Mo-99 Presentation to NSAC

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U.S. Department of Energy

Office of Science

Outline

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

Charge to NSAC

- What is the current status of implementing the goals of the NNSA-M^3 Mo-99 Program?
- What progress has been made since the 2nd NSAC assessment?
- Is the strategy for continuing to implement the NNSA goals complete and feasible, within an international context?
- Are risks identified in implementing those goals being appropriately managed?
- Has the NNSA-M^3 Program addressed concerns and/or recommendations articulated in the 2015 NSAC assessment of the Mo-99 Program appropriately and adequately?
- What steps should be taken to further improve NNSA program effectiveness in establishing a domestic supply of Mo-99?

Subcommittee Members

Carolyn Anderson, University of Pittsburgh

Jeff Binder, University of Illinois

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

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Steve Mattmuller, Kettering Medical Center

Berndt Mueller, Brookhaven National Laboratory

Ken Nash, Washington State University

Joseph Natowitz, Texas A&M University

Thomas Ruth, TRIUMF

Susan Seestrom, Chair, Los Alamos National Laboratory

Expertise of the Subcommittee

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

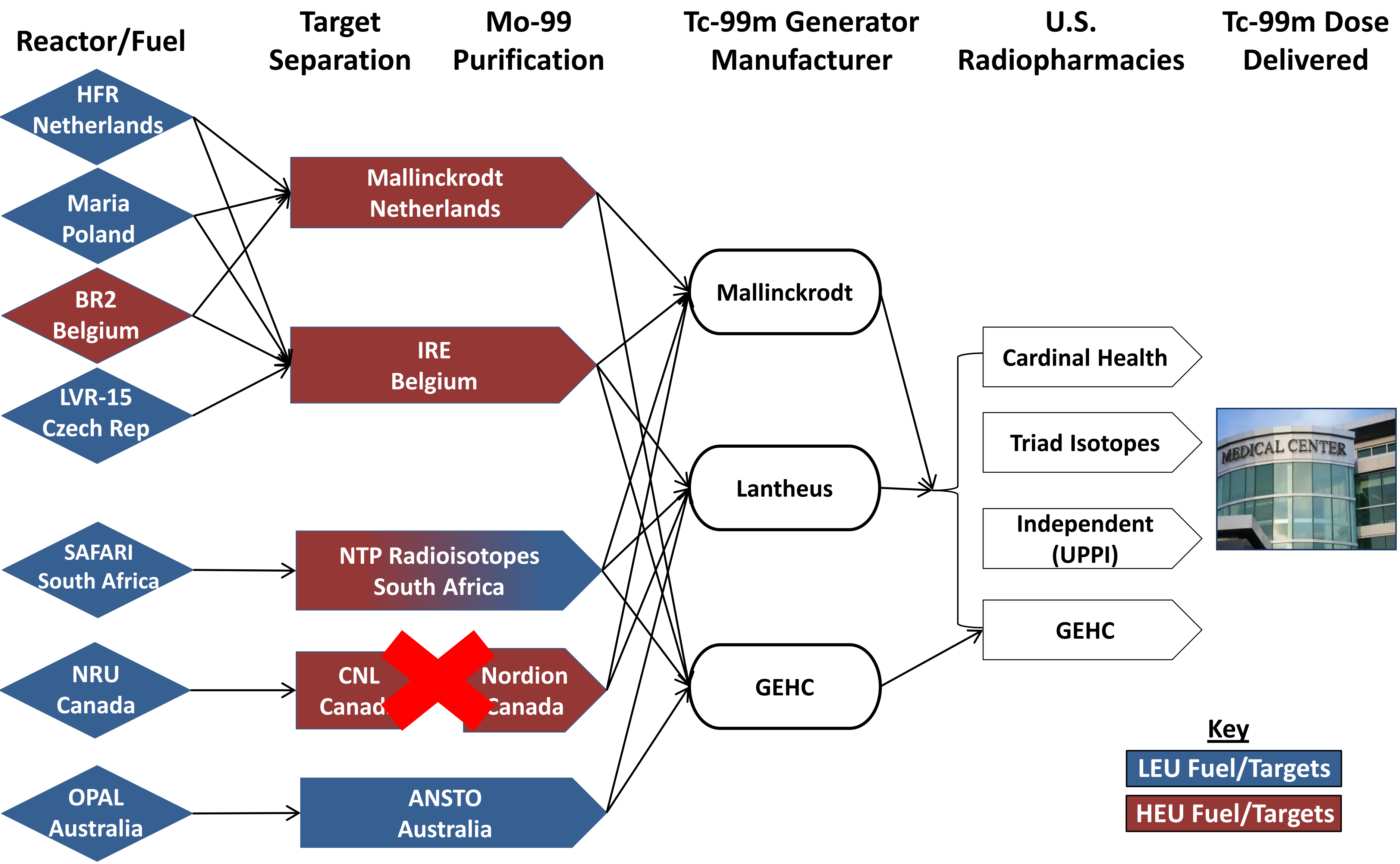
Subcommittee Process

- The Subcommittee met in Bethesda MD on September 29-30, 2016.
- We were briefed by NNSA as well as DOE-EM, representatives of the OECD, and the NAS study group.
