GOVERNMENTAL COMMITTEE AND SNM PANEL ADDRESS GOVERNMENT RADIATION EXPERIMENTS

Under new program of "openness," Presidential panel of experts reviews millions of documents and advises agencies on compensation

ON APRIL 20, THE PRESIDENT'S Advisory Committee on Human Radiation Experiments (ACHRE) held its first meeting, in Washington, DC, to begin the gargantuan task of assessing millions of relevant documents. President Clinton had called for such a committee earlier in the year, and appointed Ruth R. Faden, PhD, professor of health policy and management at Johns Hopkins School of Hygiene and Public Health, as committee chair. The committee has the charge of evaluating the ethics of a gamut of (partly or wholly) government-sponsored experiments spanning the 1940's to the 1970's, arbitrarily grouped only because they all involved some sort of radiation and, usually though not always, human subjects.

The committee must answer to a task force of representatives from seven agencies connected to the experiments—the Departments of Defense, Energy, Veterans Affairs, Justice (connected primarily because it must determine possible remunerations to victims), and Health and Human Services; the Central Intelligence Agency; and the National Aeronautics and Space Administration. Besides making recommendations about compensating human subjects, the committee must also work with the seven task-force agencies on sifting through their warehouses of documents to find pertinent material.

"There are extraordinary numbers of documents that the committee must figure out how to search," said Steven Klaidman, counselor to the committee-designate and director of the communications-designate. "The committee must decide which cases to focus on and devote more energies to." Each of the fourteen ACHRE members (Table 1) are experts in a particular field related to the task and include SNM member Henry D. Royal, professor of radiology and associate director of the Division of Nuclear Medicine, Mallinckrodt Institute of Radiology (St. Louis, MO). They must accomplish this onerous task in one year, with a possible six-month extension.

Nuclear medicine practitioners are watching the course of the committee's operations: not only has the mass media confused the government radiation experiments with nuclear medicine (see *Newsline*, March 1994, p. 9N), but, because the specialty involves radiation and health physics, several nuclear medicine practitioners or researchers have been connected to the experiments.

In fact, for its first task, the committee concentrated on strategies for collecting data for three cases: 1) the Cincinnati studies; 2) the plutonium injection trials; and 3) the so-called "Green Run" case. The Cincinnati experiments were led by Eugene L. Saenger, professor emeritus of radiology at the University of Cincinnati and SNM member.

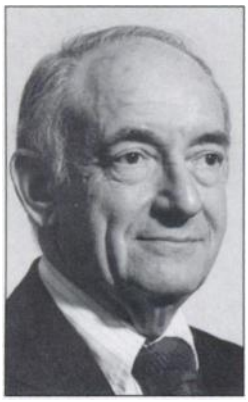
Secretary of Energy, Hazel O'Leary

Dichotomy of Purposes: Soldier or Patient?

In Cincinnati, on April 11, the House Judiciary committee held a hearing on radiation tests on humans conducted there in the 1960's and 1970's. In an effort to develop cancer treatment, Dr. Saenger's team evaluated the effect of whole body radiation on 88 cancer patients. All but one were terminally ill with inoperable breast, lung, gastrointestinal, or other tumors, and all but that one have since died. The Pentagon gave funding to the experiments, not because it was interested in the cancer-treating effects of the radiation, but because it wanted data on how high dosages of radiation affected the human body.

This Pentagon connection has stigmatized the Cincinnati experiments as if the federal government were experimenting on its citizens solely to see the effects of radiation—a stigma that is magnified with a general lack of agreement on the

causes of the patients' deaths. Some critics have stated that the radiation—hour-long exposures, of up to 300 rads—caused many of the patients to die, whereas the researchers contend that the patients died of their underlying illnesses. The critics argue that the doses were too high for an era when such treatment had been generally ruled as ineffective, and state the experiments had been carried out primarily to evaluate radiation toxicity for the government. David S. Egilman, PhD, clinical assistant professor of community health at Brown University, stated that the study was specifically designed to test the effect of radiation on soldiers. Yet the researchers maintain that it was done primarily for cancer treatment, and only secondarily for the federal government.



