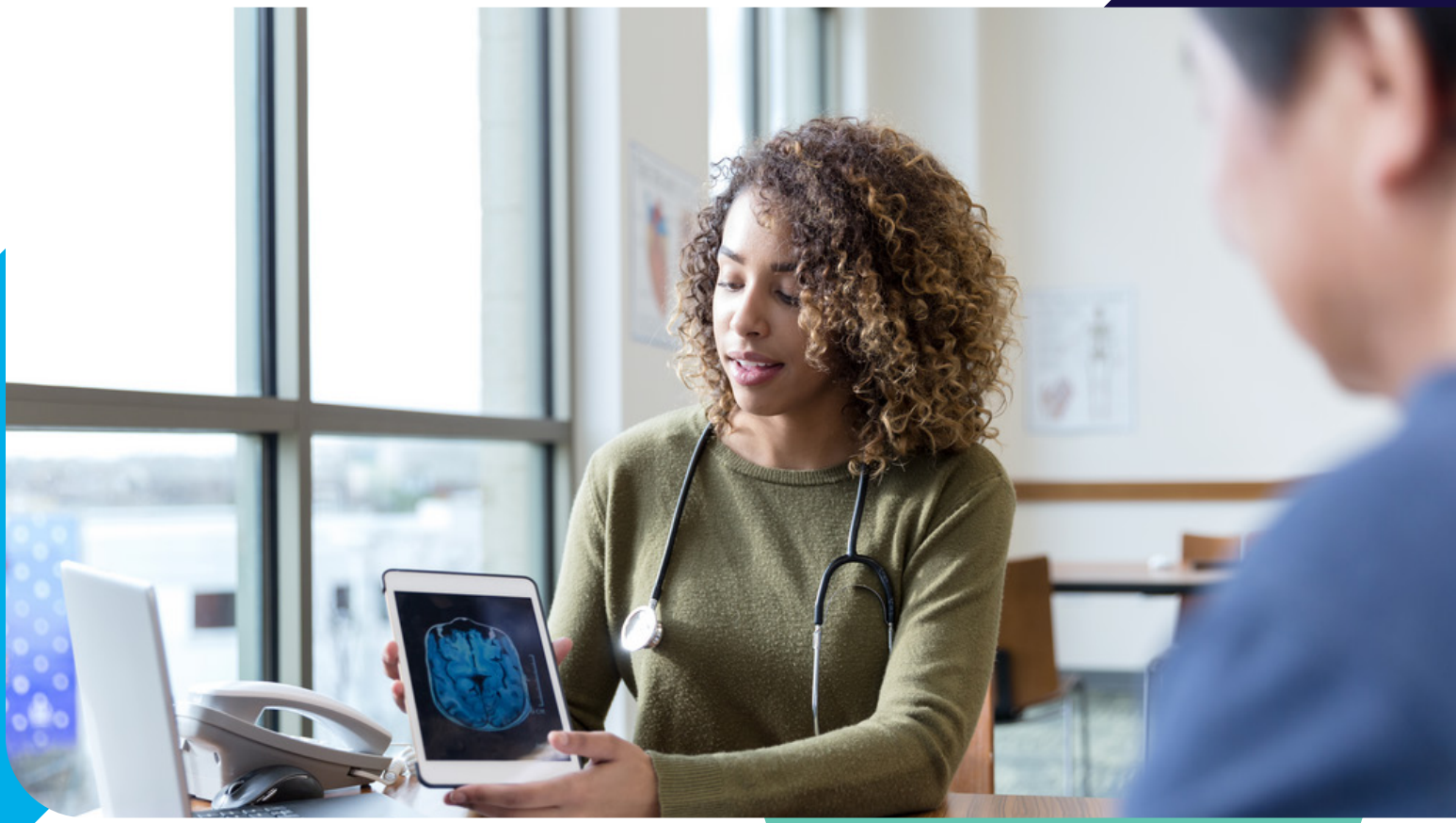
Insight Brief

Real World Evidence for Medical Device Regulatory Submissions

Gain insight into the key principles from the FDA draft guidance to evaluate the relevance and reliability of real world data for regulatory decision-making.

CHRISTINA MACK, PhD, MSPH, FISPE, Chief Scientific Officer, Real World Solutions, IQVIA
JOANNA WILLS, Global Director, MedTech Real World Evidence Solutions, IQVIA MedTech
TIFFANY MERCADO, Associate Principal, Regulatory Science Strategy and Innovation, IQVIA
NILSA LOYO-BERRÍOS, PhD, MSc, Principal, Epidemiology and Drug Safety, Regulatory Science Strategy and Innovation, IQVIA MedTech



Real World Evidence (RWE) for medical device regulatory submissions: draft guidance considerations

Background

In December 2023, the FDA issued a draft guidance document titled "Use of RWE to Support Regulatory Decision-Making for Medical Devices." This update builds upon their original guidance issued in 2017. Given the rapid technological advancements within MedTech, including our improved capacity to access and curate real world data (RWD), the FDA's release of this guidance document is timely and important. This guidance document addresses the growing need to utilize RWD to inform regulatory decisions.

