February XX, 2022

The Honorable Patty Murray
United States Senate
Committee on Health, Education, Labor and Pensions
428 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Richard Burr
United States Senate
Committee on Health, Education, Labor and Pensions
428 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Frank Pallone
United States House of Representatives
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Cathy McMorris Rodgers
United States House of Representatives
Committee on Energy and Commerce
2322 Rayburn House Office Building
Washington, DC 20515

Dear Chair Murray, Ranking Member Burr, Chairman Pallone, and Ranking Member McMorris Rodgers:

The undersigned childhood cancer organizations are members of the Alliance for Childhood Cancer, consisting of patient advocacy groups, healthcare professionals and scientific organizations, representing Americans who care deeply about childhood cancer. We write to provide analysis and policy recommendations for inclusion on the upcoming authorization of the Prescription Drug User Fee Agreement VII (PDFUA VII). Our recommendations address the next five-year cycle and fiscal years 2023-2027.

Each year in the U.S., approximately 16,000 children are diagnosed with cancer. Approximately 1 in 264 children in the U.S. will develop cancer before their 20th birthday. Annually, there are more than 300,000 children diagnosed with cancer worldwide. Unfortunately, cancer remains the most common cause of death by disease among children in the United States.

We have made significant advances to develop better treatments for the most common forms of childhood cancer. There are many different types of childhood cancers, and for many, progress is limited, leaving too many children with no available cure. Unfortunately, 1 in 5 children diagnosed with cancer in the U.S. will not survive, and for the ones who do, the battle is never over. By the age of 50, more than 99% of survivors have had a chronic health problem, and 96% have experienced a severe or life-threatening condition caused by the toxicity of the treatment that initially saved their life, including brain damage, loss of hearing

and sight, heart disease, secondary cancers, learning disabilities, infertility and more. By the time a child in treatment for cancer today reaches the age of 50, we want these statistics to be far less grim.

The pharmaceutical industry is market-driven, and as such, there is more incentive to develop drugs for certain diseases than others. Childhood cancer provides little market incentive for the pharmaceutical industry to develop pediatric oncology drugs because the population of those impacted is comparatively small. Therefore, current treatments for children were developed decades ago for adults and were not based on modern understanding of the biology of pediatric cancers. With these challenges in mind, the Alliance for Childhood Cancer puts forward the following policy recommendations:

Recommendation 1: Ensure the Successful Implementation of the RACE for Children Act Through Appropriate FDA Resourcing

The Research to Accelerate Cures and Equity (RACE) for Children Act ("RACE Act"), passed in 2017, went into effect August 2020. The RACE Act amended the Pediatric Research Equity Act (PREA) so that FDA could require companies to conduct pediatric evaluations of new adult cancer drugs and biologics whose molecular targets are substantially relevant to pediatric cancers. Prior to passage of the RACE Act, PREA in effect excluded almost all oncology drugs from pediatric testing because cancers were understood by their location in the body (e.g., breast, prostate) and considered not relevant to children's diseases.

If FDA determines that a product is directed at a molecular target that is substantially relevant to the growth or progression of a pediatric cancer, sponsors of adult oncology drugs seeking FDA approval may be required to conduct RACE Act studies as specified in pediatric study plans (PSPs). To meet the implementation of the RACE Act, FDA must respond rapidly and effectively to: (1) the increase in the number of oncology agents in sponsors' pipelines that require pediatric discussion and planning in Early Advice Meetings as well as later initial Pediatric Study Plans (PSPs); (2) the increase in the potentially multiple pediatric cancer evaluations for a single oncology product; (3) and the growing number of Cluster Calls and Common Commentaries, FDA's mechanisms critical for coordinating global pediatric oncology clinical trials (necessary because eligible patient populations shrink with the discovery of molecular subgroups of disease).

Ensuring that sufficient resources are allocated to FDA's pediatric activities authorized under the RACE Act is essential to the effective implementation of the RACE Act. Congress must critically assess the user fee agreements between FDA and industry to ensure that they are

sufficient to adequately resource the considerable workload required. Congress should also provide appropriate oversight over the implementation of RACE Act to ensure that it is efficient, timely, and effective.

