July 9, 2014

MEMORANDUM TO: ACRS Members

FROM: Cayetano Santos, Chief /RA/
Technical Support Branch
Advisory Committee on Reactor Safeguards

SUBJECT: TRIP REPORT 2014 Mo-99 TOPICAL MEETING ORGANIZED BY NNSA

The enclosed trip report provides a summary of the highlights from the 2014 Mo-99 Topical Meeting held on June 24-27, 2014, at Washington, DC. The meeting program and abstracts of the technical papers presented at the meeting are published in a handout, which is available for perusal.

Enclosure: As stated

cc: E. Hackett
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I attended the 2014 Mo-99 Topical Meeting organized by the Argonne National Laboratory (ANL) for NNSA on June 24-27, 2014, at the Hamilton Crowne Plaza, Washington D.C. Over 200 people from 13 countries were in attendance. Representatives of the medical and pharmaceutical companies representing the radioisotope producers and end users, government agencies and regulators, national laboratories and the insurance industry had their voices heard. In addition to SHINE Medical Technologies, NorthStar Medical Technologies, and Coqui Radiopharmaceuticals, also present at the conference were three potential producers that have previously engaged with the NRC: General Atomics, Flibe Energy, and Eden Radioisotopes. In addition to three ACRS staff (Kathy Weaver, Quynh Nguyen and myself), staff from the NRC Offices of NRR, Research, and NMSS attended the meeting. William Shuster, NRR, presented the NRC activities in the area of licensing new Mo-99 production facilities.

Ann Harrington from DOE-NNSA opened the meeting, and Cindy Atkins-Duffin from the President’s Office of Science and technology communicated White House support to non-HEU production of Mo-99. The American Medical Isotope Production Act promotes transition to non-HEU production methods to reduce proliferation risks. There are 50 million world-wide and 18 million US radioisotope imaging studies done every year, 80% of which use TC-99m (50% in cardiology and 25% in oncology). The medical community considers TC-99m as the most effective imaging isotope due to its 140kev gamma that yields high quality pictures and 6 hour half-life (decays quickly in the body), while the mother isotope Mo-99 has a 66 hour half-life ideal for minimal decay during transportation. In addition to the neutron capture process \([\text{Mo}_{98}(n, \gamma)\text{Mo}_{99}]\) in reactors, non-HEU production of Mo-99 can be accomplished using the linear accelerator (LINAC) based photon capture process with enriched Mo-100 \([\text{Mo}_{100}(\gamma, n)\text{Mo}_{99}]\). However, the use of cyclotron/accelerator sources was noted to have some logistical issues and higher doses.

Loss of European reactors caused shortages of Mo-99. Also, major producers in Canada (Chalk River reactor) and France are scheduled to exit the market during 2015-2020 timeframe. Unless new production sources are created, risk to the reliable supply of Mo-99/Tc-99m as early as 2015 is foreseen. A survey conducted by the Society of Nuclear Medicine and Molecular Imaging found only a small percentage of isotope users use non-HEU generated Mo-99. Responders noted their concern with the price increase expected in the transition. Competition with cost subsidized European products was a concern.

Currently there are three FDA approved US products for TC-99m: GE Healthcare; Mallinckrodt Pharmaceuticals; and Lantheus Medical Imaging. FDA approval process seemed to be quite involved and goes into the manufacturing process (neutron flux profile, placement and definition of targets,
holdup time, purification process, etc.) as it could affect the purity of Mo-99. Assurance of sterility and non-pyrogenic property are addressed in review.

Due to similarity of fission products from nuclear explosions and medical isotope production using reactors, the later use creates radio-Xenon fog background causing challenges for verifying compliance with the Comprehensive Nuclear Test Ban Treaty. The two communities are working together to find ways to mitigate this impact. Xenon weather is larger in some areas in the world like the Northeast US, South Africa and Western Europe. New radio-Xenon trapping system is one of the technical challenges. Various producers like IRE in Belgium, Coqui, NorthStar, ANSTO (Australian) signed a pledge to reduce emission and provide stack monitoring data.

