ACT-AD
Accelerate Cure/Treatments for Alzheimer's Disease

February 10, 2015

The Honorable Fred Upton
Chairman
U.S. House of Representatives
Committee on Energy and Commerce
2368 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Representative DeGette,

The coalition to Accelerate Cure/Treatments for Alzheimer's Disease (ACT-AD) is comprised of more than 50 national organizations representing patients, caregivers, researchers, health professionals, and other health advocates. For the past ten years we have supported efforts to expedite the development, review, and approval of transformational therapies for Alzheimer's disease (AD). Thank you for the opportunity to provide feedback on the 21st Century Cures discussion draft released on January 27, 2015. We applaud your interest in accelerating the development of treatments, particularly for diseases with high unmet need. We recognize that the impetus for this legislation is a common frustration caused by delayed patient access to new interventions. There is no area where this frustration has been felt more deeply than among those endeavoring to find more effective treatments for people suffering with Alzheimer's disease.

We appreciated the chance to submit comments to you when this process began in 2014, reflecting areas specific to Alzheimer's disease where legislative action could be beneficial. Since then we have had productive discussions with committee staff on various aspects of the drug development process and their relationship to Alzheimer's disease treatment. There are some provisions in the discussion draft that we would like to highlight and others we would suggest revising.

TITLE I- PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADRESSING UNMET NEEDS

Subtitle A- Patient-Focused Drug Development

During stakeholder discussion convened by FDA before the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA V), we supported the concept of creating a series of meetings that would bring patient and caregiver voices as early as possible into the drug development process. We were pleased that these meetings were included as part of the final PDUFA V agreement and that the patient-focused drug development (PFDD) meetings held to date covered aspects of disease that are most important to those living with diseases like Narcolepsy, Fibromyalgia and Lung Cancer. These meetings were largely driven by the FDA and patient groups and resulted in valuable publicly-available resources written in the voice of patients to help inform new endpoint

development, outcome measure selection in clinical trials, and benefit/risk decision making by regulators.

There is a desire by some to shift away from the PFDD meetings and instead add more scientific rigor to these discussions through the development of methodologies to guide structured interactions with patients and their caregivers. While there may be value in making the process more data driven, it should not be at the expense of experiences learned from interaction reflecting actual disease burden. Subtitle A would be improved by continuing PFDD meetings when warranted.

A parallel may be found with the public comment process, which does not restrict who may provide feedback based on a methodology or level of expertise of the commenter. Agencies gather information through unstructured processes and informal conversations with people and organizations interested in the issues. The current PFDD meetings allow for both structured and unstructured interactions, and Subtitle A should permit that process to continue even after a methodology is developed.

Section 1001 under Subtitle A currently only involves patients, caregivers, and patient advocacy groups as agents for collecting "patient experience data" and does not specifically list them as entities that could lead the development of methodologies behind the "patient experience data" collection or suggest research concepts to the Secretary where "patient experience data" would be useful. We would recommend adding the definition of an "entity" under subsection (y) to include patients, caregivers, and patient advocacy groups, members of the scientific and medical research communities.

Subtitle B-Surrogate Endpoint Qualification and Utilization

FDA established a process several years ago through which drug development tools like biomarkers, outcome assessments and other endpoints could be qualified for a specific use and then incorporated into clinical trials. Through this process a company, group of companies or other organization could opt to work with regulators in a collaborative fashion to reduce the cost of developing these tools individually and produce a tool that once qualified became publicly available. Even with the qualification process in place, there is still the ability for a company, group of companies or other organization to talk directly with the FDA's medical product review divisions on the use of unqualified biomarkers and unqualified endpoints in specific clinical trials. FDA frequently approves the use of unqualified biomarkers and endpoints in trials and unqualified tools served as the basis of many drug approvals.

The process of qualification takes time. The process is driven by the slow pace of science and often delayed by a lack of data. The lengthy timeline for qualification has been particularly challenging in diseases where there is a paucity of biomarkers and other valid endpoints. Sections 1021-1024 of Subtitle B are intended to address the length of time it takes to qualify surrogate endpoints and allow FDA to enter into public-private partnerships (PPPs) to qualify surrogate endpoints. These sections are troubling for several reasons.

