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

Suzanne Lapi, PhD

Professor of Radiology and Chemistry

The University of Alabama at Birmingham

Outline

- Charge and Subcommittee process
- Background – the ^{99}Mo issue
- Overview of the NNSA Material Management and Minimization ^{99}Mo program
- Findings and comments
- Recommendations

Charge to NSAC

- What is the current status of implementing the goals of the NNSA-MMM Mo-99 Program? What progress has been made since the 6th NSAC assessment?
- Is the strategy for continuing to implement the NNSA goals complete and feasible, within an international context?
- Are risks identified in implementing those goals being appropriately managed?
- Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2019/2020 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?

Subcommittee Members

- Ronald Crone, Idaho National Laboratory
- Gail Dodge, Old Dominion University
- Mitch Ferren, Oak Ridge National Laboratory
- Silvia Jurisson, University of Missouri - Columbia
- Suzanne Lapi, Chair, University of Alabama at Birmingham
- Steve Mattmuller, Kettering Medical Center
- Alan Packard, Boston Children’s Hospital
- Thomas Ruth, TRIUMF

Expertise of the Subcommittee

Committee Expertise		
Nuclear Medicine	**Radioisotope Production**	**Radiopharmacy and Clinical Use**
Alan Packard Suzanne Lapi Silvia Jurisson	Mitch Ferren Suzanne Lapi Thomas J. Ruth	Steve Mattmuller Alan Packard
Nuclear and Radiochemistry	**Commercial Isotope Sales**	**Project Management**
Silvia Jurisson Suzanne Lapi Thomas J. Ruth	Mitch Ferren Suzanne Lapi	Gail Dodge Ron Crone

Subcommittee Process

- The Subcommittee met virtually on May 10th, 2021
- We were briefed by:
  - NNSA (both open and closed sessions)
  - DOE-EM (both open and closed sessions)
  - All active cooperative agreement partners (written reports)

A follow up meeting was held with subcommittee members virtually on June 21st, 2021 for additional discussion about the report.

Background

- ^{99m}Tc is the daughter of ^{99}Mo and is widely used for nuclear medicine diagnostic imaging.
- Today, ^{99}Mo is mainly produced by fission of ^{235}U (until recently using Highly Enriched Uranium (HEU).
- There is U.S. government interest in reducing the use of HEU.
- American Medical Isotopes Production Act (AMIPA) aims establish a technology-neutral program to provide assistance to commercial entities to accelerate production of ^{99}Mo (without the use of HEU).
- Until recently, there was no U.S. producer of ^{99}Mo.

Image courtesy of J. McConathy, UAB

NNSA ^{99}Mo Objectives and Strategy

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 reactor fuel and by accelerating the establishment of commercial non-HEU-based ^{99}Mo production in the United States.

With respect to the former objective, it does appear that all of the major global ^{99}Mo producers will be using LEU targets by the end of 2022.

Changes in the international context

- The most dramatic change in the international landscape since the prior report was the impact of the COVID-19 pandemic. However, this caused minimal disruption of ^{99}Mo production.
- There was an impact on international transportation of processed ^{99}Mo, primarily becase of the large decrease in the number of international flights available to carry the processed ^{99}Mo.
- This disruption was resolved relatively quickly and only modestly impacted ^{99}Mo availability in the US.

Changes in the international context (OECD)

“The Supply of Medical Radioisotopes: 2019 Medical Isotope Demand and Capacity Projection for the 2019-2024 Period”.

- Global demand growth has been maintained as in earlier reports.
- The conclusion on supply is similar to the previous report, “When facilities are well-maintained, well-scheduled and when unplanned outages are avoided, total irradiator and processor capacity should be sufficient.” ……… “However, when no additional processing capacity is added above the present level, the capability to manage adverse events will remain low and will be further reduced with time.”
- Longer term OECD projections point to the possibility of a significant overcapacity internationally as additional facilities come on-line.

Current NNSA Co-operative Partners

	Neutron Capture Technology	Accelerator Technology	Accelerator with LEU Fission Technology	Photonuclear LEU fission
Cooperative Agreement Partner	NorthStar Medical Radioisotopes	NorthStar Medical Radioisotopes	SHINE Medical Technologies	Niowave
Cooperative Agreement Status	Active	Active	Active	Active
Anticipated Market Entry*	November 2018	2023	2022	2024/2025

*Market entry dates provided by CA partners in 2021

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

- Despite challenges presented by COVID-19, the program is continuing to make progress towards improving the reliability of domestic ^{99}Mo supply. While there is now U.S. produced ^{99}Mo in the market, establishment of a large-scale domestic supply (1000 6-day Ci/week) has not yet occurred.

- In addition to its support of CA partners, the NNSA-M3 continues to provide non-proprietary technical support at the DOE National Laboratories that benefits both the CA and non-CA projects.

