Advancing the Development of Therapeutics Through Rare Disease Patient Community Engagement

Virtual Public Meeting
December 14, 2023

Meeting Summary

U.S. FOOD & DRUG ADMINISTRATION

Center for Drug Evaluation and Research

Duke Margolis Institute for Health Policy

EXECUTIVE SUMMARY

Many rare diseases are progressive, considered serious or life-threatening, and nearly half affect children. With only a small portion of rare diseases having an approved treatment, advancing the development of treatments for people living with rare disorders is critical. However, factors such as small patient populations and wide variation in disease symptoms and progression create significant challenges for rare disease drug development.

Patient input can help inform researchers, sponsors, and regulators about meaningful clinical trial endpoints, the feasibility of different trial designs, and aspects of therapeutic context such as level of risk tolerance within patient populations where the disease may not be well characterized or widely known. There are a number of ongoing activities at the U.S. Food and Drug Administration (FDA) to advance meaningful patient engagement, such as Patient Listening Sessions and Patient-Focused Drug Development (PFDD) meetings. This report's Appendix contains a more detailed list of FDA initiatives and meeting programs related to rare disease drug development. These opportunities for engagement (among others) can serve as important starting points for furthering sponsor and regulator understanding of patient communities' priorities and experiences, which can in turn inform clinical trial designs and ultimately generate robust evidence to support a marketing application. However, further opportunities to enhance meaningful interactions between patients, regulators, sponsors, and researchers can be explored to better support rare disease drug development.

As part of a requirement in the Food and Drug Omnibus Reform Act of 2022 (FDORA), FDA in cooperation with the Duke-Margolis Institute for Health Policy convened a one-day virtual public meeting to discuss approaches and opportunities for engaging patients, rare disease experts, and experts in small population studies during rare disease drug development. The meeting also focused on how best to collect and incorporate patient input and lived experiences throughout the drug development process.

The following key themes emerged from participant discussion throughout the workshop:

1. Regulator and sponsor activities can benefit from engagement with patient communities before the trial design process begins as well as throughout the drug development process.
2. Patient engagement activities can help support clinical trial designs that reflect patient needs and priorities and that minimize the burden of trial participation.
3. Communication in all directions between patients, sponsors, rare disease experts, and regulators can better support the rare disease drug development process.

Introduction and Background

The Orphan Drug Act defines a rare disease as a condition that affects fewer than 200,000 people in the United States. Altogether, rare diseases affect more than 300 million people worldwide, including around 30 million people in the United States. Yet, the vast majority of rare diseases have no FDA-approved treatment. Small patient population size, poorly understood natural history, heterogeneity of symptoms and disease progression, and difficulties obtaining timely diagnoses, among other factors, can make drug development challenging for many rare disease populations.

Given these factors, a collaborative approach to drug development that includes meaningful input from patients and other experts at numerous points throughout the process can support more efficient and effective rare disease drug development activities. Opportunities for meaningful patient engagement exist throughout the drug development process as a product moves from the discovery phase to pre-clinical studies, clinical trials, and ultimately to a marketing application for FDA review.

Engaging with patient communities and other experts early in the process, and on an ongoing basis, can help all participants in drug development understand what endpoints matter most to patients and caregivers, what clinically meaningful improvement entails, and other components essential to drug development. Engagement may also inform FDA's regulatory advice and decision making, as considerations of patient burden, available treatment options, and evaluation of side effects are taken into account in the development and review of drugs and biologics for rare diseases.

Several mechanisms exist for rare disease communities to share their perspectives on drug development with FDA, especially early in the process, such as Patient-Focused Drug Development (PFDD) meetings and Patient Listening Sessions. Additional interactions through scientific meetings, working groups, public-private partnerships, and research roundtables bring together multidisciplinary groups to inform rare disease drug development and help advance regulatory science. Patient groups can organize such meetings and invite or inform regulators to further FDA's familiarity with a given rare disease topic. In addition to informing FDA about key considerations for rare disease drug development, these types of convenings can serve as a starting point for pre-clinical research and discussions about clinical trial design and the inclusion of patient experience data (PED). Activities that take into account patient priorities and other relevant condition-specific expertise help generate rigorous, robust evidence to research questions.

