EXECUTIVE SUMMARY OF THE REPORT BY THE EXPERT PANEL ON MEDICAL ISOTOPE PRODUCTION[1]

The Expert Review Panel on Medical Isotope Production (the Panel) was established on June 19, 2009, to advise the Government of Canada on the most viable options for securing a predictable and reliable supply of the key medical isotope technetium-99m (Tc-99m) in the medium to long term. This report is the culmination of that work, and presents recommendations that, in our opinion, will move Canada toward a new model for sustainable and secure long-term production of medical isotopes. We recognize that the government must ultimately select the best path forward for Canada, taking into account the broader nuclear energy and health care policy considerations that are outside the mandate of the Panel.

As part of this work, an expression of interest (EOI) process was launched to solicit ideas for alternative production of molybdenum-99 (Mo-99)/technetium-99m (Tc-99m) for the Canadian market in the medium to long term. We received 22 EOIs from a range of public and private sector organizations and reviewed the EOIs against specified criteria:

- Technical Feasibility;
- Business Implementation;
- Timeliness;
- Regulatory Issues; and
- Benefits to Canadians.

The EOIs proved very useful in identifying broad classes of technology options available. We greatly appreciated the time and effort invested by the proponents - we reviewed and assessed every EOI, and they played an important role in forming the content and recommendations presented here.

We also engaged medical, technical and regulatory experts to enhance our understanding of the many considerations involved in a long-term plan to secure medical isotope supplies. Among others, we received information from:

- Atomic Energy of Canada Limited;
- the Canadian Association of Medical Radiation Technologists;
- the Canadian Association of Nuclear Medicine;
- the Canadian Association of Radiologists;
- the Canadian Association of Radiopharmaceutical Scientists;
- the Canadian Institutes of Health Research;
- the Canadian Medical Association;
- the Canadian Society of Nuclear Medicine;
- the Canadian Society of Senior Engineers;
- individual nuclear medicine specialists;
- International Safety Research Inc.;
- the Ontario Association of Nuclear Medicine;
- the Royal College of Physicians and Surgeons of Canada - Nuclear Medicine Specialty;
- SECOR Inc.;
- SNC Lavalin Inc.;
- 15 independent and internationally known technical experts;
- other national and international stakeholders; and
- a Tc-99m generator manufacturer.

Throughout, our focus and attention remained on the best interests of patients and their families and the health care needs of Canadians.

Our report is structured around major classes of technology, with each technology option assessed against the specified criteria. The technologies are:

- Reactor technology
  1. New multi-purpose research reactor - fission option
  2. Dedicated Isotope Facility - fission option
  3. Existing reactors - fission option
- Accelerator technology
  4. Linear accelerator - photo-fission option
  5. Linear accelerator - Mo-100 transmutation option
  6. Medical cyclotron - direct Tc-99m option

SUSTAINABILITY AND SECURITY

Through our work and our assessments, we established parameters to define a sustainable and secure supply of Tc-99m in the medium to long term. A sustainable supply of Tc-99m to serve the needs of Canadian patients would:

1. be viable for the foreseeable future, likely for at least 15 to 20 years, and may include options that begin producing in the short to medium timeframe but that promise to remain viable;
2. comprise options that could each meet a meaningful portion of the Canadian demand, but that would not necessarily be exclusively Canadian-based and may or may not serve the U.S. or other markets;
3. have a sound business model that may or may not include government involvement; and
4. be free of highly enriched (weapons-grade) uranium (HEU) because of Canadian and global commitment to non-proliferation.

1. A copy of the full report and background information can be found at http://nrcan.gc.ca/eneene/sources/uranuc/mediso-eng.php (English) or http://nrcan.gc.ca/eneene/sources/uranuc/mediso-fra.php (français).

A **secure** supply of Tc-99m would:

5. improve redundancy at all points in the supply chain to avoid the "single point of failure" risk associated with a linear supply chain;
6. use diverse technologies to hedge against a failure that could arise if all suppliers used the same technology;
7. collocate irradiation and processing facilities to minimize decay losses and avoid shipping losses and risks; and
8. ensure sufficient capacity to accommodate short-term outages of some sources.

Establishing these parameters for sustainable and secure supply helped to frame how we assessed the likelihood of various technology options contributing to a stable isotope supply in the long term.

KEY FINDINGS FOR TECHNOLOGY OPTIONS

The most significant findings for each technology are given below. A full assessment of each technology option against all established criteria is given in Chapter 5.

1. New Multi-purpose Reactor Option

The lowest-risk path to new Mo-99/Tc-99m production capacity is to build a new multi-purpose research reactor. The research reactor also promises the most associated benefits to Canadians based on its multiple purposes.

