DEPARTMENT OF PHYSICS
UNIVERSITY *of* WASHINGTON
College of Arts & Sciences

Box 351560 *Tel: 206-543-0839*
Seattle, WA 98195 *Fax: 206-685-0635*

March 16, 2020

Dr. Chris Fall
Director, Office of Science
U.S. Department of Energy
1000 Independence Ave., SW
Washington, DC 20585

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 October 4, 2019, you charged NSAC to reconvene its standing Subcommittee on Mo-99 to conduct its sixth annual assessment of the effectiveness of the National Nuclear Security Administration, Office of Material Management and Minimization (NNSAMMM) Domestic Molybdenum-99 Program. I attached the report from the NSAC Subcommittee, which was chaired by Professor Suzanne Lapi, from the University of Alabama at Birmingham. The committee membership was composed of a small number of experts in nuclear medicine, nuclear and radio chemistry, radioisotope production, commercial isotope sales, and radio pharmacy and clinical use.

Fact finding for this report was facilitated by a Subcommittee meeting held February 3-4, 2020, which featured briefings by NNSA, DOE-EM, and all active cooperative agreement (CA) partners. NNSA stated that their program objective is to bring online two U.S. producers, each capable of producing 3000 6-day Ci/week of ^{99}Mo (approximately equal to the entire U.S. demand, plus reserve). The Subcommittee found that NNSA continues to move the program forward. NorthStar, a CA partner, has already entered the commercial market. However long-term financial viability concerns exist owing to the Uranium Lease and Take Back (ULTB) program and/or compliance with the full cost recovery (FCR) mandate in an international context. Nevertheless, the Subcommittee heard evidence of vibrant activities by several CA partners and is optimistic that the NNSA objectives will be met.

Two recommendations are made. One is related to the uncertainties in the Take-Back aspect of the DOE-EM program. The second recommendation encourages NNSA to prioritize future funding awards toward accelerating time-to-market of the CA partners in order to support the

NNSA stated program objectives.

The Subcommittee report was presented to NSAC during its March 2, 2020 meeting. Following discussion, the report was approved unanimously.

Sincerely,

David W. Hertzog

Chair, NSAC

cc: Steve Binkley, DOE
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 (M^3) ^{99}Mo Program

February 24, 2020
Report of the NSAC ^{99}Mo Subcommittee

Executive Summary

The Nuclear Science Advisory Committee (NSAC) Molybdenum-99 (^{99}Mo) Subcommittee met February 3-4, 2020, to address the charge to NSAC requesting that a sixth annual review of the National Nuclear Security Administration's (NNSA) ^{99}Mo program be performed. The Subcommittee found that NNSA has continued to make progress over the course of the year in the context of the specific requirements of the American Medical Isotopes Production Act of 2012 (AMIPA).

Since the last review, the international context for ^{99}Mo availability has continued to evolve. The Organisation for Economic Cooperation and Development's Nuclear Energy Agency (OECD-NEA) has updated its assessment of the international ^{99}Mo production capacity and demand curves [1]. Longer term, OECD projections still 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, particularly if not all parties are operating in a full-cost recovery mode. However, because the ^{99}Mo supply chain is complex, while a producer might have the capacity to produce a larger amount of ^{99}Mo, that product might not get to market if all of the contracts and validations are not in place.

The Subcommittee found that NNSA has partially addressed its concerns and recommendations from the previous review. The Subcommittee still believes that the Uranium Lease and Take Back (ULTB) program requires significant attention in order to provide Cooperative Agreement (CA) partners well-defined, predictable, and stable costs for disposition and storage of waste from leased low enriched uranium (LEU).

Additionally, the Subcommittee encourages NNSA to focus their strategy and resources on the stated objective during this review, which is to bring online two U.S. producers, each capable of producing 3000 6-day Ci/week of ^{99}Mo.

The Subcommittee has two recommendations:

Recommendation 1

The limitations of the ULTB program continues to be one of the biggest risks 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.

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.