Eugene L. Saenger, MD

This dichotomy between certain critics' interpretations of the allegedly governmental origination of many experiments and the researchers' views about the purposes of their work runs through much of the current controversy. One aim of the advisory committee's document research is to determine the ethics of the studies and answer questions concerning their motivation and origination.

The Society held a panel discussion at the annual meeting in Orlando to help members "understand just what these experiments are were about," said A. Bertrand Brill, MD, PhD, professor of Nuclear Medicine at University of Massachusetts Medical Center (Worchester, MA), organizer of the panel. Each panel member presented documents and the published literature, describing just what each experiment was about. For example, Dr. Brill spoke about the 1970's Oak Ridge whole-body radiation studies, which had many parallels to the Cincinnati studies: they involved whole-body radiation on cancer patients and also provided data to government agencies interested in problems other than cancer. "The *idea* was that if you exposed the patient to a low-dose rate, normal cells would be able to repair naturally and cancer cells would not, so they would die," said Dr. Brill. "It turns out that whole-body radiation didn't provide a cure—it didn't hurt, though. This did lead into methods we use now to cure leukemia with high levels of radiation followed by bone-marrow transplant."

On the other hand, the data had secondary uses. "The data collected on this were used to estimate damage from radiation exposure," Dr. Brill said. NASA wanted this data for their astronauts exposed to cosmic radiation. The government decided to pay researchers at Oak Ridge to collect this information—thus they didn't irradiate the patients to get the data for the government. Furthermore, Dr. Brill said, Oak Ridge researchers did not just collect the data from their, but from hospitals all over the country. The Oak Ridge people were simply contractors who coordinated all this research.

Table 1. Members of the Advisory Committee on Human Radiation Experiments.

Kenneth R. Feinberg	Lawyer and expert in compensation
Eli Gladstein	Chairman, Department of Radiological Oncology, Southwest Medical Center, Dallas
Jay Katz	Psychiatrist, Yale University
Patricia A. King	Professor of Law, Georgetown University
Susan E. Lederer	Historian of Science, College of Medicine, Pennsylvania State University
Ruth Macklin	Historian of Science, College of Medicine, Pennsylvania State University
Lois Noris	Bank vice president
Nancy Oleinick	Professor of radiology, Washington University, St. Louis
Henry D. Royal	Professor of radiology, Washington University, St. Louis
Phillip K. Russell	Professor, Department of International Health, Johns Hopkins School of Public Health
Mary Ann Stevenson	Assistant Professor of radiological oncology, Harvard Medical School
Ray Tuckson	President, Charles R. Drew University of Medicine and Science, Los Angeles
Duncan C. Thomas	Professor, Department of Preventative Medicine, University of Southern California school of Medicine

Cases with Government as Prime Mover

ACHRE has already found that determining the ethics of the radiation experiments in terms of whether they were performed to benefit the patients is no easy task. They also must compare the standards of the time "with current standards [to see] whether the people behaved within the ethical standards of the time," said Mr. Klaidman. They will then "use this standard to judge the experiments."

