U.S. Department of Energy
Office of Science

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

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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 4th NSAC assessment?
- Is the strategy for continuing to implement the NNSA goals complete and feasible, within an international context?
- Are risks identified in implementing those goals being appropriately managed?
- Has the NNSA-MMM Program addressed concerns and/or recommendations articulated in the 2017 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?

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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
- 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
- Susan Seestrom, Chair, Sandia 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

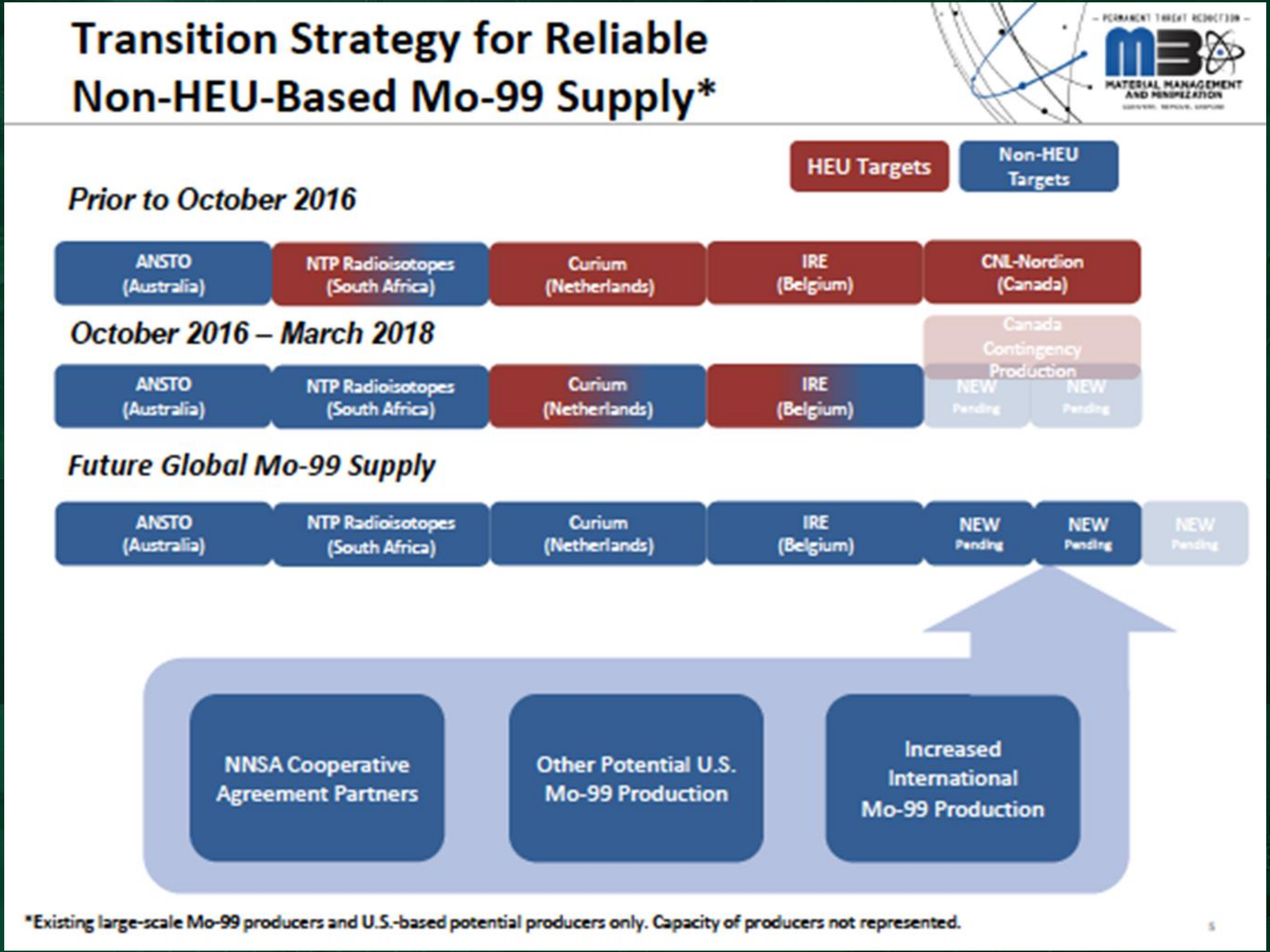
Subcommittee Process

- The Subcommittee met in Gaithersburg, MD on December 6-7, 2018.
- We were briefed by NNSA, representatives of the OECD, and all active cooperative agreement partners.
- We devoted a session to input from the broad stakeholder community.