Introduction

The Nuclear Science Advisory Committee (NSAC) Molybdenum-99 (^{99}Mo) Subcommittee began its work in 2014. Additional members were added in 2015 and 2016 to address stakeholder input and additional meetings were held in 2017 and 2018. The creation of this subcommittee was motivated by the American Medical Isotopes Production Act (AMIPA) legislation contained in the National Defense Authorization Act for Fiscal Year 2013, which required 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 ^{99m}Tc in the United States without the use of highly enriched uranium (HEU). This Act also called for an annual review of the NNSA ^{99}Mo program by the NSAC. The National Nuclear Security Administration (NNSA) was given the responsibility for development of this program in 2009. Following an NNSA reorganization, the ^{99}Mo program is now within NNSA's Office of Material Management and Minimization (NNSA-M^3).

The ^{99}Mo Subcommittee began its work in 2019 in response to a charge letter dated October 4, 2019 (Appendix 1). The 2019/2020 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 February 3-4, 2020, in Arlington, VA, and built on the extensive work of the previous five reviews. At this meeting, the Subcommittee was briefed by NNSA on details of their program. The Subcommittee invited input from all current CA partners, all of which presented briefings. 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 2019 Report

The OECD-NEA issued a new report "The Supply of Medical Radioisotopes: *2019 Medical Isotope Demand and Capacity Projection for the 2019-2024 Period"* [1]. As seen 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 existing facilities are well maintained and well scheduled, and when unplanned outages are avoided, total irradiator capacity should be sufficient. That said, the supply chain must fully implement the recommended levels of paid Outage Reserve Capacity (ORC) in order to be able to manage unplanned processor outages. 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."

Almost all projects, including conventional technologies and those supported by NNSA, have reported delays with variable impact on the current and future ^{99}Mo supply.

The OECD report 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 U.S. producers.

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. However, because the ^{99}Mo supply chain is complex, while a producer might have the capacity to produce a larger amount of ^{99}Mo, that product might not get to market if all of the contracts and validations are not in place.

Developments in the NNSA Program

The organization and goals of the NNSA-M^3 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-M^3 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. As in previous reviews, it is the latter of these issues that was the main concern of this review. With respect to the former objective, it does appear that the majority of global ^{99}Mo production facilities will convert to the use of LEU targets by the 2022.

Sections 3173 (c) and (e) of the FY13 National Defense Authorization Act directed 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 ^{99}Mo for medical uses. The Act 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. The 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 ^{99}Mo 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 ^{99}Mo production. The cost recovery models DOE will utilize for the ULTB Program are of particular interest to potential ULTB users because these users need to incorporate these costs into their business models. There have been significant delays in developing the “take-back” component of the ULTB program. Although the program was defined when AMIPA was signed in 2011, it was not actually established until the 2016 NSAC review, and significant challenges remain in defining the costs of the take-back portion of the program, particularly for greater-than-Class-C low-level radioactive waste (GTCC LLW), to domestic ^{99}Mo producers.

The DOE has assisted with technology and funding for the conversion of HEU to LEU targets for foreign producers of ^{99}Mo, and the problem of disposing of the resulting GTCC LLW waste has been addressed by these producers. Thus, while the problem of disposal of GTCC LLW has been addressed in other countries; the DOE has yet to provide a cost-effective disposal path for US ^{99}Mo producers, which is a potentially serious impediment to their commercial viability.

There has been some instability in the global market over the last year. This highlights the importance of this program in establishing a stable U.S. supply of ^{99}Mo. The initial movement of ^{99}Mo 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 3000 6-day Ci/week goal for at least several years.

As reported last year, 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 challenge of achieving wide-spread market acceptance for the NorthStar RadioGenix generator technology, the slow rate of progress in the global move toward FCR and the longer-term potential for overcapacity.

The NNSA-M^3 program is a mature program. Perhaps the most significant remaining challenge that is within DOE's purview is the "take-back" component of the ULTB program. As noted previously, the inability of DOE-EM to establish a well-defined process that results in predictable costs for the disposal of leased uranium target residue presents a significant challenge to the financial viability of several of the CA partners. Timely resolution of this issue will require focus and coordination across organizational entities within the Department of Energy.

Following the previous reviews of this program to bring a stable supply of ^{99}Mo to the US, it is clear that the CA partners have underestimated the time required to achieve the goal of producing 3000 6-day Ci/week. All projects are significantly behind schedule and all projects need large infusions of funds, both in terms of government support and private investment. Any new entity wishing to become a Cooperative Agreement partner is looking at ^{99}Mo being available in 2025 or beyond unless they already have a mature technology in hand.

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 ^{99}Mo Program? What progress has been made since the 2018/2019 assessment?

