U.S. FOOD & DRUG ADMINISTRATION

Rare Disease Innovation Hub

FDA Rare Disease Educational Materials: A Landscape Assessment, Gap Analysis, and Recommendations

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1. EXECUTIVE SUMMARY

In support of efforts to expand upon existing educational resources and address the needs of the rare disease product development community, the U.S. Food and Drug Administration's (FDA) Rare Disease Innovation Hub (the Hub) worked with an independent third-party contractor to conduct a comprehensive assessment of the current rare disease educational landscape. This assessment included (1) a review of existing, public-facing rare disease educational resources; (2) listening sessions with the rare disease product development community; and (3) a qualitative analysis of public comments on FDA's February 2026 rare disease docket, FDA-2026-N-1584, to identify educational gaps across topics in rare disease product development and regulation, with a particular emphasis on biologics and the role of patients and disease advocates in the development of rare disease therapies.[1] This report summarizes the findings from the engagements and outlines recommendations to expand educational offerings for those involved in rare disease product development.

A. Summary of Findings by Topic Area

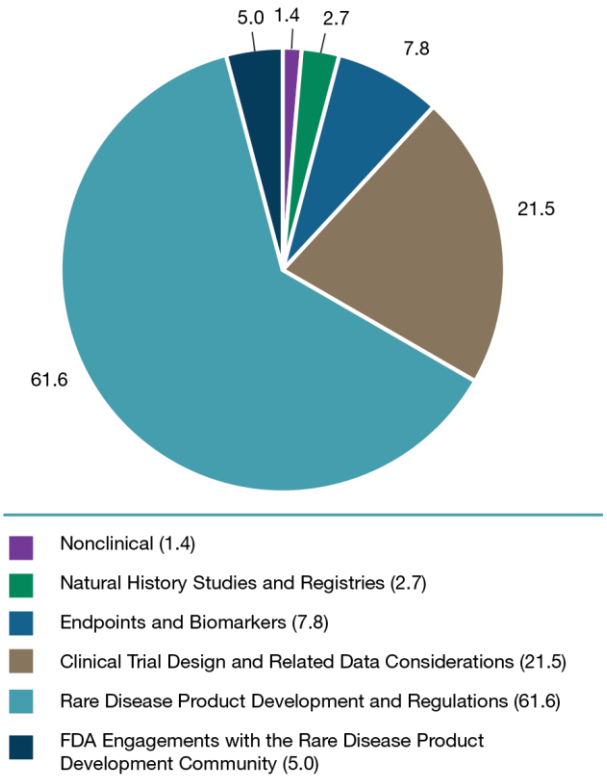
Nonclinical

Less than 2% of the 219 total resources captured in the landscape assessment pertained to nonclinical topics (e.g., discovery, dose-finding). Engagement efforts with the rare disease product development community revealed interest in more educational resources on nonclinical development. Industry representatives communicated a need for more information on the regulatory standards for nonclinical studies to mitigate the risks and uncertainty associated with early product development. Patient advocates urged FDA to develop plain-language resources on nonclinical development for the public.

Natural History Studies and Registries

A limited number of resources (~3%) identified through the landscape assessment discussed natural history studies

Figure 1: Distribution of Existing Educational Resources by Topic Area



***Note**: Topic area distribution presented as percentages*

[1] Opportunity for Public Comment on Rare Disease Educational Materials from the Center for Drug Evaluation and Research's Accelerating Rare disease Cures Program and the Rare Disease Innovation Hub (https://www.regulations.gov/docket/FDA-2026-N-1584)

(NHS) and registries in rare disease product development. The community voiced high interest in resources clarifying how NHS and registry data can support product development (e.g., addressing practical questions about how NHS can mitigate rare disease clinical trial challenges and support product submissions). Participants expressed uncertainty about the regulatory standards that apply to the use of NHS and registries to inform regulatory decision making, which they deemed essential to improve industry and patient advocacy group (PAG) collaboration. Furthermore, the community requested greater communication from FDA on how NHS and registry data are used to inform regulatory reviews of clinical trial data and approvals of marketing applications.

Endpoints and Biomarkers

The landscape assessment captured a small number (~8%) of resources on endpoints and biomarkers. Resources covered common topics discussed during community interviews such as endpoint development, selection, validation or qualification, and use in product submissions. Interview participants consistently requested additional information on these topics.

Clinical Trial Design and Related Data Considerations

Clinical trial design and related data considerations comprised ~21% of resources collected. These resources focused on data science topics, patient involvement and patient experience data, and innovative and adaptive trial designs. Industry voiced limited quantity of resources related to innovative and adaptive trial designs, an observation substantiated by the landscape assessment findings. Topics with a limited number of resources included the roles of PAGs in clinical investigations, considerations for pediatric clinical trials, and clinical trial ethics.

Rare Disease Product Development and Regulations

Findings from the landscape assessment indicated that over 60% of the educational resources identified were related to rare disease product development and regulation. Topics covered across the resources identified were funding mechanisms, FDA organizational structure and initiatives, biologics, priority designations, and patient-focused product development. However, the community voiced interest in audience-specific resources, as well as a need for more informational materials describing FDA's rare disease programs, medical product centers and their respective regulatory purview, and the financial incentives (e.g., vouchers) available to support rare disease product developers. The combined findings suggest a disconnect between the results of the landscape assessment and the community feedback, which may be partially explained by the cited challenges of locating and navigating fragmented educational content disseminated by U.S. Government organizations.

Information on engagement with FDA is an educational gap corroborated by both the landscape assessment findings and community feedback. Five percent of all the resources pertained to engagement opportunities for the rare disease product development community, and participants expressed confusion regarding availability and timing of FDA engagement opportunities for both sponsors and patient communities.

2. INTRODUCTION

There are over 10,000 rare diseases that collectively impact approximately 30 million Americans, or almost 1 in 10 people in the U.S., approximately half of whom are children. Rare diseases represent a high unmet need: approximately 5% of all diagnosed rare diseases have an approved treatment.

Rare disease product development is complicated, facing inherent challenges including slowly progressive and poorly understood natural history, genotypic and/or phenotypic heterogeneity within a disease state, and small and geographically dispersed patient populations. These unique challenges make the planning, design, conduct, and interpretation of clinical investigations complex.

Through its Rare Disease Innovation Hub (the Hub) and rare disease programs, FDA maintains its commitment to enhancing regulatory science and advancing development of medical products for rare diseases. FDA created the Hub to serve as a point of collaboration and connectivity between FDA's medical product centers (i.e., the Center for Biologics Evaluation and Research [CBER], Center for Drug Evaluation and Research [CDER], and Center for Devices and Radiological Health [CDRH]) and rare disease programs with the goal of improving outcomes for rare disease patients. The Hub enhances collaboration across FDA to address shared scientific, clinical, and policy issues related to rare disease product development, including relevant cross-disciplinary approaches related to product review, and promote consistency across centers, offices, and programs.

To expand on the identification of the challenges and educational needs of the rare disease product development community, FDA engaged a third-party independent contractor, Booz Allen Hamilton (Booz Allen), to perform an assessment of existing public-facing rare disease educational resources. This report presents Booz Allen's findings on the educational gaps and needs specific to the rare disease product development community. The assessment included (1) identifying and reviewing existing educational materials, (2) conducting focus groups and interviews, and (3) analyzing public comments on a rare disease docket to understand currently available rare disease

educational resources and identify topics to consider for development into future educational materials.[2]

This report synthesizes feedback from the rare disease product development community via comments in the FDA public docket and the focus group interviews with members of industry (e.g., small-to-medium pharmaceutical and biotechnology companies), PAGs, and U.S. Government (USG) individuals engaged in rare disease clinical research and research administration (i.e., program officers). Booz Allen (the project team) collected and organized insights into six topics relevant to rare disease medical product development: (1) nonclinical, (2) NHS and registries, (3) novel endpoint and biomarker development, (4) clinical trial design and related data considerations, (5) rare disease product development and regulations, and (6) FDA engagements with the rare disease product development community. The findings will inform the Hub's future engagement and education strategy as well as initiatives.

3. ASSESSMENT METHODOLOGY

This section describes the landscape analysis methods. This assessment involved two primary components: (1) a landscape assessment of available educational materials related to rare disease product development and regulation, and (2) engagement with the rare disease product development community (i.e., small-to-medium biopharmaceutical and biotechnology companies, patient advocacy groups [PAGs], and U.S. Government representatives) to assess their needs.[3] The **Detailed Assessment Methodology Appendix** describes the methods used for this report.

Overview of Our Approach

The project team performed targeted research (informed by prespecified inclusion and exclusion criteria) to characterize the landscape of existing rare disease educational resources, enhancing it through interviews with the rare disease product development community and review of docket comments posted on regulations.gov.[4] The approach included: (1) specifying the scope of the assessment, (2) reaching out to the rare disease product development community, (3) collecting and analyzing data, (4) generating findings and recommendations, and (5) verifying recommendations with the rare disease product development community.

Identify Scope of Assessment

Informed by the Hub's Strategic Agenda, Booz Allen defined the scope of the landscape assessment and prespecified inclusion and exclusion criteria, focusing on educational

[2] Opportunity for Public Comment on Rare Disease Educational Materials from the Center for Drug Evaluation and Research's Accelerating Rare disease Cures Program and the Rare Disease Innovation Hub (https://www.regulations.gov/docket/FDA-2026-N-1584)
[3] Small-to-medium industry: Companies with fewer than 3,000 global workforce headcount.
[4] Opportunity for Public Comment on Rare Disease Educational Materials from the Center for Drug Evaluation and Research's Accelerating Rare disease Cures Program and the Rare Disease Innovation Hub (https://www.regulations.gov/document/FDA-2026-N-1584-0001)

materials addressing the development and regulation of rare disease drugs and biologics that targeted patient communities and product developers[5,6] (see **Identify Scope of Assessment** subsection of Appendix D).[7]

Engagement with the Rare Disease Product Development Community

The project team identified several rare disease organizations and individuals within each organization to participate in the Hub's Educational Assessment and Resource Development (HEARD) listening sessions, randomly selecting 9 individuals from industry (small-to-medium pharmaceutical and biotechnology companies), 9 from PAGs, and 8 USG staff for a total of 26 participants.

Booz Allen developed three HEARD interview guides tailored to industry, PAGs, and USG staff to (1) augment understanding of available educational resources for rare disease product developers, patient communities and advocates; (2) identify gaps in the community's understanding of rare disease product development and regulatory review; and (3) identify rare disease topics of interest.

The project team structured the interview guides to include the following core topic areas:

- Baseline Questions (on educational resource awareness)
- Product Development and Regulation
- Biologics
- Drugs

To extend the reach of the rare disease product development community engagement and broaden the perspectives captured, the Hub and CDER's Rare Diseases Team posted a joint public docket for comment on regulations.gov from 2/11/2026 – 4/3/2026 (Docket No. FDA-2026-N-1584).[8] Following the closing of the docket, comments underwent qualitative analysis. The project team included in this analysis public comments that (1) provided information on availability of educational resources for patients/patient organizations and developers of rare disease biologics or (2) provided information on where gaps in available resources may exist.

