Rare Disease Innovation Hub

Strategic Agenda 2025

FDA

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Rare Disease Innovation Hub Mission

FDA created the Rare Disease Innovation Hub (Hub) to serve as a point of collaboration and connectivity between the Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) with the goal of improving outcomes for rare disease patients. The Hub will enhance collaboration across FDA to address common scientific, clinical, and policy issues related to rare disease product development, including relevant cross-disciplinary approaches related to product review, and promote consistency across offices and Centers. Although the Hub will work across all rare diseases, it will particularly focus on challenges within smaller populations or for diseases where the natural history is variable and not fully understood.

Rare Disease Innovation Hub Establishment

Rare Disease Innovation Hub Launch

The Hub was created in 2024 to promote collaboration across FDA and advance a shared vision and comprehensive approach to address common challenges such as identifying and utilizing innovative scientific approaches to drug development and to streamline communications with the rare disease community. The Hub is led by the Directors of CBER and CDER. They serve as co-chairs for the Rare Disease Innovation Hub Steering Committee, which also includes relevant leadership from within the Centers and other offices within the FDA, including the Center for Devices and Radiological Health (CDRH), Oncology Center of Excellence (OCE), Office of Orphan Products Development (OOPD), and the Office of Combination Products (OCP). The strategic operations of the Hub are led by the Director of Strategic Coalitions (DSC), who is accountable to both Center Directors.

The first phase of the Hub launch was to receive input from the rare disease community. The Reagan-Udall Foundation, in collaboration with FDA, hosted a public meeting to discuss the Hub and to receive feedback on community priorities for the Hub. The public meeting also included the opening of a Federal Register docket to receive written comments on the mission and function of the Hub. The feedback provided to the FDA on the need for and intended purpose of the Hub demonstrates the strong support for this new FDA program; there were over 3000 registrations for the public meeting[1] and over 60 in-depth comments submitted through the Federal Register docket.[2] In addition, the registrations and feedback represented a broad cross-section of the rare disease community, with 40% of the registrations for the public meeting being from the regulated industry and over half of the public docket comments being from patient and disease organizations. For more details on input from the rare disease community, see Community Input section below.

The second phase of the Hub launch is the drafting of this Strategic Agenda. Building upon the feedback already received, and knowing that the Hub is in its infancy, CBER and CDER leadership

[1] https://reaganudall.org/news-and-events/events/advancing-rare-disease-therapies-through-an-fda-rare-disease-innovation-hub
[2] https://www.federalregister.gov/documents/2024/08/12/2024-17924/advancing-rare-disease-therapies-through-a-food-and-drug-administration-rare-disease-innovation-hub

have homed in on the priority areas of focus for the first year of this Hub. This document outlines the actions that the Hub plans to undertake in its first year, with extensive involvement from the rare disease community, while simultaneously addressing the many questions about the ultimate structure and programs of the Hub. At the end of 2025, the Hub will assess the results of its activities and create a new strategic agenda for 2026.

External socialization of the Hub, its goals, and its functions will involve communicating clearly what the Hub's functions will and will not be to patient advocacy groups, researchers, drug developers, and federal research partners. While the Hub aims to provide a centralized point of entry for broad conversations regarding treatment approval and authorization processes and challenges in the rare disease space, drug developers and patient groups will still communicate directly with the Centers about specific approvals and authorizations. Clarifying the outward-facing role of the Hub will require consistent engagement with the patient community and drug developers.

Rare Disease Innovation Hub Infrastructure

The Hub's primary function is to play a coordinating role between two well-established rare disease efforts within CDER and CBER, but the Hub will also work with the many FDA programs in the rare disease space.[3] The Hub's task is neither to supplant nor to take over any major operations from existing programs, but instead to ensure coordination and alignment between FDA's rare disease teams. It is likely that the Hub may encounter some duplication of efforts between programs, differences in review criteria between Centers, or siloed programs and will need to facilitate alignment between them. This knowledge will help guide Hub activities in 2025 and beyond.

