The Use of Real-World Data for Prescription Drug Regulatory Questions

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FDA U.S. FOOD & DRUG ADMINISTRATION

Disclaimer

- **This talk reflects the views of the author and should not be construed to represent FDA's views or policies.**

FDA Real-World Evidence and COVID-19

- **COVID-19 Evidence Accelerator**
  https://www.evidenceaccelerator.org/

- **FDA Sentinel Initiative**
  https://www.sentinelinitiative.org/

Topics

- US legal and regulatory background
- US Food and Drug Administration efforts
- Sources and uses of real-world data

21st Century Cures Act

- **Signed into law on December 13, 2016**
- **Designed to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently**

https://www.fda.gov/regulatory-information/selected-amendments-fdc-act/21st-century-cures-act

21st Century Cures Act: Real-World Evidence

Establish a program to evaluate the potential use of real world evidence-

- **to help to support the approval of a new indication for a drug approved under section 355(c) of this title; and**
- **to help to support or satisfy postapproval study requirements.**

No change in evidentiary standard

SEC. 505F. UTILIZING REAL WORLD EVIDENCE. Amended by Food and Drug Administration Reauthorization Act 2017

Prescription Drug User Fee Act VI (PDUFA VI)

- **Signed into law on August 18, 2017**
- **Provides FDA with the necessary resources to maintain a predictable and efficient review process for human drug and biologic products**
- **FDA commits to goals**

https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vi-fiscal-years-2018-2022

Prescription Drug User Fee Act VI (PDUFA VI): Real-World Evidence

- Workshops
  - Benefits to patients, regulators, companies
  - Data and methodology issues
  - Context of use
- Activities to address outstanding issues
  - Pilot studies
  - Methodology projects
- Guidance for use in safety and effectiveness for regulatory submissions

Real-World Data/Evidence: What Are the Goals?

- Traditional randomized clinical trials (RCTs) typically
  - Use select groups of patients
  - Involve special infrastructure and data collection
  - Maximize sensitivity

- RWE study Goals
  - Reflect the diversity of patients and actual health-care practices
  - Improve efficiency by making use of existing data and infrastructure
  - Maintain evidentiary standards

Bring proven safe and effective drugs to people faster and more efficiently.

US FDA Definitions

US FDA Definitions

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.

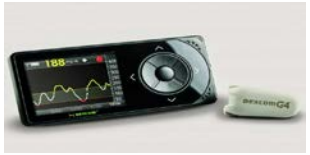
Examples:

- **Electronic health records (EHRs)**
- **Medical claims and billing data**
- **Product and disease registries**
- **Patient-generated data**
- **Wearable devices**

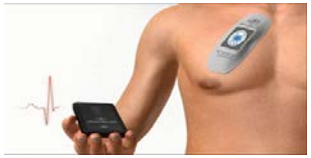
Digital Health Technology in Health and Clinical Trials

