

January 19, 2018

Scott Gottlieb, MD
Commissioner
Food and Drug Administration
C/O Dockets Management Staff (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: **Docket No. FDA-2017-D-6380**, Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases; Draft Guidance for Industry; Availability

Dear Commissioner Gottlieb:

On behalf of the following organizations who are dedicated to the health and well-being of children, we write to applaud the Food and Drug Administration (FDA) for the publication of the Draft Guidance on the Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases and to offer the following comments.

Children are not just small adults. Drugs work differently in children than in adults and must be studied specifically for their use. The Best Pharmaceuticals for Children Act (BPCA) and the Pediatric Research Equity Act (PREA) are two laws that encourage and require the study of drugs in children. Data resulting from BPCA and PREA studies are added to drug labels to give parents and providers essential information on the safety and efficacy of drugs used in children. The lives of millions of children have been improved because of BPCA and PREA, which have resulted in more than 640 drugs and biologics being relabeled with important information about their use in children. Children are safer because of what we have learned through BPCA and PREA studies and the pediatricians who care for them are better equipped to make clinical decisions for their patients.

Despite that progress, today, roughly 50 percent of all drugs used in children still lack FDA-approved pediatric information. For some populations, such as neonates, over 90 percent of drugs still lack approved labeling. Children should not have to wait 10 years or more for FDA-approved treatments that are safe and effective for their use. Yet, that is the average time lag between when a product is FDA-approved for adults and when it is approved for children. Some drugs never receive pediatric approval.

We are pleased that the draft guidance states that FDA will no longer continue to grant pediatric-subpopulation designation for drugs that are used to treat common diseases. FDA's draft guidance ends an outdated practice that has allowed sponsors to avoid their obligation to conduct pediatric studies of commonly-used drugs in adults. Currently, a drug for a common disease, that would otherwise not be eligible for orphan status, can receive orphan status for just the pediatric population with that disease, if such population is under 200,000. After receiving that designation, the sponsor can decide not to pursue pediatric drug studies at all, despite requesting the pediatric designation. Since the designation makes the drug exempt from PREA, FDA in turn has no authority to require that sponsor to conduct the needed pediatric studies. This loophole allows sponsors to exploit the process and this must change. We strongly support this action by FDA to close the orphan drug loophole. With this guidance, FDA is taking an important step forward in ensuring that more drugs are studied in children.

Addressing this narrow loophole, however, does not go far enough. The vast majority of orphan drugs will be still exempted from PREA. In recent years, roughly 40 percent of all drugs approved by FDA annually were designated as orphan drugs, meaning FDA cannot require these drugs to be studied in children under PREA despite the fact that 50-75 percent of orphan diseases occur in children. We understand that many orphan drugs are studied, approved, and labeled for use in children. However, sponsors do so only voluntarily, without being subject to the provisions of Section 505B of the Federal Food, Drug, and Cosmetic Act. Specifically, sponsors are not required to submit an Initial Pediatric Study Plan and have an Agreed Initial Pediatric Study Plan, have any interaction with FDA's internal Pediatric Review Committee, and labeling changes are generally not considered by FDA's Pediatric Advisory Committee. So, while a sponsor may choose to perform studies of an orphan drug in one pediatric subpopulation, as a result of the blanket exemption from PREA, FDA cannot require the sponsor to conduct studies in other pediatric subpopulations, most often younger age groups, who are affected by the disease.

Section 505B(k) gives FDA the authority to apply PREA to orphan drugs through regulation. We urge FDA to initiate such rulemaking as soon as possible. While we understand the challenges associated with drug development for orphan diseases, the number of orphan drug designations and orphan drug approvals has increased over time so these challenges can be overcome. PREA also gives FDA extensive authorities to waive and defer pediatric study requirements when studies would not be feasible or advisable. With close to 7,000 rare diseases without a treatment, and the majority of orphan diseases affecting children, PREA is a vitally important tool for ensuring that orphan disease drugs are studied and labeled for use in children. We look forward to working with you to ensure that all children, including children with rare diseases, have the benefit of research into how drugs can most effectively treat those conditions.

Thank you again for releasing this draft guidance and for the opportunity to comment. We look forward to working with you to improve and strengthen BPCA and PREA for all children. If we can be of further assistance, please contact Tamar Magarik Haro or James Baumberger with the American Academy of Pediatrics at tharo@aap.org or jbaumberger@aap.org.

Sincerely,

American Academy of Pediatrics
Academic Pediatric Association
American Pediatric Society
American Thoracic Society
Association of Medical School Pediatric Department Chairs
Children's Hospital Association
Elizabeth Glaser Pediatric AIDS Foundation
National Association of Pediatric Nurse Practitioners
March of Dimes
Pediatric Infectious Diseases Society
Pediatric Policy Council
PPAG: the Pediatric Pharmacy Association
Society for Pediatric Research
Treatment Action Group