Information collected in these ways – including PED – is consistently referenced by FDA during meetings with sponsors and in reviewing applications. FDA encourages sponsors to engage with the Agency early and often during rare disease drug development. Patient input, as well as researcher and clinician expertise, is particularly valuable in informing how the sponsor approaches scientific discussions concerning trial protocols, trial design, and clinical endpoints. When a sponsor submits an application, FDA reviewers may rely on PED to understand therapeutic context and patient priorities, ultimately helping to inform the benefit-risk analysis. FDA has taken internal steps to ensure that review staff are aware of PFDD meetings, Patient Listening Sessions, and other interactions that provide PED to inform the review process.

FDA has also created and continues to develop policies, programs, and public resources that support meaningful engagement with external communities and experts during rare disease drug development. Examples include CDER's Accelerating Rare disease Cures (ARC) Program, Support for clinical Trials Advancing Rare disease Therapeutics (START) Pilot Program, and the recently announced CDER's Genetic Metabolic Diseases Advisory Committee (GeMDAC). More examples can be found in this report's Appendix.

Meeting Objectives

The Duke-Margolis Institute for Health Policy and the FDA, through a cooperative agreement, convened a one-day virtual public meeting to discuss approaches and opportunities for engaging patients, patient advocacy groups, rare disease or condition experts, and experts on small population studies during the drug development process for rare diseases. This meeting was convened to facilitate rare disease drug development, and as part of a requirement in the Food and Drug Omnibus Reform Act of 2022 (FDORA). The meeting also focused on how to best understand patients' experiences living with a rare disease and how to incorporate those experiences and patient priorities throughout the drug development process. This included understanding patient perspectives on the burden of their condition and any existing treatment options, as well as how their current health status and risk of disease progression may impact willingness to accept risks from treatment side effects.

It is critical that discussions on enhancing meaningful patient and expert engagement continue beyond this meeting. The opportunities for improvement and recommendations discussed during the meeting (and submitted to the associated docket) are summarized in this report and can be used to inform ongoing efforts that support meaningful engagement amongst all those involved in the rare disease drug development process.

Developments, Opportunities for Improvement, and Recommendations Across the Rare Disease Drug Development Process

Through presentations, case studies focused on stakeholder engagement, and several panel discussions, speakers explored common challenges and key considerations in rare disease drug development. Speakers also shared recommendations for improving communication and collaboration between patients, regulators, sponsors, and other collaborators throughout rare disease drug development.

Important developments, opportunities for improvement, and recommendations shared throughout meeting discussions and those submitted via comments to the public docket (FDA-2023-N-4718) for this event are captured below.

Discovery and Pre-Clinical Stages – Researchers discover a potential therapeutic and conduct initial non-clinical studies to determine whether it should be tested in people.

Developments

In discussions regarding the discovery and pre-clinical stages of drug development, speakers representing patient groups noted that patient communities have helped to guide researchers toward drug development targets that matter most to patients. Several speakers cited examples in which patient communities have helped facilitate connections between academic experts and potential sponsors through activities such as desktop research and cold-calling or cold-emailing. Other representatives from patient communities cited successes stemming from increased involvement in pre-clinical research, with concrete contributions to research infrastructure, such as establishing laboratory-based genetic models.

FDA speakers noted that, in an effort to help rare disease communities navigate drug development, the FDA has created centralized public resources to help demystify the drug development and regulatory process particularly for those newer to the space. These include, for example, the ARC Program resources available on FDA's website and the CBER RegenMedEd and Town Hall webinar series on cell and gene therapies. These resources may be used by patient communities and others involved in the design and conduct of rare disease clinical trials.

Opportunities for Improvement

While patient groups can have an important impact by participating in these early stages of drug development, it can be challenging, especially for newer or smaller groups with limited resources. Several speakers representing patient groups mentioned supporting the development of patient-reported outcome (PRO) instruments and other clinical outcome assessments (COAs) as priority activities for their organizations. However, they also agreed it can be a costly and lengthy process. One such speaker noted that Critical Path Innovation Meetings (CPIM) with FDA can be a productive early-stage step for patient communities seeking to receive feedback on new approaches in drug development – though the particular example cited resulted in a disappointing disconnect when the proposed endpoint did not gain traction at that time.

