

Report to the Nuclear Science Advisory Committee

Annual Assessment of the NNSA-Material Management and Minimization (M³) ⁹⁹Mo Program

**March 19, 2018
Report of the NSAC ⁹⁹Mo Subcommittee**

Executive Summary

The Nuclear Science Advisory Committee (NSAC) ⁹⁹Molybdenum (⁹⁹Mo) Subcommittee met December 14-15, 2017 to address the charge to NSAC requesting that a fourth annual review of the National Nuclear Security Administration (NNSA) ⁹⁹Mo program be performed. The Subcommittee found that the NNSA has continued to make progress over the course of the year based on the specific American Medical Isotopes Production Act of 2012 (AMIPA) requirements.

The international context for ⁹⁹Mo availability has changed somewhat since the last review. The Organization for Economic Cooperation and Development's Nuclear Energy Agency (OECD-NEA) has updated [1] its assessment of the ⁹⁹Mo production capacity and demand curves as well as its assessment of the global supply chain [2] and progress toward full cost recovery (FCR). The Canadian government has ceased production of ⁹⁹Mo at the National Research Universal Reactor (NRU). There have been some unexpected outages of both irradiators and processors during the last year; in spite of this, the demands of the market have mostly been met during this period.

The Subcommittee found that while the NNSA had considered the previous recommendation of the Subcommittee regarding limiting the liability to the Cooperative Agreement (CA) partners from the Uranium Lease and Take Back (ULTB) program, progress on this recommendation has been less than needed to maintain momentum in the program. All of the active CA projects have incurred additional delays of approximately one year in the projected dates for first ⁹⁹Mo commercial production over what was stated at the last Subcommittee meeting fifteen months ago. It is probable that one or more of the NNSA supported projects will enter the market eventually, and perhaps as early as the first half of 2018, although likely not with sufficient capacity to mitigate potential shortages in the period before 2020. We note that as this report was being finalized, the Food and Drug Administration announced [3] the approval of the RadioGenix generator, developed by NorthStar and supported by the NNSA.

The Subcommittee has one recommendation:

Recommendation:

Various potential U.S. producers of ⁹⁹Mo, including several of the CA partners, will need to use the capabilities of the ULTB program. In order to develop their business models, they must have well-defined, predictable, and stable costs for disposition of the waste they produce. In the 15 months since the last NSAC review (September 2016), no contract for ULTB waste has been shared with potential producers.

For this reason, the single recommendation of the Subcommittee is that the Department of Energy should:

- a) In a timely manner, issue a waste *take back* contract to the CA partner with whom they have been engaged for the last year *and*
- b) use the lessons learned in this process to identify opportunities for improvement of the ULTB process.

Introduction

The Nuclear Science Advisory Committee (NSAC) ⁹⁹Molybdenum (⁹⁹Mo) Subcommittee began its work in 2017 in response to a charge letter dated September 27, 2017 (Appendix 1). This letter was motivated by the American Medical Isotopes Production Act (AMIPA) legislation contained in the National Defense Authorization Act for Fiscal Year 2013. This Act requires the Secretary of Energy to establish a technology-neutral program to provide assistance to commercial entities to accelerate production of ⁹⁹Mo (aimed at ensuring a reliable domestic supply of the isotope ⁹⁹Mo) used to supply the medical diagnostic isotope ^{99m}Tc in the United States, without the use of Highly Enriched Uranium (HEU). The National Nuclear Security Administration (NNSA) Global Threat Reduction Initiative (GTRI) was given the responsibility for development of this program in 2009. This Act also called for an annual review of the NNSA GTRI ⁹⁹Mo program by the NSAC. Following an NNSA reorganization, the ⁹⁹Mo program is now within the NNSA Material Management and Minimization (NNSA-M³) program.

NSAC established a Subcommittee to perform this review in 2014. Additional members were added in 2015 and 2016 to address stakeholder input. The 2017 Subcommittee membership and relevant experience are given in Appendix 2. The full text of previous reports can be found at <http://science.energy.gov/np/nsac/reports/>.

The Subcommittee met December 14-15, 2017 in Crystal City, VA and built on the extensive work of the previous three reviews. At this meeting, the Subcommittee was briefed by NNSA on details of the program and received input from representatives of the Organization for Economic Cooperation and Development's Nuclear Energy Agency (OECD-NEA) High Level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) and the National Academy of Sciences (NAS) Committee on the State of Molybdenum-99 Production and Utilization and Progress Toward Eliminating Use of Highly Enriched Uranium. The Subcommittee invited input from all three current CA partners; they all presented briefings. Finally, the Subcommittee solicited feedback from a broad set of ⁹⁹Mo stakeholders, devoting a session to stakeholder input. Appendix 3 contains the agenda of the Subcommittee meeting.

Considerable information on ⁹⁹Mo production and the events leading to the AMIPA legislation was presented in the 2014 NSAC report. The reader is directed to Appendix 4 for a summary of this information.