[5] Drug: small molecules, monoclonal antibodies, protein-based therapies, DNA/RNA antisense oligonucleotides, RNA-based therapies, and non-vaccine immunotherapies.
[6] Biologics are generally large and complex molecules derived from living systems such as microorganisms, plant cells, or animal cells and are regulated by CDER and CBER. Examples of CBER-regulated biologics include cell and gene therapies, tissue and tissue products, blood and blood products, xenotransplants (i.e., transplantation, implantation, or infusion of live non-human animal cells, tissues, or organs into humans, or human materials that have contacted live animal cells or tissues ex vivo), and vaccines.
[7] Rare Disease Innovation Hub Strategic Agenda – 2026 (https://www.fda.gov/media/185144/download?attachment)
[8] Opportunity for Public Comment on Rare Disease Educational Materials from the Center for Drug Evaluation and Research's Accelerating Rare disease Cures Program and the Rare Disease Innovation Hub (https://www.regulations.gov/docket/FDA-2026-N-1584)

Collect and Analyze Data

For the landscape assessment, Booz Allen captured key data elements including resource format, technical level, topic alignment, and usability (i.e., ease of navigation, user interface) and accessibility (i.e., learning accommodations) ratings.[9] The project team evaluated usability and accessibility using selected domains from the Learning Object Review Instrument (LORI), a standardized framework for assessing the quality of educational resources.[10] Two team members independently reviewed and rated each resource, and scientific subject matter experts (SMEs) reviewed a randomly selected sample. The project team collaboratively discussed and adjudicated discrepancies between reviewer ratings and SME ratings; then analyzed the landscape assessment data, summarizing findings to identify patterns and gaps.

From HEARD interviews, Booz Allen received input from 26 individuals across 3 rare disease product development community groups (i.e., PAGs, developers, USG). Following the completion of the listening sessions, Booz Allen aggregated feedback across all sessions and analyzed the data to identify common themes, trends, and areas of alignment and divergence across the rare disease product development community.

After the closing of the public docket (Docket No. FDA-2026-N-1584), Booz Allen reviewed all 69 submissions and, in consultation with the Hub and CDER's Rare Diseases Team, determined their relevance to both the scope of the assessment and CDER's LEADER 3D educational initiative.[11] Of the 69 submissions, 14 comments were in scope for this assessment and subsequently analyzed. Comments requesting feedback on the Rare Diseases Team's existing LEADER 3D educational materials were considered separately to inform the LEADER 3D educational initiative and are therefore not reflected in this assessment.

Generate Findings and Recommendations

Booz Allen used data from the landscape assessment, HEARD listening sessions, and public docket comments to elucidate shared themes and identified:

- Areas where educational needs are currently well met and high-quality resources are available
- Trends in challenges experienced within and across the rare disease product development community

[9] The design of controls and presentation formats to accommodate disabled and mobile learners.
[10] Leacock, T. L., & Nesbit, J. C. (2007). A Framework for Evaluating the Quality of Multimedia Learning Resources. Educational Technology & Society, 10(2), 44–59.
[11] Learning and Education to ADvance and Empower Rare Disease Drug Developers (LEADER 3D) (https://www.fda.gov/about-fda/accelerating-rare-disease-cures-arc-program/learning-and-education-advance-and-empower-rare-disease-drug-developers-leader-3d)

- Gaps in existing educational materials, including the nature and extent of those gaps
- Recommendations for future educational material development to address identified gaps and opportunities

Verifying Recommendations with the Community

To maintain alignment between the report findings and the priorities of the rare disease product development community, the project team and the Hub hosted three working sessions with six industry and seven PAG participants that previously contributed to the data collection interviews (i.e., HEARD Interviews).

The project team developed two working session guides tailored to each target audience (i.e., industry and PAGs) and provided the working session guides to participants prior to their session. Each guide summarized the audience-specific educational gaps identified in the assessment, recommendations to address each gap, and questions designed to assess the accuracy, relevance, and identify prioritization of the recommendations. Booz Allen then analyzed working session insights to identify key takeaways specific to the community groups, to refine the final set of educational gaps and recommendations.

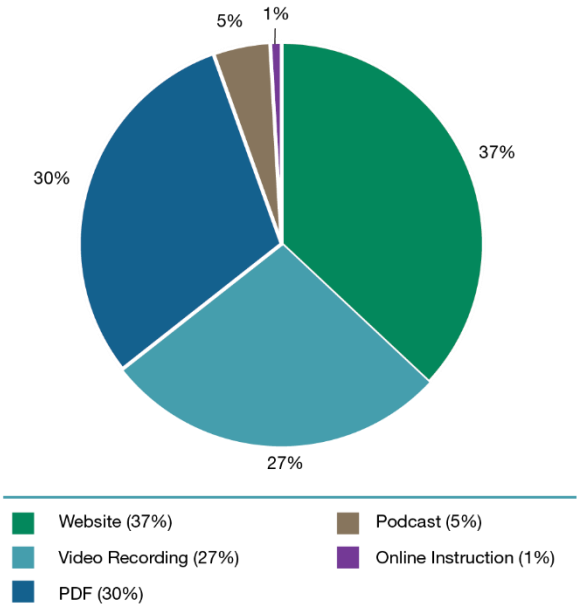
4. FINDINGS

This report summarizes findings organized across six topic areas derived from a landscape assessment of available resources, community insights obtained through interviews and docket comments from the public.

A. Overview of Findings and Recommendations

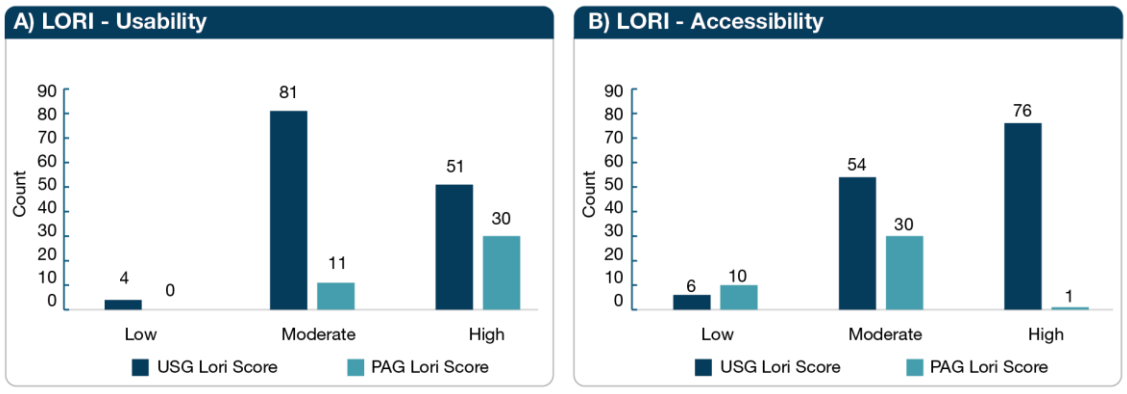
The landscape assessment identified and collected a total of 219 in-scope educational resources available through website pages (37%), video recordings (27%), PDF documents (30%), podcasts (5%), and online instructional modules (1%) (**Figure 2**). Across these resources, content suitable for beginner, intermediate, and advanced audiences accounted for 38%, 35%, and 27% of all materials, respectively (see **Table 6-3** for suitability determination criteria).

Figure 2: Delivery Format of Educational Resources



The project team conducted a LORI scale assessment to determine the usability (i.e., ease of navigation, user interface) and accessibility (i.e., learning accommodations) of each educational resource. Collectively, nearly all resources captured demonstrated moderate or high usability (44% and 53%, respectively) and moderate or high accessibility (52% and 37%, respectively). Booz Allen assessed the usability and accessibility ratings of resources attributed to USG (136) and PAGs (42) because, among all organization types captured (refer to the **Identify Scope of Assessment** subsection of Appendix D; **Figure 4**), they disseminated the greatest number of educational materials. USG-disseminated resources predominantly scored moderate on usability and high on accessibility (**Figure 3**).[9] Meanwhile, resources disseminated by PAGs scored high on usability but moderate-to-low on accessibility, indicating easy to use resources with limited learning accommodations (**Figure 3**).

Figure 3: Usability and Accessibility of Resources Disseminated by USG and PAGs



Landscape Community Engagement

The HEARD interview sessions were held between January – March 2026 and included 26 individuals from industry, PAG, and federal health agencies, and comments from FDA's rare disease docket were also captured**.** During the HEARD interview sessions, community members responded to questions about their preferred educational materials and suggested areas needing additional information. Community members identified the following resources as their initial sources for educational content:

- Industry referenced FDA guidance documents and the Learning and Education to ADvance and Empower Rare Disease Drug Developers (LEADER 3D) case studies as prominent educational materials.
- PAGs voiced preference for their self-developed, patient-centered educational materials, or they referred their constituents to rare disease umbrella organizations.[12]
- USG intramural staff also cited directing their patients to rare disease umbrella organizations while extramural USG staff refer their awardees/grantees to FDA guidance documents to inform the planning of their research programs.

In June 2026, the project team held working sessions with 13 individuals from industry and PAGs to validate the assessment findings. Industry individuals focused on evidentiary standards, especially regarding heterogeneous or pediatric diseases. Meanwhile, PAG participants emphasized that the knowledge level and educational needs across the patient advocacy community were dependent on organizational experience and expertise. PAG participants requested a tiered approach to educational content that caters to varying PAG expertise levels (see **Additional Insights**).

Community members identified the following topics as their priorities:

- Industry unanimously identified *Endpoints and Biomarkers* as the topic of greatest need, followed by *Natural History Studies and Registries* and *Clinical Trial Design and Related Data Considerations*.
- PAGs identified *Natural History Studies and Registries* as their topic of highest priority, followed by *FDA Engagements with the Rare Disease Product Development Community*, then *Endpoints and Biomarkers*.

[12] Rare disease umbrella organizations: Associations of groups or institutions focused on rare disease therapy development and who formally pool their resources to advocate for community needs, accelerate innovation, and provide access to relevant information.

B. Topics

Nonclinical

Existing Rare Disease Educational Materials

During the landscape assessment efforts, the project team identified few in-scope resources on nonclinical development, with 1.4% (n=3) of the total focused on nonclinical topics. Two of these resources provided content on dose-finding strategies for product development programs, while one was an FDA guidance document on product development tools (i.e., Drug Development Tools [DDTs]).[13]

HEARD Engagement with the Rare Disease Product Development Community

Insights from the HEARD listening sessions supported landscape assessment findings identifying a limited availability of nonclinical educational materials. Industry identified a need for additional nonclinical FDA guidance and educational materials targeting nonclinical development. Participants further observed there are a limited number of guidance documents clarifying the evidentiary expectations prior to entering clinical phases, particularly around the data required to initiate clinical investigations. Industry participants also voiced the need for more resources on the challenges in chemistry, manufacturing, and controls standards that can adversely impact the transition from nonclinical to clinical development.