There is currently no budget designated specifically for Hub activities and staff. Apart from the Director of Strategic Coalitions, who is fully devoted to the Hub, all Hub staff are currently CBER and CDER full-time employees whose work for the Hub is in addition to other duties. While this reflects CBER and CDER's commitment to the establishment of the Hub, accomplishing many of the goals and activities in this Agenda and the long-term success of the Hub will require additional financial support and dedicated personnel.

Community Input

The Strategic Agenda content reflects extensive input from, and partnership with, the larger rare disease community. On October 16, 2024, the Reagan-Udall Foundation for the FDA, in collaboration with FDA, hosted a public meeting for rare disease advocacy groups, academia, regulated industry, and other external partners to discuss how the Hub might best engage with the rare disease community and prioritize its work. During the meeting, 37 rare disease community partners contributed comments and, in connection with the meeting, more than 60 provided comments to a federal docket.

Rare disease community comments at the meeting and in the written docket coalesced around the following "5 Cs", with some specific suggestions for implementing them. A full summary of the

[3] GAO-25-106774, RARE DISEASE DRUGS: FDA Has Steps Underway to Strengthen Coordination of Activities Supporting Drug Development

key themes can be found on Reagan Udall's Meeting Page; the material below provides highlights.

Communication. Effective and transparent communication is foundational for addressing the complexities of rare disease drug development. To this end, the rare disease community recommended that FDA:

- Provide information on the scope of the Hub to clarify what is and is not under its purview;
- Establish a centralized communication platform with updates on regulatory guidance and policy changes;
- Engage in educational outreach to the rare disease community, e.g., by providing training to drug developers on regulatory requirements for rare diseases; plain language resources for patients and caregivers on regulatory requirements; and guidance on surrogate endpoints, accelerated approval, and rare versus “ultra-rare” diseases.

Community. Building an inclusive and engaged community is critical for sustained progress in rare disease drug development initiatives. The rare disease community recommended that FDA:

- Implement targeted outreach to underserved and underrepresented populations, such as ultra-rare disease groups and pediatric patients; and
- Address systemic barriers, such as geographic and economic disparities, to broaden clinical trial participation.

Coordination. Enhanced coordination with external organizations and across FDA’s Centers and review divisions is pivotal for reducing inefficiencies and aligning efforts in the rare disease drug development space. To this end, the rare disease community recommended that FDA:

- Strengthen partnerships among FDA, industry, academia, and advocacy groups through joint workshops;
- Focused Drug Development (PFDD) meetings, and advisory boards;
- Foster public-private partnerships to advance research and drug development; and
- Coordinate with global regulators to harmonize standards, reducing duplicative efforts and expediting drug approvals.

Creativity. Innovative approaches to clinical trial design and drug development are essential for addressing the unique challenges of rare diseases. FDA could:

- Create a mechanism for early engagement with non-sponsors in the noncompetitive space for practical advice on subjects such as the development of biomarkers, clinical trial design, registries, and natural history studies that contain quality fit-for-purpose data.

Cooperation. Collaboration among the rare disease community is a critical driver of progress in rare disease drug development. FDA could enhance collaboration by:

- Working with international partners on shared goals, such as improving diagnostic tools and establishing cross-border clinical trial frameworks.

It is important for FDA to stay continuously engaged with the rare drug community throughout the year to ensure that they receive the information needed to guide their drug development efforts and to build enduring relationships. To that end, the Hub will sponsor public meetings and workshops with the rare disease community, as well as respond to speaking requests and opportunities to collaborate.

Rare Disease Innovation Hub Goals

Goal 1: Further Advance Regulatory Science of Rare Disease Therapies

Create and enhance opportunities for consideration of novel endpoints, biomarker development and assays, innovative trial design, real world evidence, and statistical methods. Initiate engagement with federal research partners and the broader rare disease research community with the purpose of sharing scientific innovations and enhancing collaboration in regulatory science.

Goal 2: Enhance and Strengthen Coordination and Alignment Between Medical Product Centers, with Particular Focus on CDER and CBER

In an effort to move the agency towards greater cross-Center consistency on rare disease standards and decisions, facilitate regular collaboration between leadership and review teams between CBER and CDER, with CDRH joining when relevant. Promote cross-Center information sharing and, where possible, alignment between Centers on review standards and decision-making. Where scientific reasons exist for differences in review procedures between CBER and CDER, promote clarity about those reasons with the rare disease community. Encourage transparency and communication between FDA Centers and drug developers throughout the review process.

