

Return of the Radionuclide Shortage

In what is becoming a perennial news cycle and a growing threat to the stability of nuclear medicine practice, new shortages of radionuclides resulting from unexpected interruptions in supply are providing challenges for North American physicians and their patients. Atomic Energy of Canada Limited (AECL) reported on May 16 that its National Research Universal (NRU) reactor at Chalk River, Ontario, had shut down on May 14 as a result of an electrical power outage in eastern Ontario and western Quebec. On May 15 a routine inspection during restarting activities revealed a small leak (5 kg/h) of heavy water at the base of the reactor vessel in a location with corrosion on the outside wall of the vessel. The leak was contained, and on May 18 AECL announced that the NRU, the world's oldest reactor, would remain out of service for more than 1 mo. The NRU produces approximately 30%–40% of the world's medical isotopes and approximately 50% of those used in North America. It is 1 of only 5 reactors in the world with the current capacity to produce significant commercial quantities of ^{99}Mo . A shutdown of the reactor in 2007 and scheduled and unscheduled interruptions in supplies from other reactors caused a worldwide shortage of radioisotopes for nuclear medicine studies in 2008.

Reaction from Canadian law- and policy-makers was swift, with many condemning the previous administration's decision to end plans to go ahead with the twin MAPLE reactors that would have replaced and/or supplemented NRU production at Chalk River. Scientists expressed skepticism that the current shutdown would be restricted to 1 mo. The AECL confirmed these fears on May 27, announcing that the reactor would be offline for "at least 3 months" and possibly longer. To compound the rising level of anxiety among manufacturers, nuclear medicine physicians, and health care observers, the High Flux Reactor (Petten, The Netherlands) announced a 4-wk maintenance shutdown during the month of July. The Petten facility usually supplies one-third of the world's ^{99}Mo needs.

"The situation really is day-to-day at this point," Ontario Association of Nuclear Medicine President Christopher O'Brien, MD, told Canada AM TV on May 26. Clinics and hospitals in some parts of Canada were already postponing bone scans and other tests because of the shortage. "This is becoming a routine event almost every 6 months or so," added O'Brien. "What needs to be done is the government needs to ensure that Chalk River will be repaired, because although it's an old reactor, it's still a vital link in the medical isotope production chain. But the government also needs to find alternate sources for a long-term, stable supply of isotopes for Canadian patients. So far we have seen no concrete plans from the government on either issue."

Robert Atcher, PhD, MBA, outgoing SNM president, told the Reuters news service on May 26 that "about 8 million of our studies are imperiled because that reactor is

offline." Michael Graham, MD, PhD, who would assume the SNM presidency on June 23, noted that in past emergencies the remaining reactors and generator manufacturers have shipped small supplies from Europe and South Africa so hospitals can "limp along." He added that many physicians would be constrained to use less efficient and more costly procedures and, in some cases, no adequate substitutes are available.

On June 1, MDS Nordion (Ottawa), for which the AECL was the primary provider of ^{99}Mo for manufacture of $^{99\text{m}}\text{Tc}$ generators, released a statement indicating its concern for physicians and patients who might be affected by shortages. The company urged the government of Canada and AECL to consult with international experts and obtain assistance toward reactivating the MAPLE project, both to address the current shortage of medical isotopes created by the NRU shutdown and to avoid similar occurrences in the future. "The current NRU shutdown—and the shutdown of November 2007—illustrates the fragility and unpredictability of the global medical isotope supply system and highlights the requirement for new research reactor capacity to deliver a reliable long-term supply of medical isotopes," said Steve West, President of MDS Nordion. "The solution to the global medical isotope crisis is in Canada. The infrastructure is in place, and with the assistance of an international consortium of nuclear experts, the MAPLE facilities could be producing medical isotopes to the benefit of patients worldwide."

SNM Response Aimed at U.S. Domestic Self-Supply

In the United States, attention is increasingly being directed at domestic self-sufficiency in isotope supplies. At a press conference held on June 15 at the SNM 56th Annual Meeting in Toronto, Canada, leaders and researchers in the field of molecular imaging addressed the latest developments in the shortage. Atcher, Graham, and Peter S. Conti, MD, PhD, past-president of SNM, discussed the likely effects of the interruptions in supply and pointed to the SNM's organized efforts—predating the current crisis—to increase awareness about the need for sustainable domestic supplies of isotopes in the United States.

