



Advancing Molecular Imaging and Therapy

## Preliminary Draft Report of the SNM Isotope Availability Task Group June, 2008

### Introduction

The initiation of this project – researching alternative means for isotope production within the United States – began with the late 2007 shutdown by the Atomic Energy of Canada Limited (AECL) of the aging National Research Universal (NRU) reactor. At that time, it was noted that the US capacity for domestic reactor-produced medical radioisotope production in support of nuclear medicine had declined sharply over the past 10 years. This, coupled with recent efforts to curtail the use of highly-enriched uranium (HEU) in radioisotope production as a non-proliferation strategy and to deter terrorism, now poses a significant threat to Molybdenum-99 (Mo-99) availability within the US. The subsequent cancellation in May 2008 of the MAPLE Reactors at the Chalk River Laboratories has made the need for an alternative domestic source for Mo-99 production more acute. *Currently there are no facilities in the US that are dedicated to manufacturing Mo-99 for Mo-99/Tc-99m generators.*

The following draft report of possible Mo-99 suppliers for the US market was put together by an SNM task group and does not contain suggested solutions to the problem. Instead, it provides a summary of discussions held with six potential sources that have the physical and intellectual resources to develop Mo-99 production capabilities, where those facilities are located, and estimates on development/production costs: University of Missouri Research Reactor Center (MURR), Australian Nuclear Science and Technology Organisation (ANSTO) and ANSTO Radiopharmaceutical and Industrials (ARI), Babcock & Wilcox Technical Services Group, the Annular Core Research Reactor (ACRR) at Sandia National Laboratories (SNL), the resources of the Department of Energy's (DOE) National Nuclear Security Administration (NNSA), and the Atomic Energy of Canada Limited (AECL) and MDS Nordion. The task group will continue its research over the next few months, and will be adding further information to the report as necessary.

### University of Missouri Research Reactor Center (MURR)

**Anticipated Level of Medical Isotope Production:** MURR could meet approximately 50% of the current market need for Mo-99, with little change to the current reactor. The reactor runs 24 hours a day, 7 days a week, with a scheduled 12 hour maintenance shutdown on Mondays. MURR could also help to fill gaps made by planned shutdowns of other reactors, for up to about 75% of the market, with shifts in production schedule, in the short term only.

**Physical Plant:** Currently MURR is working on the design of a processing center, which would be approximately 30 feet from the reactor building.

**Funding:** The processing center would be solely owned by the University of Missouri, however how to fund the center has not yet been decided. A mix of several options is being considered, including public-private partnership, federal support, and donations. MURR believes that production of Mo-99 could begin by 2012.

**Switch to LEU:** If required to switch to low-enriched uranium (LEU) fuel for the reactor, the impact will be minimal. MURR would expect to be producing Mo-99 before any reactor fuel conversion to LEU would be required.

**Timeline:** MURR hopes to have the design of the processing center completed in 4 to 6 months. MURR is waiting for an NRC license amendment in order to do a sample target irradiation. They are expecting the amendment by the end of July, and will select a target design soon thereafter.

**Other Issues:** The proximity to the University of Missouri campus and the town might create issues during environmental impact statement development.

**Australian Nuclear Science and Technology Organisation (ANSTO) and  
ANSTO Radiopharmaceutical and Industrials (ARI)**

**Anticipated Level of Medical Isotope Production:** By October 2008, the reactor will be able to produce enough Mo-99 for the Australian market with one manufacturing run per week. If there is a need to produce for the US market as well, the manufacturing process can be run multiple times per week with multiple targets.

**Physical Plant:** The "Mini-Moly" reactor is already in place and by October 2008 will be producing 100% of Australia's market for Mo-99.

**Funding:** Since a reactor is already in place and functioning, funding is not currently an issue. However, if ANSTO was to build a larger reactor ("Mega-Moly"), then the financial returns would come into play. With the decline in the US dollar, it is uncertain as to whether or not making an investment would make sound financial sense.

**Switch to LEU:** Already uses LEU, and has no regulatory issues with Australian regulators.

**Timeline:** US manufacturers will have to file supplements to their New Drug Applications (NDAs) to the FDA in order to use the Mo-99 made by ARI. The application process could take between 4 and 6 months, then it would be up to the FDA. In parallel, ANSTO would submit a Drug Master File (DMF) with the FDA.

**Other issues:** Politically, it may be difficult to convince the current Australian government to allow export to the US given its "anti nuclear" position. Additionally, there may be public push back regarding the production of nuclear waste to "provide health care to Americans."

**Babcock & Wilcox Technical Services Group (B&W)**

**Anticipated Level of Medical Isotope Production:** Using Aqueous Homogenous Reactors ("Solution" Reactors) with LEU fuel, could supply 50% of the US market using 3 200Kw units. Production could be staggered and linked with radiopharmacies so that they receive the product in a timely fashion.

**Physical Plant:** The AHR's are modular. It takes approximately 120 hours to get the Mo-99 at optimal concentration. The units use conventional purification techniques. Additionally, the units can be used as backups for one another. First facility will be built somewhere near either St. Louis or Boston to achieve proximity to Mo-99 manufacturing sites.

**Funding:** B&W is already investing, and will work with a pharmaceutical partner and private investments. Overall cost estimate is less than \$100 million, including research and development. Not looking for government funding.

**Switch to LEU:** The AHR's use LEU fuel already.

**Timeline:** Five year timeline starting this past February. Currently in discussions with NRC regarding the early phases of the license process. Current nuclear reactor regulations do not specifically address Aqueous Homogeneous Reactors so licensing under current regulation may require clarifications. New regulations may become necessary to appropriately address this relatively low hazard type of reactor.