Goal 3: Create a Centralized Point of Contact for External Partners

Serve as a primary point of connection and engagement with the rare disease community, including patient and caregiver groups, trade organizations, and scientific/academic organizations, for matters that intersect rare disease drug development within CDER and CBER. Promote engagement with the rare disease community via enhancements to rare disease information publicly available throughout the Agency's webpage and facilitate the development of educational materials on rare disease drug development regulatory innovations.

Rare Disease Innovation Hub Actions

Goal 1: Further Advance Regulatory Science of Rare Disease Therapies

Rare disease Innovation, Science, and Exploration Workshop Pilot

Medical product development can be a long and difficult process, and only more so for rare diseases where the populations are small and are often heterogeneous. It is also well understood that the 'gold standard' of two large, well-controlled clinical trials is often not feasible, or even possible, in small populations. Yet rapidly evolving science offers opportunities for treatments and cures for rare diseases unimaginable even a few short years ago.

The Rare Disease Innovation Hub will design and implement multi-partner education and engagement opportunities for drug developers, FDA reviewers and staff, patient organizations, other federal agencies, including NIH and ARPA-H, and researchers to engage and collectively educate about novel approaches to therapy development for rare diseases. These engagement opportunities will create a platform for sharing expertise and promoting alignment on complex

scientific challenges, evolving science, and novel clinical trial approaches, particularly for issues common to multiple diseases or a class of diseases. Such an approach will seek broader understanding and consensus from all participants to inform future drug development.

The Hub will launch a pilot for a Rare disease Innovation, Science, and Exploration (RISE) workshop series.[4] In 2025, the Hub will sponsor up to three multi-partner workshops on challenges that are common to multiple diseases or a class of diseases and for which evolving science offers innovative solutions. The workshops will be open to the public and designed for interaction and discourse between the various rare disease community members and perspectives, including drug developers, patient and disease organizations, academics, FDA regulators and reviewers, and relevant staff from other federal agencies. All workshops will include coordination between CBER and CDER and address the Centers' approaches to the relevant issues. The workshops will also include a discussion of the role of patients and patient/disease organizations in the design and implementation of innovative solutions. The workshops will primarily focus on cross-cutting or common issues and will not be focused on any specific product under review by the Agency.

To establish and demonstrate the intended cross-partner and common issues themes for the RISE workshops, the first workshop will be on a topic derived from feedback already received from the stakeholder community. For the remaining workshop(s), the topic(s) will be selected from proposals submitted by the rare disease community. In reviewing the proposals, preference will be given to proposals submitted jointly by multiple organizations, individuals, or companies, either within a rare disease community group or across groups.

For the 2025 pilot RISE workshops, proposals will be received via the Hub website. However, the pilot phase of the program will include the design and implementation of a portal through which proposals can be submitted, beginning in 2026. The portal will include requirements for workshop proposals and timelines for review. In preparing for the 2025 workshops, the Hub will consider utilizing external partners to plan, execute, and facilitate the workshops.

RISE Workshop #1: The first workshop for 2025 will be on the design of clinical trials when you have a small and diminishing population of eligible trial participants. The meeting will consider recurring issues raised with smaller trial design. Potential topics include the use of alternatives to placebo (historical controls and natural history studies), as well as utilization of adaptive trial designs. It could also address the use of master protocols when the population for potential trial participants is ultra-small, and incentivizing drug developers to coordinate individual trials, without disclosing proprietary information.

RISE Workshops #2 and #3: The topics for the remaining one or two RISE workshop(s) in 2025 will be chosen by the Hub from proposals submitted by the rare disease community.

Patient and Patient Organization Engagement in the Development and Review of Drugs for Rare Diseases

FDA currently has many ways for patients, patient organizations, and disease organizations to engage with the Agency and to provide input on patient experience and preferences. FDA's most

[4] The RISE meetings are based on the concept the rare disease community often refers to as "Science-Focused Drug Development Meetings."

utilized programs are FDA-led Patient-Focused Drug Development (PFDD) Public Meetings, Externally-led Patient-Focused Drug Development Meetings, and Patient Listening Sessions. These patient engagement opportunities provide the Agency with valuable information about patient experience, risk tolerance, and the relevance of clinical endpoints to the lived experience of the patients who are using medical products.

