

Reliable Domestic & Global Supplier of Molybdenum-99 (Mo-99) and Switch from Highly Enriched Uranium (HEU) to Low-Enriched Uranium (LEU) to Produce Mo-99

A White Paper by a Coalition of Professional Organizations

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A coalition made up of the Society of Nuclear Medicine (SNM), American Association of Physicists in Medicine (AAPM), American College of Radiology (ACR), American Nuclear Society (ANS), American Society of Nuclear Cardiology (ASNC), American Society for Radiation Oncology (ASTRO), Council on Radionuclides and Radiopharmaceuticals (CORAR), Health Physics Society (HPS), and the Nuclear Energy Institute (NEI) are concerned with two key issues regarding production of Molybdenum-99 (Mo-99) within the United States: an inherent need for reliable domestic suppliers of Mo-99, and the recent efforts to curtail the use of high-enriched uranium (HEU) in radionuclide production as a non-proliferation strategy and to deter terrorism.

Mo-99 decays into Technetium-99m (Tc-99m), which is used in approximately 16 million nuclear medicine procedures each year in the United States. Such procedures include: detection and staging of cancer; detection of heart disease; detection of thyroid disease; study of brain and kidney function; and imaging of stress fractures. In addition to pinpointing the underlying cause of disease, physicians can actually see how disease is affecting other functions in the body. Because Mo-99 is produced through the fission of uranium and has a half-life of 66 hours, it cannot be produced and stored for long periods of time. Unlike traditional pharmaceuticals, which are dispensed by pharmacists or sold over-the-counter, nuclear reactors produce radioactive isotopes that are processed and provided to hospitals and other nuclear medicine facilities based on demand.

Concern has been building over the last several years about supply interruptions of Mo-99 from foreign vendors and the lack of a reliable supplier of Mo-99 in the United States. The initial concerns were raised when the MAPLE X reactor deployment dates were extended by years back in the late 1990s. The most recent concerns began in late 2007, with a three-week shutdown by the Atomic Energy of Canada Limited (AECL) of the National Research Universal (NRU) reactor, and continued with the recent unanticipated shutdown of the High Flux Reactor (HFR) in Petten, The Netherlands. The subsequent cancellation in May 2008 of the construction of the Canadian MAPLE Reactors at the Chalk River Laboratories, which were intended to replace the aging NRU reactor, has made the need for additional Mo-99 production capacity more acute. While, both the NRU and the HFR reactors were back online in February 2009, this does not negate the need for additional capacity, which will increase the reliability of the medical radionuclides supply. Most recently, the NRU reactor was shut down for an undetermined amount of time due to a heavy water leak and the HFR reactor is scheduled to be down for maintenance beginning in June 2009, under the existing supply situation, any incident, which would necessitate the closing of our borders to radioactive shipments, would cripple the practice of nuclear medicine in this country. In addition, although there may be alternatives to certain diagnostic procedures using Tc-99m (including substitution of other isotopes for Tc-99m, and some computed tomography (CT) and invasive angiography procedures), clinicians routinely choose the most accurate, most useful and most dose-efficient imaging technique. It is a disservice to patients to deny them access to the most appropriate study due solely to the non-availability of Tc-99m in the United States. Thus, to preserve patient care, we are advocating for the development of a domestic production capability within the United States.

1. Reliable Domestic Supply of Mo-99

In order to ensure that patient needs are not compromised, a continuous reliable supply of medical radioisotopes is essential. Currently there are no facilities in the United States that are dedicated to manufacturing Mo-99 for Mo-99/Tc-99m generators. The industry must develop additional capacity for Mo-99 production, and not rely solely on current suppliers. A Public-Private partnership should be explored to speed the availability of Mo-99 to ensure the continued availability of diagnostic imaging for patients with cancer, heart disease, neurologic conditions, and other medical problems.

For the purposes of this discussion, the coalition has decided to focus on those sources that could be located within the United States with additional backup of new foreign sources. The Australian Nuclear Science and Technology Organisation (ANSTO) and ANSTO Radiopharmaceutical and Industrials (ARI) is potentially an option, for a new foreign source, given Mo-99's short half-life, coupled with the likelihood that at this point they only have the capacity to supply a small part of the United States market, it is counterintuitive to rely on a Mo-99 supplier located half-way around the world. They are working on a plan to dramatically increase the production capacity which would change this concept, but there is no guarantee that they can expand their production nor has a timetable been released. The NRU reactor is almost 50 years old and is approaching the end of its useful life. Over the course of the past two years it has been shut down three times for extended periods in addition to shorter outages, NRU may face obstacles when applying for license renewal in 2011. AECL has also rejected suggestions to install a different reactor design into the existing facility, which was built for the MAPLE system.