Recommendations

Speakers suggested that engagement between rare disease communities, sponsors, and regulators should begin as early as possible. Though FDA cannot discuss specific products under development with anyone but the sponsor, patient communities can meet with regulators to help such regulators become more familiar with the key considerations and challenges associated with their rare condition. It was also recommended that patient groups think strategically and early about the desired outcomes of a listening session or PFDD meeting with FDA and other stakeholders. This planning may help to determine the best timing for and specific goals of these meetings, which can help identify clinically meaningful trial endpoints.

Clinical Research Stages – Clinical trials and other studies are conducted in humans to test whether the investigational product is safe and effective for its proposed indication.

Developments

Speakers again emphasized that in recent years, more sponsors have been increasingly engaged with patient groups, which has helped generate transformative therapies for some rare conditions and generally has made clinical trials more accessible to potential participants. Presentations during the meeting and comments from the docket both noted that

development of innovative trial designs can help to balance the need for rigorous clinical trials with the challenges of small populations inherent to rare disease drug development. Representatives from sponsor companies and patient communities suggested that reducing the size of the placebo group tends to help increase recruitment and decreases dropout rates, as receiving a potentially effective treatment is often a priority for trial participants. FDA staff possess expertise in small population trial designs and actively engage with experts developing innovative ways to design effective trials with small populations. One developing novel trial design – the small "n" sequential multiple assignment randomized trial (snSMART) - was presented during the meeting. Although promising, innovative designs like snSMART need to be rigorously tested before real-world implementation and may not be appropriate for all rare disease drug development programs.

Opportunities for Improvement

Designing and executing a clinical trial for a rare disease therapeutic that generates robust evidence while balancing what's feasible for patients and caregivers remains challenging. Speakers discussed a tension between sponsors' desire to measure numerous outcomes with a high degree of precision and patients' and caregivers' need to minimize the burden of clinical trial participation – a challenge sponsors and caregivers alike described. Patients and caregivers also described the daily challenges associated with living with, or caring for someone with, a rare disease and stated that participating in a clinical trial can add to that burden. Trial participation may also complicate or disrupt existing care strategies. In many cases, people living with rare diseases may be unable or less able to communicate with others about their condition (pediatric conditions, for example), so measuring outcomes accurately can be challenging. Despite increased engagement between sponsors and patient communities, speakers generally agreed there is still more work to be done to gain a full and comprehensive understanding of day-to-day life for both patients and caregivers.

Recommendations

Speakers from companies and patient communities recommended trial designs take into account what is viable or feasible for patients and caregivers, what endpoints are meaningful to patients and caregivers, safety concerns balanced with risk tolerance, disease characteristics such as rate of progression, and the anticipated impact and mechanism of action of the investigational product (i.e., the therapeutic being tested in the clinical trial). Speakers agreed that early engagement between patient communities, sponsors, and academic and clinical experts can set a trial up for success by ensuring that a sound plan for collecting and analyzing evidence is developed and documented, and that the endpoints used are both meaningful to the community and measurable. Generating quality data helps answer key research questions and potentially supports marketing applications. In order to improve trial recruitment and retention, it was suggested that sponsors should continue to pursue trial designs that minimize burden on participants (especially by reducing the frequency and duration of in-person visits) and offer the investigational product to as many as possible. Additionally, patient representatives and caregivers recommended sponsors communicate clearly with potential trial participants what trial participation entails, not only in terms of time commitments, treatment administration, etc., but also how it could change their care and the progression of their disease. These conversations should include participants themselves but may also require inclusion of family and health care providers already caring for the patient. Speakers recommended sponsors empower trial participants to be active research partners as much as possible by explaining how the data they contribute will further understanding of the investigational product's safety and efficacy and potentially help improve care for others with the same condition.

Marketing Application and FDA Review Stages – A sponsor submits a marketing application for FDA approval of their product. FDA reviews the application and determines whether or not to approve the product.

Developments

During pre-clinical and clinical development, the collaboration between sponsors, rare disease communities, and regulators can support sponsors in establishing the right research questions, collecting high-quality data, and generating the evidence necessary to answer those research questions and potentially submit a marketing application. FDA speakers described how reviewers at FDA often look for the patient voice to be included in submissions, and FDA remains committed to prioritizing input from a representative sample of the patient community. Though these forms of patient community input cannot replace the required evidence collected through rigorously conducted clinical trials, they can provide valuable therapeutic context for regulators.