Background

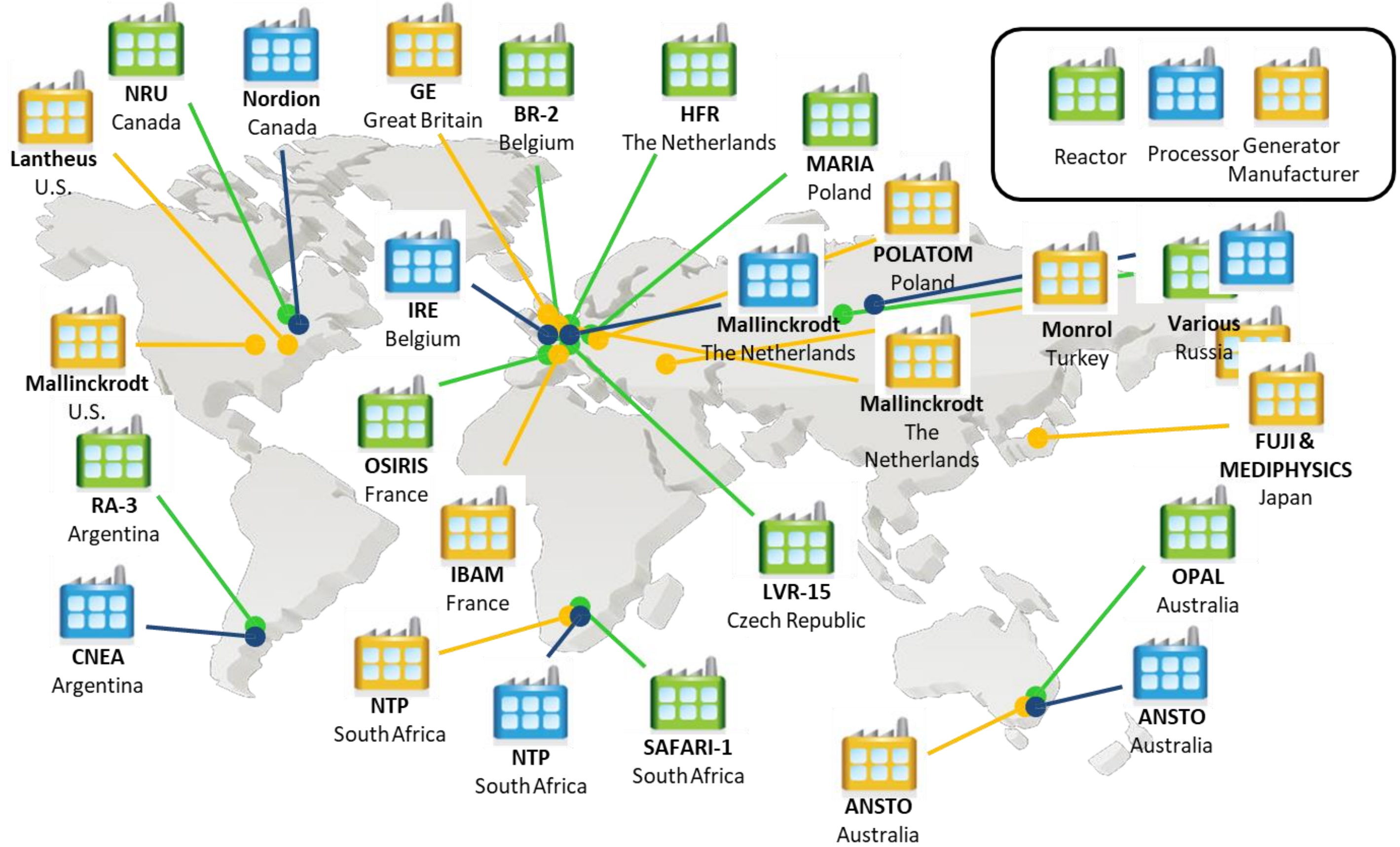
- ^{99m}Tc is the daughter of ^{99}Mo and is widely used for nuclear medicine diagnostic imaging.
- Today, ^{99}Mo is mainly produced by fission of ^{235}U.
- There is U.S. government interest in reducing the use of Highly Enriched Uranium (HEU).
- There was concern in the medical community that this 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 2005-2017.
- Until recently, there was no U.S. producer of ^{99}Mo.

