

LEADING THE FIGHT TO END DUCHENNE

Center for Drug Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave, Bldg 51, Rm 1146
Silver Spring, MD 20993-0002
Docket No. FDA-2016-N-1895
RE: Prescription Drug User Fee Act; Public Meeting

August 19, 2017

To Whom It May Concern,

On behalf of Parent Project Muscular Dystrophy (PPMD), we are most grateful to the Food and Drug Administration

- for the commitment to integrating patient perspectives within the drug development lifecycle through the implementation of PDUFA V;
- for the multiple opportunities to reflect on our experiences as we innovated within the patient focused drug development (PFDD) framework over these last five years; and
- for the opportunities to actively engage in the exchange of ideas as to how to build upon the transformational PFDD foundation as we move ahead to PDUFA VI.

PPMD is overall very pleased with the recommendations contained within the FDA PDUFA VI commitment letter and recognizes the tremendous effort Agency personnel have devoted to these proceedings. We are most grateful.

PPMD is the world's largest organization focused on ending Duchenne muscular dystrophy. Duchenne is a progressive disease diagnosed in early childhood that affects skeletal muscle and the cardiac and pulmonary systems. There currently are no FDA-approved, disease-modifying treatments, and children diagnosed with Duchenne typically live only into their 20s. In short, Duchenne is 100% fatal.

Though Duchenne-specific treatments have eluded us to date, PPMD and our partners have worked tirelessly to build a robust therapeutic pipeline and regulatory infrastructure. The FDA Safety & Innovation Act (FDASIA) and PDUFA V aligned perfectly with the dawning of a new day for our Duchenne community – one in which basic laboratory breakthroughs have developed into clinical trials, enabling the Duchenne pipeline of experimental therapies to become more robust than ever. We immediately embraced the opportunities presented to us through PDUFA V and have worked over the past few years to evolve the science of patient input and advance the field of Patient-Focused Drug Development.

As we look ahead to PDUFA VI – and Patient-Focused Drug Development (PFDD) 2.0 – and build upon the tremendous foundation of patient preference work that has been laid to date, we see an opportunity to address questions that have arisen over the past few months as to where and how this information fits into the overall development plans, application, and review process.

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As noted in our previous Federal Register comment submissions, public stakeholder meeting testimony, and through our efforts around the Patient Focused Impact Assessment Act (S. 1597), we would like to see greater transparency in how FDA reviewers are or are not using such information. Such feedback would be valuable to all stakeholders. Patients would benefit by being able to see how their inputs are – or are not – factoring into FDA reviewer and management decisions. When the answer is that such inputs are not informative to reviews or not being used as patients would like, the explanation could be particularly valuable in helping communities develop patient engagement tools that better respond to the needs and standards of the agency. Industry stakeholders also would obtain a similar benefit from such feedback, particularly as they consider how to properly collaborate with patients, researchers, and others on such tools.

Beyond such agency reporting, we would like to see the following items considered for and reflected within the final performance goals for FY 2018 through 2022:

Promoting Innovation Through Enhanced Communication Between FDA and Sponsors During Drug Development

Clarity and guidance from FDA as to how, exactly, patient preference data can be entered into the review process of a specific application – including instances where such information is supported by the sponsor and situations where it is not product-specific yet highly relevant to the issues being considered – is needed. The draft agreement emphasizes the need for enhanced agency communications with sponsors. We would urge the agency to recognize that the patient must be at the center of therapeutic development efforts by expanding this section further to include communications with patient stakeholders as integral participants in the regulatory decision-making process. Specifically, we would urge that the planned assessment looking at agency communications practices include how the agency communicates with patient communities, particularly those communities actively involved in PFDD efforts connected to one or more applications, as well as whether and how the FDA might encourage sponsors to pursue more transparency with patient communities across development phases and programs.

While we recognize the confidential nature of many FDA-sponsor communications, including those that are governed by statute, we must balance that protection with equal attention to the patient interests, particularly as patient engagement continues to evolve as a field. Patients deserve to be included during the review process, particularly when they have been clinical trial participants or are playing a material role through one or more PFDD tools. We would strongly encourage the agency to establish the procedures and parameters for patient communities to engage fully in the development and review process, particularly where the community brings a critical perspective to the table, but does so in a way that is not product-specific and not attached to an applicant's submission. We recognize that this can be a very complicated topic but encourage the agency to address it within its larger plans in this space.

Finally, we would encourage the FDA and industry to give serious consideration to ways the regulatory communications processes can be improved, particularly when a PDUFA date deadline has passed. The Duchenne community is in the midst of such a situation at this writing,

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and the lack of official updates has generated much frustration and created a void that unfortunately has been filled by rumors and speculation. This is not good for patients, not good for the FDA, not good for the sponsor, and not good for other stakeholders. We recognize the complexity of such reviews, particularly when they run past the PDUFA date, and appreciate the efforts team leaders and others are making to reach a thorough decision as quickly as possible. At the same time, we believe better communications would help address these challenges.

Specifically, we recommend that the agency consider the merits of issuing a brief update 30 days following a PDUFA deadline and every 30 days thereafter until the agency issues an approval or a complete response letter. This approach could help fill the damaging information void that exists in these circumstances and would extend the commitment to enhanced communications that is included in the draft performance goals.

