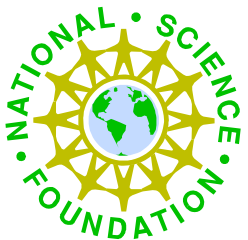


Mo-99 Presentation to NSAC

March 12, 2018

Susan J. Seestrom



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-M³ Mo-99 Program?
- What progress has been made since the 3rd 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 2016 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, 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

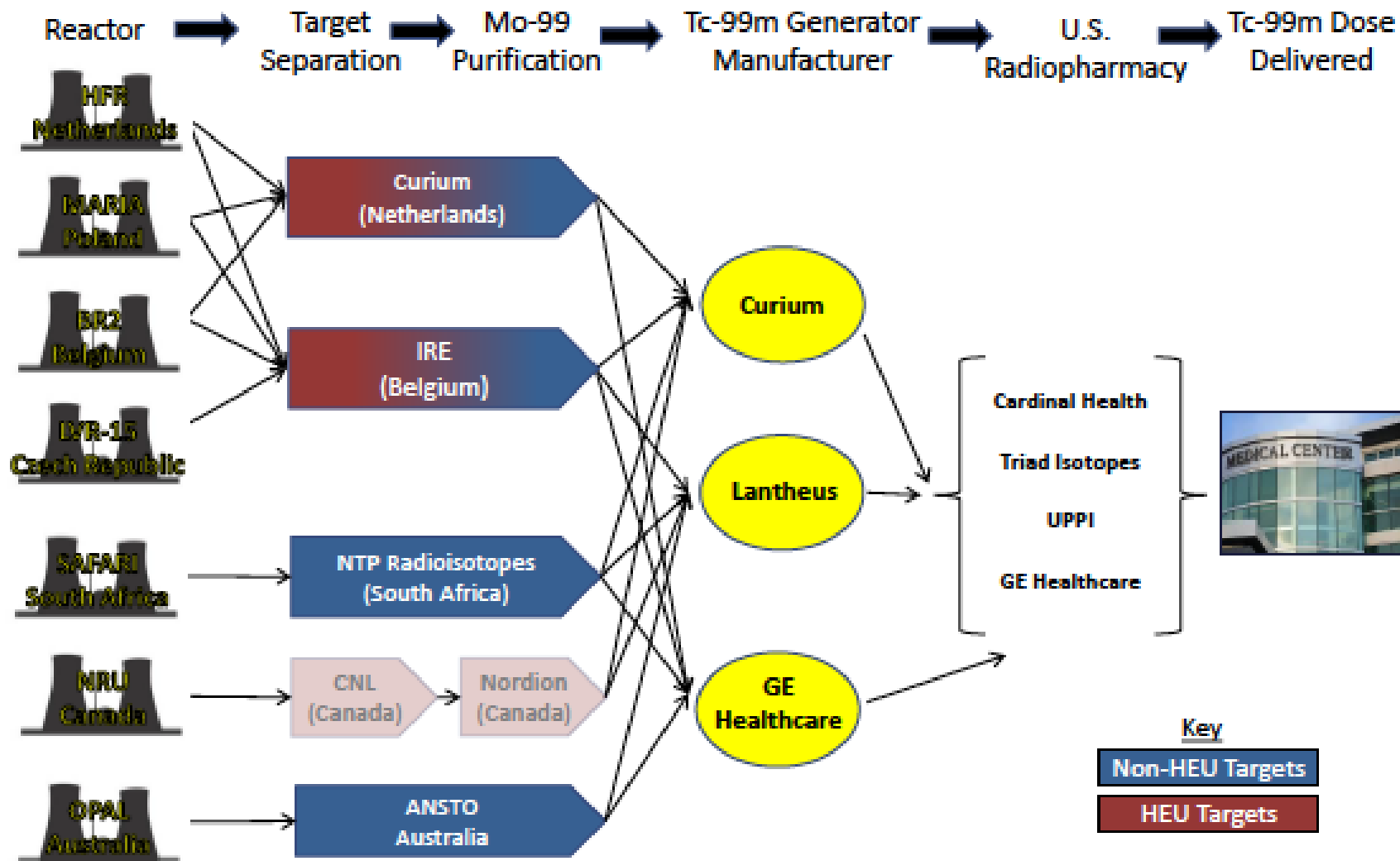
Subcommittee Process

- The Subcommittee met in Crystal City, VA on December 14-15, 2017.
- 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.