NorthStar neutron capture project:

- ^{99}Mo currently in the US market
- Received FDA approval to implement enriched ^{98}Mo targets at MURR for ^{99}Mo production to enhance capacity

NorthStar accelerator project:

- Electron linac and production of ^{99}Mo via the $^{100}Mo(\gamma,n)$ reaction.
- Completed construction of the electron accelerator production building and the concrete bunker for the beam line and target station
- Commissioning activities, qualification production runs of ^{99}Mo and submissions to the FDA are scheduled in 2022

SHINE Accelerator with LEU Fission project:

- Construction of the production facility’s concrete structures is nearly complete
- SHINE expects to be able to produce 1,500 6-day Ci/week of ^{99}Mo with the first two neutron driver assembly system by the end of 2022.

Niowave project:

- Produce ^{99}Mo and other isotopes via photonuclear fission of LEU.
- Scaling up the ^{99}Mo process at their R&D facility
- They have added a new GMP Quality system that will allow them to provide active pharmaceutical ingredients (radioisotopes) to the pharmaceutical community in 2021

Northwest Medical Isotopes project:

- Over the past year, Northwest Medical Isotopes (NWMI) had changes in management as well as to their original plan/process. Given these changes, NWMI and NNSA are working together to determine the best path forward for the cooperative agreement. NWMI did not submit a report for this time period.

The CA partners acknowledge the importance of the assistance from the national labs.

NNSA issued a new Funding Opportunity Announcement (DE-FOA-0002303) in July 2020

- Criterion 1 – Commercial Deployment (weighted 50%): The applicant's proposal will be evaluated to measure the degree to which the applicant's approach will enable the project to produce and sell above quantities [3,000 6-day Ci/week].
- Criterion 2 – Technology Maturity (weighted 30%): The applicant's proposal will be evaluated to measure the degree to which the applicant's technical approach is able to produce and deliver above quantities.
- Criterion 3 – Business Strategy and Management Capabilities (weighted 20%): The applicant's proposal will be evaluated to measure the degree to which the company's business strategy and management capabilities will enable the project to achieve commercially approved ^{99}Mo in the above quantities.

This FOA process is underway, and awards are expected to be announced by the fall of 2021.

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

- The Subcommittee finds the dual goals of the NNSA program to be on track to realize both a significant domestic ^{99}Mo supply and a global conversion to non-HEU sources. The conversion of world producers to LEU targets has been very successful.
- The Uranium Lease and Take Back (ULTB) program has made progress in resolving the major outstanding issue related to the disposition of the returned uranium/waste and the costs associated with this transfer. At this point only one of the CA partners is pursuing this approach.
- The significant U.S. production of ^{99}Mo and entrance of NorthStar into the U.S. market – even with their unique generator system – does establish that the NNSA program of CA partner support can work.

Are the risks identified in implementation being appropriately managed?

- NNSA has identified a comprehensive set of risks; these were discussed in previous reports and no new risks have been identified.
- Some of these risks are beyond the direct control of the NNSA. All risks within the scope of their program are now being well managed.

Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2019/2020 NSAC assessment of the ^{99}Mo Program appropriately and adequately?

- *Prior Recommendation 1*

The limitations of the ULTB program continues to be one of the biggest risks to the program's success. The ULTB contract templates should be reviewed and revised as necessary; in particular, with respect to reducing the continuing significant uncertainties in the take-back aspects of the DOE-EM program. The results of this review should be presented to the NSAC ^{99}Mo Subcommittee at the next program assessment.

The lease contract between NNSA and SHINE and the take-back contract between EM and SHINE are expected to be signed following issuance of the Operating License by the U.S. Nuclear Regulatory Commission (NRC). Because SHINE will only be producing minimal amounts of greater than type C waste, their ULTB contract negotiations with DOE-EM was somewhat simplified.

The Subcommittee found that the NNSA has partially addressed its concerns and recommendations from the previous review. The program has established a ULTB concept for those CA partners that might require it with an anticipated first contract to be finalized in 2021. However, while all the current partners have a path forward, the ULTB program is still incomplete as there is still no disposal path for greater than Class C waste

- *Prior Recommendation 2*

The NNSA stated during this review that a program objective was to have at least two US producers, each capable of producing 3000 6-day Ci/week of ^{99}Mo. The third FOA for this program is anticipated in 2020. After 10 years of significant investment in this program, the NNSA should focus their strategy on prioritizing future awards such that time-to-market, consistent with the stated objective, is considered as the most important review criteria. This strategy should be reflected in the approach to allocation of CA funding and national laboratory resources.

The review committee considers this recommendation addressed. The NNSA FOA issued on July 30, 2020, included 3 separate merit review criteria: Commercial Deployment (Weighted 50%), Technology Maturity (Weighted 30%), Business Strategy and Management Capabilities (Weighted 20%). In addition, the FOA clearly stated that it was not intended to support Research and Development (R&D) projects.

