

| DOE 2017 MO-99 TOPICAL MEETING

CHALLENGES AND OPPORTUNITIES ON THE PATH TO LEU CONVERSION

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INTRODUCING CURIUM

| INTRODUCTION

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 Molybdenum-99 production facility, three large SPECT manufacturing facilities, and close to 40 SPECT and PET radiopharmacies

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**CHALLENGES FACED
DURING LEU
CONVERSION PROJECT**

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 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 contaminate, 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-231 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

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PROGRESS ON CONVERSION TO LEU

STEADY PROGRESS ON CURIUM'S LEU CONVERSION

- Process development was completed in 2015.
- Cold and hot testing completed in 2016.
- Drug regulatory submissions made in early 2017.
- EU drug regulatory approvals for LEU Mo-99 have been received.
- FDA drug regulatory approval for LEU Mo-99 has been received.
- Health Canada drug regulatory approval for LEU Mo-99 has been received.
- Asia drug regulatory submissions had to wait until we received EU approvals, but have been filed.
- New Marianne container approval for LEU targets has been received.
- Nuclear Validation runs are nearing completion.
- Completion of LEU conversion project still anticipated by the end of 2017.



Curium's Petten Mo-99
Production Operation



Marianne Transport Container

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 is on schedule to be completed by the end of 2017.