Original 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



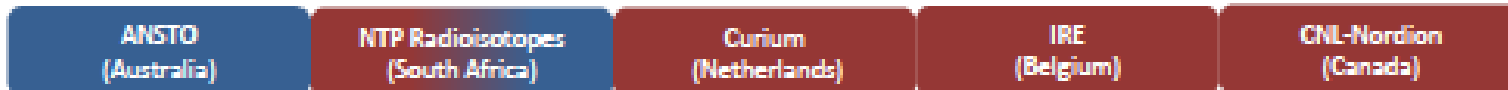
Transition Strategy for Reliable Non-HEU-Based Mo-99 Supply*



HEU Targets

Non-HEU Targets

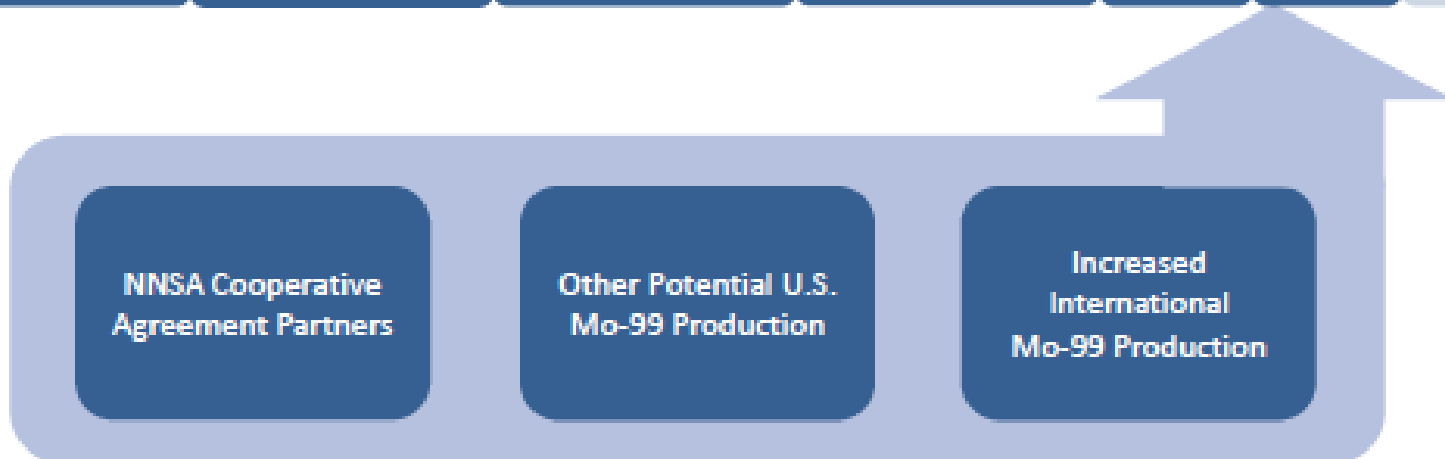
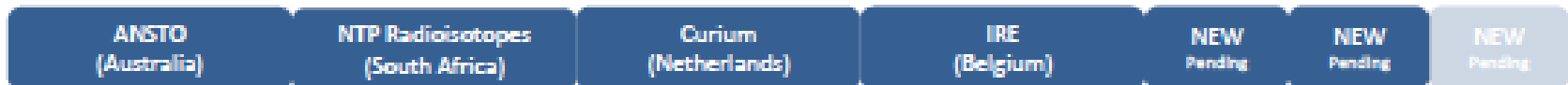
Prior to October 2016



October 2016 – March 2018



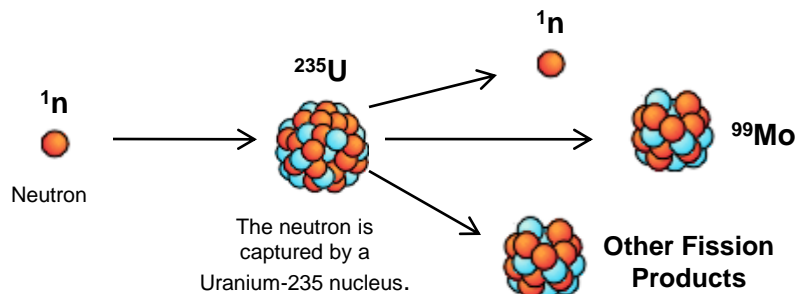
Future Global Mo-99 Supply



*Existing large-scale Mo-99 producers and U.S.-based potential producers only. Capacity of producers not represented.