US Efforts in Non-HEU Based Mo-99 Production:

- Lantheus Medical Imaging was the first to obtain the FDA approval for its LEU-sourced TechneLite generators in 2010. They have agreements with NTP Radioisotopes in South Africa and the Australian Nuclear Science and Technology Organization (ANSTO) to receive an increasing supply of LEU-sourced Mo-99. Lantheus plans to increase its use of LEU-sourced Mo-99 each year, with a goal of eventually eliminating HEU-sourced Mo-99 from its supply chain.
- Mallinckrodt, a Dutch company operating in US, is producing Mo-99 since 1994 using HEU in Patten high flux reactor in the Netherlands. The other two reactors in use are the Belgian BR2 high-flux research reactor, and Polish MARIA research reactor that played an important role when Patten experienced unexpected technical problems and was shutdown. Their LEU conversion work started in 2010 and had some challenges, including the uranium filter redesign required for manufacturing LEU target, loss of efficiency in HEU to LEU conversion, and increased waste volume.
- SHINE will use an accelerator-driven, LEU solution (uranyl sulfate) in a geometry optimized for high efficiency isotope production (includes I-131 and Xe-133, in addition to Mo-99). Very high neutron yield is produced by a deuterium-tritium fusion reaction in the accelerator gas target that drives fission in the subcritical LEU solution. SHINE plans to supply over half of the US demand for Mo-99. SHINE’s construction permit application is under NRC review. LANL is doing extensive subcritical target modeling. NRC approval of the Construction Permit and project financing for the balance of work were noted as a risk factors. SHINE is pursuing government support and commercial partnership. They made a supply agreement with GE Healthcare and an MOU with an Indonesian producer of Mo-99.
- NorthStar Medical Technologies has two parallel efforts to establish domestic supply of Mo-99 from non-Uranium based sources. One involves the neutron capture process at the Missouri University Research Reactor (MURR), and the other is LINAC based photon capture process using enriched Mo-100 at their Beloit, Wisconsin, site. The low specific activity of Mo-99 solution requires a new type of generating system in their RadioGenix platform which uses an automated radionuclide separation system.
- Northwest Medical Isotopes in Corvallis, OR plans to irradiate targets made from LEU procured from DOE in existing University reactors like MURR and OSU, and produce fission based Mo-99.
Part 50 and 70 license applications to the NRC are being prepared while the facility site is being secured.

- GE Global research center provided a review of the landscape and potential future supply models. A 35% outage/reserve capacity is deemed necessary for a predictable supply. Challenges involve the regulatory path, cost and waste management.
- Coqui has secured a 25 acre site in Alachua, Florida, within the University of Florida Progress Industrial Park. They plan to use two small research reactors with the University of Florida research reactor in mind.

Technical Support of US National Labs (not all inclusive):

