ALZHEIMER DISEASE (AD), the most common form of dementia, affects about four million Americans and has been estimated to cost US society $100 billion per year, exceeded only by the costs of heart disease and cancer.1,2 The prevalence of AD has been predicted to reach 14 million by 2050 unless a treatment is found, and overall costs may increase four-fold.1,2 While considerable debate remains about the pathogenesis, nosology, and treatment of AD,3 there is no doubt that this research has the potential for enormous financial and professional gains. Thus, there is a need to balance the interests of both researchers and society in conducting AD research.

Although the financial interests of clinical investigators have not necessarily affected the validity of trial results, experiences with some AD drug trials have prompted the development of organizational guidelines to limit the appearance or reality of financial conflicts of interest. Based on a trial of tacrine4 and other drugs, a multidisciplinary panel was convened to study the financial relationship between academia and industry.5 Its recommendations included proactive disclosure of both personal and organizational conflicts in all clinical trials, particularly as a way to build public trust in the drug development process.6 The Parkinson Study Group, a not-for-profit physicians’ group that coordinates research at 85 sites across the United States and Canada, has adopted similar principles and has published the results of some 25 multicenter trials for diagnostic methods and experimental interventions in Parkinson disease.7 This group further mandates review of all research by outside health care providers and the release of both positive and negative results to the public.

Guided in part by the approach of the Parkinson Study Group, a large multisite study—the National Institute on Aging (NIA) Cooperative Study—has developed and internally disseminated conflict-of-interest guidelines. These include a $10000 annual cap on consulting fees for investigators and stringent limitations on ownership of equity in companies involved in the studies. Those leading the studies are subject to stricter guidelines. However, the blanket exclusion of experts with some industry ties from the design of trials might make drug development less efficient. Therefore, the Cooperative Study’s guidelines reflect a need to balance access to scientific expertise with the goal of mitigating conflicts of interest. The group is currently studying the impact of its guidelines on the conduct of clinical trials.

Novel targets of AD pathogenesis, however, would present a new set of challenges even if all appearances of conflict were to be addressed. A recent trial of a vaccine-based treatment for AD8 was viewed by many as a critical test of the amyloid hypothesis, a popular model of AD pathogenesis. Vaccination of transgenic mice against components of human amyloid, a protein at the core of senile plaques in AD, led to clearance of this protein from the brain.9 However, in phase II human trials with this same vaccine, some subjects developed autoimmune encephalitis, an adverse effect that prompted termination of the trial.10 As others have suggested, the public health can best be served in this case by a full disclosure of the disease course and clinical response of all trial participants,11 rather than analyses of single cases or subsets of subjects.12 Equipped with as complete a set of positive and negative findings as possible, clinical investigators would be better able to anticipate potential problems with mechanistically novel agents in future trials.

REFERENCES

©2003 American Medical Association. All rights reserved.

(Reprinted) JAMA, July 2, 2003—Vol 290, No. 1 115