last week's advisory panel meeting in Rockville, Md. Although measures of cognitive ability showed that THA provided some clinical benefit in both trials, another type of cognitive test revealed no improvements from THA compared with placebo. After deliberating for nearly 14 hours, the FDA panel decided the slight improvements seen on some tests did not outweigh the drug's small but potentially serious threat of liver damage (SN: 11/7/87, p.292).

In one of the studies, led by Kenneth L. Davis at the Mount Sinai School of Medicine in New York City, investigators at 16 U.S. clinical centers randomly assigned 112 Alzheimer's patients to placebo and 103 to THA. Neither the researchers nor the volunteers knew who got the active drug. After six weeks, the team found that people on THA, compared with placebo recipients, scored an average of three points higher on the Alzheimer's Disease Assessment Scale, a test measuring memory, language and other thinking abilities that progressively fail among victims of the disease. While this difference was small, the researchers call it significant.

However, THA's performance faltered on the Clinical Global Impression of Change, a test commonly used to gauge the general state of psychiatric patients, including thinking skills. Scrutiny of those scores revealed no difference between THA treatment and placebo.

In the British study, a 29-week trial involving 92 people with Alzheimer's, researchers led by Raymond Levy of the Institute of Psychiatry in London randomly assigned half the participants to a placebo and the remainder to THA plus lecithin, a substance thought to boost THA's efficacy. Halfway through the trial, they switched the two groups so that people on the placebo got the active drug and vice versa. Using a test called the Mini-Mental State Examination, the investigators discovered that 44 percent of the volunteers improved their scores by three or more points after treatment. Only 11 percent showed a similar rise in scores after receiving the placebo.

Despite the varying results measured on different cognitive tests, some clinicians say their own experience has convinced them of THA's promise. Nancy L. Earl, a neurologist at Duke University in Durham, N.C., told the FDA panel that some of her patients with Alzheimer's show enhanced cognitive abilities with THA treatment. "I know that I saw significant improvement in some patients at my site," she said.

But such testimony remains purely anecdotal, and the FDA remains unswayed. Officials at the agency want to see more hard data proving THA's potency and safety before granting Warner-Lambert the go-ahead to market this treatment to an estimated 4 million people in the United States who suffer from Alzheimer's disease. — *K.A. Fackelmann*

Low-level radiation: Higher long-term risk?

A new study of workers at a federal research laboratory strengthens the evidence linking cancer with long-term exposure to low levels of ionizing radiation.

Steve Wing, an epidemiologist at the University of North Carolina in Chapel Hill, headed the new study, which looked for statistical correlations between cause of death and the cumulative radiation exposures of nearly all white men hired by Oak Ridge (Tenn.) National Laboratory (ORNL) between 1943 and 1972. His team followed 8,318 men through 1984, by which time 18 percent had died.

The risk of dying from cancer increased by almost 5 percent for each rem of radiation exposure incurred over the course of employment at this Department of Energy (DOE) facility — at least a 10-fold greater risk than the Japanese atomic-bomb-survivor data would suggest, the researchers report in the March 20 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.

A previous analysis of the same ORNL population by several of Wing's coauthors failed to find a correlation between cancer risk and worker radiation exposures. Wing says his additional seven-year follow-up primarily explains the trend's emergence, and he suggests researchers should follow future populations longer than they have in the past.

Though the new analysis also identified a 63 percent higher leukemia death rate in the ORNL workers than in U.S. white males as a whole, leukemia risk did not increase consistently with radiation exposure, Wing notes. He speculates that exposure to some other toxic chemical may account for the high number of ORNL deaths from this disease.

The researchers also did not have smoking histories or the cause of death for some workers — factors that potentially weaken the findings, Wing says.

The new study took longer than usual to publish, Wing says, because its unexpected results prompted an in-depth review of his methods by DOE. Because the new results challenge a belief held by many epidemiologists — that low-level radiation does not cause cancer — "there was certainly a lot of concern about the findings," he says.

Such findings are not, however, unprecedented. In 1989, DOE provided the Senate Governmental Affairs Committee 14 studies reporting elevated cancer mortality rates among employees at nuclear facilities run by DOE and its predecessor agencies.

Epidemiologist Alice M. Stewart of the University of Birmingham in England says the findings by Wing's team resemble the increased cancer risks in radiation-exposed workers at DOE's Hanford facility in Richland, Wash., that she, Thomas F. Mancuso and George W. Kneale reported more than a decade ago (SN: 2/25/78, p.117).

Mancuso, a University of Pittsburgh epidemiologist, had worked under contract with the Atomic Energy Commission, one of DOE's predecessor agencies. Mancuso lost that contract in 1977 when he refused to support his contract officers' contention that the Hanford data showed no evidence for a cancer-radiation link (SN: 2/10/79, p.93).

Mancuso's dismissal is not the only case of DOE interference in epidemiologic studies of workers at its facilities. In the summer of 1989, the Senate Governmental Affairs Committee uncovered information showing that half of some 40 filing cabinets of ORNL workers' medical records in storage at Oak Ridge Associated Universities (ORAU) had been deliberately destroyed at some time after 1977, according to Robert Alvarez, a member of the committee's staff. The absence of these data could affect the statistical strength of the Wing team's study, Alvarez contends. (Although some of Wing's coauthors work at ORAU, Wing said he was unaware of the records' destruction.)

Finally, in February 1990, epidemiologist Gregg S. Wilkinson of the University of Texas in Galveston testified before a federal panel investigating DOE epidemiologic research that DOE officials pressured him not to publish findings linking cancer and exposure to plutonium at the Rocky Flats nuclear weapons plant outside Golden, Colo.

As these and other problems have come to light, many scientists and politicians have actively challenged DOE's objectivity in managing studies of its workers' health. On Jan. 8, responding in part to a 1989 hearing by the Senate's Governmental Affairs Committee, DOE agreed to turn over responsibility for worker-health studies to the Department of Health and Human Services.

"Complex Cleanup," a February report by the congressional Office of Technology Assessment, further recommends establishing independent federal investigatory teams to evaluate environmental health and safety at DOE defense facilities.

But because DOE will continue to control the kind of information researchers can collect, these measures represent only a partial solution, Alvarez contends. Researchers still have no way to ensure the accuracy and completeness of the information they receive from DOE, he notes.

In the past, DOE has been accused of attempting to cloak adverse worker-health impacts in "secrecy," acknowledged Paul L. Ziemer, the assistant DOE secretary for health and safety. At a March 19 press briefing on Wing's study, he said, "We're trying to make [such analyses] more open." — *W. Gibbons*