The Food and Drug Administration's Role in Advancing Rare Diseases Therapies

The FDA has been instrumental in building the regulatory framework and institutional expertise needed to accelerate innovation and development of rare disease therapies. Leveraging key legislative milestones like the Orphan Drug Act of 1983 and the FDA Safety and Innovation Act of 2012, the FDA has enabled remarkable progress in which the number of approved orphan-designated products has grown to over 1300, serving about 400 different communities[1]. Advancements in regulatory policy, the FDA's embrace of patient-focused drug development, and the recent formation of the Rare Disease Innovation Hub are just a few of the examples that demonstrate the FDA's commitment to creating a robust rare disease therapy development environment.

FDA's Commitment to Rare Disease Therapy Development

FDA's Focus on Patient-Focused Drug Development

Patient-focused drug development (PFDD) and the use of patient experience data have experienced a tremendous evolution since being introduced in PDUFA V – codified as a part of FDA's mission in 21st Century Cures and PDUFA VI – and further expanded through the implementation of PDUFA VII. The FDA's commitment to patient-focused drug development has resulted in:

- Deepened engagement and understanding of the patient perspective via Patient Focused Drug Development workshops, the FDA Benefit Risk Framework development, the Patient Experience Data (PED) checklist implementation, and the PFDD Guidance series.
- Opportunities for meaningful participation in formal service on advisory committees

> The EveryLife Foundation and a steering committee of 23 scientific and regulatory experts published the *Guide to Patient Involvement in Rare Disease Therapy Development* in 2022. The Guide is the product of four workshops in which 88 subject matter experts examined 20 FDA guidance documents, leading to 8 cross-cutting topics and action steps for patient advocacy leaders and sponsors to consider as they plan and implement patient-focused drug development strategies in rare disease therapy development. The Guide also has robust framing content and extensive resources across the stages of integrating patient-focused drug development into therapy development.

- The establishment of the FDA's Patient Representative Program and CDRH's Patient Engagement Advisory Committee

Rare Disease Innovation Hub

[1] FDA Office of Orphan Products Development (OOPD). (n.d.). *Orphan Drug Designations and Approvals*. Orphan Drug Product Designation Database. https://www.accessdata.fda.gov/scripts/opdlisting/oopd/

The Rare Disease Innovation Hub was established to enhance collaboration across the FDA to address common scientific, clinical, and policy issues related to rare disease product development[2]. Strategic goals for 2025 include:

- Further Advance Regulatory Science of Rare Disease Therapies
- Enhance and Strengthen Coordination and Alignment Between Medical Product Centers, with Particular Focus on CDER and CBER
- Create a Centralized Point of Contact for External Partners

The Rare Disease Innovation Hub at the FDA was established following years of community and Congressional engagement. A formal policy proposal grew from the 2018 EveryLife Foundation Scientific Workshop discussion. Previous community work to make the vision for a collective rare disease home at the FDA includes:

- ✓ Community support for the STAT Act, a bill that would improve rare disease coordination, stakeholder engagement, and policy development within FDA by expanding existing authority to create a Rare Disease Center of Excellence
- ✓ The publication of a community based white paper entitled: A Community Vision for a Rare Disease Center of Excellence at the FDA
- ✓ The submission of report language, along with a community letter to Congress, to request the development of an intercenter institute to support rare disease therapy development at the FDA, as authorized to the FDA in the 21st Century Cures Act.

Rare Diseases Across the Product Review Centers

Center for Drug Evaluation and Research (CDER):

- 50 novel drug approvals in 2024 - 18 of these therapies focus on non-oncology, non-infectious rare diseases[3]. Two of those therapies are the first for their respective conditions[4].
- Orphan new molecular entity (NME) approvals have increased in the last decade. The Division of Rare Disease & Medical Genetics has the highest rate of orphan approvals that are NME[5].
- Less than 10% of products approved using the accelerated approval pathway are for non-oncology, non-infectious, rare diseases[6].