Biosensors

Continuous glucose monitor



Continuous ECG monitor



Continuous blood pressure monitor

Fall detector

Actigraphy

Interactive mobile

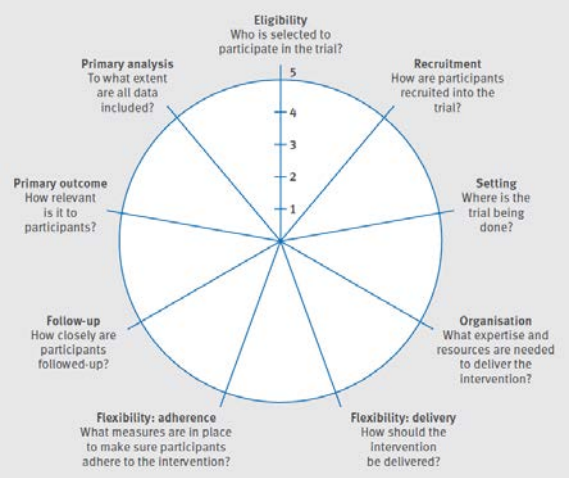
Patient reported outcome

Cellphone camera

Coordination test in Parkinson's

US FDA Definitions

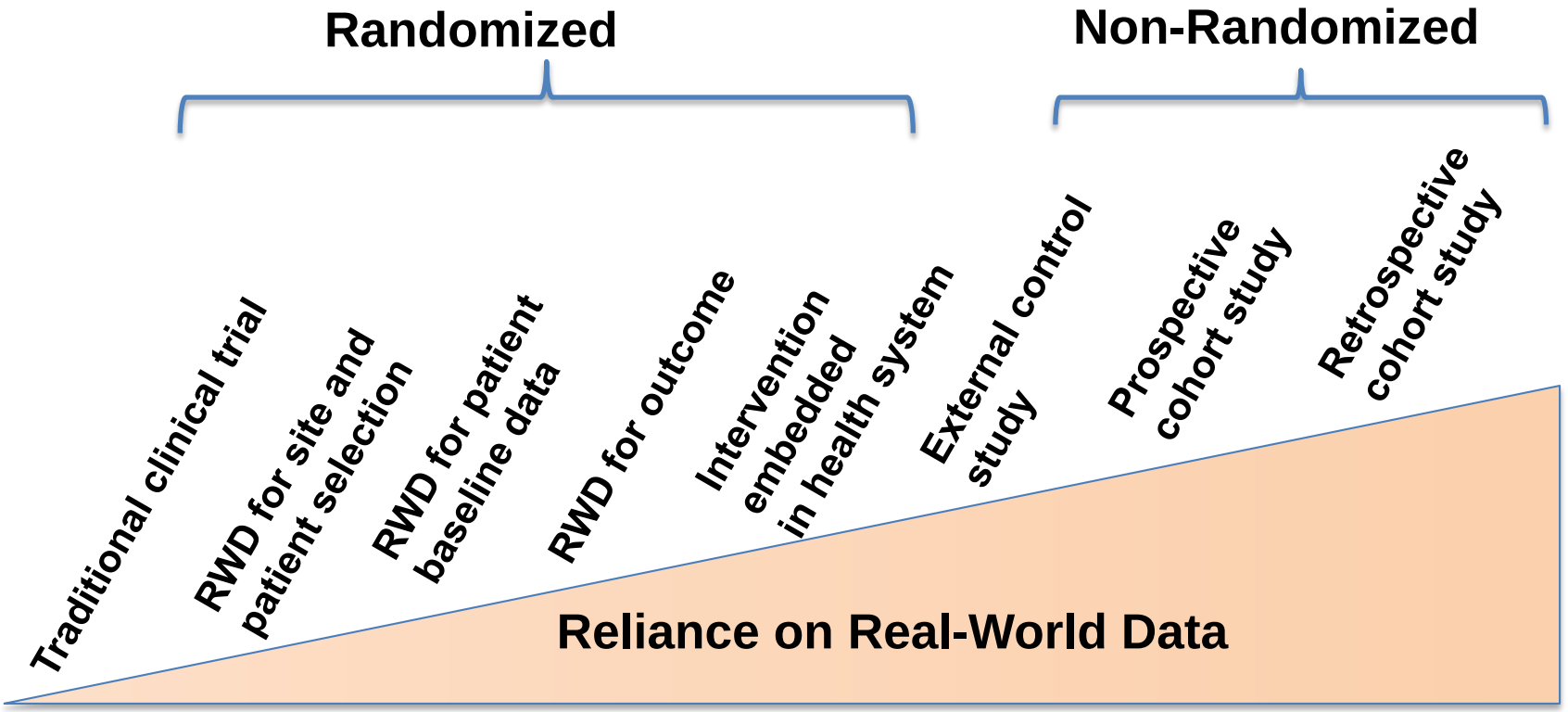
Real World Evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.