Enhancing the Incorporation of the Patient's Voice in Drug Development and Decision-Making

PPMD applauds the agency for the progress it has made in the field of benefit/risk and patient preferences during the 5-year PDUFA V timeframe. The framework has established a foundation for structured consideration of these most important issues, a foundation upon which we must build further in the years ahead. We also commend the agency's plan, as noted in its draft performance goals, to develop a series of guidance documents to move PFDD toward an era of "fit-for-purpose tools to collect meaningful patient and caregiver input ultimately for use in regulatory decision making." It is this involvement in the regulatory process that PPMD and other patient communities desire most.

As an early adopter and leader in the field of patient engagement and PFDD, PPMD knows well the challenges the agency has faced in recent years determining how to encourage development of a nascent field, simultaneously ensuring appropriate levels of guidance and oversight. While we are pleased to see the agency proposing to move forward with multiple guidances to provide much-needed advice and definition to this sector, we are concerned that the timelines for those milestones are simply too remote and will not align with the fact that products are currently under review for which patient focused drug development tools designed with disease-specificity and methodological rigor exist.

Absent near-term guidance, we are concerned that uncertainty and confusion will continue, potentially deterring or delaying patient or industry efforts to develop groundbreaking PFDD and related tools. Rather than risk this scenario, we encourage the FDA to accelerate this work and would propose the issuance of best practices in the form of an interim guidance that could be particularly useful. Guidance in the areas of collecting patient input, patient preferences, patient-reported outcomes, and clinical outcomes measures, for example, would be most useful to patients, researchers and industry seeking to advance the field of patient engagement. Additionally, while we recognize the need for a standardized approach to much of this work, we are concerned that a significant component of this activity will be highly tailored and vary greatly from patient community to patient community and even patient to patient. For example,

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based on our own landmark work in patient preferences, we could envision significant variation among patients and caregivers on topics like burden of disease, burden of treatment and the like and would caution against setting a standard that is simply not possible to reasonably achieve.

Enhancing Benefit-Risk Assessment in Regulatory Decision-Making

Complete Benefit-Risk Evaluation

One concern we have noted within the current benefit-risk paradigm has been the lack of a structured benefit-risk evaluation for at least one NDA in the Duchenne muscular dystrophy arena that proceeded to an accepted application and an advisory committee meeting. Unfortunately, during this process, the FDA stated that it did not complete a formal benefit/risk evaluation even though it accepted the application. This lack of an evaluation limited discussion about benefit/risk and related patient preferences during the advisory committee meeting. As a result, we believe that the review omitted valuable information and patient perspective.

Advisory Committee and Benefit-Risk Considerations

We recommend that as the agency refines its proposed performance goals, that it commit to conduct a complete benefit/risk evaluation for every candidate therapy that would address an unmet medical need, even in situations where the agency may question the overall benefit or efficacy of a candidate therapy. If this is the case, such perspectives can and should be noted within the review, but would still enable the agency to put forward an evaluation.

Related to the point above, we believe that each advisory committee session focused on a first-in-class product and/or a product to address an unmet medical need should include a defined portion of time to present and discuss further a benefit/risk evaluation. Current procedures place the burden on either the sponsor or the patient community to dedicate time during respective Advisory Committee review presentations or Open Public Hearing (OPH) to allow for the presentation or discussion of such data. Given the importance of this information, we believe there must be a dedicated time and place for such a discussion, perhaps at the conclusion of the agency's presentation.

Doing this would not preclude the sponsor from focusing on benefit/risk and related patient preferences during their presentation time, nor would it preclude patient and other stakeholders from doing so during the OPH. Rather, this action would simply have the agency present its benefit/risk evaluation as part of its presentation. This will ensure benefit/risk evaluations receive the essential level of attention from an advisory committee and sends an important message to industry and patients that the agency values such quantitative data from both traditional clinical trials and new, innovative preference assessments.

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Advisory Committee on Patient Engagement

We were encouraged when the FDA moved forward in 2015 to establish a patient engagement advisory committee (PEAC) focused on medical device issues. While we are concerned that this committee has yet to be constituted, we strongly believe in the merits of such a panel and would urge the agency to consider establishing a similarly oriented patient engagement advisory committee under the Human Drug Advisory Committee umbrella. This action will provide the agency with the tools and processes needed to gather necessary expert input to develop this field going forward.

Advancing Development of Drugs for Rare Diseases

PPMD appreciates the proposal to integrate the CDER Rare Disease program staff within the review teams working on applications in rare disease. This integration will help maximize the likelihood that review decisions incorporate the unique challenges and limitations of rare disease patient populations, particularly when it comes to clinical trial size and power and the need for a greater level of regulatory flexibility within statutory parameters. PPMD believes the agency should go beyond the agreement text to develop pilot programs focused on specific disease areas to evaluate the impact of these approaches and develop recommendations for further refinement.

PPMD also applauds the proposed PDUFA VI plan to increase staffing for support of breakthrough product reviews, which may often be applicable to unmet needs for rare diseases. PPMD endorses the plan to enhance both the evaluation and communication of post-marketing safety findings related to new drugs, especially noting the importance of this information to patient communities having access to drugs which were introduced via the accelerated approval processes.

On behalf of our Duchenne community, we are extraordinary grateful to all those who have worked tirelessly to implement the transformational framework which yielded from PDUFA V and we are delighted to build on this critical foundation through the refinements and enhancements proposed within the FDA PDUFA VI commitment letter.

Sincerely,



President & CEO
Parent Project Muscular Dystrophy