March 15, 2013

Jennifer L. Watson
Senior Public Affairs Specialist
National Institute on Aging (NIA)
31 Center Drive
Room 5C27
Bethesda, MD 20892-2292

VIA ELECTRONIC DELIVERY

Dear Ms. Watson:

I am writing in response to **Request for Information: Increasing Enrollment in Alzheimer's Disease and Related Clinical Trials and Studies (NOT-AG-12-017)**.

Leaders Engaged on Alzheimer's Disease (LEAD) is a diverse and growing coalition of 57 member organizations including patient advocacy and voluntary health non-profits, philanthropies and foundations, trade and professional associations, academic research and clinical institutions, and biotechnology and pharmaceutical companies. LEAD works collaboratively to focus the nation's strategic attention on Alzheimer's disease and related disorders and to accelerate transformational progress in care and support, detection and diagnosis, and research leading to prevention, effective treatment and eventual cure. LEAD Coalition members stand ready to work with NIA and all other stakeholders to develop and implement actionable strategies that will increase and diversify enrollment in clinical trials, safeguard participants, strengthen efficacy, and translate evidence into meaningful benefits for individuals, families, and communities in the United States and around the world.

Alzheimer's disease clinical trial recruitment does not function in isolation; rather it is tied to broader questions and challenges. Development of a National Institutional Review Board for Neurodegenerative Disease (NIRB-ND) is well underway but additional resources are necessary for a 2013 launch, and then to sustain and build the effort. Similarly, the Clinical Data Interchange Standards Consortium (CDISC) provides a promising pathway but one not yet fully realized. There is sore need for expanded data sharing in the pre-competitive, "failed" trials, and dormant drug spaces. Simultaneously, we need to expedite development and utilization of effective look-back informed consent options, more combination therapy trials, and a soul-searching reexamination of how functional access to clinical trial enrollment can be democratized. Recently, the LEAD Coalition submitted recommendations to Secretary Sebelius for ways to strengthen the National Plan to Address Alzheimer's Disease. Among the recommendations was a call to develop standardized informed consent to allow participants in clinical trials to

authorize their de-identified data be used for research purposes broader than a single study in order to advance understanding, treatment and prevention of Alzheimer's disease. LEAD recommended pooling of individual de-identified data into larger Alzheimer's disease databases – globally available to qualified researchers – to allow data mining and to increase statistical significance, provide information on the natural history of Alzheimer's disease, identify promising biomarkers and response or non-response to treatment.

Many of the potential reforms intended to improve the representative diversity of clinical trial participants may also address more generalizable challenges to clinical trial recruitment, participation, retention, and completion. For example, we all could stand to be more thoughtful about the painful Tuskegee legacy by not using it as an excuse for a lack of diversity but rather as an impetus to invest additional resources necessary to reach, build trust with, and demonstrate genuine collaborative engagement with under-represented communities. Some communities may believe the lessons of Tuskegee have been learned and be quite welcoming of genuine access to promoting participation in clinical trials of pharmacological interventions. Other communities may be more welcoming of clinical trials focused on non-pharmacological interventions that also serve broader and more widely accepted health and social good goals such as fitness and nutrition interventions.

It is not enough for professionals to demand changes in attitudes toward the value of detection and diagnosis among the general population and communities of color in particular. These same attitudes must change among many medical professionals and public and private payers who all too frequently appear to downplay or fundamentally underappreciate the importance of detection and diagnosis due to the absence of effective disease modifying pharmacological interventions. Payers, medical professionals, patients and families (regardless of socio-economic status) would benefit from heightened recognition that more widespread, timely, and accurate detection and diagnosis would decrease stigma and encourage more people to utilize vital, proven interventions such as care planning, legal and financial planning, and social support services. Expanding detection and diagnosis also would expand the pool of people available to participate in clinical trials. The degree of success or failure for anything NIA and other stakeholders embark upon in the clinical trial space will be determined in no small measure by the degree of investment we make collaboratively to stigma reduction and confronting the pernicious myth that only the existence of disease-modifying pharmacological interventions warrant detection and diagnosis. The National Plan to Address Alzheimer's Disease devotes considerable attention to reducing stigma, increasing awareness, improving detection and diagnosis, and strengthening clinical practice; the recent LEAD Coalition recommendations to Secretary Sebelius offer extensive additional suggestions and are available in their entirely at http://www.leadcoalition.org/?wpfb_dl=98.

Access to both clinical care and trial sites is inadequate for many people who might otherwise be willing to participate in trials. Sometimes, this is an issue of geography, transportation, or personal economic circumstance. Other times, it may be an issue of the disease stage or whether a caregiver is available to accompany the potential trial participant. None of these challenges are overcome easily but will be remediated only when their identification ceases to be treated as a fait accompli and instead when systems are redesigned out of a collective recognition of necessity. Systemic overhaul offers the proverbial opportunity to make lemons into lemonade by engaging community-

wide collaboration in under-represented communities. Clinical trial recruitment done in sincere, committed partnership with organizations serving the needs of disenfranchised people (e.g. faith communities, public hospitals and clinics, social services organizations) likely will have greater trust and credibility leading to greater access and success in recruitment, enrollment, retention, and completion of study protocols. The complexities and challenges notwithstanding, Alzheimer's clinical trials should give strong consideration to expanding collaboration with voluntary health associations focused on other medical conditions which disproportionately impact underserved and under-represented communities, especially when such conditions have a high correlation with dementing disorders and potentially even a causal relationship (e.g. diabetes, hypertension).

Government, industry, and patient advocacy organizations should work together to develop a large-scale, open-source patient registry of subjects who can be approached for recruitment in prevention trials. One option worth pursuing would be a broader healthy aging registry, similar to the Framingham study for cardiovascular disease, to follow asymptomatic individuals and those with correlated diseases such as diabetes (the new European Medical Information Framework – Innovative Medicines Initiative consortium has a similar aim). Trials focused on identifying early stages of Alzheimer's disease should be based on development of quantitative clinical trial models designed for studies in early Alzheimer's disease.

Undoubtedly, NIA must and will utilize a highly diverse and dedicated advisory committee to evaluate all the recommendations solicited by this RFI with the goal of developing an implementable and financially feasible protocol with clear goals and structure for evaluation.

In isolation, none of these recommendations provide a panacea. Some, in fact, may not be worth pursuing and others simply may fail to garner the necessary resources of funding, know-how, or commitment to be implemented effectively. Our best chance to identify the best ideas also happens to be our best chance to produce effective implementation and the desired outcomes: genuine, candid, persistent, inclusive collaboration. With that in mind, on behalf of the LEAD Coalition, I commend NIA for issuing this Request For Information and pledge to collaborate with NIA and all stakeholders to develop and implement actionable strategies that will increase and diversify enrollment in clinical trials, safeguard participants, strengthen efficacy, and translate evidence into meaningful benefits for individuals, families, and communities in the United States and around the world.

Respectfully,

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