2018 Mo-99 TOPICAL MEETING

LESSONS LEARNED DURING CONVERSION FROM HEU TO LEU

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September 24, 2018

INTRODUCING CURIUM

CURIUM – UNITING IBA MOLECULAR AND MALLINCKRODT NUCLEAR MEDICINE LLC

- January 27, 2017 – Mallinckrodt Pharmaceuticals completed the sale of its Global Nuclear Imaging business to IBA Molecular.
- 100 years of combined experience in the nuclear medicine industry.
- Singular focus – to develop, manufacture and supply SPECT, PET and therapeutic radiopharmaceuticals.
- More than 1,600 dedicated employees work to provide nuclear medicine products for over 14 million patients worldwide each year through 6,000 customers in 70 countries.
- Largest vertically integrated radiopharmaceutical manufacturing network with one global Mo-99 production facility, three large SPECT manufacturing facilities, and more than 40 SPECT and PET radiopharmacies.

LEU TARGET COMPOSITION

- The new LEU target was designed so it would meet the needs for Mo-99 production, reactor compatibility and fabrication.
- The Al alloy cladding chosen for metallurgy principles contained a metallic impurity which created a new chemistry removal challenge in the process development.
- The target manufacturing process at CERCA (Framatome) introduced another metallic impurity into the LEU targets, which created a new chemistry removal challenge.
- Similar issues were also faced by Mo-99 processors NTP and IRE in their conversion efforts, leading to longer development time.

RESOLVED METALLIC IMPURITY ISSUE IN ALLOY

- We confirmed the metallic impurity in the LEU targets formed oxides and clogged the uranium filter, slowing the filtration process.
- We did not want to change the AG3 alloy in the new LEU target because it would have added at least 12-18 months to the conversion.
- We designed/tested/validated a new uranium filter which could handle the metallic impurity load and still optimize waste disposal.

RESOLVED METALLIC IMPURITY ISSUE IN TARGET

- Metallic contamination from target manufacturing process caused problems in the radiochemistry process.
- Although Y-12 (Oak Ridge National Lab – U.S.) can control the level of metallic impurity in the bulk LEU, that same metal was being added as part of the target manufacturing process.
- Any of this metallic impurity contained in the target as a contaminant, is activated to a radionuclide of concern during the target irradiation process.
- Any of this radionuclide of concern present in the finished Mo-99 presents a problem.
- We added an additional sorbent column to remove this metallic contaminant, and to ensure the absence of any of this metal in the finished product.

OTHER CHALLENGES OVERCOME

- Unexpected shutdowns of the HFR and MARIA and the Be matrix replacement in the BR2 during time scheduled for validation runs caused delays in the irradiation schedules.
- Previously drug regulatory agencies had a final material specification check for gross alphas, whereas new requirements specified development of methods for sampling and measuring Pu-239, Am-241 and U-235 individually.
- Updated approval by the French transport competent authority (ASN/IRSN) was needed for the Type B container we use to transport irradiated LEU targets from the reactors to our Petten site.

MARIANNE target transport container

REGULATORY APPROVALS

Key Country/Region	RA Submissions to Health Authority (Master File + Variation / Supplement)	Approval Date
EU	16-January-17	25-April-17
Switzerland	16-January-17	31-October-17
US	31-January-17	27-April-17
Canada	21-March-17	31-May-17
Asia	31-May-17	21-June-17

Experiences from previous drug regulatory submissions

EU - Work sharing with National MA. Grouped submissions. ASMF and Type IB Variation as prospectively agreed by Reference Authority.