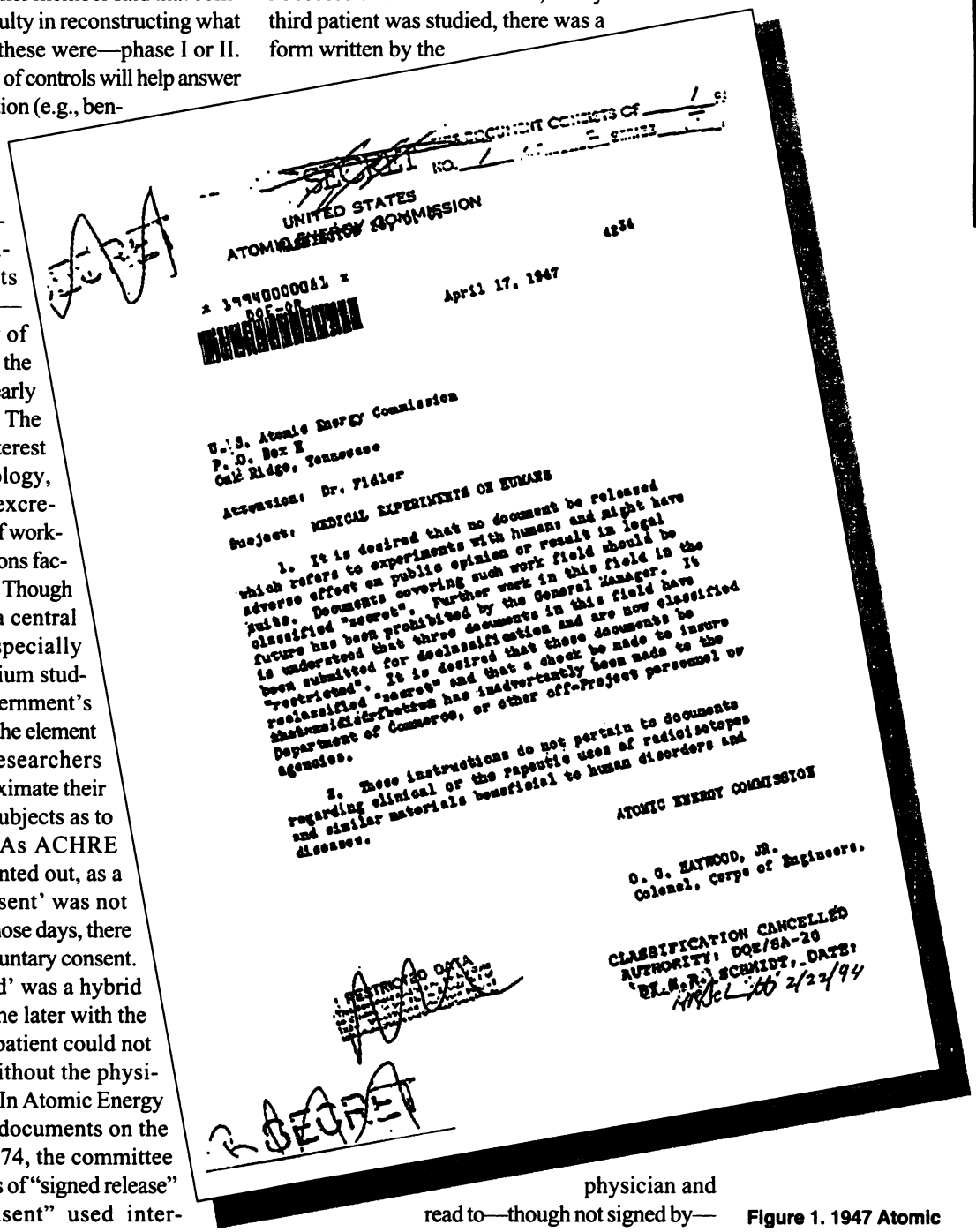
The committee met on May 18-19, in Washington, DC, to discuss their findings on the three tests cases, providing more questions than answers as to how to approach their own research and handle a different era's ethics and methodology. Concerning the question of controls in the Cincinnati experiments, ACHRE brought up the problem of whether "the terms 'Phase I, Phase II, Phase III' were used then. We have to get a picture of what research design was like in those days... to see if this [study] deviated from the contemporary methodology."

Many questions of ethics and methodology are intimately intertwined. For example, as the committee meeting brought to light, if the study was designed to help the patients, different considerations must be used in evaluating it, compared to those studies done for other reasons. More specific to the Cincinnati case, the clinical trial phase of the study would also effect the ethical evaluation. One committee member, pointing out that there is renewed interest in whole-body radiation, said that

from a historical perspective, one could not expect controls in the Cincinnati study because it was a Phase I study. Yet another member said that committees have had difficulty in reconstructing what kinds of experiments these were—phase I or II. Answering the question of controls will help answer the study's ethical relation (e.g., benefit) to the patient.