- As part of the NNSA’s Global Threat Reduction Initiative (GTRI) program, LANL is providing engineering design support to NorthStar’s accelerator generated Mo-99 production effort. Process optimization includes target performance at the ANL electron linear accelerator with different enrichments of Mo-100 and beam energies, and improving production facility design. The electron beam positioning and profile affect production. They are also helping SHINE in the area of system modeling, design support, irradiation and separation chemistry, CFD modeling of the Target Solution Vessel thermal performance, simulation of gas bubbles in fissile solution, and fabricating Zr-clad DU disks for testing at ANL.
- ORNL is supporting fabrication of accelerator target disks for NorthStar using Mo powder metallurgy approaches that minimize waste. The targets are very thin wafers (29 mm diameter and 0.5 mm thick) with very stringent dimensional tolerances.
- In 1944 Enrico Fermi operated a solution reactor at LANL. A time dependent dynamic system simulation model of fissile solution system was discussed. It is composed of four coupled sub-models: neutron kinetics; radiolytic gas generation; core thermal; and plenum models. Performance of the model is compared against experimental data. LANL is doing model extension to address accelerator-driven subcritical systems and will publish it later in summer.
- ANL has developed an experimental setup called mini-SHINE (subcritical hybrid intense neutron emitter) using ANL’s LINAC (35 Mev, 10 KW beam) and 5L of LEU uranyl sulfate solution, and successfully produced 1-2 Ci of Mo-99. A modified CINTICHEM process is used for purification. Reportedly, ANL has optimized potential waste streams to minimize cost and waste disposal. Modeling for bubble formation and precipitation of uranyl peroxide are being examined.
- ORNL at Y-12 is developing the high density LEU targets for Mo-99 production. After testing several technologies, the current design target is undergoing irradiation testing at the MURR.
- LANL has refined the technique for analysis of uranium in sulfate medium for SHINE to complement the labor intensive Davis and Gray titration techniques. Increase in uranium is required for LEU production and they developed a process for removal of excess uranium post-irradiation prior to Mo-99 purification. 10 CFR Part 74 requires material control and accounting of special nuclear material.
Non-US Producers of Mo-99:

- Representatives from IAEA, OECD/NEA, and isotope producers from Belgium, Australia, Argentina and South Africa provided the status of Mo-99 supply situation and their efforts in conversion to non-HEU production of Mo-99.

- Euratom Supply Agency (ESA) role was enlarged in 2013 to cover the aspects of medical isotope supply in EU, and to recommend policy options. Stamatios Tsalas, the Director-General of ESA, mentioned that transition from HEU to LEU to be problematic and the need for DOE cooperation for additional supply of HEU during transition beyond 2015. Their long term supply agreement with DOE includes 20% LEU-sourced Mo-99. He mentioned the new European players coming on line to be the German high-flux research reactor FRM-II in 2017; new material testing reactor JHR under construction at Cadarache, France in 2019; new high flux reactor PALLAS in the Netherlands in 2023; and the world’s first prototype of a nuclear reactor MYRRHA that is driven by a particle accelerator in 2023.

- INVAP in Argentina, developed a process for Mo-99 production from LEU in a solution nuclear reactor. This work was done for B&W and demonstrated the feasibility of producing high activity high purity Mo-99.

- Russia provides only 0.1% of world supply of Mo-99, and may not move out of HEU use.

- South Africa has been involved in a LEU conversion process at the Pelindaba NTP facility (SAFARI-1 research reactor) for last four years, and experienced slower uptake of LEU-based Mo-99. It is concerned about economic uncertainty and long term sustainability.

- Linear accelerator generated Mo-99/Tc-99m production is being developed in Canada with a target date of early 2016. They consider this method of generation as more environment-friendly, cheaper, more secure, with purer Mo-99 stream, and easier to license. They studied both natural (10%) and 97% enriched Mo-100 discs at various beam energy and power levels. In addition, a consortium in Canada is pursuing direct production of Tc-99m using small medical cyclotrons and enriched Mo-100 targets [Mo100(p, 2n)Tc99m] before Chalk River reactor ceases Mo-99 production in 2016. While a 97.39% Mo-100 enrichment is optimized for production efficiency, the beam current and energy band need to be optimized with additional patient dose considerations.

- Alan Kuperman of University of Texas at Austin discussed what he termed as “European foot dragging.” Despite Dutch and Belgian government’s commitment at the 2012 Nuclear Security Summit to ensure that Mallinckrodt eliminates by 2015 its use of HEU to produce Mo-99, the Netherland had rejected an US government’s offer on technical and financial support, only to reverse course after European TV networks reported on it. He noted protectionism may be playing a role in European regulator’s delay in approving non-HEU Mo-99 from South Africa, while US did it 4 years ago. This meant South Africa could not sell LEU-based Mo-99 in Europe, thus providing a chilling effect. He opined that US should halt export of HEU to Europe if they do not expedite LEU use.