- We were briefed by all active cooperative agreement partners.
- We devoted a session to input from the broad stakeholder community.

Background

- There is widespread use of ^{99m}Tc for nuclear medicine diagnostic imaging. ^{99m}Tc is the daughter of ^{99}Mo.
- Today, ^{99}Mo is produced by fission of ^{235}U.
- There is U.S. government interest in reducing the use of Highly Enriched Uranium (HEU)
- There was concern in the medical community that this could lead to shortages or a significant increase in price.
- This issue was addressed in the 2009 National Academy study.
- Supply chain disruptions have occurred 2005-2014
- There is currently no U.S. producer of ^{99}Mo

Current U.S. Mo-99 Supply Matrix



U.S. DEPARTMENT OF ENERGY

National Nuclear Security Administration

Transition Strategy for Reliable Non-HEU-Based Mo-99 Supply

HEU | Non-HEU

Today*

ANSTO (Australia) | NTP Radioisotopes (South Africa) | Mallinckrodt (Netherlands) | IRE (Belgium) | CNL-Nordion (Canada)

Nov 2016 to Mar 2018

ANSTO (Australia) | NTP Radioisotopes (South Africa) | Mallinckrodt (Netherlands) | IRE (Belgium) | Canada Contingency Production | NEW Pending | NEW Pending

Future Global Mo-99 Supply

ANSTO (Australia) | NTP Radioisotopes (South Africa) | Mallinckrodt (Netherlands) | IRE (Belgium) | NEW Pending | NEW Pending | NEW Pending

NNSA Cooperative Agreement Partners

Other New U.S. and/or International Mo-99 Producers

Increased International Mo-99 Production

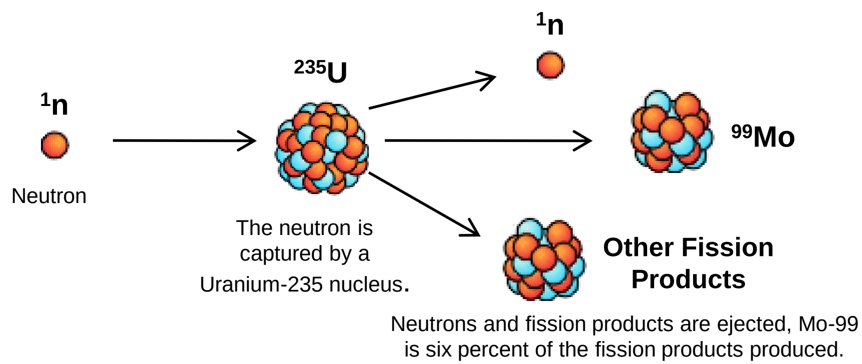
*Existing large-scale Mo-99 producers only. Capacity of existing and new potential producers not represented.