The second sample case that ACHRE studied—the plutonium injection experiments on 18 patients across the country—lacked the ambiguity of the government's role: the federal government clearly instigated the studies. The government had an interest in plutonium's toxicology, biodistribution, and excretion rates for the sake of workers handling it in weapons factories and laboratories. Though informed consent is a central issue, this issue is especially dicey with the plutonium studies because of the government's top-secret handling of the element in the 1940's. The researchers then could only approximate their descriptions to their subjects as to what was to occur. As ACHRE member Dr. Katz pointed out, as a term, 'Informed consent' was not used until 1957... In those days, there was the concept of voluntary consent. The idea of 'informed' was a hybrid legal concept that came later with the understanding that a patient could not truly give consent without the physician's full disclosure. In Atomic Energy Commission (AEC) documents on the experiments up to 1974, the committee has uncovered the uses of "signed release" and "informed consent" used interchangeably, though the former term does not imply the latter.

Robert J. Lull, MD, chief of nuclear medicine, San Francisco General Hospital, addressed the plutonium experiments in SNM's panel discussion. "Possibly earlier patients didn't have advised, written informed consent," he said. "It's *possible* some of them didn't know—the written informed consent is not available today. But later on, [the researchers] developed a written informed consent." He said that the first two of the three California patients (so-called "CAL-1, -2, and -3) have no record of informed consent, but by the time the third patient was studied, there was a form written by the physician and read to—though not signed by—the patient. "I speculate [the patients] didn't sign for the studies because they were top-secret," Dr. Lull said. However, "It's unclear whether there was oral consent when there is no written record."


UNITED STATES
ATOMIC ENERGY COMMISSION

April 17, 1947

U. S. Atomic Energy Commission
P. O. Box E
Oak Ridge, Tennessee

Attention: Dr. Fidler

Subject: MEDICAL EXPERIMENTS ON HUMANS

1. It is desired that no document be released which refers to experiments with humans and might have adverse effect on public opinion or result in legal suits. Documents covering such work field should be classified "secret". Further work in this field in the future has been prohibited by the General Manager. It is understood that three documents in this field have been submitted for declassification and are now classified "restricted". It is desired that these documents be reclassified "secret" and that a check be made to insure that classification has inadvertently been made to the Department of Commerce, or other off-Project personnel or agencies.

2. These instructions do not pertain to documents regarding clinical or the reparatic uses of radioisotopes and similar materials beneficial to human disorders and diseases.

ATOMIC ENERGY COMMISSION

O. G. HAYWOOD, JR.
Colonel, Corps of Engineers.

CLASSIFICATION CANCELLED
AUTHORITY: DOE/SA-20
BY: R.J. SCHMIDT, DATE: 2/22/94

SECRET

Figure 1. 1947 Atomic Energy Commission letter.

Secrecy, Mistrust, Confusion

Understanding these experiments within the context of the peculiar top-secret milieu of the time may be essential in evaluating them ethically. Pursuant to this idea, ACHRE released a 1947 docu-

ment revealing the government's explicit intentions to keep the nature of the human experiments completely hidden from the public (Figure 1). This document was declassified February 22, 1994 as part of Sec. O'Leary's openness campaign. "If nuclear medicine physicians saw this, they would understand why it's necessary to make this information about the government's radiation experiments available," Dr. Royal said. "The government has been hiding things from the American people." In a May 23, 1994 letter, Dr. Royal wrote that this document "raises several important questions: 1) What was the nature of these experiments? 2) Did the government have a secret program to suppress scientific information about the effects of radiation? 3) Why did it take until... 1994 to declassify this document? 4) Were additional experiments performed and classified as "secret" despite the prohibition stated in this letter?" Dr. Royal added that, "The shroud of secrecy surrounding nuclear weapons development and radiation experiments has been a major factor contributing to the distrust of the government's nuclear activity."

