2022 Mo-99 TOPICAL MEETING

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REFLECTIONS ON FIVE YEARS OF LEU-BASED PRODUCTION OF MEDICAL RADIONUCLIDES

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INTRODUCING CURIUM

CURIUM – UNITING IBA MOLECULAR AND MALLINCKRODT NUCLEAR MEDICINE LLC

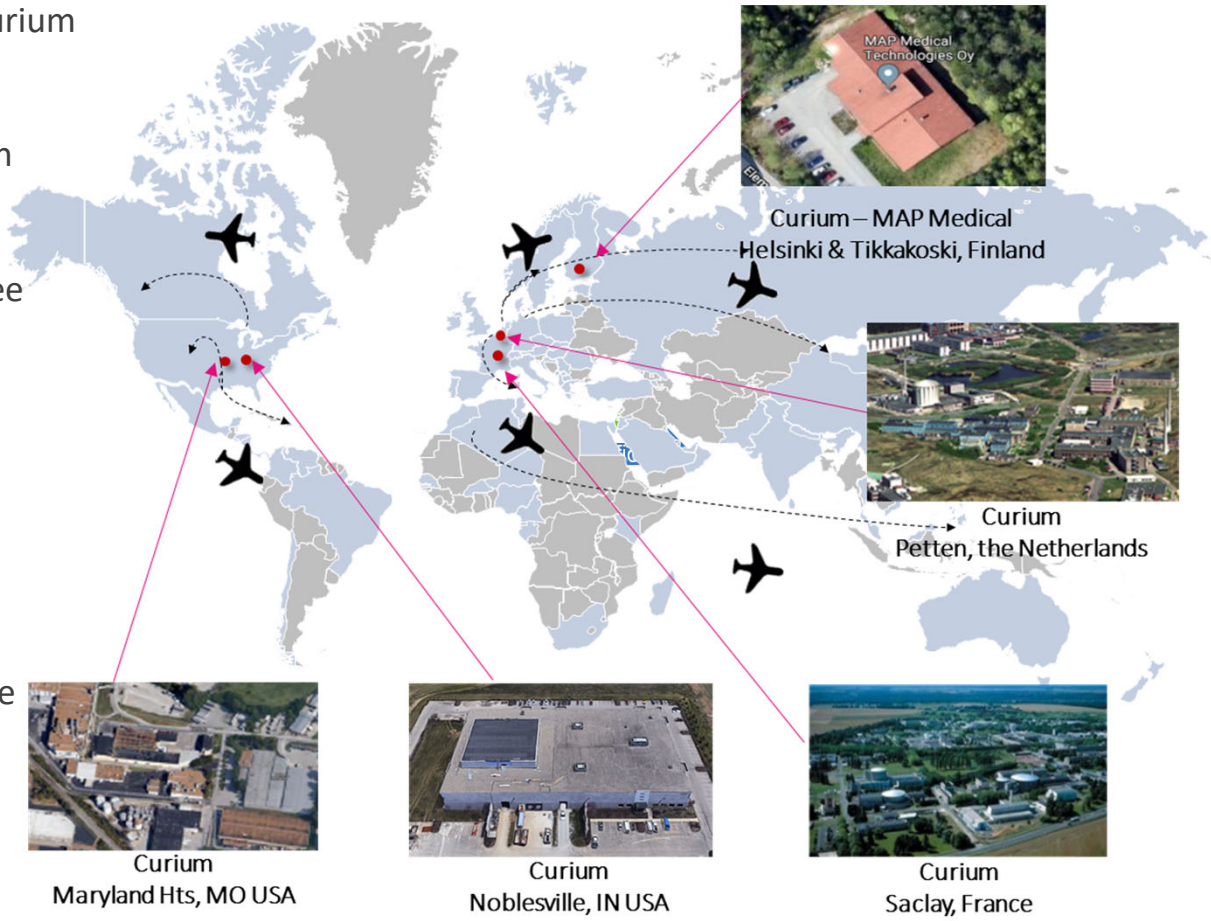
- January 27, 2017 – Mallinckrodt Pharmaceuticals completed the sale of its Global Nuclear Imaging business to IBA Molecular.
- 100 years of combined experience in the nuclear medicine industry.
- Singular focus – to develop, manufacture and supply SPECT, PET and therapeutic radiopharmaceuticals.
- More than 2,500 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 45 SPECT and PET radiopharmacies.