Non-industry individuals noted that patients and non-experts (in rare disease drug development) may have a limited understanding of early development requirements. PAG participants identified that their constituents experience challenges in understanding why some investigational products remain in nonclinical stages while other products advance to human clinical trials. As a result, some patient advocacy organizations invest time and financial resources to translate scientific and/or regulatory resources (e.g., FDA guidance documents) into easily digestible educational materials for patients and caregivers. Patient advocates stated that advocacy organizations range in size and expertise, with various levels of scientific understanding, regulatory science background, and experience in successful medical product development and regulatory submission. PAGs recommended that FDA consider developing simplified explanations of early drug development stages (e.g., toxicology studies) for patients and non-scientific audiences.

Gap Analysis of Nonclinical Aspects

Both findings from the landscape assessment and feedback from the rare disease product development community identified an educational gap in information

[13] Qualification Process for Drug Development Tools Guidance for Industry and FDA Staff (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/qualification-process-drug-development-tools-guidance-industry-and-fda-staff)

describing nonclinical aspects of rare disease product development. Product developers sought educational resources clarifying nonclinical evidentiary standards — an especially important consideration for small-to-medium sized developers who communicated less ability (compared to large counterparts) to absorb delays in timelines and increases in capital costs associated with recompleting or supplementing an underinformed study.

The nonclinical findings expand on FDA's February 2024 LEADER 3D Public Report of External Stakeholder Analysis, where the rare disease drug development community cited the absence of suitable animal models and information on alternative methods (i.e., new approach methodologies) as key challenges to nonclinical drug development. Given that the scope of the current landscape assessment extended to biologics, the results of this 2026 assessment cover a broader product development audience than previously assessed and provide additional insight into the depth of the nonclinical knowledge gap identified by the CDER Accelerating Rare Disease Cures (ARC) Program's LEADER 3D educational initiative.

PAGs expressed a need for resources providing an overview of nonclinical product development and the circumstances that allow investigational products to advance into clinical development. Further, the technical nature of content on nonclinical topics, such as FDA guidance documents, is a barrier that patient communities and advocates with limited experience in regulatory science face. Thus, creating more foundational content on nonclinical product development would benefit the patient and patient advocacy communities.

Natural History Studies and Registries

Existing Rare Disease Educational Materials

Booz Allen found a limited number of educational resources focused on NHS and rare disease registries, with 2.7% (n=6) of all resources. Four resources included information on the design and use of NHS and registry data in rare disease product development, while one provided an introductory perspective. One resource focused on the Rare Diseases Registry (RaDaR) program, intended to provide patient organizations with tools and step-by-step guidance to facilitate the setup of rare disease registries.[14]

HEARD Engagement with the Rare Disease Product Development Community

HEARD respondents requested clarity on the use of natural history and registry data. They voiced needing additional FDA guidance on how natural history data can be used as external comparators in clinical investigations. Since rare diseases are often heterogeneous and slowly progressive, understanding their progression

[14] Rare Diseases Registry (RaDaR) Program (https://ncats.nih.gov/research/research-activities/RaDaR)

and patient experiences requires lengthy NHS from limited populations to boost statistical power. This increases complexity of drug development further beyond the already intricate development of a drug for small patient populations. The rare disease product development community requested that FDA clarify how NHS can be used as a source of Real-World Evidence (RWE).

Participants from small-to-medium industry indicated the importance of collaborating with PAGs when collecting natural history data. However, they expressed concerns about the limitations of obtained data due to perceived ambiguity concerning FDA's data quality expectations and regulatory acceptability.

Patient organizations, which often lead collection of or support NHS, face difficulties understanding the evidentiary standards the Agency requires for NHS data to be suitable in the regulatory setting. PAG interviewees requested that FDA increase audience-appropriate communication on evidentiary standards for NHS so that their sponsored data collection efforts can meaningfully inform rare disease medical product development. Comments from the docket corroborated these findings, with respondents requesting practical tools and educational resources to help patient advocacy organizations effectively contribute to NHS and registry data collection efforts. Docket feedback from PAGs emphasized that NHS data are critical to understanding disease progression and called for greater communication on how these data can inform clinical trial design and regulatory decision-making.

Gap Analysis of Natural History Studies and Registries

Limited available information on NHS and registries suggests an educational gap, comprising less than 3% of the total educational resources identified. Community interviews supported the observed scarcity, as participants expressed a perception of limited information on the design and use of NHS and registry data. This knowledge gap highlights the need for resources discussing specific aspects of the design and use of NHS and registries including evidentiary data standards, design and implementation challenges, the use of real-world data (RWD) and RWE, and sponsor-PAG collaboration.

Endpoints and Biomarkers

Existing Rare Disease Educational Materials

Educational resources about endpoints and biomarkers made up 7.8% (n=17) of the resources captured. Eight out of the seventeen resources focused on endpoint selection and novel endpoint development. Of these eight, three focused on FDA's Rare Disease Endpoint Advancement (RDEA) Pilot Program, which focuses on supporting novel endpoint development for drugs that treat rare diseases. Two FDA guidance documents focused on oncology therapeutic area endpoint selection, with one providing advanced content on novel efficacy endpoints, and the other focusing on the grouping and analysis of grouped endpoints. One

resource was an introductory video on important considerations for endpoint selection in rare disease drug development. In addition, clinical outcome assessments, including patient-reported outcomes, were captured by four resources, two of which were FDA guidance documents, one a case study, and another a specialized panel discussion.

The project team found five resources related to biomarker development, validation, and use in product development. Two of these resources were specialized case studies on the use of biomarkers to demonstrate substantial evidence of effectiveness in new product applications. Two resources were FDA guidance documents, with one focusing on the general considerations in the development of biomarkers for qualification, and the other focusing on the use of biomarkers in clinical trials for hematologic malignancies. Lastly, one resource captured the distinctions between biomarkers and endpoints, as well as how each contribute to medical product development.

HEARD Engagement with the Rare Disease Product Development Community

All participants highlighted challenges in selecting biomarkers and developing novel endpoints due to the unique challenges rare diseases pose (e.g., small patient population, limited comparative data) and understood the importance of early engagement with FDA to discuss endpoints and biomarkers.

Both industry and USG participants acknowledged the existence of resources on developing novel endpoints and using biomarkers as surrogate endpoints. However, in their opinion, they stated that existing materials lack actionable suggestions for product developers. Industry emphasized the need for FDA to consider a broader range of evidence when evaluating rare disease products and noted that more case studies on endpoint selection can help developers understand FDA's current thinking on key regulatory policies.

USG participants also noted that communicating technical concepts related to endpoints and clinical trial design to patients and non-experts was challenging. PAG participants echoed this concern and emphasized the need for patient-centered approaches to endpoint selection that reflect outcomes important to patients (e.g., preservation of quality of life and delayed disease progression).

Gap Analysis of Endpoints and Biomarkers

Endpoint and biomarker-related materials represented less than 10% of resources captured in the landscape assessment and was a prominent topic discussed during HEARD community engagement. The community expressed a need for resources providing foundational knowledge on endpoints and biomarkers, as well as real-world examples on the successful use of endpoints in rare disease medical product submissions.

The landscape assessment found that some resources address existing community needs, including case study examples of endpoint development,

validation, and use. However, most of the available resources identified targeted intermediate or advanced audiences and did not provide an overview of foundational concepts related to endpoints and biomarkers for less experienced audiences. Moreover, PAGs prominently cited a limited number of materials describing the patient community's role in endpoint selection.

Clinical Trial Design and Related Data Considerations

Existing Rare Disease Educational Materials

Clinical trial design and clinical trial data considerations comprised the second largest topic area in the landscape assessment, representing 21.5% (n=47) of the resources captured. Approximately half focused on three areas: (1) data science, (2) patient involvement in clinical investigations and patient experience data, and (3) innovative and adaptive trial designs.

Fifteen out of the forty-seven resources focused on data science topics including data sharing and data repositories (n=7), computational modelling (n=5), and Bayesian methods (n=3). Five resources discussed patient involvement in clinical investigations and patient experience data. Of these, three outlined opportunities and challenges for patient involvement in clinical trial design and participation, while two were FDA guidance documents describing methods and best practices for collecting patient preference data.[15,16] In addition, four resources focused on innovative and adaptive clinical trials. Of these, two focused on the use and challenges of innovative clinical trial designs and two were FDA guidance documents on the use of adaptive clinical and innovative clinical trial designs to establish substantial evidence of the effectiveness and safety of drugs and biologics, as well as cell and gene therapies for small populations.

Topics with lower prevalence among the resources Booz Allen captured included sponsor and patient advocate collaboration in clinical trials, pediatric populations, and clinical trial eligibility and rare disease clinical trial ethics. Four resources focused on the collaboration between patient advocates and developers, how collaboration can help developers incorporate patient perspectives into clinical trial design, or the distinct roles patient advocates can play throughout the clinical phase. Only 2 of the 47 resources discussed information on pediatric considerations or clinical trial eligibility and ethics.

HEARD Engagement with the Rare Disease Product Development Community

[15] Patient-Focused Drug Development: Collecting Comprehensive and Representative Input (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-collecting-comprehensive-and-representative-input)
[16] Patient-Focused Drug Development: Methods to Identify What Is Important to Patients (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-focused-drug-development-methods-identify-what-important-patients)

Participants reported that FDA's expectations and policies on clinical trial design and data collection were difficult to understand and apply in practice. Both PAG and industry respondents identified this as a particular challenge for biologics and requested case-based examples of clinical trials specific to biologics, such as gene therapies.

Patient advocates voiced that technical language — often directed toward industry — makes it difficult for organizations with limited scientific expertise to understand content on relevant clinical trial topics, including how to establish PAG-sponsor collaborations, and the collection and analysis of clinical trial data. In addition, because PAGs are increasingly involved in leading or supporting the NHS and registries that can inform clinical trial designs (e.g., study endpoints, biomarkers, treatment comparator), understanding the evidentiary standards that the Agency expects from these efforts is challenging. As such, PAGs requested practical guidance to help them align their work to Agency expectations.

PAGs highlighted the need for patient-centered educational materials on clinical trial design and processes. Patient advocates noted that patients, caregivers, and families have a limited understanding of the distinctions between nonclinical development, clinical trial phases, and the regulatory approval processes. PAGs indicated that patient-centered content on the clinical trial lifecycle could address common misconceptions regarding product development and post-trial access. They noted that patients may not always be aware that access to investigational products can be discontinued after a trial concludes, leading to confusion and frustration given the time-consuming nature of the product development process. PAGs also emphasized the importance of clearer communication and education around post-trial processes, long-term follow-up, and post-trial safety monitoring.