Of those sources located within the U.S, at this time two stand out as being the most viable solutions to provide a domestic supply of medical radionuclides: the University of Missouri Research Reactor Center (MURR) in Columbia, Missouri, and the Babcock & Wilcox (B&W)—Covidien collaboration. It is important to note that even though we are currently focusing on these two potential domestic suppliers, there continues to be a need for reliable suppliers located outside of the United States that would be in a position to help supply the United States market in case of anticipated preventive maintenance or an unforeseen shutdown of one, or more, of the domestic suppliers. We recommend that assistance be given for expedited regulatory approval by the United States Nuclear Regulatory Commission (NRC), the U.S. Food and Drug Administration (FDA) and any other regulatory agency that will need to grant approval to those entities seeking to supply the United States with Mo-99.

The MURR reactor has undergone evaluation for potential supply of Mo-99. The findings are- the reactor could meet approximately 50% of the current United States market need for Mo-99, with little change. 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 United States market, with short term-shifts in production schedule. Currently MURR is working on the design of a processing center, to be located adjacent to the reactor building. Provided funding is arranged and the regulatory requirements are met, the facility could be in operation by the end of 2011. The reactor currently operates on HEU fuel. If a requirement to switch to LEU fuel is implemented, the impact will not be minimal, but it will be feasible. A new processing center for Mo-99 would be solely owned by the University of Missouri; however funding has not been arranged. This presents an opportunity for the government to initiate a private-public partnership. Federal funding of the construction and development of the processing center would accomplish two significant government objectives. First, it would demonstrate the government support for educational institutions. Second, it would promote a large-scale demonstration project for the worldwide conversion of Mo-99 production using LEU fuel and targets.

Just as important, the coalition believes that the U.S. Department of Energy (DOE) should be directed to work with MURR and B & W (discussed below) on a disposal path for the radioactive waste. This

issue will most likely be included in the environmental impact statement; however, DOE participation could help with expedited approval of the processing center. As noted, there currently are limited disposal paths for Class B and C radioactive waste that is generated by private entities in 36 states in the United States. Hence, if the National Nuclear Security Administration (NNSA) is to succeed in conversion of fuel and targets to LEU, and if a domestic producer of Mo-99 is to be developed, this can only occur if the domestic producer(s) are able to dispose of their radioactive waste. DOE can provide a path forward by opening up its low-level waste facility(s) for the waste generated by these two projects if commercial facilities are not available.

In February, B & W and Covidien jointly announced their intent to work on the development of an Aqueous Homogeneous Reactor (AHR). This proven type of reactor design would run on LEU, and would not require separate targets to be irradiated for Mo-99 production, as is the case for conventional reactors. Their plans are to build several small units capable of supplying 50% of the United States need for Mo-99. There have been more than 30 AHRs built and successfully operated, including reactors at Los Alamos National Lab, Lawrence Livermore National Lab, Brigham Young University, University of Wyoming and Walter Reed Army Hospital. An AHR reactor in Russia has successfully demonstrated production of high quality Mo-99 in 2002-2003¹. This reactor and radiochemical processing operation is expected to generate less low-level radioactive waste than conventional reactors, and no spent fuel waste except at the end of its useful life. B & W is estimating the facility can be operational within five years.

The coalition understood that Covidien and B & W were not originally pursuing government funding for this effort. However, if they choose to do so, the coalition would support that approach as well. Development of this reactor and the associated radiochemistry has been underway for several years, and has benefited from the assistance of Argonne National Laboratory and the International Atomic Energy Agency (IAEA). In addition to support for the domestic production of Mo-99 and other medically useful fission products, we also are advocating government assistance in expediting the regulatory approval process, including the licensing process by the NRC and the FDA. Assistance in waste disposal from the DOE is essential for the development effort and ongoing operation of the facility, as we suggested above.

