NEWSLINE

Medical Research Delayed As Brookhaven Grapples With Management Change

Aerial view of Brookhaven National Laboratory in Upton, NY.

Citing safety and health concerns, the Department of Energy (DOE) announced on May 1 that it was dismissing the nonprofit organization that has run Brookhaven National Laboratory (BNL) since the laboratory first opened 50 years ago. The announcement shocked the laboratory's contractor, Associated Universities, Inc. (AUI), who had held a press conference just three days earlier to announce the appointment of Lyle H. Schwartz, president of AUI, as interim director of Brookhaven. The DOE (which owns all of the National Laboratories) appointed John Wagoner, manager of the Richland Operations Office in Washington state, to oversee operations at Brookhaven for the DOE until a new manager was hired. Energy Secretary Federico F. Peña based his decision to terminate AUI's contract on a DOE report that found environmental, safety and health programs at Brookhaven were not a high priority. Specifically, the assessment alleged that Brookhaven scientists and managers believed that any funds spent on improvements in worker safety and environmental protection were funds that could have been spent on research. "The findings in this report and the ongoing problems here at Brookhaven are unacceptable," said Peña at the news conference held on May 1 at Brookhaven. "There need not—and will not—be a trade-off between award winning scientific research and environment, safety and health."

One of the major reasons for the dismissal of AUI was, in the DOE's opinion, its slow and inefficient response to an underground plume of water laced with low-level tritium that is believed to be leaking from the spent-fuel storage tank of Brookhaven's High-Flux Beam Reactor (HFBR). The reactor was shut down indefinitely in January, which has severely hampered the capability for research-level production of such medical isotopes as ^{117m}Sn, which is used for studies on bone cancer pain. "Many of our research projects involving HFBR-produced isotopes had to be stopped midstream," said Suresh Srivastava, PhD, a senior scientist and head of the radioisotope and radiopharmaceutical research division in the medical department at Brookhaven. "Although our highest priority projects have not come to a standstill, we've been slowed down tremendously."

Adding to Brookhaven's troubles, three separate safety incidents occurred in June prompting Peña to shut down all lab facilities during June 20-23. In the first incident, six workers were exposed to a small amount of ^{38}Cl while irradiating a sample of plastic wrap in preparation for an experiment. In the second incident, two workers were found to be contaminated with a negligible amount of ^{60}Co on their clothing. The third and latest incident occurred on June 20 when a construction worker was run over and killed by a payloader. (Neither the construction worker nor payloader operator worked for

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A Half-Century of Research at Brookhaven

This year marks Brookhaven National Laboratory's 50th anniversary. Nuclear medicine, as it is practiced today, was widely advanced by the discoveries of new radionuclides and development of new radiopharmaceuticals at Brookhaven. Here is a timeline of some important events:

1947	1950	1958	1961	1970
Brookhaven National Lab was founded and ground was broken for the Brookhaven Graphite Research Reactor.	The Graphite Research Reactor and the first hospital devoted to nuclear medicine open at Brookhaven.	Technetium-99m is discovered accidentally by Brookhaven researchers. The Medical Research Center opens.	The first order for a ^{99m}Tc generator produced at Brookhaven came from the Argonne Cancer Research Hospital.	The instant kit concept using Sn(+2) for preparing ^{99m}Tc radiopharmaceutical is developed and made available to industry.

first, with any available funds left over to be allocated for ^{99}Mo production. Based on DOE estimates, the SNM has proposed that $11 million be earmarked for these research programs.

These provisions, which are part of the larger Energy and Water Development Appropriations bill, are expected to be addressed by the full House and Senate over the next month.

Allied Health Funding, Title VII

The House Appropriations Subcommittee on Labor, Health and Human Services, Education and Related Agencies as well as the full House Appropriations Committee have forwarded their recommendations for the funding of the Allied Health Project Grants. The funding for Allied Health received an increase to $3.926 million and the Health Professions Training grants increased from $292.8 million to $306.5 million.

The House is expected to consider the bill this month with the Senate action expected shortly afterwards. The funding is then used to support grants from educational institutions for the training of allied health personnel such as nuclear medicine technologists.

The Clinton administration remains concerned about approving individual line items in the appropriations bills, such as allied health funding. Legislation was proposed last year that would have clustered all health professions training under one line item in the budget, then allowed staff at the Health Resources and Services Administration to make determinations about funding levels in each area.

