

August 14, 2026

Robert F. Kennedy, Jr.
Secretary
Department of Health and Human Services

Submitted via Regulations.gov

HHS Request for Comment on the Update to the National Plan To Address Alzheimer's Disease

Docket ID: HHS-ASPE-2026-0298-0001

Dear HHS Secretary Robert F. Kennedy, Jr.:

We write on behalf of Science Advancement and Outreach, a division of People for the Ethical Treatment of Animals—PETA entities have more than 10 million members and supporters globally, and PETA U.S. is the largest animal rights organization in the world—to make recommendations that will advance Alzheimer’s disease and Alzheimer’s disease-related dementias (AD/ADRD) research and the development of new interventions to prevent and treat dementia.

1. What opportunities or challenges exist in advancing research and development of interventions to prevent or treat AD/ADRD, including translating scientific progress into effective and scalable treatments and care?

In order for HHS to achieve its goal of “translating scientific progress into effective and scalable treatments and care” for Alzheimer’s disease, the National Plan must include language stating that HHS will no longer conduct or fund Alzheimer’s research that uses other animals and will instead prioritize research that uses only human-based approaches.

The clinical failure rate for Alzheimer’s disease drug candidates remains extraordinarily high, with estimates of 99.6% failure.^{1,2,3} One major reason for this is the inability of experiments on animals to recapitulate human AD biology. AD is a uniquely human condition, and other animals do not naturally acquire it. Transgenic mouse models, which are widely used in AD research, do not replicate the human disease and have not led to effective treatments.^{4,5} Attempts to model AD-like pathology in nonhuman primates, who are more closely related to humans, have reproduced only one or two of the symptoms observed in Alzheimer’s patients.^{6,7,8,9} Hallmarks of

AD—including extensive neuronal loss, tau pathology, progressive cognitive decline, and dementia—are rarely observed in animals used in AD experimentation.^{10,11,12}

These shortcomings are compounded by species-specific differences in gene expression and protein function,¹³ immune responses,¹⁴ neurodevelopment,¹⁵ neuroanatomy,¹⁶ age-related changes in hormone production,¹⁷ and neurodegeneration.^{18,19} As such, these differences make it impossible for another animal to accurately represent AD and prevents the translation of findings from experiments using other animals to human clinical use.

AD also varies substantially among individuals in its clinical presentation,^{20,21,22} age at onset and rate of progression,^{23,24,25} and genetic,^{26,27,28} environmental,^{29,30,31} and epigenetic^{32,33} influences. Consequently, research approaches that are based in human biology—particularly patient-derived systems that can capture individual variation—are needed to improve the identification and testing of potential treatments.

Human-based approaches are already being used to address these challenges. For example, researchers have developed 3D human cell models to study late-onset AD,³⁴ which accounts for the vast majority of cases; conducted proteomic analyses of cerebrospinal fluid from patients with AD to identify biomarkers that may be detectable decades before symptoms emerge;³⁵ engineered human organ-on-a-chip systems to evaluate the brain permeability of nanotherapeutics and support more personalized approaches to AD research and treatment;³⁶ and used patient neuroimaging data to develop and validate a computational model linking dementia symptoms to patterns of neurodegeneration in the brain in AD.³⁷

The National Plan should therefore include prioritizing the continued development and implementation of patient-derived and other human-based approaches for identifying and testing AD/ADRD interventions instead of the use of animals. This should include support for studies that use advanced human cell and tissue models, organoids, organ-on-a-chip systems, patient-derived induced pluripotent stem cell models, human biomarker and clinical datasets, and computational approaches that can integrate and analyze human data.

8. What workforce or infrastructure challenges most affect:

a. AD/ADRD research and intervention development

A significant challenge for researchers interested in using non-animal approaches to study Alzheimer’s disease is the lack of infrastructure, training, and institutional support available to them. Many federally funded researchers continue to receive training primarily in animal-based methods and have limited exposure to advanced non-animal technologies. Transitioning to these approaches can require new technical training, laboratory equipment, computational resources, and access to interdisciplinary expertise.