FDA speakers also described internal efforts to familiarize reviewers with innovative methods being used in rare disease drug development and to standardize and improve approaches to reviewing applications for rare diseases. These efforts include holding regularly scheduled internal cross-divisional and cross-center meetings and trainings. FDA also utilizes cross-cutting teams to work with different review divisions. These cross-cutting teams can consist of experts including biostatisticians, psychometricians, clinicians, and others to support a rigorous review. FDA speakers noted the importance of PED and patient engagement activities such as PFDD meetings, listening sessions, and natural history studies in providing regulators with patient perspective, priorities, and therapeutic context while conducting their review.

Opportunities for Improvement

When discussing FDA Advisory Committee meetings, some speakers representing patient groups felt that the inclusion of advisory committee members with clinical expertise in the specific indication being discussed is critical to informing regulators' decision-making. However, conflict of interest policies may rule out their participation if they've been involved with the development of the medical product under review. Another challenge speakers noted was related to the use of natural history data as an external control. Natural history studies can serve an important role in informing sponsors and regulators of foundational information on disease progression and presentation as well as supporting efficient conduct of clinical trials by potentially serving as an external control. But natural history studies may not always be sufficiently fit for purpose relative to the trial population and study design, and therefore may not be able to serve as an external control for a given trial. Researchers and supporting organizations should consider what use cases are desirable at the outset of natural history study design so that such studies can best support relevant clinical trial efforts in the future.

Recommendations

Speakers and docket respondents representing sponsor companies and patient groups identified a number of ways those involved in rare disease drug development can help sponsors in establishing the right research questions and collecting the high-quality data necessary to support marketing applications. Some suggested that as part of natural history studies, patient communities collect caregiver perspectives and outcome measures that satisfy both the patient community's and FDA's respective needs. They recommended that sponsors should more regularly seek to leverage natural history studies as an external control, though this approach may not be feasible in all cases. Some FDA speakers recommended that sponsors work to incorporate patients into their meetings with FDA to ensure continued opportunities for regulators to hear from patients directly, better understand a rare condition, and ultimately make the most informed decision in review. One patient group representative alluded to an EMA effort in which reviewers are encouraged to reach out to patient communities proactively, immediately in advance of application review, to gain an understanding of specific disease and patient community priorities. This representative recommended FDA adopt a similar approach.

Several speakers and docket respondents provided further recommendations specific to FDA. Some speakers representing patient groups emphasized the importance of reviewers being informed and familiar with all available PED and patient input received through PFDDs, listening sessions, and other means- before starting the review process to better understand the condition and preferences of the patient population. One patient group representative recommended adjustments to existing conflict of interest policies that apply to advisory committees to ensure that relevant disease-specific experts are leveraged for informing regulatory thinking.

Speakers also proposed that a more streamlined and consistent process of utilizing and reviewing patient input across regulatory review divisions could further benefit rare disease drug development. As described by one patient group representative, this might be achieved through formalized tracking of the use of PED during the review process, or assessments by FDA leadership of how patient input is used during review across different divisions. Although FDA cannot generally comment on submissions under review, speakers and docket respondents representing patient groups and sponsor companies encouraged FDA to consider opportunities for sharing information about the use of PED after an approval. One common recommendation was for FDA to more frequently share how the input received through patient listening sessions and PFDD meetings was used in review without revealing confidential information. Some recommended building upon PED tables, which are located within FDA review documents, to more specifically describe how such data was used to support the regulatory decision.

Post-Approval Stages – Additional studies after approval are used to monitor the product's safety and efficacy.

Recommendations

Speakers briefly touched on recommendations beyond the review phase. It was noted that long-term follow-up can reveal real-world impacts that may not have been captured during the shorter time frame of clinical trials. After a therapy is approved, some speakers suggested that sponsors consider further studies to improve the understanding of how the therapy affects different subsets of the patient population given the significant heterogeneity that is common among rare diseases. One docket respondent representing a patient group recommended sponsors and FDA continue to engage closely with patient communities after a product is approved to understand how eligibility, access, and uptake develop – especially since these points may affect patients' attitudes toward the development of additional treatments for their rare condition.