U.S. DEPARTMENT OF ENERGY

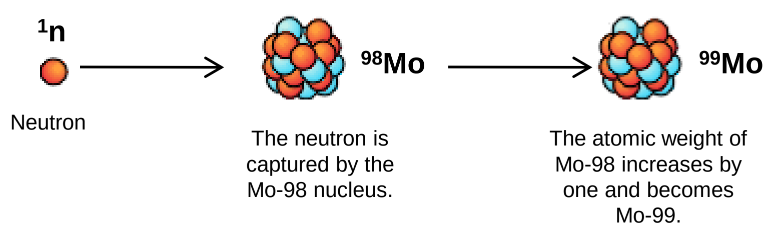
GTRI and U.S. Domestic Mo-99
Implementing a Technology-Neutral Program

National Nuclear Security Administration
Defense Nuclear Nonproliferation

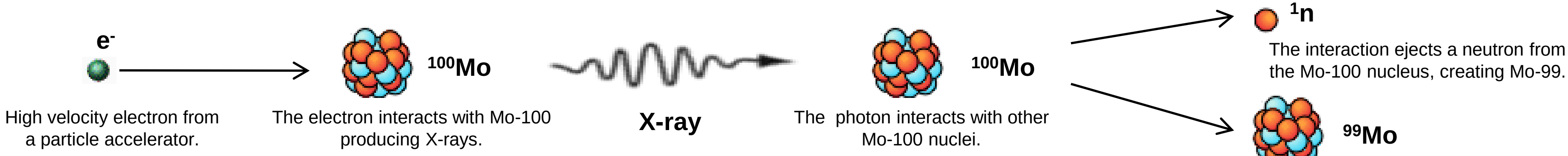
LEU Fission Based: ^{235}U (n,f)



Neutron Capture:(n,γ)



Accelerator Based: (γ,n)



NNSA has 3 Cooperative Agreement Partners

- NorthStar – two projects continuing
- SHINE – one project continuing
- General Atomics – new project started since last years review

