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April 17, 2019

Dr. J. Stephen Binkley
Acting Director, Office of Science
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1000 Independence Ave., SW
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Dr. Anne Kinney
Assistant Director
Directorate for Mathematical and Physical Sciences
National Science Foundation
2415 Eisenhower Avenue
Alexandria, Virginia 22314

Dear Drs. Binkley and Kinney,

In the letter from your offices dated September 12, 2018, you charged NSAC to reconvene its standing Subcommittee on Mo-99 to conduct its annual assessment of the effectiveness of the National Nuclear Security Administration, Office of Material Management and Minimization (NNSAMMM) Domestic Molybdenum-99 Program. The attached report from the NSAC Subcommittee convened to carry out this charge is the fifth such annual assessment. The Subcommittee was chaired as before by Dr. Susan Seestrom. Its composition was broad, including expertise in reactor design, nuclear and radio chemistry, nuclear physics, radiopharmacy, radioisotope production, nuclear engineering, and clinical end use of Mo-99/Tc99m. In the last phase of the writing of the report, Professor Suzanne Lapi from the University of Alabama at Birmingham assumed leadership for its completion due to a practical exigency unrelated to the Subcommittee's work.

Fact finding for this report was facilitated by a Subcommittee meeting held December 6-7, 2018. Progress on the overall program was presented by NNSA leaders. The Subcommittee found that since the review in 2017, NNSA has moved the NNSA-M3 program forward, consistent with the AMIPA language. Over the last year there have been successes: notably NorthStar has begun to deliver ⁹⁹Mo to the U.S. market on a small scale, the first domestic supply since the beginning of the NNSA program to assist with the development of a domestic supply. There have also been setbacks, such as the fact that General Atomics has withdrawn from the program for stated reasons which included continued uncertainty about the paths for radioactive waste storage and disposal. The latter finding led in part to one of the report's recommendations related to the Uranium Lease and Take Back (ULTB) program. While a ULTB program has been formally established, an effective model for practical implementation of this program remains elusive and

NNSA does not appear to have a working strategy for proactively addressing the waste acceptance criteria and disposal options with CA partners. Hence, the recommendations read:

- NNSA must encourage CA partners and others interested in ULTB to engage with them early on so that a plan including take back can be developed in a timely fashion.
- NNSA must develop a waste take back process document to formalize the commitment to this process, including a model timeline and an estimate of costs under a set of well-defined scenario templates, in order to formalize communications with potential users. This must be presented to the subcommittee in advance of its next meeting.

There are additional issues related to the financial viability of any producers that succeed in entering the market. They include product-specific concerns, such as achieving wide-spread market acceptance for NorthStar's RadioGenix generator technology. As well, there are compliance implications related to the mandated full cost recovery (FCR) principles. The Subcommittee supports the U.S. commitment to FCR, but also recognizes that measuring and implementing it will be challenging and that the slow progress and/or uncertain commitment to FCR by the international community could impact the ultimate financial viability of any U.S. producers. The Subcommittee recommends:

- NNSA should require existing and new CAs (or potential producers supported by national lab research) to agree to adhere to the OECD principles of FCR and to submit to self-reporting to the OECD FCR survey as soon as they have provided product to U.S. or other markets.

The Subcommittee report was presented to NSAC during its April 8, 2019 meeting. Following discussion, the report was approved unanimously.

Sincerely,



David W. Hertzog
Professor of Physics
Chair, NSAC

cc: Tim Hallman, DOE
Allena Opper, NSF
Denise Caldwell, NSF

Report to the Nuclear Science Advisory Committee

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

**April 1st, 2019
Report of the NSAC ⁹⁹Mo Subcommittee**

Executive Summary

The Nuclear Science Advisory Committee (NSAC) Molybdenum-99 (⁹⁹Mo) Subcommittee met December 6-7, 2018 to address the charge to NSAC requesting that a fifth 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 its assessment of the ⁹⁹Mo production capacity and demand curves [1]. There have been worrisome negative trends, e.g. multiple problems at NTP Radioisotopes SOC Limited, South Africa (NTP) led to "chronic" shortage situations in some markets for ⁹⁹Mo/^{99m}Tc. Almost all international projects, including those supported by NNSA, have reported delays. Supply shortages of up to 15% of world demand occurred in some weeks.