[2] U.S. Food and Drug Administration. (n.d.). FDA Rare Disease Innovation Hub. https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/fda-rare-disease-innovation-hub

[3] Center for Biologics Evaluation and Research. (2025a, February 7). *2024 Biological License Application Approvals*. U.S. Food and Drug Administration. https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2024-biological-license-application-approvals

[4] Ibid

[5] Domike R, Raju GK, Sullivan J, Kennedy A. Expediting treatments in the 21st century: orphan drugs and accelerated approvals. Orphanet J Rare Dis. 2024 Nov 8;19(1):418. doi: 10.1186/s13023-024-03398-1. PMID: 39516878; PMCID: PMC11549740.

[6] Ibid

- The Accelerating Rare disease Cures (ARC) Program provides strategic coordination of CDER's rare disease activities. LEADER 3D produces training resources for sponsors, patient organizations, and agency teams involved in rare disease therapy development.

Center for Biologics Evaluation and Research (CBER):

- 9 novel drug approvals in 2024 - 5 approvals for non-oncology non-infectious rare diseases[7].

Center for Devices & Radiological Health (CDRH):

- Enables innovation and ensures the safety of medical devices and diagnostics for the rare disease community, including newborn screening and laboratory-developed tests[8].

The Office of Orphan Products Development

The Office of Orphan Products Development (OOPD) implements the Orphan Drug Act and oversees a targeted grant program whose research has led to over 80 FDA-approved therapies[9].

- In 2024, 481 conditions received an orphan disease designation, and 231 therapies received a rare pediatric disease designation[10].
- In 2024, the Orphan Products Grant program and the Rare Neurodegenerative Diseases Grant Program provided 11 grants to support innovative clinical trials, natural history studies, and research on rare neurodegenerative diseases. These investments enable non-traditional, academic, and non-profit models of therapy development to be viable, even when commercial interests are not feasible[11].

[7] Center for Biologics Evaluation and Research. (2025a, February 7). 2024 Biological License Application Approvals. U.S. Food and Drug Administration. https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/2024-biological-license-application-approvals
[8] https://www.fda.gov/about-fda/fda-organization/center-devices-and-radiological-health
[9] Office of Orphan Products Development (OOPD). (n.d.). Grants awarded. Orphan Products Grants Awarded. https://www.fda.gov/industry/orphan-products-grants-program/orphan-products-grants-awarded
[10] FDA. (n.d.). *FDA-track: Office of the Chief Medical Officer - Office of Orphan Products Development Dashboard*. U.S. Food and Drug Administration. https://www.fda.gov/about-fda/fda-track-agency-wide-program-performance/fda-track-office-chief-medical-officer-office-orphan-products-development-dashboard
[11] U.S. Food and Drug Administration. (n.d.). *Orphan Products Grants Awarded*. FDA Office of Orphan Products Development (OOPD). https://www.fda.gov/industry/orphan-products-grants-program/orphan-products-grants-awarded

EVERYLIFE FOUNDATION FOR RARE DISEASES

Select EveryLife Foundation for Rare Diseases Publications and Comments

1. Orphanet Study reviewing the use of expedited pathways and accelerated approvals -Expediting treatments in the 21st century: orphan drugs and accelerated approvals. https://pubmed.ncbi.nlm.nih.gov/39516878/
2. Response to Rare Disease Innovation Hub solicitation: Advancing Rare Disease Therapies Through an FDA Rare Disease Innovation Hub
    a. https://everylifefoundation.org/wp-content/uploads/2024/11/EveryLife-Foundation-RDIH-Comment-Final.10.31.24.pdf
3. Proceedings from the 2024 Scientific Workshop – Therapy Development for Small Populations: Evidence, Implications, & Policy in Characterizing Ultra-Rare
    a. https://everylifefoundation.org/wp-content/uploads/2024/12/UltraRareSummary.pdf
4. Response to FDA Solicitation: Optimizing FDA's Processes for Advisory Committees
    a. https://everylifefoundation.org/wp-content/uploads/2024/07/FDA-Advisory-Committee-Reform-ELF-Written-Submission-Final.pdf
5. Community Whitepaper Outlining the Original Vision for an FDA Rare Disease Center of Excellence
    a. https://everylifefoundation.org/wp-content/uploads/2022/04/COE-White-Paper-4.6.22.Final_.pdf