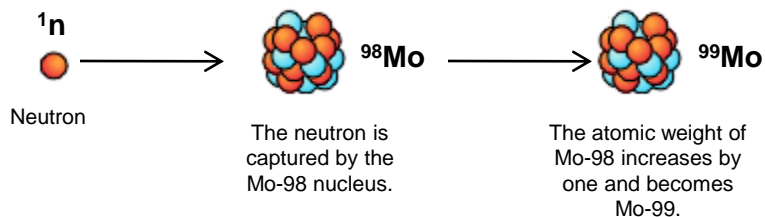


LEU Fission Based: $^{235}\text{U} (n,f)$

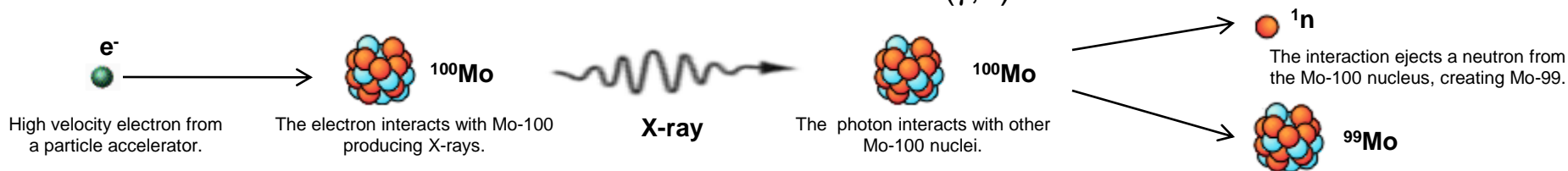


Neutrons and fission products are ejected, Mo-99 is six percent of the fission products produced.

Neutron Capture: (n,γ)



Accelerator Based: (γ,n)



NNSA has 3 Cooperative Agreement Partners

- NorthStar – two projects continuing
- SHINE – one project continuing
- General Atomics – one project continuing

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.

NNSA Cooperative Agreement Partners Progress



*RadioGenix™ – NorthStar™ Tc
Generating System*

Since 2009, NNSA has partnered with U.S. commercial entities to accelerate domestic Mo-99 production.

NorthStar Neutron Capture Technology:

- Final submittal to FDA for use of its RadioGenix™ System to produce Tc-99m from non-HEU based Mo-99
- Anticipated FDA approval in early 2018
- Anticipated market entry: first half of 2018

NorthStar Accelerator Technology:

- Downselected Accelerator type
- Began ordering long lead procurement items
- Anticipated market entry: end of 2019

SHINE Accelerator with LEU Fission Technology:

- Broke ground on its Building One Testing and Training Facility in July 2017
- Estimated completion date is February 2018
- Anticipated market entry: 2020

General Atomics LEU Target Technology:

- Submitted License Amendment Request (Part I) to the NRC in Spring 2017 for in-reactor operations at MURR
- Anticipated market entry: end of 2019



*SHINE Medical Technologies
Accelerator-Driven LEU Subcritical
Assembly for Medical Isotope Production*

Changes in the international context since 2014

- The OECD-NEA HLG-MR issued two new reports: *The Supply of Medical Radioisotopes: 2017 Medical Isotope Supply Review: 99Mo/99mTc Market Demand and Production Capacity Projection 2017-2022* and *The Supply of Medical Radioisotopes: Results from the Third Self-assessment of the Global Mo-99/Tc-99m Supply Chain*
 - the assessed demand was kept constant from previous years at 9,000 6-day Ci per week
 - “Overall, the current irradiation and processor supply chain capacity should be sufficient and if well maintained, planned and scheduled, be able to manage an unplanned outage of a reactor, or a processor throughout the whole period to 2022. When no additional capacity is added, then from mid-2018, the level of capability to manage adverse events reduces, in particular when considering processing capacity.”
 - the conclusion on progress toward full cost recovery is less positive: “showing continued but slow progress towards implementing the six HLG-MR policy principles”
- “Nuclear Technology Products in South Africa has been off-line since the end of November 2017 and as of early February 2018 it was still not processing 99Mo”
 - OECD/NEA ““During the recent unexpected outages the remaining suppliers are mostly working at maximum levels and there are still some limited shortages in some markets.
 - They have now resumed production