The Subcommittee found that NNSA has partially addressed its concerns and recommendations. A draft take-back contract was not issued with the CA partner with whom they were in negotiations before that partner requested termination of the CA. The NNSA has made an attempt to capture lessons learned from the initial attempt to create a takeback contract for a CA partner. The committee believes that the effort thus far will be insufficient to increase the likelihood that a takeback contract can be issued in a timely way with well-defined, predictable, and stable costs for disposition and storage of waste from leased LEU.

Longer term, OECD projections point to the possibility of a significant overcapacity internationally as additional facilities come on-line. Such an overcapacity could threaten the sustained economic viability of the fledgling domestic projects.

The Subcommittee has two recommendations:

Recommendation 1

The slow implementation of full cost recovery (FCR) worldwide continues to be a risk to the financial viability of U.S. producers. NNSA has supported the development of a technology with a U.S. producer of ⁹⁹Mo who has now entered the U.S. market. It is an appropriate time for NNSA to ensure that the U.S. producers they have supported adhere to the tenets of full cost recovery to which the United States has agreed [2]. Therefore, the subcommittee recommends:

NNSA should require existing and new CAs (or potential producers supported by national lab research) to agree to adhere to the OECD principles of FCR and to submit self-reporting to the OECD FCR survey as soon as they have provided product to U.S. or other markets.

Recommendation 2

Although the ULTB has been established, and LEU has been leased under this program, the NNSA has not successfully executed a take back contract with any CA partner. Nor has the NNSA executed a take back contract with any of the other potential new (non-CA partner) US producers of ⁹⁹Mo because no other U.S. producer has approached DOE/NNSA for a ULTB contract. One CA partner has withdrawn from the program, stating there were multiple factors “including the business implication of the continued uncertainty around the costs and timing associated with the uranium take back agreement.” For this reason, it is imperative that NNSA take additional actions aimed at improving the transparency and predictability of this program. This requires working closely with DOE-EM. The subcommittee recommends:

- NNSA must encourage CA partners and others interested in ULTB to engage with them early on so that a plan including take back can be developed in a timely fashion.
- NNSA must develop a waste take back process document to formalize the commitment to this process, including a model timeline and an estimate of costs under a set of well-defined scenario templates, in order to formalize communications with potential users. This must be presented to the subcommittee in advance of its next meeting.

Introduction

The Nuclear Science Advisory Committee (NSAC) Molybdenum-99 (^{99}Mo) Subcommittee began its work in 2018 in response to a charge letter dated September 12th, 2018 (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 which requires the Secretary of Energy to establish a technology-neutral program to provide assistance to commercial entities to accelerate production of ^{99}Mo (aimed at ensuring a reliable domestic supply of the isotope ^{99}Mo) used to supply the medical diagnostic isotope $^{99\text{m}}\text{Tc}$ in the United States, without the use of Highly Enriched Uranium (HEU). The National Nuclear Security Administration (NNSA) was given the responsibility for development of this program in 2009. This Act also called for an annual review of the NNSA ^{99}Mo program by the NSAC. Following an NNSA reorganization, the ^{99}Mo 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 and an additional meeting was held in 2017. The 2018 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 6-7 in Gaithersburg, Maryland and built on the extensive work of the previous four reviews. At this meeting, the Subcommittee was briefed by NNSA on details of the program and received input from the Organization for Economic Cooperation and Development's Nuclear Energy Agency (OECD-NEA) The Subcommittee invited input from both current CA partners, both of which presented briefings. Finally, the Subcommittee solicited feedback from a broad set of ^{99}Mo stakeholders, devoting a session to stakeholder input. Appendix 3 contains the agenda of the Subcommittee meeting.

Considerable information on ^{99}Mo 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 2017 Report

The OECD-NEA issued a new report “The Supply of Medical Radioisotopes: 2018 Medical Isotope Demand and Capacity Projection for the 2018-2023 Period” [1]. In Reference [1] the 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. When the supply chain has fully implemented the recommended paid levels of ORC, the supply chain should be able to manage a limited unplanned outage of a reactor or a processor during the period to 2023. However, when no additional processing capacity is added above the present level, the capability to manage any adverse events, particularly concerning ORC will be low and will reduce progressively with time.”

That said, the presentation from OECD representative Kevin Charlton pointed to some worrisome negative trends, e.g. multiple NTP problems led to a “chronic” shortage situation in some markets for $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ and some shortages of ^{131}I . Almost all international projects, including those supported by NNSA, have reported delays. The world-wide supply has been stabilized to a certain degree due to the efforts of existing supply chain participants and the coordination activities of the Association of Isotope Producers and Equipment Suppliers (AIPES), but challenges remain. A measure of the instability is that the AIPES Emergency Response Team (ERT) convened more than 45 times and that supply shortages of up to 15% of world demand occurred in some weeks.

