November 24, 2025

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA-2017-D-6159: Expedited Programs for Regenerative Medicine Therapies for Serious Conditions; Draft Guidance for Industry

Dear Sir or Madam,

On behalf of the Pediatric Inclusion Alliance, we are pleased to submit comments on FDA's "Expedited Programs for Regenerative Medicine Therapies for Serious Conditions" Draft Guidance for Industry. We appreciate FDA's updates with additional examples and clarification on FDA's recommendations on expedited development and review of regenerative medicine therapies. Of specific importance for the Pediatric Inclusion Alliance is that therapies intended to treat children with rare diseases will have eligibility to these expedited programs.

About the Pediatric Inclusion Alliance

The Pediatric Inclusion Alliance (Alliance) is devoted to full, active collaboration among all stakeholders committed to achieving earlier inclusion of children in clinical trials across all diseases and conditions without compromising safety. For far too long, children have had to wait years for access to safe, effective therapies, often already approved for adult populations. These therapies might well have been even more effective for younger patients if administered at the best time for them.

By combining a deep understanding of the needs of pediatric patients and their families, technical expertise, and real-world experience in medical research and therapy development, knowledge of regulatory guidance and processes, public policy, regulatory knowledge, and public policy understanding, the Alliance is a united collaborative of stakeholder groups committed to ensuring that children have the earliest opportunity to access safe and effective therapies when those therapies are most likely to have maximum benefit to them. This is especially true for early onset genetic disorders, the affected populations for which could benefit from earlier inclusion of children in CGT clinical trials.

Recommendations for Pediatric Inclusion

The Alliance appreciates new examples included in the guidance, some with applicability to rare pediatric diseases, including the CRISPR and non-integrating replication-incompetent viral vector-based gene therapy examples. **We would encourage FDA to provide additional examples that relate directly to rare pediatric diseases (for example Angelman Syndrome, Prader-Willi Syndrome, Rett Syndrome, Batten Disease, Sanfilippo Syndrome), in the Breakthrough Therapy Designation section starting on page 6.** By including examples that are specific and relevant to pediatric populations, FDA would send the important signal that pediatric inclusion is encouraged and a priority in development programs seeking to utilize expedited programs.

Other Recommendations

FDA has been very vocal on the need to improve chemistry, manufacturing, and controls (CMC) and integrate CMC early within gene therapy product development programs, stating the agency cannot compromise on safety.[1] Moreover, FDA has indicated that the prospect of direct benefit and a positive benefit-risk profile are fundamental to enable early inclusion of pediatrics in rare disease clinical trials.[2,3] Therefore, we encourage FDA to be

[1] JS Eglovitch. FDA official: Clinical, CMC teams should be on the same page when developing CGTs. Regulatory News. 26 Sept. 2025. https://www.raps.org/news-and-articles/news-articles/2025/9/fda-official-clinical,-cmc-teams-should-be-on-the

[2] FDA. Benefit-Risk Assessment for New Drug and Biological Products, Guidance for Industry. October 2023. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/benefit-risk-assessment-new-drug-and-biological-products

[3] FDA. Ethical Considerations for Clinical Investigations of Medical Products Involving Children. Draft Guidance for Industry, Sponsors, and IRBs. Sept. 2022. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ethical-considerations-clinical-investigations-medical-products-involving-children

more explicit in the guidance about how CMC readiness ties into the regulatory framework, especially for pediatric diseases. This could include building on the discussion on page 4 to include the importance of CMC for regenerative medicine therapies as a critical component to the overall benefit-risk assessment and consideration of prospect of direct benefit for rare diseases that manifest in childhood.

Also of critical importance to the Alliance is the prompt Congressional reauthorization of rare pediatric disease priority review voucher (PRV) program, which expired in December 2024. Developing safe and effective treatments for rare pediatric diseases is complex and requires significant resources. Along with the expedited programs described in this guidance, the rare pediatric disease PRV program was created in 2012 as another mechanism to incentivize investments and reward rare pediatric disease drug development. There are two parts to the program, the designation and then the award upon approval. Since the rare pediatric disease PRV program was created, FDA has awarded 53 vouchers for rare pediatric diseases, most of which did not have previously approved treatments.[4] Moreover, the non-partisan Government Accountability Office found that the rare pediatric disease PRV program incentivizes biotech companies to invest in drug development for rare diseases.[5]

With the lapse in reauthorization, designations have stopped and awards will no longer be permitted after September 30, 2026. Without the financial award of the rare pediatric disease PRV program, biotech companies, especially small companies, may not be able to overcome challenges to incentivizing development. Simultaneously, reductions in government funding for overhead have made it increasingly challenging for disease-associated nonprofits, including the many small private foundations supporting individual rare diseases, to sustain drug discovery and development efforts. These changes have affected operating nonprofits that depend on federal grants and non-operating nonprofits that support research at academic institutions, some of which are now shifting unrecovered overhead costs onto nonprofit funders, further stretching limited resources generated through private fundraising. Consequently, some promising treatments may not be developed, prolonging morbidity and mortality in children with rare diseases. We appreciate FDA's successful implementation of the rare pediatric disease PRV program, and we urge Congress to reauthorize it before the end of this year.

[4] propharma. The End of the FDA's Rare Pediatric Disease Priority Review Voucher Program. March 11, 2025. https://www.propharmagroup.com/thought-leadership/fda-rare-pediatric-disease-priority-review-voucher-prv-program/

[5] U.S. Government Accountability Office. Drug Development: FDA's Priority Review Voucher Programs. GAO-20-251. Jan 31, 2020. https://www.gao.gov/products/gao-20-251

Conclusion

Children with rare diseases deserve timely access to evidence-based therapies that are scientifically developed and tailored to pediatric patients. The Alliance believes that pediatric inclusion at the outset is the most effective way to achieve this goal and the expedited programs discussed in this guidance will incentivize pediatric inclusion in development programs.

The Alliance appreciates FDA's work on this important guidance. We look forward to future discussions with you as you finalize this and other guidance documents that will help ensure children with rare diseases are included as early as possible in clinical trials. If you have any questions or would like to discuss this further, please contact Sara Singleton at Sara.Singleton@Leavittpartners.com.

Sincerely,

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