Industry respondents cited challenges in clinical trial design unique to rare diseases, including smaller trial sample sizes, geographically dispersed patient populations, and endpoint selection due to disease heterogeneity. Although clinical trial design educational materials exist, industry requested more case studies of successful uses of innovative trial designs (e.g., single-arm trials) which they believe can help overcome rare disease clinical trial challenges.

Gap Analysis of Clinical Trial Design and Data

Resources on clinical trial designs and data considerations represented an estimated 21% of the materials captured. Data science topics were represented to a greater extent than the gaps identified by the community which included patient advocacy involvement in clinical investigations, PAG-developer partnerships, non-traditional clinical trial designs, and foundational content on clinical trial phases. The landscape assessment findings corroborated this observed divergence, as few materials covered developer and patient advocate collaboration in clinical trials (n=4), innovative and adaptive clinical trial designs (n=4), and foundational clinical trial content (n=3). Additional knowledge gaps for patients and patient advocates

include foundational content on the importance of clinical trial eligibility criteria and related ethical considerations.

Rare Disease Product Development and Regulations

Existing Rare Disease Educational Materials

Of the resources identified through the landscape assessment, 61.6% (n=135) pertained to product development and regulation, representing the topic area with the highest concentration of available resources. Over half of these resources focused on (1) funding mechanisms, (2) FDA organization and programs/initiatives, (3) biologics, (4) priority designations, and (5) patient-focused product development.

Seventeen of the resources focused on topics related to funding mechanisms including FDA grants programs (n=8), ARPA-H programs supporting rare disease innovation (n=7), and general funding databases or investment strategies to support research and development (n=2). Sixteen resources focused on FDA's role in rare disease product development. Some of these resources focused on the Agency's infrastructure supporting rare disease product development such as the Hub, CDER's ARC Program, and CBER's Office of Therapeutic Products (OTP) and Rare Disease Program. Other resources focused on individual FDA initiatives such the Hub's Rare Disease Innovation, Science, and Exploration (RISE) Workshop Series, CDER/CBER's Rare Disease Evidence Principles (RDEP), CDER's Genetic Metabolic Diseases Advisory Committee (GeMDAC), and the ARC Program's LEADER 3D educational initiative. Fifteen resources involved biologic products, ten of which represented specific product types such as cell and gene therapies and monoclonal antibodies, including four guidance documents. In addition, five resources conveyed broad information related to biologics product development, regulation, and compliance programs (e.g., CBER compliance programs).

Fifteen of the resources disseminated information related to priority designations. Of these, ten resources focused on the Orphan Drug Act, orphan product development, and orphan product designation, while the remaining five described other priority designations. Lastly, 13 resources touched on patient-focused product development topics including patient engagement and collaboration (n=5), patient advocacy (n=3), patient-centered development (n=4), and representativeness in clinical trials (n=1).

Topics with less representation included pediatric product development, general challenges in rare disease product development, and drug repurposing. Five of the materials on this topic area applied to pediatric populations, which included three FDA guidance documents on pediatric product development and ethics and two general resources.

HEARD Engagement with the Rare Disease Product Development Community

An overarching sentiment across HEARD participant groups was the challenge related to the absence of integrated, user-friendly, and audience-specific resources on rare disease product development and regulation. Several participants noted that existing materials are often fragmented across different FDA medical product centers, causing searchability difficulties for the community. They also noted that existing materials target industry and developers, despite non-industry community members also being key contributors to rare disease product development. Participants suggested that the barriers to finding the necessary information may slow development timelines, increase inefficiencies, and limit the effective translation of scientific and patient insights into approved therapies.

Some patient advocates expressed a limited understanding of the regulatory pathways supporting rare disease product development, the general submission process, and how their contributions (e.g., collecting patient experience data or natural history data), can inform FDA's decision-making. These participants suggested that this knowledge gap can hinder their meaningful participation in product development. PAGs also noted that the limited number of easy-to-understand resources across USG websites, combined with the technical language used in many existing educational materials, makes it challenging for newer organizations with limited scientific or regulatory expertise to engage in the product development process. HEARD interview participants and docket respondents requested easy-to-understand explanations of biologics regulatory pathways, particularly for cell and gene therapies.

For industry, particularly for small and mid-sized developers, major challenges they reported facing are regulatory uncertainty and cost burden. Developers reported difficulty interpreting FDA requirements across the product lifecycle, including a perceived variability in expectations between review divisions, limited alignment across FDA medical product centers, and lack of clarity on evidentiary standards for rare disease products. This uncertainty increases development risk and can delay or deter investment altogether. Furthermore, in the HEARD interviews and the docket, industry sought to address some financial burdens by requesting additional information about the availability of incentive vouchers and clarity on the ability to combine different vouchers simultaneously (e.g., Commissioner's National Priority Voucher [CNPV], Rare Pediatric Disease [RPD]); these vouchers lessen the cost of entry and mitigate commercial viability concerns, an especially important consideration for small-to-medium-sized developers.

Gap Analysis of Rare Disease Product Development and Regulations

Most resources in the landscape assessment related to rare disease product development and regulation. The landscape assessment revealed that educational materials focused on pediatric populations, real-world examples of product

development challenges faced by developers, and drug repurposing are gaps in the educational curricula, representing less than 8% of resources identified for this topic area. Although several resources captured by the landscape assessment refer to topics related to funding mechanisms, FDA organization and initiatives, and priority designations, the community emphasized a need for educational content clarifying FDA's rare disease infrastructure (i.e., cross-Agency versus Center-specific programs), the regulatory pathways available to rare disease medical product developers, and available funding opportunities (e.g., the Orphan Products Grants Program) and regulatory designations (e.g., Fast Track, Regenerative Medicine Advanced Therapy, and Breakthrough Therapy) that can help developers de-risk development programs. This need was further underscored by developer requests for FDA to communicate more regularly and clearly on regulatory trends that can help improve alignment between development programs and the Agency.

A total of 63 resources captured in the landscape assessment disseminated information on such topics, highlighting that existing educational offerings are already available to the community. The disconnect between the community's educational needs and the quantity of resources identified by the landscape assessment may reflect usability challenges across the USG websites offering such content. The majority (59%) of USG-disseminated resources scored in the *moderate* usability range (**Figure 3**), with this percentage increasing to 62% when FDA websites were assessed in isolation. In comparison, 71% of all the resources disseminated by PAGs received *high* usability ratings and HEARD interview session participants repeatedly observed that locating information from PAGs or rare disease umbrella organizations is not challenging. Several HEARD interview participants recommended that, to improve reach, FDA consider rare disease umbrella organizations as points of reference for how to enhance the organization and cataloguing of existing Agency resources. Together, these findings suggest that USG and FDA websites are difficult to navigate and search, partially due to confusing user interfaces.

In addition, patient advocates observed that sourcing easy-to-comprehend content related to product development and regulation was challenging for their constituents and requested more educational resources targeting general audiences with a lower technical background. Findings from the landscape assessment demonstrate this need, as under the adapted Dreyfus model (see **Collect and Analyze Data** subsection of Appendix D; **Table 6-3**), 51% of FDA-disseminated resources were suitable for advanced audiences, while 19.4% and 29.6% were suitable for intermediate and beginner audiences, respectively.

These findings indicate that the rare disease product development community encounters challenges locating information, which presents as potentially attributable to difficulty navigating the USG platforms and a high technical knowledge entry point.

FDA Engagements with the Rare Disease Product Development Community

Existing Rare Disease Educational Materials

Educational resources on FDA engagements with the rare disease product development community made up 5% (n=11) of resources identified. Four of these resources discussed FDA's patient engagement programs (e.g., patient listening sessions), four were FDA guidance documents for developers and interested parties on engagement opportunities with the Agency during product development, two were general resources for patients and developers, and one focused on FDA's Support for clinical Trials Advancing Rare Disease Therapeutics (START) Pilot Program.

HEARD Engagement with the Rare Disease Product Development Community

The heterogeneity of rare diseases also presents inherent challenges for the Agency in developing FDA guidance documents. Feedback from HEARD interviews and the docket noted that most of the existing guidance documents are scoped for general medical product development, and a limited number of available guidance documents anchor content around rare disease product development. Participants observed that the limited number of guidance documents centering on rare disease product development leads to a reliance on direct Agency interactions to address complex, product-specific questions about how their programs can meet evidentiary standards designed for general product development. Respondents encouraged continued FDA participation in scientific conferences and publication of regulatory perspectives, as these efforts help communicate clearer expectations across therapeutic areas.

Many PAG participants reported that prior to consulting FDA-disseminated resources, they relied on their network of peers and other advocacy organizations to interpret regulatory expectations and development pathways. This reflects a broader gap in user-friendly content across FDA resources, including the existing resources that guide the public on how to engage with the Agency. PAGs also emphasized the need for more opportunities to directly engage FDA without the formal FDA-sponsor paradigm; they requested enhanced dialogue through public workshops and listening sessions.

Industry participants reported challenges in understanding how to effectively engage FDA, as well as how to leverage existing regulatory programs in a consistent and predictable manner. Feedback from the HEARD interviews and the docket recommended a practical resource describing how to prepare for meetings with FDA. They requested clarity on the different expectations for precompetitive meetings (e.g., Critical Path Innovation (CPIM) and Initial Targeted Engagement for Regulatory Advice on CBER/CDER Products [INTERACT]) and formal meetings between FDA and sponsors (e.g., Pre-Investigational New Drug [Pre-

IND], Type B) to improve the quality of meeting requests and meaningfully engage FDA throughout a development program.

Although FDA provides educational materials and means to engage the community, participants perceived these resources as difficult to navigate and not tailored to their individual needs, which contributes to underutilization and reliance on intermediaries. Furthermore, interviewees recognized the importance of FDA and developers involving patient communities and PAGs throughout the product development process, including formal meetings where patient experience data are discussed and considered. As such, participants expressed interest in increased PAG inclusion in product development discussions and guidance and educational material development.

Gap Analysis of FDA Engagements with the Rare Disease Product Development Community

The landscape assessment revealed that 11 out of the 219 resources (5%) focused on engagement opportunities with FDA. Most resources identified targeted patient-specific engagement opportunities, such as patient listening sessions and CBER's patient engagement program. Although limited resources exist explaining FDA meeting types, industry requested more informative and practical resources clarifying the types of meetings available and best practices to maximize the utility of meetings. These quantitative and qualitative findings may indicate: (A) that information on how to engage FDA is a need for the community; (B) that existing resources could benefit from increased promotion to improve visibility; or (C) that existing resources could benefit from revisions informed by community input.

