CHALLENGES AND OPPORTUNITIES ON THE PATH TO LEU CONVERSION

Roy W. Brown
September 11, 2017
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
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.
PROGRESS ON CONVERSION TO LEU
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 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.