This cluster approach is still being discussed now and the Society of Nuclear Medicine-Technologist Section (SNM-TS) has supported it. In testimony submitted by the Allied Health Roundtable, in which the SNM-TS participates, the group supported a cluster of allied health, rural health and geriatrics. These three groups would be clustered together under one line item, potentially creating an opportunity for more allied health funding in the future. This issue is still being debated, however, and it is unclear whether Congress will address this issue this year in spite of its continuing to appropriate funds based on individual line items.

—David Nichols is the director of the ACNP/SNM government relations office

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Brookhaven, but were working under an outside contractor on the Brookhaven site.) All Brookhaven employees attended safety seminars during the lab shutdown.

Public Pressure for Safety Measures

In one of his most highly visible acts since taking office in March, Peña's dismissal of AUI was based on a history of highly publicized incidents of environmental and safety lapses at Brookhaven. As cited in the DOE report, Brookhaven was declared a Superfund site in 1989. A mishap at one of the experimental stations near the reactor caused a small electrical fire in 1994 that caused a negligible amount of radiation to be released. Brookhaven's beam reactor has also been leaking a small amount of tritium into the groundwater on the site.

"We found multiple indications of safety taking a back seat to science," said Glenn Podonsky, DOE Deputy Assistant Secretary for Oversight whose department conducted the evaluation. The report criticized Brookhaven for not dealing with the tritium leak as a top priority when tritium was first detected in a monitoring well south of the reactor in 1986. In 1992, an engineering analysis recommended building three additional wells further south of the reactor. These wells were not installed, according to the report, for reasons that are unknown. "In 1994, BNL made a commitment to the Suffolk County Department of Health Services...to install two monitoring wells south of the HFBR, but did not follow through," said the report. The next year, Brookhaven managers decided to delay installation of the wells because of funding reductions.

The report also criticized the DOE for not following up on the tritium leak. "No one from the Department validated that the monitoring wells had been built," said Podonsky. "There was a calamity of errors that took place, and our report stressed that improvement is needed within the DOE in terms of accountability for the managers that the DOE goes into contract with."

The tritium plume currently stretches 1.5 miles south of the reactor and contains a total of 10 curies of tritium, according to Kara Villamil, a press officer at Brookhaven. Since mid-May, water has been pumping into the southern-most tip of the plume, which has diluted the concentration of tritium to 6000 picocuries/liter. (The EPA's drinking water limit is 20,000 picocuries/liter.) The diluted tritium will then be pumped back to a recharge basin, where it will inch southward again, winding up in the southern-most site in 19 years. By that time, the tritium, with a half-life of 12.3 years, will have a concentration of 2000 picocuries/liter. The process, called the Tritium Plume Recovery Plan, has been approved by the Suffolk County and New York State Departments of Health and the EPA. All three agencies are in agreement that the plume poses no threat to the drinking water wells serving the nearby community, said Villamil.

Senator Alfonse D'Amato (R-NY) has promised to commit $6 million in Brookhaven funds to hook up houses closest to the plume to the public water supply. "This funding completely ignores the fact that the tritium has not left this site," said Mona Rowe, a spokesperson for Brookhaven. Senator D'Amato and other politicians are being swayed by a small, but vocal, group of environmental and community activists who have been picketing the reactor site. Rowe said anywhere from 2 to 80 protestors have been gathering on a regular basis to lobby for the permanent closure of the reactor.

Delays in Nuclear Medicine Research

The climate of public discontent and the shutdown of the reactor has interrupted a large body of research involving radionuclides used in nuclear medicine, as well as projects in other fields. "We were supposed to be celebrating Brookhaven's 50th Anniversary this year—which is particularly relevant to nuclear medicine since over 80% of radioisotopes used in nuclear

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medicine were developed at Brookhaven," said Srivastava. "Instead we're dealing with delays and are burdened with new regulations."

Since the DOE brought in John Wagoner, manager of the Richland Operations Office in Washington state, to serve as a transition manager of the Brookhaven Group, paperwork requirements have increased. "We now have increasing layers of approvals to go through before we can embark on a new experiment," said Srivastava. "There have been certain occasions recently where we were not been able to predict with absolute certainty the dosimetry of new radioisotopes which were to be produced for the first time. We were informed that such experiments may have to be delayed or abandoned pending such information."

Even more troubling have been the delays in ongoing research projects. For instance, Brookhaven is coordinating a randomized multicenter trial of ^{117m}Sn-DPTA for the treatment of bone cancer pain. In order to produce the radiopharmaceutical, Brookhaven must ship the raw material to Oak Ridge National Laboratory in Oak Ridge, Tennessee for irradiation in Oak Ridge's nuclear reactor. Oak Ridge then ships the material back to Brookhaven for processing. Other researchers are performing preliminary studies to see if ^{117m}Sn-DPTA could be a potential therapy for bone cancer, but they have been slowed considerably due to the logistics of shipping samples in a cycle that usually takes about three weeks.

