August 15, 2024

Chair Cathy McMorris Rodgers
House Energy and Commerce Committee

Chairman Robert Aderholt
House Appropriations Subcommittee on Labor, Health and Human Services, and Education

by electronic delivery: NIHReform@mail.house.gov

Dear Chair McMorris Rodgers and Chairman Aderholt:

Thank you for the opportunity to comment on "**Reforming the National Institutes of Health Framework for Discussion."**

As the uniting voice of over 260 members and allied organizations serving people with dementia and their families, along with hundreds of researchers dedicated to furthering our understanding of the prevention, causes, and effective treatment of dementia, Leaders Engaged on Alzheimer's Disease (the LEAD Coalition),[i] is grateful for the Committees' steadfast support of research on Alzheimer's disease and related disorders (AD/ADRD). Your support has made the National Institutes of Health (NIH) and our American research enterprise the envy of the world. Your ongoing commitment to this research has improved health for Americans and bolstered American competitiveness globally.

It is essential that any organization as large, complex, and important as the NIH be reviewed periodically to ensure that its design and governance support optimal results, and that changes can be considered carefully in consultation with stakeholders to optimize effectiveness while mitigating any risks for potential unintended consequences. We offer questions and comments about the Framework in the spirit of helping to inform the important process you have begun, and we look forward to continued dialogue.

Among the most consequential structural changes for our community would be the reorganizations of the National Institute on Aging (NIA) and National Institute of Neurological Diseases and Stroke (NINDS). We are grateful for your recognition that dementia, which affects a third of older Americans, is a cancer-sized problem requiring bold and effective leadership with commensurate resources and authority. Therefore, we appreciate the potential benefits motivating you to create the National Institute on Dementia (NID) to parallel the National Cancer Institute and the important achievements it has catalyzed. Because the proverbial devil is in the

details, we are dedicated to ensuring that none of these details cause harm or limit scientific advances, particularly given the inextricable link between dementia and the science of aging. Dementia – including younger onset dementia – is a condition of aging, so it would be vital that the proposed NID maintain and expand NIA's existing biomedical, behavioral, and social science research portfolio, to develop interventions to extend human health span, address the needs of caregivers, and prevent disease onset with age. We offer a representative handful of comments and questions intended to contribute to a deliberative, collaborative, and constructive process to identify all relevant questions and solutions across the full range of NIH institutes and centers (ICs).

- We agree wholeheartedly that science should not be conducted in silos. NIH has a strong record of collaboration across relevant ICs. NIA and NINDS exemplify ensuring research silos do not exist, collaborating routinely, closely, and productively with each other and with nearly all other ICs. Over the past decade, wise and sustained investments by Congress have enabled NIA to grow and diversify its research portfolio. With support and partnership from NIA and NINDS, vital AD/ADRD research is carried out across 24 ICs. This collaboration across NIH is essential to engaging researchers from other disciplines in joining the AD/ADRD research community, lending their expertise in oncology, cardiology, pulmonology, psychiatry, and other fields to the risk factors and co-occurring conditions that influence the lived experience of dementia. In Fiscal Year 2023 alone, NIA partnered on 458 research projects led by sister ICs. We are deeply concerned that, without necessary additional details and clarification, the proposed reframing to a NID would create precisely the sort of siloing effect and destabilizing consequences that both Congress and the patient advocacy community are determined to prevent. **Would the NID absorb the AD/ADRD-relevant work of all other ICs, including biomedical, behavioral, and social science research, or would collaborative science funding across ICs be able to continue at current or even expanded levels?**

- The Framework would merge NINDS, the National Eye Institute, and the National Institute of Dental and Craniofacial Research, to create the new National Institute of Neuroscience and Brain Research (NINBR). Currently, NINDS is the primary home to research on several major forms of dementia including dementia with Lewy bodies (DLB), frontotemporal degeneration (FTD), and vascular dementia. Millions of Americans have one or more of these forms of dementia and millions of people with a primary diagnosis of Alzheimer's disease also have one or more of these so-called "related dementias." Additionally, NINDS is the primary home to research on epilepsy and stroke. Important gaps remain in understanding the correlation between these conditions and dementia and the potential for therapeutics at the intersections. **Would LBD, FTD, vascular dementia, and epilepsy research move to the NID or would it move to the new NINBR? If this research**

moved to the NID, what portions of the current NINDS research portfolio would move to the new NINBR?