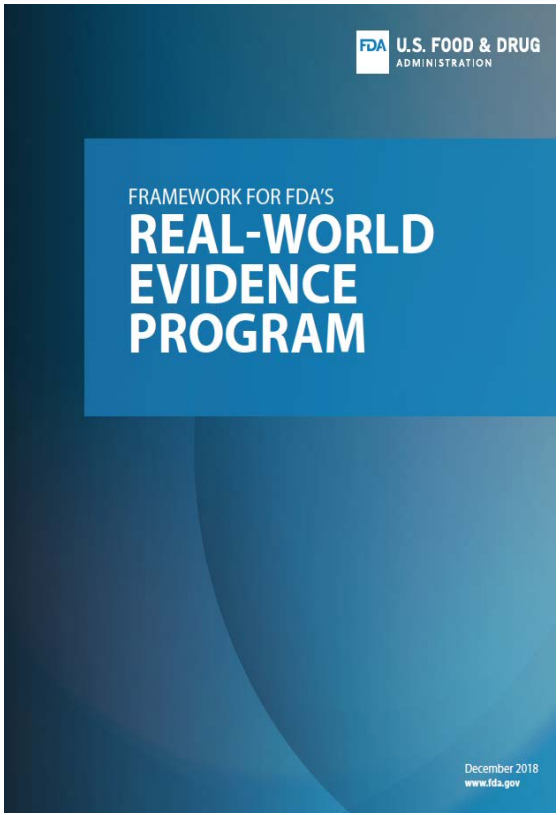
Study designs to generate RWE:

- **Randomized trials including:**
  large simple trials, pragmatic clinical trials
- **Externally controlled trials**
- **Observational studies**

Real-World Evidence Design Spectrum



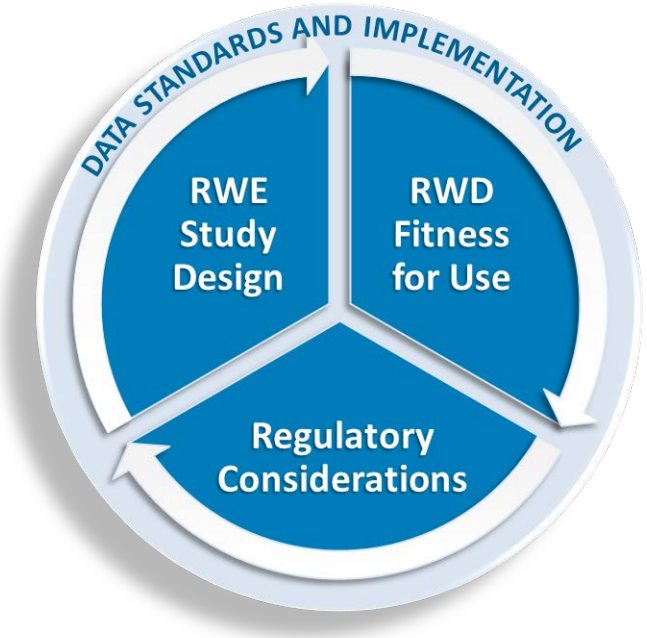
US FDA Real-World Evidence Program



- Outlines FDA's plan to implement the RWE program
- For drug and biological products
- Multifaceted program
  - Internal processes
  - Guidance development
  - Stakeholder engagement
  - Demonstration projects

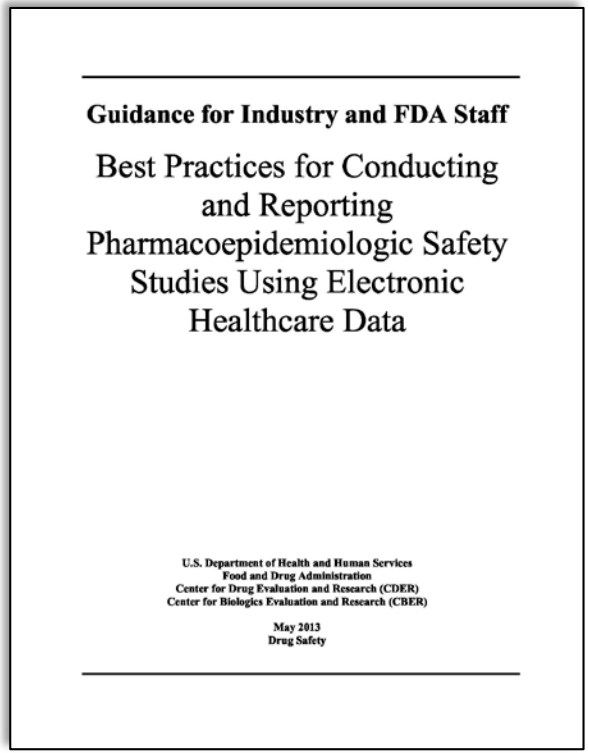
https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RealWorldEvidence/UCM627769.pdf

