

**Agency Guidance Snapshot: Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices: Draft Guidance for Industry and Food and Drug Administration Staff (*Draft Guidance*)**

The Yale Human Research Protection Program (HRPP) has launched the “**Agency Guidance Snapshot**” series. The purpose of the Agency Guidance Snapshots is to highlight recent agency guidance from the Food and Drug Administration (FDA)<sup>1</sup>, Office for Human Research Protections (OHRP), and other federal agencies that specifically impacts Yale University and affiliate stakeholders who conduct or oversee **human subjects research**.

**Please Note:** Yale University does not expect any immediate changes to policies due to this guidance; however, this guidance will be taken into consideration as policies and procedures are reviewed and revised in the future. Yale University may have additional requirements related to the topics covered in this guidance. For more information, please refer to the following Yale University Human Research Protection Program (HRPP) documents located on the HRPP website ([Policies, Procedures, Guidance, and Related Documents](#)) and in the Yale HRPP IRES-IRB Library ([IRES IRB LOGIN](#)): **1) Yale HRPP Policy and Standard Operating Procedure Manual**; **2) Yale HRPP Investigator Manual**; **3) Yale IRB Members and Chairs Manual**; and **4) HRPP Supplemental Guidance Manual**. Please also refer to [University Policies & Procedures](#) and policies published by the various Yale University schools and departments.

<b>Title of Document:</b>	Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices: Draft Guidance for Industry and Food and Drug Administration Staff ( <i>Draft Guidance</i> )
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<b>Hyperlink to Document:</b>	<a href="https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-use-real-world-evidence-support-regulatory-decision-making-medical-devices">https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-use-real-world-evidence-support-regulatory-decision-making-medical-devices</a>

**Overview of Guidance Document:**

FDA is issuing this draft guidance to clarify how FDA evaluates real-world data to determine whether they are of sufficient quality for generating real-world evidence that can be used in FDA regulatory decision-making for medical devices, such as new or expanded indications for use or postmarket surveillance. The draft guidance also provides expanded recommendations to sponsors considering using real-world evidence to support a regulatory submission for medical devices.

<sup>1</sup> FDA Guidance documents represent the Agency’s current thinking on a particular subject. They do not create or confer any rights for or on any person and do not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

## **Terminology:**

**Real-world data (RWD)** are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Examples of RWD sources include data derived from electronic health records (EHRs), medical claims data, data from product and disease registries, and data gathered from other sources (such as digital health technologies) that can inform on health status. RWD sources can be used as data collection and analysis infrastructure to support many types of study designs, including, but not limited to, randomized and non-randomized controlled trials; single-arm studies with or without comparison to an objective performance criterion, performance goal, or extended control; observational studies; and hybrid designs which combine elements of multiple study designs.

**Real-world evidence (RWE)** is the clinical evidence regarding the usage, and potential benefits or risks, of a medical product derived from analysis of RWD.

This draft guidance includes factors that FDA considers important to demonstrate whether the RWD are fit-for-purpose for a particular regulatory decision relating to medical devices, as well as FDA's recommendations on how FDA intends to assess these factors. When finalized, the recommendations and considerations in this draft guidance will apply regardless of the RWD source and encompass processes for conducting studies to generate RWE. A fit-for-purpose assessment should evaluate both the relevance and reliability of the RWD. FDA recognizes that there may be other approaches to address the considerations identified in this document and encourages sponsors to discuss their approach with FDA, especially if the approach diverges from the recommendations in this draft guidance, when finalized.

## **Key Points for Sponsor-Researchers:**

FDA recognizes that a wealth of clinical data in the form of RWD are routinely collected in the course of clinical practice during the treatment and management of patients. Although these data typically have different quality controls compared to data collected within a traditional clinical study, under certain circumstances RWD may be used to generate RWE to help inform or augment FDA's understanding of the benefit-risk profile of devices at various points in their life cycle.

RWE derived from relevant and reliable RWD may constitute valid scientific evidence, depending on the study question, regulatory decision, data source(s), and design and analysis of the specific dataset derived from RWD source(s), and thus may be used to support regulatory decisions.