Research reactors are shared facilities that have all the benefits associated with multi-use facilities, including the benefit of costs being spread over a large base of activities. However, this is the most expensive of the options, with high capital and operating costs. Costs associated with the processing facility, training, licensing requirements, security, and waste management are also very significant.

Revenue from isotope production would likely offset only approximately 10–15% of the costs of the reactor; building a new reactor would have to be justified, in large part, based on its other missions.

Given the established parameters for sustainability, any new reactor-based source of Mo-99 should be based on low enriched uranium (LEU) targets; some research and development (R&D) would be required to optimize the process and deal with the increased volumes of waste.

Of all the technology options, this one has the highest potential for concomitant benefit to Canadians based on the promise of the broad-based research that would be undertaken, and its associated potential for generating intellectual property, job creation and training.

2. The Dedicated Isotope Facility (DIF) Option

This option involves restarting the DIF project, which included two Multi-purpose Applied Physics Lattice Experiment (MAPLE) reactors, the New Processing Facility (NPF) and associated waste management structure. These facilities were never fully commissioned, and are in an extended shutdown state.

The DIF was designed and optimized to use HEU targets. Moreover, the design of the MAPLE reactors, the NPF and the associated waste management structure was heavily customized and dedicated to isotope production. This customization would pose significant challenges for possible modification and conversion to LEU, which, in our opinion, is mandatory for any medium- to long-term plan.

Furthermore, even if the existing infrastructure were to come at no cost, the ongoing economics for this project remain questionable because high operating costs cannot be shared across multiple uses. The fact that no dedicated isotope production reactors have been built and operated or are in planning anywhere in the world (with the exception of the DIF) suggests that others recognize the economic difficulties of this option.

Estimates for the timeline range from two to eight years. Although the best-case scenario of two years to market is attractive, we expect the timeline to be longer given the challenges with the processing facility, in addition to the licensing challenges.

3. Existing Reactor Option

Other existing research or power reactors, either domestically or internationally, could be used to irradiate targets for the production of Mo-99. Generally, projects associated with existing reactors are based on the use of modified processing facilities at AECL and the existing supply chain. Because research reactors are less powerful and consequently less efficient for isotope production, they require the use of HEU targets to achieve worthwhile yields.

While conversion to LEU would be possible, it may not be justifiable based on the limited remaining lifespan of the facilities. Nonetheless, HEU-based options in this category should be considered as options to address short-term supply shortages.

4. Linear Accelerator — Photo-fission Option

A particle accelerator is a device that uses electric fields to accelerate ions or charge subatomic particles to high speeds in well-defined beams to bombard targets for research and isotope production.

In this option, a high-power electron linear accelerator is used to bombard a converter to produce an intense photon beam to generate Mo-99 through nuclear interactions with natural uranium.

The required accelerator is not currently available, but the development is technically low risk. Substantial R&D is needed for the target and converter design, the cooling capacity and overall process optimization.

To meet the required production levels, the accelerators would be dedicated to isotope production, and would not be available for research or any other purpose. This option suffers from poor economics because capital investment is relatively high and cannot be shared across multiple missions.

Although the cost of an individual accelerator is much less than that of a reactor, as many as four accelerators would be needed to meet Canadian demand, and they would be relatively expensive to build and operate based on the high power requirement. When costs associated with processing and waste management are included, the total costs of the option could exceed $500M.

As a fission-based approach, this option would likely fit well into the existing supply chain; however, significant quantities of nuclear waste would be generated.

5. Linear Accelerator — Mo-100 Transmutation Option

An electron linear accelerator can produce Mo-99 through the transmutation of enriched Mo-100.

The Mo-100 option requires significant R&D regarding targetry and cooling capacity, as well as the development and marketing of a new type of generator. There is some concern that hospitals may not accept the new generators, and that this new product may not be able to compete with the traditional generators, presenting significant business risk.

Currently, there is no commercial production of purified Mo-100. The cost of the quantity needed could be substantial and may prove to be a barrier to commercialization. A full recycling of Mo-100 could reduce the cost substantially by minimizing loss, but recycling is yet to be demonstrated, and significant R&D would be required.

As in the case of photo-fission, the accelerators used for Mo-100 transmutation would likely need to be dedicated to isotope production to achieve the desired production levels, making this a single-use option. Return on investment would be difficult given the current price for Mo-99 and the significant costs, which cannot be shared across multiple missions.

A significant advantage of this option from an environmental and cost point of view is that it does not generate nuclear waste.