Changes in the International Landscape Since the 2016 Report

The OECD-NEA HLG-MR issued two new reports “The Supply of Medical Radioisotopes: 2017 Medical Isotope Supply Review: $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ Market Demand and Production Capacity Projection 2017-2022” [1] and “The Supply of Medical Radioisotopes: Results from the Third Self-assessment of the Global $\text{Mo-99}/\text{Tc-99m}$ Supply Chain” [2]. In Reference [1] the assessed demand was kept constant from previous years at 9,000 6-day Ci per week. The conclusion on adequacy of supply is positive: “Overall, the current irradiator and processor supply chain capacity should be sufficient and if well maintained, planned and scheduled, be able to manage an unplanned outage of a reactor, or a processor throughout the whole period to 2022. When no additional capacity is added, then from mid-2018, the level of capability to manage adverse events reduces, in particular when considering processing capacity.” In reference [2], the conclusion on progress toward full cost recovery is less positive: “showing continued but slow progress towards implementing the six HLG-MR policy principles”. The report also notes that the lack of full implementation of full cost recovery sends negative signals to potential investors in future commercially-based production. This fact has the potential to impact the success of the present CA partners supported by NNSA. The OECD-NEA representative noted that there are also potential negative consequences of FCR if resulting cost increases relative to income squeeze some suppliers out of the market. This has the potential to impact the supply of ^{99}Mo in the U. S. if it were to happen prior to the entry of new producers into the market.

Nuclear Technology Products in South Africa has been off-line since the end of November 2017 and as of early February 2018 it was still not processing ^{99}Mo . The Subcommittee was told during the presentation by the OECD-NEA representative that, “During the recent unexpected outages the remaining suppliers are mostly working at maximum levels and there are still some limited shortages in some markets. “. These events underscore the vulnerabilities in the global supply chain that the NNSA-M³ program was created to address.

Developments in the NNSA Program

The organization and goals of the NNSA-M³ program with respect to ^{99}Mo remain unchanged since the previous review: to achieve HEU minimization and to assist in establishing reliable domestic supplies of ^{99}Mo produced without the use of HEU. The NNSA-M³ program seeks to achieve these objectives through assisting global ^{99}Mo production facilities to convert to the use of low-enriched uranium (LEU) targets and accelerating the establishment of commercial non-HEU-based ^{99}Mo production in the United States. As in previous reviews, it is the latter of these issues that was the main concern of this review.

Sections 3173 (c) and (e) of the FY13 National Defense Authorization Act direct DOE to establish a Uranium Lease and Take Back (ULTB) program by January 2016 to make LEU available, through lease contracts, for irradiation to enable the production of ⁹⁹Mo for medical uses. The Act also requires DOE to retain responsibility for the final disposition of spent nuclear fuel (SNF) and to take title to and be responsible for the final disposition of radioactive waste that is created by the irradiation, processing, or purification of the leased uranium for which the Secretary determines the producer does not have access to a disposal path. The Act also requires DOE to recover the costs associated with the ULTB Program.

This ULTB Program is coordinated between different organizations within DOE; the NNSA Production Office (NNSA-PO) provides the management and leasing of LEU required for domestic fission-based ⁹⁹Mo production, while the DOE Office of Environmental Management (DOE-EM) manages the disposition of SNF and radioactive waste that does not have an existing disposal path, both of which may be generated by ⁹⁹Mo production. The cost recovery models DOE will utilize for the ULTB Program are of particular interest to potential ULTB users (including two CA partners of the ⁹⁹Mo program) because the users need estimated program costs to assess and incorporate into their business model planning. NNSA has established an intra-agency working group to coordinate the completion of various activities in order to establish the ULTB program; the ULTB program was officially established at the time of the NSAC review of 2016. In spite of this, significant challenges remain in defining the cost of the take-back portion of the program, particularly for greater-than-Class-C low-level radioactive waste (GTCC LLW).

As required by AMIPA, the NNSA-M³ program has continued to provide assistance to commercial entities to pursue several technologies to accelerate production of ⁹⁹Mo in the United States without the use of HEU. This program involves creating cooperative agreements with a set of commercial entities based on a 50/50 cost share between the government and the commercial entity. NNSA continues to operate using a total funding limit of \$25M to each commercial project it supports; this is in accordance with the OECD-NEA guidelines on full cost recovery (FCR) principles.

At the time of the 2017 review, all cooperative agreements have been awarded at \$25M and funds have been obligated in the following amounts:

- NorthStar Neutron Capture project fully funded at \$25M
- NorthStar Accelerator project funded at ~\$15M
- SHINE Accelerator with LEU Fission project funded at ~\$22M
- General Atomics LEU Target project funded at ~\$21M

The technical approaches of the four CA projects have been described in previous reports. These descriptions will not be repeated here. All four projects have made progress since the last Subcommittee meeting. In spite of this, the expected dates of first ⁹⁹Mo from all projects to enter the market have been

delayed by approximately one year for all projects since the last Subcommittee meeting. The specific progress of each project is described below.

