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Large-Scale Cancer Study Urged on Nuclear Power Industry

The nuclear power industry has long debated the need for a comprehensive epidemiological study of the effects of chronic exposure to low-level radiation. No large-scale effort has yet been mounted, but the prospects for such a study have improved with vigorous endorsement from a National Research Council (NRC) panel, which urged U.S. utility companies to take part in an ambitious industry-wide survey proposed by epidemiologists at New York University (NYU) Medical Center.

The survey of nuclear power workers, whose radiation exposures are well documented, would be the largest ever to directly compare recorded dose equivalents of ionizing radiation with observed cancer incidence. In a recently published report, the NRC panel of radiation biologists and epidemiologists asserted that the massive study would ease widespread concerns about the dangers of radiation, and would answer lingering questions about the risks to workers from dose equivalents permitted by regulatory authorities. The amount of information collected would allow statistically sound estimates of at least the upper bounds of low-dose radiation risks. As proposed, the study would cost about \$6 million and take at least five years to complete.

Commencement of the study, however, depends on cooperation and funding from the nuclear power industry, which is far from guaranteed. A decision from the utilities isn't expected until early 1992, according to Leeka Kheifets, PhD, project officer for the Electric Power Research Institute (EPRI), which funded a pilot study of the NYU proposal. Roy Shore, PhD, doctor of public health and professor at NYU's Institute of Environmental Medicine, who designed the proposal, believes that only a small minority of the

nuclear utilities oppose an industry-wide study.

Commonly cited reasons to oppose the effort include fears that the analysis will yield false-positive results that could lead to bad press and unfounded lawsuits. Others have said the costs of such a study aren't justified since the biological effects of ionizing radiation are well characterized. Dr. Shore says that there are sound scientific and public health reasons for embarking on the study. "If there were any risks associated with radiation exposures [among nuclear power workers], we would want to know," he says. He expects the study to rule out assertions that risks are greater than currently estimated. "In the most likely scenario there won't be any detectable risk."

The NRC panel pointed out that decades of experiments confirm the risks of high-dose effects, but added that the dangers of low-doses remain difficult to assess. Estimates of the cancer risks from low-level radiation are typically extrapolated from data on human populations exposed to high radiation levels, primarily the survivors of the atomic bombings on Hiroshima and Nagasaki, Japan. The rules for extrapolating from acute high levels to chronic low-level exposures create large uncertainties in the calculated risks.

Many smaller studies have directly examined populations exposed to protracted doses of low-level radiation, "but small studies don't answer the questions," said Richard B. Setlow, vice-chairman of the NRC panel and associate director for life sciences at Brookhaven National Laboratory in Upton, New York. "The only way to eliminate uncertainty is to get lots of data."

Ideally, the NRC panel reported, the study would include all industry workers, including contract workers—the industry has dosimetry files on an estimated 1.2 million individuals—and provide analysis of exposures to other carcinogens. The study data would be

recorded in a format compatible with the format developed by the International Agency for Research on Cancer (IARC). The NRC group concluded that the NYU study adequately provided for these recommendations.

Dr. Setlow said that an industry-wide study of nuclear power workers is the only large-scale epidemiological survey possible to measure the risks of environmental radiation, about which he added, "it's time to quit guessing." ■

Time to Chart the Brain

Given the pace of advances in brain imaging and computer science, the time is right to launch a nationally coordinated effort to chart and catalog the human brain, computer scientists and neuroscientists declare in a recent report published by the Institute of Medicine.

The goal of the initiative is no less than organizing the entire hierarchy of brain research—from genetic expression and molecular function to anatomy and behavior—in computerized atlases of text and three-dimensional maps of the brain.

Armed with this battery of linked data bases, a researcher could efficiently navigate the already overwhelming sea of information on the brain, concluded the review committee in the report, *Mapping the Brain and Its Functions*. The report was funded by the National Institute of Mental Health, the National Institute on Drug Abuse, and the National Science Foundation.

With access to extensive computer-managed information, a researcher could, for example, overlay anatomical maps with chemical and physiological maps, or relate positron-emission tomography (PET) images of the patterns of chemical receptor distribution to known paths of neurocircuitry. The report—aimed at government officials responsible for funding biomedical research—points out that the ability to connect knowledge from diverse specialties might hasten a better understanding of

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pain, vision disorders, schizophrenia, Alzheimer's disease, and other illnesses.