6. Cyclotron Option

A cyclotron is also a particle accelerator device. This option is based on bombarding Mo-100 with protons to extract Tc-99m directly from the irradiated product.

This is the only option in which Tc-99m is produced directly without first generating Mo-99.

Because the production of Tc-99m using cyclotrons is at an early stage of development, it is difficult to say how much of the Canadian market could be or would be served by cyclotrons. However, it is attractive because the cyclotron infrastructure could be in place and used for other purposes, but could still offer surge capacity to augment other sources.

Although significant R&D is required, the infrastructure to undertake the research, demonstration and initial production is presently available. Therefore, costs are relatively low and timelines for the R&D are relatively short.

This option can be implemented on a gradual basis since the model is for a distributed system with each cyclotron serving only local radiopharmacies and nuclear medicine departments. Communication and collaboration between medical cyclotron operators could ensure redundancy in supply and avoid single point of failure in the supply chain.

The cyclotron option is not a complete solution; because the half-life of Tc-99m is short, only hospitals and radiopharmacies close to a cyclotron would be served. More remote locations would continue to be served by Tc-99m generators, likely through existing supply chains. As a result there will be a need for Mo-99 to meet Canadian needs for the foreseeable future, although this could coexist with direct Tc-99m production.

Difficulties with this option include the requirement for R&D associated with target design and Mo-100 recycling. This option may require more validation from a Health Canada regulatory perspective. Currently, there is no commercial production of purified Mo-100. The cost could be high and may prove to be a barrier to commercialization.

An important consideration is that this option does not produce nuclear waste, which results in economic and environmental benefits over fission-based options.

The cyclotron option has the potential to be the timeliest option. Commercial production of Tc-99m could begin between 2011 and 2014, depending primarily on results of R&D and health regulatory issues.

GENERAL RECOMMENDATIONS

1. Strive for diversity and redundancy throughout the supply chain.

We recommend adopting a supply strategy offering technological diversity, and redundancy at every step in the supply chain.

2. Leverage multi-use infrastructure.

We recommend investing in infrastructure that is designed to have multiple purposes and is more likely to remain useful over the long term, regardless of how the use of medical isotopes evolves.

3. Continue with international coordination, and seek processing standardization within North America.

We recommend that the government continue to inform itself of all international isotope initiatives, and work with other countries to better coordinate worldwide efforts around isotope production and distribution. We also encourage the government to start laying the groundwork now for establishing target and target processing compatibility, especially for any new sources developed in North America.

4. Recognize that HEU options are viable only in the short to medium-term.

We recommend that any option reliant on HEU be dismissed as a long-term solution. As a proponent of non-proliferation, Canada must work to eliminate HEU from civilian use. Because many options associated with existing reactors are based on using HEU targets, they should be considered only within a short-term context.

TECHNOLOGY-SPECIFIC RECOMMENDATIONS

1. Make policy decisions on the requirement for a new research reactor.

We recommend that the government expeditiously engage in the replacement of the NRU reactor as we believe a multi-purpose research reactor represents the best primary option to create a sustainable source of Mo-99, recognizing that the reactor's other missions would also play a role in justifying the costs. With the National Research Universal (NRU) reactor approaching the end of its life cycle, a decision on a new research reactor is needed quickly to minimize any gap between the start-up of a new reactor and the permanent shutdown of the NRU. If the decision is to not build a new research reactor, the issue of securing supply of Tc-99m will have to be revisited in light of how cyclotron/accelerator options are advancing, and what new foreign sources of isotopes have materialized.

2. Support an R&D program for cyclotron-based Tc-99m production.

We recommend that the cyclotron option for direct production of Tc-99m, which has many attractive features, be explored further. Although this option requires significant R&D, the infrastructure and know-how to undertake that work is readily available in Canada so costs associated with the R&D remain relatively low. Assuming technical viability, the infrastructure necessary to demonstrate this approach in selected centres across Canada is already in place. Indeed, Canada has an opportunity to be a leader in this area and strengthen its existing related businesses.

3. Achieve better use of Tc-99m supply through advanced medical imaging technologies.

We recommend deployment of newer single photon emission computed tomography (SPECT) technologies (software and hardware), as well as investment in positron emission tomography (PET) technology, to reduce demand for Tc-99m now and over the longer term, which would reduce the impact of future shortages of reactor-produced isotopes.

OTHER CONSIDERATIONS

1. Linear accelerator options

The two linear accelerator options have limited prospects for multi-purpose use, require significant R&D, and may not have significant cost advantages over reactor technologies. Nonetheless, a modest R&D investment could be considered as a hedge against the risk of failure of other options. Of the two linear accelerator options, we prefer the technology based on Mo-100 transmutation since the projected economics appear better, and it largely avoids nuclear waste management issues.