The OECD representative states that progress toward full cost recovery (FCR) continues to be slow and the market continues to be economically unsustainable. The variable adherence to FCR by the various foreign producers is an additional financial challenge for US producers.

Despite the progress the NNSA-M³ program has made, these recent events seem to indicate significant vulnerabilities still exist within the ^{99}Mo global supply chain.

Longer term OECD projections point to the possibility of a significant overcapacity internationally as additional facilities come on-line. Such an overcapacity could threaten the sustained economic viability of the fledgling domestic projects.

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 ⁹⁹Mo production facilities to convert to the use of low-enriched uranium (LEU) targets and reactor fuel accelerating the establishment of commercial non-HEU-based ⁹⁹Mo production in the United States. As in previous reviews, it is the latter of these issues that was the main concern of this review. It does appear to be that case that global ⁹⁹Mo production facilities will convert to the use of low-enriched uranium (LEU) targets by the end of 2021.

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 one CA partner of the ⁹⁹Mo program) because the users need estimated program costs to assess and incorporate into their business model for 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 currently supports at the time of this review; this is in accordance with the OECD-NEA guidelines on full cost recovery (FCR) principles.

At the time of the 2017 review, all four cooperative agreements had been awarded at \$25M. Since that time, General Atomics has withdrawn for a variety of reasons which they stated included radioactive waste storage and disposal

uncertainties. The remaining three projects have been fully funded. The NorthStar neutron capture CA and the SHINE CA were completed in 2018, and will close out in 2019. The period of performance for the NorthStar Accelerator Technology Project has been extended until December 2020.

The technical approaches of all the CA projects have been described in previous reports. These descriptions will not be repeated here. NorthStar, an active CA partner of this program, has begun to deliver (on a small scale) ^{99}Mo to the U.S. market. $^{99\text{m}}\text{Tc}$ from this ^{99}Mo is being used to prepare a limited number of $^{99\text{m}}\text{Tc}$ doses for patients. This constitutes the first domestic supply of ^{99}Mo since the beginning of the program and is a very important accomplishment. The expected dates of first ^{99}Mo from NorthStar's second project has been delayed since the last meeting of this subcommittee.

The specific progress of each project is described below.

NorthStar neutron capture project:

NorthStar described the following progress:

- Three FDA approvals were received since the last meeting, including NDA 202158 for the RadioGenix System in February 2018.
- In 2018 (through the date of the Subcommittee meeting) they conducted 42 production runs, prepared 3,550 6-day Ci of ^{99}Mo , and shipped 523 source vessels.
- They initiated direct customer/commercial shipments for patient use in 4Q2018.
- NorthStar $^{99}\text{Mo}/\text{RGX}$ v1.1 is generating patient doses of $^{99\text{m}}\text{Tc}$.
- NorthStar has had extensive interactions with potential customers of the RadioGenix system.
- The College of Pharmacy at Purdue University has included the RadioGenix System in their Nuclear Pharmacy laboratory, supporting their Certificate Program in Nuclear Pharmacy.

NorthStar accelerator project:

NorthStar described the following progress:

- They received approval from their Board on December 3, 2018 to proceed with contracts for accelerator purchase and building construction.
- They ordered hot cell equipment for the new processing building, which needs to be installed, validated and FDA approved prior to testing of electron accelerators.

- They have completed specifications for the electron accelerators that will be used to produce ^{99}Mo from $^{100}\text{Mo}(\gamma, n)$.
- They began contract negotiations with their selected vendor to provide up to eight electron accelerators. The first of which they expect to be delivered in 2020.

This CA partner acknowledges the importance of work being done at the national labs in support of their basic R&D needs.

SHINE Accelerator with LEU Fission project:

SHINE reported the following progress:

- Building One construction on the SHINE campus in Janesville, Wisconsin is complete.
- The first production unit accelerator was delivered to Building One.
- SHINE received a \$150M financing commitment from Deerfield Management Company, an institutional healthcare investor, and closed on an additional \$30M+ of private funding.

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 the CA and non-CA projects. FY2018 appropriations provided \$15 million for this purpose. NNSA expanded the scope of the laboratory program to include a number of non-cooperative agreement partner technologies, including Coqui, BWXT, Niowave, Global Medical Isotopes System (GMIS), Northwest Medical Radioisotopes (NWMI) and Magneto Inertial Fusion Technology (MIFTI).