## **Data sources that may be considered RWD sources include the following:**

- Registries;
- EHRs;
- Administrative claims data;
- Patient-generated data created, reported, or gathered by patients including in-home use settings (e.g., data from digital health technologies (DHTs) such as wearables);
- Device-generated data (e.g., implantable devices, physiological monitoring devices);
- Public health surveillance data (e.g., COVID-19 case surveillance);
- Clinically annotated biobanks; and
- Medical device data repositories (e.g., imaging, electrocardiography databases).

The use of RWE for specific regulatory purposes will include assessment of the overall *relevance and reliability* of the RWD used to generate the RWE.

**For any questions, please contact HRPP Assistant Directors  
Gina Larsen ([gina.larsen@yale.edu](mailto:gina.larsen@yale.edu)) or Cathi Montano ([cathleen.montano@yale.edu](mailto:cathleen.montano@yale.edu))**

## **Assessing Data Relevance and Reliability**

To determine the potential suitability of RWD to generate RWE for regulatory decision-making, FDA assesses the relevance and reliability of the RWD source as well as the data elements, study design, and analytic components of the study. Relevance and reliability are evaluated to determine if the data are fit-for-purpose.

**Relevance** includes consideration of data availability, linkages (how data from different sources can be obtained and integrated), timeliness of the current clinical environment, and generalizability of the RWD.

**Reliability** includes consideration of data accrual (collected and processed in a consistent, methodical manner), quality assurance for the RWD source (site and data monitoring, data quality audit program) and integrity of the RWD by adherence to data collection, recording, and source verification procedures.

## **Methods for study designs using RWD**

The draft guidance provides examples of study designs to generate RWE, including:

- Single-arm studies with comparisons to external controls, in whole or part;
- Objective performance criteria or performance goals;
- Non-interventional studies (observational studies) (e.g., comparative cohort studies, case-control studies, self-controlled studies, and descriptive studies); and
- Randomized controlled trials using RWD to supplement one or more study arms.

## **Recommendations for Submitting RWE for FDA Review**

In addition to listing the factors that it intends to assess when making regulatory decisions regarding medical device submissions, the FDA's draft guidance also provides expanded recommendations for sponsors that are considering using RWE in support of their regulatory submissions. Appendix A in the guidance provides an outline of proposed elements to be included in documentation submitted for review. Two tables are provided that propose relevance and reliability factors, with each table specifying the information that sponsors should document and have available for potential inspections, as well as where this information should be included in their FDA submissions.

## **Final Note**

This current draft guidance issued by the FDA is intended to provide the parties responsible for medical devices with additional guidelines on the approach to be followed when using real-world data and real-world evidence in regulatory submissions to support claims made for their products. While FDA encourages the use of relevant and reliable data to generate clinical evidence, including RWE, this draft guidance neither mandates use of RWD and RWE nor restricts other means of providing evidence to support regulatory decision-making. This draft guidance does not affect any federal, state, or local laws or regulations, or foreign laws or regulations that may be applicable to the use or collection of RWD, or that provide protections for human subjects (including informed consent requirements) or patient privacy. When finalized, this guidance should be used to complement, but not supersede, other device-specific and GCP and guidance documents.

**For more related information, please see the following links to additional resources:**

- [FDA Guidance Documents](#)
- [Examples of Real-World Evidence \(RWE\) Used in Medical Device Regulatory Decisions.](#)
- [\*Real-world evidence for regulatory decision-making: updated guidance from around the world\*](#), Burns L, Le Roux N, Kalesnik-Orszulak R, Christian J, Dudinak J, Rockhold F, Khozin S, O'Donnell J. Real-world evidence for regulatory decision-making: updated guidance from around the world. *Front Med (Lausanne)*. 2023 Oct 30;10:1236462. doi: 10.3389/fmed.2023.1236462. PMID: 38020096; PMCID: PMC10643567.

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Gina Larsen ([gina.larsen@yale.edu](mailto:gina.larsen@yale.edu)) or Cathi Montano ([cathleen.montano@yale.edu](mailto:cathleen.montano@yale.edu))**