Statement
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Committee on Health, Education, Labor, and Pensions
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NIH Research on Alzheimer's Disease and Other Cognitive Disorders

Statement of

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Senator Mikulski and Members of the Committee:

Good afternoon. I am Dr. Elias Zerhouni, Director of the National Institutes of Health (NIH), an agency of the Department of Health and Human Services, and I am pleased to be here today to talk about the advances we are making toward defeating Alzheimer's disease (AD), a devastating condition with a profound impact on individuals, families, the health care system, and society as a whole.

Peer-reviewed reports estimate that up to 4.5 million Americans ages 65 and older are currently battling AD. Moreover, the rapid aging of the American population threatens to increase this burden significantly in the coming decades: Demographic studies suggest that if current trends hold, the incidence of AD will begin to sharply increase around the year 2030, when all the baby boomers (born between 1946 and 1964) will be over age 65. By the year 2050, the number of Americans with AD could rise to as many as 16 million.[1] In addition to the tremendous emotional and physical toll AD exacts upon patients and their caregivers, financial costs of AD are high: Some experts estimate direct and indirect costs of Alzheimer's and other dementias to be more than $148 billion annually.[2]

AD's complex pathology and relentless clinical course have presented daunting challenges for the medical and research communities. However, the National Institutes of Health is poised to

[1] Hebert, L.E., et al. Alzheimer Disease in the US Population: Prevalence Estimates Using the 200 Census. Archives of Neurology 60: 1119-1122, 2003.

[2] Alzheimer's Association, Alzheimer's Disease Facts and Figures: 2007. http://alz.org/national/documents/Report2007_FactAndFigures.pdf
Figure includes Medicare and Medicaid costs and the indirect cost to businesses when employees are burdened with the care of persons with Alzheimer's.

meet these challenges through a comprehensive program of research into the underlying causes, diagnosis, prevention, and treatment of AD.

At the most basic level, our understanding of the brain and cognition in both normal aging and disease states is increasing rapidly and exponentially. Advanced imaging technologies have opened a window into the inner workings of the brain and made it possible to visualize the brain's activity, including changes in the brain that could herald the onset of disease, with a specificity that was impossible even a few years ago. For example, the development of new tracer compounds such as Pittsburgh Compound B, the first molecule that can be used to map amyloid plaques (one of the pathological hallmarks of AD) in the brains of Alzheimer's patients, could allow earlier diagnosis of AD and facilitate the evaluation of new treatments.

Because research suggests that the earliest AD pathology begins to develop in the brain long before clinical symptoms are apparent, scientists are now searching for reliable, valid, and easily attainable biological markers that can identify cases very early in the course of disease. Early diagnosis of AD benefits affected individuals and their families, clinicians, and researchers. For patients and their families, a definitive early diagnosis provides the opportunity to plan for the future while the patient can still take an active role in decision making. For clinicians, accurate early diagnosis facilitates the selection of appropriate treatments, particularly as new interventions are developed to stop or slow progression of symptoms. And for researchers, earlier and more accurate diagnosis will facilitate clinical studies of new therapies and preventive measures by allowing clinical trials on early intervention, before cognitive loss becomes significant. We expect programs such as the ongoing Alzheimer's Disease Neuroimaging

Initiative (ADNI), a public-private partnership which Dr. Hodes discusses in his statement, to provide a wealth of information about both brain pathology and biomarkers that can aid us in early diagnosis.

Successful early diagnosis also depends upon the identification of people who are at particular risk for developing the disease. Although we do not yet fully understand what causes AD, it is apparent that genes play an important role, and NIH is supporting the development of new techniques to speed the identification of genes that are associated with AD. For example, genome-wide association studies (GWAS) rely on newly available research tools and technologies to rapidly and cost-effectively analyze genetic differences between people with specific illnesses such as Alzheimer's disease or diabetes and to healthy individuals. Identifying the differences may facilitate our understanding of genetic risk factors that influence the development or progression of disease.

Several NIH Institutes recently launched, or are planning, GWAS initiatives with the expectation that the results will eventually accelerate the development of better diagnostic tools and the design of new, safe, and highly effective treatments. NIH is also developing a data-sharing policy for GWAS to harmonize the practices NIH-wide through which data will be made available for research use.

As with other chronic diseases and conditions, however, genes are only part of the story. In addition to the genetic component, cognitive health can be influenced by concurrent medical conditions, environmental factors, and even an individual's social environment. An ongoing

NIH initiative aimed at elucidating the underpinnings of cognitive health and preventing disease is the Cognitive and Emotional Health Project. The goal of this trans-NIH initiative is to assess the state of epidemiologic research on demographic, social, and biologic determinants of cognitive and emotional health in aging populations and the pathways by which cognitive and emotional health may reciprocally influence each other so that the most likely interventions for maintenance of cognitive and emotional health may be targeted. As a first step, a comprehensive review of measures that are associated with maintenance of cognitive health has been published and was a starting point for the development of the recently published Centers for Disease Control and Prevention/Alzheimer's Association's *Healthy Brain Initiative: A National Public Health Roadmap to Maintaining Cognitive Health*.