The committee made clear that this government matrix makes it more difficult for them to research the experiments—as members have to undergo the byzantine process of requesting declassification. It also has bred skepticism and even mistrust of intentions among the public, mass media, and anyone researching it: already newspaper reports have raised the specter of a federal government experimenting on its mentally and financially challenged populace. Both the media and ACHRE have raised the question of whether the government specifically chose indigent patients as subjects for the plutonium injections. However, Dr. Lull contends that such factors as which patients to use were all chosen specifically for experimental design. "For example, the media talked about a patient injected with plutonium and two days later, doctors have to amputate his leg," Dr. Lull said. "But the fact they selected him was because he was having to have his leg amputated. In other words, the researchers were not a bunch of scientists running amok." The researchers selected "a dose that they could adequately measure yet low enough it wouldn't hurt the patients; they chose patients [who likely] would not last beyond ten years because of terminal illness. "The study was not meant to harm patients. (As it turned out, some people had a miraculous [remission] and lived many years.)"

Many media reports—including the *Albuquerque Tribune*'s—did not definitively show that the plutonium affected health. The ACHRE discussed the possibility of determining how the plutonium affected health—which will play a part in assessing the ethics of the study. The problem remains that the researchers understood there was some danger, yet how much of that danger did they communicate to the subjects. There was no question of the studies benefitting the patient—but it turned out the results were of great benefit to others. "The data did get used for years: it was a model for evaluating occupationally exposed individuals," Dr. Lull said. He also contended that the evidence was weak for harm to the patients at the dosages they received. Thus, "In light of the plutonium injections, our ideas about its toxicity must be rethought"—though history may debate this for some time.

Apparently vulnerable citizenry also were the subjects of mineral absorption studies at Massachusetts's Fernald School. But many observers assert that these studies are an entirely different sort from the plutonium experiments, because: a private company (Quaker Oats), not the federal government, sponsored them; the studies benefitted the subjects by pointing to the need for mineral supplements to their diets; the amount of radiation was extremely low—lower than background levels—and is an amount used in mineral absorption studies still carried on by nutrition departments. According to Kevin J. Donohoe, MD, in the Division of Nuclear Medicine, Beth Israel Hospital (Boston, MA), who is addressing the Fernald School issue at the SNM panel, just the mention of the word "radiation" causes concern, despite explanations about the low-activity iron and calcium isotopes that were used at Fernald. He sees more potential harm done to the subjects now by carelessly managing their alleged victimhood. "I'm not against the government studying this," he said, but certain parties "want to go at once at notify the patients. But you have a problem with a population that doesn't really understand these risks well. They will sense the fear around them, so you have some patients who are terrified because they don't fully understand the problem... By informing the patients, you risk harming them more than the effects of the radiation can do. [Interested parties] bring the media and say, 'Look at how these people are harmed,' when it was the fear invoked in them by the information" that caused the detrimental reaction.

Yet another set of radiation studies not covered by the government were some carried out at Vanderbilt University in the late 1940's. Ronald R. Price, PhD, at the department of Radiology, Medical Center, Vanderbilt University (Nashville, TN), covered the Vanderbilt studies of iron

absorption during pregnancy, which have also been lumped into the set of government radiation experiments in media reports. "The information will be based on the published [literature]," Dr. Price said. "This wasn't really a government related experiment. It was financed by the Nutrition Foundation and the State of Tennessee Health Service."

The Wages and Payoffs of Openness

To complicate matters for the ACHRE even more, some of the studies they must analyze were not only non-federal or non-governmental but were not even biomedical or involving humans at all. Their third sample case discussed at the May 18-19 meeting, the Green Run experiments, were done explicitly to test the flow of radioactive gases in the atmosphere, part of postwar classified AEC/military research into the effects of radioactive fallout and bomb debris. On December 2-3, 1949, a plant at Hanford, Washington, released off-gases from spent fuel that had been aged (stored for hot isotopes to decay) only 16 days instead of the usual 90, thus the name "green" run, since the spent fuel was younger. The released gases totaled about 27,800 curies, including 20,000 curies of xenon-133 and 7,800 curies of iodine-131. (A recent recalculation showed the amounts were probably 9,000-11,000 Ci of ^{131}I and about 16,000 Ci of ^{133}Xe.)