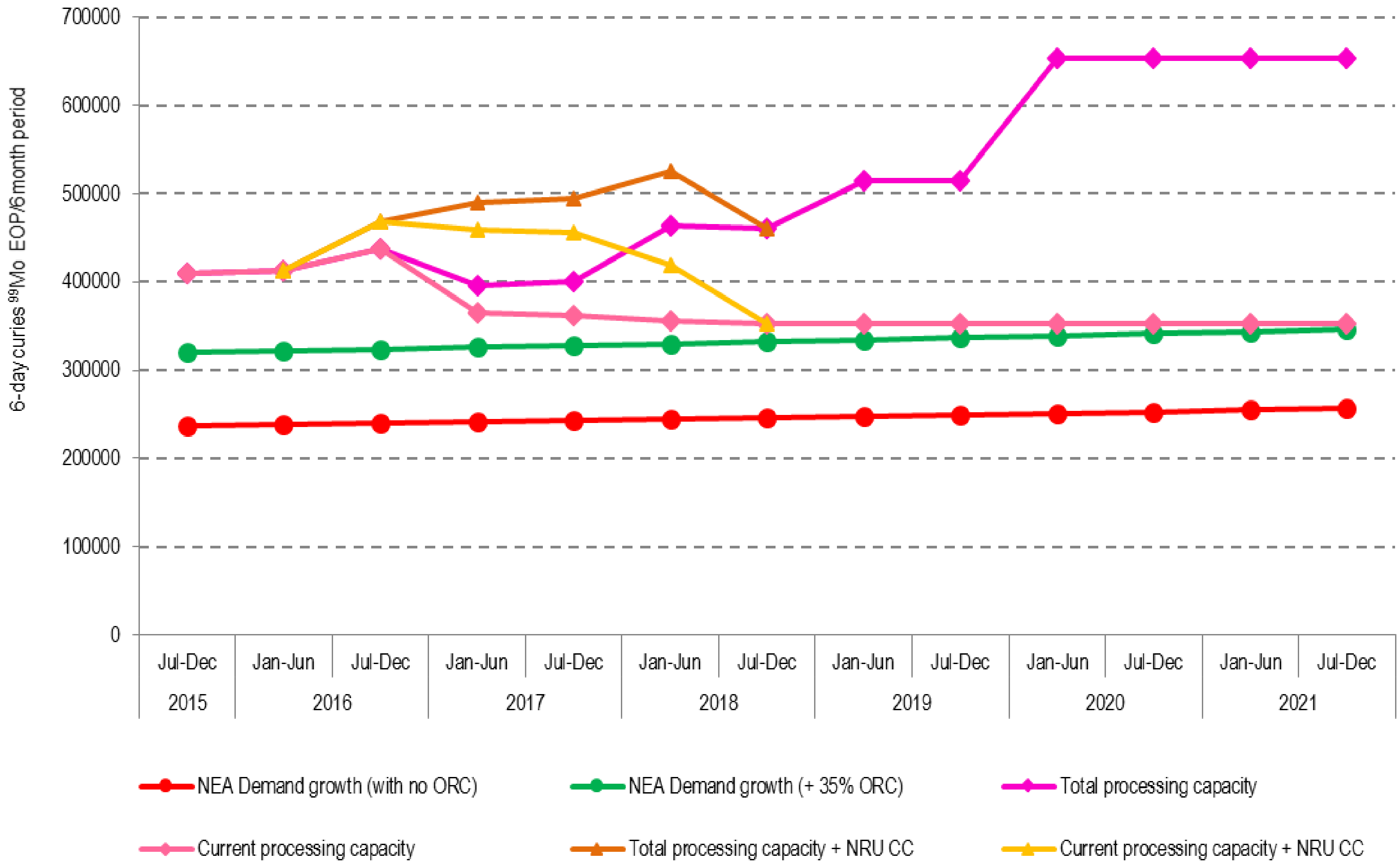
Each cooperative agreement is awarded under a 50% - 50% cost-share arrangement, consistent with the American Medical Isotopes Production Act and Section 988 of the Energy Policy Act of 2005. The cooperative agreements are currently limited to $25M each.

Changes in the international context since 2014

- OECD-NEA HLG-MR issued a new report “2016 Medical Isotope Supply Review: 99Mo/99mTc Market Demand and Production Capacity Projection 2016-2021”
  - “the current irradiator and processor supply chain capacity should be sufficient and if well maintained, planned, and scheduled, be able to maintain an unplanned outage of a reactor or processor through 2021”
- NAS issued a report entitled “Molybdenum-99 for Medical Imaging”
  - “…substantial likelihood of severe ^{99}Mo/^{99m}Tc supply shortages after October 2016.”
- The Canadian government has issued a contingency plan for emergency production of ^{99}Mo during the period 2016-2018 should a worldwide shortage develop

2016 OECD-NEA Study

Current Mo-99 Demand vs. Processing Capacity with Canada Contingency Capacity



Source: OECD-NEA Report "2016 Medical Isotope Supply Review: ^{99}Mo/^{99m}Tc Market Demand and Production Capacity Projection 2016-2021", June 2016

ORC: Outage Reserve Capacity

NRU CC: National Research Universal (Research Reactor) Contingency Capacity

NAS Study

FINDING 2D: Coordinated actions taken by governments, molybdenum-99 suppliers, technetium generator suppliers, technetium-99m suppliers, and others since the 2009-2010 supply shortages have improved the resilience of the global supply chain, minimized supply disruptions during unplanned reactor and processing facility shutdowns, and increased molybdenum-99/technetium-99m utilization efficiencies. Supply vulnerabilities remain, however, owing to the small number of participating organizations at some steps in the supply chain.

