Rare Disease Endpoint Advancement Pilot Program Workshop: Novel Endpoints for Rare Disease Drug Development

Virtual Public Workshop
June 7-8, 2023

Agenda

Event Background and Objectives

Although the Orphan Drug Act defines a rare disease as a disease or condition that affects less than 200,000 people in the United States, collectively these conditions impact an estimated 30 million people in the United States. Significant unmet treatment needs remain for many of those living with one of the 7,000-10,000 known rare diseases. Advancing the development of treatments for these individuals is critical, as many rare diseases are progressive, considered serious or life-threatening, and nearly half affect children. However, traditional clinical trials are challenging to conduct for therapies targeting small populations. Additionally, many rare disease communities have significant heterogeneity of disease presentation or poorly characterized natural history, further complicating clinical trials for products in the rare disease space. Well-developed efficacy endpoints, especially those that could apply to other rare diseases with similar manifestations, can help drive the general advancement of rare disease drug development.

In order to facilitate rare disease drug development, and as part of a performance goal and requirement related to the FDA User Fee Reauthorization Act of 2022 and the Food and Drug Omnibus Reform Act of 2022 (FDORA), respectively, the U.S. Food and Drug Administration (FDA) has established a pilot program for supporting the development of efficacy endpoints for rare disease treatments. The new Rare Disease Endpoint Advancement (RDEA) Pilot Program offers additional engagement opportunities with the FDA to sponsors of rare disease development programs that meet specific criteria. The PDUFA [Prescription Drug User Fee Act] Reauthorization Performance Goals and Procedures Fiscal Years 2023-2027, known as the PDUFA VII Commitment Letter, contains detailed requirements for participating in the program and outlines the FDA's commitment to conduct up to three public workshops by the end of fiscal year 2027 to discuss topics relevant to endpoint development for rare diseases. In addition, FDORA requires the conduct of up to three public workshops to discuss topics relevant to the development of endpoints for rare diseases by September 30, 2026. This public workshop is intended to meet a performance goal under PDUFA VII and a requirement under FDORA.

The Duke-Margolis Center for Health Policy, under a cooperative agreement with the FDA, is convening this two-day event that will illustrate challenges and opportunities in rare disease endpoint development, introduce attendees to the RDEA Pilot Program, and highlight how the RDEA Pilot Program is structured to support sponsors who may encounter challenges with endpoint development. Attendees will hear from a variety of speakers about rare disease endpoint examples to gain a better understanding of endpoint development challenges and opportunities. Workshop programming will also facilitate a shared understanding of the RDEA Pilot Program's purpose and structure, including key features of the program such as sponsor disclosure requirements. Learnings from other FDA pilot programs that share programmatic features with the new RDEA Pilot Program will also be discussed. This event is intended to serve as a resource for sponsors and other attendees interested in learning how they might engage with the FDA through this new program.

Day 1: Rare Disease Endpoint Development Challenges and Opportunities

June 7, 2023
1:00 pm – 5:00 pm ET

1:00 pm **Welcome and Overview**
Mark McClellan, Duke-Margolis Center for Health Policy

1:10 pm **Opening Remarks from FDA**
Peter Stein, U.S. Food and Drug Administration
Celia Witten, U.S. Food and Drug Administration

1:25 pm **Session 1: Considerations in Developing Rare Disease Endpoints: Digital Health Technology (DHT)**
Objective: In this session focused on exploring an example of an endpoint that involves use of a DHT, attendees will learn about relevant endpoint development challenges and opportunities. The session will end with a panel discussion where the panelists will share thoughts on opportunities and challenges with developing a rare disease endpoint that involves the use of DHT.

Topic: Actimyo/95th Stride Velocity

Moderator: Michelle Campbell, U.S. Food and Drug Administration

Presentation: Laurent Servais, University of Oxford

Panel: Damien Eggenspieler, Sysnav
Hussein Ezzeldin, U.S. Food and Drug Administration
Ami Mankodi, U.S. Food and Drug Administration
Leonard Sacks, U.S. Food and Drug Administration
Laurent Servais, University of Oxford

2:15 pm **Session 2: Considerations in Developing Rare Disease Endpoints: Biomarker Surrogate Endpoints**
Objective: In this session focused on exploring an example of a biomarker surrogate endpoint, attendees will learn about relevant endpoint development challenges and opportunities. The session will end with a panel discussion where the panelists will share thoughts on opportunities and challenges with developing a rare disease endpoint that includes a biomarker as a surrogate endpoint.

Topic: Proteinuria in adults with primary immunoglobulin A nephropathy (IgAN)

Moderator: Michael Pacanowski, U.S. Food and Drug Administration

Presentation: Patrick Nachman, University of Minnesota

Panel: Patrick Nachman, University of Minnesota
Lynley K. Thinnes, Travere
Aliza Thompson, U.S. Food and Drug Administration

3:05 pm **Break**

3:20 pm **Session 3: Considerations in Developing Rare Disease Endpoints: Clinical Outcome Assessment (COA)**

Objective: In this session focused on exploring examples of endpoints that include a COA, attendees will learn about relevant endpoint development challenges and opportunities. The session will end with a panel discussion where the panelists will share thoughts on opportunities and challenges with developing a rare disease endpoint that includes a COA.