Findings

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 (3000 6-day Ci/week) has not yet occurred.

NorthStar, a CA partner of this program, continues to deliver ^{99}Mo to the U.S. market. They will be able to increase the weekly delivery of ^{99}Mo with the recent approval of a larger fill line at the NorthStar Columbia Operations (NCO) using material irradiated at the Missouri University Research Reactor (MURR) and also plan to move to the use of enriched ^{98}Mo targets. They estimate they will be able to produce 30-35% of the US market needs by late 2020 using the neutron capture process at MURR.

NorthStar has a second project that would produce ^{99}Mo by use of an electron linac via the ^{100}Mo(γ,n) reaction. They have made progress on this project as well. Construction of their accelerator facility was initiated in 2019, and the first accelerator is scheduled to be delivered in 2020.

SHINE continues to make steady progress. They have initiated construction of their production facility and have met several significant financing milestones. SHINE states they will be able to achieve first production of ^{99}Mo by late 2021 with sales starting in 2022.

Previous CA awards to SHINE and the NorthStar neutron capture project have been closed out and the NorthStar accelerator project CA funding has been extended to 2021.

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 new cooperative agreements in order to accelerate 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. NNSA's contribution to each award was $15,000,000.

Since the last review, four new 50/50 cost-sharing awards have been issued

- NorthStar Medical Radioisotopes, LLC, located in Beloit, Wisconsin
    - Previous CA partner
    - Technology: Neutron capture and photonuclear reactions on stable Mo targets
- SHINE Medical Technologies, located in Janesville, Wisconsin
    - Previous CA partner
    - Technology: Subcritical LEU assembly
- Northwest Medical Isotopes, located in Corvallis, Oregon
    - New CA partner
    - Technology: LEU fission using 2 reactor sites
- Niowave, Inc., located in Lansing, Michigan
    - New CA partner
    - Technology: Photonuclear fission of LEU targets

Northwest isotopes will use existing research reactors (MURR and Oregon State University (OSU)) to irradiate proprietary LEU targets. Test irradiations at OSU have begun.

Niowave's goal is to produce ^{99}Mo and other isotopes via photonuclear fission of uranium targets. They have already purchased LEU for their pilot studies and aim to produce ^{99}Mo on a small scale (Ci level) by 2021.

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

In addition to its support of CA partners, the NNSA-M^3 continues to provide non-proprietary technical support at the DOE National Laboratories that benefits both the CA and non-CA projects. FY2019 and FY2020 appropriations provide $25 million in total for this purpose. In FY2019, NNSA-M^3's laboratory program included a number of non-cooperative agreement partner technologies, including Coqui, BWXT, Eden Radioisotopes, Flibe Energy, and Magneto Inertial Fusion Technology (MIFTI).

Comments

While the production capacity will meet a significant portion of U.S. market demand, both of the 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}Mo/^{99m}Tc generator that uses high specific activity ^{99}Mo. Hence, they may face an additional challenge in market acceptance of their RadioGenix system.

New cooperative agreements have been initiated with new and existing CA partners. This has resulted in expanding the technology options that the program supports. While additional funding may accelerate the more mature CA partners, it is not clear the addition of the new CA partners will result in a faster market entrance or a higher likelihood of two partners producing 3,000 6-day Ci/week.

The ULTB program is still underdeveloped, however CA partners appear to be finding alternative paths forward including purchasing material.

Recommendations

None

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

Findings

The transition to LEU from HEU by the international ^{99}Mo producers is now close to complete with 75% of the global ^{99}Mo supply now being produced from LEU. The Belgium Institute for Radioelements (IRE) is in the process of conversion to LEU, with a target date of 2022. The conversion of world producers to LEU-driven sources has been very successful.

The program has invested over $140 M over the life of the program in the national laboratories who are engaged in direct, non-proprietary, but cooperative partner prioritized strategic R&D.

The program has established a uranium lease and take back (ULTB) concept for those CA partners that might require it. In accordance with the USEC Privatization Act, the Secretary of Energy signed a determination to allow the sale, lease or transfer of up to 500 kgs of high assay LEU per calendar year in support of this program. No ULTB contracts were signed in 2019; however, two companies have contract templates for review.

The OECD High Level Group (HLG) that oversees the surveys of FCR no longer meets in a formal setting.

