Questions About the Future of DOE Isotope Production and Research

UNDER THE U.S. ENERGY Department's 1993 Budget proposal, big-ticket items like the Super Conducting Super Collider and human genome research are squeezing the funds available for nuclear medicine research in DOE's Medical Applications Program. Adding to the anxieties of the nuclear medicine community is a pattern of dwindling support for isotope production and research within DOE. Responding to these circumstances in testimony on the budget proposal to a Congressional subcommittee, The Society of Nuclear Medicine and the American College of Nuclear Physicians hammered at one urgent issue: the need for a particle accelerator facility dedicated to the production of radioisotopes for use in medicine and research.

National Accelerator Facility

On behalf of SNM and ACNP, Richard C. Reba, MD told lawmakers on March 31, 1992 of a "crisis in the availability of stable and radioisotopes." As a solution he urged the members of the House of Representatives Energy and Water Development Subcommittee of the Committee on Appropriations to support the establishment of an ambitious particle accelerator and biomedical research and teaching facility—an institution detailed in a 1991 planning and feasibility study produced by SNM and ACNP with the support of an Energy Department grant. The proposed facility has come to be known as the NBTF, or national biomedical tracer facility.

Since funding the initial NBTF report, the Energy Department has expressed little interest in taking on the expense of building and running the accelerator. "The DOE does not consider the NBTF a priority," Dr. Reba stated flatly in his testimony. "Unfortunately, it will be an emergency issue within the next two to four years," once physics research accelerators at Brookhaven National Lab and Los Alamos National Laboratory cease production. "Already we are without a reliable source of materials, but once these lab facilities shut down, there will be nothing," Dr. Reba said.

Estimating that an NBTF would take at least four years to build, Dr. Reba called upon Congress to authorize emergency funding of $2 million for a formal "request for proposal" (RFP) process to select a site for the NBTF before June.

Despite the inertia of DOE, several groups attracted to the NBTF have drafted proposals. "Interest from the community has grown by leaps and bounds," Dr. Reba said. One interested institution, Purdue University in West Lafayette, Indiana, invited nuclear medicine researchers and representatives from the radiopharmaceutical industry and the DOE to a workshop in April to define expectations for the NBTF, such as which isotopes to produce. (Although the NBTF plan calls for production of research isotopes, not radiopharmaceuticals, members of SNM's NBTF task force once again tried to lay to rest persistent notions that the facility would produce products in competition with industry.)

Another group that has expressed interest in the NBTF is the North Texas Research Institute (NTRI), a non-profit corporation affiliated with the University of North Texas in Denton. The North Texas group ruffled a few feathers with its April 1991 proposal, which suggested that NTRI could build a tracer facility

Budget Testimony of SNM and ACNP

The Society of Nuclear Medicine and the American College of Nuclear Physicians testified before the House Energy and Water Development Subcommittee of the Committee an Appropriations on March 31, 1992. The following is excerpted from that testimony on the DOE fiscal 1993 budget:

The declining financial support of research exacerbates the problem of the lack of national resources to produce radioisotopes. It is expected that DOE (Department of Energy) labs will cease to produce accelerator isotopes within the next five years. If the U.S. is to maintain a continuous supply of isotopes, the NBTF (national biomedical tracer facility) must be operational by 1997. To comply with this schedule, design, engineering, and siting must begin in 1993. Therefore, we urge the Congress to include $2 million in fiscal year 1993 appropriations for a request for proposal (RFP) to initiate siting the NBTF.

The Administration's fiscal 1993 budget proposal seeks $39,312,000 for the DOE's Medical Applications Program. . .Our total recommended budget request for fiscal year 1992 is $50 million for the Medical Applications Program, $2 million in emergency funding to be used immediately for an RFP to identify a site for the NBTF, and. . .and estimated $100 million for construction to be appropriated in fiscal 1993.

The patients who have been served by nuclear medicine, in the United States and in most other countries around the world, have benefitted from the support of the Atomic Energy Commission (AEC) and the DOE. The future of nuclear medicine is contingent upon the production and availability of stable and radioactive isotopes for both clinical and research purposes. For the United States to retain its prominent role in the application of radioactive materials in medicine, it is essential that this nation provide a reliable source and supply of radioisotopes. ■

without the government support sought by SNM and ACNP. The NTRI plan called for private investment, long-term loans, and industrial development bonds, and maintained that the facility could generate returns on investments as early as 1995. Critics say that the NTRI proposal is feasible only if the Energy Department commits to purchasing substantial quantities of isotopes and providing grants for research to be conducted at the facility, which would amount to government support. The project has not attracted enough investors to get off the ground.

In the SNM and ACNP testimony to Congress, Dr. Reba stated pointedly that the NBTF "cannot fulfill its [education and research] mission without some assistance from the federal government ...The NBTF will not be a money maker. Therefore, it would be highly unlikely that one could generate venture capital to support construction unless it were to become solely a production facility."