Key Themes and Future Directions

A few overarching themes emerged throughout meeting discussions that included observations about attitudes toward and approaches to patient engagement in rare disease drug development. Important directions for future efforts were also raised repeatedly across different presentations and panels. Speakers noted that:

- A more inclusive and holistic drug development process has become a priority for many involved in rare disease drug development, especially sponsors and FDA.
- Sponsors often engage with patient communities during pre-clinical and clinical stages of drug development.
- FDA has created mechanisms for patient input via PFDD meetings, Patient Listening Sessions, and other venues, and this input can add therapeutic context to the clinical data.
- Those involved in rare disease drug development are aligned in their focus to bring safe and effective treatments to market as quickly and efficiently as possible, and agree that incorporating the voices of patients, caregivers, and condition-specific experts into drug development are part of achieving that goal.

Still, speakers mentioned the following as persistent challenges:

- Communication between patient groups and others involved in drug development – particularly regulators – is not always consistent or bi-directional.
- Creating meaningful contributions to rare disease drug development requires a significant investment in terms of time and effort from patient groups.
- It may be unclear to patient groups how their contributions to drug development are considered, especially in regulatory decision-making.

To provide greater clarity to patient communities and identify opportunities for improvement, speakers and respondents to the docket recommended sponsors and regulators seek out additional opportunities to highlight how patient input contributes to their work.

Ultimately, discussion highlighted that meaningful input from patient communities and other experts shouldn't be a single point in time or a one-size-fits-all phenomenon. Instead, this input should inform activities throughout the drug development process, including:

- the development of patient registries and natural history studies;
- clinical trial design, conduct, enrollment, retention;
- identification of clinically meaningful benefit; and
- sponsors' and regulators' understanding of patients' tolerance for risk.

CONCLUSION

Persistent challenges in rare disease drug development can be mitigated through a collaborative approach that includes meaningful input from patients and other rare disease experts throughout drug development. This input can provide valuable information about patients' and caregivers' experiences with a condition, clinically meaningful and measurable trial endpoints, the feasibility of different trial designs, and patients' levels of risk tolerance. While there are a number of ongoing activities at the FDA to advance meaningful patient engagement to help researchers, sponsors, and patient communities overcome challenges in this space, further opportunities to enhance engagement activities between all collaborators can be explored to better support rare disease drug development.

Workshop participants discussed a number of notable developments, opportunities for improvement, and recommendations for enhancing meaningful patient and expert engagement throughout the rare disease drug development process. Of note, participants highlighted that, to the extent possible, more communication around how the patient voice is used to inform regulatory thinking and decision making would help patient communities determine what future patient engagement initiatives may be most useful in supporting their drug development activities.

Past meetings such as those listed in the **Appendix** have informed approaches to rare disease drug development. Upcoming meetings of particular importance to the Rare Disease community are listed on the Accelerating Rare disease Cures (ARC) Program website and on the FDA Meeting website, and will continue to build upon the important information shared during this meeting. These meetings bring together FDA and external rare disease experts from a wide range of backgrounds in service of the shared goal of advancing rare disease therapeutic development.

It is critical that discussions on enhancing meaningful and collaborative engagement continue beyond this workshop. The findings and recommendations shared throughout the event can inform the evolving conversation on activities and approaches needed to facilitate successful rare disease drug development. FDA and Duke-Margolis thank the meeting participants, docket respondents, and meeting attendees for their contributions to the discussion, and look forward to continued efforts to advance the development of therapeutics for rare diseases.

Acknowledgements

We would like to thank the participants who joined our meeting for sharing their expertise and insights, which are reflected in this report. The Duke-Margolis project team for this meeting includes Victoria Gemme, Gerrit Hamre, Thomas Roades, and Mia Williams.

This meeting was supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award [U19FD006602] totaling $5,045,773 with 100 percent funded by FDA/HHS. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by FDA/HHS, or the U.S. Government.

Appendix

This Appendix highlights examples of FDA initiatives, programs, and meetings related to rare disease drug development. It is not intended to be comprehensive but provides references that may be helpful to those seeking more information related to the topics discussed in this meeting.

FDA Initiatives Related to Rare Disease Drug Development

Accelerating Rare disease Cures (ARC) Program

This program brings together FDA Center for Drug Evaluation and Research (CDER) expertise and activities to provide strategic overview and coordination of rare disease activities and accelerate the availability of treatments for patients with rare diseases.

Complex Innovative Trial Design (CID) Meeting Program

The CID Paired Meeting Program was established to support the goal of facilitating and advancing the use of complex adaptive, Bayesian, and other novel clinical trial designs.