By learning more about the diverse factors that may increase risk of cognitive decline or AD, we hope to identify interventions that could delay or prevent its onset. For example, we have learned from epidemiologic studies that diabetes, a condition affecting nearly 21 million Americans,[3] is associated with cognitive decline in older people. ACCORD-MIND, an ongoing substudy of the NIH-supported Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, is currently testing whether the rate of cognitive decline and structural brain change in people with diabetes treated with standard care guidelines is different than in people with diabetes who adhere to more rigorous treatment.

[3] "National Diabetes Statistics." National Institute of Diabetes and Digestive and Kidney Diseases, 2005. http://diabetes.niddk.nih.gov/dm/pubs/statistics/index.htm

The translation of findings from basic research into new interventions to prevent or treat disease is another major focus of the NIH. In recent years, new insights into amyloid, tau, and inflammatory and oxidative stressors have enabled us, for the first time, to create highly specific treatments for AD that are targeted at particular molecules and processes in the brain; Dr. Hodes describes in his statement some of the newer targets that have been identified through this research. Some of those compounds have significant proprietary potential and are currently undergoing preclinical and clinical study by pharmaceutical and biotech companies. Others are being tested in NIH-supported clinical trials.

Finally, NIH supports the national infrastructure that makes basic and clinical research possible. For example, researchers at NIH-funded Alzheimer's Disease Centers (ADCs) are working to translate research advances into improved diagnosis and care for Alzheimer's disease patients while at the same time focusing on the program's long-term goal -- finding a way to cure and possibly prevent AD. Areas of investigation range from the basic mechanisms of AD to managing the symptoms and helping families cope with the effects of the disease. ADC staff conduct basic, clinical, and behavioral research and train scientists and health care providers who are new to AD research.

The Alzheimer's Disease Cooperative Study (ADCS) is a major Alzheimer's disease clinical trials effort. Now in its 16th year, the goal of the ADCS is to plan and conduct clinical trials on promising compounds designed to improve cognitive functioning, ameliorate behavioral disturbances, slow the rate of decline, or delay the onset of Alzheimer's disease. In general, the ADCS tests drugs that are not typically studied by large pharmaceutical companies, such as

drugs that are off patent or were patented and marketed for another use but might be useful for treatment of AD, or novel compounds from individual investigators or from small companies without adequate resources for clinical trials. ADCS studies thus fill an important resource gap between the identification of a potentially useful compound and its eventual adoption in clinical practice. In October 2006, NIH announced a $52 million award to the ADCS over the next six years to conduct several new clinical trials. Dr. Hodes describes some of these upcoming clinical trials in his statement.

An exciting trans-NIH initiative that will facilitate research into AD and other neurological disorders is the NIH Blueprint for Neuroscience Research. The Neuroscience Blueprint brings the 16 NIH Institutes, Centers, and Offices that support neuroscience research into a collaborative framework to coordinate their ongoing efforts and to plan new cross-cutting initiatives. By pooling resources and expertise, the Blueprint aims to accelerate neuroscience research and to reduce the burden of nervous system disorders. Working together, representatives from the partner Institutes, Centers, and Offices identify pervasive challenges in neuroscience and any technological barriers to solving them. This enables the Blueprint to support the development of new tools, training opportunities, and other resources to assist neuroscientists in both basic and clinical research. Each year from FY07 to FY09, the Blueprint will focus on one of three themes: Neurodegeneration, neurodevelopment, and neuroplasticity. Four funding announcements related to the neurodegeneration theme were released in FY07. These initiatives support the identification of biomarkers for neurodegeneration, the development of new ways to deliver therapeutics to the nervous system, and two interdisciplinary training programs in neurodegeneration research.

Finally, NIH conducts a number of research studies that support caregivers of AD patients. AD caregiving is highly stressful, emotionally and physically, and Dr. Hodes will tell you about some of the ways NIH works to develop and disseminate interventions to help the millions of Americans who care for a loved one with AD. To further explore the economic, social, and psychological costs of AD, the NIH supports studies such as the Health and Retirement Survey, the leading source of combined data on health and financial circumstances of Americans over age 50. Now in its 14th year, the HRS follows more than 20,000 people at two-year intervals, and gathers important data that informs health care policy regarding AD and a number of other health conditions.

It is important to note that the NIH cannot and does not conduct its important work in a vacuum. We work closely with partners in academia, in the private sector, and elsewhere in the government to develop new diagnostic tools and methodologies, to conduct clinical trials, to disseminate the results of our research, and to implement new interventions and policies resulting from our research at the community level. For example, the AD Neuroimaging Initiative is a joint venture between NIH and a number of academic and industry partners. Another is the AD Cooperative Study, which I described earlier, is conducted in close collaboration with our partners at the University of California-San Diego and scores of clinical sites across the Nation. Compared to even a decade ago, the field of neuroscience is moving at an extraordinary pace. We know, however, breakthroughs cannot come quickly enough for the millions of Americans touched by Alzheimer's disease. I can report to you today that real progress is being made, and

that we at NIH are committed to seeing that progress continues toward treatment, and ultimately prevention, of Alzheimer's disease.

This concludes my statement, and I will be happy to discuss these matters further with the Subcommittee.