NNSA issued a new Funding Opportunity Announcement (FOA DE-FOA-0001925) in July 2018, open to both new and existing cooperative agreement partners, to solicit applications to competitively award up to four new cooperative agreements worth \$10 million each in order to expedite the establishment of domestic supplies of ^{99}Mo . This FOA was supported by Congressional funding in FY18 (\$40,000,000) and FY19 (\$20,000,000 appropriated after the FOA was issued) to fund the new cooperative agreements.

Note: While this report was being written, the NNSA announced that it would begin negotiations for potential cooperative agreement awards with 4 U.S. companies:

- NorthStar Medical Radioisotopes, LLC, located in Beloit, Wisconsin
- SHINE Medical Technologies, located in Janesville, Wisconsin
- Northwest Medical Isotopes, located in Corvallis, Oregon
- Niowave, Inc., located in Lansing, Michigan

If these negotiations are successful, NNSA will divide the \$20,000,000 provided by Congress in FY19 among the four agreements, increasing NNSA's contribution to \$15,000,000 per agreement.

Findings

The Subcommittee found that since the review in 2017, NNSA has moved the NNSA-M³ program forward, consistent with the specific AMIPA requirements.

There has been increased instability in the global market over the last year. This highlights the importance of this program in establishing a stable U.S. supply of ⁹⁹Mo. The initial movement of ⁹⁹Mo produced by NorthStar into the market and the resulting ^{99m}Tc into some patient procedures is an important step forward, especially in that it involves acceptance of a new generator technology. That said, no CA partner (past or present) projects meeting the initial goal of 3000 6-day Ci /week for multiple years at a minimum.

As reported last year, there continue to be issues related to the long-term financial viability of any producers that succeed in entering the market. The reasons for this include the challenge of achieving wide-spread market acceptance for the NorthStar RadioGenix generator technology and the slow rate of progress on the global move toward FCR. Now that U.S.-produced ⁹⁹Mo has entered the market, there is an opportunity for NNSA-M³ to demonstrate the U.S. commitment to Full Cost Recovery.

The NNSA-M³ program is a mature program. The remaining major challenge that is within DOE's control concerns the ULTB program and the ability to achieve a well-defined process resulting in predictable costs for disposal of leased uranium target residues. This will be a relevant factor for any entity seeking to use this program as part of ⁹⁹Mo production (new or existing CA partners or independent entities). Timely resolution of this issue will require focus and coordination across organizational entities within the Department of Energy.

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 2017 assessment?

The program is continuing to make slow progress towards improving the reliability of domestic ⁹⁹Mo supply. Establishment of a large scale domestic supply has not yet occurred. None of the partners have achieved the original goal of producing 3000 6-day Curies per week (1/2 of the US market's needs), and none are likely to reach this level before mid-2023.

A major accomplishment of this program occurred this year. NorthStar, a CA partner of this program, has begun to deliver, on a small scale, ⁹⁹Mo to the U.S. market. ^{99m}Tc from this ⁹⁹Mo is being used to prepare a limited number of ^{99m}Tc doses for patients. This constitutes the first domestic supply of ⁹⁹Mo since the beginning of the program. NorthStar projects that they will be able to increase

this amount first with approval of an extra production line at the NorthStar Columbia Operations (NCO) using material irradiated at the MURR and later with the use of enriched ^{98}Mo targets. Both of these will require additional approvals from the FDA. They estimate they will be able to produce 30-35% of the US market needs by 2020 using the neutron capture process at MURR.

NorthStar has a second project that would produce ^{99}Mo by use of an accelerator via the $^{100}\text{Mo}(\gamma, n)$ reaction. They have made progress in this project. Construction of the accelerator building and ordering of eight accelerators has been approved by the board of directors of NorthStar. NorthStar projects having the capacity to produce 3000 6-day Ci ($\sim 1/2$ of the US market) by 2023 using the combination of production at their NCO facility, expanded Beloit operations and the new photonuclear Mo production.

Both Northstar methods produce low specific activity ^{99}Mo that requires the use of their novel Radiogenix system. This system is more complicated to operate than a standard $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator that uses high specific activity ^{99}Mo . Hence, they face an additional challenge in market acceptance of their Radiogenix system.

Shine continues to make slow but steady progress. They have completed construction of their Building One, taken delivery of their first production unit accelerator, and have met some significant milestones in financing. Shine states they will be able to achieve first production of ^{99}Mo by late 2021.

