

Conflict-of-interest problems lead to policy changes

Scientists had hoped that the discovery of a genetic link to Alzheimer disease (AD) would lead to the first reliable diagnostic test for the condition. Instead, it has yielded an intense scientific debate about the test's limits and a conflict-of-interest clash for academic researchers involved its evaluation.

Last month, a Stanford University bioethics panel concluded, after almost two years of deliberation, that genetic testing for AD is "currently inappropriate for everyday, clinical use and should be restricted to research settings." The Stanford Program in Genomics, Ethics and Society panel's recommendations were published in *Nature Medicine* last

year (*Nature Med.* 4, 757; 1998) and state that the tests do not provide enough information to be useful, especially as so few doctors are trained to perform genetic counseling.

The panel initiated the evaluation after the first Alzheimer tests became commercially available in 1996. The 35-member group concurred that healthy people should not be tested for variations in the APOE gene, which has been linked to AD. Some people have the form of the gene linked to Alzheimer but never get the disease.

Moreover, the panel determined that

the test is not useful as a diagnostic tool because it only offers a slight improvement over tools such as brain imaging and cognition tests. In addition, patients, family members and doctors can easily misinterpret the results.

As the Stanford group was releasing its report, officials at the National Institutes of Aging (NIA), Harvard University

and the Elsevier journal, *Neurobiology of Aging* (NoA), announced revisions to their conflict-of-interest rules in connection with genetic testing for AD.

Each has received detailed anonymous complaints that a 1998 NoA journal article by a 24-member NIA working group reported favorably on biomarkers for genetic testing for AD, but failed to disclose that some authors had financial relationships with Athena Neurosciences—the company that manufactures genetic test kits for the *presenilin 1* gene and APOE. The fact that the review article states clearly "The workshop and the publication of this supplement were sponsored in part by an unrestricted grant...from Athena Neurosciences" was apparently unsatisfactory to the complainant.

The NoA article was published in April 1998, but it was not until December, when a tip-off led to the *Wall Street Journal* printing a story entitled "Did ties to Alzheimer test maker sway NIH report?" that the controversy over the authors' industry links flared. Copies of the newspaper article were mailed anonymously to neurologists across the country on three separate occasions.

Within days of the newspaper piece, both NIH officials and the dean of the Harvard Medical School received the anonymous complaints. The objection submitted to Harvard charged that working groups members, Dennis Selkoe—one of the founders of Athena—and John Growdon, had violated the School's conflict-of-interest rules. However, six weeks ago, a Harvard Medical School panel decided that Selkoe did not contravene the rules because he explicitly requested that his affiliation with Athena be published in



Lawsuit reveals academic conflict-of-interest

Texan lawsuits against the manufacturer of the so-called 'phen-fen' diet drugs Redux and Pondimin, Wyeth Ayerst, have revealed yet another problem for the biomedical research community borne of conflict of interest issues.

The *Dallas Morning News* has reported that Wyeth paid Excerpta Medica—a medical publisher owned by Reed Elsevier, which also carries out contract writing—to 'ghostwrite' articles at a cost of \$20,000 each on the health problems associated with obesity. The pieces were then 'authored' by leading scientists, some of whom accepted honoraria in the range of \$1,000–\$1,500 according to the newspaper. Two of the articles were published subsequently in peer-reviewed, Excerpta Medica journals.

Wyeth voluntarily withdrew the drugs from the market on September 15th, 1997, based on reports that they caused heart valve abnormalities. Although the purpose of the lawsuit is to establish what Wyeth knew and when, and given that contract writing is standard practice within the pharmaceutical industry, the case has highlighted the need for scientific journals to adopt clear disclosure policies, to enforce them, and for researchers to adhere to them.

One of the review papers (*Am. J. Med.* 100(2), 230; 1996) was authored by Albert Stunkard, University of Pennsylvania. The journal has a clear disclosure policy that includes the statement, "Because reviews and editorials are based on selection and interpretation of the literature, the *Journal* expects that authors of such articles will not have any financial interest in a company (or its competitor) that makes a product discussed in the article." The statement continues, "Information about potential conflict of interest will be...published with the manuscript at the discretion of the editors."

Stunkard devotes paragraphs to the weight-reducing effects of *d*-fenfluramine, but no disclosure statement is made. According to the *Dallas* newspaper, Stunkard claims "Excerpta did not tell him that the honorarium came from Wyeth." Stunkard did not respond to requests from *Nature Medicine* to discuss the issue.

The other review article (*Clin. Ther.* 18(6), 1006; 1996) by F. Xavier Pi-Sunyer, St Luke's Hospital Center, New York, was accompanied by an editorial that referred to the risk of pulmonary hypertension caused by dexfenfluramine as "small (28 cases per million person years)." Again, the journal in question states, "Upon submission authors will be required to disclose, in writing, any financial interests (e.g employment, consultancies, stock ownership, honoraria, expert testimony)..." but adds, "...This information, in whole or in part, may be published at the discretion of the Editor-in Chief after consultation with the author..."

Publisher Stan Heimberger, explained that "only if, in the opinion of the Editor-in-Chief or the Editors, disclosure has a impact, would the journal feel the need to add this in the text itself." Pi-Sunyer told *Nature Medicine* that he did not accept the honorarium, and therefore no disclosure appeared in the article.

KAREN BIRMINGHAM, LONDON