



February 18, 2018

Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2017-D-6380-0005: Guidance: Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases

Dear Sir or Madam:

On behalf of the 30 million Americans with one of the nearly 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the Food and Drug Administration (FDA) for the opportunity to provide comments on the Agency's "Guidance: Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases."

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

There is nothing more foundational to our mission than ensuring proper incentives are in place for researching and developing treatments for individuals with a rare disease. NORD was founded in 1983 by the very same patients, caregivers, and family members who successfully advocated for the passage of the Orphan Drug Act (ODA). Ever since, NORD has served as the lead supporter of the ODA and the incentives within.

Approximately 50 percent of individuals with rare diseases are children, and about two-thirds of all rare diseases affect individuals 18 years of age or younger. Therefore, ensuring rare pediatric disease drug development incentives are strong is particularly critical for the development of treatments for the rare disease patient population.

For these reasons, we take accusations of loopholes in the system for incentivizing drug development for rare pediatric patients extremely seriously and are committed to ensuring that these incentives are not only working as intended when they were created, but are also resulting in the robust development of innovative orphan therapies for our patients.

In this draft guidance put forward by FDA, the agency is attempting to close what they argue is a loophole that can occur at the intersection of the ODA and the Pediatric Research Equity Act (PREA). FDA argues that drug and biologic developers are able to avoid PREA requirements for testing therapies in pediatric populations by exploiting this loophole. FDA claims that by

receiving orphan designation for the pediatric subpopulation of a common disease, but then declining to move forward with testing in this additional orphan indication, drug and biologic developers are able to evade testing the therapies in children because orphan designated therapies are exempt from PREA.

We support closing any and all loopholes that may exist within the laws and regulations intended to spur rare and pediatric therapeutic development. However, we request the following items from FDA before the finalization of this guidance.

Additional Evidence Is Needed:

First, it is difficult for us to ascertain the severity of this potential loophole due to the lack of evidence FDA has put forward. In this draft guidance, and in accompanying materials, FDA claims this loophole exists and must be closed, but does not offer any substantive examples of these actions.

Before FDA moves forward with finalizing this guidance, we request that FDA offer further evidence of the exploitation of this loophole, including how many therapies that received a pediatric subpopulation orphan designation did not complete additional pediatric testing, but were also exempt from PREA.

Additional Cost/Benefit Analysis Is Needed:

Second, the additional evidence FDA will provide on the frequency and extent of the exploitation of this loophole will allow outside stakeholders to weigh the costs and benefits of no longer providing orphan designation to pediatric subpopulations. While several incentives exist to encourage pediatric drug development, such as PREA and the Best Pharmaceuticals for Children Act (BPCA), orphan designation is accompanied by seven years of exclusivity for the additional pediatric indication, a 25 percent tax credit on the clinical testing, and more.

We are concerned that there may be rare pediatric subpopulations of common diseases that would have been tested under the previous incentive structure that would now no longer receive such attention. Both PREA and BPCA exist to encourage these studies, but PREA requirements can be avoided using the sometimes unpredictable waiver and deferral process, and the six months of exclusivity offered by BPCA has not shown to be an adequate incentive in every case.

We request that FDA offer the stakeholder community additional analysis on the possibility for pediatric drug development and research to actually be weakened by this move rather than strengthened.

Ambiguity Within the Draft Guidance Should Be Addressed:

Finally, we are concerned that certain ambiguities within the draft guidance could result in the lack of virtually any incentive for therapeutic development for pediatric subpopulations of rare diseases.

We are thankful FDA is clear that they will continue to designate pediatric populations if they meet the one of the following criteria:

1. “due to one or more properties of the drug, the remaining persons with such disease or condition would not be appropriate candidates for use of the drug”¹; or
2. “the sponsor can adequately demonstrate that the disease in the pediatric subpopulation is a different disease in the adult population”²

We anticipate the vast majority of orphan therapies intended to treat pediatric populations for which there is also an adult population would meet one of these two categories, and we thank FDA for clearly delineating their continued intention to designate these products.

However, there are additional pediatric rare disease populations for which FDA is unclear: rare pediatric populations of rare diseases. On page 4 of the draft guidance, FDA states, “In order to close the loophole created by the interaction of the practice of granting pediatric–subpopulation designation and the PREA orphan exemption, FDA intends to no longer continue to grant pediatric-subpopulation designation.” FDA notably does not specify this only applies to pediatric subpopulations of common diseases, for which PREA would require pediatric studies.

If a sponsor gains orphan designation for the adult population of a rare disease but not the pediatric population (which could occur for any number of reasons), and the pediatric population does not meet one of the above two criteria for designation, there will be barely any incentive for the company to conduct pediatric studies later on. PREA will not apply due to the orphan exemption, and FDA is unclear whether their declination to designate pediatric subpopulations, as is explained on page 4 of the draft guidance, also applies to pediatric subsets of rare diseases.

We ask FDA to ensure these pediatric subpopulations of rare diseases continue to receive orphan designation since there are few other incentives for development.

We thank FDA for the opportunity to comment and we look forward to working with FDA to ensure pharmaceutical incentives are working properly and as intended. For questions regarding NORD or the above comments, please contact me at pmelmeyer@rarediseases.org, or 202-545-3828.

Thank you in advance for your consideration.

Sincerely,



Paul Melmeyer
Director of Federal Policy

¹ 21 CFR 316.20

² Clarification of Orphan Designation of Drugs and Biologics for Pediatric Subpopulations of Common Diseases Draft Guidance for Industry pg. 4