While RWD is collected under different quality controls compared to data collected as part of a clinical trial, the FDA recognizes its value and volume.[1] The forthcoming final version of this guidance document aims to clarify how the FDA will assess the quality of RWD for use in regulatory decision making.[1]

When use of RWE may be appropriate

The application of RWD and RWE extends across the entire product lifecycle of medical devices. Examples of RWE utilization in regulatory decision-making include the following[1]:

1

Example 1: New or expanded indications for use

- Data from a registry outside of the US was available for nearly 300 patients with more than two years of follow up data.
- This RWD was used as the primary clinical evidence to support the Pre-Market Approval (PMA) submission to the FDA. An Investigative Device Exemption (IDE) study was not required.

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Example 2: 522 submissions

- A single-arm, prospective observational study was designed to assess real world safety of a device. A comparator group was established from systematic literature review.
- The study met its safety endpoints with no unanticipated adverse device effects.

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Example 3: Control group

- A sponsor submitted a PMA for an indication expansion using a single study arm design.
- The control group was formed from a US registry with patients receiving alternative devices for this indication.
- Propensity-score analysis was performed using 20 pre-specified variables.

Assessing RWD quality: relevance and reliability

The principles of relevance and reliability are critical to assessing 'fit-for-purpose' to support regulatory decisions. Relevance and reliability are defined as follows:

Source: Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices, Federal Food, Drug, and Cosmetic Act_Draft Guidance December 19, 2023

RELEVANCE

Relevance of the data is assessed based on the research question that needs to be addressed. The FDA evaluates this relevance using criteria such as data availability, timeliness, and generalizability to ensure the data is suitable for addressing the research question.

Data availability refers to the sufficiency of detail within the data to evaluate the specified research question. The FDA assesses if relevant exposures, outcomes, and co-morbidities are present at the required time-points and intervals to adequately address the research question. It is imperative that the research question clearly defines the target population, the exposures and outcomes of interest, as well as the duration of follow-up.

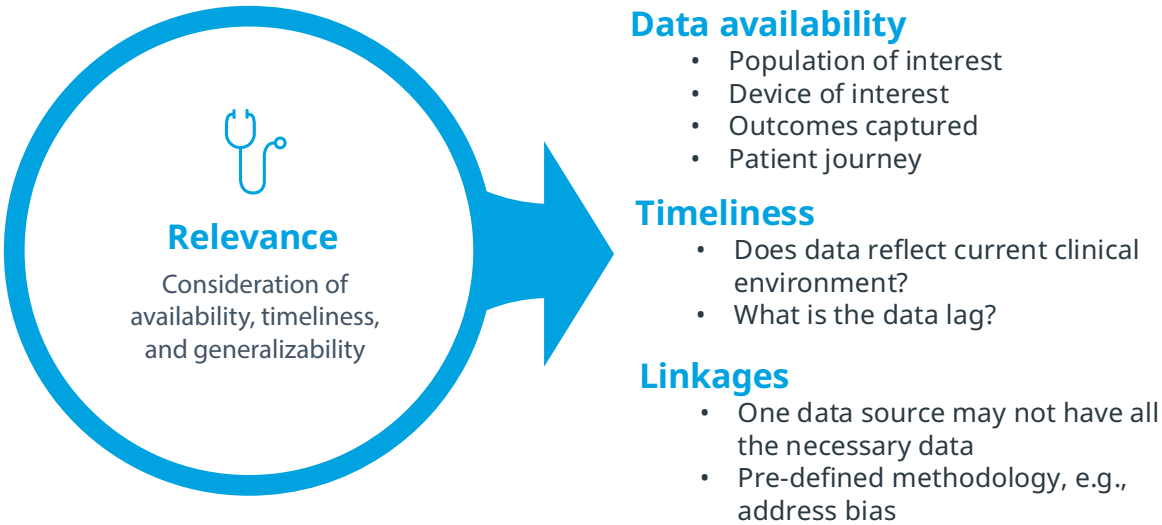
The FDA also considers timeliness when assessing data relevance and wants evidence that a reasonable time frame passed between data collection and release for research.

Data must also reflect current clinical practice. For example, if data are collected before a substantial change in medical guidelines, it may not be considered timely (relevant).

In line with diversity guidelines, study samples must represent the population of the RWD source relative to the specific device indication for use. Furthermore, to ensure relevance, the data should be generalizable to the broader patient population affected by the disease or condition under investigation.

