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

Resources

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

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

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 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

Monitoring

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.

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