Image courtesy of J. McConathy, UAB

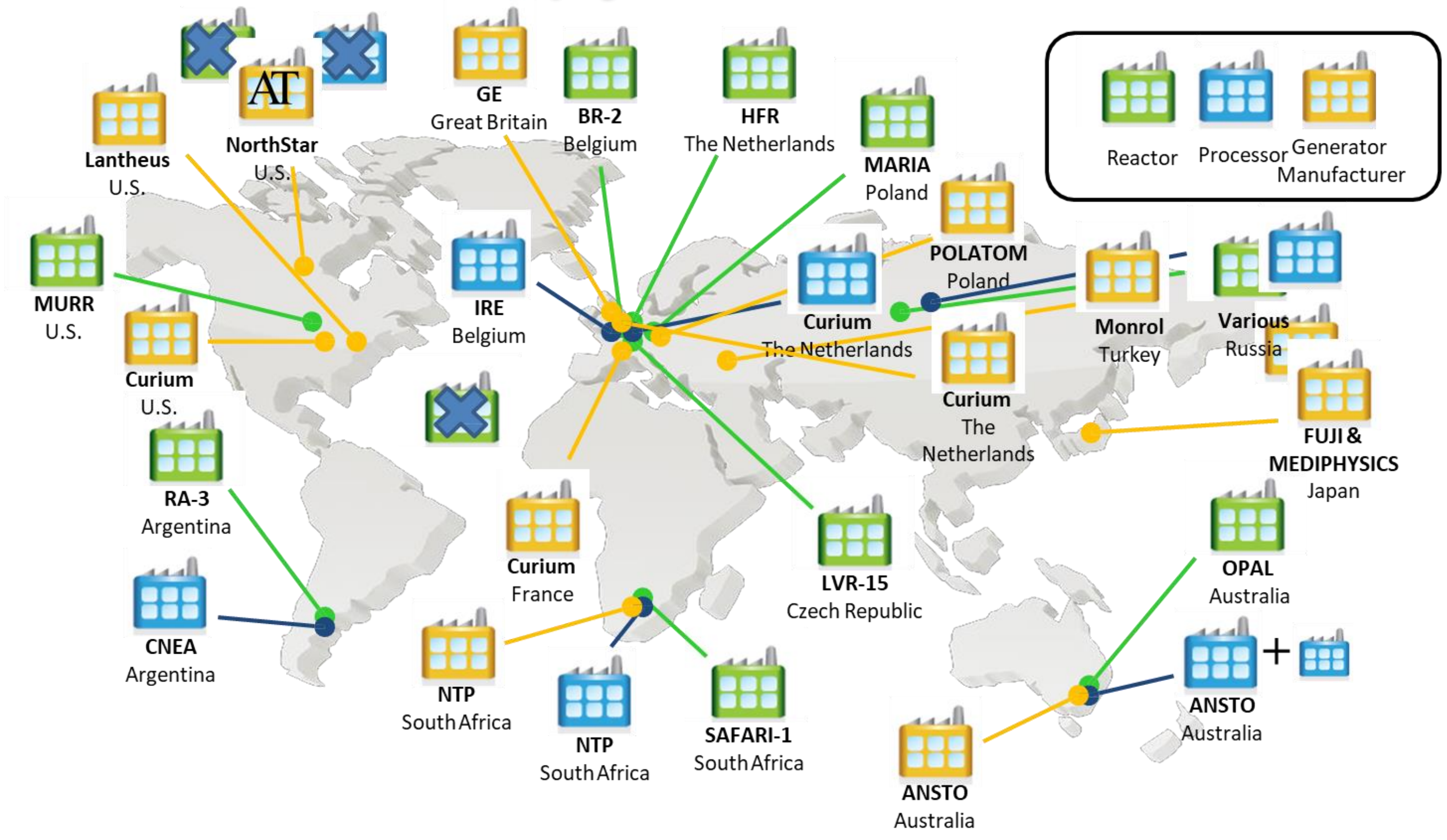


From NNSA ^{99}Mo 2016 presentation

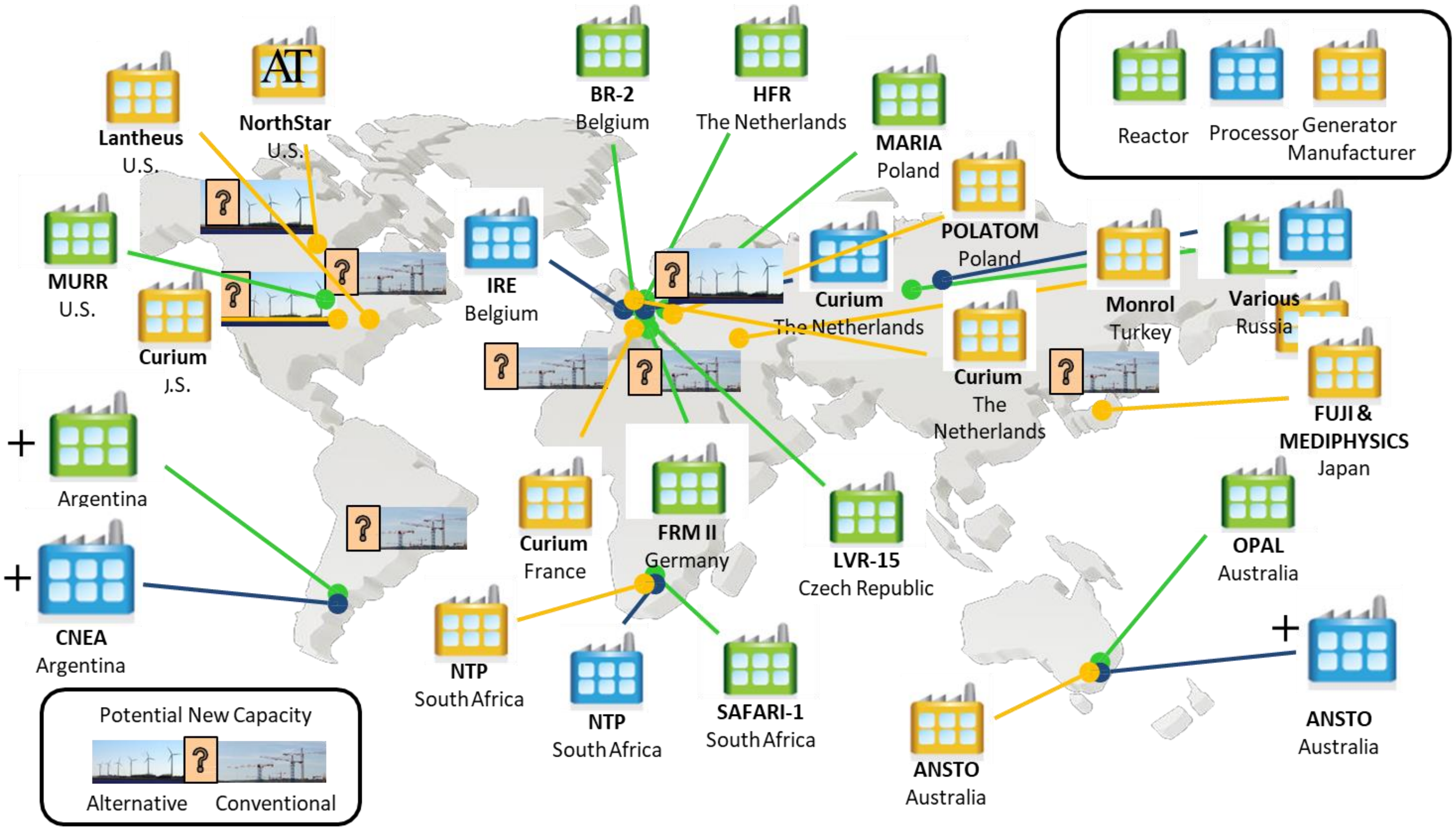
Global Supply Chain – around 2014



Global Supply Chain – around 2018



Global Supply Chain – around 2022



Changes in the international context (OECD)

“The Supply of Medical Radioisotopes: 2018 Medical Isotope Demand and Capacity Projection for the 2018-2023 Period”.

