Muscular Dystrophy Association Comment  
Docket No. FDA-2016-N-1895: Prescription Drug User Fee Act  
August 22, 2016


MDA is the nation’s leading nonprofit organization dedicated to saving and improving the lives of children and adults living with neuromuscular disease. MDA fulfills its mission by funding biomedical research, providing expert clinical care and support through a network of more than 150 specialty care centers nationwide, and championing public policies and programs that benefit those living with neuromuscular disorders and the people who love them. For more than 65 years, MDA has been on the frontlines of research for neuromuscular disease, taking a unique, big picture perspective to find breakthroughs across disorders. Since inception, MDA has invested more than $1 billion in research grants to accelerate treatments and cures for neuromuscular disorders, making MDA one of the largest sources of neuromuscular disease funding.

MDA appreciates the Food and Drug Administration’s (FDA or Agency) commitment to engage the community throughout the process of PDUFA VI. Over the past 13-months the Agency has provided the opportunity for stakeholders to participate—resulting in a commitment letter that incorporates the perspectives of patients, advocates, and other stakeholders in a meaningful way.

MDA supports the PDUFA VI commitment letter, particularly with regard to the following provisions.¹

Enhancing Development of Drugs for Rare Diseases.

¹ Subsections referenced herein are set forth in PDUFA VI, Parts I, II, and III (Ensuring the Effectiveness of the Human Drug Review Program, Enhancing Management of User Fee Resources, and Improving Hiring and Retention of Review Staff, respectively).
Each of the more than 40 disorders under MDA’s umbrella—including muscular dystrophy, amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy (SMA)—are classified as rare diseases, for which there are few treatments—and no cures. MDA is committed to helping change that paradigm, and is pleased to see the commitment to rare disease therapy development in PDUFA VI.

Drug development for rare disorders is especially challenging due to the complexities and (often unknown) underlying mechanisms of disease, the relatively few number of individuals eligible to participate in clinical trials, the geographic distribution of potential trial participants, the challenges of traveling (especially by air) to clinical trial sites, and a myriad of other considerations. FDA’s recognition of the challenges of rare disease drug development in the advent of the Rare Disease Program (RDP) and other programs, offices, and policies, has significantly impacted the rare disease drug development pipeline. MDA supports a continued concerted effort to strengthen these and other approaches that would help further accelerate treatments and cures for rare disorders.

MDA applauds the concept of integrating RDP staff into the Agency’s development and review teams, and anticipates that this will result in meaningful incorporation of rare disease considerations into the full scope of the development and review cycles. The continuation of training to both drug and biologic department staff by RDP about the challenges with rare disease development and reviews as well as sharing guidance and strategies for best practices and flexibility to handle such considerations is also important. MDA is pleased that RDP staff will continue to engage in outreach to stakeholder groups including industry and patient groups to share information about RDP, and anticipates that prioritizing this outreach will result in staff engagement with stakeholder groups in various venues such as meetings and conferences.

**Enhancing Drug Development Tools Qualification Pathway for Biomarkers.**

Biomarkers are critical to rare disease drug development and MDA supports the focus on accelerating the qualification and application of biomarkers. Efforts to improve the Agency’s capacity to review biomarkers and to make clear the evidentiary standards for qualification are positive developments. MDA also appreciates the Agency’s commitment to incorporating stakeholder input in the process by committing to a public meeting to address tools for biomarker qualification.

The development, qualification and use of biomarkers for neuromuscular disorders including muscular dystrophy, ALS, SMA and others are important factors in the development and review process. As such, MDA is committed to working collaboratively with the Agency and other stakeholders to continue to develop and strengthen this area.²

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² MDA convened a group of stakeholders in May 2015 to submit a joint response to FDA’s Notice and Request for Comment Identifying Potential Biomarkers for Qualification and Describing Contexts of Use to Address Areas Important to Drug Development (FDA-2014-N-2187), which set out biomarker information for multiple disorders.
Early Consultation on the Use of New Surrogate Endpoints.

As neuromuscular disease science evolves, and as approaches and lessons learned from past trials and development efforts emerge, it is critical that a clear path exists early in the cycle to determine whether a given biomarker may be appropriately relied upon as a new surrogate endpoint for approval purposes.

PDUFA VI emphasizes the importance of early consultation between the drug developer and the Agency to determine whether the proposed surrogate end point may serve as the primary basis for product approval. This, along with multiple other provisions in PDUFA VI that encourage and facilitate early, clear and transparent interactions among industry and the FDA are important to MDA, as such lines of communication are critical to ensure that safe and effective therapies are available to patients as quickly as possible.

Ensuring Sustained Success of the Breakthrough Therapy Program.

MDA supports the allocation of additional resources to the breakthrough therapy program. Breakthrough therapy designation expedites development and review of therapies for serious disorders when evidence from preliminary clinical study demonstrates “substantial improvement over existing therapies.” A therapy receiving a designation of this type benefits from certain features of the fast track program and additional engagement with and input from the FDA in the development and review cycle. The breakthrough therapy program focuses on the rapid development and review of therapies for serious diseases such as neuromuscular disorders, and MDA supports the provisions in PDUFA VI that would strengthen this program.

