence is traditionally comprised of non-clinical and in some cases, clinical studies conducted and

provided to FDA by the device manufacturer or sponsor. However, FDA recognizes that a wealth of data covering medical device experience exists and is routinely collected in the course of treatment and management of patients. Under certain circumstances, these real-world data (RWD) may constitute real-world evidence (RWE), or clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD, that may be of sufficient quality to help inform or augment FDA's understanding of the benefit-risk profile of devices at various points in their life cycle, and could potentially be used to aid FDA in regulatory decision-making.

This document describes the characteristics and sources of RWD and characteristics of RWE that may be sufficient for use in making various regulatory decisions. Because of its nature, the quality (i.e., relevance and reliability) of RWD can vary greatly across sources. Likewise, there are many types of regulatory decisions with varying levels of evidentiary needs. FDA's evidentiary standards for regulatory decision-making are not changing. FDA encourages the use of RWE where appropriate, and will evaluate whether the available RWE is of sufficient relevance and reliability to address the specific regulatory decision being considered.

This guidance does not affect any Federal, State or local laws or regulations or foreign laws or regulations that may otherwise be applicable to the use or collection of RWE and that provide protections for human subjects or patient privacy. This guidance should be used to complement, but not supersede, other device-specific and good clinical practice guidance documents. FDA considered comments received on the draft guidance that published in the *Federal Register* of July 27, 2016 (81 FR 49228). FDA revised the guidance as appropriate in response to the comments.

II. Significance of Guidance

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. This guidance is not subject to Executive Order 12866.

III. 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/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>. Guidance documents are also available at <https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm> or <https://www.regulations.gov>. 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 1500012 to identify the guidance you are requesting.

IV. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations and guidance. These 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-

3520). The collections of information in 21 CFR part 807, subpart E, have been approved under OMB control number 0910-0120; the collections of information in 21 CFR part 814, subparts A through E (premarket approval), have been approved under OMB control number 0910-0231; the collections of information in 21 CFR part 814, subpart H (humanitarian device exemption), have been approved under OMB control number 0910-0332; the collections of information in 21 CFR part 812 (investigational device exemption) have been approved under OMB control number 0910-0078; the collections of information in 21 CFR part 822 (postmarket surveillance) have been approved under OMB control number 0910-0449; the collections of information in 21 CFR 50.23 (exception from general requirements for informed consent) have been approved under OMB control number 0910-0586; the collections of information in 21 CFR part 54 (financial disclosure by clinical investigators) have been approved under OMB control number 0910-0396; the collections of information in 21 CFR 56.115 (institutional review boards records) have been approved under OMB control number 0910-0130; and the collections of information in 21 CFR parts 50 subpart B (informed consent of human subjects) and 56 (institutional review boards) have been approved under OMB control number 0910-0755. The collections of information in the guidance "Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff" have been approved under OMB control number 0910-0756.

Dated: August 25, 2017.

Leslie Kux,

Associate Commissioner for Policy.

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