Topic: Multi-luminance mobility test (MLMT) for RPE65-mediated inherited retinal dystrophy

Moderator: Naomi Knoble, U.S. Food and Drug Administration

Presentation: David Rousso, Spark Therapeutics

Panel: Yuqun "Abigail" Luo, U.S. Food and Drug Administration
Lindsey Murray, Critical Path Institute
David Rousso, Spark Therapeutics
Lei Xu, U.S. Food and Drug Administration

4:10 pm **Session 4: Considerations in Developing Rare Disease Endpoints: Multiple Endpoints, with a Focus on Multicomponent Endpoints**

Objective: In this session focused on discussing the use of multiple endpoints in rare disease drug development, attendees will learn about relevant multiple endpoint development challenges and opportunities, with a focus on multicomponent endpoints. The session will end with a panel discussion where the panelists will share thoughts on opportunities and challenges with such endpoint development as it relates to the RDEA program.

Moderator: Laura Lee Johnson, U.S. Food and Drug Administration

Presentations: Kathleen Fritsch, U.S. Food and Drug Administration
Lili Garrard, U.S. Food and Drug Administration
Kevin Weinfurt, Duke University, U.S. Food and Drug Administration

Panel: Kathleen Frisch, U.S. Food and Drug Administration
Lili Garrard, U.S. Food and Drug Administration
Naomi Knoble, U.S. Food and Drug Administration
Kevin Weinfurt, Duke University, U.S. Food and Drug Administration

4:55 pm **Closing Remarks**
Mark McClellan, Duke-Margolis Center for Health Policy

5:00 pm **Adjournment**

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Day 2: RDEA Pilot Program Orientation

June 8, 2023
1:00 pm – 4:30 pm ET

1:00 pm **Welcome and Overview**
Mark McClellan, Duke-Margolis Center for Health Policy

1:10 pm **Session 5: RDEA Pilot Program Overview**
Objective: During this session, the FDA will orient workshop attendees to the new RDEA Pilot Program. Presentations will cover a high-level introduction to the program, including program structure and intended goals.

Presentations: Kerry Jo Lee, U.S. Food and Drug Administration
Julienne Vaillancourt, U.S. Food and Drug Administration

1:40 pm **Session 6: RDEA Pilot Program – Process Overview**
Objective: Attendees will learn about the RDEA program proposal process in this session. Presentations in this session will cover a high-level overview of the process for building and submitting a proposal and engaging through the pilot program.

Presentations: Mary Jo Salerno, U.S. Food and Drug Administration
Julienne Vaillancourt, U.S. Food and Drug Administration

2:10 pm **Session 7: Elements of RDEA Proposals and Meetings**
Objective: In this session, attendees will learn about the required elements for a complete RDEA proposal and meeting package. Speakers will also describe available resources to assist sponsors with the development of a complete RDEA proposal and meeting package.

Presentation: Sepideh Haghpanah, U.S. Food and Drug Administration

2:40 pm **Session 8: RDEA Pilot Program Q&A**
Objective: The session will consist of a brief Q&A to answer previously submitted questions about the RDEA program as well as clarifying questions on the information presented on the RDEA program during sessions 5, 6, and 7.

Moderator: Nancy Allen Lapointe, Duke-Margolis Center for Health Policy

Panel: Sepideh Haghpanah, U.S. Food and Drug Administration
Stefanie Kraus, U.S. Food and Drug Administration

Kerry Jo Lee, U.S. Food and Drug Administration
Mary Jo Salerno, U.S. Food and Drug Administration
Julienne Vaillancourt, U.S. Food and Drug Administration

3:05 pm **Break**

3:20 pm **Session 9: Experiences and Lessons Learned from Other Meeting Pilot Programs**

Objective: This session will include a presentation and discussion about lessons learned from other PDUFA pilot meeting programs with features similar to the newly established RDEA Pilot Program. The session will provide an overview of the Complex Innovative Trial Design (CID) and Model-Informed Drug Development (MIDD) programs and experience to date, including discussion of disclosure agreement aspects of the CID meeting program. The session will conclude with a brief Q&A to answer previously submitted questions as well as clarifying questions on the PDUFA pilot program experience.

Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Presentations: Rajanikanth Madabushi, U.S. Food and Drug Administration
Dionne Price, U.S. Food and Drug Administration

Panel: Rajanikanth Madabushi, U.S. Food and Drug Administration
Dionne Price, U.S. Food and Drug Administration
Susan Warner, Eli Lilly and Company

4:00 pm **Session 10: Public Comments**

Objective: This public comment period provides an opportunity for sponsors and other relevant stakeholders to share thoughts and questions about the RDEA Pilot Program, how the program may address stakeholder needs, and reflections on potential remaining gaps in support for rare disease endpoint development.

4:25 pm **Closing Remarks**

Mark McClellan, Duke-Margolis Center for Health Policy

4:30 pm **Adjournment**

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