2. Dedicated Isotope Facility (DIF) infrastructure

Cost and timeline estimates associated with the commissioning and licensing of the DIF varied widely. Although it may be possible to bring them into operation, the business case is such that even if the DIF facilities could be licensed immediately at no cost, the ongoing revenues from isotope sales would be insufficient to cover the ongoing operating expenses, particularly with the anticipated reduced throughput from future conversion to LEU targets. A dedicated isotope facility based on a private sector cost-recovery model would be a good solution assuming a private sector organization would be willing to accept the full commercial risk associated with this model.

The Expert Review Panel on Medical Isotope Production was comprised of Mr. Peter Goodhand (Chair), Mr. Richard Drouin, Dr. Thom Mason, and Dr. Eric Turcotte.

CREATING THE FUTURE OF CHALK RIVER

BY ZIN TUN, ON BEHALF OF CREATE (CHALK RIVER EMPLOYEES *AD HOC* TASKFORCE)

With the federal government planning to restructure Atomic Energy of Canada Limited and split off the CANDU reactor business from Chalk River Laboratories (CRL), the future of Canada's main nuclear research infrastructure is uncertain. Furthermore, the 52-year old NRU reactor is showing its age, being shutdown for repairs since May 2009. The NRU reactor is the flagship of CRL, performing three missions simultaneously: (1) It produces neutrons beams for advanced materials research, (2) it is a platform for in-core testing of materials for nuclear R&D, and (3) it is the word's largest producer of medical isotopes. While the National Research Council is responsible for research with neutron beams, AECL is the owner and operator of the reactor and performs the latter two missions.

In response to the restructuring of AECL and to the need for a new, multi-purpose research reactor, the Chalk River Employees *Ad hoc* TaskforcE for a national laboratory (CREATE) was formed in August 2009. CREATE is a grass-roots, non-partisan group of volunteers that includes current and former employees at Chalk River. These volunteers developed a concept for a future Chalk River National Laboratory (CRNL), consulted with CRL staff, and obtained their support. CRNL would include a new multipurpose reactor for research and isotope production. Such a reactor is otherwise known to CAP as the Canadian Neutron Centre proposed by the Canadian Institute of Neutron Scattering (http://www.cins.ca/CINSplan.html).

In October 2009, CREATE submitted its report to Natural Resources Canada and Cheryl Gallant, Member of Parliament for Renfrew-Nipissing-Pembroke (Figure 1). The report in both French and English is available at www.futurecrl.ca.

"CREATE has provided Canadians with a vision of what the future of science at Chalk River could be, by evolving

SUMMARY

In response to the restructuring of AECL and to the need for a new, multi-purpose research reactor, the Chalk River Employees *Ad hoc* TaskforcE for a national laboratory (CREATE) was formed in August 2009. This is a summary of this initiative.

Fig. 1 CREATE presents its report proposing its concept for the future of Chalk River to MP Cheryl Gallant (centre). Left to right: John Hilborn, Gordon Tapp, Zin Tun, and Blair Bromley.

its mission to one of a national laboratory. I intend to make sure the report is widely circulated among my colleagues on Parliament Hill," Gallant said.

In CREATE's proposed vision, CRNL will be Canada's premier laboratory for nuclear and related sciences (illustrated in Figure 2) and an international centre of excellence. It will be a resource for researchers from across a broad spectrum, from fundamental sciences to industrial applications, rather than being restricted to research and development that is mainly focused on supporting CANDU nuclear power reactors, as is the case today.

The new mission of CRNL will be very outward looking, partnering and impacting at all levels of Canadian society. That outward focus includes several new functions: leading diverse research programs beyond nuclear energy; partnering broadly with universities, industries, and government; commercializing knowledge; providing a training ground for Canada's future generation of research scientists and engineers; and fostering a science and technology culture in Canada. By serving as a unique, major resource for science and industry, CRNL will deliver enduring value for Canada.

While the need for a new facility has long been recognized, the Expert Review Panel on Medical Isotope Production concluded in November "a multi-purpose research reactor represents the best primary option to create a sustainable source of Mo-99, recognizing that the reactor's other missions would also play a role in justify-

Zin Tun, a Principal Research Officer with the NRC's Canadian Neutron Beam Centre at Chalk River, is acting on behalf of the volunteer working group CREATE in submitting this article to *Physics in Canada*. With regard to this article he can be reached through the website at www.futurecrl.ca .