FDA Rare Disease Day Public Meetings

The purpose of these meetings is to raise awareness about rare diseases, the challenges encountered by those affected, the importance of research to develop diagnostics and treatments, and the impact of these diseases on patients' lives.

Model-Informed Drug Development (MIDD) Paired Meeting Program

The MIDD Paired Meeting Program advances and integrates the development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources in drug development and regulatory review.

Patient-Focused Drug Development (PFDD) Meetings

Patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation.

Patient Listening Sessions

These sessions are a resource for the medical product Centers to engage with patients and their advocates. Patient Listening Sessions are one of many ways the patient and advocacy community can share their experiences and perspectives by talking directly with FDA staff.

Rare Disease Endpoint Advancement (RDEA) Pilot Program

The RDEA Pilot Program is designed to advance rare disease drug development programs by providing a mechanism for sponsors to collaborate with FDA; promote innovation and evolving science by sharing learnings on novel endpoint development; and develop FDA staff capacity to enable and facilitate the development and use of novel endpoints.

Support for Clinical Trials Advancing Rare Disease Therapeutics (START) Pilot Program

The purpose of the START Pilot Program is to further accelerate the pace of development of novel drug and biological products that are intended to address an unmet medical need as a treatment for a rare disease.

Selected Meetings Related to Rare Disease Drug Development

May 2024 - Natural History Studies and Registries in the Development of Rare Disease Treatments
This workshop brought together rare disease patient advocates, academic researchers, regulated industry, and other key stakeholders to discuss considerations for the use of natural history study and registry data in rare disease drug development programs.

April 2024 - Streamlining Drug Development and Improving Public Health through Quantitative Medicine: An Introduction to the CDER Quantitative Medicine Center of Excellence
The purpose of this workshop was to introduce the Center for Drug Evaluation and Research (CDER) Quantitative Medicine Center of Excellence (QM CoE), providing an overview of the scope, goals, and current state, while gaining feedback from the public on needs and opportunities in education, outreach, and policy.

March 2024 - Enhancing Adoption of Innovative Clinical Trial Approaches
This meeting covered efforts to advance innovation of clinical trial design and conduct. The meeting covered regulatory and compliance considerations, patient-centricity and recruitment innovations, and clinical trial infrastructure and organizational culture.

March 2024 - Advancing the Use of Complex Innovative Designs in Clinical Trials: From Pilot to Practice
The purpose of this public workshop was to facilitate discussion on the use of external data sources, Bayesian statistical methods, and simulations in complex innovative trial designs as well as trial implementation.

June 2023 - Rare Disease Endpoint Advancement Pilot Program Workshop: Novel Endpoints for Rare Disease Drug Development
This meeting illustrated challenges and opportunities in rare disease endpoint development, introduced the RDEA Pilot Program, and highlighted how the RDEA Pilot Program is structured to support sponsors who may encounter challenges with endpoint development.

May 2023 - Creating a Roadmap to Quantitative Systems Pharmacology-Informed Rare Disease Drug Development
The purpose of this workshop was to discuss the potential utility of quantitative systems pharmacology (QSP) in rare disease drug development and brainstorm the potential path to address associated challenges and facilitate its use.

May 2023 - Addressing Challenges in the Design and Analysis of Rare Disease Clinical Trials: Considerations and Tools
This workshop covered broadly recognized challenges in rare disease drug development and the potential for innovative trial designs and analysis methods to address those challenges.

April 2023 - Methods and Approaches for Capturing Post-Approval Safety and Efficacy Data on Cell and Gene Therapy Products
This meeting solicited input on methods and approaches (e.g., use of real-world evidence [RWE] registries) for capturing post-approval safety and efficacy data for cell and gene therapy products.

November 2022 - FDA CBER OTAT Patient-Focused Drug Development Listening Meeting — Patient Perspectives on Gene Therapy Products
The purpose of this meeting was to better understand patient perspectives on gene therapy products, including cell-mediated gene therapies.

May 2022 - Translational Science in Drug Development: Surrogate Endpoints, Biomarkers, and More
This meeting focused on best practices and provided use cases for successfully bringing forward evidence generated through translational science for regulatory submissions.

May 2022 - FDA CDER & NIH NCATS Regulatory Fitness in Rare Disease Clinical Trials Workshop
This workshop focused on academic investigators and those looking to learn how to bridge the gap between academic investigation and the regulatory aspects of drug development.