NorthStar neutron capture project:

NorthStar described the following progress:

- 26 full production runs were completed, producing ~2,000 6D Ci of ⁹⁹Mo by the exact processes that will be used upon Food and Drug Administration (FDA) approval of NorthStar's pending New Drug Application (NDA).
- Installation and site acceptance of a new fill line at the Missouri University Research Reactor (MURR) that will yield a factor of four increase in production throughput was completed. NorthStar expects this fill line to receive FDA approval for commercial use during 2Q 2018.
- Submission of a revised NDA to the FDA was completed.
- The FDA completed required Pre-Approval Inspections (PAI) at NorthStar and selected vendors' facilities.
- NorthStar completed and closed responses to all FDA observations from PAI on Dec 5.
- They responded to all 2017 Information Request (IR) from the FDA by Dec 21.
- Hot cells to be installed in their Beloit facility were ordered to expand operational capabilities and potentially increase ⁹⁹Mo available to market.

In addition, as this report was being finalized, the FDA announced [3] the approval of the RadioGenix generator. This is a very significant step forward for ⁹⁹Mo produced by NorthStar to enter the U.S. market.

NorthStar accelerator project:

NorthStar described the following progress:

- Experiments at Argonne National Laboratory (ANL) benchmarked Monte Carlo calculations of produced activity.
- Successful tests of a Helium blower system at Los Alamos National Laboratory (LANL) showed that a liquid Helium plant will not be necessary.

SHINE Accelerator with LEU Fission project:

SHINE reported the following progress:

- SHINE headquarters moved to Janesville, Wisconsin.
- Building One groundbreaking occurred and construction was begun. SHINE Building One is the first building built on the SHINE campus. SHINE will utilize it to demonstrate actual production equipment, serve as an employee training facility, and allow SHINE to develop operating history with equipment. SHINE expects occupancy in Q1 2018.
- Baker Concrete Construction was chosen as prime contractor for the primary production facility. Baker is a civil firm with nuclear experience.
- In 2017, SHINE went from 23 employees to over 60 employees and expects to hire 10 more in the next few months.

General Atomics LEU Target project:

GA reported the following progress:

- Full-scale target assembly flow and pressure drop have been verified in a simulated reactor pool.
- Target irradiation testing and post irradiation examination has verified design calculations.
- Rapid Mo-99 extraction yield from full-scale selective gas extraction (SGE) target batch was demonstrated to be greater than 90%.
- Part 1 License Amendment Application and Round 1 Request for Additional information have been submitted to Nuclear Regulatory Commission (NRC).
- Process and waste hot cells have been designed and are being fabricated.
- A technical data package supporting a *take back* disposal pathway was provided to DOE.

In addition to its support of CA partners, the NNSA-M³ continues to support foundational research at the DOE National Laboratories that benefits the CA projects. This year support aimed at research identified by other potential producers that are not CA partners has been provided for the first time. Given the importance of understanding the costs of waste take back in the ULTB program, the Subcommittee encourages DOE-M³ to consider supporting research that could help in resolving these waste issues.

Findings

The Subcommittee found that since the review in 2016, NNSA has moved the NNSA-M³ program forward, consistent with the specific AMIPA requirements.

There continue to be issues related to the long-term financial viability of any producers that *do* succeed in entering the market. The reasons for this include the relative stability of the present supply of ⁹⁹Mo, the challenge of achieving market acceptance for a new generator technology (for one CA partner), and the slow rate of progress on the global move toward FCR.

The NNSA-M³ program is a mature program that is expected to reach its goals in the next two-three years. The remaining major challenge that is within DOE's control concerns the ULTB program and the ability to achieve predictable costs for disposal of leased uranium residues. Resolution of this issue will require focus and coordination across organizational entities within the Department of Energy. Given the maturity of the program and the advanced state of technical progress of CA projects focused on demonstrating feasibility for domestic ⁹⁹Mo production, it is unlikely that future NSAC reviews would identify new recommendations that could impact the program's success.

In the next sub-sections, the Subcommittee addresses the specific questions presented in the NSAC charge.

What is the current status of implementing the goals of the NNSA-MMM ⁹⁹Mo Program? What progress has been made since the 2016 assessment?

All four Cooperative Agreement projects have been awarded at \$25M to support LEU fission production by reactor and accelerator irradiation, reactor neutron capture in ⁹⁸Mo, and electron accelerator irradiation of ¹⁰⁰Mo. The first delivery of LEU under ULTB was made in January 2017 and take-back options at DOE and commercial sites are being evaluated. In the international market, South Africa has certified in August 2017 that it is using 100% LEU targets. In January of 2018 Curium announced the capability for 100% LEU production of ⁹⁹Mo. The program continues to hold public stakeholder and technical topical meetings, and issued a report to Congress in October 2017. All four CA projects have made technical and business development progress, with anticipated market entry ranging from the first half of 2018 through 2020. The program continues to support national laboratory collaborative projects at ANL, LANL, Oak Ridge, Pacific Northwest, Savannah River, and Y-12.

