

A Conversion Development Program
to LEU Targets for Medical Isotope Production
in the MAPLE Facilities

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A CONVERSION DEVELOPMENT PROGRAM TO LEU TARGETS FOR MEDICAL ISOTOPE PRODUCTION IN THE MAPLE FACILITIES

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ABSTRACT

Historically, the production of molybdenum-99 in the NRU research reactors at Chalk River, Canada has been extracted from reactor targets employing highly enriched uranium (HEU). The molybdenum extraction process from the HEU targets provided predictable, consistent yields for our high-volume molybdenum production process. A reliable supply of HEU for the NRU research reactor targets has enabled MDS Nordion to develop a secure chain of medical isotope supply for the international nuclear medicine community. Each link of the isotope supply chain, from isotope production to patient application, has been established on a proven method of HEU target irradiation and processing.

To ensure a continued reliable and timely supply of medical isotopes, the design of the MAPLE facilities was based on our established process – extraction of isotopes from HEU target material. However, in concert with the global trend to utilize low enriched uranium (LEU) in research reactors, MDS Nordion has launched a program to convert the MAPLE facilities to LEU targets. An initial feasibility study was initiated to identify the technical issues to convert the MAPLE targets from HEU to LEU. This paper will present the results of the feasibility study. It will also describe future challenges and opportunities in converting the MAPLE facilities to LEU targets for large scale, commercial medical isotope production.

1. INTRODUCTION

The health care industry continues to discover innovative ways to improve the lives of people globally. Medical research using isotope based technologies have enabled scientists; physicians and clinicians to research, develop and apply advanced therapies. Isotopes have enabled research into the functioning of the human body, evaluation of organs that are critical to normal human development, and the ability to apply leading-edge therapies in areas such as cancer treatment and pain control.

The radiopharmaceutical industry continues to develop treatment that relies on medical isotopes for accurate diagnosis, cancer therapy and pain control. Advanced techniques such as brachytherapy and radioactive implants have proven to be effective therapies. Recent explorations using monoclonal antibodies radiolabeled with isotopes – the “magic bullet” – have demonstrated the value of continued medical research using isotope-based technologies.

Research and development of these new medical techniques has been enabled by the secure, reliable supply of isotopes. To provide continued support to the nuclear medicine community, MDS Nordion, a leader in global supply of molybdenum-99 and other medical isotopes, is providing the investment to construct and operate two MAPLE reactors and a new processing facility in Chalk River, Ontario, Canada. The MAPLE facilities will be the first privately owned reactors in the world dedicated to medical isotope production.

The MAPLE reactors are reliant on a low cost, reliable source of uranium to produce molybdenum-99 from the uranium based reactor targets. All of the major isotope producing reactors rely on high-enriched uranium (HEU) for this purpose. The MAPLE reactors have been designed to operate with low enriched uranium (LEU) fuel and to produce isotopes based on known HEU target processing technology.

This paper will provide a brief overview of the importance of molybdenum-99 to the nuclear medicine community. It will then give some background on the MAPLE project. Finally, it will discuss some of the challenges of MDS Nordion's HEU to LEU target development and conversion program for the MAPLE facilities.

2. MEDICAL ISOTOPES IN HEALTH CARE

Nuclear medicine imaging is unique in that it documents organ function and structure, in contrast to diagnostic radiology, which is based upon anatomy. It is a way to gather medical information that may otherwise be unavailable, require surgery, or necessitate more expensive diagnostic tests. There are nearly 100 different nuclear medicine imaging procedures available today. Nuclear medicine imaging procedures often identify abnormalities very early in the progression of a disease – long before some medical problems are apparent with other diagnostic tests. This early detection allows a disease to be treated early in its course when there may be a more successful prognosis.

In the United States alone, it is estimated that about one of every four hospital patients receive the benefit of nuclear medicine, and over 12 million nuclear medicine procedures are performed each year.

Molybdenum-99 (Mo-99) is the backbone of the nuclear medicine industry. It is used to make Mo-99/Technetium-99m. (Tc-99m) generators, which are used in most nuclear medicine departments around the world. Tc-99m is, by far, the most widely used radioisotope in nuclear medicine. It is estimated that 50,000 people worldwide benefit daily from the use of this isotope.

