



The Honorable Diana DeGette
House of Representatives
2111 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Fred Upton
House of Representatives
2183 Rayburn House Office Building
Washington, D.C. 20515

December 30, 2021

Dear Representatives DeGette and Upton:

On behalf of the Alzheimer's Association and the Alzheimer's Impact Movement (AIM), including our nationwide network of advocates, thank you for your continued leadership on issues and legislation important to Americans living with Alzheimer's and other dementia, and their caregivers. We appreciate the opportunity to provide input on the bipartisan 21st Century Cures 2.0 updated text, released on November 16, 2021, which aims to further improve the way our nation delivers new life-saving treatments to the people that need them. Our comments to the updated text are below, but most notably we urge you to include the bipartisan ENACT Act (H.R. 3085/S. 1548) in the final legislation, which would increase the participation of underrepresented populations in Alzheimer's and other dementia clinical trials.

Section 203: Increasing Diversity in Clinical Trials

The Alzheimer's Association and AIM strongly support the inclusion of this section in the bill, which among other priorities, requires the Department of Health and Human Services (HHS) to conduct a clinical trial public awareness campaign, particularly in underrepresented communities, and establish a task force to make Clinicaltrials.gov more user- and patient-friendly. As noted in our previous comments, we again urge the inclusion of the bipartisan Equity in Neuroscience and Alzheimer's Clinical Trials (ENACT) Act (H.R. 3085/S. 1548), which would increase the participation of underrepresented populations in Alzheimer's and other dementia clinical trials by expanding education and outreach to these populations, encouraging the diversity of clinical trial staff, and reducing participation burden in clinical trials, among other priorities. We are grateful that this legislation was discussed by bill sponsor Rep. Lisa Blunt Rochester and National Institute on Aging (NIA) Director Dr. Richard Hodes at the House Energy and Commerce Health Subcommittee July 29 hearing on "The Path Forward: Advancing Treatments and Cures for Neurodegenerative Diseases."

In addition to the growing bipartisan support on Capitol Hill, the ENACT Act is also supported by the American Academy of Neurology, Black Nurses Rock, National Asian Pacific Center on Aging, National Caucus and Center on Black Aging, Inc., National Hispanic Council on Aging, National Hispanic Medical Association, National Indian Council on Aging, SAGE (Services & Advocacy for LGBT Elders) and UsAgainstAlzheimer's.

Alzheimer's and other dementia disproportionately affect older Black and Hispanic Americans compared to older Whites. Black Americans are about twice as likely to develop Alzheimer's and Hispanic Americans are about one and a half times more likely to develop the disease. However, much of the Alzheimer's research to date has not included sufficient numbers of Blacks, Hispanics, Asian Americans/Pacific Islanders and Native Americans to be representative of the U.S. population. The underrepresentation of these populations not only hinders the ability of researchers to understand these health disparities, it also restricts their knowledge of how an approved therapy or diagnostic may affect the population most likely to need the treatment. There is therefore an urgent need for current and future research to include increased numbers of Blacks, Hispanics, Asian Americans/Pacific Islanders, and Native Americans in clinical trials to ensure everyone benefits from advances in Alzheimer's science.

According to the [*Alzheimer's Association 2021 Alzheimer's Disease Facts and Figures special report*](#), nearly two-thirds of Black Americans (62%) believe medical research is biased against people of color — a view shared by substantial numbers of Asian Americans (45%), Native Americans (40%), and Hispanic Americans (36%) as well. In fact, only half of Black Americans (53%) trust a future cure for Alzheimer's will be shared equally regardless of race, color or ethnicity. This underscores the need to build and restore trust in underrepresented communities. Strong community relationships can serve to address misconceptions and mistrust about research because the community has a sense of ownership in the research initiative.

The NIA has established a good foundation of centers across the country that offer local resources, support, and opportunities to participate in Alzheimer's and other dementia research. NIA currently funds over 30 Alzheimer's Disease Research Centers (ADRCs) at major medical institutions across the United States and four Exploratory ADRCs that are designed to expand and diversify research and education opportunities to new areas of the country, new populations, and new areas of science and approaches to research. There are also eight Alzheimer's disease-focused Resource Centers for Minority Aging Research (RCMARs) which focus on enhancing the diversity of the aging research workforce by mentoring promising scientists from underrepresented groups for sustained careers in aging research. These ADRCs and RCMARs are well-positioned to increase education and outreach activities to underrepresented populations within their communities.

Specifically, the ENACT Act would provide funding for NIA to expand the number of ADRCs in areas with higher concentrations of underrepresented populations, such as through entities like Historically Black Colleges and Universities (HBCUs), Hispanic-Serving Institutions, Tribal Colleges and Universities (TCUs), or centers of excellence for other underrepresented populations. The ENACT Act would provide funding for ADRCs and RCMARs to increase

education and outreach to underrepresented communities and primary care physicians to let them know about current trial opportunities, the importance of participation, and the disparate impact of the disease on their populations. Importantly, ADRCs and RCMARs would use community-based engagement strategies in their outreach to underrepresented populations.