- We appreciate the Framework's reference to "encouraging each IC to use a holistic life stage approach" and to "ensure that each IC is considering the whole individual and all populations across the lifespan." Currently, NIA and NINDS conduct and fund vital and highly productive lines of research regarding life-course health events that contribute to AD/ADRD later in life. Similarly, NIA and NINDS research supports investigation of health conditions that frequently co-occur with AD/ADRD and further compromise quality of life for people with AD/ADRD and their families. **Would research into health events and conditions that are not dementia, but which increase risk for dementia or exacerbate morbidity and mortality for people with dementia, stay at the NID or be relocated to other ICs?**

- Most people who develop dementia begin with a condition called Mild Cognitive Impairment (MCI). Although MCI is a debilitating precursor to dementia, by definition, MCI is not dementia. While many people who have MCI do go on to develop clinical dementia, other people with MCI never develop dementia, and some people with MCI return to normal cognitive function altogether. NIH-funded research has been critical in understanding MCI. **Would MCI research stay at the NID or be relocated to other ICs?**

- NIA and NINDS actively partner with the National Institute of Mental Health (NIMH) to foster research focusing on the assessment and treatment of behavioral and psychological symptoms (BPS) of dementia. BPS drive down quality of life for people with dementia and drive up both caregiver burden and health care utilization. BPS often is present but underrecognized in the MCI and early dementia stages of Alzheimer's disease. And while BPS most commonly are recognized as being associated with later stages of Alzheimer's disease and affecting morbidity and mortality, they often are among the first warning signs of FTD and LBD. **How would the Framework facilitate NID expanding its capacity to collaborate with the NIHM to foster urgently needed BPS of AD/ADRD research?**

- Currently, NIA (through the Division of Behavioral and Social Research and Division of Neuroscience) and NINDS conduct and fund a large number of research projects focused on reducing risks for (or preventing) later development of dementia. For example, NIA and NINDS were essential to generating the necessary evidence to change clinical practice in terms of aggressively treating hypertension to reduce risk of vascular dementia, which also affects most people with Alzheimer's disease. Similarly, NIA and NINDS are driving essential research about interventions relating to nutrition, exercise, social isolation/depression, hearing impairment, and other known AD/ADRD risk factors. But, again, these conditions are not dementia. **Would**

AD/ADRD and dementia risk-reduction or prevention research stay at the NID or be relocated to other ICs?

- Currently, NIA conducts and funds over 100 research trials and many more projects focused on better equipping and supporting caregivers of people with MCI or dementia; NINDS also conducts and funds extensive and critically important research relevant to the differentiated challenges of caregiving in the context of the related dementias. These caregivers do not have dementia, but their ability to give care well and in a sustainable manner directly affects quality of life for people with MCI or dementia, the degree to which publicly funded Older Americans Act services and nursing home care may be required, and – of course – the physical and mental health, wellbeing, and economic participation of these caregivers. **Would MCI and dementia caregiving research stay at the NID or be relocated to other ICs?**

- Currently, NIA and NINDS fund numerous multi-year grants. **When would ICs begin and conclude the reorganization process? How would management and oversight of multi-year grants be transferred between ICs? Would there be a phase-in period and, if so, of what duration?**

- While we appreciate and share the Framework's commitment "to continue to bolster and support early-career investigators," we are troubled by the proposal to limit primary investigators (PIs) to a maximum of "three ongoing concurrent NIH engagements." Such a limit necessarily threatens innovation and collaboration, may inadvertently drive PIs to silo their research within a single IC, and potentially underutilizes many of the most productive scientists who have the experience to lead cutting-edge, large-scale, multi-institution, collaborative research while mentoring and training as many early-career investigators as possible. Additionally, we are concerned that specific types of infrastructure grants would suffer if those scientists who are leading innovative research were to be discouraged from leading training programs or center grants that are geared toward building the field rather than a specific line of science. We would encourage NIH to consider ways to engage PIs with several concurrent NIH grants to serve regularly on NIH study sections, contributing their skills and experience to NIH grant review committees. It is hard to offer alternatives without examples of a problem. **Do the Committees have examples of underperformance of grants in which a PI is managing four or more engagements? Would the Committees consider distinguishing between an investigator's lead role on a training award (F, K, and T grant mechanisms) and a research grant to avoid disincentivizing senior scientists from mentoring emerging and mid-career scientists?**