The National Plan should therefore include increased support for training and career development opportunities focused exclusively on non-animal methods for AD/ADRD

research and intervention development. Such support would enable both early-career scientists and established researchers to develop the skills needed to conduct human-relevant Alzheimer's research and accelerate the adoption of these approaches in the field. It would also help ensure that the U.S. Alzheimer's research community remains competitive with international advances in human-based research technologies.

There are a number of educational programs that HHS could refer to when developing and implementing training on non-animal methods for AD/ADRD research, such as the Summer School on Non-Animal Approaches³⁸ held by the European Commission Joint Research Centre and the Summer Immersion on Innovative Approaches in Science³⁹ held by the Physicians Committee for Responsible Medicine.

Resources for expanded training and infrastructure could be redirected from expenditures currently supporting AD/ADRD experiments on animals, which have not shown predictive value. In addition to supporting research training and infrastructure, these resources could be used to strengthen other components of the national AD/ADRD strategy, including risk reduction, early detection, patient care, and support for families and caregivers.

These recommendations can help HHS advance research strategies that accurately reflect human disease biology and have potential to improve treatment and quality of life for individuals affected by Alzheimer's disease and related dementias. Additional information on the recommendations outlined in this response is available in our policy roadmap, [Research Modernization NOW](#) (available at science.peta.org), which provides a comprehensive action plan for advancing biomedical research in the U.S. across multiple research areas, including [Alzheimer's disease](#). You may also reach us at info@scienceadvancement.org.

¹ Cummings JL, Morstorf T, Zhong K. Alzheimer's disease drug-development pipeline: few candidates, frequent failures. *Alzheimers Res Ther*. 2014;6(4):37. doi:10.1186/alzrt269

² Mullane K, Williams M. Preclinical models of Alzheimer's disease: relevance and translational validity. *Curr Protoc Pharmacol*. 2019;84(1):e57. doi:10.1002/cpph.57

³ Pistollato F, Ohayon EL, Lam A, et al. Alzheimer disease research in the 21st century: past and current failures, new perspectives and funding priorities. *Oncotarget*. 2016;7(26):38999-39016. doi:10.18632/oncotarget.9175

⁴ Franco R, Martínez-Pinilla E, Navarro G. Why have transgenic rodent models failed to successfully mimic Alzheimer's disease. How can we develop effective drugs without them?. *Expert Opin Drug Discov*. 2019;14(4):327-330. doi:10.1080/17460441.2019.1581169.

⁵ Pippin, J. J., Cavanaugh, S. E., & Pistollato, F. (2019). Animal research for Alzheimer disease: failures of science and ethics. In K. Herrmann & K. Jayne (Eds.), *Animal experimentation: Working towards a paradigm change* (pp. 480-516). Boston: Brill.

⁶ Ridley RM, Baker HF, Windle CP, Cummings RM. Very long term studies of the seeding of beta-amyloidosis in primates. *J Neural Transm (Vienna)*. 2006;113(9):1243-1251. doi:10.1007/s00702-005-0385-2

⁷ Wu J, Basha MR, Brock B, et al. Alzheimer's disease (AD)-like pathology in aged monkeys after infantile exposure to environmental metal lead (Pb): evidence for a developmental origin and environmental link for AD. *J Neurosci*. 2008;28(1):3-9. doi:10.1523/JNEUROSCI.4405-07.2008

⁸ Tuszyński MH, U HS, Amaral DG, Gage FH. Nerve growth factor infusion in the primate brain reduces lesion-induced cholinergic neuronal degeneration. *J Neurosci*. 1990;10(11):3604-3614. doi:10.1523/JNEUROSCI.10-11-03604.1990

⁹ Sato K, Oiwa R, Kumita W, et al. Generation of a nonhuman primate model of severe combined immunodeficiency using highly efficient genome editing. *Cell Stem Cell*. 2016;19(1):127-138. doi:10.1016/j.stem.2016.06.003