Since the 2016 NSAC assessment, SHINE began construction on their research and development building; GA/MURR/NORDION has demonstrated chemistry at production levels of uranium and using trace amounts of ⁹⁹Mo, and NorthStar has introduced lines 2 and 3 at MURR and began construction for accelerator production.

At the time of this review, NorthStar continued to seek FDA approval of their new RadioGenix $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator technology. When FDA approval is granted, NorthStar will be ready to enter the market with ^{99}Mo produced by the neutron capture project. (Note: as this report was being finalized, the FDA announced [3] the approval of the RadioGenix generator). The NorthStar project to produce ^{99}Mo with accelerators is on schedule to be on line in two years. NorthStar anticipates being able to produce at least 1000 6-day Ci by mid 2019, which has the potential to mitigate potential shortages in global supply. However, given the delays seen by all CA partners over the course of these NSAC reviews, it is likely that unanticipated delays will continue to occur for all CA projects. For this reason, the Subcommittee concludes that although it is probable that one or more of the NNSA supported projects will enter the market eventually, and perhaps as early as the first half of 2018, it will likely not be with sufficient capacity to mitigate potential shortages in the period before 2020.

Even with this significant progress, there will continue to be a gap for any CA partners to reach the original 3000 6-Day Ci goal for an undetermined period of time, at least through 2020.

Is the strategy for continuing to implement the NNSA goals complete and feasible, within an international context?

The Subcommittee concludes that the NNSA strategy is complete and feasible:

- The NNSA-M³ Domestic Molybdenum-99 Program has achieved the objective of the program: to provide assistance to commercial entities to accelerate production of ^{99}Mo in the United States without the use of HEU. We consider it likely that one or more of the CA partners will begin potentially sustainable production of ^{99}Mo for the domestic radio-pharmacy market.
- Completion of the ULTB program is an important part of the NNSA strategy. This is essential for some CA projects.
- Three of the four major international suppliers have transitioned to the use of LEU targets, and the fourth is expected to make the transition soon. Two reactors continue to use HEU fuel (Belgium Reactor 2 and MURR)

Are the risks identified in implementing those goals being appropriately managed?

In the Subcommittee meeting, NNSA presented a summary of risks and the actions taken addressing those risks.

The Subcommittee finds that the major outstanding risk to the successful completion of the goals of the NNSA program is the finalization of the ULTB program. As discussed elsewhere, the lease aspect of the program appears to

be in place while the *take back* has not been finalized, in part due to the complex nature of involving multiple departments within and outside the DOE. Timely communication is essential for successful resolution.

This risk is of significance because two of the CA partners will most likely rely on this program, and both of these projects will produce ⁹⁹Mo that would seamlessly fold into the existing supply chain because they can use existing generator technology. Failure to complete the contracts for the CA partner(s) in a timely fashion could result in the withdrawal of CA partners before completion of their projects.

There remain other risks to the success of the NNSA goals, as have been addressed elsewhere in this report or earlier reports, but for the most part these are outside of the control of the NNSA. In particular, we note the risk posed by the need for the market to accept new generator technology in order to use the low specific activity ⁹⁹Mo produced by NorthStar. These risks should continue to be monitored.

Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2016 NSAC assessment of the ⁹⁹Mo Program appropriately and adequately?

The NNSA has responded that they agree that the recommendation from the previous report (*The costs associated with the take-back portion of the ULTB program must be defined in a way that potential customers have predictable costs. The subcommittee considers it extremely urgent that DOE identify a way to cap the liability associated with spent nuclear fuel (SNF) and radioactive waste in the ULTB program for potential US ⁹⁹Mo producers*) is important, and they have been working with one of the cooperative agreement (CA) partners on this issue. It was emphasized that determining costs for taking back uranium has been very challenging, as there are many facets that include crafting a contract that is acceptable to the CA partner and the U. S. Government. NNSA must work closely with DOE Environmental Management (DOE-EM) during the communication process with any customer wanting to use the ULTB program. One CA partner has been working with NNSA for over a year with limited progress on a take back contract. NNSA has leased material to this CA partner, but so far it may not be irradiated because there is no contract for taking back that material. Further, a *draft* contract has not even been shared with the partner as of the time of the subcommittee meeting. NNSA acknowledges the slowness of the process but emphasized the technical challenges as well as the sensitivity of communication as a factor.

The complexity and diversity of waste that is generated by the various CA partners and other companies that need the ULTB program precludes a way to identify a generic cap on the liability. It is the view of the Subcommittee that for a

given contract and producer, the costs must be well defined, predictable, and stable in order for the potential producers to put together the required business plans.