A November 1993 GAO report, "Examples of Post World War II Radiation Releases at U.S. Nuclear Sites," stated that a search through classified and nonclassified documents revealed no intentions of a field test of radiobiological effects on humans. But nuclear medicine physicians and others interested in the follow-up to the government's human radiation experiments may want to know the outcome of the research into Green Run, because ACHRE must deal with it, and the outcome will affect public relations concerning radiation. The Green Run experiments became an issue because, according to the GAO report, "the offsite populace was not forewarned of the event or made aware of it for decades. The test was also conducted despite less-than-optimal weather conditions, which limited the test results and may have exposed greater-than-expected numbers of the population to the radioactive cloud." Yet "test participants noted the release was considered to be well within the standards of the time for human exposure to radiation." Furthermore, the release was only a fraction of the estimated 45,000 Ci of iodine released per month at Hanford during 1945—a fact, along with the misjudged weather condition, complicating the assessment of the ethics of the experiment. "The then-existing local Hanford tolerance for continuous deposition on vegetation" was temporarily exceed in certain areas, the GAO report stated (Figure 2), but "it has not been determined whether the test exceeded present limits for off-site radiation doses and emissions." Similarly to the human radiation experiments, the ACHRE obviously must assess the ethics of an experiment conducted during an era of different ethics, methodology, assumptions, and knowledge; and as with all the other cases, it must evaluate one that has a set of intentions and outcomes that make it completely unique and incomparable to the others.

These new complexities, with their concomitant potential for misunderstanding and new mistrust among the public and mass media, are one side effect that comes from the Administration's campaign for openness. Granted, Secretary O'Leary reportedly read the *Albuquerque Tribune* reports before her December announcement that began the openness campaign. These experiments, being mostly in the published literature, have been discussed and reported on for years. But the campaign to disclose government files long sequestered from the public will inevitably release documents which will be hard for the public to assimilate or handle.

Addressing the National Press Club in Washington, May 18, Sec. O'Leary said that the process