The SNM Isotope Availability Work Group began in 2008 to draft a report on possible ^{99}Mo suppliers for the U.S. market. Plans for this report began with the late 2007 shutdown of the NRU. At that time, it was noted that U.S. capacity for domestic medical radioisotope production in support of nuclear medicine had declined sharply over the past decade, with no facilities in the country dedicated to manufacturing ^{99}Mo for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generators. The announcement in May 2008 of the cancellation of the MAPLE Reactors at the Chalk River Laboratories made the need for an alternative domestic source for ^{99}Mo more

acute. The report, reviewed last month at the SNM Annual Meeting in Toronto, does not contain suggested solutions to this problem. Instead, it provides a summary of detailed discussions held with 6 potential sources (both U.S. and international) with the physical and intellectual resources to develop ^{99}Mo production capabilities, as well as the locations of those facilities and estimates on development/production costs. The task group will continue its research and add information to the report as necessary.

In an open letter to Congressman Edward Markey (D-MA) dated March 23 (well ahead of the current crisis), Atcher and SNM leaders outlined the challenges and focused on the potential of 2 of the 6 sources identified in the draft report: the University of Missouri Research Reactor Center (MURR; Columbia) and a collaboration between Babcock and Wilcox (B&W; Lynchburg, VA) and Covidien (Hazelwood, Mo). SNM recommended that assistance be given for expedited regulatory approval by the Nuclear Regulatory Commission, the Food and Drug Administration, and any other regulatory agency that will need to grant approval to those entities seeking to supply the United States with ^{99}Mo .

Information provided by Ralph Butler, director of the MURR, indicated that with the addition of a processing facility, the center could meet approximately 50% of the market need for ^{99}Mo , with little change to the current reactor. The reactor runs 24 h/d, 7 d/wk. except for a 12-h maintenance shutdown on Mondays. When other reactors have planned shutdowns, MURR could also help to fill gaps for up to about 75% of the U.S. market, with short-term shifts in production schedule. Scientists at MURR are now working on the design of a processing center to be located adjacent to the reactor building. Although the new processing center would be solely owned by the University of Missouri, a funding source has not yet been obtained. SNM recommended to Markey that the National Nuclear Security Administration (NNSA) fund the construction and development of the processing facility. In addition to increasing the supply of much-needed radio-nuclides, NNSA funding of the MURR reactor could serve as a large-scale demonstration project for the worldwide conversion of ^{99}Mo production using low-enriched uranium (LEU). SNM advocated funding for initial design and planning for fiscal year 2009, as well as the designation of stimulus funding and a commitment of \$35 million in 2010 to construct the facility and initiate operational activities.

SNM leaders also reviewed a Babcock & Wilcox and Covidien February announcement of a joint effort to

develop an aqueous homogeneous reactor that would run on LEU and would not require separate targets to be irradiated for ^{99}Mo production as do conventional reactors. The effort includes plans to build several small units capable of supplying 50% of the U.S. need for ^{99}Mo . Babcock & Wilcox and Covidien estimated that the facility could be operational within 5 y. Because this is a corporate effort, SNM did not recommend government funding. Instead, the society advocated government assistance in expediting the regulatory approval and licensing processes. Finally, the letter to Markey urged that any regulatory switch from highly enriched uranium to LEU include consideration of economic and environmental factors and other concerns, including the possibility of additional supply problems during the transition period.

Resolution Unclear

At Newsline press time in early June, the extent of radionuclide shortages and their effects on nuclear medical practice remained unclear, as did the projected time of restart for the NRU. Some facilities report shifting to ^{201}Tl for myocardial perfusion imaging and ^{82}Rb PET for selected cardiac applications, and others are rescheduling some studies from morning hours to the afternoon, to take advantage of the ability of suppliers to “milk” generators twice. Some facilities report that patients shortages are resulting in switches to nonnuclear studies, such as CT angiography.

European reactors have offered to step up production to supplement dwindling North American supplies. Experts were not optimistic about a short-term remedy. Jean-Luc Urbain, MD, president of the Canadian Association of Nuclear Medicine, told the *Wall Street Journal* on June 4 that the NRU could be down much longer than anticipated and that he views the current problem as “symptomatic” of additional issues that need investigation. SNM President Graham, who was contacted for the same article, was more blunt: “There’s a real possibility it will never restart.”

SNM maintains a dedicated and frequently updated section on the isotope shortage on its Web site at www.snm.org. A full copy of the draft report of the SNM Isotope Shortage Work Group is available there along with other documents.

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