FDA Funding Opportunity Announcement: “Exploring the use of Real-World Data to Generate Real-World Evidence in Regulatory Decision-Making (U01) Clinical Trials Optional”

Article By

Erica Abshez Moran
Chanda A. Miller
Michael C. Zogby

Faegre Drinker
Faegre Drinker on Products

Related Practices & Jurisdictions

- Biotech, Food, Drug
- Environmental, Energy & Resources
- All Federal

Friday, April 3, 2020

The U.S. Food & Drug Administration (FDA) has released a Funding Opportunity Announcement (FOA) titled “Exploring the use of Real-World Data to Generate Real-World Evidence in Regulatory Decision-Making (U01) Clinical Trials Optional.” The FOA relates to the FDA’s RWE Framework published in December 2018, and is issued
“to support research projects that examine real-world data (RWD), real-world evidence (RWE), and related issues such as data analytics, the use of digital health tools, and innovative trial designs utilizing healthcare settings.”

The FOA specifically seeks the submission of proposed projects that explore the utility of RWD and RWE in the generation of evidence supporting regulatory approval of new indications of use or post-approval study requirements for approved medicines. The FDA defines RWD as “data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.” RWE is “clinical evidence about the use and potential benefits or risks of a medical product derived from analysis of RWD.”

The FOA encourages innovative approaches to further explore the use of RWD while making sure that scientific evidence supporting marketing approvals meets the FDA’s high evidentiary standards. By way of example, and as discussed in more detail below, the FDA is interested in projects that accomplish the following:

- Explore and conduct innovative clinical trials using RWD
- Explain ways to address challenges to using RWD in research studies
- Explore methods to address challenges of using RWD in research studies
- Evaluate reliability considerations around the use of RWD.

The FDA “is particularly interested in projects that compare use of RWD and generation of RWE with more traditional approaches and methods for data collection and evidence generation.”

The deadline for submissions is May 11, 2020.

**Background Regarding RWE Framework and Issuance of the FOA**

The FDA issued the FOA “to address a diversity of topics related to FDA’s RWE Program ... and to enable FDA to assess and validate the potential utility of RWD and RWE.” In December 2018, the FDA published its strategic RWE Framework, which outlined the FDA’s multifaceted RWE program to explore the potential regulatory uses of RWD and RWE. As acknowledged in the RWE Framework, data collected in health care systems, referred to as “clinical practice data,” has the potential to be used in clinical trials submitted for regulatory purposes. Traditional clinical trials that have been used historically to support regulatory submissions increase demand for resources and burden sites, clinical investigators, study personnel and trial participants.

The RWE Framework recognizes that using RWD sources in randomized trials, as well as innovative trial designs that could take advantage of the clinical practice infrastructure, have the potential to improve efficiencies in clinical development of therapeutics. The RWE Framework outlines the potential use of “pragmatic clinical trials” that more closely resemble routine clinical practice to gather evidence in support of regulatory approval; such trials “often rely on RWD and have the potential to generate RWE.”
The RWE Framework also recognizes that health data from medical claims, electronic health records (EHRs), data captured using digital tools, data from registries, and other sources should be further explored for their potential utility in producing or augmenting RWE regarding the safety and effectiveness of a product using non-interventional (observational) study designs. The FDA describes such observational studies as “non-interventional clinical study designs that are not considered clinical trials,” and provides the examples of natural history studies for diseases, studies in which treatment is determined in clinical practice, and variables and outcomes of interest derived from RWD.

**Scope of the FOA**

The FDA states that the “primary objective of this [FOA] announcement is to encourage a variety of projects exploring the utility of RWD and RWE in evidence generation.” The FDA notes that the scope of the FOA:

“...includes, but is not limited to, projects that focus on the following:

- Exploring and conducting innovative clinical trials, or parts of clinical trials, utilizing RWD, such as trials that incorporate ‘pragmatic’ elements and utilize RWD to generate RWE.

- Exploring and elucidating ways and methods to address challenges to utilizing RWD in research studies, such as data processing, standardization, and analytics.

- Exploring the use of innovative technologies, such as digital health tools, predictive algorithms, and sensors to provide reliable data.

- Designing and conducting pilot projects and collaborations that further the development of a shared understanding and clarity on key components of trials utilizing RWD, including intervention selection, outcome measurement, feasibility of blinding, statistical techniques, and data integrity.

- Determining and evaluating endpoints (or composite endpoints) that can be captured reliably from RWD.

- Evaluating reliability considerations around the use of RWD, such as methodologies to assist in the standardization and analyses of the typically fragmented and variable RWD sources.”

The FDA welcomes a variety of project types under the FOA, “including clinical trials, ancillary studies in parallel to planned or ongoing clinical trials, and other clinical study types.” The FDA states that it “is particularly interested in projects that compare use of RWD and generation of RWE with more traditional approaches [and] methods for data collection and evidence generation.”

**Details Regarding the FOA Application Process**

The FDA states that it “is anticipated that up to 2 awards will be made, not to exceed $2 million in total cost . . . per award.”
The FOA contains detailed guidance regarding the application process and criteria, but interested applicants should be aware of the following:

- The award will result in a Cooperative Agreement with the FDA, with substantial post-award involvement from FDA scientific or program staff in assisting, guiding, coordinating, or participating in project activities.
- The maximum proposed project period is three years.
- The application budget should not exceed $4 million in total costs in each of years 1 through 3.

The FDA explains that applications “will be evaluated for scientific and technical merit by (an) appropriate Objective Review Committee.” This committee will consider each of the following review criteria in the determination of scientific merit, in addition to other listed review considerations:

- **“Significance (20 Points)"** Does the project address an important problem or a critical barrier to progress in the field? Is the prior research that serves as the key support for the proposed project rigorous? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?”

- **“Investigator(s) (20 Points)"** Are the PD(s)/PI(s), collaborators, and other researchers well suited to the project? If Early Stage Investigators or those in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?”

- **“Innovation (25 Points)"** Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?”

- **“Approach (25 Points)"** Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Have the investigators included plans to address weaknesses in the rigor of prior research that serves as the key support for the proposed project? Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed? Have the investigators presented
adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects? If the project involves human subjects and/or FDA-defined clinical research, are the [sic] plans to address 1) the protection of human subjects from research risks, and 2) inclusion (or exclusion) of individuals on the basis of sex/gender, race, and ethnicity, as well as the inclusion or exclusion of individuals of all ages (including children and older adults), justified in terms of the scientific goals and research strategy proposed?”

- “Environment (10 Points) Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed? Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?”

The submission deadline is **May 11, 2020**, by 11:59 PM Eastern Daylight Time. The earliest start date for awarded projects is September 2020.

© 2021 Faegre Drinker Biddle & Reath LLP. All Rights Reserved.

National Law Review, Volume X, Number 94