Additional Insights

Pediatric Medical Product Development

Because nearly half of people with a rare disease in the U.S. are children, a noteworthy finding of this assessment is the limited educational content on product development for pediatric populations. Out of the 219 resources captured, a total of 26 (11.8%) included information pertinent to pediatric populations, while only 10 (4.5% of all materials) focused exclusively on pediatric product development. Industry observed that the limited number of existing educational materials focusing on pediatric product development was an educational gap that FDA should consider addressing. Thus, pediatric medical product development represents a cross-cutting area of need for future educational content.

Knowledge and Experience Across the Patient Advocacy Community

Across all engagement efforts with the rare disease product development community, PAG participants emphasized that the educational needs of patient advocacy organizations are varied. Most participants agreed that the findings from

this assessment (see **Table 5-1**) reflected the needs of specialized advocacy organizations and that foundational content on rare disease product development and regulation was an unmet educational need for newer PAGs and their patient communities.

Several participants suggested that FDA consider a centralized and targeted educational curriculum where content is presented across specialized tracks to address the spectrum of knowledge needs across the rare disease product development community (i.e., new PAGs, experienced PAGs, industry, researchers). Participants stated that developing educational materials targeted to groups within the community can expand the reach and uptake of FDA's rare disease educational curriculum: easy-to-understand videos and infographics (e.g., guidance snapshots) for foundational content and more in-depth case studies for technical content.

5. CONCLUSIONS AND CONSIDERATIONS

Figure 1 illustrates the distribution of existing educational resources by rare disease topic area, and **Table 5-1** summarizes the main gaps identified through the landscape assessment and third-party recommendations. Recommendations outlined below reflect the quantitative and qualitative findings from the landscape assessment and engagement efforts with the rare disease product development community.

Table 5-1: Gaps in Educational Curricula and Third-Party Recommendations for FDA's Consideration

Topic Area	Gaps	Frequency of Mentions at HEARD Interviews	Third-Party Recommendations and Intended Beneficiary

Nonclinical	• Insufficient resources outlining the key steps for the transition from nonclinical to clinical studies.
	• Insufficient examples of evidentiary standards for nonclinical studies.
		Low (1-3 mentions)	• For Patient Community: Develop introductory educational content on the progression from nonclinical to clinical development and partner with rare disease umbrella organizations to disseminate this content to the community.
			• For Product Developers:
			  ○ Develop case studies on nonclinical topics including dose-finding approaches and evidentiary standards (e.g., animal models and new approach methodologies), as well as case studies illustrating challenges that may arise during nonclinical rare disease product development.
			  ○ Increase promotion of the LEADER 3D case study on clinical dose escalation strategies for rare disease drug development.[17]

Natural History Studies and Registries	• Limited examples of strategies to overcome challenges on the use of NHS and	High (7+ mentions)	• For Patient Community:

[17] LEADER 3D – A Clinical Dose Escalation Strategy for a Rare Disease Drug Program (Olipudase alfa-rpcp [Xenpozyme]) (https://www.fda.gov/media/185753/download?attachment)

Topic Area	Gaps	Frequency of Mentions at HEARD Interviews	Third-Party Recommendations and Intended Beneficiary
	registry data in rare disease product development. • Lack of information on the evidentiary standards for the use of NHS and registry data to support product submissions. • Limited guidance on what constitutes acceptable external control data when NHS data are limited or unavailable.		○ Promote existing FDA educational resources (e.g., LEADER 3D video) on considerations for collection and use of NHS in rare disease drug development. [18] ○ Create new case studies on considerations for the use of NHS in rare disease product development (e.g., using NHS and registry data to identify surrogate endpoints and establish predictability of clinical outcomes, and how NHS can be used as an external control to support substantial evidence of effectiveness). ○ Develop a resource that informs PAGs on how to collect and maximize the use of natural history data to meet evidentiary standards. ○ Supplement existing curricula with new content (e.g., short-form videos, podcasts, and snapshot summaries) on the evidentiary standards for the use of NHS and registries during product development, focusing on RWD, developer-patient advocacy collaboration, and data quality. • For Product Developers: ○ Develop targeted case studies on the challenges of NHS and registry data use, highlighting successful approaches and FDA engagement opportunities. ○ Create educational resources addressing practical limitations in NHS data availability, including guidance on what constitutes acceptable external control data when NHS data are limited or unavailable.
Endpoints and Biomarkers	• Limited patient-centered content on the importance of endpoints and patient	High (7+ mentions)	• For Patient Community: ○ Develop introductory educational content on endpoints and biomarkers that prioritizes the patient perspective, including the role of patient experience data in endpoint selection and

[18] LEADER 3D – Considerations for Collecting/Using Natural History Data Fit for Use in the Regulatory Setting (https://www.youtube.com/watch?v=VJu0-N6alil)

Topic Area	Gaps	Frequency of Mentions at HEARD Interviews	Third-Party Recommendations and Intended Beneficiary
	input for endpoint selection. • Limited resources on the effective use of endpoints to support product submissions. • Limited resources demonstrating how patient experience data can be integrated into endpoint selection and used to support regulatory decision making throughout rare disease product development.		meaningful opportunities for patient engagement in endpoint development and selection. ○ Promote existing educational resources such as the Patient-Focused Drug Development (PFDD) Glossary and the guidance snapshots.[19,20] ○ Create a case study that includes information on how a developer successfully engaged with the patient community (i.e., PAGs and patients) throughout rare disease product development program. • For Product Developers: ○ Develop case studies on how patient experience data may inform endpoint selection. ○ Promote the CDER ARC Program's LEADER 3D educational resources on endpoint selection and use on the Hub's webpage (e.g., connecting readers to the case studies and videos). ○ Supplement existing case studies with new content (i.e., additional case studies, speaking engagements, and RISE workshops) on the common challenges to the use of endpoints in product submissions including: ▪ Validating endpoints and outcome measures. ▪ Use cases for composite endpoints. ▪ Pediatric considerations.
Clinical Trial Design and Related Data Considerations	• Insufficient information to guide patient communities'	High (7+ mentions)	• For Patient Community: ○ Engage with patient advocacy organizations to host informational sessions (e.g., workshops) and develop specialized plain-language documents for patient

[19] https://www.fda.gov/drugs/development-approval-process-drugs/patient-focused-drug-development-glossary (https://www.fda.gov/drugs/development-approval-process-drugs/patient-focused-drug-development-glossary)
[20] Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments (https://www.fda.gov/media/159516/download?attachment)

Topic Area	Gaps	Frequency of Mentions at HEARD Interviews	Third-Party Recommendations and Intended Beneficiary
	involvement in clinical trials. • Lack of materials explaining eligibility criteria and ethical considerations for clinical trials. • Low number of resources on innovative and adaptive clinical trial designs in rare disease product development. • Limited resources to support clinical trials in pediatric populations.		communities and advocates on ways to increase patient representation and input during clinical trial design. ○ Leverage FDA communication channels (e.g., listservs, newsletters, speaking engagements) to raise awareness about existing resources that describe patient-centered clinical trial design approaches. ○ Create introductory content (e.g., online educational modules explaining why clinical trial participation is important and how patients can meaningfully engage) on clinical trial eligibility criteria and related ethical considerations. • For Product Developers: ○ Disseminate existing resources on clinical trial designs for rare disease product development (e.g., RISE workshops and CDER Center for Clinical Trial Innovation [C3TI]). ○ Develop case studies and host public engagements (e.g., RISE workshops) to address special considerations related to clinical trials in pediatric populations, highlighting challenges, analytical approaches, and evidentiary standards. ○ Develop case studies on successful uses of adaptive and innovative clinical trial designs.
Rare Disease Product Development and Regulations	• Challenges in using educational websites and engagement channels to distribute foundational knowledge on rare disease product development and regulation. • Lack of examples on strategies to	Medium (4-6 mentions)	• For Patient Community: Collaborate with external rare disease organizations to disseminate educational resources on rare disease product development and regulation intended for patients. • For Product Developers: ○ Increase awareness of existing grant programs supporting rare disease product development and innovation. ○ Promote LEADER 3D curriculum, which includes videos and case studies highlighting challenges and strategies for rare disease product development.

Topic Area	Gaps	Frequency of Mentions at HEARD Interviews	Third-Party Recommendations and Intended Beneficiary
	overcome product development challenges and drug repurposing.		○ Create case studies on drug repurposing for rare disease indications. ○ Create a Guidance Directory on the Hub's website to direct the rare disease product development community to commonly used FDA guidance documents for rare disease biologics development.
FDA Engagements with the Rare Disease Product Development Community	• Limited awareness within the community about existing FDA engagement opportunities available to patient communities and patient advocates. • Limited awareness of early engagement opportunities with FDA prior to clinical development.	High (7+ mentions)	• For Patient Community: ○ Increase communications to improve visibility and awareness of existing FDA engagement opportunities such as PFDD meetings, patient listening sessions, and CBER's Patient Engagement Program. ○ Develop educational content on the different types of engagement opportunities that are available to rare disease patient communities and improve ease of navigation to access existing resources. • For Product Developers: ○ Participate in public forums (e.g., workshops, conferences) to promote the formal engagement pathways available to patients, PAGs, and developers. ○ Develop case studies highlighting the different types of FDA engagement opportunities available to product developers – including early engagement – focusing on purpose, best practices, and timing (i.e., when along the development process these opportunities are most useful).

During working sessions, individuals from industry and PAGs reviewed the proposed recommendations to prioritize based on their needs. The three highest priority recommendations, from **Table 5-1** above, are presented below:

Table 5-2: Patient Community's Prioritized List of Recommendations

Priority Ranking	Topic Area	Recommendation Identified
1	Natural History Studies and Registries	Develop a resource that informs PAGs on how to collect and maximize the use of natural history data to meet evidentiary standards.
2	FDA Engagements with the Rare Disease Product Development Community	Develop educational content on the different types and scope of engagement opportunities available to patient communities and patient advocacy organizations.
3	Endpoints and Biomarkers	Develop introductory educational content on endpoints and biomarkers that prioritizes the patient perspective, including the role of patient experience data in endpoint selection and meaningful opportunities for patient engagement in endpoint development and selection.

Table 5-3: Product Developers' Prioritized List of Recommendations

Priority Ranking	Topic Area	Recommendation Identified
1	Endpoints and Biomarkers	Supplement existing case studies with new content (i.e., additional case studies, speaking engagements, and RISE workshops) on the common challenges to the use of endpoints in product submissions including: • Validating endpoints and outcome measures • Use cases for composite endpoints • Pediatric considerations
2	Endpoints and Biomarkers	Promote the CDER ARC Program's LEADER 3D educational resources on endpoint selection and use on the Hub's webpage (e.g., connecting readers to the case studies and videos).
3	Clinical Trial Design and Related Data Considerations	Develop case studies on successful uses of adaptive and innovative clinical trial designs.

6. APPENDIX

This section includes: (1) a glossary containing the acronyms used in this document along with the corresponding definitions, (2) Additional Resources, (3) docket language, (4) and detailed assessment methodology.