Steps to further improve the NNSA program effectiveness in establishing the domestic supply of ^{99}Mo

- Two CA partners, NorthStar and SHINE are projected to be capable of producing 3,000 6-day curies/week during 2023. This is on track with NNSA's focus on commercial development rather than technology development.
- The NNSA should consider the methodology for ending the FOA process beyond what is already approved to align with two successful producers in the market in 2023.
- The pathways for disposal of greater than Class-C nuclear waste remain an issue and should continue to be investigated along with refinements to the disposal cost model.

Recommendation 1

- The NNSA-Material Management and Minimization (M3) ^{99}Mo Program has been underway since 2009 with several FOAs and rounds of funding to develop a domestic source of ^{99}Mo. Several companies that have or have had cooperative agreements with the NNSA for funding are in various stages of completion. The NNSA should define the metrics for an exit strategy from this program. This should be presented to the NSAC ^{99}Mo Subcommittee at the next program assessment.

Acknowledgements

- Thanks to our committee members who were very engaged and passionate about this topic and did a great job.
- Thanks to NNSA, EM and all the CA partners.
- Thanks to Brenda May for her support in organizing our meeting.

Back up slides

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

March 1, 2021

Professor Gail Dodge
Chair, DOE/NSF Nuclear Science Advisory Committee
College of Sciences
Old Dominion University
4600 Elkhorn Avenue
Norfolk, Virginia 23529

Dear Professor Dodge:

This letter is to request that, in accordance with direction given to the Department of Energy (DOE) in the National Defense Authorization Act (NDAA) for FY 2013, 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 NDAA for FY 2013. 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 DOE and the National Science Foundation very much appreciate NSAC's six previous assessments as described in reports transmitted to the agencies on May 8, 2014, July 30, 2015, November 3, 2016, March 19, 2018, April 17, 2019, and March 16, 2020.

We request that NSAC provide a seventh 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 6th 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?
- Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2019/2020 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 spring of 2021.

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,

JOHN BINKLEY Digitally signed by JOHN BINKLEY Date: 2021.03.01 11:27:27 -05'00'

J. Stephen Binkley
Acting Director
Office of Science

Sean L. Jones Digitally signed by Sean L. Jones Date: 2021.03.01 13:19:51 -05'00'

Sean Jones
Assistant Director
Directorate for Mathematical and Physical Sciences
National Science Foundation

What is ^{99}Mo?

Molybdenum-99 (Mo-99) is the parent product of Tc-99m, a radioisotope used in approximately 50,000 medical diagnostic tests per day in the U.S. (over 18 million per year in the U.S.)

Primary uses include detection of heart disease, cancer, study of organ structure and function, and other applications.

Mo-99 has a short half life (66 hours) and cannot be stockpiled

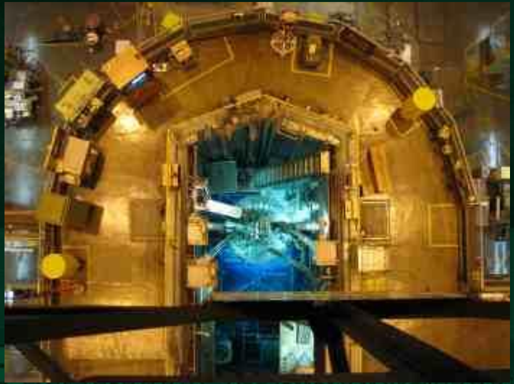
U.S. demand is approximately 50% of the world market

- The historic global demand is ~12,000 6-day curies per week.
- Since the 2009-2010 shortages, global demand has been ~10,000 6-day curies per week.

Mo-99 is produced at only 5 processing facilities worldwide, in cooperation with 8 research reactor facilities

- Processing facilities located in Canada (HEU), The Netherlands (HEU), Belgium (HEU), South Africa (HEU and LEU), and Australia (LEU)
- Research reactors used for irradiation located in Canada, The Netherlands, Belgium, France, Poland, Czech Republic, South Africa, and Australia

Tc-99m generator and labeling kits



SAFARI-1 Reactor (South Africa)

The American Medical Isotopes Production Act of 2012

- The Act was incorporated in the National Defense Authorization Act for Fiscal Year 2013 and enacted on January 2, 2013.

- Intended to help establish a reliable domestic supply of Mo-99 produced without the use of HEU and includes a number of short, medium, and long-term actions.

    - Requires the Secretary of Energy to establish a technology-neutral program to provide assistance to commercial entities to accelerate production of Mo-99 in the United States without the use of HEU
    - Requires annual public participation and review
    - Requires development assistance for fuels, targets, and processes
    - Establishes a Uranium Lease and Take Back program
    - Requires DOE and NRC to coordinate environmental reviews where practicable
    - Provides a cutoff in exports of HEU for isotope production in 7 years, with possibility for extension in the event of a supply shortage
    - Requires a number of reports to be submitted to Congress