If government funding is made available to MURR, it is important to remember that, while they will only be able to routinely supply 50% of the United States market and up to 70 % for short periods, there is still 50% that will need to be supplied. Having 100% of the United States market supplied by domestic sources, with backup supplies from international sources, will ensure that patient needs are not compromised.

2. Switch from HEU to LEU

A continuous, reliable supply of medical isotopes is essential; any change from HEU to LEU must be undertaken in such a way that we ensure that patient needs are not compromised.

Forcing a change from HEU to LEU reactor fuel and targets must be done with adequate time made available for the research and development needed for the transition period. There also must be consideration of economic and environmental factors to prevent, first and foremost, putting patients at risk because of delays in production of much needed radionuclides, such as Tc-99m which is made from Mo-99. Currently, no large-scale, commercial processes using LEU targets for medical isotopes have been developed, demonstrated, and implemented. In order to establish this process there are two critical elements that must be accomplished. First, the technology must be proven to be robust and reliable, which requires a significant transition period to demonstrate its efficacy. Second, the system must be able to

¹ The Kurchatov Institute, Moscow, Russia

provide commercial quantities of Mo-99 (thousands of curies per week, every week). Otherwise patients—the ultimate consumers of Tc-99m—will be put at risk.

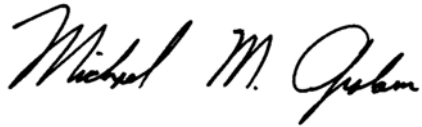
The financial impact of forcing a change from HEU to LEU targets remains vague. Although it is technically feasible to produce Mo-99 from LEU targets, it may not be commercially viable without federal subsidies. In addition to structural and technological changes that must be made, the new technology would require NRC approval and the actual production process would have to be approved by the FDA. Any new technology will not be considered complete until it receives approval from both the FDA and the NRC, which is expensive both in terms of time and the expected fees associated with the application process. It has been estimated that the cost of verifying and generating approval for a different production process will be in the millions of dollars.

The environmental impact such a switch would cause has not yet been determined. A switch to LEU targets will not only increase the amount of plutonium produced due to the increase in neutron capture by U-238 during Mo-99 production, but will also increase the amount of radioactive waste produced since nearly five times more uranium will be put into the reactor than is required by the HEU process. Both the plutonium and the radioactive waste will have to be disposed of properly, further increasing costs, which will ultimately be passed on to the patient.

The age of the NRU and HFR reactors, which are responsible for nearly all of the US supply of Mo-99, also complicates a potential LEU conversion for the Mo-99 production process. Both of these reactors are approaching the end of their operating life cycle and a premature forced conversion to the LEU Mo-99 production process may force them to shut down prematurely or at least abandon Mo-99 production for the United States market. Again patients—the ultimate consumers of Tc-99m—will be put at risk.

If a switch from HEU to LEU is required to be implemented prematurely, even those users outside of the United States will be adversely affected, by requiring either financial and/or regulatory support from United States regulatory agencies in order for their product to be used domestically. As we have mentioned earlier, it is imperative that patients are not put at risk. Forcing a change to a new, and as yet unproven, technology without the proper research and development, or regulatory and financial support will most certainly cause harm.

Signed,



Michael M. Graham, MD
President, SNM



Maryellen L. Giger, Ph.D., FAAPM, FAIMBE
President, The American Association of Physicists
in Medicine (AAPM)



James H. Thrall, MD, FACR
Chair, Board of Chancellors
American College of Radiology (ACR)



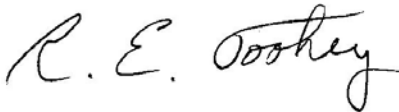
William E. Burchill
President, American Nuclear Society (ANS)



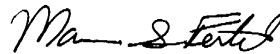
Jennifer Mieres, MD, FASNC, FACC
President, American Society of Nuclear
Cardiology (ASNC)



Laura Thevenot, CAE
Chief Executive Officer
American Society for Radiation Oncology (ASTRO)



Richard E. Toohey, Ph.D., CHP
President, Health Physics Society (HPS)



Marvin S. Fertel
President and Chief Executive Officer
Nuclear Energy Institute (NEI)



Franklin B. Yeager
Chairman, Council on Radionuclides &
Radiopharmaceuticals (CORAR)