FARA leads the Neuromuscular Community in Important FDA Recommendation:

Early this fall, the FDA announced its intention of meeting over the next five years with representatives from 20 "disease areas" so as to learn enough about disease severity and unmet medical needs in those diseases to be helpful in the benefit-risk evaluations the FDA must make when considering an application for clinical trials or drug approval. When FARA saw that the list of disease areas the FDA nominated for consideration consisted mostly of single diseases and that the FDA requested public comments on this list and process, we immediately assembled some of our key advocacy partners to recommend that the FDA take a different, more comprehensive approach. FARA drafted public comments proposing that, rather than meeting with only 20 individual diseases, the FDA identify 20 "clusters" of diseases that are so similar in terms of severity and unmet medical needs, etc., that the agency would learn enough about all the diseases in such a "cluster" to reach appropriate judgments regarding benefit and risk in any one of them, permitting the FDA to learn about hundreds of diseases rather than only 20. The illustrative "cluster" we offered was "Degenerative Neuromuscular Disorders Affecting Children," none of which were among the individual diseases listed by the FDA for consideration. In addition to FA, our proposed "cluster" included the muscular dystrophies, ataxia telangiectasia; spinal muscular atrophy; Charcot-Marie-Tooth disease; congenital myasthenia gravis; congenital myopathies, and severe pediatric onset forms of metabolic diseases of muscle such as mitochondrial myopathies. FARA's partner advocacy organizations representing the other diseases in this illustrative "cluster" (Muscular Dystrophy Association, Parent Project Muscular Dystrophy, National Organization for Rare Disorders, and the Ataxia Telangiectasia Children's Project) joined us in approving and signing the recommendation in the public comments below and we submitted the comments on November 1, 2012.

Docket No. FDA-2012-N-0967
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
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via electronic submission

These public comments are submitted to the docket number above in response to the Food and Drug Administration (FDA) notice of public meeting and request for comments dated September 14, 2012. These comments are endorsed by the undersigned and are offered respectfully for your consideration as you implement the FDA's patient-focused drug development initiative.

As stated in the public notice, the recent reauthorization of the Prescription Drug User Fee Act (PDUFA) includes performance goals and procedures that represent FDA's commitments during FY 2013-2017, and Section X of these commitments relates to enhancing benefit-risk assessment in regulatory decision making. The public notice also makes clear that a key part of regulatory decision making is establishing the context in which the particular decision is made -- a context that must include a thorough understanding of the severity of the treated condition and the adequacy of the existing treatment options.

We applaud the FDA's undertaking of these commitments and your prompt initiation of a process for obtaining patient perspectives on disease severity and unmet medical needs, including nomination of a preliminary set of disease areas that could benefit from a more systematic and expansive approach to obtaining such patient perspectives. We would also like to commend the FDA for acknowledging publicly that, "Though several programs exist to facilitate patient representation, there are currently few venues in which the patient perspective is discussed outside of a specific product's marketing application review." We wholeheartedly agree that it is terribly important that we work together to ensure that the patient perspective is taken fully into account at every regulatory stage of therapy development.

The FDA's notice invites public comments on the preliminary list of disease areas and requests that those who propose additional disease areas for consideration describe how they applied the criteria identified by the FDA. We would like, first, to offer an overarching suggestion we believe would enhance significantly the FDA's ability to accomplish the stated objectives of the patient-focused drug development initiative. Our suggestion is aimed directly and solely at the key targets the FDA has identified for the initiative.

Those key targets are made clear in the FDA's public notice -- a thorough understanding of the severity of the treated condition and the unmet medical needs so as to set the context of regulatory decision making in regards to benefit and risk. If the FDA's key targets in this initiative were, instead, a more thorough understanding of such factors as the genetics or pathology of particular diseases, a list of 20 specific diseases might seem sensible. However, given the clearly stated key targets of the initiative, we feel strongly that a far more effective approach would be to identify "disease areas" that involve clusters of diseases that have profiles that are identical or very close to identical in terms of disease severity and unmet medical needs. This approach would enable FDA personnel, in a single meeting with patients and advocates representing a number of disorders, to develop a thorough understanding of severity and unmet medical needs held in common by all in this "disease area" and to set the context for benefit-risk evaluation and decision making for each of them.