FDA has also issued multiple guidance documents on patient-focused drug development, offering insight on multiple topics including collecting input from patients, patient representatives serving on advisory committees, identifying what is important to patients, fit-for-purpose clinical outcome assessments, and incorporating clinical outcome assessments into endpoints for regulatory decision-making. These guidance documents are intended to encourage patient organizations to engage in the drug development process, and to encourage drug developers to voluntarily involve patients and patient organizations throughout the drug development process.

While this active involvement with patients and patient organizations has had a strong and positive impact on FDA's incorporation of the patient perspective on drug development, there remains a strong interest among patient and disease organizations and many drug developers for deeper and more substantive involvement of patients and the patient voice in drug development and review processes. The feedback provided to the Hub during the public meeting and through the open docket sends a clear message that many external partners seek greater substantive involvement of patients and patient organizations in policy decisions, including regulatory processes.

Rare disease community partners understand that FDA's ability to involve non-drug developers in the drug review and approval process, beyond what it already does, is guided by law and regulation. That said, the Hub is interested in engaging with both patient organizations and drug developers to learn how, within existing boundaries, the Agency can engage in continuous and meaningful conversations throughout the drug development process.

The Hub will work with members of the rare disease community in 2025 to discuss ways that FDA might build on engagement efforts and to envision strategies to better engage the rare disease community in regulatory processes, as allowed by law. Topics should include both opportunities for further engagement by patients and patient organizations, as well as discussion about enhancing drug developer opportunities to more deeply involve the relevant rare disease community members in their interactions with FDA. The Hub's engagement on this topic should result in a better understanding by all of what is envisioned and what is possible, along with some preliminary ideas for an even more substantive role for patients and patient organizations in the drug review process, either independently or through drug developers.

Goal 2: Enhance and Strengthen Coordination and Alignment Between Medical Product Centers, with Particular Focus on CDER and CBER

Promote Knowledge-Sharing Around Rare Disease Treatment Review Between CDER and CBER

CBER and CDER share a vision of a drug review process that takes full advantage of the deep knowledge and experience of all of FDA and its clinical and scientific staff. One aspect of that

vision is ensuring that our comprehensive drug reviews are conducted within the context of other applications, approval decisions, and related information within the Agency, particularly when it comes to innovative approaches in the areas of novel endpoints, biomarker development, and trial designs for rare diseases. It is imperative that internal expertise be shared within and across Centers so that knowledge gained in a single IND, NDA, or BLA review, or during a Patient-Focused Drug Development Meetings and Patient Listening Sessions can be retained and utilized across the Agency as institutional knowledge.

The Hub will work with CDER and CBER to put in place best practices that promote drug review information sharing opportunities that will have broader cross-Center implications throughout the rare disease drug review process, from IND through NDA or BLA. The Hub has already launched the Rare Disease Policy and Portfolio Council (RDPPC), which is a senior level forum to promote cross-Center dialogue on challenging and complex rare disease drug development program-related issues. The RDPPC meetings bring together technical experts from across both Centers to discuss, on an as-needed basis, scientific, regulatory science, and policy issues related to rare disease product development that are common to both Centers. Building upon the early success of the RDPPC meetings, the Hub will work with CDER and CBER leadership, and CDRH as appropriate, to put in place additional practices and policies to regularize cross-Center communication regarding the same or related diseases or issues, particularly regarding innovative approaches in rare disease, to ensure that drug review within the Centers have common approaches when approaching similar populations or issues. While the drug product reviews within each Center remain separate, the Hub will work with the Centers to create systems that proactively share information useful to others and provide access to those seeking information regarding disease states or populations.

We anticipate that establishing proactive information sharing will translate into more consistent communication with drug developers on various applications across the Centers. We will continually seek feedback on whether external parties, such as drug developers and patient organizations, are hearing similar advice when approaching similar populations or issues.