Chapter 7 of our report describes the potential supply vulnerabilities referenced in the last sentence of Finding 2D. These include the following:

- A reduction in the number of global Mo-99 suppliers from five to four after October 2016.
- The continued heavy reliance on aging reactors for the production of Mo-99.
- The reliance on single reactors for production of Mo-99 by two global suppliers.
- The potential for unexpected Mo-99 supply disruptions as two global suppliers convert from highly enriched uranium to low enriched uranium targets and another global supplier starts up a new target processing facility.
- Further delays in bringing new U.S. supplies of Mo-99 to market.

Progress in NNSA program

- NNSA has taken a leadership role in the interagency working group developing the Uranium Lease and Take Back Program (ULTB) and this year the ULTB officially started
- The projected dates of production from the CA projects active have incurred delays ranging from 1-2 years since the 2015 review
  - However, CA partners have made some significant progress
- A project has begun with General Atomics

NorthStar Neutron Capture Summary

- Completion of more than 30 ^{99}Mo production runs of 100 6-day Ci each
- Prepared more than 12,000 Ci of ^{99}Mo
- Filled about 300 generator Source Vessels (SV)
- Tested and validated their shipping logistics
- Mounted and ran ^{99}Mo produced at MURR using the RGX system, eluted ^{99m}Tc and performed multiple labeling runs
- Initiated clean room SV production operations at Beloit
- Initiated expansion of the MURR fill line operations to 4 times current production rate
- Ordering Six MIDUS Type B shipping containers for enriched targets for ^{99}Mo production
- Pre-Approval Inspection readiness audits were performed by outside experts

NorthStar expects to complete submission of responses to the FDA in 4QTR16. They state that when approval is granted they will be ready to provide ^{99}Mo to the U.S. market.

SHINE Summary

- Issuance of a Construction Permit by the US Nuclear Regulatory Commission (NRC). This is the first Construction Permit issued for a non-power facility since 1985.
- Running an accelerator demonstration for 132 consecutive hours of operation with 97% uptime.
- Producing ^{99}Mo at Argonne National Laboratory using the SHINE process and shipping the product to General Electric Health Care (GE). GE then tested the ^{99}Mo in their DryTec generator and found that both the ^{99}Mo and the resulting ^{99m}Tc met all specifications.
- Executing a supply agreement with HTA Co., Ltd., the largest distributor of radiopharmaceuticals in China.

Although SHINE reports that it has raised enough funds to complete design, the progress of this project has been hindered by the limited availability of investment funds.

General Atomics Summary

- Performance and accident analyses have been completed for target assembly
- Design reviews of target assembly, cooling & collection systems are complete
- 1/10 scale experiments on ^{99}Mo-doped pellets have measured yields higher than required
- Curie quantities have been extracted by SGE from irradiated pellets
- A LEU lease agreement between MURR and NNSA was signed, and delivery of 20 kg LEU is imminent.
- Hot cell equipment was defined and a vendor selected

GA has stated that there must be a resolution of waste take-back costs in the coming months that provides a limitation on the final liability they might have for waste disposal costs if they are to proceed on schedule in pursuing new technology based on the fissioning of LEU

General Conclusions

- NNSA has worked diligently and proactively over the course of the program based on the specific AMIPA requirements, especially considering the many complex factors outside their direct control
- NNSA is working with the international community to achieve full cost recovery and thus a level playing field for new U.S. producers.
- NNSA is trying to accelerate development of new domestic suppliers – funding seems to be an issue for one.
- Subcommittee finds that there is a significant chance that NNSA will meet their goal of achieving U.S. production of ^{99}Mo with FDA approval for use in the U.S. Market during 2017

What is the current status of implementing the goals of the NNSA-MMM ^{99}Mo *Program? What progress has been made since the 2nd assessment?*