Recommendation

Various potential U.S. producers of ⁹⁹Mo, including several of the CA partners, will need to use the capabilities of the ULTB program. In order to develop their business model, they must have well-defined, predictable, and stable costs for disposition of the waste they produce. In the approximately 15 months since the last NSAC review (September 2016), no contract for ULTB waste has been shared with potential producers.

For this reason, the single recommendation of the Subcommittee is that the Department of Energy should:

- a) In a timely manner, issue a waste *take back* contract to the CA partner with whom they have been engaged for the last year *and*
- b) use the lessons learned in this process to identify opportunities for improvement of the ULTB process.

References

- [1] OECD/NEA (2017), *The Supply of Medical Radioisotopes: 2017 Medical Isotope Supply Review: ⁹⁹Mo/^{99m}Tc Market Demand and Production Capacity Projection 2017-2022*, NEA/SEN/HLGMR (2017) 2, Paris, France.
- [2] OECD/NEA (2017), *The Supply of Medical Radioisotopes: Results from the Third Self-assessment of the Global Mo-99/Tc-99m Supply Chain*, NEA/SEN/HLGMR (2017) 5, Paris, France.
- [3] Press release by the Food and Drug Administration February 8, 2018
<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm595996.htm> .

Appendix 1 – Charge Letter



U.S. Department of Energy
and the
National Science Foundation



September 27, 2017

Professor David Hertzog
Chair, DOE/NSF Nuclear Science Advisory Committee
Department of Physics
University of Washington
Seattle, Washington 98195

Dear Professor Hertzog:

This letter is to request that, in accordance with direction given to the DOE in the National Defense Authorization Act (NDAA) for FY2013, the Nuclear Science Advisory Committee (NSAC) standing Subcommittee on Mo-99 conduct its annual assessment of the effectiveness of the National Nuclear Security Administration, Office of Material Management and Minimization (NNSA-MMM) Domestic Molybdenum-99 (Mo-99) Program (formerly known as the Global Threat Reduction Initiative).

The American Medical Isotopes Production Act of 2012 (Act), formerly known as S. 99 and H.R. 3276, was incorporated into the National Defense Authorization Act (NDAA) for FY2013. On January 2, 2013, President Obama signed the NDAA into law, enacting this legislation. A stipulation of the NDAA under section 3173 – *IMPROVING THE RELIABILITY OF DOMESTIC MEDICAL ISOTOPE SUPPLY* is that:

“...the Secretary [of Energy] shall...use the Nuclear Science Advisory Committee to conduct annual reviews of the progress made in achieving the [NNSA MMM] program goals and make recommendations to improve effectiveness.”

The Department of Energy (DOE) and National Science Foundation (NSF) very much appreciate NSAC’s three previous assessments as described in reports transmitted to the agencies on May 8, 2014, July 10, 2015 and November 6, 2016.

Subsequently, we request that NSAC reconvene the Subcommittee to provide a fourth annual assessment addressing the following charge elements:

- What is the current status of implementing the goals of the NNSA-MMM Mo-99 Program? What progress has been made since the 2016 NSAC assessment?
- Is the strategy for continuing to implement the NNSA goals complete and feasible, within an international context?
- Are the risks identified in implementing those goals being appropriately managed?




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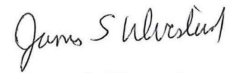
- Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2016 NSAC assessment of the Mo-99 Program appropriately and adequately?
- What steps should be taken to further improve NNSA program effectiveness in establishing a domestic supply of Mo-99?

It is requested that this assessment be submitted by January 31, 2018.

We are aware that this charge represents an additional burden on your time. However, the involvement of NSAC is essential to inform the Agency regarding the effectiveness of efforts to steward Mo-99, and isotope essential for the health and well-being of the Nation.

Sincerely,


J. Stephen Binkley
Acting Director
Office of Science


James S. Ulvestad
Acting Assistant Director
Directorate for Mathematical
and Physical Sciences

Appendix 2 – Membership of the NSAC Molybdenum-99 Subcommittee

Susan Seestrom, Chair, Sandia National Laboratories
 Carolyn Anderson, University of Pittsburgh
 Jeff Binder, Argonne National Laboratory
 Ronald Crone, Idaho National Laboratory
 Frederic Fahey, Boston Children's Hospital
 Jack Faught, LINDE
 Mitch Ferren, Oak Ridge National Laboratory
 David Hertzog, University of Washington
 Suzanne Lapi, University of Alabama at Birmingham
 Meiring Nortier, Los Alamos National Laboratory
 Steve Mattmuller, Kettering Medical Center
 Berndt Mueller, Brookhaven National Laboratory
 Ken Nash, Washington State University
 Joseph Natowitz, Texas A&M University
 Thomas Ruth, TRIUMF