Goal 3: Create a Centralized Point of Contact for External Partners

Assess Options for Website-Based Rare Disease Roadmap

FDA currently has numerous rare disease-specific programs across the Agency.[5] While many are housed in CDER and CBER, some are within other FDA offices. Some of these programs have very specific purposes and other programs have overlapping jurisdiction and offerings. The public feedback regarding the launch of the Hub was generally positive regarding the wealth of rare-disease programs offered by the Agency. Yet there was also a consistent theme of the need for a clear entry point to FDA's rare disease programs that would provide greater clarity regarding where external community members should go for their issue or questions, and guidance on the distinctions between many of these programs. For example, one commenter suggested that the Hub be a "…centralized "First Stop" webpage for comprehensive rare disease resource." Another focused on the numerous FDA programs from the drug developer's perspective, suggesting that "we would recommend FDA to prepare a road map to help drug developers navigate the various regulatory science initiatives and opportunities and delineate the linkage across centers."

[5] GAO-25-106774, RARE DISEASE DRUGS: FDA Has Steps Underway to Strengthen Coordination of Activities Supporting Drug Development

In 2025, the Hub will conduct an assessment of options to meet the need for a "one-stop shop" for FDA rare disease programs and information. The recommendations resulting from the assessment could include resource-intensive options such as the design of a single website that encompasses all FDA rare disease programs and which is searchable and valuable to all rare disease community members, as well as less comprehensive alternatives that place all programs in one website location comprised primarily of brief explanations and links to existing programs. The overarching theme of this assessment and resulting recommendations will be to ensure that FDA information regarding its many rare disease programs is accessible, understandable, and useful to the rare disease community. Accordingly, an outcome of the assessment will also be recommendations as to whether current CDER and CBER outreach and communication efforts are effective, valuable, and not duplicative.

Encourage Hub Interaction with the Community at Multiple Meetings and Conferences

A key purpose of the Rare Disease Innovation Hub is to engage directly with the rare disease community, including drug developers, patients, patient organizations, and researchers to ensure that FDA is informed of the concerns and needs of the rare disease community and that the community is given all appropriate opportunities to engage with FDA. This engagement is fundamental to the Hub's ultimate mission of facilitating the development, evaluation, and availability of safe and effective therapies for rare diseases. In 2025, the Hub, through its Director of Strategic Coalitions (DSC) as well as other rare disease program staff, will seek opportunities to engage directly with the rare disease community. This engagement will include conferences, meetings, webinars, and similar gatherings, and will provide opportunities for the DSC to educate about Hub activities and hear feedback from the community on this Strategic Agenda, other FDA rare disease programs, and areas where the Agency needs to enhance its access and communication.

Gaps Analysis for Rare Disease Community Educational Materials

FDA currently has numerous written and virtual education programs focused specifically on rare diseases, which are offered by the many offices and divisions in the Agency. Yet, there continues to be requests for additional educational materials focused on FDA regulatory processes and procedures, particularly focused on the unique issues regarding rare and very small disease populations.

In 2025, the Hub will work with members of the rare disease community, including patient organizations and drug developers, to serve on an informal educational materials committee that will assess FDA-wide rare disease educational materials and define gaps and redundancies in those materials. This work will build upon the recent LEADER 3D[6] effort that assessed existing and needed rare disease educational materials available to the rare disease community. The Hub will then work with relevant FDA Centers and offices and the rare disease community to, within their own programs and using their own resources, design and create the needed educational materials. The cross-Center nature of the gaps analysis and resulting new educational materials

[6] https://www.fda.gov/about-fda/accelerating-rare-disease-cures-arc-program/learning-and-education-advance-and-empower-rare-disease-drug-developers-leader-3d

is needed to ensure that FDA's rare disease educational materials are viewed comprehensively, and as inter-related, as external viewers see them.

Conclusion

This Rare Disease Innovation Hub Strategic Agenda is intended as a guidebook for the first year of the Hub. It is the hope and expectation of FDA leadership and the Hub that this Agenda will evolve as the Hub evolves. It is also the expectation that the rare disease community will remain heavily engaged in this evolution. Throughout the year, there will be multiple ways for the community to engage with and offer suggestions to the Hub, both for its immediate use, and for the Hub to consider for the 2026 Strategic Agenda. We encourage all rare disease community members to be partners in the growth and establishment of the Hub.