The ENACT Act would direct the NIA to enhance the diversity of principal investigators and study staff conducting Alzheimer's and other dementia clinical trials, so they are more representative of the populations they're trying to enroll. The bill directs the NIA to provide training to principal investigators from underrepresented populations on topics like clinical protocols and how to apply for grants, so they have the necessary expertise. NIA would also ensure senior researchers from underrepresented populations are included when making awards for leadership and excellence in Alzheimer's research.

The ENACT Act would reduce participation burden to make it easier for underrepresented populations to participate in Alzheimer's and other dementia clinical trials by providing incentives for locating Alzheimer's clinical trial sites in areas with high concentrations of underrepresented populations, as identified by data from the U.S. Census and Medicare claims data. The bill would direct NIA to ensure grantees use community-based engagement strategies in their outreach to underrepresented populations. The bill also encourages the use of remote health technology in communities, such as remote patient monitoring, to ease the burden of participation. Importantly, the bill would direct NIA to ensure grantees appropriately budget for outreach activities to underrepresented populations and include a description of outreach plans. NIA would also encourage grantees to engage with community-based organizations in efforts to increase clinical trial participation of underrepresented populations.

Finally, the ENACT Act would ensure inclusion and exclusion criteria are not unnecessarily restrictive so that older adults and individuals with a mild form of comorbid conditions are included, unless there is a strong clinical or scientific justification to exclude them. The bill also encourages the use of adaptive clinical trial design which could expand to include broader populations as the trial progresses through Phases I, II and III. This is important because Black and Hispanic Americans with Alzheimer's have higher rates of comorbid conditions, such as cardiovascular disease and diabetes, and these conditions should not unnecessarily disqualify these populations from participating in clinical trials. This is consistent with FDA's November 2020 guidance, "[Enhancing the Diversity of Clinical Trial Populations - Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry.](#)"

The Alzheimer's Association and AIM also appreciate the bill's inclusion of a provision to establish a task force to make Clinicaltrials.gov more user- and patient-friendly. The Alzheimer's Association has learned many lessons through [TrialMatch](#), a free, easy-to-use clinical studies matching service that connects individuals living with Alzheimer's disease, caregivers and healthy volunteers with current research studies. The continuously updated database of Alzheimer's and dementia clinical studies includes hundreds of pharmacological and non-pharmacological studies being conducted at sites across the country.

Currently Clinicaltrials.gov is only searchable by condition, but we again recommend adding additional filters and search criteria to make it easier for people to see which trials within those conditions may be relevant and open to them. For example, if a person currently searches for dementia clinical trials they must navigate the hundreds of results to see what type of trial could be right for them, such as a prevention trial or a trial for those with mild cognitive impairment, especially given their age and location. That can be cumbersome for many people and discourage them from taking the additional time to find a trial in which to participate. We also recommend efforts to make the information on Clinicaltrials.gov more easily understood for the layperson and less reliant on dense scientific terms. Finally, we reemphasize our recommendation that the information on Clinicaltrials.gov is required to be regularly updated. There should be accountability for trial sponsors to regularly update their data and report their results at the completion of a study. There are instances when a study has been marked as completed on Clinicaltrials.gov for years but there is no information on whether the trial was successful or if it failed, which is not conducive to learning or data sharing. It would also be helpful if Clinicaltrials.gov listed recruitment goals for underrepresented populations and updates on recruitment results to ensure accountability and adherence to the initial recruitment goals.

Section 201: Educational Programs and Training for Caregivers

The Alzheimer's Association and AIM strongly support the inclusion of this section in the bill, which would authorize \$25 million per year for three years to provide grants for educational programs and training for caregivers. We are encouraged to see the updated text include an expanded list of educational and training programs that would be accessible to caregivers, including caregiver psychosocial support - like cognitive-behavioral, supportive, and bereavement counseling - and caregiver health self-management.

The burden of living with Alzheimer's and other dementias extends to millions of Americans caring for those with the disease. In 2020, more than 11 million unpaid caregivers provided 15.3 billion hours of care valued at nearly \$257 billion. Alzheimer's caregivers also report higher levels of stress, depression and worse health outcomes when compared to others who are providing care to individuals without dementia. The physical and emotional impact of dementia caregiving is estimated to have resulted in \$11.8 billion in health care costs in the United States in 2018. The more caregivers understand Alzheimer's disease or other dementia, the better they can care for their loved ones and themselves.

The Alzheimer's Association and AIM also support the bipartisan Alzheimer's Caregiver Support Act (H.R. 1474/S. 56) which would provide caregivers and their families much needed support by providing grants to public and non-profit organizations to expand and improve training and support services. These services can empower caregivers to provide quality care for their loved ones while giving them tools to manage and improve their own health.

Section 204: Patient Experience Data

The Association and AIM appreciate the inclusion of this section, which would require the transparent and uniform collection and consideration of patient experience data as part of clinical trials. Patient experience data provides meaningful information that sponsors can use to improve upon the patient experience and incorporate that feedback into the trial benefits, providing value to participants. We recommend that the patient experience data is collected in a thoughtful, uniform way at consistent intervals, which does not unnecessarily add to the patient burden.

