



February 5, 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-N-6476-0001: Pediatric Rare Diseases-A Collaborative Approach for Drug Development Using Gaucher Disease as a Model; Draft Guidance for Industry; Availability**

Dear Sir or Madam:

On behalf of the 30 million Americans with one of the nearly 7,000 known rare diseases, NORD thanks the Food and Drug Administration (FDA) for the opportunity to provide comments on the Agency's "Pediatric Rare Diseases-A Collaborative Approach for Drug Development Using Gaucher Disease as a Model; Draft Guidance for Industry."

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.

We thank FDA for putting forward this draft guidance as it once again reflects FDA's commitment to fostering innovative rare disease therapeutic development. FDA already reviews over 75 percent of orphan therapies using an expedited review pathway, and a similar percentage of orphan therapies are evaluated and approved using innovative clinical trial designs. FDA is also continuing its long history of support for the rare disease community perhaps best exemplified by the efforts of the Office of Orphan Product Development, the Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research's (CDER and CBER) Rare Diseases Programs, and the ongoing Orphan Drug Modernization Plan.

We particularly appreciate FDA's efforts to further facilitate and encourage therapeutic development within rare pediatric diseases. Approximately half of the rare disease patient population are children, and an estimated two-thirds of rare diseases affect children. Rare pediatric disease therapeutic development is also particularly difficult due to the small patient populations, the complex biology of these diseases, and the additional ethical implications that must be considered when testing therapies in children.

The following comments on this guidance will pertain specifically to the implications of the guidance on the broader rare pediatric disease patient community. We will not comment on the aspects of this draft guidance specific to Gaucher disease as we are not experts in this condition. Instead, we encourage FDA to consider the viewpoints of the patients, caregivers, physicians, researchers, and companies who are experts on Gaucher disease as FDA moves forward on finalizing this guidance.

NORD strongly supports FDA's stated goal of "minimizing the number of patients necessary to be treated with placebo." We believe using placebos as the control group within rare disease clinical trials is antiquated and often avoidable, and we have long supported innovative trial designs that avoid the use of placebos. This is particularly important within pediatric populations as we view unnecessarily delaying or denying access to potentially effective therapeutic interventions for kids as unethical. We support all efforts to facilitate access to the experimental therapy within clinical trials while still maintaining the validity and rigor of the trial.

We also support the stated proposed method of collaborative trial design within this draft guidance. This model, if implemented effectively and broadly, has the potential to dramatically lower the number of kids subjected to placebos. We do believe, however, that there are several aspects of this draft guidance that can be improved.

First, much of the draft guidance is very specific to Gaucher disease and may be difficult to easily extrapolate to other diseases. While FDA outlines the structure of this collaborative model within Gaucher disease, it does not specify which characteristics of this model could also apply to other disease areas. Given the regulatory caution and restraint of many biotechnology and pharmaceutical companies, we can imagine many companies choosing not to pursue this model as they would be unsure of what translates to their specific disease or development pathway.

Second, FDA does not discuss the many hurdles to collaborative drug development that would prevent this model from gaining popularity. Collaborating with drug development competitors, and all of the intellectual property, patent, and propriety barriers that would need to be overcome, is extremely difficult. We do not see any guidance from FDA on how to overcome these obstacles. While these impediments largely fall outside the scope of this specific draft guidance, if left unaddressed, we imagine this model may not be utilized extensively without further guidance or assistance.

Finally, FDA does not address how to incorporate the entity that is often the unifying participant in drug development; the patient organization. Patient organizations have become much more involved in the development of orphan therapies, and have the potential to facilitate the very arrangements FDA is encouraging within this draft guidance. Patient organizations are creating and administering therapy-agnostic natural history data registries, as is recommended within this draft guidance. For example, NORD has collaborated with many of our member patient organizations to create these exact registries for their populations. Patient organizations can also act as the broker between companies to ensure honest interactions. FDA should amend this guidance to incorporate specific suggestions on involving patient organizations in encouraging the use of this model.

We thank FDA for the opportunity to comment, and we look forward to working with FDA in refining and encouraging the use of this innovative collaborative model. For questions regarding NORD or the above comments, please contact me at [pmelmeyer@rarediseases.org](mailto:pmelmeyer@rarediseases.org), or 202-545-3828.

Thank you in advance for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read 'P. Melmeyer', with a long horizontal flourish extending to the right.

Paul Melmeyer  
Director of Federal Policy