Medical Radioisotopes—What Steps Can We Take to Ensure a Secure Supply?

Earlier this year, Alexander McEwan, MD, immediate past president of SNM, and I attended the workshop "Security of Supply of Medical Radioisotopes," which was convened by the Nuclear Energy Agency (NEA), a specialized agency within the Organization for Economic Co-operation and Development (OECD), at the request of the Canadian government. More than 80 participants representing a variety of international organizations—including government regulatory agencies, nuclear medicine, allied health industries, and nuclear reactors—met to discuss present challenges facing the reliable supply of ^{99m}Tc and to identify measures to be taken to ensure a secure supply for the future.

The workshop was organized with the assistance of the International Atomic Energy Agency (IAEA) and included participants from 13 OECD countries and 3 non-OECD countries.

During the course of the workshop, participants underscored the vulnerability of the global medical isotope supply chain, which depends on a limited number of aging nuclear reactors as well as a complex processing and distribution method for delivery of these short-lived isotope products to the health system. The inherent weakness in this processing and delivery system has been made even more evident over the last few years after several reactors were shut down unexpectedly and for longer-than-anticipated time frames. Because a number of these reactors are scheduled to go permanently offline because of their age and the increasing expense of maintenance, this situation is not likely to improve.

Workshop participants identified a number of measures that could help to ensure a short-term, uninterrupted global supply of medical radioisotopes. These include:

- Encouraging reactor owners and operators to continue to share information with one another and enhance coordination of maintenance schedules;
- Promoting an increase in production from existing reactors;
- Reviewing current economic conditions for irradiation services to provide better incentives to reactor operators, especially where the mission is in support of scientific programs;
- Removing impediments to distribution, such as restrictions in transport capabilities and denial of shipment by airline companies; and
- Urging radiopharmacies, hospitals, health product regulators, and the medical community at large to explore options for more efficient patient scheduling and generator utilization.

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Although these actions should have a favorable response in the near term, the group discussed the need to develop, deepen, and share contingency plans to avoid future supply disruptions. Increasing the supply of ^{99m}Tc to hospitals and clinics and, ultimately, patients will require that industry step up efforts to improve the flexibility and efficiency of the distribution chain and provide more transparency in the production of isotopes.

Questions naturally arose about the wisdom of replacing or supplementing aging reactors in light of uncertainties regarding long-term global demand and competing—albeit more expensive—production techniques. It is difficult to forecast whether capital-intensive additional nuclear capacities, which are designed to last approximately 50 y, would be judicious. The present economic model relies mainly on government-run reactors that typically charge marginal fees for irradiation services. Although it was agreed that governments have a responsibility to establish an environment conducive to private and/or public sector investments, participants recognized that a long-term isotope supply presents a global challenge requiring a global response.

The workshop closed with recognition of the importance of collaborating with colleagues around the world. Participants requested that the NEA consider establishing a working group, which would include the IAEA, to carry forward the workshop's agenda and to review additional measures to be taken. They requested that special attention be given to the economics of the supply chain and to increasing its flexibility through improved standardization.

I must confess that I wanted a more concrete set of action items than simply establishing a working group. OECD is a bureaucracy, and it is not unexpected that they would choose such a path forward. In light of the fact that ^{99}Mo production is a global enterprise, international cooperation is needed, and that will only come through extended communication.

Within SNM, we have been gathering information about the options available in the near, mid, and long terms to

(Continued on page 18N)

SNM Molecular Imaging Summit Introduces Clinical Trials Network

More than 150 experts from molecular imaging, regulatory agencies, and the pharmaceutical industry came together on February 8 and 9, immediately after the SNM Mid-Winter meeting in Clearwater, FL, to advance the use of imaging biomarkers in multicenter drug development trials. The intensive 2-d workshop was organized by the SNM Molecular Imaging Center of Excellence and the SNM Clinical Trials Network leadership. The objectives were to discuss the need for imaging biomarkers in the development of therapeutic pharmaceuticals, to examine the challenges of imaging in multicenter trials, and to discuss the path forward to successful biomarker imaging for large multicenter clinical trials.

The summit was an opportunity to learn how SNM's new Clinical Trials Network can facilitate faster and more cost-effective drug and biologics development through improved integration and standardization of imaging biomarkers into Phase 1, 2, 3, and 4 therapeutic clinical trials. The workshop outlined details of clinical sites' participation in the network and examined the critical need for imaging standardization and harmonization across clinical trial sites.

Gustav von Schulthess, MD, kicked off the meeting with a keynote address highlighting the importance of choosing the appropriate imaging modality and biomarker to address the clinical question being evaluated in the therapeutic clinical trial. He also emphasized the need for standardization of imaging protocols between different imaging centers and different types of imaging equipment (different vendors or performance levels).

The formal program for the meeting then continued with a series of presentations highlighting both the needs and challenges associated with incorporating imaging into clinical trials. Of particular interest were presentations by pharmaceutical developers, including Diane Jorkasky, MD (formerly of Pfizer); Jeff Evelhoch, PhD (Merck); Dan Skovronsky, MD, PhD (Avid); Sudha Kadiyala, PhD (Advanced Technologies & Regenerative Medicine, a subsidiary of Johnson & Johnson); and Susan Galbraith, MB, BChir, PhD (Bristol-Myers Squibb). U.S. Food and Drug Administration (FDA) participants also shared their perspective on challenges they have experienced with the use of imaging biomarkers in multicenter clinical trials.

After listening carefully to the needs of these varied but interconnected communities, leaders of the Clinical Trials Network have focused on the issue of standardization of imaging protocols between and across multiple imaging centers participating in clinical trials. The Clinical Trials Network will work to ensure the use of a consistent methodology and protocol across the multiple clinical trial sites, which is key to quality data generation and ultimate FDA approval of investigational therapeutics and imaging diagnostics.

The network is encouraging imaging centers and PET radiopharmaceutical manufacturers to get involved at this time in order to maximize the impact of the network standardization programs.

A complete list of presentations is available at www.snm.org/clinicaltrials. Additional educational sessions are planned during the SNM Annual Meeting this June in Toronto.

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(Continued from page 17N)

increase availability of ^{99}Mo for generator production. After the recent release of the National Academy of Sciences panel report on low-enriched uranium (LEU) for ^{99}Mo production and with the U.S. presidential election and musical chairs of committee assignments in Congress now over, we are starting a program to educate stakeholders in Congress and the executive branch on the current crisis. Some bright spots have appeared, including the announced partnership of Covidien with Babcock and Wilcox and continued progress at the Missouri University Research Reactor on developing an LEU process.

We continue to work with stakeholders to identify shorter-term solutions to the ^{99}Mo supply for SNM members and their patients. Although no obvious solution is in sight, we are assisting those who are working on this problem by communicating with regulators and others about the need for rapid implementation of new processes and capabilities.

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