A. Glossary of Acronyms

Acronyms	Definition
ARC	Accelerating Rare Disease Cures
ARPA-H	Advanced Research Projects Agency for Health
BGTC	Bespoke Gene Therapy Consortium
C3TI	Center for Clinical Trial Innovation
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CNPV	Commissioner's National Priority Voucher
CPIM	Critical Path Innovation Meeting
DCI	Data Collection Instrument
DDT	Drug Development Tools
FDA	The U.S. Food and Drug Administration
GeMDAC	Genetic Metabolic Diseases Advisory Committee
HEARD	Hub's Educational Assessment and Resource Development
Hub	FDA Rare Disease Innovation Hub
INTERACT	INitial Targeted Engagement for Regulatory Advice on CBER/CDER ProducTs
LEADER 3D	Learning and Education to ADvance and Empower Rare Disease Drug Developers
LORI	Learning Object Review Instrument
NCATS	National Center for Advancing Translational Sciences
NHS	Natural History Studies
NIH	National Institutes of Health
OTP	CBER's Office of Therapeutic Products
PDF	Portable Document Format
PFDD	Patient-Focused Drug Development
Pre-IND	Pre-Investigational New Drug
RaDaR	Rare Diseases Registry

Acronyms	Definition
RDEA	Rare Disease Endpoint Advancement Pilot Program
RDEP	Rare Disease Evidence Principles
RISE	Rare Disease Innovation, Science, and Exploration
RPD	Rare Pediatric Disease Priority Review Voucher
RWD	Real-World Data
RWE	Real-World Evidence
SME	Subject Matter Expert
START	Support for clinical Trials Advancing Rare Disease Therapeutics Pilot Program
TRND	Therapeutics for Rare and Neglected Diseases
U.S.	United States
USG	U.S. Government

B. Additional Resources

The tables below represent a non-exhaustive list of existing educational resources that address or partially address the needs of the rare disease product development community, as identified by this assessment. Each table is tailored to the distinct needs expressed by industry and the patient community, listing informational resources by topic area.

Table 6-1: List of Selected Additional Resources for Industry by Topic Area

Topic Area	USG Resources Available	Covered Product Area(s)
Nonclinical	• LEADER 3D: A Clinical Dose Escalation Strategy for a Rare Disease Drug Program (Olipudase alfa-rpcp [Xenpozyme]) (https://www.fda.gov/media/185753/download?attachment) • Qualification Process for Drug Development Tools Guidance for Industry and FDA Staff (https://www.fda.gov/media/133511/download) *	• Drugs • Drugs & Biologics
Natural History Studies and Registries	• LEADER 3D: Leveraging Natural History and Registry Data to Inform Endpoint Selection for a Rare Disease (Lumasiran [Oxlumo]) (https://www.fda.gov/media/193493/download?attachment) • LEADER 3D: Leveraging Existing Biomarker and Natural History Data to Support Drug Repurposing for a Rare Disease (Chenodiol [Ctexli]) (https://www.fda.gov/media/193803/download?attachment) • LEADER 3D: A Natural History Study External Control as Confirmatory Evidence for a Rare Disease Drug Approval (Omaveloxolone [Skyclarys]) (https://www.fda.gov/media/193804/download?attachment) • Rare Diseases: Natural History Studies for Drug Development *Guidance for Industry* (https://www.fda.gov/media/122425/download) *	• Drugs • Drugs • Drugs • Drugs & Biologics
Endpoints and Biomarkers	• BEST (Biomarkers, EndpointS, and other Tools) Resource (https://www.ncbi.nlm.nih.gov/books/NBK326791/) * • Rare Disease Endpoint Advancement Pilot Program (https://www.fda.gov/drugs/development-resources/rare-disease-endpoint-advancement-pilot-program) * • Biomarker Qualification: Evidentiary Framework (https://www.fda.gov/media/122319/download) • Multiple Endpoints in Clinical Trials (https://www.fda.gov/media/162416/download) * • LEADER 3D: Use of the Win Ratio Method to Demonstrate Clinical Benefit from a Composite Endpoint for a Rare Disease (Mavorixafor [Xolremdi]) (https://www.fda.gov/media/193494/download?attachment) • LEADER 3D: A Novel Approach to Identifying a Clinically Meaningful Outcome in a Heterogeneous Population (Inebilizumab-cdon [Uplizna]) (https://www.fda.gov/media/193805/download?attachment)	• General • Drugs & Biologics • Drugs & Biologics • Drugs & Biologics • Drugs • Drugs

Topic Area	USG Resources Available	Covered Product Area(s)
	• LEADER 3D: Developing Novel Clinical Outcome Assessment Instruments for Use in the Demonstration of Substantial Evidence of Effectiveness for a Rare Disease (Odevixibat [Bylvay]) (https://www.fda.gov/media/186133/download?attachment) • LEADER 3D: Use of a Surrogate Endpoint to Demonstrate Substantial Evidence of Effectiveness for an Accelerated Approval (Tofersen [Qalsody]) (https://www.fda.gov/media/186135/download?attachment) • LEADER 3D: Use of Biomarkers as Surrogate Endpoints for Approval in the Avalglucosidase alfa-ngpt (Nexviazyme) and Seladelpar (Livdelzi) Development Programs (https://www.fda.gov/media/186136/download?attachment)	• Drugs • Drugs • Drugs
Clinical Trial Design and Related Data Considerations	• Adaptive Design Clinical Trials for Drugs and Biologics Guidance for Industry (https://www.fda.gov/media/78495/download) • Innovative Designs for Clinical Trials of Cellular and Gene Therapy Products in Small Populations (https://www.fda.gov/media/188892/download) • Use of Bayesian Methodology in Clinical Trials of Drug and Biological Products (https://www.fda.gov/media/190505/download) • E11A Pediatric Extrapolation (https://www.fda.gov/media/161190/download) • LEADER 3D: Bayesian Statistics in Rare Disease Clinical Investigations (Belimumab [Benlysta]) (https://www.fda.gov/media/193802/download?attachment)	• Drugs & Biologics • Biologics • Drugs & Biologics • Drugs & Biologics • Drugs
Rare Disease Product Development and Regulations	• Guidance Documents for Rare Disease Drug Development (https://www.fda.gov/drugs/guidances-drugs/guidance-documents-rare-disease-drug-development) • Cross-cutting Topics: Rare Diseases Regulatory Science Research (https://www.fda.gov/science-research/focus-areas-regulatory-science-report/cross-cutting-topics-rare-diseases-regulatory-science-research) • Rare Diseases: Considerations for the Development of Drugs and Biological Products (https://www.fda.gov/media/119757/download) * • Human Gene Therapy for Rare Diseases (https://www.fda.gov/media/113807/download) • Postapproval Methods to Capture Safety and Efficacy Data for Cell and Gene Therapy Products (https://www.fda.gov/media/188891/download) • CDER/CBER Rare Disease Evidence Principles (RDEP) (https://www.fda.gov/industry/fda-rare-disease-innovation-hub/cdercber-rare-disease-evidence-principles-rdep) • Innovative Therapeutics: Gene Therapy (https://youtu.be/mU25qAsYwu0?si=PXnUGDEyY3ctvV7Z) • Considerations for the use of the Plausible Mechanism Framework to Develop Individualized Therapies that Target	• Drugs • Drugs, Biologics, & Medical Devices • Drugs & Biologics • Biologics • Biologics • Drugs & Biologics • Biologics • Biologics

Topic Area	USG Resources Available	Covered Product Area(s)
	Specific Genetic Conditions with Known Biological Cause (https://www.fda.gov/media/191247/download)	• Drugs, Biologics, & Medical Devices
	• Rare Disease Innovation, Science, and Exploration (RISE) Workshop Series (https://www.fda.gov/industry/fda-rare-disease-innovation-hub/rare-disease-innovation-science-and-exploration-rise-workshop-series)	• Drugs, Biologics, & Medical Devices
	• Ethical Considerations for Clinical Investigations of Medical Products Involving Children (https://www.fda.gov/media/161740/download)	• Drugs
	• E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population (https://www.fda.gov/media/101398/download)	• Drugs, Biologics, & Medical Devices
	• Rare Pediatric Disease Priority Review Vouchers (https://www.fda.gov/media/90014/download)	• Drugs
	• Accelerated Approval – Expedited Program for Serious Conditions (https://www.fda.gov/media/184120/download)	• Biologics
	• Expedited Programs for Regenerative Medicine Therapies for Serious Conditions (https://www.fda.gov/media/188874/download)	• Drugs, Biologics, & Medical Devices
	• Funding Opportunities for Rare Diseases at FDA (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/funding-opportunities-rare-diseases-fda)	• Drugs
	• Learning and Education to ADvance and Empower Rare Disease Drug Developers (LEADER 3D) (https://www.fda.gov/about-fda/accelerating-rare-disease-cures-arc-program/learning-and-education-advance-and-empower-rare-disease-drug-developers-leader-3d)	• Drugs & Biologics
	• Designating an Orphan Product: Drugs and Biological Products (https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/designating-orphan-product-drugs-and-biological-products)	• Drugs, Biologics, & Medical Devices
	• Flexible Requirements for Cell and Gene Therapies to Advance Innovation (https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/flexible-requirements-cell-and-gene-therapies-advance-innovation)	• Biologics
	• CBER's CMC Considerations for Early Phase Studies of Cell and Gene Therapy Products (https://www.youtube.com/watch?v=Ua9dT1Bi6kI)	• Drugs & Biologics
	• Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases (https://www.fda.gov/media/109496/download)	• General
	• Rare Disease AI/ML for Precision Integrated Diagnostics (https://arpa-h.gov/explore-funding/programs/rapid)	• Biologics
	• Genetic Medicines and Individualized Manufacturing for Everyone (https://arpa-h.gov/explore-funding/programs/give)	• Biologics & Medical Devices
	• Treating Hereditary Rare Diseases with In Vivo Precision Genetic Medicines (https://arpa-h.gov/explore-funding/programs/thrive)	
FDA Engagements	• Formal Meetings and Requests for Feedback for CBER-Regulated Products (https://www.fda.gov/vaccines-blood-	• Biologics