- Global demand growth has been maintained as in earlier reports.
- The conclusion on supply is similar to the previous report, “When facilities are well-maintained, well-scheduled and when unplanned outages are avoided, total irradiator and processor capacity should be sufficient.” ……… “However, when no additional processing capacity is added above the present level, the capability to manage any adverse events, particularly concerning ORC will be low and will reduce progressively with time.”

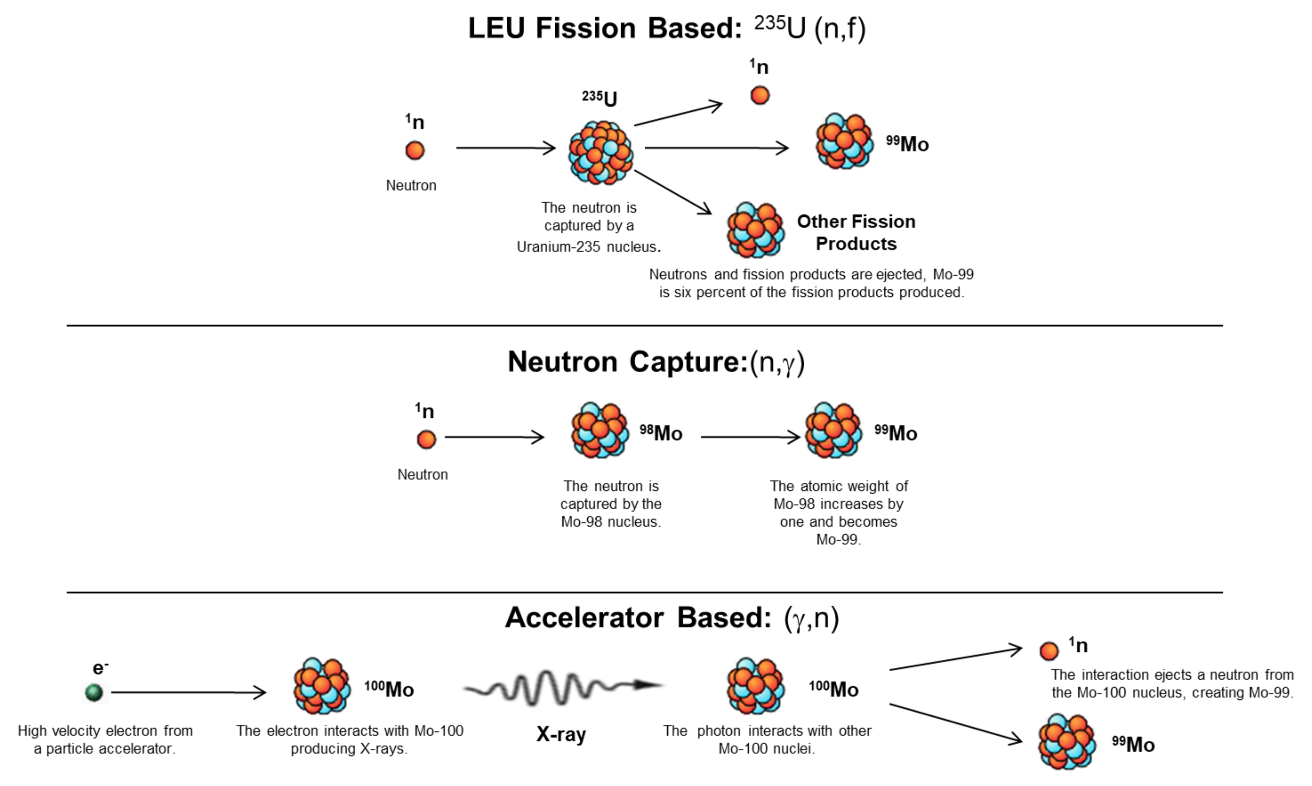
Changes in the international context (OECD)

- NTP problems led to a “chronic” shortage situation in some markets
- 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.

Changes in the international context (OECD)

- 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.
- 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.