As noted in last year's report, one U.S. producer – NorthStar – has a product in the U.S. market. Their business model is based on neutron capture of natural Mo, with a plan to use enriched ^{98}Mo in the near future. Their process creates ^{99}Mo with a lower specific activity than other methods, which requires use of a proprietary generator system by the radiopharmacy.

Comments

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. Notably, the CA partners (e.g., NorthStar and SHINE) have developed novel production methods that will produce low-level waste or minimal greater than Class-C waste volume.

The national laboratory program has been very effective and should be continued with a focus on R&D specific to advancing ^{99}Mo production. CA partners who are engaged with the laboratories strongly reinforced this assertion, giving numerous technical examples of successful projects.

The ULTB program has not been effectively implemented. This is both a combination of the fact that it is not needed by most of the CA partners and because of the difficulty of establishing the costs of the “take-back” aspect of the program, in particular, full-cost recovery by DOE-EM, including financial assurance, and the open-ended cost provisions in the proposed contract.

The demise of the OECD HLG hampers any attempt to establish FCR by foreign producers. While the NNSA hopes to reconvene the HLG, FCR remains a significant challenge to establish and to enforce.

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. There is also evidence that other CA partners that are close to market, suggesting that the strategy appears to be successful.

Recommendations

The limitations of the ULTB program continues to be one of the biggest risks 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.

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

Findings

NNSA has identified a comprehensive set of risks; these were discussed in previous reports and no new risks have been identified.

Comments

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.

Recommendations

None

Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2018 NSAC assessment of the ^{99}Mo Program appropriately and adequately?

Findings

DOE-EM did not provide the committee a waste takeback model and contract template as requested by the Subcommittee in the last report.

NNSA indicated that the OECD has ended its formal mandate for FCR and discontinued its FCR self-assessment surveys. NNSA continues to directly support FCR by requiring U.S. companies to compete in the market without U.S. government subsidies and reminding each company of the importance of adhering to OECD FCR principles. NNSA has not put a formal FCR requirement in funded cooperative agreements because such a requirement is not enforceable.

Should the OECD choose to restart these surveys at any point, NNSA will strongly encourage CA partners to contribute to the U.S. response.

NNSA continues to highlight the need for potential ULTB customers to engage with DOE/NNSA at least two years prior to its first LEU delivery needs. The current CA partners indicated that NNSA staff have been very cooperative with respect to understanding and working the logistics of the lease aspects of ULTB. Some CA partners have opted to not use the ULTB citing the complexity and the uncertainty of waste disposal costs. This is primarily due to the length of time needed to develop a draft contract and the uncertainties associated with the costs of potential long-term storage and ultimate disposition of the waste generated. The lack of a U.S. permanent repository for spent nuclear fuel continues to complicate the take-back portion of the ULTB.

Comments

The Subcommittee believes NNSA has addressed the concerns and recommendations within the scope of their program.

FCR for ^{99}Mo should continue to be a worldwide goal; however, the difficulty of accomplishing this task cannot be overstated.

The Subcommittee notes that DOE-EM's progress on the "take-back" portion of the ULTB program continues to be a concern, that the absence of a cost-effective take-back program continues to be a challenge for at least one of the CA partners.

Recommendations

None

<u>What steps should be taken to further improve the NNSA program effectiveness in establishing the domestic supply of ^{99}Mo?</u>

Findings

One CA partner, NorthStar, has brought the RadioGenix generator to market, with a number of systems currently installed. They estimate that they will have the capacity to supply a significant fraction of the U.S. market in 2020.

A second CA partner, SHINE, has submitted their NRC operating license application (Q2 of 2019) and had a successful NRC construction site inspection. They have conducted a successful test of their production process at Argonne National Laboratory. They have also successfully tested the accelerator at their facility and aim to have ^{99}Mo in the U.S. market in 2022.

A third CA partner, Niowave, has their production facility underway and a superconducting electron LINAC in place at their research facility. They have verified their gamma and neutron production methods. LEU needed for ^{99}Mo pilot production has been purchased from Y-12. While ^{99}Mo production is not their primary mission, they aim to have ^{99}Mo in the US market in the 2024/2025 timeframe.

A fourth CA partner, Northwest Medical Isotopes, has their site and land lease agreements for future construction set at Discovery Ridge in Columbia, MO. They have collaborated with Polish partners to run test irradiations and target processing. They aim to have ^{99}Mo into the US market in 2023.