First, the rigid guidance parameters in Section 1021 requiring pre-determined evidentiary standards for what constitutes a surrogate endpoint could potentially impact FDA's flexibility to determine the validity and use of unqualified surrogate endpoints. Second, the short timeframe provided to FDA for issuing this guidance is not reasonable to allow for meaningful consultation with patients, industry, providers, and researchers. This consultation would be essential to

ensuring that proposed standards meet the needs of all stakeholders. Third, there are no resources provided to assist FDA in implementing these changes. As written, it would not be possible for FDA to positively improve the qualification process in the aggressive timeframe set forth by this bill. Lastly, FDA and other external stakeholders already participate in public-private partnerships (PPPs) on biomarkers and endpoint development, validation and qualification. Three examples of PPPs already doing this work to some degree in the area of Alzheimer's disease are the Critical Path Institute's Coalition Against Major Disease (CAMD), the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the Accelerating Medicine's Partnership for Alzheimer's Disease (AMP-AD). Caution should be taken in creating additional PPPs with the goal of endpoint development and qualification so as not to supplant successful efforts like these.

A lack of predictable timeline and the length of time it takes to successfully complete qualification are very valid concerns. Such uncertainty raises questions among drug developers about the value of investing in qualification, particularly if the impression is that endpoints may not be qualified in time for incorporation into their drug development programs. These are process issues that need to be discussed in the context of the personnel and resources necessary to meet set timeframes and this discussion should not just be limited to surrogate endpoints, but also include other endpoints. We recommend removing Section 1021-1024 from the next iteration of the 21st Century Cures bill. Instead, we suggest that improvements to the qualification process and necessary resources should be addressed as part of PDUFA VI negotiations set to begin this summer.

Subtitle K-Cures Acceleration Network

In 2010, we and our colleagues in the advocacy community called on Congress to create the National Center for Advancing Translational Sciences (NCATS) Cures Acceleration Network at NIH because of its unique ability to aid in the translation of basic scientific discoveries into treatments for diseases like Alzheimer's. One approach taken by NCATS is drug repurposing under its "Discovering New Therapeutic Uses for Existing Molecules" program. Repurposing has had very promising results in treating difficult diseases including HIV/AIDS and certain cancers. We hope for similar success in repurposing drugs for the treatment of Alzheimer's disease.

One NCATS project was started in 2013 to use a repurposed drug to block activity of a certain Alzheimer's-linked protein in mice. The results of this study have not been released and the effects of this treatment in humans are not yet known. There have not been additional repurposing projects for Alzheimer's disease funded by NCATS since 2013.

Section 1202 under Subtitle K would authorize additional funding in fiscal years 2016-2018 for drug repurposing. If authorized and appropriated, we feel this additional funding may enable more opportunities for the use of therapeutic repurposing for AD.

TITLE II- BUILDING THE FOUNDATION FOR 21ST CENTURY MEDICINE, INCLUDING HELPING YOUNG SCIENTISTS

Subtitle G-Utilizing Real-World Evidence

Section 2101 of Subtitle G is intended to establish a program at FDA under which evidence from observational studies or registries could be utilized to support approval of a new use for a drug or to satisfy post-approval study requirements. This section is concerning because there is not agreement on the best methods for the collection of real-world evidence for use in supporting regulatory decision-making.

Rather than requiring FDA to issue guidance and establish a program predicated on a lack of consensus, Section 2101 should be modified to start as a pilot program laying the foundation for future guidance on the application of real-world data in approval decisions. One could see potential use for a well-designed, real-world evidence program in the area of Alzheimer's disease and many other diseases in the future.

TITLE IV- ACCELERATING THE DISCOVERY, DEVELOPMENT, AND DELIVERY CYCLE AND CONTINUING 21ST CENTURY INNOVATION AT NIH, FDA, CDC, AND CMS

Subtitle E-FDA Hiring, Travel, and Training

For the FDA to be effective, the agency must be populated with highly capable staff that is constantly up to date on new scientific knowledge and developments. Right now, Section 4101 of Subtitle E is a placeholder for provisions related to FDA hiring, travel, and training. In the next iteration of the bill, Section 4101 should grant FDA direct hiring authority. Currently, it can take eight to twelve months for the FDA to hire a professional for which they do not already have direct hiring authority. During that time, they often lose talented individuals to other employers. This hiring process must be streamlined to better serve those who depend on the FDA.

In recent years budgetary limitations and sequestration have led to restrictions on the number of outside conferences FDA employees can attend and the number of people FDA is able to send to each conference. Scientific conferences and annual meetings are venues where emerging discoveries and the latest breakthroughs are presented. They also provide the opportunity for regulators to interact with the medical research community. This is particularly important for Alzheimer's disease because the science is evolving rapidly. Section 4101 of Subtitle E should lift any policies in place limiting FDA's participation in meetings and conference.

Chairman Upton and Congresswoman DeGette, thank you for your leadership on behalf of patients and your careful consideration of the views expressed above. We hope the committee will contemplate the suggested modifications when it releases its next draft and moves forward with legislative action on 21st Century Cures. Please feel free to contact us at (202) 293-2856 with any questions.

Sincerely,

Daniel Perry
Chairman

Cynthia Bens
Vice President, Public Policy