Recommendation 2: Congress Must Ensure that RACE Studies are Completed on Time

While PREA and RACE are premarket requirements, under the law, sponsors are permitted to request a deferral allowing them to submit pediatric studies after a drug is approved for adults. However, when sponsors do not complete required studies by the deadline specified in the deferral or deferral extension, FDA's existing authorities to enforce these deadlines have proven insufficient. In 2012, PREA was amended to require FDA to issue and publicly post non-compliance letters to companies that have failed to submit their assessments on time. The law was also changed to allow FDA to extend deferral deadlines for good cause, meaning that sponsors with reasonable delays are not included among those that receive non-compliance letters.

The issuance of non-compliance letters has unfortunately not resulted in the completion of delinquent pediatric studies, and many required studies are still outstanding after being years overdue.[1] While this problem has yet to impact RACE Act studies since deferral deadlines for those products have not yet been reached, it will inevitably affect RACE Act studies in the coming years. FDA is allowed to assess civil monetary penalties for late post-market study requirements for adults, but the law currently forbids FDA from doing the same for children. This is an inequity that must be addressed.

Congress should address the problem of delinquent pediatric studies now to ensure that it does not later become a problem with RACE Act studies. FDA needs the authority to penalize companies that do not complete their required pediatric studies.

Additionally, delays can result when sponsors request deferrals of required studies under PREA. While deferrals may legitimately be needed in many cases, we must ensure that deferrals are appropriate and do not unnecessarily delay the development of critical information for pediatric cancer research community and timely access to potentially life-saving products.

[1] https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/prea-non-compliance-letters; https://www.fda.gov/drugs/development-resources/non-compliance-letters-under-505bd1-federal-food-drug-and-cosmetic-act; https://www.fda.gov/about-fda/center-biologics-evaluation-and-research-cber/prea-non-compliance-letters; http://web.archive.org/web/20150608194838/http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm343203.htm

Congress should require FDA to assess the appropriateness of deferrals for RACE Act studies as well as compliance with RACE Act deadlines through the reporting requirement authorized under Section 508 of the Food and Drug Administration Safety and Innovation Act.

Recommendation 3: Authorize a New Public-Private Partnership to Develop Drugs for Rare Pediatric Cancers

Many rare pediatric cancers have molecular and genetic characteristics that are unique to children, such as tumors with gene fusions, embryonic tumors, germline tumors and many brain tumors. Developing new therapies for such rare cancers is unlikely to offer companies economically beneficial opportunities, leaving children with rare tumors with no therapeutic options. The RACE Act requires pediatric assessments only for those new agents in development for adults' cancers when they are molecularly relevant to a childhood cancer.

A new public-private partnership (PPP) would drive and catalyze the scattered resources in academia, the nonprofit sector and industry to assume responsibility for conducting pediatric oncology drug development programs when agents may have no associated adult cancer indications. A January 2020 GAO report on pediatric vouchers made this specific recommendation: "A collaborative agreement to share development risk and reward between a public or quasi-public organization and one or more private developers." Subsequent to the GAO report, the COVID-19 pandemic demonstrated the potential of public-private partnerships as in Operation Warp Speed's rapid deployment of vaccine options.

The Alliance recommends that Congress create a PPP to assume responsibility for conducting pediatric oncology drug development programs that may not be commercially advantageous for industry to develop on its own, bringing precision oncology and hope to children with many rare types of cancer.

As described above, the discovery and development of new effective treatments for children will require innovative collaborations among academia, government and industry. One approach is a bill introduced by Representative G.K. Butterfield (D-NC) and Representative Michael McCaul (R-TX) – H.R. 5416, the Give Kids a Chance Act which calls for reinforcing FDA's authority to require pediatric trials of combination drugs. We recognize the need for such trials, but wish to emphasize the importance of the clinical research community's traditional role in determining which trials are done and the manner in which they are conducted. As this legislation evolves, we look forward to working with the bill's sponsors to ensure that kids with cancer have access to the most cutting-edge clinical trials.

Thank you for your consideration of our recommendations. The Alliance for Childhood Cancer welcomes the opportunity to further discuss the unique challenges of childhood cancer drug development and research. Please contact Sarah Milberg, Co-Chair of the Alliance for Childhood Cancer, at smilberg@allianceforchildhoodcancer.org or Dr. Michael Link, Co-Chair of the Alliance for Childhood Cancer, at mlink@stanford.edu for any additional information.

Sincerely,

The Alliance for Childhood Cancer