Comments

NorthStar plans to utilize enriched ^{98}Mo targets, which would allow them to make higher activity generators (~19 Ci loading, based on their assessment) upon FDA approval. Their accelerator method to produce ^{99}Mo would allow them to further increase ^{99}Mo capacity while still using the same RadioGenix generator. Thus, the implementation of the photonuclear production route is likely to be faster than the time-to-market of the neutron-capture ^{99}Mo.

SHINE's recycling process allows them to minimize radioactive waste production. Their production method builds on two existing, well-established methods and is innovative. This technology produces high specific activity ^{99}Mo that can be used in current generators.

Niowave's process builds on their expertise in superconducting electron LINACs. Their process is relatively simple and straight-forward and produces high specific activity ^{99}Mo, which can be used in existing generators. However, they aim to produce ^{99}Mo in addition to a number of other isotopes and they stated that full-scale ^{99}Mo production is dependent upon the commercial success of other isotopes; it is not clear that ^{99}Mo is the top priority.

Northwest Medical Isotopes' process uses standard LEU irradiation method to produce fission ^{99}Mo in existing U.S. university reactors. The Subcommittee found the 2023 timeline to market optimistic.

Several current CA partners noted that the restriction (prohibition) on using the award funds toward construction costs is problematic.

The pathways for disposal of greater than Class C nuclear waste remain an issue.

Recommendation

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.

References

[1] OECD/NEA (2019), The Supply of Medical Radioisotopes: *2019 Medical Isotope Demand and Capacity Projection for the 2019-2024 Period,* NEA/SEN/HLGMR (2019) OECD Publishing, 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

October 4, 2019

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 five previous assessments as described in reports transmitted to the agencies on May 8, 2014, July 30, 2015, November 3, 2016, March 19, 2018, and April 17, 2019.

We request that NSAC reconvene the Subcommittee to provide a sixth 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 5th 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 2018/2019 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 2020.

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,

Christopher Fall
Director
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

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

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 Radio Chemistry	**Commercial Isotope Sales**	**Project Management**
Silvia Jurisson Suzanne Lapi Thomas J. Ruth	Mitch Ferren Suzanne Lapi	David Hertzog Ron Crone

Appendix 3 – Meeting Agenda

Meeting Agenda
2020 DOE/NSF Nuclear Science Advisory Committee Mo-99 Program Review

<u>February 3, 2020</u>

OPEN SESSION

8:30 – 8:45 Discussion of Charge and Introductions (NSF and DOE/NP)

8:45 – 9:45 Review of 2018 Recommendations (Lapi)

9:45 – 10:15 NNSA Response to 2018 NSAC recommendations (NNSA)

10:15 – 10:30 **Break**

10:30 – 11:30 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)

11:30 – 12:30 **WORKING LUNCH (Committee, NSF, DOE/NP only)**

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

12:30 – 1:00 Closed-session updates from NNSA

1:00 – 5:00 Updates from NNSA Cooperative Agreement Partners

- 1:00 – 2:00 NorthStar Medical Radioisotopes

2:00 – 2:15 **Break**

- 2:15 – 3:15 SHINE Medical Technologies
- 3:15 – 4:15 Niowave
- 4:15 – 5:15 Northwest Medical Isotopes (Zoom Session)

OPEN SESSION

5:15 – 6:00 Mo-99 Stakeholder Input and Public Comment Session

DOE/NSF Nuclear Science Advisory Committee
Mo-99 Program Review
February 3-4, 2020
Agenda

February 4, 2020

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

8:30 – 10:00 Committee Discussion

10:00 – 10:15 **Break**

10:15 – 10:45 Committee Discussion / Q&A/NNSA

10:45 – 12:00 Committee Working Session (Committee, NSF, and DOE/NP only)

12:00 – Adjourn

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

The technetium-99m isomeric state (^{99m}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 ^{99m}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 ^{99m}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 ^{99m}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 ^{99m}Tc generator in 1958 [1]. At this time the head of the radioisotope production effort, Powell Richards, realized the potential of ^{99m}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 ^{99m}Tc generator in 1961, and the boom began.

The ^{99m}Tc generators allow a quick and convenient chemical separation of ^{99m}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 ^{99m}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 ^{99m}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 ^{99m}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 ^{99}Mo 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 ^{99}Mo 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

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[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-M^3 - 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

OSU – Oregon State University

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