"We envision this to be a national resource that will provide education and respond to the changing and unpredictable radioisotope requirements of researchers," Dr. Reba told *Newsline*. "I'm hopeful we'll get it in this year's budget—I think it's realistic."

Molybdenum-99

The lack of a U.S. supplier of molybdenum-99 (^{99}Mo) continues to trouble nuclear medicine professionals in this country. The DOE is taking steps to produce radioisotopes of molybdenum, iodine, and xenon in a reactor at the Los Alamos National Laboratory—despite DuPont-Merck Pharmaceuticals Co.'s recent agreement to buy ^{99}Mo exclusively from Nordion International of Canada. Radiopharmaceutical companies use ^{99}Mo to make technetium-99m generators used in hospitals for an estimated 80% of all nuclear medicine procedures.

The DOE plan had originally required some funding and guarantees of substantial ^{99}Mo purchases from the big three radiopharmaceutical makers—Mallinckrodt Medical, Inc., Medi-Physics, Inc., and DuPont. Then last October, Mallinckrodt announced plans to produce the isotope at a reactor in The Netherlands (see Newsline, December 1991, p.13). Now that DuPont has withdrawn, the criticism that the DOE asked for too much from industry seems to have been borne out.

Although Donald E. Erb, director of DOE's Isotope Production and Distribution Program, says he "would have been much more comfortable with a commitment from industry," the DOE is proceeding with modifications to the reactor core at the Omega West Reactor at Los Alamos, New Mexico. Mr. Erb estimates that the first test batches of ^{99}Mo will be ready for evaluation by the end of this year, and ^{125}I even sooner.

Isotec Petition

The Energy Department's Isotope Production and Distribution Program, has in the meantime, unequivocally rejected the petition of a company that had asked the DOE to quit the business of selling several stable isotopes, including stable forms of carbon, nitrogen, and oxygen. Granting the petition would have given the company, Isotec, Inc. of Miamisburg, Ohio, a virtual monopoly on a number of markets in the U.S. and that prospect caused widespread alarm among scientists from a variety of disciplines whose research depends on stable isotopes.

Within nuclear medicine, many users of positron emission tomography (PET) in particular were concerned due to their complete dependence on Isotec for oxygen-18 (^{18}O), the cyclotron target material (used to make the positron-emitting isotope fluorine-18) that has been in short supply for over two years. The DOE discontinued production of ^{18}O water at the end of 1989.

The rejection of Isotec's petition became final on April 18, despite pleas by Isotec to extend the deadline. For the most part, researchers seem pleased with The Energy Department's stance. "I hope it means that the DOE has plans to begin production of ^{18}O again," says

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R. Edward Coleman, MD, director of nuclear medicine and professor of radiology at Duke University Medical Center, Durham, North Carolina. "We need ^{18}O and having a single source is always problematic...[Isotec] is a single source that has been unable to meet our needs."

In response to such remarks, Isotec's president, Vincent L. Avona says, "The government went out of the ^{18}O business, not Isotec, so why is everybody pointing their finger at us." Isotec filed its petition in July 1990, and the DOE posted a request for comments on the petition in the *Federal Register* in September 1991, spurring a flood of letters of protest from the research community (see *Newsline*, December 1991, p. 15N).

The DOE published a sharply worded and exhaustive denial of Isotec's petition in the *Federal Register* on March 2, 1992. The DOE maintains that Isotec could not meet market demand for many of the isotopes and that if DOE agreed to the petition, the lack of competition would result in price increases prohibitive of scientific and medical research. The notice went on at great length citing claims of various scientists that Isotec's prices have proven to be "considerably higher" than DOE's, and that, in some instances, the quality of Isotec's products has been inferior to the DOE.