| Committee Expertise | | |
|---|--|--|
| Reactor Design and Operation | Radioisotope Production | Radiopharmaceutical Chemistry |
| Ron Crone Jeff Binder | Mitch Ferren Jeff Binder Suzanne Lapi Meiring Nortier Thomas J. Ruth | Carolyn Anderson Suzanne Lapi Thomas J. Ruth |
| Nuclear and Radio Chemistry | Commercial Isotope Sales | Project Management |
| Carolyn Anderson Suzanne Lapi Ken Nash Joe Natowitz Meiring Nortier Thomas J. Ruth | Jack Faught Mitch Ferren | Berndt Mueller David Hertzog Susan Seestrom Ron Crone |
| Nuclear Physics | Nuclear Engineering | Radiopharmacy and Clinical Use |
| David Hertzog Berndt Mueller Joe Natowitz Susan Seestrom | Ron Crone Jeff Binder Meiring Nortier | Steve Mattmuller Frederic Fahey |

Appendix 3 – Meeting Agenda

Meeting Agenda
2017 DOE/NSF Nuclear Science Advisory Committee Mo-99 Program Review
December 14-15, 2017
Crystal City Marriott, Salons A&B
1999 Jefferson Davis Highway
Arlington, Virginia

December 14, 2017

OPEN SESSION

- 08:15 – 08:30 Discussion of Charge and Introductions (DOE NP)
- 08:30 – 09:00 Review of 2016 Recommendations (Seestrom)
- 09:00 – 10:15 Developments in the Mo-99 Program since 2016 review (NNSA)
- Current status of cooperative agreement projects
 - NNSA response to 2015 NSAC recommendations
- 10:15 – 10:30 Break
- 10:30 – 11:00 Status of the Uranium Lease and Take-Back Program (Peter Karcz, DOE-EM)
- 11:00 – 12:00 Review of NAS 2016 Report (Thomas Ruth, TRIUMF)

CLOSED SESSION (Committee, NSF and DOE NP)

- 12:00 – 1:00 WORKING LUNCH

CLOSED SESSION (Committee, NSF, DOE NP, and DOE NNSA)

- 1:00– 2:00 Closed-session updates from NNSA
- 2:00 – 5:00 Updates from NNSA Cooperative Agreement Partners
- 2:00-3:00 General Atomics (MURR and Nordion)
 - 3:00-4:00 NorthStar Medical Radioisotopes
 - 4:00-5:00 SHINE Medical Technologies
- 5:00 – 5:30 Committee Discussion (Committee, NSF, and DOE NP)**2017**

December 15, 2017

OPEN SESSION

08:30 – 9:00 Q&A on OECD projections of supply and demand (Kevin Charlton, OECD-NEA)

9:00 – 10:30 Mo-99 Stakeholder Input and Public Comment Session

10:30 – 11:00 Committee Discussion / Q&A for Open Session Participants

CLOSED SESSION

11:00 – 12:00 Committee Working Session (Committee, NSF, and DOE NP only)

12:00 – 1:00 WORKING LUNCH (Committee, NSF, DOE NP, and NNSA)

1:00 – 3:00 Committee Working Session (Committee, NSF, and DOE NP only)

3:00 Adjourn

Appendix 4 – Background on ^{99}Mo from the NSAC 2014 Report

The technetium-99m isomeric state ($^{99\text{m}}\text{Tc}$) is the most common radioisotope used in nuclear medicine procedures in the U.S. It is employed in about 14 million procedures per year. The isomeric decay produces a 140 keV gamma-ray that is well suited for gamma camera imaging and the half-life, 6.0 hours, allows sufficient time for preparing radiopharmaceuticals while being short enough to assure relatively rapid physical decay following the procedure. There are a variety of radiopharmaceuticals containing $^{99\text{m}}\text{Tc}$ for planar gamma scintigraphy and single photon emission computed tomography (SPECT) imaging in patients having multiple types of diseases. Technetium-99m has found extensive use in nuclear cardiology (50% of procedures), nuclear oncology (25%) and in other imaging of the brain, endocrine system, lungs, gastro-intestinal (GI) and genito-urinary (GU) and bones. Technetium-99m can be produced directly on a cyclotron or other type of particle accelerator, but is most conveniently obtained from the beta-decay of ^{99}Mo with a half-life of 66 hours.

The development of the ^{99}Mo generator for producing $^{99\text{m}}\text{Tc}$ is a success story of the DOE National Laboratories. In the late 1950's scientists at Brookhaven National Laboratory were working on improving a separation process for materials produced in the Brookhaven Graphite Research Reactor. They detected a trace contaminant of $^{99\text{m}}\text{Tc}$, which was coming from contaminant ^{99}Mo . Based on the similarities with the chemistry of the tellurium-iodine parent-daughter pair, they developed the first $^{99\text{m}}\text{Tc}$ generator in 1958 [1]. At this time the head of the radioisotope production effort, Powell Richards, realized the potential of $^{99\text{m}}\text{Tc}$ as a medical radiotracer and promoted its use among the medical community. Dr. Paul Harper of the Argonne Cancer Research Hospital ordered and used the first $^{99\text{m}}\text{Tc}$ generator in 1961, and the boom began.