¹⁰ Walker LC, Jucker M. The exceptional vulnerability of humans to Alzheimer's disease. *Trends Mol Med*. 2017;23(6):534-545. doi:10.1016/j.molmed.2017.04.001

-
- ¹¹ Drummond E, Wisniewski T. Alzheimer's disease: experimental models and reality. *Acta Neuropathol.* 2017;133(2):155-175. doi:10.1007/s00401-016-1662-x
- ¹² Neha, Sodhi RK, Jaggi AS, Singh N. Animal models of dementia and cognitive dysfunction. *Life Sci.* 2014;109(2):73-86. doi:10.1016/j.lfs.2014.05.017
- ¹³ Bailey J. Monkey-based research on human disease: the implications of genetic differences. *Altern Lab Anim.* 2014;42(5):287-317. doi:10.1177/026119291404200504
- ¹⁴ Kametani Y, Shiina T, Suzuki R, Sasaki E, Habu S. Comparative immunity of antigen recognition, differentiation, and other functional molecules: similarities and differences among common marmosets, humans, and mice. *Exp Anim.* 2018;67(3):301-312. doi:10.1538/expanim.17-0150
- ¹⁵ Sakai T, Komaki Y, Hata J, et al. Elucidation of developmental patterns of marmoset corpus callosum through a comparative MRI in marmosets, chimpanzees, and humans. *Neurosci Res.* 2017;122:25-34. doi:10.1016/j.neures.2017.04.001
- ¹⁶ Charvet CJ, Palani A, Kabaria P, Takahashi E. Evolution of brain connections: integrating diffusion MR tractography with gene expression highlights increased corticocortical projections in primates. *Cereb Cortex.* 2019;29(12):5150-5165. doi:10.1093/cercor/bhz054
- ¹⁷ Abbott DH, Barnett DK, Colman RJ, Yamamoto ME, Schultz-Darken NJ. Aspects of common marmoset basic biology and life history important for biomedical research. *Comp Med.* 2003;53(4):339-350.
- ¹⁸ Chen X, Errangi B, Li L, et al. Brain aging in humans, chimpanzees (Pan troglodytes), and rhesus macaques (Macaca mulatta): magnetic resonance imaging studies of macro- and microstructural changes. *Neurobiol Aging.* 2013;34(10):2248-2260. doi:10.1016/j.neurobiolaging.2013.03.028
- ¹⁹ Sherwood CC, Gordon AD, Allen JS, et al. Aging of the cerebral cortex differs between humans and chimpanzees. *Proc Natl Acad Sci U S A.* 2011;108(32):13029-13034. doi:10.1073/pnas.1016709108
- ²⁰ Mega MS, Cummings JL, Fiorello T, Gornbein J. The spectrum of behavioral changes in Alzheimer's disease. *Neurology.* 1996;46(1):130-135. doi:10.1212/wnl.46.1.130
- ²¹ Nelson PT, Alafuzoff I, Bigio EH, et al. Correlation of Alzheimer disease neuropathologic changes with cognitive status: a review of the literature. *J Neuropathol Exp Neurol.* 2012;71(5):362-381. doi:10.1097/NEN.0b013e31825018f7
- ²² Keller JN. Age-related neuropathology, cognitive decline, and Alzheimer's disease. *Ageing Res Rev.* 2006;5(1):1-13. doi:10.1016/j.arr.2005.06.002
- ²³ Storandt M, Grant EA, Miller JP, Morris JC. Rates of progression in mild cognitive impairment and early Alzheimer's disease. *Neurology.* 2002;59(7):1034-1041. doi:10.1212/wnl.59.7.1034
- ²⁴ Jacobs D, Sano M, Marder K, et al. Age at onset of Alzheimer's disease: relation to pattern of cognitive dysfunction and rate of decline. *Neurology.* 1994;44(7):1215-1220. doi:10.1212/wnl.44.7.1215
