

Guidance from the FDA on the Use of Real-World Evidence (RWE) in Non-Interventional Studies : A Visual Guide to the Published Resources



The FDA is continually publishing and updating guidance to allow for and encourage the generation of RWE specifically for regulatory decisions. In August 2023, they issued new guidelines for industry: [Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products](#).

These guidelines cover the incorporation of RWE in both pre- and post-market regulatory decisions regarding the effectiveness and safety of a drug and focus primarily on non-interventional studies.

Here we provide a quick visual summary of the resources referenced in that guidance:



Pre-market

Investigational New Drug (IND) applications

RWE can be used to:

- Identify potential control group population for a randomized, controlled trial
- Understand the natural history of diseases and act as historical control arms
- Act as comparator arms in an externally controlled trials

Resources

[Choice of Control Group and Related Issues in Clinical Trials](#)

[Rare Diseases: Natural History Studies for Drug Development Guidance for Industry](#)

[Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products](#)



Post-market

Safety & effectiveness evidence

Early engagement

- If a non-interventional study is to be submitted to support a marketing application, early engagement with the FDA is encouraged.

Resources

[Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products](#)

Protocol & statistical analysis plan (SAP)

- Protocols should be posted on publicly available websites
- Final reports should present all analysis in the SAP; additional analysis should be described as exploratory

Resources

[Postmarketing Studies and Clinical Trials—Implementation of Section 505\(o\)\(3\) of the Federal Food, Drug, and Cosmetic Act Guidance for Industry](#)

[Clinicaltrials.gov](#)

[European Medicines Agency](#)

Transparency

Data sources:

- All data used should be assessed for fit for purpose
- Codes and algorithms to allow replication of analytic approach should be provided and should follow data standards required for submission
- Compliance of electronic health records collected

Resources

[Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products](#)

[Data Standards for Drug and Biological Product Submissions Containing Real-World Data](#)

[Part 11, Electronic Records; Electronic Signatures - Scope and Application](#)

[Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers](#)

[Use of Electronic Health Record Data in Clinical Investigations Guidance for Industry](#)

Reporting

- A log of researchers who have significant involvement in the design or conduct of the study should be retained, including:
 - Researcher's name and affiliations
 - Description of roles or activities performed
 - Qualifications regarding education, training, and experience to perform the proposed study role

Resources

[Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drug and Biological Products](#)

Safety reporting process

- Studies that investigate post-market drug use must comply with post-marketing safety reporting requirements

Resources

[Postmarketing Safety Reporting for Human Drug and Biological Products Including Vaccines](#)

[Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application](#)

[Postmarketing Safety Reporting for Combination Products](#)

Monitoring

Monitoring process

- A risk-based quality management approach to study is encouraged:
 1. Processes critical to human subject protection relevant when additional protocol-specified activities or procedures are included in a non-interventional study
 2. Preventing or mitigating important and likely risks to study quality

Resources

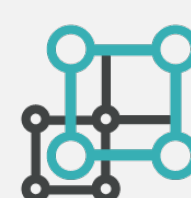
[Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring](#)

[A Risk-Based Approach to Monitoring of Clinical Investigations Questions and Answers](#)

[E6\(R2\) Good Clinical Practice: Integrated Addendum to ICH E6\(R1\)](#)

If you need expert advice on incorporating real world evidence in your regulatory decision applications Broadstreet HEOR can help.

Contact us: info@broadstreetheor.com



BROADSTREET
HEALTH ECONOMICS
& OUTCOMES RESEARCH