Tc-99m is a versatile isotope that can be incorporated into a variety of radiopharmaceuticals to assist the diagnosis of problems in many parts of the body including, heart, brain, liver, lungs, thyroid gland, kidneys and bone. This popularity is due principally to the combination of its versatility, low cost, high-quality imaging and reliable availability. Moreover, its very short life (6-hours) allows viable analyses without risk to the patient.

3. THE MAPLE FACILITIES – DEDICATED TO MEDICAL ISOTOPE PRODUCTION

Today, MDS Nordion is the worlds' largest supplier of molybdenum-99, using the NRU reactor owned by AECL at Chalk River. Molybdenum-99 supply in the pre-1980 era was supported by four capable suppliers: Cintichem and GE in the United States, IRE in Belgium, and MDS Nordion in Canada, which produced isotopes in the NRU and NRX reactors. All of the reactors involved in isotope production are old and some of them have encountered insurmountable circumstances that resulted in their permanent shutdown. The GE reactor was found to be located on a seismic fault and it was shutdown in 1980. The Cintichem reactor experienced a contamination incident that resulted in its permanent shutdown in 1990.

Consequently, global molybdenum supply became reliant on two producers - IRE, and MDS Nordion - with MDS Nordion supplying most of the market needs. Supply reliability concerns created by shutdown of the Cintichem and GE reactors were heightened when the NRX reactor in Canada was shutdown in 1993 resulting in no viable backup supply of medical isotopes.

As a result, a number of initiatives to broaden molybdenum-99 supply were taken. Mallinckrodt established a contract with HFR at Petten; IRE increased its production capacity to provide a larger volume back up; AEC in South Africa began to produce molybdenum-99 in 1993.

In response to concerns the nuclear medicine community had about the long term, secure supply of molybdenum-99; in 1996 AECL and MDS Nordion announced an agreement that will ensure reliable and economic supply of radioisotopes to hospitals and clinics worldwide. The terms of the agreement between MDS Nordion and AECL provided for construction of two MAPLE reactors and a high volume, commercial, processing facility at AECL's Chalk River site. MDS Nordion will own the reactors and processing facility and be responsible for developing the isotope production planning activities. AECL have been contracted to design, build, and operate the facilities. The MAPLE reactors will be the only reactors in the world totally dedicated to the commercial production of medical radioisotopes. The significant investment being made by MDS Nordion at the AECL site at Chalk River, Canada, will capitalize in the extensive infrastructure, expertise and experience of MDS Nordion and AECL for the reliable, continuous supply of isotopes.

Overall, completion of the MAPLE project was planned to be about fifty months in duration. These new, one-of-a-kind facilities had several challenges to meet during the execution of the project. Advanced technology, a new licensing environment, and a compressed schedule created challenges in licensing, design, construction and commissioning. It is encouraging to report that the project is generally progressing well, with several key milestones achieved.

Figure 1: MAPLE Project Key Milestones

• Project Start	September	1996
• Environmental Approval	April	1997
• Construction Approval	December	1997
• MAPLE 1 Reactor		
- Operating License	April	1999
- First Sustained Nuclear Reaction	February	2000
• New Processing Facility		
- Operating License	April	1999
• MAPLE 2 Reactor		
- Operating License	June	2000

An environment assessment for the facilities was completed in April 1997 and construction approvals for these facilities were granted in December 1997. MAPLE 1 achieved its first sustained nuclear reaction on February 19, 2000. This was a significant milestone in the project. The MAPLE 1 reactor has been achieving all of its performance objectives at the 2 kW level and power has been increased to the 500 kW level. Also, the operating license for MAPLE 2 was received in June 2000. While there have been some delays in construction along the way, as with any large project introducing new technology in a changing regulatory environment, work is proceeding apace. For the MAPLE 1 reactor and the New Processing Facility (NPF) commissioning and acceptance testing are the next major milestones to complete. We expect first sample quantities of molybdenum-99 to be available in spring of 2001 for customer qualification testing.

The MAPLE reactors are 10 Mw, open pool, light water reactors. The reactor has a compact core, about the size of a 90 litre (20 gallon) drum, and is surrounded by a heavy water reflector tank.

The reactor assembly consists of five major components: the inlet plenum; the grid plate; the core structure consisting of vertical flow tubes containing LEU driver fuel bundles and HEU target assemblies for medical isotope production; the heavy water reflector tank; and the chimney.