**Other issues:** Going to LEU means producing small amounts of plutonium and how to deal with that? The same solution is being used for a long time before being discarded. In the end, it could be reprocessed into oxide fuel. A solution reactor will need NRC approval but cannot be licensed as a "research reactor" as it will not be 50% dedicated to research. Regarding FDA approval, the machine will first need to be built, then operated, and then the material can be tested and submitted to FDA for approval. B&W plans to work with FDA to optimize the product approval process.

### **Annular Core Research Reactor (ACRR) at Sandia National Laboratories (SNL)**

**Anticipated Level of Medical Isotope Production:** The ACRR has the capability of meeting 100% of the need for the US market. However, the reactor is currently being used by the Defense programs group at the Department of Energy (DOE). To free the ACRR for production of medical radionuclides would require DOE to reassign the mission of the ACRR and make significant investment in the reactor and the processing facilities.

**Physical Plant:** The ACRR is currently operating in a pulse mode for the testing of materials response to neutron fields. It can operate at 30,000 MW in pulse mode or 4 MW in a steady state mode. Hotcells were modified in the 1990's at the ACRR in order to allow for the production of Mo-99. This Mo-99 project was later dropped by the DOE. It may be possible to locate a new LEU reactor for the production of Mo-99 at Sandia, rather than try to change the mission of the ACRR.

**Funding:** It would require \$10-\$50 million to convert the ACRR into a steady state reactor and finish and equip the existing Hotcells in order to process Mo-99. This would also require DOE to reassign the ACRR from Defense Program uses to isotope production use.

**Switch to LEU:** The current fuel is 35% enriched U-235, which is considered HEU. The reactor fuel could be converted to LEU fuel for the production of Mo-99.

**Timeline:** Three things would have to happen for the ACRR to produce Mo-99. The DOE would have to change the mission for the reactor, the facilities and reactor would have to be modified to allow for the production of Mo-99, and the funding for those changes would have to be developed by industry or a possible consortium with industry and DOE.

**Other Issues:** A new reactor could be sited at Sandia or at another national lab. The time frame for licensing may be shortened, but the cost may be higher. Possible partnerships with National Nuclear Security Administration (NNSA) and DOE could be explored.

### **National Nuclear Security Administration (NNSA)**

**Anticipated Level of Medical Isotope Production:** The NNSA is charged with minimizing the use of HEU in the civilian sector, while at the same time ensuring that there is technology to produce an indigenous supply of Mo-99. The NNSA is not charged with developing the supply of the isotope.

**Physical Plant:** Would not be possible at this time to use an existing Department of Energy (DOE) reactor for the production of Mo-99. The DOE would have to go through a long process to determine where the best location would be and whether this would be the best use of federal funds.

**Funding:** The economic feasibility of producing Mo-99 with LEU will be discussed in an upcoming National Academies of Science (NAS) report, due to be released sometime in the fall. The NNSA would entertain unsolicited proposals for federal funds to be used to develop an industry consortium to research LEU use for Mo-99 production using publicly available information.

**Switch to LEU:** One of the missions of the National Nuclear Security Administration (NNSA) is to reduce the use of HEU in the civilian sector, primarily in research and test reactors, and the production of Mo-99. One way to accomplish this is to look for alternate technologies using LEU for the current technologies being used to make Mo-99 with HEU.

**Timeline:**

**Other issues:** The NNSA is limited to using research and development that is available in a public format.

**Atomic Energy of Canada Limited (AECL) / MDS Nordion**

**Anticipated Level of Medical Isotope Production:** The National Research Universal (NRU) reactor is operated by AECL in Chalk River, Ontario. Targets are processed by AECL, and then the Mo-99 solution is shipped to MDS Nordion in Ottawa for purification. AECL/Nordion currently provides about 40% of the world's supply of Mo-99. The NRU can supply about 80% of world's needs on a sustained basis.

**Physical Plant:** The NRU reactor, originally commissioned in 1957, currently operates at up to 130 MW. The Mo-99 targets still utilize HEU.

**Funding:** AECL is a Canadian Crown corporation, which is federally subsidized. MDS Nordion is publicly owned and traded on the NYSE.

**Switch to LEU:** The NRU fuel was converted from HEU to LEU a few years ago. The MAPLE reactors had also planned to use LEU fuel and HEU targets.

**Timeline:** Although the MAPLE project was recently canceled, AECL plans to extend the license of the NRU reactor, which currently expires in 2011.

**Other issues:**

### Conclusion

At this point the task group has spoken to 80-90% of the organizations that the task group has identified as having a realistic opportunity in the near- to mid-term to supply Mo-99 to the domestic market. The task group will continue to broaden the current discussion by speaking to other producers of Food and Drug Administration (FDA)-approved medical radioisotopes as well as those potentially capable of producing FDA-approvable material. During the next phase of this project, the task group will begin to explore the technical side of this issue, as well as the feasibility of different options for production of Mo-99, including industry consortiums, public/private partnerships, government funding and other programs. It is anticipated that a larger consortium will be involved in making any recommendations regarding a long-term solution to this problem. Obviously, SNM anticipates being an active member in that activity. The task group will continue to develop as much background material as possible to facilitate a reasoned approach to this dilemma. The upcoming national elections may also have an impact on the future course, as there will be a change in administration and in the Congress that will affect the future course of government participation.

The task group is eagerly anticipating the release of the National Academy of Science (NAS) report entitled "Medical Isotope Production Without Highly Enriched Uranium", and will work to incorporate the recommendations and findings made as it moves into the second phase of the project.

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