Various, May 2021-Present – OTP RegenMedEd Series
The OTP Virtual Town Halls aim to engage with product development stakeholders and researchers. These town halls have a question-and-answer format with the goal of providing regulatory information to stakeholders to help advance development of OTP-regulated products.

Selected Guidances Related to Rare Disease Drug Development

December 2023 - Rare Diseases: Considerations for the Development of Drugs and Biological Products (final guidance)
The purpose of this guidance is to assist sponsors of drug and biological products for the treatment of rare diseases in conducting more efficient and successful drug development programs through a discussion of selected issues commonly encountered in rare disease drug development.

July 2023 - Inborn Errors of Metabolism That Use Dietary Management: Considerations for Optimizing and Standardizing Diet in Clinical Trials for Drug Product Development (draft guidance)
This guidance describes the Food and Drug Administration's (FDA's) current recommendations regarding how to optimize and standardize dietary management in clinical trials for the development of drugs that treat inborn errors of metabolism (IEM) for which dietary management is a key component of patients' metabolic control.

April 2023 - Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making (PFDD Guidance 4, draft)
Guidance 4 addresses methodologies, standards, and technologies that may be used for the collection, capture, storage, and analysis of COA data. The guidance also addresses methods to better incorporate COAs into endpoints that are considered significantly robust for regulatory decision-making. This includes methods to define meaningful change in a COA-based endpoint and interpretation of results. The guidance includes information on the format and content required for regulatory submissions incorporating patient experience, COA data.

June 2022 - Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments (PFDD Guidance 3, draft)
Guidance 3 discusses approaches to selecting, modifying, developing, and validating COAs to measure outcomes of importance to patients in clinical trials.

February 2022 - Patient-Focused Drug Development: Methods to Identify What Is Important to Patients (PFDD Guidance 2, final)
Guidance 2 discusses approaches to identifying what is most important to patients with respect to their experience as it relates to burden of disease/condition and burden of treatment.

January 2020 - Human Gene Therapy for Rare Diseases (final guidance)
This guidance provides recommendations to sponsors developing human gene therapy products intended to treat a rare disease in adult and/or pediatric patients regarding the manufacturing, preclinical, and clinical trial design issues for all phases of the clinical development program.

July 2019 - Rare Pediatric Disease Priority Review Vouchers (draft guidance)
This guidance provides information on the implementation of section 908 of the Food and Drug Administration Safety and Innovation Act (FDASIA), which added section 529 to the Federal Food, Drug, and Cosmetic Act (the FD&C Act). Under section 529, FDA will award priority review vouchers to sponsors of certain rare pediatric disease product applications that meet the criteria specified in that section.

March 2019 - Rare Diseases: Natural History Studies for Drug Development (draft guidance)
This guidance is intended to help inform the design and implementation of natural history studies that can be used to support the development of safe and effective drugs and biological products for rare diseases.

October 2018 - Rare Diseases: Early Drug Development and the Role of Pre-IND Meetings (draft guidance)
This guidance is intended to assist sponsors of drug and biological products for the treatment of rare diseases in planning and conducting more efficient and productive pre-investigational new drug application (pre-IND) meetings.

July 2018 - Slowly Progressive, Low-Prevalence Rare Diseases with Substrate Deposition That Results from Single Enzyme Defects: Providing Evidence of Effectiveness for Replacement or Corrective Therapies Guidance for Industry (final guidance)
This document provides guidance to sponsors on the evidence necessary to demonstrate the effectiveness of investigational new drugs or new drug uses intended for slowly progressive, low-prevalence rare diseases that are associated with substrate deposition and are caused by single enzyme defects.

June 2018 - Patient-Focused Drug Development: Collecting Comprehensive and Representative Input (PFDD Guidance 1, final)
Guidance 1 discusses methods to collect patient experience data that are accurate and representative of the intended patient population.

December 2017 - Pediatric Rare Diseases--A Collaborative Approach for Drug Development Using Gaucher Disease as a Model; Draft Guidance for Industry (draft guidance) The purpose of this guidance is to facilitate drug development in pediatric rare diseases. In particular, it discusses a new possible approach to enhance the efficiency of drug development in pediatric rare diseases using Gaucher disease as an example.

FDA updates guidances periodically. For the most recent version of a guidance, check the FDA guidance web page.