- Dates of anticipated ^{99}Mo production have slipped 1-2 years since the last review
- The existing CA partners have nonetheless all made progress during the last year, with a number of important milestones
- An agreement has been signed with a new partner
- ULTB program has started
- The Canadian government has issued a contingency plan for emergency ^{99}Mo production and NNSA has transmitted an HEU export license application to the NRC

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

- The Subcommittee concludes that the NNSA strategy is complete and feasible based on the actions listed below:
  - The NNSA strategy has been adjusted based on the delays incurred by the CA partners.
  - A three-pronged approach was presented and the Subcommittee agrees that it should achieve the goals stated by the program. GA has been brought in as a fourth CA project and they have made progress.
  - The ULTB Program has been established in coordination with DOE-EM.
  - The Canadian government has created a contingency start-up plan for NRU production of ^{99}Mo, and NNSA has transmitted an HEU export license application for 3 kg HEU to the NRC.
  - NNSA made a thorough evaluation considering whether to raise the cap on CA project funding above $25M as recommended by the NSAC review in 2015; NNSA considered raising the cost share in the context of AMIPA and elected to maintain the cap at $25M and the 50/50 cost share. The Subcommittee found this evaluation to be a reasonable and acceptable response.

Are the risks identified in implementation being appropriately managed ?

- NNSA has taken action on a number of risks :
  - NNSA has taken an active role in the development of the ULTB program and that program is active
  - NNSA have worked with the Canadian government on planning for emergency production of ^{99}Mo
  - They work with interagency partners as needed
- The slow progress toward full cost recovery in the global ^{99}Mo supply chain threatens long term viability any U.S. producers who enter the market
- The risk due to costs in the take-back portion of the ULTB is a significant challenge

Overall, the Subcommittee finds that NNSA is appropriately managing the risks identified in implementing the ^{99}Mo program

Response to 2015 Recommendations

- The Subcommittee recommended that DOE should increase funds available to individual CA projects sufficient to significantly accelerate their ability to rapidly establish domestic production.
  - NNSA considered this carefully, but decided not to increase funding
  - The Subcommittee found this evaluation to be a reasonable and acceptable response.
- The Subcommittee recommended in 2015 that DOE must support NNSA in their continued efforts to advocate for the timely establishment of the ULTB Program.
  - This program was established in January of 2016.

Response to 2015 Recommendations

- The Subcommittee recommended in 2015 that NNSA should document a contingency plan to ensure a supply of ^{99}Mo from Canada within a few months if a significant shortage of ^{99}Mo appears imminent during the period 2016-2018.
  - The Canadian government has issued such a plan
  - NNSA has transmitted an HEU export license application to NRC for 3 kg HEU, consistent with the Government of Canada's 'NRU Contingency' Plan.
- The subcommittee recommended in 2015 that NNSA should develop a contingency plan to adapt the program should OECD-NEA continue to determine that the global community is not making adequate progress toward FCR in order for domestic production to be economically feasible.
  - NNSA has not acted on this recommendation.

Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2015 NSAC assessment of the ^{99}Mo Program appropriately and adequately?

- The NNSA-M^3 program has paid attention to the 2015 assessment
- Three of four recommendations were addressed adequately
- No action was taken on the fourth recommendation

The report lacks a conclusion on this point. Although this was not explicitly discussed (*an oversight*), I think the answer would be that the recommendations have been addressed appropriately and adequately…

Recommendation

The NNSA-M^3 program is working toward their high-level goal to accelerate domestic production of ^{99}Mo. It is possible that one of the CA partners will enter the market with U.S. produced ^{99}Mo in 2017. A new CA project based on fission production of ^{99}Mo has been initiated this year. The success of some projects based on fissioning of LEU may depend critically on the costs associated with waste disposal through the ULTB.