US FDA Real-World Evidence Program: Guidance



1. **Whether the RWD are fit for use**
2. **Whether the trial or study design can provide adequate scientific evidence to help answer the regulatory question**
3. **Whether the study conduct meets FDA regulatory requirements (e.g., for study monitoring)**

US FDA RWE Existing Guidances (More Coming)

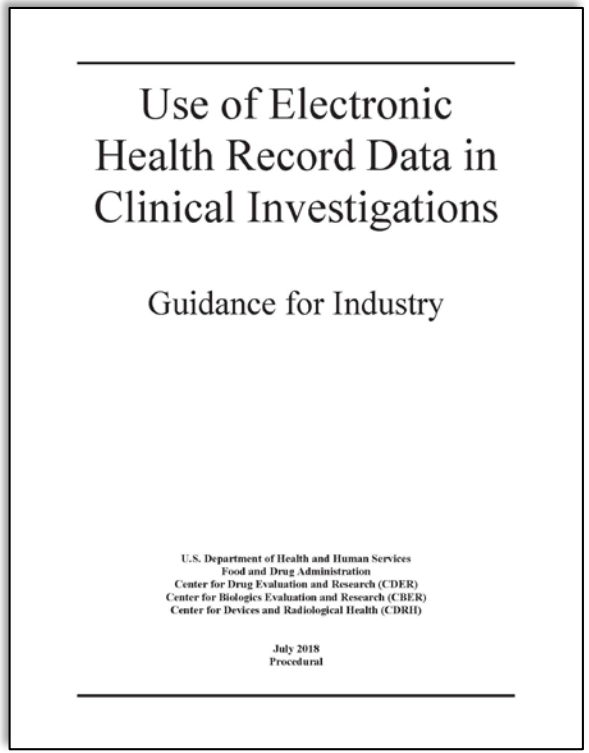


Guidance for Industry and FDA Staff

Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2013
Drug Safety

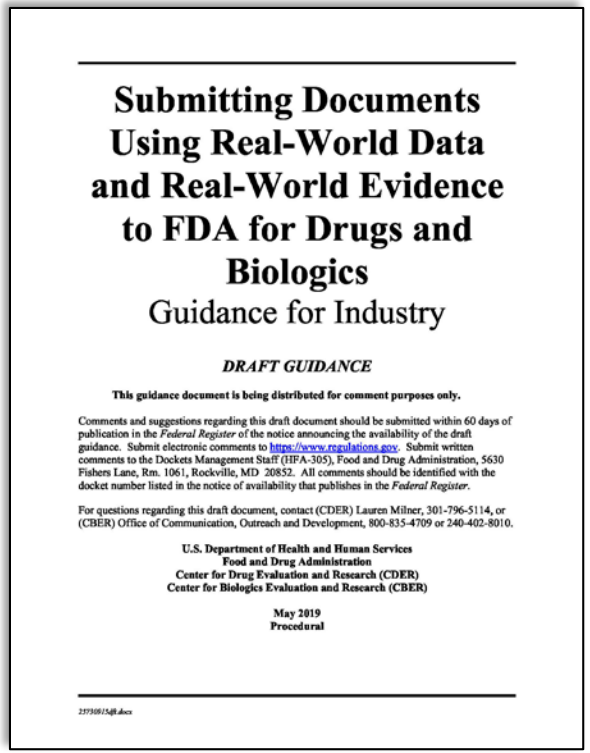


Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

July 2018
Procedural



Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Lauren Milner, 301-796-5114, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2019
Procedural

Substantial Evidence Effectiveness

- **"evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involve on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof."**

  Federal Food, Drug, and Cosmetic Act 1962

- **US Drug Regulation History**

  https://www.fda.gov/AboutFDA/History/ProductRegulation/ucm593465.htm

Adequate and Well-Controlled Study

- **Clear objectives, summary of methods and results**
- **Design permits a valid comparison with a control (concurrent and historical controls)**
- **Adequate selection of patients**
- **Assigning patients to treatment and control groups minimizes bias**
- **Adequate measures to minimize biases on subjects, observers, and analysts**
- **Well-defined and reliable assessment of subjects' responses**
- **Adequate analysis to assess drug results**

Regulations 21CFR314.126

Thank You

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