One CA partner, General Atomics, has withdrawn for reasons which they stated included radioactive waste storage and disposal uncertainties.

A new FOA for cooperative agreements was launched and attracted multiple applications from new and existing CA partners. Four have recently been selected to begin negotiations leading to a potential award. This could result in expanding the technology options that the program supports. At this time, it is not clear to the committee whether this substantially improves the feasibility of the present strategy.

A positive development is that more than 70% of ^{99}Mo produced world-wide is currently met using non-HEU targets, according to OECD [1].

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

If the goal is defined broadly, as the establishment of an economically viable and lasting domestic production of ^{99}Mo covering approximately one-half of the domestic demand, the strategy is incomplete, and its feasibility still needs to be demonstrated:

- While a ULTB program has been formally established, an effective model of implementation remains elusive and there is no strategy for proactively addressing the waste acceptance criteria and disposal options with CA partners.
- There has been slow progress on establishing the principle of full cost recovery in the international context; this could impact the long term viability of U.S. producers. However, it should be noted that while NNSA's program can help advance the goal of full cost recovery in the global ⁹⁹Mo market, the cooperation of numerous governments and market participants is necessary to develop a ⁹⁹Mo market based on full cost recovery principles.
- The sole domestic producer, who started production in 2018, still relies on a US research reactor using HEU fuel (MURR), and has not yet participated in the OECD FCR survey as they were not in production at the time of the last survey. NorthStar's business model is based on a novel generator that yet has to reach significant market penetration.
- A new Funding Opportunity Announcement has been published. It is not clear to the committee whether this substantially improves the feasibility of establishing a domestic supply of ⁹⁹Mo.

Given the continued inability to execute a waste take back contract under the ULTB program in a timely way, and the lack of progress internationally on FCR, the committee has concerns about the completeness and feasibility of the strategy.

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

NNSA has identified a comprehensive set of risks; these were discussed in previous reports. Some of these risks are beyond the direct control of the NNSA, and many have been well managed. There are two areas for which the committee believes risks management could be improved. These are:

- While a ULTB program has been formally established, an effective model of implementation remains elusive and there is no formal strategy for proactively addressing the waste acceptance criteria and disposal options with CA partners. The risk associated with the application of the take-back portion of the ULTB program to the needs of a specific party is still too high. The uncertainty associated with length of time needed to develop a draft contract and the uncertainty associated with the costs of ultimate disposition (and possible long term storage) of the waste generated may contribute again to withdrawal of a party needing these resources.
- On an international level, perhaps one of the biggest risks is adherence to the OECD's goal of full cost recovery during the production of ⁹⁹Mo. This, in principle, would make for an even playing field for all of the producers.

However, measuring and implementing FCR has proven to be very challenging. The slow progress and/or uncertain commitment toward full cost recovery by the international community could impact the ultimate financial viability of any U.S. producers.

- Additionally, OECD predictions show that this is a possibility of a significant overcapacity in the world supply in the 2021 to 2023 period. This scenario would lead to economic risks for newcomers to the market.

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

NNSA has partially addressed our concerns and recommendations.

A draft contract was not been issued with the CA partner with whom they were in negotiations prior to the CA partner requesting termination of its CA. NNSA states there were multiple factors for delaying finalization of a take-back contract, including “insufficient knowledge of the waste and its packaging”.

The NNSA has made an attempt to capture lessons learned from the initial attempt to create a takeback contract for a CA partner. The committee believes that the effort thus far will be insufficient to increase the likelihood that a takeback contract can be issued in a timely way with well-defined, predictable, and stable costs for disposition and storage of waste from leased LEU.

Recommendations

Recommendation 1

The slow implementation of full cost recovery (FCR) worldwide continues to be a risk to the financial viability of U.S. producers. NNSA has supported the development of a technology with a U.S. producer of ⁹⁹Mo who has now entered the U.S. market. It is an appropriate time for NNSA to ensure that the U.S. producers they have supported adhere to the tenets of full cost recovery that the United States has signed on to [2]. Therefore, the subcommittee recommends:

NNSA should require existing and new CAs (or potential producers supported by national lab research) to agree to adhere to the OECD principles of FCR and to submit self-reporting to the OECD FCR survey as soon as they have submitted product to U.S. or other markets.