Significant improvements, however, are needed in databases and computer networks to make such an ambitious brain mapping effort possible, the committee concluded. Computerized imaging techniques, such as PET and magnetic resonance imaging, are sufficiently advanced, but current database programs and networks cannot easily handle these images. Nor can different databases communicate effectively enough to enable the kind of cross-referencing envisioned for the brain mapping initiative.

The first phase of the initiative calls for pilot projects around the country to develop powerful new software and improved networks, as well as standardized formats for storing and exchanging text and images. The second phase would involve the construction of integrated sets of brain maps for humans, rats, and monkeys.

The initiative would require about \$10 million a year over a test period of five years—less than 1% of the total annual U.S. spending on neuroscience, according to the report. The committee recommends an appropriation of funding beyond what's already budgeted for neuroscience, so as not to pose another "big-science" threat to basic research. ■

FDA Scrutinizes Physician Role in Drug Promotion

Clinical investigators involved in the promotion of drugs can expect heightened scrutiny and even the possibility of criminal prosecution by the Food and Drug Administration, according to Commissioner David A. Kessler, MD.

Departing from previous FDA policy, the commissioner said the agency will investigate physicians and scientists involved in illegal promotional efforts as well as the companies that sponsor them. The FDA has traditionally focused on

the sponsors of promotional activities, rather than individual researchers—"to minimize the chilling effect... on the free exchange of scientific information," as Dr. Kessler put it. That restraint is no longer FDA policy, the commissioner announced. Offenders, Dr. Kessler wrote, "may be subjected to civil injunctions or criminal prosecution."

His warning of the FDA's determination to crack down on drug promotions disguised as scientific presentations appeared in the July 18 issue of *The New England Journal of Medicine*.

Dr. Kessler focused on industry-sponsored symposiums, press conferences, continuing education classes and publications designed to promote drugs rather than present unbiased data. The number of medical symposiums sponsored by pharmaceutical firms and the money spent on these events have increased "dramatically" since the 1970s, according to Dr. Kessler. He acknowledged the importance of some industry-funded presentations in educating medical professionals, but expressed concern that mounting numbers of promotional events threaten to "undermine the unbiased exchange of scientific information."

The FDA plans to publish guidelines to help physicians and drug companies steer clear of activities that the agency considers "promotional" and illegal. Commissioner Kessler listed the following criteria necessary for industry-sponsored events to pass muster:

- Scientific content should be free of control by sponsors.
- Information presented should be objective—the FDA looks favorably on events that receive industry funding through educational organizations such as recognized professional societies. Funding from more than one sponsor also scores points for objectivity.
- A balanced range of diverse views should be presented.
- Data presented should be rigorous enough to inform medical decision

making. (For more information from the FDA, call Ann Witt, acting director of the Division of Drug Marketing, Advertising, and Communications, 301-295-8226.)

Commissioner Kessler's written commentary follows his pledge in June to fully enforce laws that prohibit companies from promoting drugs for alternate uses not listed on the label, as well as products that have not received FDA approval. The commissioner testified before the House Subcommittee on Human Resources and Intergovernmental Relations, which is investigating the adequacy of FDA monitoring of promotion of drugs and devices for off-label uses. The subcommittee is also determining if the agency should be given greater enforcement powers.

A bill proposed by Reps. Henry Waxman (D-California) and John Dingall (D-Michigan) would increase FDA authority to inspect company records and to seize, embargo, and recall products. The legislation would also expand the FDA's power to impose new civil penalties for violations.

Dennis Swanson, MS, co-vice chairman of government relations for The Society of Nuclear Medicine, is concerned that the FDA's actions may be wrongly interpreted to mean that the agency is trying to limit the practice of prescribing medications for off-label uses. He stresses that "physicians certainly have the right to use approved drugs for non-approved uses so long as the decision is based on sound scientific principles."

Recent media accounts have suggested that the FDA is stepping into the practice of medicine. When asked about this possibility, a spokesman for the FDA maintained that the agency had neither the authority, nor the intention to regulate the ways that doctors prescribe drugs in caring for patients. Potential for legal and ethical problems arises, he said, when physicians accept payment to promote pharmaceutical products. ■