The FDA recognizes that relevant data will likely stem from multiple sources. Linking of multiple data sources can augment the relevance of data but could introduce bias. To minimize this risk, when linking two or more data sources, sponsors must include in the protocol a predefined **linkage methodology.**

Relevance



Source: Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices, Federal Food, Drug, and Cosmetic Act_Draft Guidance December 19, 2023

RELIABILITY

Reliable data exhibits high levels of **quality and integrity.** The protocol must explain data accrual methods used for extraction and processing. The protocol should confirm the data processed in a consistent and methodical manner. Data collection methods can vary based on the source type; secondary sources like registries or claims databases may have different protocols compared to primary sources such as clinical notes.

Other reliability factors to consider include sample size calculations and an assessment of the impact of any missing data.

Reliability

Data accrual

- Data collected and processed in a consistent and methodical manner
- Quality control procedures, site and data monitoring

Data quality and integrity

- Sample size to address the study question
- Impact of missingness of data
- Access to the RWD source from the first instance

Source: Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices, Federal Food, Drug, and Cosmetic Act_Draft Guidance December 19, 2023

Case study: ThermoCool SmartTouch® SF catheter

The FDA granted premarket approval of the ThermoCool SmartTouch® Surround Flow Catheter from Johnson & Johnson (J&J) MedTech in 2016 to treat Type I atrial flutter in patients aged 18 or older.[2]

J&J MedTech wanted to expand the device's indications to include drug refractory recurrent symptomatic paroxysmal atrial fibrillation. Working in partnership with the National Evaluation System for Health Technology Coordinating Center (NESTcc), J&J MedTech used RWD from patient electronic health records. The unique device identifier (UDI) was used to identify the device within the health records.[3]

The FDA concluded that the approach was feasible, and the data were sufficient to demonstrate reasonable assurance of safety and effectiveness. As a result, J&J MedTech received its expanded indication faster than studying the new indication using traditional methods.[4]

When to start FDA dialog

When preparing for an RWE-based study, it is best to engage with the FDA at the initial stages of the design process. Specifically, this means initiating contact during the preliminary planning phase, before finalizing the study protocol and data collection methodologies. Medical device companies should take advantage of the Q-Submission program to discuss the research question, proposed study outline/synopsis, proposed data sources, and any questions related to data relevance and reliability.

In addition, developing a cross-functional team, beyond your clinical operations and biostatistians, to participate in these conversations is helpful. For example, an epidemiologist can discuss study design and methods topics with the regulatory reviewers, while a data scientist can ask questions related to data collection and standardization.

Conclusion

This newly release FDA RWE guidance document for medical device submissions provides more detail and context around what constitutes scientifically valid data as well as what it considers appropriate use of RWE. This information allows sponsors to make the best use of relevant, reliable data to generate high-quality RWE.

References

1. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices Draft Guidance for Industry and Food and Drug Administration Staff. United States Food & Drug Administration, December 19, 2023. https://www.fda.gov/media/174819/download

2. Summary of Safety and Effectiveness Data. https://www.accessdata.fda.gov/cdrh_docs/pdf3/P030031S100B.pdf

3. Jiang G, Dhruva SS, Chen J, et al. Feasibility of capturing real-world data from health information technology systems at multiple centers to assess cardiac ablation device outcomes: A fit-for-purpose informatics analysis report. J Am Med Inform Assoc. 2021;28(10):2241-2250. doi:10.1093/jamia/ocab117

4. J&J used RWE for an expanded indication— and you can, too (medicaldesignandoutsourcing.com)

Additional resources

1. Procedures for handling Post-Approval Studies Imposed by Premarket Approval on Order, Final Guidance October 7, 2022

2. Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act, Final Guidance October 7, 2022

3. Examples of Real-World Evidence (RWE) Used in Medical Device Regulatory Decision, March 6, 2021

About the authors

CHRISTINA MACK
PhD, MSPH, FISPE, Chief Scientific Officer, Real World Solutions, IQVIA

Dr. Mack is an engineer and epidemiologist with expertise in the development of global evidence platforms and novel studies. She has over 20 years of experience in medical devices, diagnostics, and healthcare research including using real world evidence for decision-making.

JOANNA WILLS
Global Director, MedTech Real World Evidence Solutions, IQVIA MedTech

Wills brings over 18 years of experience working in the MedTech industry in commercial, research and real world evidence. She earned her Bachelor of Mechanical Engineering and Management at McMaster University in Canada.

TIFFANY MERCADO
Associate Principal, Regulatory Science Strategy and Innovation, IQVIA

Tiffany Mercado leads consultative support in the design and execution of various studies that leverage real world evidence for regulatory decision making. Prior to joining IQVIA, Tiffany worked closely with CDRH developing RWE studies for medical devices while at NESTcc.

NILSA LOYO-BERRÍOS
PhD, MSc, Principal, Epidemiology and Drug Safety, Regulatory Science Strategy and Innovation, IQVIA MedTech

Dr. Loyo-Berríos is an epidemiologist, with 20 years of experience, including 18 years at FDA/CDRH with the regulation of medical devices, regulatory research, and post market surveillance. She earned her PhD in Epidemiology from Johns Hopkins Bloomberg School of Public Health.

CONTACT US

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