Progress in NNSA program

- At the time of the 2017 review, all cooperative agreements have been awarded at \$25M
- NNSA has not yet issued a contract for take-back of Uranium under the Uranium Lease and Take Back Program (ULTB)
- All of the active CA projects have incurred additional delays of approximately one year in the projected dates for first ^{99}Mo commercial production over what was stated at the last Subcommittee meeting fifteen months ago.
 - However, CA partners have made some significant progress
 - Since our review, the Food and Drug Administration announced the approval of the RadioGenix generator developed by NorthStar

General Conclusions

- NNSA has moved the NNSA-M3 program forward, consistent with the specific AMIPA requirements
- There continue to be issues related to the long-term financial viability of any producers that do succeed in entering the market.
 - Market acceptance of new technology
 - Slow progress toward full cost recovery internationally
- Subcommittee finds that it is probable that one or more of the NNSA supported projects will enter the market eventually, and perhaps as early as the first half of 2018, although likely not with sufficient capacity to mitigate potential shortages in the period before 2020.
- The remaining major challenge that is within DOE's control concerns the ULTB program and the ability to achieve predictable costs for disposal of leased uranium residues

What is the current status of implementing the goals of the NNSA-MMM ⁹⁹Mo Program? What progress has been made since the 3rd assessment?

- Dates of anticipated ⁹⁹Mo production have slipped ~1 year since the last review
 - The existing CA partners have all made technical and business development progress during the last year
 - anticipated market entry ranges from the first half of 2018 through 2020.
- The first delivery of LEU under ULTB was made in January 2017 and take-back options at DOE and commercial sites are being evaluated.
- The program continues to support national laboratory collaborative projects

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-M3 Domestic Molybdenum-99 Program has achieved the objective of the program: to provide assistance to commercial entities to accelerate production of ^{99}Mo in the United States without the use of HEU.
 - We consider it likely that one or more of the CA partners will begin potentially sustainable production of ^{99}Mo for the domestic radio-pharmacy market.
 - Completion of the ULTB program is an important part of the NNSA strategy. This is essential for some CA projects.
 - Three of the four major international suppliers have transitioned to the use of LEU targets, and the fourth is expected to make the transition soon.
 - Two reactors continue to use HEU fuel (Belgium Reactor 2 and MURR)

Are the risks identified in implementation being appropriately managed ?

- The Subcommittee finds that the major outstanding risk to the successful completion of the goals of the NNSA program 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
 - two of the 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.
 - We note the risk posed by the need for the market to accept new generator technology in order to use the low specific activity ^{99}Mo produced by NorthStar.
 - NNSA should continue to monitor these risks

Response to 2016 Recommendations

- The NNSA has responded that they agree that the recommendation from the previous report (*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 US 99Mo producers*)
 - NNSA emphasized that determining costs was challenging
 - NNSA acknowledges the slowness of the process but emphasized the technical challenges as well as the sensitivity of communication as a factor
 - A draft contract for take back had not been issued at the time of the subcommittee review
- It is the view of the subcommittee that for a given contract and producer, the costs must be well defined, predictable, and stable in order for the potential producers to put together the required business plans

Recommendation

Various potential U.S. producers of 99Mo, including several of the CA partners, will need to use the capabilities of the ULTB program. In order to develop their business model, they must have well-defined, predictable, and stable costs for disposition of the waste they produce. In the approximately 15 months since the last NSAC review (September 2016), no contract for ULTB waste has been shared with potential producers.

Recommendation:

For this reason, the single recommendation of the Subcommittee is that the Department of Energy should:

- a) In a timely manner, issue a waste take back contract to the CA partner with whom they have been engaged for the last year and
- b) use the lessons learned in this process to identify opportunities for improvement of the ULTB process.

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