Recommendation 2

Although the ULTB has been established, and LEU has been loaned under this program, the NNSA has not successfully executed a take back contract with any CA partner. Nor has the NNSA executed a take back contract with any of the other potential new (non-CA partner) US producers of ⁹⁹Mo because no other U.S. producer has approached DOE/NNSA for a ULTB contract. One CA partner has withdrawn from the program, stating there were multiple factors “including the business implication of the continued uncertainty around the costs and timing associated with the uranium take back agreement.” For this reason, it is imperative that NNSA take additional actions aimed at improving the transparency and predictability of this important program. The subcommittee recommends:

- NNSA must encourage CA partners and others interested in ULTB to engage with them early on so that a plan including TB can be developed in a timely fashion.
- NNSA must develop a waste take back process document to formalize the commitment to this process, including a model timeline and an estimate of costs under a set of well-defined scenario templates, in order to formalize communications with potential users. This must be presented to the subcommittee in advance of its next meeting.

References

[1] OECD/NEA (2018), *The Supply of Medical Radioisotopes: 2018 Medical Isotope Demand and Capacity Projection for the 2018-2023 Period*, NEA/SEN/HLGMR (2018) 3, Paris, France.

[2] OECD Joint Declaration on the Security of Supply of Medical Radioisotopes online at <https://www.oecd-nea.org/med-radio/jointdeclaration.html>

Appendix 1 – Subcommittee Charge



U.S. Department of Energy
and the
National Science Foundation
September 12, 2018



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 four previous assessments as described in reports transmitted to the agencies on May 8, 2014, July 30, 2015, November 3, 2016, and March 19, 2018.

We request that NSAC reconvene the Subcommittee to provide a fifth 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 4th 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 2017/2018 NSAC assessment of the Mo-99 Program appropriately and adequately?

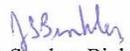


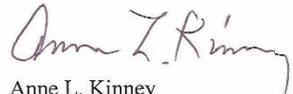
- What steps should be taken to further improve NNSA program effectiveness in establishing a domestic supply of Mo-99?

It is requested that this assessment be submitted by February 2019.

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
Deputy Director for Science Programs
Office of Science


Anne L. Kinney
Assistant Director, Directorate for
Mathematical and Physical Sciences
National Science Foundation

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
2018 DOE/NSF Nuclear Science Advisory Committee Mo-99 Program
Review

December 6-7, 2018

Gaithersburg Marriott Washingtonian Center, Salons A-D
9751 Washingtonian Boulevard
Gaithersburg, Maryland

December 6, 2018

OPEN SESSION

- 08:15 – 08:30 Discussion of Charge and Introductions (NSF and DOE/NP)
- 08:30 – 09:00 Review of 2017 Recommendations (Seestrom)
- 09:00 – 9:30 NNSA Response to 2017 NSAC recommendations (NNSA)
- 09:30 – 10:30 OECD-NEA Demand and Capacity Projection (Kevin Charlton, OECD-NEA)
- 10:30 – 11:00 **Break**
- 11:00 – 12:00 Review of Progress in the NNSA Mo99 Program
- Current status of cooperative agreement projects
 - ULTB status
 - National lab support for CA partners and others

CLOSED SESSION (Committee, NSF and DOE/NP)

- 12:00 – 1:00 **WORKING LUNCH (Committee, NSF, DOE/NP only)**

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

- 1:00– 1:30 Closed-session updates from NNSA
- 1:30 – 3:30 Updates from NNSA Cooperative Agreement Partners
- 1:30-2:30 NorthStar Medical Radioisotopes
 - 2:30-3:30 SHINE Medical Technologies

- 3:30 - 4:00 **Break**

OPEN SESSION

- 4:00 – 5:30 Mo-99 Stakeholder Input and Public Comment Session

Meeting Agenda
2018 DOE/NSF Nuclear Science Advisory Committee Mo-99 Program
Review

December 6-7, 2018

Gaithersburg Marriott Washingtonian Center, Salons A-D
9751 Washingtonian Boulevard
Gaithersburg, Maryland

December 7, 2018

CLOSED SESSION (Committee, NSF, and DOE/NP only)

08:30 – 10:00 Committee Discussion

10:00 – 10:30 **Break**

10:30 – 12:00 Committee Working Session (Committee, NSF, and DOE/NP
only)

12:00 – 1:00 **WORKING LUNCH (Committee, NSF, DOE/NP only)**

1:00 – 2:00 Committee Working Session (Committee, NSF, and DOE/NP
only)

2:00 **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 AMIPA 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

NTP – NTP Radioisotopes SOC Limited, South Africa

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