NORD Statement at the FDA Pediatric Stakeholder Meeting
November 21, 2019

Hello and good morning,

On behalf of the 25 to 30 million Americans with one of the over 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the U.S. Food and Drug Administration (FDA) for the opportunity to speak here today at the Pediatric Stakeholder Meeting.

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare – also known as "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.

The Best Pharmaceuticals for Children Act[1] or "BPCA" and the Pediatric Research Equity Act of 2003[2] or "PREA" are landmark pieces of legislation designed to improve information about how to safely and effectively use therapeutics in children. Both laws were enacted at a time in which many drugs that were not directly approved for pediatric populations were being used on children without adequate information on safety and efficacy nor proper dosage.

The two laws operate differently. As Dr. McCune mentioned, they are often referred to as a "carrot and stick" approach. BPCA, or "the carrot," offers an incentive in the form of an additional 6 months of exclusivity for the conduct of pediatric studies that would be beneficial for children. Under PREA, or "the stick," FDA can *require* a sponsor to conduct certain pediatric studies and to submit such studies with the marketing application. As a result of these two important laws, there have been 765 labeling changes to include pediatric information.[3] NORD recognizes the importance of these successes and supports efforts to ensure the continued efficacy of these laws.

Although not the central focus of this meeting today, I want to discuss another law for which NORD has a long history of support: the Orphan Drug Act. In 1983, there was a serious lack of treatments for those living with rare diseases - only 34. Out of a sense of desperation, a small group of patient advocates – many of whom were parents, led by Abbey Meyers, mobilized. Abbey founded NORD, and she and NORD played a pivotal role in the enactment of the ODA that same year. The goal of the Act is to encourage the development of drugs for rare diseases and it has been a huge success, going from less than 35 in 1983 to over 800 FDA approved indications for rare disease treatments today.

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[1] P.L. 107-109
[2] P.L. 108-155
[3] FDA. New Pediatric Labeling Information Database. https://www.accessdata.fda.gov/scripts/sda/sdNavigation.cfm?sd=labelingdatabase. Accessed on November 19, 2019.

But other numbers suggest there is more work to be done. There are still over 7,000 rare diseases that afflict almost 30 million people in the United States alone. More than 90% of these diseases still have no FDA-approved therapy.

Patients with rare diseases live this reality on a daily basis. With this serious unmet need in mind, NORD has continued its fight for policies that foster orphan drug development from 1983 to today.

Of course, rare diseases impact adults and children alike. Estimates suggest that anywhere between half to two-thirds of the 7,000 rare diseases begin in childhood.[4,5] Many continue to be fatal in these young children.[6] Yet, scientific advancements leading to early diagnosis and improved treatments have resulted in more children with rare diseases surviving into adulthood. And we hope that someday treatments will allow all children with rare diseases to live to adulthood.

When PREA was enacted in 2003, Congress decided to exempt orphan products from its requirements.[7] In other words, when a sponsor pursues an orphan designation and approval, that sponsor is not required to conduct the pediatric studies that would otherwise apply to sponsors of non-orphan products. Under the law, FDA has the authority to revoke or change this exemption through regulation.

In the 2017 passage of the FDA Reauthorization Act, Congress required FDA to report on the lack of pediatric information in the labeling of drugs for indications that have received an orphan designation. In August 2019, FDA issued its report entitled "Pediatric Labeling of Orphan Drugs" responding to this mandate. FDA found that of the 548 total approved orphan indications (from 1999-August 2018), 200 did not warrant pediatric labeling, while 348 did warrant pediatric labeling. Of the 348 approved orphan indications that warranted pediatric labeling, FDA found that 221 (or roughly 2/3) were fully labeled. The other 127 were incompletely labeled, with 81 having no pediatric information and 46 missing some pediatric information.[8]

NORD applauds FDA for completing this comprehensive and thorough report.

NORD is extremely concerned about FDA's findings in this important report. It is unacceptable that roughly 1/3 of all orphan products that warranted it had inadequate pediatric labeling and ¼ failed to contain any pediatric labeling at all. NORD recognizes that children are not just small adults. Ensuring that pediatric patients, their families, and their providers have the information they need to make not only dosing decisions, but treatment decisions is of utmost concern to

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[4] Sanford Research. Pediatrics & Rare Diseases. https://research.sanfordhealth.org/fields-of-research/pediatrics-and-rare-diseases. Accessed on November 19, 2019.
[5] Bavisetty S., Grody, W., Yazdani, S. Emergence of pediatric rare diseases. Rare Dis. 2013; 1: e23579. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3932940/. Accessed on November 19, 2019.
[6] Institute of Medicine. Rare Diseases and Orphan Products. Pp. 89-91. https://www.ncbi.nlm.nih.gov/books/NBK56189/pdf/Bookshelf_NBK56189.pdf. Accessed on November 19, 2019.
[7] 21 USC 355c(k)(1)
[8] Department of Health and Human Services, Food and Drug Administration. Pediatric Labeling of Orphan Drugs. Report to Congress. Table 5. https://www.fda.gov/media/130060/download, downloaded on November 13, 2019.

NORD. Without adequate labeling for children, health care providers and caregivers are put in the difficult position of guessing whether and how much of a drug to provide. This could have dangerous consequences for children.

This is a situation that cannot be sustained. NORD supports efforts to ensure that adequate and complete information on pediatric uses for all appropriate age groups can be obtained for orphan drugs.

Orphan therapies represent an increasing number of products approved by FDA. That is good news for all patients with rare diseases, especially given the 90% of rare diseases with no approved drugs. But, under current law and regulations, this means that more products coming to market will be exempt from PREA, potentially exacerbating the concerns highlighted in FDA's report.

As we explore ways to remedy the lack of pediatric information on orphan drug labeling, NORD believes it is critical to keep in mind some key considerations.

Again, we must remember that 90% of 7,000 rare diseases still do not have a treatment that has been developed and is FDA-approved. We need to ensure that any requirements to increase pediatric information about therapies do not impede innovation in the rare disease space. Any such requirements must also be applied only when necessary. Studies in children shouldn't just be interesting—they must be necessary. There must also be transparency and predictability around requirements with respect to pediatric studies. Companies in this space must know the requirements in advance and understand when and how such studies might be required. Some therapies do not necessarily lend themselves to pediatric studies and incorporating children may not be practicable. All of these factors must be considered carefully, incorporated into the process, and communicated and applied clearly and consistently across the centers and review divisions. Such protections are in the interest of both children and adults with rare diseases.

NORD stands ready to work with FDA, Congress, and other stakeholders to achieve the dual goals of ensuring that innovation in the orphan drug space continues and that more robust pediatric labeling makes its way onto orphan products. The status quo as detailed in FDA's report is unacceptable and we need to find a way to address it.

Thank you.