We would like to illustrate the potential strength of this approach by suggesting one such "disease area" in which all the disorders listed have profiles that are identical or very close to identical in terms of disease severity and unmet medical needs and the patients and advocates of those disorders are in agreement that such is the case. We would also like to describe how this "disease area" meets all the criteria identified in the FDA public notice.

Illustrative Disease Area -- Degenerative Neuromuscular Disorders Affecting Children

The disorders in this disease area would include: 1) the muscular dystrophies such as Duchenne muscular dystrophy, Becker muscular dystrophy, myotonic muscular dystrophy, congenital muscular dystrophy, Emery-Dreifuss muscular dystrophy, fascioscapulohumeral muscular dystrophy, and limb girdle muscular dystrophy; 2)

Friedreich ataxia; 3) ataxia telangiectasia; 4) spinal muscular atrophy; 5) Charcot-Marie-Tooth disease; 6) congenital myasthenia gravis; 7) congenital myopathies, and 8) severe pediatric onset forms of metabolic diseases of muscle such as mitochondrial myopathies.

This disease area and all the disorders listed within it clearly and fully meet all the criteria identified in the FDA's public notice and they meet those criteria in identical or very close to identical ways:

- Disease areas that are chronic, symptomatic, or affect functioning and activities of daily living -- Each of these disorders is chronic, affecting these children severely throughout their disease-shortened lives. Each of these disorders involves multi-system symptoms with devastating impact on functioning and activities of daily living. Mobility, energy, strength and coordination are all severely limited, requiring full-time care givers for most basic activities.

- Disease areas that reflect a range of severity -- While the patients with each of these life-shortening disorders are very severely affected, the individual patients with each of them experience a range of severity in such factors as age of onset of symptoms, rate of progression, age at which full-time assistance is needed for activities of daily living, and age at death.

- Disease areas for which aspects of the disease are not formally captured in clinical trials -- Patients with each of these disorders experience multiple debilitating aspects not formally captured in clinical trials. For example, as a result of their conditions, they experience pain, depression, decreased confidence and self esteem, isolation, diminished ability to communicate, inability to perform many of the basic activities of daily living and care for themselves, as well as tremendous impact on their families. Furthermore, many of these young patients suffer life-threatening cardiomyopathies for which there are no widely accepted clinical care guidelines or clinical trial end points that satisfactorily reflect therapeutic efficacy. Finally, most clinicians believe that we will need to treat presymptomatic patients with these conditions because so much of the biological damage is done by the time symptoms manifest. However, to date, clinical end points and biomarkers have been inadequate to support the conduct of clinical trials in presymptomatic patients.

- Disease areas that have a severe impact on identifiable subpopulations (such as children or the elderly) -- each of the disorders listed affect children, severely impact their quality of life and greatly reduce the length of their lives.

- Disease areas that represent a broad range in terms of size of the affected population -- Each of the disorders listed is rare, affecting a range from a few thousand to tens of thousands of American patients at any given time.

- Disease areas for which there are currently no therapies or very few therapies, or the available therapies do not directly affect how a patient feels, functions, or

survives -- None of the disorders listed in this disease area have any approved treatment at all.

We believe that, in the disorders listed in this particular illustrative "disease area," the key factors of severity of disease and impact on quality of life as well as unmet medical needs are so close to identical that the stated objectives of the public meetings to be scheduled over the next five years could be accomplished for this whole set of disorders in a single meeting. Further, we believe that other "disease areas" could be readily defined so that, without adding to the number of meetings, the FDA's patient-focused drug development initiative could be extremely effective in setting the benefit-risk decision-making context for far more than 20 specific diseases.

We would welcome the opportunity to work closely with you on this approach. Again, we applaud and thank you for your active and energetic implementation of the commitments you have undertaken under the recently enacted Food and Drug Administration Safety and Innovation Act.

Signed:

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