The light water primary coolant enters the inlet plenum, flows upwards through the grid plate, the flow tubes and fuel and target assemblies, and is directed back to the suction of the primary cooling pump via the outlet arms of the chimney.

The MAPLE reactor is composed of 13 hexagonal and six circular flow tubes. Four of the 13 hexagonal flow tubes are used for irradiating HEU targets; the remaining nine contain 36 element LEU driver fuel assemblies. The six circular flow tubes contain 18 element driver fuel assemblies.

Two reactors were built to ensure a secure and continuous supply of medical isotopes. Isotopes will be produced in one reactor while the other is being maintained and prepared for its next production run. The operating cycle of each reactor will have a period of two to four weeks depending on isotope demand. HEU targets irradiated in the MAPLE reactors will be transferred in shielded containers to the processing facility for isotope extraction. The radioactive waste from the extraction process will be solidified within the processing facility and transferred to the waste management area on the Chalk River site for storage in concrete canisters.

The processing facility will extract the radioisotopes produced in the HEU feedstock target material, process the residuals, and transfer the product to containers for shipment to MDS Nordion's Kanata facility. At our Kanata operations, the isotopes are further processed, packaged, and distributed to MDS Nordion's nuclear medicine customers around the world. The timeline from start of target processing to product delivery to the hospital can be as little as 41 hours.

4. HEU TO LEU TARGET CONVERSION PROGRAM

The MAPLE reactors have been designed to operate with low enriched uranium (LEU) fuel and the isotope production process has been designed using highly enriched uranium (HEU) targets clad in zirconium alloy. HEU target technology is an integral part of the reactor operating system. It is a proven and reliable process for molybdenum production in the reactors operated by all of the commercial isotope producers.

Predictable, consistent yields of molybdenum from HEU targets are the foundation for a reliable supply of isotopes. Furthermore, all of the requisite licensing has been approved by national nuclear regulators and by health care regulators such as the U.S. Food and Drug Administration (USFDA), and the European national authorities. All of these links have been developed to provide a secure chain of medical isotopes for the international nuclear medicine community.

All the while that HEU target technology is well established, there is significant international interest in reducing reactor reliance on HEU feedstock material. The only known commercial sources of HEU are the United States, Russia and South Africa. Concerns with international safeguards and non-proliferation of HEU material have caused the U.S. to enact legislation that will encourage reactor operators to convert to LEU and create increased difficulty for non-U.S. organizations to access U.S. sourced HEU. Furthermore, there is increasing difficulty in the logistics of sourcing HEU material worldwide. Generally, HEU material is government controlled, lead-time to access material is long, and the reliability of supply is uncertain. All of the above, coupled with a public perception that favours the use of LEU material, has caused MDS Nordion to initiate a program to examine the feasibility of, and address the issues to, converting those reactors and their associated processing facilities to operate with low enriched uranium (LEU) targets. Conversion from HEU to LEU targets must be done while the facilities are operating reliably, providing the primary source of molybdenum-99 and other radioisotopes used annually in thousands of medical procedures.

To achieve the objective of converting the MAPLE facilities to LEU targets, MDS Nordion has established a three-phase *LEU Target Development and Conversion Program*. The three phases are:

- Initial Feasibility Study
- Conversion Development Program
- Conversion Implementation Program

The *LEU Target Development and Conversion Program* must be accomplished within certain boundary conditions and inputs. The first condition is that there must be minimum change to the MAPLE reactor design and operation, as well as the downstream processing system, all of which have been designed and built based on HEU target technology. A second condition is that the design isotope production capacity must be maintained. As a consequence of these two conditions, the same number of targets will be used and the mass of uranium in the LEU targets will be 4.7 times greater than in an HEU target. The processing facility must be able to handle the increased uranium mass from the LEU targets and achieve acceptable performance characteristics in the areas of uranium dissolution, molybdenum-99 recovery yields, waste solidification and waste storage. Any incremental operational burden placed on the isotope production and processing system must ensure that the rigorous equipment preventative maintenance program is not compromised.

Over the past year, MDS Nordion, together with AECL has completed the Initial Feasibility Study through a series of technical studies and programs. With the MAPLE reactors, the objective was to determine the LEU target design as well as the technical and regulatory conversion constraints.