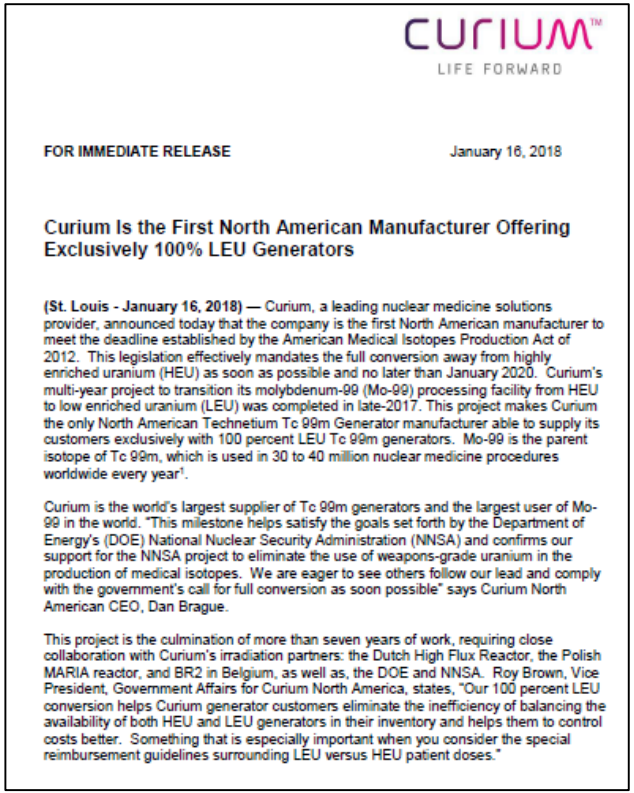
US – DMF and Prior Approval Supplement

Canada – DMF and Notifiable Change

The commitment and collaboration between Global Drug and Nuclear governing bodies was outstanding and served as a solid foundation for LEU regulatory success

CURIUM IS NOW FULLY CONVERTED

- After all the regulatory approvals were received, Curium burned the last of our HEU targets late last year.
- As of early January 100% of the Mo-99 produced by Curium is from LEU targets.
- We have already seen the lower yield and higher cost associated with producing LEU Mo-99.
- We appreciate the technical and financial assistance provided by the U.S. Department of Energy during our conversion effort.



CURIUM™
LIFE FORWARD

FOR IMMEDIATE RELEASE January 16, 2018

Curium Is the First North American Manufacturer Offering Exclusively 100% LEU Generators

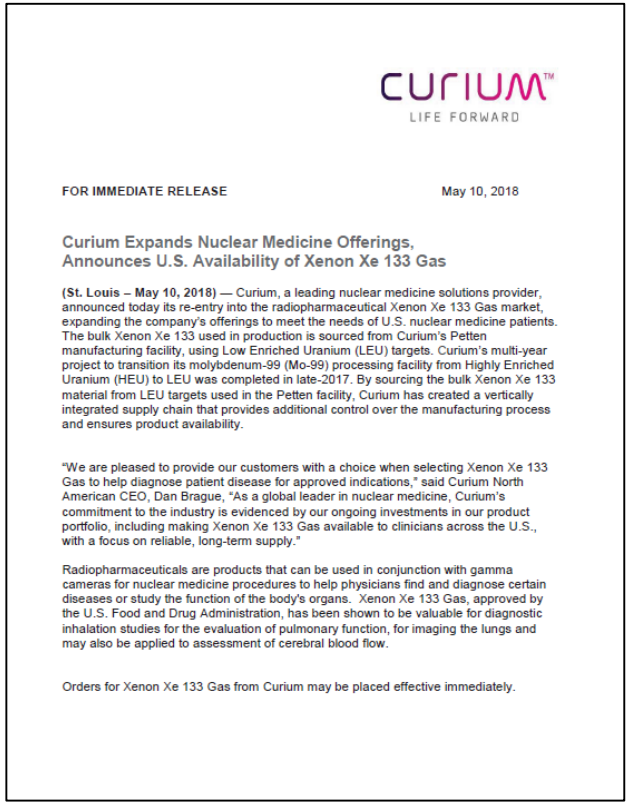
(St. Louis - January 16, 2018) — Curium, a leading nuclear medicine solutions provider, announced today that the company is the first North American manufacturer to meet the deadline established by the American Medical Isotopes Production Act of 2012. This legislation effectively mandates the full conversion away from highly enriched uranium (HEU) as soon as possible and no later than January 2020. Curium's multi-year project to transition its molybdenum-99 (Mo-99) processing facility from HEU to low enriched uranium (LEU) was completed in late-2017. This project makes Curium the only North American Technetium Tc 99m Generator manufacturer able to supply its customers exclusively with 100 percent LEU Tc 99m generators. Mo-99 is the parent isotope of Tc 99m, which is used in 30 to 40 million nuclear medicine procedures worldwide every year[1].