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

MDA applauds the focus on promoting systematic approaches for incorporating the patient voice in the drug development and regulatory review cycle. PDUFA V facilitated incorporation of the patient voice in the Patient Focused Drug Development (PFDD) effort, which resulted in a fixed number of FDA led PFDD meetings. With the FDA’s invitation for externally led PFDD meetings, greater opportunity now exists for sharing the patient’s voice, and MDA appreciates this opportunity. MDA is pleased to see the role of patient engagement incorporated in a meaningful way into PDUFA VI, and looks forward to working with the Agency and other stakeholders to develop externally led PFDD meetings and to continue to engage in sharing the patient voice.

MDA also supports the Agency’s interest in strengthening its capacity to apply patient-focused methodology. The multidisciplinary nature of the proposed staff as well as the

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integration of such staff into the regulatory review teams is an approach MDA believes will facilitate integration of the patient voice throughout the regulatory review cycle.

The proposed development of a series of guidance documents that will set forth (1) mechanisms for collecting input from patients and caregivers that reflect representative and comprehensive input; (2) processes to develop patient impact data such as burden of disease and treatment; (3) measures for an identified set of impacts; and (4) clinical outcomes assessments and ways to incorporate such outcomes into clinical trial endpoints, as long term goals will provide helpful frameworks. MDA anticipates that stakeholders including patients and advocates will have an opportunity to help inform the approach taken in the guidance.

The repository proposed to publicly share tools and resources is supported by MDA, and the intent to include staff training on the application of the tools is key to ensuring such resources are employed consistently. MDA appreciates the effort to convene a workshop that would aim to enhance patient engagement in clinical trials and looks forward to participating.


MDA agrees that benefit-risk assessments are important in the development and review cycle and appreciates the recognition of benefit-risk in PDUFA VI. The goal to clarify the Agency’s approach to benefit-risk assessment and to increasing transparency in the process are supported by MDA. MDA looks forward to participating in the public meeting set out in the terms that would include allowing stakeholder input on how such information is applied through the entire drug development and review cycle.

Enhancing Use of Real World Evidence for Use in Regulatory Decision-Making.

MDA agrees that real world evidence (RWE) represents an opportunity unlike any other currently available to potentially impact the drug development and review process. While there are many unanswered questions about RWE (i.e. how to collect, apply, analyze), MDA applauds the Agency’s interest in engaging stakeholders in a public forum to begin to consider a framework for RWE.

Advancing Development of Drug-Device and Biologic-Device Combination Products Regulated by CBER and CDER.

MDA is glad to see Agency coordination as part of PDUFA VI as we understand this type of effort can be an obstacle to the review of combination products. The approaches set out that include streamlining processes and updating procedures for combination products review will contribute to consistent reviews across the Agency for both drugs and biologics. Uniformity in approach and coordination across centers are important elements in facilitating timely and predictable review processes.
Enhancing Capacity to Review Complex Innovative Designs.

MDA is pleased to see the FDA committed to considering complex innovative trial design and to ensuring that staffing will be sufficient for the commitment to be carried out. The approach to hold a public meeting regarding the use of various study designs and to conduct a pilot program for highly innovative trial designs that require simulations are also welcome as they capitalize on transparency and openness to new and creative ideas and approaches.

Improving FDA Hiring and Retention of Review Staff.

PDUFA VI sets out goals and processes that MDA believes are critical to increasing efficiencies in the drug development and review process, thereby getting safe and effective therapies to patients as quickly as possible. The obligations on the Agency, however, cannot be accomplished without sufficient staffing. Historically, the Agency has had below optimal staffing in critical departments, and MDA is pleased that the terms of PDUFA VI specifically call out the need for sufficient staff in terms of the number of staff needed to fulfill the objectives as well as identifying skill sets staff will need to carry out the obligations set out in the agreement.

Focus on Industry/Sponsor and FDA Communication.

MDA applauds the focus on early, frequent and sustained communication between drug developers and the FDA. Ongoing communication of this nature is critical to ensuring that all stakeholders are apprised of the information necessary for reviews to be carried out in the most efficient and effective manner possible.

PDUFA VI sets out multiple approaches aimed at ensuring sufficient communication, including the concept of a Formal Communication Plan that would be developed collaboratively with the FDA and the drug developer in the pre-submission timeframe. Also included is a commitment to either revise or finalize guidance for best practices for communication with the FDA. Moving a therapy into the regulatory review space is a significant undertaking for applicants and for the individuals who have participated in the development process and clinical trials, and ensuring that the applicant and the reviewer have open lines of communication is critical.

MDA applauds the significant effort that the Agency, industry, and stakeholders have invested into developing the performance goals and procedures set forth in PDUFA VI. MDA is pleased to see the inclusion of many provisions that advance the engagement of patients, continue to focus on rare disease drug development, prioritize clear and transparent communication practices, and address agency staffing needs to make implementation of the goals possible. For questions about MDA’s comments or for additional information, contact Kristin Stephenson, MDA’s Vice President, Policy & Advocacy, at kstephenson@mdausa.org.