Curium Combined Mallinckrodt Nuclear Medicine and IBA Molecular

> 100 yrs History	▪ Combination of two well-respected names in the industry ▪ 100% focus on Nuclear Medicine
> 50 Sites	▪ Producing more than 30% of Moly needs worldwide ▪ Producing more than 120,000 Tc-99m Generators p.a. (+ cold kits, hot products) ▪ Producing more than 320,000 doses of FDG p.a.
> 50 Products	▪ Broad product portfolio across SPECT (generators, cold kits, hot products) and PET
14 mil patients p.a.	▪ Serving +6,000 hospitals and Centers Of Excellence around the world
> 60 Countries	▪ Main markets are USA, France, Germany, Spain, Italy and Benelux
> 2500 Employees	▪ Engineers, Radiopharmacists, Radiochemists, …

Overview of Curium's Operations

- Molybdenum (Mo-99) facility in Petten makes Curium the only global vertically integrated SPECT manufacturer.
  - Very high reliability for the key isotope used in approximately 85% of all nuclear medicine procedures.
- Leading SPECT manufacturing footprint with three Tc-99m generator facilities, 2 in Europe and 1 in the U.S.
- 10 High Energy Cyclotrons across the network enabling a broad offering of complex medical isotopes.
- Delivering SPECT products to >60 countries worldwide.
- 45 SPECT and PET radiopharmacies across Europe dispensing unit doses.
- 50+ products in portfolio for a wide diversity of medical applications (e.g. cardiovascular, oncology, bone).



Curium's History of Producing Mo-99

- We have operated two Mo-99 production lines in Petten four days a week since the 1990's.
- We continue to produce the majority of our Mo-99 needs utilizing the HFR in the Netherlands, the BR2 in Belgium and Maria reactor in Poland.
- We maintain the ability to purchase Mo-99 from all four of the major global Mo-99 producers as part of our routine supply, and backup if needed.
- We are always looking for new partners to increase reliability or reduce costs.

One of Curium's Mo-99 Production lines in Petten

Curium's Conversion from HEU to LEU Targets

- Curium began its LEU target conversion project in 2010.
- Between 2010-2017 we resolved several technical development challenges in the radiochemistry and analytical testing.
- LEU conversion for Mo-99 was fully achieved in early January of 2018, and Xe-133 in May of 2018.
- We have established arrangements with a diverse network of reactors to irradiate targets for our Mo-99 production process and are working with new reactors to develop that capability.
- Curium has taken steps to steadily increase reliability and capacity of Mo-99 production to meet market demands, including periods of Mo-99 shortages.
- DOE provided valuable financial and technical assistance to help with our conversion efforts.