Topic Area	USG Resources Available	Covered Product Area(s)
	biologics/development-approval-process-cber/formal-meetings-and-requests-feedback-cber-regulated-products) • Support for clinical Trials Advancing Rare disease Therapeutics (START) Pilot Program (https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/support-clinical-trials-advancing-rare-disease-therapeutics-start-pilot-program) * • Rare Diseases: Early Drug Development and the Role of Pre-IND Meetings (https://www.fda.gov/media/117322/download) * • Interacting with the FDA on Complex Innovative Trial Designs for Drugs and Biological Products (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/interacting-fda-complex-innovative-trial-designs-drugs-and-biological-products) • Best Practices for Communication Between IND Sponsors and FDA During Drug Development (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/best-practices-communication-between-ind-sponsors-and-fda-during-drug-development) • Meetings with the Office of Orphan Products Development (https://www.fda.gov/media/111946/download) • Regulatory Resources and Avenues for Obtaining Early Guidance from CBER/OTP (https://youtu.be/6XWhXdErP6o?si=KkVVHAzrM_KXlZ0B)	• Drugs & Biologics • Drugs & Biologics • Drugs & Biologics • Drugs • Drugs, Biologics, & Medical Devices • Biologics
Patient-Focused Product Development	• Patient-Focused Drug Development: Collecting Comprehensive and Representative Input (https://www.fda.gov/media/139088/download) * • Patient-Focused Drug Development: Methods to Identify What Is Important to Patients (https://www.fda.gov/media/131230/download) * • Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments (https://www.fda.gov/media/159500/download) * • Patient-Focused Drug Development: Incorporating Clinical Outcome Assessments Into Endpoints for Regulatory Decision-Making (https://www.fda.gov/media/166830/download) * • Incorporating Voluntary Patient Preference Information over the Total Product Life Cycle (https://www.fda.gov/media/92593/download)	• Drugs & Biologics • Drugs & Biologics • Drugs, Biologics, & Medical Devices • Drugs, Biologics, & Medical Devices • Biologics & Medical Devices

* *Asterisk denotes FDA rare disease drug development informational resources referenced in Table 3 of the 2024 LEADER 3D Public Report of External Engagement Analysis.*

Table 6-2: List of Selected Additional Resources for the Patient Community by Topic Area

Topic Area	USG Resources Available	Covered Product Area(s)
Natural History Studies and Registries	• LEADER 3D: Considerations for Collecting/Using Natural History Data Fit for Use in the Regulatory Setting (https://www.youtube.com/watch?v=VJu0-N6alil) • Rare Diseases Registry Program (RaDaR) (https://ncats.nih.gov/research/research-activities/RaDaR)	• Drugs • Drugs, Biologics, & Medical Devices
Endpoints and Biomarkers	• LEADER 3D: Understanding Endpoints in Rare Disease Drug Development (https://www.youtube.com/watch?v=lHQ66qjXPoU)	• Drugs
Clinical Trial Design and Related Data Considerations	• LEADER 3D: Challenges, Strategies & Regulatory Considerations for Rare Disease Clinical Trial Design (https://www.youtube.com/watch?v=KKm2hG7foQw) • NIH Clinical Research Trials and You (https://www.nih.gov/health-information/nih-clinical-research-trials-you) • What is Clinical Research? (https://youtu.be/lJOQB_G15Jc?si=vG0y5EOM_bUExjxn) • What are the different types of clinical research? (https://youtu.be/BBTqkHQjUzg?si=qhfPMBefDfMbcCrR) • Rare Diseases Clinical Research Network (RDCRN) (https://ncats.nih.gov/research/research-activities/rdcrn) • Infographic: Why do researchers do different kinds of clinical studies? (https://www.nih.gov/sites/default/files/2024-12/infographic-why-researchers-different-kinds-clinical-studies.pdf) • An Introduction to Clinical Trials (https://vimeo.com/442123256)	• Drugs • General • General • General • General • General
Rare Disease Product Development and Regulations	• Rare Diseases at FDA (https://www.fda.gov/patients/rare-diseases-fda) • 9 Things to Know About CDER's Efforts on Rare Diseases (https://www.fda.gov/drugs/things-know-about/9-things-know-about-cders-efforts-rare-diseases) • Cellular & Gene Therapy Products (https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products) • What is Gene Therapy? (https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy) • Postmarketing Clinical Trials (https://www.fda.gov/vaccines-blood-biologics/biologics-post-market-activities/postmarketing-clinical-trials) • Guidance Snapshot Pilot (https://www.fda.gov/drugs/guidances-drugs/guidance-snapshot-pilot) • Regulatory Fitness in Rare Disease Clinical Trials Workshop Day 1 (https://videocast.nih.gov/watch/c6845c66-d5db-11f0-9cf9-12c45c580ad9) • Regulatory Fitness in Rare Disease Clinical Trials Workshop Day 2 (https://videocast.nih.gov/watch/c68658d5-d5db-11f0-9cf9-12c45c580ad9) • Bespoke Gene Therapy Consortium (BGTC) (https://ncats.nih.gov/research/research-activities/gene-targeted-therapies/bgtc-bespoke-gene-therapy-consortium)	• Drugs, biologics, & medical devices • Drugs • Biologics • Biologics • Biologics • Drugs • Drugs • Drugs • Biologics

Topic Area	USG Resources Available	Covered Product Area(s)
	• Therapeutics for Rare and Neglected Diseases (TRND) (https://ncats.nih.gov/research/research-activities/TRND) • Our Impact on Rare Diseases (https://ncats.nih.gov/research/our-impact/our-impact-rare-diseases) • Resources for Rare Disease Patients and Advocates (https://ncats.nih.gov/resources/for-rare-disease-patients-and-advocates) • Working with the FDA in the Conduct of Clinical Trials (https://vimeo.com/633111212) • Working with Industry in the Conduct of Clinical Trials (https://vimeo.com/523808848) • Rare Disease Drug Development Series: What Patients and Advocates Need to Know (https://learn.rarediseases.org/courses/rare-disease-drug-development-series/) [21]	• Drugs • General • General • General • General • General
Patient Community Engagement	• FDA Patient Listening Sessions (https://www.fda.gov/patients/learn-about-fda-patient-engagement/fda-patient-listening-sessions) • Center for Biologics Evaluation and Research Patient Engagement Program (https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/center-biologics-evaluation-and-research-patient-engagement-program) • For Patients (https://www.fda.gov/patients) • The Critical Role of Patients in Advancing Gene Therapy Treatments for Rare Diseases (https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/regenmeded-webinar-critical-role-patients-advancing-gene-therapy-treatments-rare-diseases-03092022) • National Center for Advancing Translational Sciences (NCATS) Toolkit for Patient-Focused Therapy Development (https://toolkit.ncats.nih.gov/) • Clinical Trials - Working with your Patient Community (https://vimeo.com/494316926)	• General • Biologics • Drugs, Biologics, & Medical Devices • Biologics • Drugs, Biologics, & Medical Devices • General

[21] Resource created by the National Organization for Rare Disorders (NORD) in collaboration with FDA's Center for Drug Evaluation and Research (CDER) and the Critical Path Institute. Funding was made available through the Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP), a collaborative agreement with the Critical Path Institute funded by FDA.

C. Docket Language

Docket Description
Title: Opportunity for Public Comment on Rare Disease Educational Materials from the Center for Drug Evaluation and Research's Accelerating Rare disease Cures Program and the Rare Disease Innovation Hub **Background** Rare diseases affect an estimated 25 to 30 million individuals in the United States, approximately half of whom are children. Despite scientific advances and existing incentives, the majority of rare diseases lack approved therapies. Drug development for rare diseases presents unique scientific, clinical, and regulatory challenges that require tailored educational resources for multiple stakeholder communities. FDA has undertaken multiple efforts to support rare disease drug development through education, outreach, and regulatory science. In December 2022, as part of CDER's Accelerating Rare disease Cures (ARC) Program, FDA published a public docket (FDA-2022-N-3226-0001) seeking input on knowledge gaps and priority topics in rare disease drug development and related regulatory considerations. Input received through that docket informed a landscape assessment published as a public report in 2024, and the subsequent development of publicly available educational materials, including case studies and videos addressing scientific, clinical, and regulatory topics relevant to rare disease drug development. Building on the 2022–2023 LEADER 3D public docket and the educational materials developed as a result of that engagement, CDER ARC is now seeking targeted input through a new public docket focused on feedback on Learning and Education to ADvance and Empower Rare Disease Drug Developers (LEADER 3D) educational materials. **Request for Feedback on Existing LEADER 3D Educational Materials** In this docket, CDER ARC is seeking feedback on the resulting educational materials developed under the LEADER 3D Program. This request represents a next phase of engagement focused on evaluating existing LEADER 3D materials, to inform future iterations of program-specific educational resources for stakeholders engaged in rare disease drug development. FDA invites comments from stakeholders involved in rare disease drug development, including industry, academia, and other federal partners, on topics such as: • The relevance and clarity of existing LEADER 3D educational materials • The effectiveness of current formats, such as case studies and videos

• Suggestions for additional topics or formats for potential future materials that would further support rare disease drug development

With input from stakeholders actively engaged in the design and conduct of rare disease drug development programs, including industry, academia, and other federal partners, FDA intends to evaluate and refine the educational materials developed under the LEADER 3D Program. Feedback received will be used to identify areas where existing materials could be expanded, or supplemented, as well as to inform the prioritization and development of the next phase of publicly available LEADER 3D educational resources. Through this iterative approach, FDA seeks to build on prior engagement and support the ongoing development of safe and effective therapies for rare diseases.

Additional Opportunity for Public Comment from the Rare Disease Innovation Hub

The FDA Rare Disease Innovation Hub (Hub) works across FDA medical product centers and programs to promote coordination and alignment to advance safe and effective rare disease therapies. In 2022, the Food and Drug Administration (FDA) issued a request for public input on scientific, clinical, and regulatory challenges and priority topics in rare disease drug development (Docket No. FDA-2022-N-3226). FDA appreciates the input received through that effort. Accordingly, The Hub is seeking information to better understand what educational resources are currently available for patients/patient organization and developers of CBER-regulated rare disease biologics. FDA is also interested in understanding where gaps in available resources may exist.

Educational Resources for Patients and Patient Organizations

The Hub invites stakeholders to identify existing educational resources intended for patients and patient organizations that relate to rare disease product development. Submissions should identify specific resources (for example, by name and where they can be accessed) and briefly describe the aspects of rare disease product development they address. The Hub is also asking patients and patient organizations to highlight areas of rare disease product development where desired educational resources for patients may not exist.

Educational Resources for Rare Disease Biologics Developers

The Hub invites stakeholders to identify existing educational resources intended to support developers engaged in rare disease biologics development. Feedback should identify specific resources and where they can be accessed and may address any stage of development.

The Hub is also interested in understanding areas of rare disease biologics development where educational resources are limited or absent.

Feedback should focus on identifying existing resources and highlighting areas where there are gaps in educational materials. FDA is not seeking proposals for new programs or initiatives through this request.

Submission of Comments

Responses to both queries may be submitted within one document. Comments submitted in response to this notice should clearly indicate whether they pertain to:

• CDER ARC's LEADER 3D Program educational materials for rare disease drug developers, or

• The Rare Disease Innovation Hub's request for input on educational resources that support patients and patient advocates, and those related to CBER-regulated biologics in the development of rare disease therapies.