Curium is the world's largest supplier of Tc 99m generators and the largest user of Mo-99 in the world. "This milestone helps satisfy the goals set forth by the Department of Energy's (DOE) National Nuclear Security Administration (NNSA) and confirms our support for the NNSA project to eliminate the use of weapons-grade uranium in the production of medical isotopes. We are eager to see others follow our lead and comply with the government's call for full conversion as soon possible" says Curium North American CEO, Dan Brague.

This project is the culmination of more than seven years of work, requiring close collaboration with Curium's irradiation partners: the Dutch High Flux Reactor, the Polish MARIA reactor, and BR2 in Belgium, as well as, the DOE and NNSA. Roy Brown, Vice President, Government Affairs for Curium North America, states, "Our 100 percent LEU conversion helps Curium generator customers eliminate the inefficiency of balancing the availability of both HEU and LEU generators in their inventory and helps them to control costs better. Something that is especially important when you consider the special reimbursement guidelines surrounding LEU versus HEU patient doses."

CURIUM HAS BEGUN LEU Xe-133 GAS PRODUCTION

- Curium (Mallinckrodt) previously manufactured Xe-133 gas from an HEU process.
- During the Mo-99 HEU conversion project Curium also developed a method for separating LEU produced Xe-133 from our process in Petten.
- Curium has now re-entered the Xe-133 market utilizing LEU produced Xe-133, used for pulmonary function, lung imaging, and cerebral blood flow scans.
- Curium's Xe-133 provides customers with the only 100% Low Enriched Uranium (LEU) offering.



CURIUM™
LIFE FORWARD

FOR IMMEDIATE RELEASE May 10, 2018

Curium Expands Nuclear Medicine Offerings, Announces U.S. Availability of Xenon Xe 133 Gas

(St. Louis – May 10, 2018) — Curium, a leading nuclear medicine solutions provider, announced today its re-entry into the radiopharmaceutical Xenon Xe 133 Gas market, expanding the company's offerings to meet the needs of U.S. nuclear medicine patients. The bulk Xenon Xe 133 used in production is sourced from Curium's Petten manufacturing facility, using Low Enriched Uranium (LEU) targets. Curium's multi-year project to transition its molybdenum-99 (Mo-99) processing facility from Highly Enriched Uranium (HEU) to LEU was completed in late-2017. By sourcing the bulk Xenon Xe 133 material from LEU targets used in the Petten facility, Curium has created a vertically integrated supply chain that provides additional control over the manufacturing process and ensures product availability.

"We are pleased to provide our customers with a choice when selecting Xenon Xe 133 Gas to help diagnose patient disease for approved indications," said Curium North American CEO, Dan Brague, "As a global leader in nuclear medicine, Curium's commitment to the industry is evidenced by our ongoing investments in our product portfolio, including making Xenon Xe 133 Gas available to clinicians across the U.S., with a focus on reliable, long-term supply."

Radiopharmaceuticals are products that can be used in conjunction with gamma cameras for nuclear medicine procedures to help physicians find and diagnose certain diseases or study the function of the body's organs. Xenon Xe 133 Gas, approved by the U.S. Food and Drug Administration, has been shown to be valuable for diagnostic inhalation studies for the evaluation of pulmonary function, for imaging the lungs and may also be applied to assessment of cerebral blood flow.