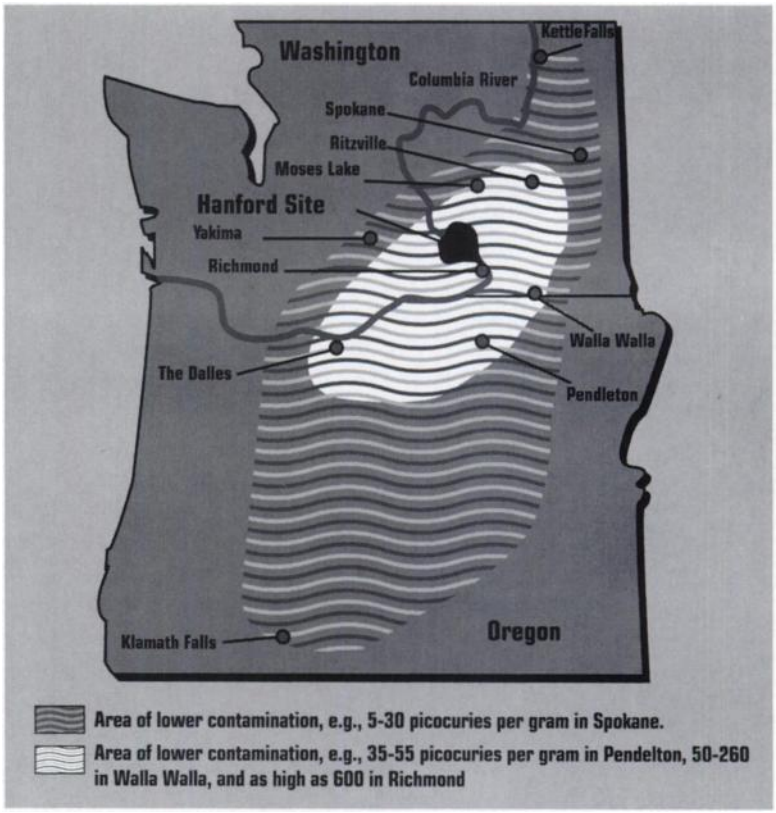


Figure 2. Levels of radioactive iodine found on vegetation in the Hanford area following the Green Run test.

is worth the effort. "It is more than the ends, it is the means," she said. "The department [DOE] and government suffers from a lack of public trust. People don't believe us when we say we can transport nuclear weapons waste... Lack of openness has hampered the work of brilliant scientists in national labs and prevents them from discussing research with international colleagues. Secrecy alone costs over one billion dollars. I recognize the importance of secrecy in protecting national interests. [But] we must rethink the balance between secrecy on the one hand and openness on the other." (See also *Newsbriefs*, P. 25N)

Dr. Donohoe sees the SNM panel as an important step in this public education process as concerns the human radiation experiments. "The REIR [Radiobiological Effects of Ionizing Radiation] committee is concerned that as patients approach the nuclear medicine community, we need to be able to educate the nuclear medicine community about what happened." Although this may generate yet another burden on an already overloaded community of physicians, Dr. Royal feels that, in light of the opportunity to ease public distrust, nuclear medicine should embrace this openness. "The nuclear medicine community should enthusiastically support the current Administration's efforts to tell the complete story of medical experiments on humans."

Lantz Miller

(Newsline will continue its four-part series on health care reform next month.)

US Investigators Contribute to the Silver Jubilee Meeting of the Society of Nuclear Medicine-India

THE SOCIETY OF NUCLEAR MEDICINE-India reached a landmark in its history with its Silver Jubilee meeting in New Delhi, December 14-18, 1993, in which many prominent US investigators participated. The local organizing committee, led by Dr. A. K. Padhy, welcomed the American participation and offered them eight plenary lecture slots in the scientific program. In keeping with a tradition, the delegation was organized by the Indo-American Society of Nuclear Medicine (IASNM) and led by its current president, Mathew Thakur. The delegation consisted of Drs. Steven Larson of Memorial Sloan-Kettering Center (New York, NY); Carol Marcus of Harbor-UCLA Medical Center (Torrance, CA); Lalitha Ramanna of Tucson Medical Center (Tucson, AZ); Suresh Srviastava of Brookhaven National Laboratories (Upton, NY); Mathew Thakur of Thomas Jefferson University Hospital (Philadelphia, PA); and Michael Welch of Washington University (St. Louis, MO). Additional presentations in continuing medical education sessions were made by Drs. G.V.S. Rayudu of Rush Medical Center (Chicago, IL) and G. Aurora of East Carolina University Medical Center (Greenville, NC). Scientific presentations were also made from groups at Roswell Park Institute, SUNY Buffalo, the University of Missouri, Columbia, and the University of Dallas.

Drs. Steven Larson, Carol Marcus, Michael Welch, Mathew Thakur, A.K. Basu (Chairman, SNM-India Organizing Committee), Lalitha Ramanna, Suresh Srivastava, and S.M. Sharma (Bombay)

Over the past 25 years, there has been steady and significant growth in nuclear medicine in India, as assessed by increased radionuclide procedures and availability of radiopharmaceuticals and the growing number of related equipment, now totaling 13 SPECT machines and about 60 gamma cameras. Indian nuclear medicine has gained a respectable image and spread its scope, not only in the public sector but also in private hospitals. Although General Electric and Siemans share the major equipment market, one local company, ECIL, has begun to market its gamma cameras at an affordable price with their own computer and software. This will promote the continued growth of nuclear medicine in India, where practicing physicians have accepted the fact that the specialty has an important role in patient management.