The $^{99\text{m}}\text{Tc}$ generators allow a quick and convenient chemical separation of $^{99\text{m}}\text{Tc}$ daughter nuclei from the ^{99}Mo parent material. The longer half-life of the ^{99}Mo makes it possible for ^{99}Mo to be produced at central large capacity locations and then transported to centralized radiopharmacies, which produce $^{99\text{m}}\text{Tc}$ radiopharmaceuticals and distribute them to hospitals and other imaging facilities. ^{99}Mo production is traditionally measured in "6-day Curies" based on the activity of the material six days after it is shipped (22% of the activity at the time of shipping). The historical worldwide demand has been about 12,000 6-day Ci per week with the U.S. demand at 6,000 6-day Ci per week; recent estimates show reduced demand of 10,000 6-day Ci per week worldwide (5,000 U.S.).

Molybdenum-99 is a fission fragment that is abundantly produced in the neutron-induced fission of ^{235}U (6% of all fissions). The last commercial production of ^{99}Mo in the U.S. ended in 1989. Since that time U.S. supply has relied on international producers who took advantage of the high efficiency of irradiating highly enriched uranium (HEU) targets, using material often exported from the U.S., at eight existing multi-purpose research reactors, with six of these sites

being over 45-55 years old. Approximately half of the U.S. supply of ^{99}Mo has typically come from the National Research Universal (NRU) reactor in Canada. As part of its nuclear non-proliferation efforts, the U.S. plans to minimize the export of HEU, which is used both for targets for isotope production and for fuel for reactors. This has been a primary mission of the NNSA Global Threat Reduction Initiative. When concern arose that this reduction in HEU exports would negatively affect the supply of radioisotopes in the U.S., Congress asked the National Research Council in the Energy Policy Act of 2005 to deliver a report on the feasibility and likely cost of non-HEU production of ^{99}Mo . This report, "Production of Medical Isotopes without Highly Enriched Uranium"[2] concluded that production with low enriched uranium (LEU) targets was feasible and estimated the additional cost for each procedure if LEU was used.

Around the same time, the ^{99}Mo supply underwent a series of shocks. In 2005, a U.S. based technetium generator producer shut down production for 5 months for a product recall. The NRU reactor shut down for one month in 2007. In August 2008 the High Flux Reactor at Petten (Netherlands) was shut down for six months. The NRU reactor was unexpectedly shut down in May 2009 as a result of a leak in the reactor vessel and only returned to service in August 2010. Simultaneously the HFR reactor in Petten was again shut down for more than 6 months. The global supply of ^{99}Mo could not meet the demand during these periods and some hospitals and clinics were forced to postpone or cancel imaging procedures. In some cases alternative-imaging procedures could be used and some even gave better results (e.g. ^{82}Rb for cardio-perfusion imaging). However, many of these alternatives involve higher radiation dose rates and often give lower quality results to the patient, e.g. ^{201}Tl cardiac scans. Additionally, most of these alternative-imaging agents were more expensive than $^{99\text{m}}\text{Tc}$ radiopharmaceuticals. Under this pressure, pharmacies did learn to use the ^{99}Mo they had more efficiently. As a result of the adaptation to these issues, and with the growth of alternative procedures, while the number of $^{99\text{m}}\text{Tc}$ procedures has continued to increase, ^{99}Mo demand in the U.S. is now calculated by OECD Nuclear Energy Agency (OECD-NEA) to be reduced to about 5,000 6-day Ci/week. [3]

To coordinate the international efforts to address these shortages, the OECD-NEA set up an international group to look at issues concerning the supply of medical isotopes, the High Level Group on the Security of Supply of Medical Radioisotopes (HLG-MR), in April 2009. This group performed detailed economic analyses of the ^{99}Mo supply [4] and concluded that the fundamental issue in the market was an unsustainable pricing structure based on government subsidization. The HLG-MR developed six principles and supporting recommendations to improve the reliability of the supply [5] (See *Appendix 4*). The first principle proposed is the implementation of full cost recovery pricing, including costs related to capital replacement. At the time of this review, Parrish Staples of NNSA was serving as the chairman of this group.

In the U.S., growing concern over supply of medical isotopes led to the introduction of the American Medical Isotopes Production Act (AMIPA). A bill, H.R. 3276, which passed the House of Representatives in November 2009, directed the Secretary of Energy to establish a program to evaluate and support projects for the production of significant quantities of ⁹⁹Mo in the U.S. for medical use, without the use of highly enriched uranium. It also directed the creation of a lease and take-back program to make low enrichment uranium available for the production of medical isotopes and proposed to end the export of highly enriched uranium for medical isotope production in the future. The bill died without action in the Senate. On November 17, 2011 the Senate passed S. 99, The American Medical Isotopes Production Act of 2011 which contained similar language. Neither of the proposed actions carried the force of law.