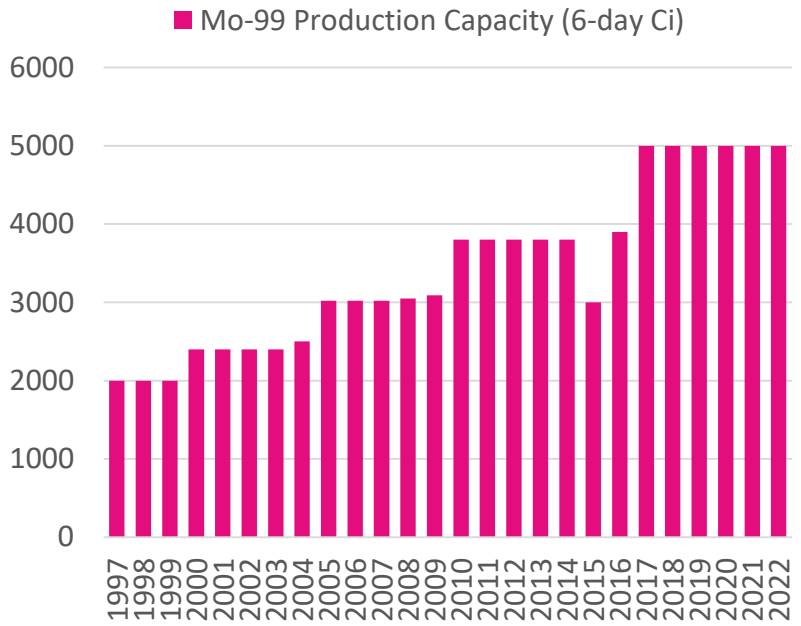
Orders for Xenon Xe 133 Gas from Curium may be placed effective immediately.

CURRENT Mo-99 SUPPLY OUTLOOK

- Curium has increased the number of Mo-99 production runs in Petten from four days per week to five. We have the ability to add a sixth production.
- Those extra production days coupled with the increased Outage Reserve Capacity creates even more reliability for Curium.
- We increased Mo-99 production during the recent NTP operational challenges in S. Africa, enabling Curium to provide additional coverage to patients.

CURIUM Mo-99 SUPPLY METRICS

- Curium Mo-99 production began in the Netherlands in the late 1990s.
- Production capacity has steadily increased since then.
- Additional capacity has been recently added.
- Capacity added to account for loss of the OSIRIS and NRU reactors.
- Capacity has been added to account for loss of efficiency due to LEU conversion.



PRODUCTION OF LEU Mo-99 DURING MARKET TRANSITION

- Production of Mo-99 with LEU versus HEU is less efficient and generates significantly more radioactive waste.
- Another Mo-99 producer reported at the EU Observatory meeting in April they may not be fully converted to LEU until late 2020.
- This higher cost of LEU production of Mo-99 impacts Curium in making Tc-99m generators at its plants in Petten, the Netherlands, Maryland Heights, MO and Saclay, France.
- Curium is now at a competitive disadvantage because we are producing LEU-based Mo-99, while our principle competitor in Mo-99 production continues to produce HEU-based Mo-99 at lower cost.

Mo-99 PRODUCERS WHO HAVE ALREADY CONVERTED TO LEU ARE AT A COMPETITIVE DISADVANTAGE

SUMMARY

- Curium began its LEU conversion project in 2010.
- During that time we have resolved several technical development challenges in the radiochemistry and analytical testing.
- Regulatory approvals from drug agencies and transport authorities were needed for the new LEU targets.
- We have established arrangements with a diverse network of reactors to irradiate targets for our Mo-99 production process.
- Curium has taken steps to steadily increase reliability and capacity of Mo-99 production to account for loss of older reactors and for the loss of efficiency due to LEU conversion.
- LEU conversion for Mo-99 was fully achieved in early January of 2018, and Xe-133 in May of 2018.
- Mo-99 producers who have already converted to LEU are at a competitive disadvantage until all are converted.