A design for an LEU target for the MAPLE reactors has been produced. Furthermore, the Initial Feasibility Study determined that operation of the MAPLE reactors with LEU targets is technically feasible and identified the key Canadian regulatory conditions that must be met to use LEU targets in those reactors. Before LEU targets may be used in the MAPLE reactors, the Canadian Nuclear Safety Commission (CNSC) must review and approve environmental assessments and safety analyses performed by AECL, including critical heat flux tests and irradiation tests. It is anticipated that a public licensing process could be carried out by the CNSC in connection with its consideration of whether the MAPLE reactors will be authorized to use LEU targets. Based on consultation with the CNSC, it is expected that completion of their licensing process could require a minimum of three years. In addition, the drug certification requirements of the USFDA and the European national authorities must be satisfied for production of molybdenum-99 from a new target source material comprised of LEU.

However, the situation with the processing facility is more challenging and complex. The isotope processing hot-cell system and equipment is custom designed and solely dedicated to the processing and extraction of molybdenum-99 from HEU targets. Therefore a thorough investigation of the processing facility to explore the technical viability of converting to LEU was required.

MDS Nordion commissioned AECL to perform the investigation and established three key objectives:

- Determine whether the equipment designed for the New Processing Facility can process LEU targets.
- Determine the production capacity with LEU targets.
- Determine changes that should be implemented prior to the introduction of radioactivity into the NPF.

Assessment Plan

The study was comprised of the following tasks:

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| Task 1 | Develop the chemical processing requirements and assess process equipment design for dissolution of LEU targets and recovery of molybdenum-99. Perform scoping laboratory tests to verify the chemical process flowsheet. |
| Task 2 | Assess the design of waste treatment equipment, comprising calcination and cementation solidification systems, liquid waste storage system and off-gas delay system. Assess the processing equipment design for treatment of wastes generated from the LEU chemical flowsheet developed in Task 1. |
| Task 3 | Assess the design of the waste transfer and storage system and equipment for loading and storage of calcined and cemented waste identified in Task 2. |

Process Employed to Perform the Assessment

The feasibility assessment included technical experts from AECL, the system design integrators, SGN in France, designers of the waste process system, and MDS Nordion.

AECL had the lead role in performing the chemistry process experiments. SGN was asked to review their waste process system design, in particular the waste cycle time and the calcining equipment throughput. On an ongoing basis, MDS Nordion scientists and technical experts met with AECL and reviewed in detail the work that was carried out. AECL and MDS Nordion also visited SGN in France for a technical review of the work that had been undertaken by SGN. The objective of this meeting was to determine if any changes to the waste processing equipment/facility could be done, prior to NPF active operation, which would facilitate conversion from HEU to LEU at a later date.

Assuming that LEU targets could be irradiated in the MAPLE reactors, 4.7 times more uranium than in HEU targets will be chemically processed in the NPF to extract a similar quantity of medical isotopes. This additional mass must also be calcined to solidify the waste in stable form for long-term storage.

The conversion of the NPF from HEU to LEU requires increasing its weekly uranium processing capacity to meet current production levels and maintain its design production

capacity. Since the design capacity of the NPF was defined and since the LEU target contained additional uranium that would need to be processed to meet MDS Nordion's current market requirements, the assessment sought to define these parameters that gave rise to the limitations in system capacity. Furthermore this facility was built with an expected useful life of 40 years. In the natural course of events it is expected that MDS Nordion and AECL will find ways to improve the process capacity of the facility to accommodate any additional process demands to meet market growth projections.

In many respects, the results of the Initial Feasibility Study are quite promising, as shown following.

Uranium Dissolution

Dissolution tests were performed with varying molarity. It was determined that complete uranium dissolution from an LEU target could be achieved within the volumes used for an HEU target.

Molybdenum-99 Recovery

Several molybdenum recovery tests were performed and molybdenum recovery efficiencies comparable to those with HEU targets were obtained. However, although it was determined that the mass of uranium in an LEU target can be dissolved within the volume of nitric acid used for an HEU target, the uranium concentration in solution must be diluted for comparable molybdenum recovery efficiencies. The greater uranium concentration in the fissile waste liquid from LEU targets increases the demands on the waste solidification and storage systems.