- ²⁵ Koss E, Edland S, Fillenbaum G, et al. Clinical and neuropsychological differences between patients with earlier and later onset of Alzheimer's disease: a CERAD analysis, part XII. *Neurology.* 1996;46(1):136-141. doi:10.1212/wnl.46.1.136
- ²⁶ Van Cauwenberghe C, Van Broeckhoven C, Sleegers K. The genetic landscape of Alzheimer disease: clinical implications and perspectives. *Genet Med.* 2016;18(5):421-430. doi:10.1038/gim.2015.117
- ²⁷ Panpalli Ates M, Karaman Y, Guntekin S, Ergun MA. Analysis of genetics and risk factors of Alzheimer's Disease. *Neuroscience.* 2016;325:124-131. doi:10.1016/j.neuroscience.2016.03.051
- ²⁸ Naj AC, Schellenberg GD; Alzheimer's Disease Genetics Consortium (ADGC). Genomic variants, genes, and pathways of Alzheimer's disease: An overview. *Am J Med Genet B Neuropsychiatr Genet.* 2017;174(1):5-26. doi:10.1002/ajmg.b.32499
- ²⁹ Yegambaram M, Manivannan B, Beach TG, Halden RU. Role of environmental contaminants in the etiology of Alzheimer's disease: a review. *Curr Alzheimer Res.* 2015;12(2):116-146. doi:10.2174/1567205012666150204121719
- ³⁰ Alford S, Patel D, Perakakis N, Mantzoros CS. Obesity as a risk factor for Alzheimer's disease: weighing the evidence. *Obes Rev.* 2018;19(2):269-280. doi:10.1111/obr.12629
- ³¹ Pistollato F, Iglesias RC, Ruiz R, et al. Nutritional patterns associated with the maintenance of neurocognitive functions and the risk of dementia and Alzheimer's disease: a focus on human studies. *Pharmacol Res.* 2018;131:32-43. doi:10.1016/j.phrs.2018.03.012
- ³² Nativio R, Donahue G, Berson A, et al. Dysregulation of the epigenetic landscape of normal aging in Alzheimer's disease. *Nat Neurosci.* 2018;21(4):497-505. doi:10.1038/s41593-018-0101-9
- ³³ Watson CT, Roussos P, Garg P, et al. Genome-wide DNA methylation profiling in the superior temporal gyrus reveals epigenetic signatures associated with Alzheimer's disease. *Genome Med.* 2016;8(1):5. doi:10.1186/s13073-015-0258-8
- ³⁴ Sun Z, Kwon JS, Ren Y, et al. Modeling late-onset Alzheimer's disease neuropathology via direct neuronal reprogramming. *Science.* 2024;385(6708):adl2992. doi:10.1126/science.adl2992
- ³⁵ Shen Y, Timsina J, Heo G, et al. CSF proteomics identifies early changes in autosomal dominant Alzheimer's disease. *Cell.* 2024;187(22):6309-6326.e15. doi:10.1016/j.cell.2024.08.049
- ³⁶ Palma-Florez S, López-Canosa A, Moralez-Zavala F, et al. BBB-on-a-chip with integrated micro-TEER for permeability evaluation of multi-functionalized gold nanorods against Alzheimer's disease. *J Nanobiotechnology.* 2023;21(1):115. doi:10.1186/s12951-023-01798-2
- ³⁷ Jones D, Lowe V, Graff-Radford J, et al. A computational model of neurodegeneration in Alzheimer's disease. *Nat Commun.* 2022;13(1):1643. doi:10.1038/s41467-022-29047-4
- ³⁸ Joint Research Centre. Summer School on Non-Animal Approaches in Science. ec.europa.eu. 2026. Accessed August 13, 2026. https://joint-research-centre.ec.europa.eu/work-us/training-and-workshops/jrc-summer-school-non-animal-approaches-science_en

³⁹ Physicians Committee for Responsible Medicine. Summer Immersion on Innovative Approaches in Science. PCRM.org. 2026. Accessed August 13, 2026. <https://www.pcrm.org/ethical-science/summer-immersion>