Although Oak Ridge is also producing other radionuclides for preliminary stages of research, Srivastava said that the coordination of shipments is not conducive to preliminary studies where small samples of isotopes are produced, modified and produced again. Another study was planned to evaluate the use of ^{47}Sc radioimmunotherapy, "but this effort has practically stopped now," said Srivastava. Brookhaven was also the sole producer of some radioisotopes such as ^{195m}Pt and ^{127}Xe, "which have now virtually disappeared from the market," he said.

The reactor shutdown has frustrated the hope that Brookhaven could become a leader among the national labs for radioisotope production and research. Last December, Brookhaven's Isotope Distribution Office sent out a letter to universities, research centers and industrial users informing them that five radioisotopes would be offered routinely to be produced in the HFBR, but the solicitation was rescinded three weeks later when the reactor was shut down.

Furthermore, the DOE had decided three years ago to upgrade Brookhaven's linear accelerator after the proposed $100 million National Biomedical Tracer Facility project was abandoned by Congress. This three-year upgrade was completed last September at a cost of $6 million and was supposed to serve (along with the beam reactor) as the centerpiece for the National Isotope Center to be formed at Brookhaven. A national advisory committee was formed to prioritize the list of new radioisotopes for research. Until the fate of the Brookhaven reactor is decided, however, many routine as well as new isotopes may have to be put on hold, according to Srivastava.

The recent management shake-up coupled with the reactor closure has left many scientists uncertain of their future at Brookhaven. "We're very concerned that some top scientists will leave and that the new management will take the attitude that if we're doing good science we can't be doing it safely," said Joanna S. Fowler, PhD, a senior chemist at Brookhaven and winner of the 1997 Paul C. Aebersold Award for her research in PET brain imaging. When asked about staff turnover, Martha Krebs, PhD, Director of the Office of Energy Research for the DOE, said, "I want to encourage our scientists to stick it out and realize that Brookhaven will continue on with its important scientific programs."

Using Research Funds for Cleanup

The most immediate concern is where the money will come from to pay for the $21 million clean up effort. "There's no question that some of the costs for the tritium recovery have already come out of energy research funding," said Krebs. "The Department has been trying to identify funds so that research programs will be nominally impacted." One of the possibilities could be to use the $25 to $30 million that was set aside by Congress to build the superconducting supercollider, which was never built. "Unfortunately, Congress has not acted on our proposal and does not appear to be interested," said Krebs.

Unless an alternate source of funding is found, money will be diverted from research funds. In terms of the current impact, Krebs said that she has reduced the amount of materials and shipments that will be available to researchers through the end of this year and has put some research projects on hold. "Our highest priority right now is to maintain our current staff of scientists at Brookhaven," said Krebs. "We have no plans for staff reductions at this point."

The DOE has not yet made a decision on when or whether it will re-open the 32-year-old reactor. Discussions are ongoing,

DOE to Evaluate All National Labs

In the DOE report issued by its Office of Oversight, the Department seems to be singling out Brookhaven National Lab for harsh criticism. In reality, the Office of Oversight has been undertaking a review of all 17 Multi-Program National Laboratories as well as its 15 Dedicated Laboratories. (All 32 federally-owned labs are under the jurisdiction of the DOE and, unlike privately-owned reactors, are not subject to regulation by the Nuclear Regulatory Commission.) "In the two and a half years since our office was founded, we have been looking at the managers at all the labs to see if there is a strong sound system in place for dealing with problems," said Glenn Podonsky, Deputy Assistant Secretary for Oversight. Brookhaven was one of the first labs to undergo review because of the problems with the tritium plume. Los Alamos National Lab in New Mexico has also been evaluated and was found to have extensive safety problems related to numerous accidents. "We found a very similar situation to what we found at Brookhaven, except that Los Alamos had even more hazards," said Podonsky. He said safety problems also have been found at several other laboratories. The Office of Oversight is currently reviewing Sandia National Lab in Albuquerque, NM and Lawrence Livermore National Lab in Berkeley, CA and plans to have all facilities reviewed by early next year.

but the reactor will be closed at least until the end of this year and probably until the public concerns over the tritium plume are put to rest. "Secretary Peña will make a decision on the reactor by December after consulting with the scientific and local community," said Krebs. "If we decide to propose restarting the reactor, there's no question that we will have to do expensive upgrades first." She said the cost for the upgrades has not yet been determined, nor has the source for the funding.

