From Catalyst to Clarity: Restoring the Intent of the Orphan Drug Act

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Introduction

Orphan drugs are therapeutics that treat rare diseases, defined as affecting 200,000 or fewer people in the United States, that normally would not receive investment given the small patient population. Passed in 1983, the Orphan Drug Act (ODA) promoted orphan drug development through incentives, including seven years of exclusivity.[1] However, a 2021 court decision undermined the original spirit of the ODA, resulting in fewer incentives for researching and developing critical therapeutics necessary for treating patients suffering from rare diseases, particularly children. The Retaining Access and Restoring Exclusivity Act (RARE Act),[2] would rectify the impacts of this decision and restore the ODA to its original intent. This would also fulfill the state's obligations to justice under the application of the difference principle to drug development priority-setting.

Background

Under the ODA, drug companies obtain an orphan designation prior to clinical trials.[3] If the drug is proven to be safe and effective, then the FDA approves the drug for a specific use or indication. For example, the FDA could approve a cystic fibrosis drug for adults with a given genetic mutation. The exclusivity would then apply only to the use of the drug in that population.[4] The orphan drug designation gives the pharmaceutical company seven years of market exclusivity.

[1] Katie Cohen, "A Catalyst For Reform: Charting A Future For Orphan Drug Exclusivity," *University of Pennsylvania Law Review* vol. 173, iss. 3 (2025): 909. https://scholarship.law.upenn.edu/cgi/viewcontent.cgi?article=9883&context=penn_law_review

[2] Now included as Section 6 of the Give Kids a Chance Act (H.R. 1262),

[3] Karin Hoelzer, "Congress should protect the intent of the Orphan Drug Act and pass the RARE Act," *NORD*, https://rarediseases.org/pass-the-rare-act/

[4] Ibid.

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Catalyst v. Becerra

In 2009, Catalyst received an orphan drug designation for its drug Firdapse (amifampridine) for the treatment of Lambert-Eaton Myasthenic Syndrome (LEMS), an autoimmune disease that affects less than 0.001 percent of the population. The FDA approved Firdapse for adults with LEMS in 2018 and granted Catalyst exclusivity through 2025. Jacobus had developed Ruzurgi (amifampridine, the same drug) to treat LEMS and received an orphan drug designation in 1990. In 2019, the FDA approved Ruzurgi for patients less than 17 years old.[5] Catalyst sued the FDA, challenging the FDA's long-standing interpretation of market exclusivity.

The case, *Catalyst Pharmaceuticals v. Becerra*, centered on how broad exclusivity is and sought to answer the question of whether or not the statutory phrase "same disease or condition" contained in the ODA was ambiguous.[6] The 11th Circuit determined that the phrase was not ambiguous, broadening the traditional FDA interpretation of "same disease or condition." The court found that FDA approval of Ruzurgi for pediatric patients violated Catalyst's exclusivity. The court held that Congress would have included specific language for "use or indication" if it had intended the statutory phrase to be interpreted to limit exclusivity to the specific use and indication and to allow other brands to market to subgroups after demonstrating safety and efficacy in those groups.[7]

Prior to *Catalyst*, the FDA interpreted the ODA to limit exclusivity to particular uses and indications. The FDA encouraged other companies to engage in clinical trials to serve subpopulations and approve existing drugs for additional subgroups within a disease. That way, FDA approval of a drug for adults would not discourage others from researching the same drug for pediatrics.[8] The RARE Act would clarify and codify the FDA's long-standing interpretation of the ODA limiting exclusivity to use or indication.

The Ramifications of *Catalyst*

The court's interpretation of orphan drug development has created a policy landscape that deters orphan drug research, straying from the ODA's intent. For example, a company that studies an existing drug with an orphan designation but for a different population subgroup, such as children, and demonstrates its safety and effectiveness, would be unable to receive a period of exclusivity.[9] Without that key incentive, many companies would likely focus on other areas of research. Exclusivity is meant to promote rare disease research and eventually lead to new treatments for patients, not constrain them. The court's ruling has jeopardized the underlying purpose of the ODA in serving the needs of rare disease communities. The downstream effects of *Catalyst* on drug development are already being

[5] Catalyst Pharmaceuticals, Inc. v. Becerra, No. 20-13922 (11th Cir. 2021), 7-9.

[6] Catalyst Pharmaceuticals, Inc. v. Becerra, No. 20-13922 (11th Cir. 2021), 2.

[7] Catalyst Pharmaceuticals, Inc. v. Becerra, No. 20-13922 (11th Cir. 2021), 13.

[8] "FDA's Overview of Catalyst Pharms., Inc. v. Becerra," https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/fdas-overview-catalyst-pharms-inc-v-becerra

[9] Ibid.

observed in FDA approval rates for new drugs. In the 16 months preceding the *Catalyst* decision, the FDA approved 217 orphan drugs.[10] After *Catalyst*, that dropped to only 95 drugs being approved.[11]

The interpretation proposed by Catalyst and held by the 11th Circuit also ignores important scientific truths recognized by both medical experts and Congress. Children are not simply "small adults."[12] Children can have different manifestations of the same diseases as adults, as well as respond differently to treatment.[13] In the context of rare diseases, advancing drug treatments is especially important for pediatric populations, as many rare diseases develop during childhood.[14] Congress has sought to address the need to promote drug treatment research in children by passing both the Best Pharmaceuticals for Children Act and Pediatric Research Equity Act.[15] The interpretation in *Catalyst* ignores this fact and errs in ignoring the critical need to distinguish indications for granting exclusivity.