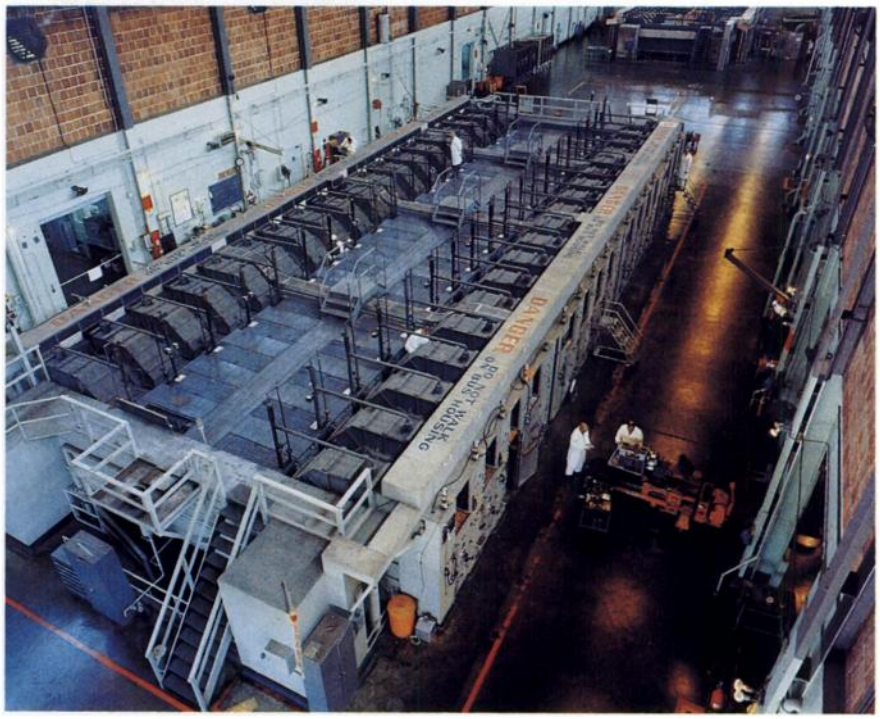
Isotec's Mr. Avona scoffs at these claims, calling them irrelevant, false and misleading. He says Isotec's ^{18}O water, for example, is of higher quality and freer of contaminants than that formerly sold through DOE's Mound Laboratories. He maintains that prices for ^{18}O water are reasonable. As for the supply of ^{18}O, Mr. Avona says, "Yes, there is indeed a shortage, but Isotec has been working very hard for the last two years to improve our production capacity. We made the decision to [build new enrichment plants] after we heard DOE closed down the Los Alamos facility."

Investigators at PET centers around the world are becoming increasingly frustrated with the lack of ^{18}O water. "I think it's going to hit us pretty badly—we have a lot of studies backed up," says PET investigator Jogeshwar Mukherjee, PhD, of the University of Chicago, where some 400 PET studies are performed per year. Dr. Mukherjee says he was told by Isotec to expect to wait six months for delivery of an order of ^{18}O water placed in April.

Isotec's Mr. Avona says that part of the blame for the ^{18}O dilemma lies with the institutions that setup PET centers. "Nobody really planned ahead," he says, "They would go ahead and buy a multimillion dollar facility, and nobody even came to us asking about the availability of ^{18}O water." Looking back, however, he concedes that the timing of the petition his company filed "was wrong—we didn't realize the demand [for ^{18}O] would be so high."

The emergence of new PET centers is just one reason for the growing demand for ^{18}O; the isotope is used as a tracer in physiology and other research. Isotec sells about a third of its ^{18}O for a research application that the company declines to disclose.

Whether the DOE will produce ^{18}O again is uncertain. The Energy Department's plans to lease the cryogenic distillation columns at Los Alamos National Laboratory to a private sector firm have stalled. According to industry sources, the terms offered by DOE failed to attract any serious interest.



The calutrons for enriching stable isotopes at Oak Ridge National Lab have been shut down since August 1991 due to lack of funds.

Despite the shortage, Isotec stridently objects to the re-entry of DOE in the ^{18}O market. Mr. Avona defends this stance by saying that his company will be able to meet the demand for ^{18}O. He points out that the company has opened a new cryogenic distillation plant in Ohio, and that Yeda of Israel is expected to begin selling ^{18}O water in North America again.

Isotec requested DOE withdrawal based on a 1965 Atomic Energy Commission (AEC) document that outlines a policy against government competition with the private sector. Much of the petition focused on the commercially valuable stable isotope helium-3 (^{3}He). Isotec got its start in 1972 by purchasing ^{3}He in bulk from the DOE and selling it at a profit to a variety of industries. The company went on to build plants to enrich stable isotopes.

Over the past ten years, Isotec has with some success plied the Energy Department with requests for withdrawal from marketing various isotopes. Despite the DOE's decision to reject the most recent petition, Mr. Avona says his company plans to pursue their case, but doesn't specify how. "I say let the private sector make the [isotopes] that are in demand in bulk quantities," he says, "and let the government do the ones that are research curiosities."

Oak Ridge Calutrons

Herein lies the dilemma. Under pressure to manage isotope production costs, Congress in 1989 made a one-time appropriation of $16 million for a "revolving fund" that would be replenished by sales of isotopes. Under this arrangement, the DOE's Office of Isotope Production and Distribution has to make enough money on isotope sales to cover its costs. Scientists argue that if the DOE were to withdraw from the sale of isotopes that are in demand in bulk quantities, it wouldn't have the money to produce scientifically important, but commercially unprofitable isotopes.