As of presstime, the DOE's Office of Energy Research had just released an action plan addressing the Oversight Report on Brookhaven. The plan included the appointment of a DOE associate director of environment, safety and health who would report to Krebs. The plan also recommended broadening the DOE's role as landlord of Brookhaven to ensure that decisions regarding the safety of the Lab are "thoughtful, timely, and part of the everyday work performed."

The DOE also issued a request for prospective managers to file contract bids and stated that the Department would only consider a bid from a nonprofit organization such as a university. A new manager for Brookhaven is expected to be in place by November 1.

—Deborah Kotz

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50 Years of Nuclear Medicine

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the $^{99}Mo/^{99m}Tc$ parent/daughter pair followed similar chemistry to $^{132}Te/^{132}I$ pair and that the aluminum oxide generator could be used with only minor modification as a source of ^{99m}Tc. Therefore, the ^{99m}Tc, with its 6-hour half-life, could still be shipped to user institutions around the world with adequate time for use.

Even with production and distribution of the radionuclide made possible by the generator, the usefulness of ^{99m}Tc was not recognized early on. In fact, in 1958, the AEC decided against preparing a patent application on the ^{99m}Tc separation process on the grounds that they could foresee no use for it.

Technetium-99m was used briefly by Brookhaven in 1960 to study thyroid physiology. Then in 1961, Argonne Cancer Research Hospital ordered the first ^{99m}Tc generator for tracer studies in the body. Word about ^{99m}Tc spread rapidly, and institutions in this country and abroad began sending in orders for generators. Finally, the demand grew so great that in 1966, Brookhaven turned generator production and distribution over to commercial suppliers.

Today, more than 85% of the 13 million nuclear medicine procedures performed annually in the U.S. involve ^{99m}Tc. Several characteristics make ^{99m}Tc ideal for clinical work. For example, it emits a single 140-keV gamma ray with no accompanying beta particle, which minimizes radiation exposure to the body. In addition, its gamma energy is well-suited for use with scintillation cameras. Another advantage is that ^{99m}Tc has a short half-life, six hours, which results in a low radiation dose to the patient. However, the short half-life makes radiopharmaceutical transporting and patient scheduling more difficult.

During the 1970s, Brookhaven introduced the first of several easy-to-use kits for labeling various compounds with ^{99m}Tc. An improved version, developed in the 1980s, simplifies the labeling operation and improves the incorporation of ^{99m}Tc into cells. A kit for labeling red blood cells was approved for commercial distribution in 1991. In 1994 alone, the kit formulation was used in more than 200,000 patients to diagnose internal bleeding and cardiovascular problems.

Current Research on Bone Cancer Pain

Since the late 1980s, Brookhaven researchers, in collaboration with the University Medical Center at Stony Brook in New York and the Veterans Affairs Medical Center in Tucson, AZ, have been conducting ^{117m}Sn-DTPA studies on bone cancer patients and have found that it offers substantial pain relief without the severe sedation of conventional drugs.

In clinical trials, about 80% of the 40 bone cancer patients treated with a single dose of ^{117m}Sn-DTPA experienced substantial relief from their pain. Some patients were completely free of pain for as long as one year. When given to patients intravenously, ^{117m}Sn-DTPA has no sedative effect and localizes preferentially in bone rather than in normal soft tissue or bone marrow. Moreover, ^{117m}Sn emits electrons that have a very short range in tissue, so bone tumors receive up to 50 times more dose than radiation-sensitive bone marrow. Thus, ^{117m}Sn-DTPA does not suppress the bone marrow's production of white blood cells or platelets, thereby retaining the body's ability to fight infection and clot blood and eliminating another major side effect of other radiopharmaceuticals used for bone pain palliation.

Since the results from the clinical trial were promising, Diatride Inc., located in Londonderry, NH, has decided to sponsor large-scale clinical trials set to begin this year involving major medical centers worldwide. In these randomized double-blind trials, patients will be given either a single therapeutic dose of ^{117m}Sn-DTPA or one of the other radiopharmaceutical products already on the market to relieve bone cancer pain. A separate trial conducted jointly by Brookhaven and Stony Brook will use higher doses of the tin compound to see if increasing the doses leads to a better response rate.

As Brookhaven scientists look back on the past 50 years, they can see how far they have advanced the field of nuclear medicine. However, they can also look ahead to see what they have yet to accomplish. Over the next 50 years, they hope to continue the commitment to nuclear medicine that has enabled the medical specialty to become indispensable to the practice of medicine.

—Excerpted from articles written by the staff in the Public Affairs Office at Brookhaven National Laboratory in Upton, New York.