FDA Queries Alzheimer's Trial Results

The Food and Drug Administration has notified California physician William Summers that it is considering barring him from conducting clinical trials of new drugs. The agency took this action because of questions it has about a previous study in which Summers and his colleagues tested the effects of the experimental drug THA in patients with Alzheimer's disease. The results, which were published in the high-profile *New England Journal of Medicine* in November 1986, indicated that the THA treatment could alleviate the patients' symptoms to a degree not seen with other experimental Alzheimer's therapies.

The study generated a firestorm of interest. It was a major stimulus to the initiation of a multi-center clinical trial under the joint sponsorship of the National Institute of Aging, the Warner-Lambert Company of Morris Plains, New Jersey, and the Alzheimer's Disease and Related Disorders Association. That trial began in September 1987, but was halted by the FDA in November when 20% of the first patients showed signs of liver damage.

Meanwhile, doubts about the methodology used by Summers in his earlier THA study had surfaced in several letters-to-the-editor that the *New England Journal* published in May. In addition, the FDA had begun its own investigation at least partly because agency officials were concerned that the physician was commercializing an as yet unproven therapy. He had formed a for-profit corporation and was charging patients up to $12,000 for a full year of THA therapy. Summers maintains that the fees covered only the cost of the research.

The FDA conducted an audit of the Summers data from the THA study in the summer of 1987. As a result, the agency presented the physician with an FDA-483 form that lists a large number of patient records and data that the FDA inspectors said that they could not locate. The 483 form also raised questions about whether the THA trial was truly double-blinded, as the *New England Journal* report claimed. To avoid compromising the integrity of drug trials, they are usually conducted in a double-blind fashion, with neither the patients nor the individuals who assess their conditions knowing when a patient is receiving the test drug and when a placebo.

An investigator who is issued a 483 form is entitled to reply, and if he can supply the missing information to the FDA's satisfaction, the matter can end. However, according to a report by Gina Kolata in the *New York Times*, Frances Kelsey of the FDA's Office of Scientific Investigations has now sent Summers a letter that lists 14 findings that she says cast doubt on conclusions of the study he conducted. If all the problems cannot be cleared up, the investigator may be barred from conducting new drug trials.

Kelsey declined to discuss the Summers investigation, saying, "It's still an open file and I have no comment." Summers confirmed that he had received the letter, but he, too, declined to discuss the situation at this time. He had, however, previously sent *Science* a copy of a letter that he wrote in November to a *Wall Street Journal* editor.

Summers states in this letter that some 55% of the items of information—out of a total of 355 by Summers' count—listed in the 483 form were already provided in the material examined by the FDA inspectors. Summers could supply corroborative material for another 29%, leaving 16% still outstanding.

While all this has been going on, the FDA has given permission for the resumption of the multi-center THA trial, in which Summers is not participating. There are theoretical reasons for thinking that the drug might be of some use in treating Alzheimer's disease. It bolsters the concentration of a brain chemical that is deficient in the patients. The FDA is requiring that lower doses of the drug be used in the resumed trial and that the patients are to be monitored very closely for signs of liver damage or other side effects. ■ JEAN L. MARX

Second Chance for Rice Research Center

The West Africa Rice Development Association (WARDA) has a new headquarters near Bouaké in Côte d'Ivoire. Besides moving to a new location, the problem-ridden organization has put into effect a number of reforms aimed at giving it a fresh start.

WARDA has been regarded as the least effective of the international agricultural research centers operating under the CGIAR* organization. Founded in the early 1970s to foster self-sufficiency in rice production in West Africa, it earned scathing evaluations for both its research performance and management. A variety of proposals were considered for WARDA including outright abolition or merger with other organizations. A decision was finally made to restructure WARDA and revise its strategy (*Science*, 5 Dec. 1986, p. 1190).

The problems with WARDA's scientific program started with its original strategy which was pitched to improving rice production in West Africa by adapting high-yielding varieties of rice developed elsewhere, mostly in Asia. As it turned out, these varieties did poorly under African environmental conditions. They also proved ill-suited economically, because the exotic varieties required water, fertilizer, and pesticides in amounts usually not available in African agriculture.

*The Consultative Group on International Agricultural Research is sponsored by the World Bank and other United Nations agencies and funded mainly by the United States and and other industrial countries.

Eugene Terry. *New director general of the West Africa Rice Development Association.*