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

Overview of FDA Draft Guidance Issued for Comment

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Why is This Draft Guidance Needed?

- Availability of real-world data (RWD) and evolving analytical techniques to generate real-world evidence (RWE) have created interest within research and medical communities to enhance clinical research and support regulatory decision making
- 21st Century Cures Act (Section 3022) requires FDA to establish a program to evaluate the potential use of RWE to:
  - to help to support the approval of new indications for approved drugs, and;
  - to help to support or satisfy postapproval study requirements

Why is This Draft Guidance Needed?

- CDER and CBER intend to identify and track certain types of submissions using RWE to inform FDA's RWE program under the Cures Act and to help FDA understand the scope and use of RWE submitted to support regulatory decisions regarding safety and/or effectiveness
- FDA hopes that by issuing this guidance, we can maintain a dialogue and mutual learning with external stakeholders on their individual efforts in the RWE space

Terms

- **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

- **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. RWE can be generated through randomized clinical trials or observational studies

Draft Guidance Scope and Goals

- Draft guidance is intended to encourage sponsors and applicants who are using RWD to generate RWE as part of a regulatory submission to FDA to provide information on their use of RWE in a simple, uniform format
- Draft guidance applies to submissions under:
  - Investigational New Drugs (INDs)
  - New Drug Applications (NDAs)
  - Biologic License Applications (BLAs)
- FDA will use this information to internally track submissions

Submissions FDA Will Track

- FDA encourages sponsor and applicants to identify those submissions that involve RWE and are being used to support a regulatory decision regarding safety and/or effectiveness
- Relevant submissions can be in different forms such as a new protocol(s) submitted to an existing IND, a final study report submitted to an NDA or BLA supplement, or a meeting package that discusses the use of RWE
- Relevant submissions may include RWE used in different ways to support study objectives, such as:
  - IND submissions for randomized clinical trials that use RWD to capture clinical outcomes or safety data, including pragmatic and large simple trials
  - New protocols for single arm trials that use RWE as an external control
  - Observational studies that generate RWE intended to support an efficacy supplement
  - Clinical trials or observational studies using RWE to fulfill a postmarketing requirement to further evaluate safety or effectiveness and support a regulatory decision

Submissions FDA Will Not Track

- FDA does not intend to track submissions that are not tied to a specific product or are not being used to used to support a regulatory decision regarding safety and/or effectiveness.
- Submissions that sponsors and applicants need not identify as containing RWE include, for example:
  - Natural history studies for development of a clinical outcome assessment or biomarker
  - Feasibility studies using RWE
  - Studies using RWD to perform exploratory analyses and generate hypotheses

Submission Process

- In cover letter accompanying the submission, sponsor or applicant should identify that submission contains RWE by including requested RWE information
- Information can be provided as a table (see sample table in draft guidance) or otherwise highlighted in the cover letter

Purpose of Using RWE as Part of Submission

- Sponsor or applicant should list the proposed purpose(s) for using RWE in the submission as:
  - Providing evidence in support of the effectiveness or safety for a new product approval
  - Supporting labeling changes for an approved drug, including:
    - Adding or modifying an indication
    - Changes in dose, dose regimen, or route of administration
    - Use in a new population
    - Adding comparative effectiveness information
    - Adding safety information
    - Other labeling change (please specify)
  - Using as part of a postmarketing requirement to support a regulatory decision

Study Design Used for RWE

- Sponsor or applicant should list the clinical study design(s) that includes RWE as part of a submission to support a regulatory decision(s). Examples include:
  - Randomized clinical trial
  - Single arm trial
  - Observational study
  - Other study design

RWD Source Used For Submission

- Sponsor or applicant should list all the RWD source(s) used to generate the RWE. RWD sources can include the following:
  - Data derived from EHRs
  - Medical claims and/or billing data
  - Product and/or disease registry data
  - Other data sources that can inform health status (e.g., data collected from mobile technologies, patient-generated data)

Sample Table

Purpose(s) of Using RWE as Part of the Submission (Select all that apply)
☐ To provide evidence in support of effectiveness or safety for a new product approval
☐ To provide evidence in support of labeling changes for an approved drug, including:
☐ Add or modify an indication
☐ Change in dose, dose regimen, or route of administration
☐ Use in a new population
☐ Add comparative effectiveness information
☐ Add safety information
☐ Other labeling change. Specify:
☐ Use as part of a postmarketing requirement to support a regulatory decision
Study Design(s) Using RWE (Select all that apply)
☐ Randomized clinical trial
☐ Single arm trial
☐ Observational study
☐ Other study design. Specify:
RWD Source(s) Used to Generate RWE (Select all that apply)
☐ Data derived from electronic health records
☐ Medical claims and/or billing data
☐ Product and/or disease registry data
☐ Other data source. Specify:

Additional Information

Submitting Comments on Draft Guidance

- You may submit comments at any time
- Submit comments electronically through Federal eRulemaking Portal (www.regulations.gov)
- Submit written comments to Documents Management Staff at FDA
- More information on submitting comments can be found in the Notice of Availability for this draft guidance

Resources

- FDA Website (https://www.fda.gov/ScienceResearch/SpecialTopics/RealWorldEvidence/default.htm)
- Framework for FDA's Real-World Evidence Program (www.fda.gov/scienceresearch/specialtopics/realworldevidence/default.htm)

Questions

- Email: CDEROMP@fda.hhs.gov
- Phone: 301-796-2500


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