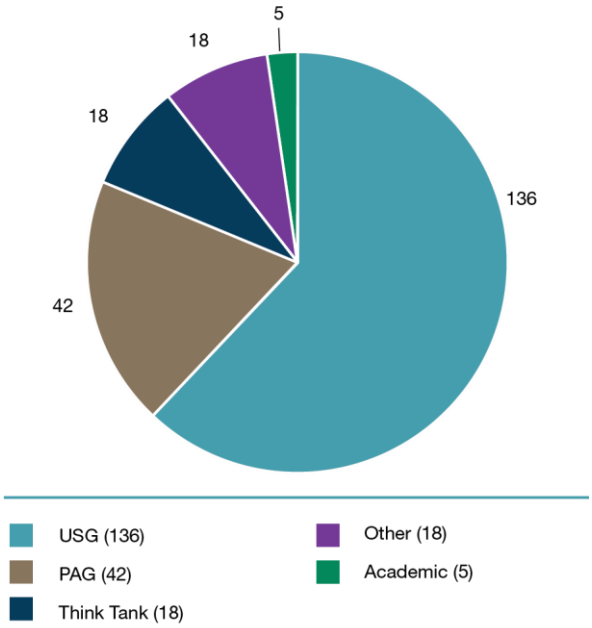
For comments to be considered, please submit them by April 3, 2026.

D. Detailed Assessment Methodology

Identify Scope of Assessment

Informed by the Hub's Strategic Agenda, Booz Allen defined the scope of the landscape assessment, and prespecified the inclusion and exclusion criteria that informed the search strategy and identification of in-scope educational materials.[22] The landscape assessment focused on educational materials related to rare disease product development and regulation, targeting rare disease patients and product developers. In-scope resources were included when all the following inclusion criteria were met: (1) content was developed by recognized rare disease organizations or thought leaders (2) resource aligned with interested party interview topics, and (3) resource was related to U.S. rare disease product development and regulation. Resources that were owned or disseminated by product developers, hyperspecialized or overly technical (i.e., peer reviewed scientific journals, law journals, economic analyses), or out-of-scope (i.e., international regulation, support services) were excluded from this project. **Figure 4** presents the categories of organizations identified during the landscape assessment and the number of resources disseminated by each.

Figure 4: Number of Educational Resources by Organization Type



Engagement with the Rare Disease Product Development Community

Booz Allen identified prospective organizations and individuals within those organizations to participate in the HEARD listening sessions, randomly selecting 9 industry (small-to-medium biopharmaceutical and biotechnology companies) representatives, 9 PAG representatives, and 8 USG representatives from a prospective pool for a total of 26 participants.

Booz Allen developed three interested party-specific HEARD interview guides for industry, PAGs, and USG staff to (1) augment understanding of available educational resources for rare disease product developers, patient communities and advocates; (2) identify gaps

[22] Rare Disease Innovation Hub Strategic Agenda - 2026 (https://www.fda.gov/media/185144/download?attachment)

in the rare disease product development community's understanding of rare disease product development and regulatory review; and (3) identify rare disease topics of interest.

Booz Allen structured the interview guides to include the following core topic areas:

- Baseline Questions (on educational resource awareness)
- Product Development and Regulation
- Biologics
- Drugs

Booz Allen and the Hub developed the public docket language, which was designed to capture broader community input on rare disease educational needs across the same topic areas covered in the interview guides. To extend the reach of the rare disease product development community engagement and broaden the perspectives captured, the Hub and CDER's Rare Diseases Team (FDA) collaborated to post a public docket for comment on regulations.gov from 2/11/2026 – 4/3/2026 (Docket No. FDA-2026-N-1584). Following the close of the docket, Booz Allen conferred with FDA to identify salient comments and then Booz Allen performed a qualitative analysis of in-scope comments.

Create Data Collection Instruments (DCIs)

Booz Allen developed three Microsoft Excel-based DCIs to capture the qualitative data gathered from the landscape assessment, HEARD listening sessions, and public docket. The first DCI was used to curate and assess educational resources identified through the landscape assessment, capturing data elements such as resource metadata, topic alignment, technical level (**Table 6-3**), and usability (i.e., ease of navigation, user interface) and accessibility (i.e., learning accommodations) ratings. The second DCI was used to capture and organize qualitative feedback collected during the HEARD listening sessions, with responses organized by the interested party and interview question to facilitate thematic analysis across sessions. The third DCI was used to track and analyze public docket submissions, capturing each comment's relevance to the assessment, reasons for inclusion, and reviewer notes. Together, the three DCIs served as Booz Allen's centralized tools for organizing, coding, and synthesizing the data collected across all three engagement channels.

Collect and Analyze Data

Booz Allen used a qualitative research approach to collect and analyze feedback from the HEARD listening sessions. The sessions were facilitated virtually, with at least one moderator leading the discussion and one team member capturing detailed notes to inform the feedback analysis. The moderator initiated each session by asking participants to provide insight into their professional background and expertise before proceeding through the interview guide questions. This approach allowed Booz Allen to collect a detailed understanding of the experiences and perspectives reflected in participant

responses. In total, Booz Allen received input from 26 individuals across three interested party groups. To facilitate data collection, coding, and analysis, Booz Allen assigned categories to participants based on their interview group. Following the completion of the listening sessions, Booz Allen aggregated feedback across all sessions and conducted a qualitative thematic analysis to identify common themes, trends, and areas of alignment and divergence across the rare disease product development community.

Booz Allen employed a structured review process to assess the educational resources identified through the landscape assessment. For each resource included in the DCI, Booz Allen captured key data elements including resource format, modality, technical level (**Table 6-3**), topic alignment, usability (i.e., ease of navigation, user interface), and accessibility (i.e., learning accommodations) ratings. Technical levels were derived from the Dreyfus model of skill acquisition, a framework that describes learner progression through distinct stages of proficiency.[23,24] For the purposes of this project, Booz Allen collapsed proficiency stages into three levels (beginner, intermediate, and advanced) to provide a practical categorization of educational resources according to the depth of knowledge presupposed in the learner. Booz Allen evaluated usability and accessibility using selected domains from the LORI, a standardized framework for assessing the quality of educational resources. Two team members independently reviewed and rated each resource, and SMEs subsequently reviewed a randomly selected sample. Reviewers and the SMEs collaboratively discussed and adjudicated any discrepancies in ratings. Booz Allen then conducted a thematic analysis of the educational resources to extract core themes to supplement a quantitative analysis of the key data elements. The qualitative thematic analysis followed Braun and Clarke's six-step approach consisting of (1) data familiarization, (2) initial code generation, (3) thematic search, (4) theme review, (5) defining and naming of themes, and (6) report.[25] **Table 6-4** provides an overview of each stage of the thematic analysis. To identify patterns and gaps in the current state of rare disease educational materials, Booz Allen executed a descriptive analysis of themes and key features.

Table 6-3: Defining Criteria for Technical Level of Knowledge

Technical Level	Regulatory	Product Development
Beginner	• Low awareness and knowledge of regulatory science and rare diseases • Requires concrete structure and simple examples for complex topics	• Low awareness and knowledge of rare disease product development, including scientific concepts • Requires concrete structure and simple examples for complex topics

[23] Kinchin, I. M., & Cabot, B. (2010). Reconsidering the dimensions of expertise: From linear stages towards dual processing. London Review of Education, 8(2).
[24] Dreyfus, H., Dreyfus, S. E., & Athanasiou, T. (1986). Mind over machine. Simon and Schuster.
[25] Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. Qualitative research in psychology, 3(2), 77-101.

Technical Level	Regulatory	Product Development
Intermediate	• Moderate awareness and knowledge of regulatory science and rare diseases • Can independently extract and contextualize information • May require moderate guidance on technical/complex information	• Moderate awareness and knowledge of rare disease product development, including scientific concepts • Can independently extract and contextualize information • May require moderate guidance on technical/complex information
Advanced	• Proficient in regulatory science for rare disease products • Can independently consume and interpret technical/complex information • Capable of using educational resources to transfer knowledge	• High awareness and knowledge of rare disease product development, including scientific concepts • Can independently consume and interpret technical/complex information • Capable of using educational resources to transfer knowledge

***Note**: Technical levels adapted from the Dreyfus model of skill acquisition.*[26, 27]

Table 6-4: Phases of Thematic Analysis

Stage	Overview
Data Familiarization	Transcription and review of raw data
Initial Code Generation	Systematically generate semantic or latent codes that reflect core features of dataset
Thematic Search	Collate semantic or latent codes into preliminary themes that represent the emerging patterns within the dataset
Theme Review	Review preliminary themes and their alignment with the defining features of the data
Defining and Naming of Themes	Iteratively analyze and refine themes, consolidating naming structure and definitions
Report	Develop narrative that presents analysis of final themes and how they relate to research question

After the closing of the public docket (Docket No. FDA-2026-N-1584), Booz Allen reviewed all 69 submissions and, in consultation with the Hub and CDER's Rare Diseases Team, determined their relevance to both the scope of the assessment and CDER's LEADER 3D educational initiative.[28] Of the 69 submissions, 14 comments were in scope for this assessment and subsequently analyzed. Other docket comments requesting feedback on the Rare Diseases Team's existing LEADER 3D educational materials were beyond the scope of this assessment.

[26] Kinchin, I. M., & Cabot, B. (2010). Reconsidering the dimensions of expertise: From linear stages towards dual processing. London Review of Education, 8(2).
[27] Dreyfus, H., Dreyfus, S. E., & Athanasiou, T. (1986). Mind over machine. Simon and Schuster.
[28] Learning and Education to ADvance and Empower Rare Disease Drug Developers (LEADER 3D) (https://www.fda.gov/about-fda/accelerating-rare-disease-cures-arc-program/learning-and-education-advance-and-empower-rare-disease-drug-developers-leader-3d)

Generate Findings and Recommendations

Booz Allen used data from the landscape assessment, HEARD listening sessions, and public docket comments to elucidate shared themes and identified:

- Areas where educational needs are currently well met and high-quality resources are available;
- Trends in challenges experienced within and across rare disease product development community;
- Gaps in existing educational materials, including the nature and extent of those gaps; and
- Recommendations for future educational material development to address identified gaps and opportunities.

Findings were organized across six topic areas: (1) nonclinical, (2) NHS and registries, (3) novel endpoint and biomarker development, (4) clinical trial design and related data considerations, (5) rare disease product development and regulations, and (6) FDA engagements with the rare disease product development community. To maintain alignment between the report findings and the priorities of the rare disease product development community, Booz Allen hosted three working sessions with six industry and seven PAG participants that previously contributed to the data collection interviews (i.e., HEARD Interviews). Booz Allen collaborated with the Hub to develop two working session guides tailored to each target audience (i.e., industry and PAGs) and provided the working session guides to participants prior to their session. Each guide summarized the audience-specific educational gaps identified in the assessment, recommendations to address each gap, and questions designed to assess the accuracy, relevance, and identify prioritization of the recommendations. Booz Allen then analyzed working session insights to identify key takeaways specific to the community groups, to refine the final set of educational gaps and recommendations.


FOOD AND DRUG ADMINISTRATION