Natural History Studies and Registries in the Development of Rare Disease Treatments

Hybrid Public Meeting
May 13, 2024

FDA and NIH Resources

General Information/ Programs

FDA Programs

CDER's Accelerating Rare disease Cures (ARC) Program

ARC's mission is to drive scientific and regulatory innovation and engagement to accelerate the availability of treatments for patients with rare diseases. Managed by the Center for Drug Evaluation and Research (CDER) Rare Diseases Team, the ARC Program brings together CDER's collective expertise and activities to provide strategic overview and coordination of CDER's rare disease activities. Those involved in the design and conduct of rare disease clinical trials will find many helpful resources on the ARC Program website, including an easily accessible list of relevant guidance documents organized by topic and links to recordings of past meetings and workshops.

- FDA CDER & JHU CERSI Workshop | Addressing Challenges in the Design and Analysis of Rare Disease Clinical Trials: Considerations and Tools - May 2-3, 2023
- FDA and Duke-Margolis Public Workshop: Translational Science in Drug Development: Surrogate Endpoints, Biomarkers, and More - May 24-25, 2022

Rare Disease Endpoint Advancement (RDEA) Pilot Program

The RDEA Pilot Program is a Prescription Drug User Fee Act (PDUFA) VII program that supports novel endpoint efficacy development for drugs that treat rare diseases. FDA welcomes RDEA proposals related to any eligible novel endpoint for a rare disease. The proposed endpoint must be a novel efficacy endpoint intended to establish substantial evidence of effectiveness for a rare disease treatment. Sponsors who do not yet have an active development program but have, or are initiating, a natural history study where the proposed endpoint is intended to be studied are eligible for the program. Any sponsor whose RDEA proposal is admitted into the RDEA pilot program will have the opportunity for increased interaction with the FDA to discuss issues associated with their proposed rare disease novel endpoint. For each RDEA proposal that FDA admits into the pilot program, the agency will conduct an initial meeting and up to three follow-up meetings.

Advancing Real-World Evidence (RWE) Program

The Advancing RWE Program is a PDUFA VII program that seeks to improve the quality and acceptability of RWE-based approaches in support of new intended labeling claims, including approval of new indications of approved medical products or to satisfy post-approval study requirements. Sponsors who are selected into the Program are provided the opportunity to meet with Agency staff—before protocol development or study initiation—to discuss the use of RWE in medical product development.

Critical Path Innovation Meetings (CPIM)

The CPIM is a means by which FDA CDER and investigators from industry, academia, scientific consortia, patient advocacy groups, and government can communicate to improve efficiency and success in drug development. The goals of the CPIM are to discuss a methodology or technology proposed by the meeting requester and for CDER to provide general advice on how this methodology or technology might enhance drug development.

NIH National Center for Advancing Translational Sciences (NCATS) Programs

NCATS' Impact on Rare Diseases

NCATS is the heart of rare diseases research at NIH. We speed the development of new rare disease treatments by focusing on approaches that can address more than one disease at a time.

Genetic and Rare Diseases (GARD) Information Center

Looking for reliable information on rare diseases? GARD is a public health resource that provides free access to easy-to-understand information in English and Spanish. Information specialists are available to answer questions and provide support through phone and email.

Therapeutics for Rare and Neglected Diseases (TRND)

The goal of the TRND program is to encourage and speed the development of new treatments for rare and neglected diseases. The program is designed to advance the entire field of therapeutic development by supporting scientific and technological innovations to improve success rates in the crucial preclinical stage of development.

Share Your Resources with the NCATS Toolkit!

The NCATS Toolkit needs your help to educate and empower patient groups!
We are looking for resources intended to help patient group leaders get started with research. Selected resources will be included in the NCATS Toolkit for Patient-Focused Therapy Development website and share across the rare disease patient community. Explore the NCATS Toolkit.

Funding Opportunities

FDA Funding

Funding Opportunities for Rare Diseases at FDA

This resource on the CDER ARC webpage contains links to a number of funding opportunities at FDA. These include opportunities from the Office of New Drugs, the Office of Regulatory Science and Innovation, the Office of Minority Health and Health Equity, the Office of Orphan Products Development, and others. For example, the Office of Orphan Products Development Natural History Studies Grant Program supports efficient and innovative natural history studies that advance medical product development in rare diseases/conditions with unmet needs. These studies can help at every stage of product development, such as identifying the patient population, identifying or developing clinical outcome assessments and biomarkers, and when appropriate, serving as external controls. This program is intended to fund well-designed, protocol-driven natural history studies with high quality and interpretable data elements that address knowledge gaps, support clinical trials and advance rare disease medical product development.

NIH Funding

NEW Funding Opportunity: Rare Diseases Clinical Research Consortia for the Rare Diseases Clinical Research Network

The objective of this Notice of Funding Opportunity (NOFO) is to invite new and renewal applications for the Rare Diseases Clinical Research Consortia (RDCRC) that comprise the Rare Diseases Clinical Research Network (RDCRN). Read more about this NOFO.

Rare Disease Conference Grant

As mandated in the Rare Diseases Act of 2002, our Division of Rare Diseases Research Innovation supports scientific workshops and symposia to identify research opportunities for rare diseases.

Specifically, we seek applications for conferences, meetings and workshops that:

- Include the active participation of relevant patient support groups in the meeting planning
- Leverage recent breakthroughs in research or support the advancement of new research endeavors

- Set clinical practice or guidelines

Refer to the current funding opportunity (**PA-24-141**) for application and submission information.

Clinical Trial Readiness (CTR) for Rare Diseases, Disorders and Syndromes

Clinical trials are key to developing and evaluating new treatments for rare diseases. Scientists, however, often do not have enough information about the symptoms and biology of rare diseases to design clinical trials. We worked with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development to create the Clinical Trial Readiness (CTR) for Rare Diseases, Disorders and Syndromes grants to address some of the obstacles scientists face, including gaps in our understanding of a rare disease's natural history and a lack of suitable biomarkers or clinical outcome measures. Learn more about funding opportunities.

Clinical Trial Readiness for Rare Neurological and Neuromuscular Diseases

This NOFO invites researchers to submit applications for support of clinical studies that address critical needs for clinical trial readiness in rare neurological and neuromuscular diseases. These studies should result in clinically validated biomarkers and clinical outcome assessment measures appropriate for use in upcoming clinical trials. Through the support of trial readiness studies, National Institute of Neurological Disorders and Stroke expects to enhance the quality and increase the likelihood of success of clinical trials in these rare diseases.

Select FDA Guidance Documents[1]

Cross-Cutting

Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products (Draft Guidance, December 2019)
https://www.fda.gov/media/133660/download

Rare Diseases

Rare Diseases: Natural History Studies for Drug Development: Draft Guidance for Industry (Draft Guidance, March 2019)
https://www.fda.gov/media/122425/download

Rare Diseases: Considerations for the Development of Drugs and Biological Products (Final Guidance, December 2023)
https://www.fda.gov/media/119757/download

Real World Data and Real-World Evidence

Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products (Final Guidance, August 2023)
https://www.fda.gov/media/171667/download

Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products (Final Guidance, December 2023)
https://www.fda.gov/media/154449/download

Externally Controlled Trials

Considerations for the Design and Conduct of Externally Controlled Trials for Drug and Biological Products (Draft Guidance, February 2023)
https://www.fda.gov/media/164960/download

[1] For the most recent versions of guidance documents, please see the FDA guidance web page https://www.fda.gov/regulatory-information/search-fda-guidance-documents