It is important to optimize the yield of molybdenum. Significant differences from the optimum would result in increased costs by proportionately increasing the number of processes required per week to attain the weekly production quantity that is required. Operational experience with active targets may allow the processing parameters to be altered and the waste volumes to be reduced. Additional information about optimum concentration will be obtained once routine operation with HEU in the NPF has been obtained.

Liquid Waste Storage Capacity

An HEU process generates about half the volume of high level liquid waste per process of an LEU process. The NPF facility has been built with adequate tanks to store the waste to reduce decay heat prior to the start of calcination. To improve the production capacity, two areas have been identified: reduction of decay time and improvement of the calcination process.

Waste Calcination

In order to determine the capability of the waste calcination system, SGN in France were asked to carry out a study of the system process parameters. The process used is a continuous batch process with the calcination taking place in a storage can that will be sealed and disposed of as solid waste. The calcination process requires the liquid from the target dissolution and

alumina column washes to be metered into a can so free water can be evaporated on-line in a controlled manner. The system must operate under stable conditions to maintain process control; this will retain the residual material in the storage can, minimize sputtering, which could cause fouling of the calcining equipment, and minimize entrainment of the off-gas. Once the free water has been evaporated, thermal energy is applied to the residual material and a solid, cinder-like mass is left in the storage can. The storage can is then seal-welded, loaded in a basket, and transported in a shielded container to a storage silo in the waste management area. SGN reported that because of the sputtering observed after the removal of free water, the total amount of uranium in the can is the limiting factor. They observed that with greater amounts of uranium there was danger of sputtering not being contained in the can and causing fouling of the calcining system. AECL and MDS Nordion scientists met with SGN in France to get a better understanding of SGN's experience in this matter. SGN confirmed that based on their knowledge about the process, a significant number of additional waste cans would be required if the change to LEU was made and the calcination process performed in a controlled manner.

Therefore, MDS Nordion's plan is to gain experience with the calcination system operation with HEU to determine what changes could be made to manage the increased mass of uranium that will be in the LEU targets. In addition, an evaluation will be made to determine if the process could be carried out more quickly.

Solid Waste Storage

Because of the processing considerations mentioned earlier, the number of waste containers will increase. Because there will be less uranium per container, the arrangement of these containers in the concrete waste storage silos can be different. Nevertheless, due to criticality considerations, it is expected that the number of silos required will be greater. This, in turn, could have an impact upon the storage capacity of the existing waste storage site. The licensing and environmental requirements to address this issue will need to be defined.

Conclusions

The assessment carried out by AECL demonstrated that an LEU target could be irradiated in the MAPLE reactors and processed to make molybdenum-99. This assessment has been discussed with and reviewed by Argonne National Laboratories (ANL). At this time, there would be a greater volume of liquid waste but the limiting factor for LEU supply capability was identified to be the speed at which waste could be calcined. This can best be addressed by establishing a process development program aimed at improving the cycle time to process the LEU waste stream. Essentially the key issue is the capacity and capability of the calcination system.

Next Steps

The next step for MDS Nordion is to proceed with the Conversion Development Program Phase. Building upon the results of the Initial Feasibility Study, the Conversion Development Program will have several challenges to address. The Program essentially consists of a waste process development program which will examine the technical, regulatory and economic

implications for dealing with the increased volume of waste arising from processing LEU targets in the NPF and identify solutions to address these issues.

The objective of the Conversion Development Program Phase is to identify and evaluate improvements to the calcining system capacity and capability to process the LEU targets. To achieve this, a waste processing development program will be established to:

1. identify improvements to the calcining system and equipment
2. identify possible process improvements in the NPF to reduce the waste arising from processing LEU targets; and
3. commence a development program to reduce the waste cycle time

The next phase must also establish the regulatory milestones for implementing a conversion program. A key outcome will be the evaluation of the technical and economic feasibility of conversion program options. The option chosen to convert to LEU targets must be both technically and economically feasible, and must ensure the reliable supply of medical isotopes, particularly molybdenum-99.

MDS Nordion will continue to provide a secure, reliable source of isotopes to the nuclear medicine community. To comply with the spirit and intent of policy and legislation intended to reduce reliance on HEU material, we are proceeding diligently with our *LEU Target Development and Conversion Program*.