

Isotope program expands activities

To meet the growing demand for isotopes and lessen dependence on foreign sources, the Department of Energy has been realigning its capabilities and connecting with universities.

The US isotope program gets a healthy dose of kudos in a recent report by the Nuclear Science Advisory Committee Isotopes Subcommittee (NSACI). A key change in the program since it moved six years ago within DOE from the Office of Nuclear Energy to the nuclear physics program in the Office of Science is that it now has a research component. The report, *Meeting Isotope Needs and Capturing Opportunities for the Future*, recommends doubling annual federal funding for the program to nearly \$40 million to cover the research and infrastructure needs that NSACI sets out for 2016–25. The program also brings in roughly \$35 million a year in isotope sales; that money goes back into producing isotopes.

Isotopes are used in many areas: medicine, energy, oil and gas drilling, border monitoring and other national security applications, fundamental nuclear physics, archaeology, and more. The isotope program has the job of meeting demand for and overseeing the distribution of both stable and radioactive isotopes that are in short supply in the US; excluded are molybdenum-99, plutonium-238, and other isotopes that have a weapons or proliferation connec-

tion. The program's mission includes developing new and better ways to produce more types and larger quantities of isotopes. Another goal is to train young scientists to do R&D on isotopes.

Filling a gap

At DOE national laboratories, isotope production is largely parasitic on machines that have other missions. The isotope program oversees production at two accelerators and two reactors—at Los Alamos and Brookhaven and at Idaho and Oak Ridge National Laboratories, respectively. Isotope processing takes place at additional DOE sites. And the program has begun working closely with universities—including funding infrastructure and offering competitive research grants—to take advantage of niche capabilities, aid in training scientists, and more effectively distribute short-lived isotopes.

Under the Office of Nuclear Energy, the isotopes program “was pure production, but it's difficult to meet the needs of the community if you don't have a means to invest in R&D,” says DOE's Jehanne Gillo, who directs the program. She and her team have turned it “upside down,” she says. “We com-

pletely changed the management organization. We have greatly increased the portfolio of isotopes produced as well as the number of sites. We have changed pricing, introduced peer review into all program activities. We have improved communication with stakeholders—we hold big meetings twice a year and coordinate among the dozens of federal agencies that use isotopes. We have created a virtual isotope center for the sales of isotopes and to serve as a customer interface—if you want an isotope, go to the website. We created a research program. We are bringing in the universities and working with them. It's a very different program now.”

Continues Gillo, “It's a small program, with a small congressional appropriation, but the impact to the nation is large. We are filling a gap, often in response to an unforeseen change in demand, or a foreign supplier that has changed its supply strategy, or a lot of sudden interest in some isotope. The program often operates in crisis mode.” One focus, she says, “is to mitigate dependence on foreign sources” of isotopes.

Dealing with metastasis

Although molybdenum-99 is not under the isotope program, the shortage of the isotope, whose decay daughter technetium-99m is used in medical imaging, prompted the DOE isotope program to support research that has turned out to be applicable for new molybdenum-99 production methods and to increase production of strontium-82 as an alternative treatment. (See PHYSICS TODAY, May 2008, page 22.)

“The biggest problem in cancer therapy today is trying to deal with metastatic disease,” says Scott Wilbur, a radiation oncology professor at the University of Washington. Alpha emitters and theranostics are two developments that may help. Alpha particles travel only a short distance and damage cells beyond repair, says Wilbur. “If you have a hit with an alpha, the cell will die. It's a big plus, but also a big minus. Targeting is the key.” Clinical studies using actinium-225 to treat leukemia and lymphoma are ongoing, and similar studies with astatine-211 are slated to start next year, he says.



A researcher handles radioactive americium-241 at Los Alamos National Laboratory, where domestic production capability is being developed. The isotope is used in home smoke alarms and oil exploration.

In theranostics, an isotope is attached to a carrier such as an antibody, peptide, or small molecule and dispatched to cancerous tissue. If it binds—as determined by imaging—then the diagnostic isotope is replaced by one that will zap the cancer. “Does the antibody make it to the tumor? You test to see if the target therapy works,” says Suzanne Lapi, a radiochemist at Washington University in St. Louis. Theranostics holds promise for personalizing cancer treatment. “The availability of more isotopes is making this idea more applicable,” Lapi says.

Stabilizing the market

Helium-3, which is obtained from weapons-related tritium and used both as a cooling agent by research scientists and as a detection tool for radioactive sources at borders, is an example of a stable isotope. The isotope program doesn’t own the helium reserves, but it pays for the extraction and is responsible for selling the isotope. Another example is lithium-7, an additive in cooling circuits for pressurized-water fission reactors. “We manage the nation’s inventory of stable isotopes,” says Gillo.