The NNSA GTRI took on the mission to address the ⁹⁹Mo production issue even before the AMPIA legislation was finally passed. There is strong overlap with their on-going work of minimizing the use of HEU. Senate report 112-17 provided a cost framework for the scope of the work, but was not an appropriation. Since the problem involved non-proliferation, health, international issues and nuclear and medical regulation issues, an inter-agency working group led by the White House Office of Science and Technology Policy (OSTP) (involving NNSA GTRI, Department of Energy (DOE)/ Office of Science, DOE/Nuclear Energy, FDA, Department of Health and Human Services (HHS)/Centers for Medicare & Medicaid Services (CMS), Department of State, Department of Homeland Security, NRC, Department of Transportation, National Institutes of Health/National Cancer Institute, and the Office of Management and Budget) was formed to coordinate activities, again even before the AMIPA legislation was passed. A stakeholders group was also formed to ensure input from and communication with the suppliers and end users.

The final version of the AMIPA was included in the Defense Authorization Act for 2013 and signed into law in January 2013. It requires the Secretary of Energy to *“establish a technology-neutral program . . . to evaluate and support projects for the production in the United States, without the use of highly enriched uranium, of significant quantities of molybdenum-99 for medical uses.”* It also required *“the costs of which shall be shared in accordance with section 988 of the Energy Policy Act of 2005.”* This latter act requires no less than a 50% cost sharing for non-R&D activities and no less than a 20% cost sharing for R&D activities, as determined by the Secretary. The act also directed the Secretary to *“use the Nuclear Science Advisory Committee to conduct annual reviews of the progress made in achieving the program goals and make recommendations to improve program effectiveness”*. The final language of the law requires the Secretary of Energy to *“establish a program to make low enriched uranium available, through lease contracts, for irradiation for the production of molybdenum-99 for medical uses and to (i) to retain responsibility for the final disposition of spent nuclear fuel created by the irradiation, processing, or purification of uranium leased under this section for the production of medical isotopes.”* However, the Secretary is only

required to be responsible for final disposition of radioactive waste for which the Secretary determines that the producer does not have access to a disposal path.

References to Appendix 4

[1] Tucker, W.D., Greene, M.W., Weiss, A.J., and Murenhoff, A.P. *Methods of preparation of some carrier-free radioisotopes involving sorption on alumina*. BNL 3746. American Nuclear Society Annual Meeting, Los Angeles, CA, June 1958. Trans. Am. Nucl. Soc. 1,1958,160.

[2] National Research Council. *Medical Isotope Production Without Highly Enriched Uranium*. Washington, DC: The National Academies Press, 2009. http://www.nap.edu/catalog.php?record_id=12569

[3] OECD/NEA (2014), *The Supply of Medical Radioisotopes: Medical Isotope Supply in the Future: Production Capacity and Demand Forecast for the 99Mo/99mTc Market, 2015-2020*, OECD, Paris, France.

[4] OECD/NEA (2010), *The Supply of Medical Radioisotopes: An Economic Study of the Molybdenum-99 Supply Chain*, OECD, Paris, France.

[5] OECD/NEA (2011), *The Supply of Medical Radioisotopes: The Path to Reliability*, OECD, Paris, France.

Appendix 5 – Acronym List

AMIPA - American Medical Isotopes Production Act of 2012

CA - Cooperative Agreement

CNL - Canadian Nuclear Laboratories

DOE - U.S. Department of Energy

DOE-EM - U.S. Department of Energy Office of Environmental Management

FCR - full cost recovery

FDA - U.S. Food and Drug Administration

FOA – funding opportunity announcement

GA - General Atomics

GE - General Electric

GTCC LLW - greater than Class C low-level radioactive waste

GTRI - the NNSA Global Threat Reduction Initiative

HEU - Highly Enriched Uranium

HLG-MR - High Level Group on the Security of Supply of Medical Radioisotopes of the OECD-NEA

LEU - Low-Enriched Uranium

MURR - Missouri University Research Reactor

NAS - National Academies of Sciences, Engineering, and Medicine

NDA - New Drug Application

NNSA - National Nuclear Security Administration

NNSA-M³ - the NNSA Material Management and Minimization Program

NNSA-PO - the NNSA Production Office

NRC - U.S. Nuclear Regulatory Commission

NRU - National Research Universal reactor

NSAC - Nuclear Science Advisory Committee

OECD-NEA - Organization for Economic Cooperation and Development's Nuclear Energy Agency

PMDA - Plutonium Management Disposition Agreement

RGX - NorthStar RadioGenix ^{99m}Tc generating system

SGE - selective gas extraction

SNF - spent nuclear fuel

SV - source vessel

TRIGA - Training, Research and Isotopes, General Atomic reactor

ULTB - Uranium Lease and Take Back P