Remarks on Prescription Drug User Fee Act (PDUFA)
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Thank you Patrick Frey and Theresa Mullin for the invitation to join today's panel of patient representatives, and for the opportunity to offer comments on the proposal to reauthorize the latest version of the Prescription Drug User Fee Act.

On behalf of the Alliance for Aging Research I extend my sincerely appreciation to the FDA employees here today for the challenging and important jobs you do each day. The impact of your work is felt by millions of older Americans.

The Alliance for Aging Research is a private, not-for-profit organization now in its 25th year working for public policies to promote medical and scientific research in human aging and chronic disease so that we might all realize better health and quality of life as we grow older.

We are all familiar by now with the unprecedented and consequential Greying of Nations, the aging of populations throughout the world. In January 2011 the first of some 77 million American Baby Boomers began turning age 65. For many years our population has been adding every day approximately 6,000 new seniors to America's Medicare rolls. Beginning this year we go from 6,000 to 10,000 people turning celebrating a 65th birthday each and every day, and we will stay at this higher level for the next 18 years.

As people grow older many will experience increasing risks of many age-related chronic ailments: coronary artery disease, stroke, heart failure, type II Diabetes, bone and joint disabilities, cancers, vision loss, and neurological diseases such as Alzheimer's and Parkinson's to name a few.

Unless we discover and put to into use more effective means to prevent, postpone or reduce the impact of diseases of aging, the U.S. faces what we call a Silver Tsunami of age-related infirmities and disabilities that carry enormous social, cultural and economic costs.

At the Alliance for Aging Research we view the federal agencies that monitor public health, and invest in medical research and regulatory science, to be America's most important defenses against the coming Silver Tsunami.

FDA's processes for evaluating and approving new and innovative therapies for chronic diseases are critical to allow discoveries from basic science to become medical breakthroughs. We recognize that the FDA can only realize this vital role if the proper resources and policies are in place. The current proposal under consideration for PDUFA V is a positive step toward enabling the Agency to conduct more patient-focused, scientifically sound, and timely reviews.

My organization has been a regular participant in the monthly stakeholder engagement process as are others here today. While patient organizations were not at the same negotiating table with industry and the FDA, we feel the Agency took seriously the directive from Congress in FDAAA to consult with members of the patient community on their views regarding the user fee program. From the time the Agency held its first public meeting in April of 2010, concerns presented by patient's advocates were received by the Agency staff and appropriately included in the enhancement proposals put forth by FDA in the negotiations. These issues included:

- accelerating drug development through greater focus on regulatory science;
- supporting the development of innovative clinical trial designs;
- reevaluating how the Agency assesses benefits and risks of therapies and how it communicates benefit-risk information; and
- ensuring that REMs do not serve as a barrier to patient access.

For the past five years the Alliance for Aging Research has chaired a coalition of more than 50 national non-profit groups focused regulatory and scientific issues related to

on one disease of aging in particular – Alzheimer's disease. This coalition is called ACT-AD, which stands for Accelerate Cure/Treatments for Alzheimer's Disease.

Our coalition is made up of organizations representing the interests of Alzheimer's patients and their families, seniors, consumers, women's health champions, caregivers, health care providers and researchers. Much of our coalition's work on Alzheimer's focuses on:

- how to select patients for clinical trials for treatments effective at earlier stages of the disease,
- how to appropriately balance the potential benefits of new therapies against the ever-present level of risk of harm from the treatment;
- how to approach the generalizability of results in a specific trial population to the larger patient population;
- and how to measure the clinical benefit of treatments for patients at the earliest discernable stages of the disease.

ACT-AD has identified the selection of endpoints in clinical trials as a critically important part of successful drug development. With respect to endpoints that capture patient reported outcomes, reliability has been a problem which results in high failure rates for these types of trials. We are encouraged that FDA would like to devote resources under PDUFA V to both increase their capacity to address trials that include PROs and engage in public consultation on qualifying PROs.

We are pleased to see that FDA will utilize PDUFA V fees to increase its capacity to advance the use of biomarkers and pharmacogenomics in drug development. This is becoming more critical as evidence accumulates supporting the use of biomarkers in order to decrease drug development time. FDA likely will continue seeing an increase in applications including the use of biomarkers in Alzheimer's clinical trials.

We support FDA's commitment in PDUFA V to developing a framework for enhancing risk-benefit decision-making that systematically and openly gathers input from patients. CDER and CBER are committed in this agreement to a total 20 meetings over

five years to receive input from patients and their representatives on disease severity and unmet medical needs. These meetings – many focused on individual diseases – will be extremely valuable to the patient community. However we regret that the original enhancements proposal of half again as many meetings – 30 over five years – was not agreed to in the negotiations.

There are many diseases and patient populations for which risk-benefit trade-offs are critical to helping chronic and terminally ill patients achieve the outcomes they want from a treatment, be it improved quality of life, increased length healthy life or other objectives. If there is no flexibility or available funds to consider additional meetings under PDUFA V, we hope the FDA will consider committing staff and resources to scale up to a point where the Agency can consider additional meetings either supported by appropriated funds or obtained in the next reauthorization round.

It is also not entirely clear to us how the FDA will analyze the proceedings from these meetings and translate them into operative procedures and decision making. The initial enhancement proposal detailed how this information would be utilized, including for new or updated guidance. We are not certain this is still the Agency's intent. Therefore we urge the FDA to clarify its plans for incorporating what it learns from these audiences into new or updated official guidance.

For those diseases where there is an established Patient Representative program, such as cancer and Alzheimer's disease, there has been an avenue for patient voices to be heard in the medical product development process. We are pleased that PDUFAV supports the increased utilization of the Patient Representative program. We strongly feel that early and frequent patient consultations will lead to more balanced evaluation of new products, particularly for FDA staff that do not regularly interact with or treat patients with a particular disease or condition.

We further hope that tighter conflicts of interest rules legislated through FDAAA do not act as a barrier to FDA's access to needed expertise either from patients or medical experts when the Agency needs its best advice for making critical decisions.

We believe that policy changes made during PDUFA IV, such as those concerning REMS for new drugs, could help regulators and clinicians to acquire more data on the known and unknown risks that drugs present, and allow FDA and industry to manage those risks appropriately in the post-market space. Unfortunately many conversations about managing risks are happening too late in the review process and are responsible for delays in drugs coming to market. We are pleased with reforms in PDUFA V to improve REMs by starting safety conversations earlier. These changes will better help sponsors and the Agency to identify safety issues in trials and make necessary adjustments.

In another capacity I serve as a founding board member of the Alliance for a Stronger FDA. The Alliance for a Stronger FDA has taken on the role of educating Congress on how unfunded mandates have put a heavy burden on the agency in recent years. In light of the difficult appropriations outlook for the foreseeable future, we understand that there is a need to remain true to what is in the PDUFA V agreement so that FDA can maintain a sound financial basis.

The merits of the current agreement certainly warrant widespread support. However, we hope that FDA has plans in place and will continue to work with patients and other stakeholders to address those issues put forward in the initial enhancements proposals but not retained in the current agreement. In particular we would like to see further effort and resources devoted to ensuring the quality of adaptive trials designs and resources devoted to informed optimal dose selection.

Thank you for the opportunity to share these comments on PDUFA V and the current reauthorization process. I welcome the opportunity to provide additional information supporting these comments and look forward to continuing to work with the Agency directly on initiatives that will help move needed treatments to patients and their families in a safe and effective manner.