For decades, many of the nation’s stable isotopes were made at Oak Ridge with calutrons—mass spectrometers



Lithium-7 hydroxide is purified by the Department of Energy’s isotope program. The country’s nuclear power plants annually use 500 kg of the stable isotope; the container here is about 50 cm across. Inset: A vial of actinium-225 is prepared for shipment to cancer researchers. The blue glow is fluorescence due to stimulation from the radioactive decay of the isotope.

for separating isotopes of uranium—left over from World War II bomb production, says NSACI chair Lawrence Cardman of the Thomas Jefferson National Accelerator Facility. “It turns out that calutrons are expensive to operate and they have been shut down for over a decade.”

According to the NSACI report, “A critical need for the U.S. is to have in place a program that can produce high-enrichment [pure] stable isotopes.” Stable isotopes are made at Oak Ridge with a separator that was built in response to recommendations made in 2009; that separator, which combines

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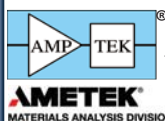
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electromagnetic and centrifuge technologies, is being upgraded to increase production by a factor of 10. NSACI also recommends that a second separator for radioactive isotopes be built.

Russia is the only supplier of americium-241, which is used in well logging to identify sites for drilling oil and gas. An industry consortium "has provided the isotope program with money to develop a method of producing americium-241 here [in the US]. We're developing it at Los Alamos," says Gillo. Similarly for lithium-7, she says, "we are dependent on the Chinese and Russian supplies. But we have been building up a reserve." That reserve is coming in handy, she says, because lithium is being sold on an emergency basis due to "a hiccup in the international market."

Isotope infrastructure

Isotope production in the US should be bolstered in other ways, too, the report says. In particular, facilities at Los Alamos and Brookhaven should be upgraded to higher energy and intensity, and the Brookhaven Linac Isotope Producer should get a second target station. NSACI also recommends that the isotope program invest in infrastructure to harvest isotopes at the Facility for Rare Isotope Beams (FRIB) under construction at Michigan State University. (See PHYSICS TODAY, February 2015, page 23.) "FRIB will have a fast development time for any new isotope of interest," says Brad Sherrill, associate director of the facility. The focus at FRIB will be nuclear physics and astrophysics. But a combination of chemical and physical techniques could harvest isotopes not needed by the main experiments. The equipment to piggyback on FRIB would cost around \$10 million, says Sherrill.

The report recommends R&D on new methods for making isotopes, including new target materials and electron accelerators. The photons emitted by accelerated electrons "could produce isotopes of great interest, such as molybdenum-99 for cardiac imaging and copper-67 to be paired with copper-64 for theranostic treatment," says Cardman. "It hasn't been done because it hasn't been cost-effective." But advances in high-intensity sources of photons give the approach new potential, he says. "The problem with electron accelerators has always been that gamma-induced reactions have very low cross sections, so you need cost-effective, high-intensity beams and thick targets."

The program sells isotopes to industrial users at full-cost-recovery prices and to academic researchers for less. It's unusual for a federal agency to run a business. "It's a careful balance between producing commercial isotopes to bring in revenue and the production of research isotopes and support of R&D," says Gillo. The program cannot legally compete with commercial interests, which means that if an isotope becomes commercially viable, DOE has to back out.

A case in point is strontium-82, which is used for cardiac imaging. DOE has produced the isotope for decades. Now a couple of companies are working to demonstrate that they can reliably meet the demand, and the isotope program is providing technical help. "It would be a success story, but if we exit, we lose a revenue stream," Gillo says. The isotope brings in about 40% of the isotope program's commercial revenues.

Connecting with universities

In its new, proactive incarnation, the isotope program is forming ties with several universities. Such collaboration, says Gillo, "is useful for cost-effectively producing a particular research isotope, or for making shorter-lived alpha emitters regionally so they don't have to be shipped far for use."

"We are still working on what our relationship [with DOE] will look like," says Washington University's Lapi. "But we are hoping for long-term collaborations and networking with other sites." The isotope program paid for a "hot cell" and an automated isotope purification system at the university, she says. And Lapi received an early-career award and funding for four graduate students through the program.

The University of Washington is the first academic partner in the isotope program's distribution network. "We have a cyclotron," says Wilbur. "We treat patients four days a week with fast neutrons, but we also have deuterons and alphas, which allows us to investigate making radioisotopes by different reactions." In joining the network, he says, "the sales of radioisotopes will go through DOE. They will decide who to call [to deliver a requested isotope]."

Advanced clinical studies "have to be done at different sites," Wilbur continues. "This is particularly difficult for astatine-211, a high-priority alpha emitter, which has a seven-hour half-life. If we set up the network, then researchers in different regions of the country can conduct preclinical and clinical studies with it."

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