Recommendation:

The costs associated with the take-back portion of the ULTB program must be defined in a way that potential customers have predictable costs. The Subcommittee considers it extremely urgent that DOE identify a way to cap the liability associated with spent nuclear fuel (SNF) and radioactive waste in the ULTB program for potential U. S. ^{99}Mo producers.

Acknowledgement

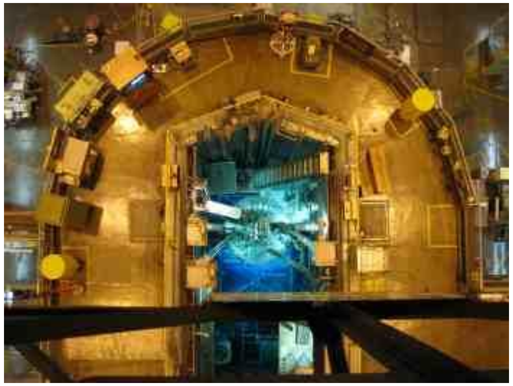
- Thanks to our committee members who did a great job developing an understanding of a complex problem, starting from very different experience and knowledge
- Thanks to Brenda May for her support in organizing our meeting!

BACKUPS

What is Mo-99?

- Molybdenum-99 (Mo-99) is the parent product of Tc-99m, a radioisotope used in approximately 50,000 medical diagnostic tests per day in the U.S. (over 18 million per year in the U.S.)
- Primary uses include detection of heart disease, cancer, study of organ structure and function, and other applications.
- Mo-99 has a short half life (66 hours) and cannot be stockpiled
- U.S. demand is approximately 50% of the world market
  - The historic global demand is ~12,000 6-day curies per week.
  - Since the 2009-2010 shortages, global demand has been ~10,000 6-day curies per week.
- Mo-99 is produced at only 5 processing facilities worldwide, in cooperation with 8 research reactor facilities
  - Processing facilities located in Canada (HEU), The Netherlands (HEU), Belgium (HEU), South Africa (HEU and LEU), and Australia (LEU)
  - Research reactors used for irradiation located in Canada, The Netherlands, Belgium, France, Poland, Czech Republic, South Africa, and Australia

Tc-99m generator and labeling kits



SAFARI-1 Reactor (South Africa)

The American Medical Isotopes Production Act of 2012

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

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

    - Requires the Secretary of Energy to establish a technology-neutral program to provide assistance to commercial entities to accelerate production of Mo-99 in the United States without the use of HEU

    - Requires annual public participation and review

    - Requires development assistance for fuels, targets, and processes

    - Establishes a Uranium Lease and Take Back program

    - Requires DOE and NRC to coordinate environmental reviews where practicable

    - Provides a cutoff in exports of HEU for isotope production in 7 years, with possibility for extension in the event of a supply shortage

    - Requires a number of reports to be submitted to Congress

GTRI's Mo-99 Objective and Strategy

Objective: Accelerate the establishment of reliable supplies of the medical isotope molybdenum-99 produced without highly enriched uranium

GTRI's strategy seeks to address weaknesses in the current Mo-99 supply chain:

- The current supply chain uses HEU to produce Mo-99
- Most Mo-99 production in today's marketplace is subsidized by foreign governments
- The current supply chain does not always have enough reserve capacity to ensure a reliable supply when one or more producers are out of operation
- The current supply chain is primarily dependent on aging facilities
- The current supply chain relies on one technology to produce Mo-99

A long-term, reliable supply of Mo-99 requires that global production of Mo-99 transition to a full-cost recovery, non-HEU-based industry

Other USG Initiatives

In addition to the American Medical Isotopes Production Act, there are other USG efforts to help achieve the objective to accelerate the establishment of reliable supplies of the medical isotope Mo-99 produced without HEU, including:

- White House Fact Sheet on Mo-99
- Participating in various domestic and international working groups
- Mo-99 stakeholder outreach
- Ensuring the implementation of OECD-NEA policy recommendations in the United States