Mo-99 Processing Diagram

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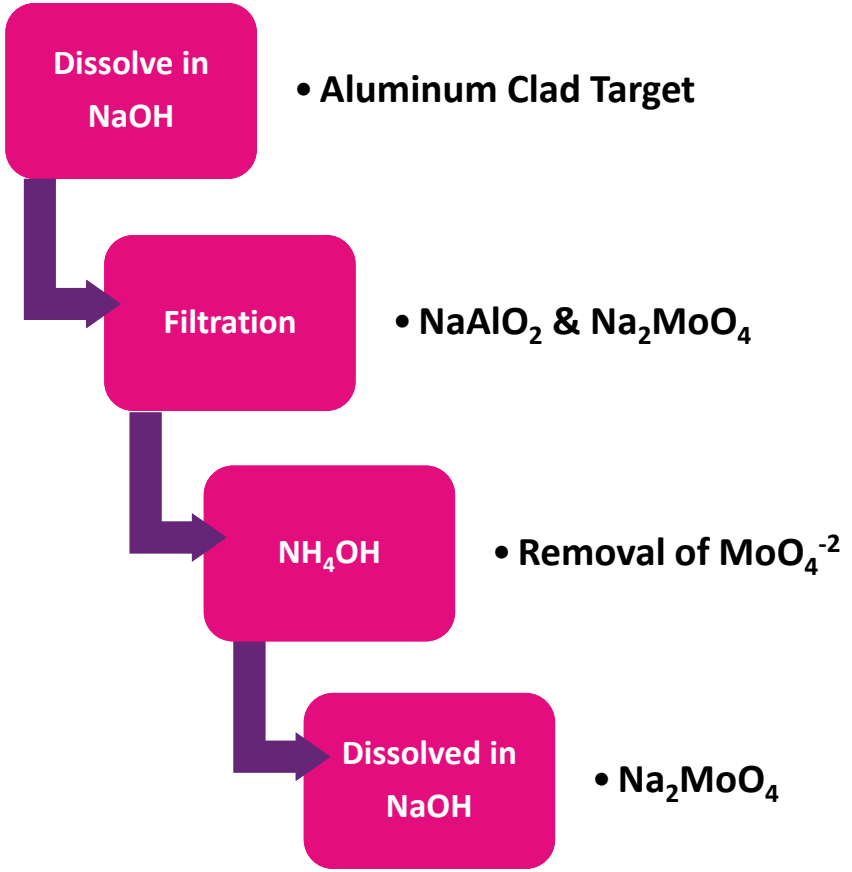
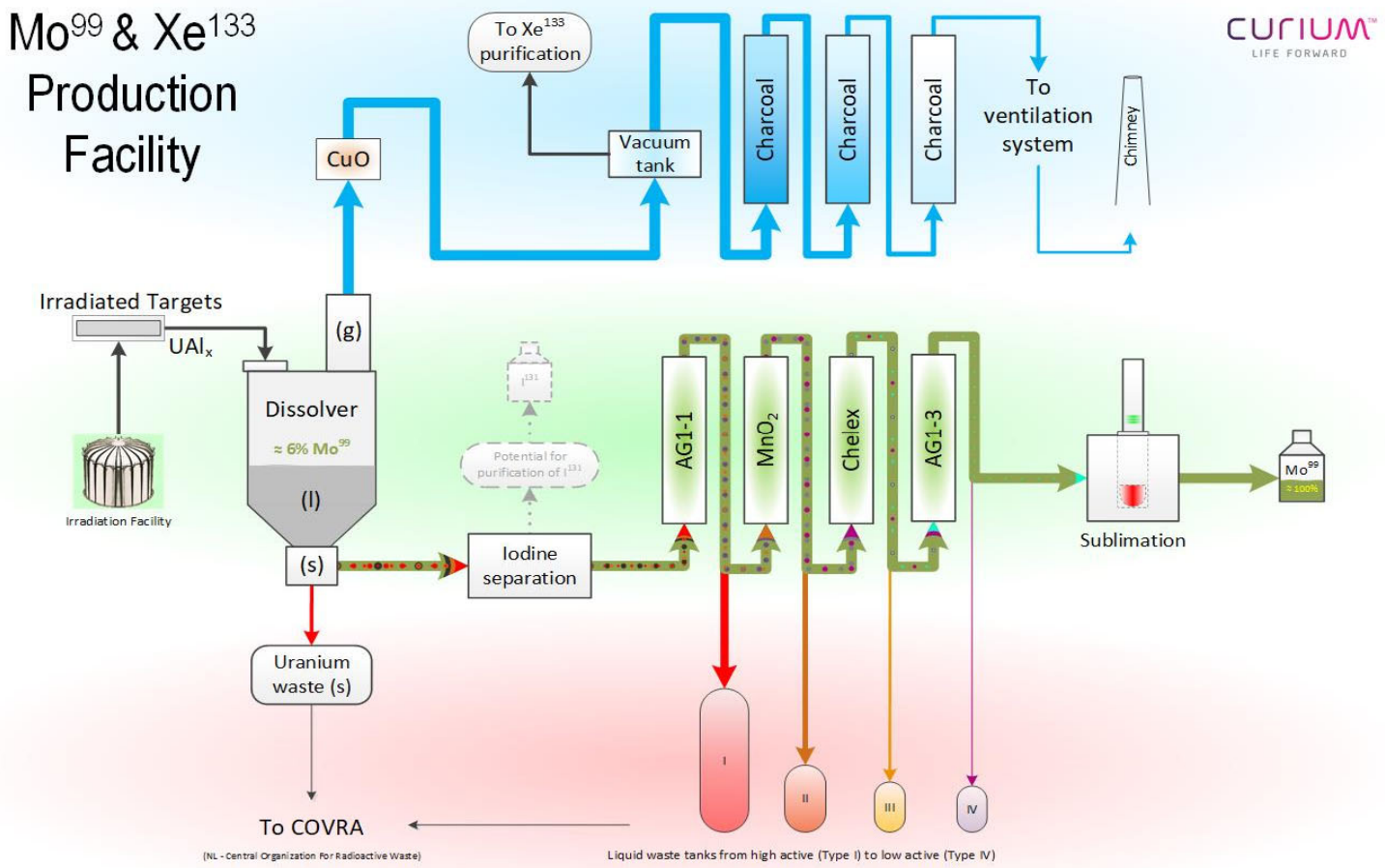
Alkaline Target Dissolution Process:

- Sodium Hydroxide is used to dissolve the entire target
- Solution is filtered to remove suspended solids
- Sorbent filters selectively remove the molybdate ion
- Molybdate washed with Ammonium Hydroxide and dissolved in Sodium Hydroxide



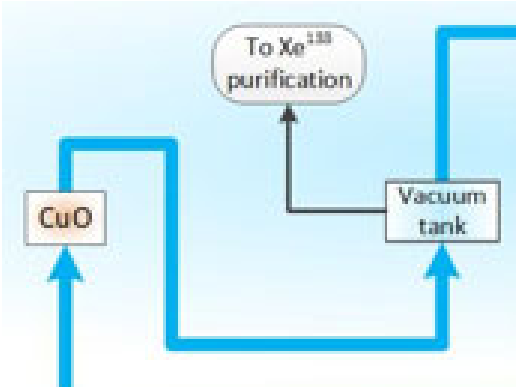
Overview of Curium's Mo-99 Process



Co-Production of Xe-133

- During the fission of U-235 for Mo-99 production, Xe-133 and many other radionuclides are co-produced.
- Although most of these fission radionuclides are discarded as radioactive waste, Xe-133 is recovered for use in nuclear medicine.
- Extensive decay beds are utilized to capture and decay the Xe-133, minimizing the release into the environment.
- This effective capture and release of Xe-133 prevents impact on the environment.
- The Xe-133 for medical use is diverted to a dedicated hotcell for capture and dispensing into coils for transfer.
- This Xe-133 is shipped to the U.S. where it is packaged into unit dose vials for use by nuclear medicine physicians.

Overview of Curium's Xe-133 Process



- The Xe-133 for production is redirected from the Copper Oxide oven to a processing glovebox.

- There it prepared as an Active Pharmaceutical Ingredient (API).

- The Xe-133 is shipped to the U.S. for use in the FDA approved product.