A recent report by Joe G. Tracy, manager of the isotope enrichment facility

at Oak Ridge National Laboratory in Tennessee put it this way: "Since the revolving fund must be self-sufficient . . . R&D activities are minimized and efforts are focused on those aspects of the program that provide revenue. Consequently, much of the technical expertise has been, and is being, lost."

From the point of view of Isotec, a company in direct competition with Oak Ridge, Mr. Avona complains that tax dollars are being used to unfairly subsidize the DOE's isotope production office. "The $16 million they have wouldn't even begin to cover the costs at the six or seven facilities where they produce isotopes," he says.

The Oak Ridge calutrons, the sole producer of many stable isotopes in the U.S., have been shut down since August 1991 due to lack of funds. Over 1000 of these electromagnetic isotope separation devices, also called high-current mass spectrometers, were built in the early 1940s for the enrichment of uranium-235 to be used in making the first atomic bomb. Only 39 calutrons remain operational.

The plight of the Oak Ridge calutrons was among the topics discussed at a closed-door workshop, held in Washington in February by the National Research Council's committee on nuclear and radiochemistry. The committee began looking last year into reports among nuclear chemists of isotope shortages and quickly realized that the problem is affecting a broad range of scientific disciplines. Workshop participants included nuclear physicians, earth scientists, nuclear chemists, physicists, physiologists, members of Congressional staff, and the DOE. The long-term outcome of the meeting is likely to be a formal study, which would take one to two years to complete and still awaits the go-ahead of the National Research Council.

Workshop participants discussed the possibility of getting the National Research Council to use its clout in Washington to muster funding for the Oak Ridge calutrons, if only to prevent the DOE from dismantling the electromagnetic enrichment facility altogether. According to Richard L. Hahn, PhD, chairman of the Council's nuclear and radiochemistry committee, the group is "still toying with a few ideas" on how to support the Oak Ridge isotope laboratories.

Competition from the countries of the former Soviet Union is one reason why the calutrons were idled—the Russians are reportedly peddling stable isotopes at prices well below those of Oak Ridge, which is still selling isotopes out of a large inventory. "We won't have a shortage of critically important isotopes unless the Soviet supply is interrupted," says DOE's Mr. Erb. The prospect of future dependence on a foreign government troubles many scientists as much or more than dependence on private sector companies. They believe that government support of isotope production is in the national interest and fear what Isotec's Mr. Avona predicts: "In the long run," the pugnacious executive says, "either Isotec will put [the DOE] out of business or the [former] Soviet Union will."

J. Rojas-Burke

FFTF On Standby

The Energy Department ordered a halt to activities at the Fast Flux Test Facility (FFTF) reactor on April 1, leaving uncertain the fate of the reactor and several medical isotope projects underway there. The reactor, located at DOE's Hanford Reservation near Richland, Washington, is now on "standby" status, meaning that temperature levels and all plant safety systems are being maintained and coolant is still circulating. But under current plans, the plant will remain on standby until at least 1996, and DOE officials have not come up with an alternative reactor in which to complete the experimental packages started at FFTF.

Among the packages are targets for making tungsten-188 and actineum-227, both of which researchers have been developing as anti-tumor agents. Another isotope under production, gadolineum-153, is used as a source in bone densitometers and is in short supply around the world. "We have a real problem," says Robert E. Schenter, PhD, fellow scientist in the isotopes program of Westinghouse Hanford Company, which operates FFTF for DOE. Dr. Schenter says the DOE has no other reactor ready to complete the irradiation of these targets, which are now sitting in the FFTF reactor and decaying.

Of all the consequences of the decision to idle the FFTF, Dr. Shenter says that the potential loss of expertise in medical isotope production is probably the most irreversible. "If we wait four years, the staff are going to all be gone," he says. FFTF personnel have been reassigned to other jobs. Dr. Schenter had devoted all of his time to medical isotope programs and is now working entirely on waste management.

Energy Secretary James Watkins has indicated that the FFTF is being kept on standby because it might be needed later to produce plutonium-238 used for power generators in space probes. The current DOE source of Pu-238, the K-Reactor at the Savannah River Plant, may not remain operational much longer.

The DOE sought to close the FFTF two years ago but Congress intervened and Washington Governer Booth Gardner began a campaign to raise funding from outside investors. Japanese sources had pledged about $8 million, and German sources at least $20 million, but the DOE decided the support wasn't adequate. The operating budget of FFTF is about $80 million.

In a letter of objection to Energy Secretary Watkins, the entire Congressional delegation of the state of Washington maintains that the "unwillingness of the [Energy] Department to engage in serious negotiations with potential partners" is the "stumbling block" that prevented the fund-raising campaign from succeeding. The lawmakers continue to pressure the DOE to reconsider the decision to idle the FFTF and call for funding to be re-established in the fiscal 1993 budget. "Either we're going to turn it around this year or it's dead," says Dr. Schenter. "I'm optimistic that were going to get it running again."