- We applaud the Framework highlighting the importance of ICs "considering distinctions and factors related to sex and age" and we would encourage having ICs report on similarly appropriate factors relating to race/ethnicity,

physical and intellectual/developmental disabilities, geography, and socio-economic status. Better understanding these and other demographic characteristics is vital to meeting the needs of all people at risk for or living with dementia. NIA, NINDS, and other ICs have done important work to improve the representativeness of clinical study cohorts, but much more progress is necessary. Progress can be achieved best through robust public-private partnerships including various federal and state agencies, industry, research universities, foundations, patient advocacy organizations, and other non-profit entities. **Are there opportunities for the Appropriations subcommittee bill, which reflects the Framework, to provide necessary additional resources for NIH to continue as a catalyst for such progress through public-private partnerships?**

Another structural change in the Framework that concerns us is the realignment the Advanced Research Projects Agency for Health (ARPA-H), which was launched less than three years ago with bipartisan support. We believe that the ARPA-H concept is strong, and that it needs to be given at least a few more years to prove its effectiveness. Any performance shortcomings should be dealt with through oversight rather than elimination, budget reductions, or absorption.

Finally, we offer suggestions regarding term limits on IC directors. Just as in the private sector, those in NIH leadership should have performance reviews. Periodic performance reviews of IC directors by the NIH director are critical, as are opportunities for the NIH director to consider opportunities for new leadership of ICs. If these are not happening today, we encourage the Committees to use oversight authority to ensure that changes. We are troubled by mandatory term limits that could destabilize strong ICs by removing effective leadership based on a calendar rather than performance. This would harm NIH's mission, Americans health, America's economy and position of global leadership.

Thanks to Congress making sustained and robust commitments, and NIA's and NINDS' strategic utilization of these resources during the current NIA and NINDS directors' service, we now have the first disease modifying medicines available to clinicians and people with early Alzheimer's disease. More than 100 additional therapies for Alzheimer's, LBD, FTD, and vascular dementia are in clinical trials. We are entering an era of advanced diagnostics, clinical and non-clinical care interventions (including the recently launched CMS GUIDE Model, which is based on evidence generated with NIA funding), and proven strategies – such as aggressive management of hypertension – to reduce risk of developing dementia. Through the experienced leadership of these NIA and NINDS directors, NIH is making remarkable progress against all six goals of the National Alzheimer's Project Act's national plan. It would be deeply unfortunate to sacrifice this valuable and high-achieving leadership in favor of artificial term limits.

Congress has been bold in providing the NIH with resources to diversify the science, take more ambitious risks, and deliver more tangible health benefits at a faster pace.

Patients, their caregivers, and those of us who have dedicated our lives to ending the scourge of dementia are forever grateful.

We share your urgency and your resolve to get NIH modernization right the first time, not through a process of trial and error. The fastest path to the right modernization is through a careful, inclusive, iterative process of dialogue with experts followed by a thoughtful, bipartisan, bicameral legislative process.

Thank you for considering our views and for your commitment to overcoming Alzheimer's disease and other forms of dementia. For any questions or additional information about these or other policy issues, please contact me at your convenience.

Sincerely,

Ian N. Kremer, Esq.
Executive Director

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[i] http://www.leadcoalition.org Leaders Engaged on Alzheimer's Disease (the LEAD Coalition) is a diverse national coalition of member and allied organizations including patient advocacy and voluntary health non-profits, philanthropies and foundations, trade and professional associations, academic research and clinical institutions, and home and residential care providers, large health systems, and biotechnology and pharmaceutical companies. The LEAD Coalition works collaboratively to focus the nation's strategic attention on dementia in all its causes -- including Alzheimer's disease, vascular disease, Lewy body dementia, and frontotemporal degeneration -- and to accelerate transformational progress in detection and diagnosis, care and support, and research leading to prevention, effective treatment, and eventual cure. One or more participants may have a financial interest in the subjects addressed.