Xe-133 Ventilation Studies in Nuclear Medicine

- Xe-133 ventilation study allows for dynamic imaging over time
  - Anterior and posterior images obtained most frequently
- Three phases of imaging:
  1. Breathing in Xe-133 and air through a closed system
  2. While Xe-133 equilibrates (wash-in)
  3. During Xe-133 exhalation (wash-out)
- Both wash-in and wash-out phases can identify ventilatory deficiencies

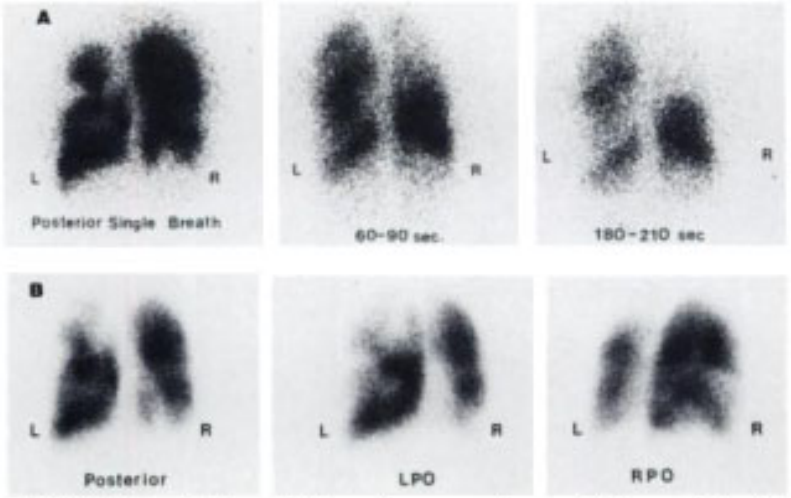


FIGURE 1. A 23-yr-old female nonsmoker on birth control pills, was referred for ventilation and perfusion scans because of sudden onset of shortness of breath. The chest x-ray showed no infiltrates. The washout images (A) reveal significant retention involving more than 50% of the lung fields. The washin ^{133}Xe image (A) shows defects matching the perfusion abnormalities seen on the posterior view (B). Pulmonary angiogram was negative for pulmonary emboli.

Elgazzar AH, et al. J Nucl Med. 1995;36:64-67

Critical Supply of HA LEU for Medical Isotope Production

- The entire industry should be converted to the use of LEU for medical isotope production by the end of this year.
- As such, the industry has become reliant on a reliable supply of High Assay LEU (HA LEU) now that we are converted.
- HA LEU is defined as U-235 enriched to a level of greater than 5% and less than 20%.
- DOE is currently providing our industry HA LEU by downblending stocks of HEU.
- The global industry is looking toward the DOE to provide us needed HA LEU after the current supply is depleted.
- The research reactors we use to irradiate targets also need HA LEU for reactor fuel.
- DOE plans to set up a consortium of interested parties for HA LEU.
- It is critical the Mo-99 producers have a seat at that table so our HA LEU needs for targets and reactor fuel can be taken into consideration.

HA LEU Supply is Also Important for Emerging Medical Radionuclides

- The nuclear medicine industry also relies on the research reactors for several new therapeutic radionuclides.
- These therapeutic radionuclides are driving the development and use of new radiopharmaceuticals for the treatment of cancer.
- Lu-177 is currently being produced is several research reactors fueled by HA LEU and is being used for the treatment of neuroendocrine tumors.
- Lu-177 is also expected to be used in drugs for the treatment of prostate cancer in the very near future.
- Tb-161, a powerful beta emitter, is also being examined for use in therapeutic radiopharmaceuticals and is produced in research reactors.

Summary

- The nuclear medicine industry made the important conversion from the use of HEU to HA LEU for medical radionuclide production in order to reduce proliferation risks.
- Mo-99, I-131 and Xe-133 still play an important in nuclear medicine and they must have a reliable supply of HA LEU for targets.
- Production of these radionuclides and new therapeutic medical radionuclides also rely on research reactors and a reliable supply of HA LEU for fuel.
- Our industry must be assured of a long term supply of HA LEU and our needs must be included in any long term projections for HA LEU by DOE.