Without clarification of the RARE Act, drug companies might also be deterred from future orphan drug development, given the existing confusion on the approval process and ambiguity in regulatory guidance. In *Catalyst*, the court ordered the FDA to set aside the drug in question. While the FDA complied with the court, it also posted a notification in the Federal Register in 2023 regarding its continued intent to grant approvals beyond the scope of *Catalyst*, using the standard of use or indication.[16] The FDA justified this decision by saying continued adherence to the ambiguous language of the statute would "best serve the public health by facilitating patient access to orphan drugs, especially for difficult-to-study patients such as young children." The RARE Act would remove any confusion in the approval process by granting the FDA the explicit statutory authority to approve the same drug from different manufacturers if they are able to treat different patient populations. It would also remove the possibility of future drug sponsors challenging competing orphan drug approvals on the basis of the reasoning in *Catalyst*.

The Difference Principle in Context

Only about 5 percent of rare diseases have an FDA-approved therapy, and this is after four decades of targeted research and development incentives through the ODA.[17] Subgroups like pediatric populations fail to attract investment and research attention from industry because barriers like confusion over exclusivity exist. Some might argue that incentivizing research into subgroups for rare diseases is a misguided approach, as it encourages

[10] Katie Cohen, "A Catalyst For Reform: Charting A Future For Orphan Drug Exclusivity," *University of Pennsylvania Law Review* vol. 173, iss. 3 (2025): 920. https://scholarship.law.upenn.edu/cgi/viewcontent.cgi?article=9883&context=penn_law_review

[11] Ibid.

[12] Thomas R. Welch, "Children are not Small Adults," *Journal of Pediatrics* vol. 271(2024).

[13] Ibid.

[14] Apoorva Kakkilaya, Mahnum Shahzad, and Florence T. Bourgeois, "FDA Approval of Orphan Drug Indications for Pediatric Patients, 2011-2023," *JAMA Pediatr*. 179, 2 (2025): 203-205. https://doi.org/10.1001/jamapediatrics.2024.5280

[15] Michael Christensen, "Best Pharmaceuticals for Children Act and Pediatric Research Equity Act: Time for Permanent Status," *J Pediatr Pharmacol Ther.* 17 (2) (2012):140.

[16] "Clarification of Orphan-Drug Exclusivity Following Catalyst Pharms., Inc. v. Becerra; Notification," Federal Register, https://www.federalregister.gov/documents/2023/01/24/2023-01179/clarification-of-orphan-drug-exclusivity-following-catalyst-pharms-inc-v-becerra-notification

[17] Hannah-Alise Rogers, "The Orphan Drug Act and Catalyst Pharmaceuticals, Inc., v. Becerra," *Congressional Research Service* (2023). https://sgp.fas.org/crs/misc/R47653.pdf

investment into drugs which would benefit only a very small population. Why should we promote the use of significant resources for these small populations when those resources could go to drug research that could benefit more people? The difference principle, as proposed by John Rawls, enriches and supports our understanding of the state's obligations in the context of drug development and priority-setting in research incentives. The principle holds that social and economic inequalities are justified only if they benefit the least advantaged members of society.[18] Applied here, it supports prioritizing research for pediatric rare diseases—even if only a small group benefits—because doing so helps those who are most disadvantaged in the healthcare system, providing them with opportunities to live a good life, as they conceive it, that they would not otherwise have. Congresswoman Doris Matsui (CA-07), co-chair of the Rare Disease Congressional Caucus, answered the question more concisely by stating that "access to medicine shouldn't be sacrificed for drug companies' bottom line."[19] If you believe that children with rare diseases deserve a fighting chance and should not be neglected for the sake of profit, the RARE Act is a necessary and urgent step to fulfilling that moral commitment.

Some argue that without broad exclusivity for an entire disease, companies might not invest in orphan drug development at all. But this concern is overstated. The FDA's earlier approach still gave companies meaningful protection for specific indications, like adults, while allowing others to step in and develop treatments for different groups, such as children. Broad exclusivity shuts that down, blocking follow-on research that could reach patients with no other options. The RARE Act would fix this by restoring a more practical balance between rewarding innovation and expanding access.

Conclusion

The House passed the RARE Act in September 2024, although it fell short of being signed into law. Although there has been consistently strong bipartisan support for the legislation, confounding political tensions concerning government inefficiency have caused these provisions to be left in a state of legislative suspension. The language of the RARE Act has been introduced once again as a part of the Give Kids a Chance Act and introduced to the House by Representative Michael McCaul (R-TX) this March. *Catalyst* has jeopardized the original spirit of the ODA as a means of helping those who need it most. Congress must pass the RARE Act to realign the function of the ODA with its intended purpose and fulfill the state's obligations under an ethical framework that is committed to prioritizing the most vulnerable and worst-off.

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[18] John Rawls, "A Theory of Justice," *Harvard University Press* (1971): 65.

[19] "Legislation Included as Part of Rare Disease Package," https://matsui.house.gov/media/press-releases/house-passes-matsuis-rare-act