Section 305: Improving FDA-CMS Communication Regarding Transformative New Therapies

The Alzheimer's Association and AIM support improved and ongoing communication between the Food and Drug Administration (FDA) and the Centers for Medicare & Medicaid Services (CMS) with regard to breakthrough therapies, fast track products, and those eligible for accelerated approval.

Section 309: Post-Approval Study Requirements for Accelerated Approval

The Alzheimer's Association and AIM appreciate the expansion of acceptable real-world evidence (RWE) that can be used to fulfill post-approval study requirements to confirm the predicted clinical benefit of a therapy approved through the accelerated approval pathway. Specifically, the updated text includes evidence based on analyses of data in clinical care data repositories, patient registries, or other sources of RWE.

In November 2021, the Alzheimer's Association, American College of Radiology, American Society of Neuroradiology, Department of Biostatistics at Brown University School of Public Health and other clinical research experts announced the formation of the [National Treatment and Diagnostic Alzheimer's Registry](#). This new national registry will be an FDA-approved-agent agnostic approach to gathering routine clinical practice data and outcomes from providers caring for patients diagnosed with Alzheimer's disease who are taking an FDA-approved disease-modifying treatment. Using data like this as RWE in post-approval study requirements could help facilitate the completion of more timely phase IV studies, and could yield greater insight to the therapy's impact on underrepresented populations and those with comorbid conditions - populations which may be harder to enroll in placebo-controlled trials.

Section 403: Extending Medicare Telehealth Flexibilities

The Alzheimer's Association and AIM appreciate the inclusion of this section, which would permanently remove Medicare's geographic and originating site restrictions and allow HHS to permanently expand the types of health care providers that can offer telehealth services and the types of services that can be reimbursed under Medicare. Flexibilities such as these allow for greater access to telehealth technology, which is especially important to the delivery of home

health for people living with Alzheimer's and other dementia. Thirty-two percent of individuals using home health services have Alzheimer's or other dementia. The ability to receive care in the home decreases visits to unfamiliar places that may cause agitation in people with dementia and can ease some burden on caregivers. This increased flexibility can reduce interruptions in access to this kind of quality care.

Section 501: Advanced Research Projects Agency for Health

The Alzheimer's Association and AIM appreciate the expanded details in this provision to establish the Advanced Research Projects Agency for Health (ARPA-H). We are encouraged to see the updated text specifically call for coordination and non-duplication of research efforts among other federal agencies, and in particular, Alzheimer's research efforts at NIH. Transparency surrounding the activities at ARPA-H will be key, as will data sharing and the open resources development of data and information. The Association and AIM are also encouraged to see the bypass budget authority given to this new agency, which allows for direct communication with Congress on the needs associated with the agency's mission.

As for the importance of research coordination and non-duplication of efforts, there are still many important unfunded targets that NIH can and should fund, as outlined in the [NIH Professional Judgment Budget for Alzheimer's Disease and Related Dementias for Fiscal Year 2022](#). One example of this work is the Accelerating Medicines Partnership Alzheimer's Disease (AMP AD). The AMP AD program is a precompetitive partnership among government, industry, and nonprofit organizations that focuses on discovering novel, clinically relevant therapeutic targets and on developing biomarkers to help validate existing therapeutic targets. AMP AD 2.0 launched in February 2021, with the goal of enabling a precision medicine approach to the discovery of novel targets and biomarkers.

We believe ARPA-H can fill an important role in supplementing the current work at NIH by driving transformational innovation in research and speeding the application and implementation of cutting edge breakthroughs. Examples of Alzheimer's-related projects ARPA-H could undertake are accelerating the discovery of brain imaging, eye imaging and blood or fluid biomarkers capable of measuring synaptic loss, neuronal death, and glial inflammatory pathways, as a means of tracking responses to potential Alzheimer's disease therapies. There are also opportunities to explore the use of digital technologies for diagnosis, assessment and disease monitoring, such as novel ways to measure and evaluate cognition and function of an individual, develop tools focused on voice recognition and other passive ways to measure changes that may be reflective of brain diseases, such as Alzheimer's. In addition, opportunities that will enable the complex modeling of contributions to risk are additional areas ripe for investment; such opportunities may help develop risk assessments based on the individual - including genetic, biologic, and clinical measures. We also urge ARPA-H to focus on activities that include providing a validated algorithm for disease risk using all available data, like biomarkers, digital and emerging technology, to support a translatable resource for clinicians and drug discovery experts.

Conclusion

Again, we thank you for your work on this important bipartisan legislation, which would benefit all Americans, including those living with Alzheimer's and other dementia, and their caregivers. We look forward to working with you as the 21st Century Cures 2.0 effort moves through the legislative process and again specifically urge you to include the bipartisan ENACT Act (S. 1548/H.R. 3085) in the bill. If you have any questions about this or any other legislation, please contact Rachel Conant, Vice President of Federal Affairs, at rconant@alz-aim.org or at 202.638.7121.

Sincerely,

A handwritten signature in black ink, appearing to read 'REgge', with a long horizontal flourish extending to the right.

Robert Egge
Chief Public Policy Officer
Executive Vice President, Government Affairs
Alzheimer's Association