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November 22, 2011

HHS Office of the Assistant Secretary for Planning and Evaluation  
Room 424E, Humphrey Building  
200 Independence Avenue, SW  
Washington DC, 20201

Re: National Alzheimer's Project Act

Dear Secretary Sebelius and Dr. Peterson,

The Society for Women's Health Research (SWHR) is writing to the Advisory Council on Alzheimer's Research, Care, and Services in regards to the National Alzheimer's Project Act (NAPA). SWHR has key scientific recommendations that it believes the Advisory Council should consider as it is establishing an integrated national plan to overcome Alzheimer's disease.

SWHR, a national non-profit organization based in Washington, D.C., is widely recognized as the thought leader in research on sex differences and is dedicated to improving women's health through advocacy, education, and research. SWHR appreciates the work NAPA is and will be doing to focus our nation's resources on Alzheimer's disease. While Alzheimer's disease is a disease of the brain, the brains of men and women are inherently different. It is common knowledge that men and women think differently; however, recent scientific discoveries have demonstrated that the difference goes beyond thought processes. Sex differences have been observed in the anatomy of the brain, behavioral traits, and in the physiological responses of the nervous system to outside stimuli and internal perturbation. These differences are also noted in the aging process and for the degenerative diseases such as Alzheimer's and Parkinson's disease.

SWHR believes that sex differences in Alzheimer's disease are critical to scientific advancements in diagnosing and treating the disease and need to be a part of the plan's scope. In October 2011, SWHR convened a one-day scientific roundtable of experts to discuss what is known about sex and gender differences in Alzheimer's disease, from both a basic and clinical science perspective as well as those of the caregiver and what research questions needed to be answered for progress to be made in the disease for all who are impacted. From the meeting it was clear that Alzheimer's disease research must account for sex as a basic biological variable and include sex-specific analyses and would be an extremely useful component of a national strategic plan to combat Alzheimer's disease. Key research

recommendations from the roundtable that NAPA should include:

- Research on the rate of progression of Alzheimer’s Disease, specifically examining sex differences in the transition from normality to early stages of disease to dementia, and from dementia to outcomes.
- Research on the influence of sex steroids, bioenergetic vulnerabilities, synaptic function, and cognition in the brain as it relates to Alzheimer’s disease.
- Re-examination of existing data for potential sex differences to help define the etiology of Alzheimer’s disease and publishing sex-specific results.
- Research on the differential impact of the caregiving role on men and women and design interventions to provide more effective services

Significant differences exist between men and women who suffer from Alzheimer’s disease. Larry Cahill, Ph.D., an associate professor in the Department of Neurobiology and Behavior at the University of California, Irvine, explained in a paper published in *Nature Reviews Neuroscience* that “Alzheimer’s disease-related neurofibrillary pathology associated with abnormally phosphorylated tau protein differs in the hypothalamus of men and women: up to 90 percent of older men show this pathology, whereas it is found in only 8-10 percent of age-matched women.” Abnormalities caused by Alzheimer’s disease may differ between the sexes and result in different symptoms or behavioral problems for men and women with the disease and may lead to the need for different treatment decisions.

Furthermore, *Biology of Sex Differences (BSD)* published research on sex differences of certain brain cells and their response to inflammation in the article, “Sex Differences in the Inflammatory Response of Primary Astrocytes to Lipopolysaccharide” on July 12, 2011. Sex differences in incidence, age of onset, symptoms or outcome are evident in many neurological and psychiatric disorders. Astrocytes, one of the glial cells of the brain, show sex difference in number of cells, function, and differentiation. Glial cells are involved with physical support for neurons, while others regulate the internal environment of the brain, and provide nutrients to neurons of the brain.

With the increasing number of known sex differences found in research in Alzheimer’s disease, SWHR recommends gaining a better understanding of the relationship between pathology and how disease presentation affects men and women differently leading to future sex-specific therapies for the disease.

Through our research recommendations above, SWHR seeks to put before the Advisory Council on Alzheimer’s Research, Care, and Services the need to advance more targeted therapies in Alzheimer’s disease for both men and women. This will lead to a greater understanding of risk factors for both men and women and more sex specific treatment of cognitive aging, Alzheimer’s disease and other dementias.

Should the Advisory Council have any questions or would like more information please contact Eileen Resnick, Director of Scientific Programs at SWHR, at 202-496-5010 or [Eileen@swhr.org](mailto:Eileen@swhr.org).

Sincerely,



Phyllis Greenberger, MSW  
President and CEO

#### References

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