NNSA and U.S. Domestic ^{99}Mo Implementing a Technology-Neutral Program



NNSA Co-operative Partners

	Neutron Capture Technology	Accelerator Technology	Accelerator with LEU Fission Technology	LEU Target Technology
Cooperative Agreement Partner	NorthStar Medical Radioisotopes	NorthStar Medical Radioisotopes	SHINE Medical Technologies	General Atomics
Funded	$25 million	$25 million	$25 million	$25 million
Cooperative Agreement Status	Completed	Period of Performance extended beyond 2018	Completed	Terminated by General Atomics
Anticipated Market Entry*	November 2018	2020	2020	N/A

*Market entry dates provided by CA partners

NorthStar neutron capture project:

- Three FDA approvals since the last meeting, including RadioGenix (February 2018)
- They initiated direct customer/commercial shipments for patient use in 4Q2018.

NorthStar accelerator project:

- Approval from their Board to proceed with contracts for accelerator purchase and building construction.
- They began contract negotiations to purchase up to eight electron accelerators. The first of which they expect to be delivered in 2020.

SHINE Accelerator with LEU Fission project:

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

NNSA issued a new Funding Opportunity Announcement (FOA DE-FOA-0001925, July 2018) open to both new and existing cooperative agreement partners

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

General Conclusions

- The Subcommittee found that since the review in 2017, NNSA has moved the NNSA-M^3 program forward, consistent with the specific AMIPA requirements.
- The initial movement of ^{99}Mo produced by NorthStar into the market and the resulting ^{99m}Tc into patient procedures is an important step forward.
- 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.
    - Some of these are related to ULTB and/or FCR

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

- The program is continuing to make progress towards improving the reliability of domestic ^{99}Mo supply.
- NorthStar has begun to deliver ^{99}Mo to the U.S. market. With additional approvals, they estimate they will be able to produce 30-35% of the US market needs by 2020 (using the neutron capture process at MURR).
- Shine has completed construction of their Building One, taken delivery of their first production unit accelerator
- One CA partner, General Atomics, has withdrawn.
- A new FOA for cooperative agreements was launched and attracted multiple applications from new and existing CA partners

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

- 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 feasibility still needs to be demonstrated:
  - While a ULTB program has been formally established, an effective model of implementation remains elusive.
  - There has been slow progress on establishing the principle of full cost recovery (FCR) in the international context; this could impact the long term viability of U.S. producers.

Are the risks identified in implementation being appropriately managed ?

- Major outstanding risk is the finalization of the ULTB program.
  - Lease aspect of the program appears to be in place while the *take back* has not been finalized.
  - One of the current (and potentially new) CA partners will most likely rely on this program.
- There remain other risks to the success of the NNSA goals, but for the most part these are outside of the control of the NNSA.
  - The risk posed by the need for the market to accept new generator technology (NorthStar).
  - The need for FCR for "level playing field".

Response to 2017 Recommendations

NNSA has partially addressed the subcommittee's concerns and recommendations.

A draft contract was not been issued with the CA partner prior to the 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.

Recommendation 1

- The slow implementation of full cost recovery (FCR) continues to be a risk to the financial viability of U.S. producers. NNSA has supported 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. 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 ^{99}Mo. 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 CAs 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.

Acknowledgements

- Thanks to Susan Seestrom for her outstanding leadership.
- Thanks to our committee members who did a great job.
- Thanks to Brenda May for her support in organizing our meeting!

Back up slides

What is ^{99}Mo?

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

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

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

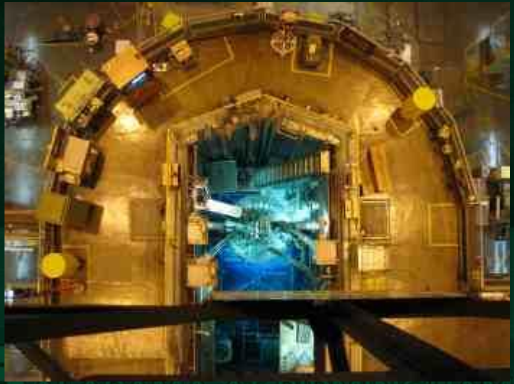
U.S. demand is approximately 50% of the world market

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

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

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

Tc-99m generator and labeling kits



SAFARI-1 Reactor (South Africa)

The American Medical Isotopes Production Act of 2012

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

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

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

NNSA Mo-99 Objective and Strategy

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

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