



50 years of dedication to Nuclear Medicine

The Path to Conversion of Low Enriched Uranium (LEU) for the Production of Mo-99

2016 Mo-99 Topical Meeting
September 13, 2016
St. Louis, Missouri

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Senior Director, Strategic Alliances



Background on Mallinckrodt and our Nuclear Medicine Business

Looking Back ... Looking Forward



1867
Established G. Mallinckrodt and Company

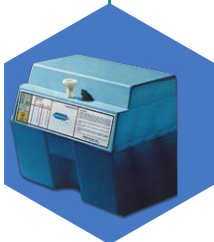
1913
Introduces barium sulfate



1966
Acquired Nuclear Medicine Consultants, entering the radiopharmaceutical business



1973
U.S. Food & Drug Administration (FDA) approves vital isotope delivery system



1977
Major Expansion at Maryland Heights, Missouri, radiopharmaceutical plant completed



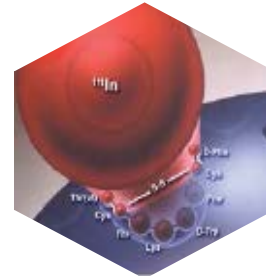
1979
Acquired cyclotron and isotope labs at Petten, facility for production of radiopharmaceuticals



1990
Introduced proprietary renal imaging agent



1991
Introduced the only FDA-approved in vitro red blood cell Tc 99m labeling agent



1994
First targeted nuclear medicine molecular imaging agent launched



2008
Enhanced nuclear products offerings with the launch of a generic cardiac imaging agent



2013
Introduced key component in PET calibration sources and vital to the future of molecular imaging



2016 & Beyond:
Mallinckrodt announces planned sale of nuclear medicine business to IBA Molecular

Mallinckrodt Enters Into Agreement to sell Nuclear Medicine Business to IBAM



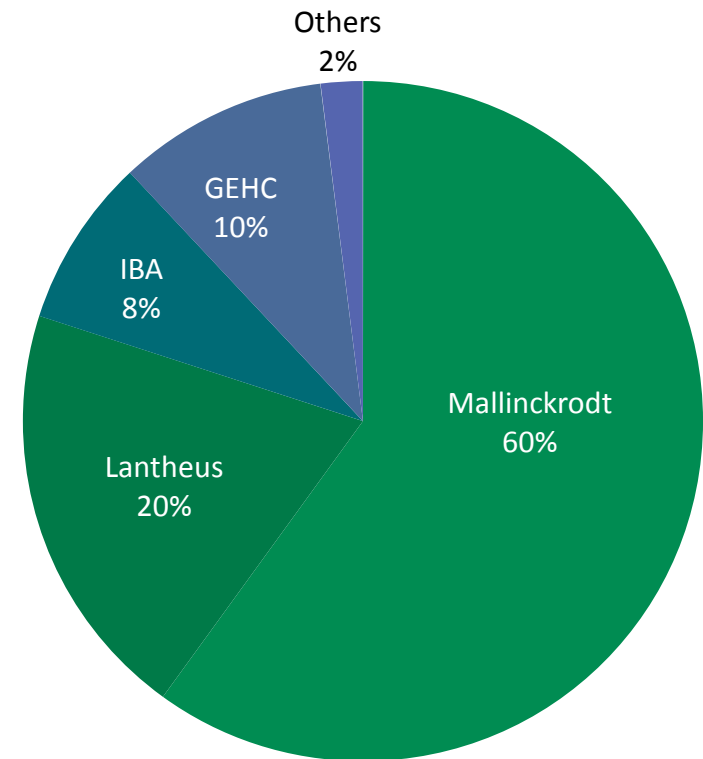
- ▶ On Aug 24, 2016 Mallinckrodt announced an agreement to sell its global nuclear medicine business to IBA Molecular (IBAM).
- ▶ The sale is subject to a number of closing conditions, including approval from the U.S. Nuclear Regulatory Commission and the U.S. Committee on Foreign Investment.
- ▶ The sale include transfer of Mallinckrodt's radiopharmaceutical plants in Maryland Heights, Missouri and Petten, Netherlands.
- ▶ The transfer of the business to IBAM is expected to close in the first half of 2017.

Mallinckrodt Plays a Key Role in Mo-99 Supply



- ▶ Mallinckrodt is the largest global Tc-99m generator manufacturer, and largest user of Mo-99.
- ▶ Mallinckrodt has provided bulk Mo-99 to key strategic markets.
- ▶ In this role, we monitor the global Mo-99 supply chain very closely.
- ▶ Last year Mallinckrodt had 75% of the U.S. Tc-99m generator market and 60% of the global market.
- ▶ We produce more than 80% of the Mo-99 used in the production of Mallinckrodt Tc-99m generators.

Global Tc-99m Generator Market – 2015*



*Source: LMI, Internal Estimates



Mallinckrodt's Production of Mo-99 in the Netherlands

Petten Site in The Netherlands



Four organizations on the premises:

- **ECN** – Energy research Center Netherlands
- **NRG** – Nuclear research and Consultancy Group
- **JRC** – Joint Research Center (European Committee)
- **Mallinckrodt Medical B.V.** – Nuclear Medicine manufacturing and distribution



Mallinckrodt Has a Long History of Producing Mo-99

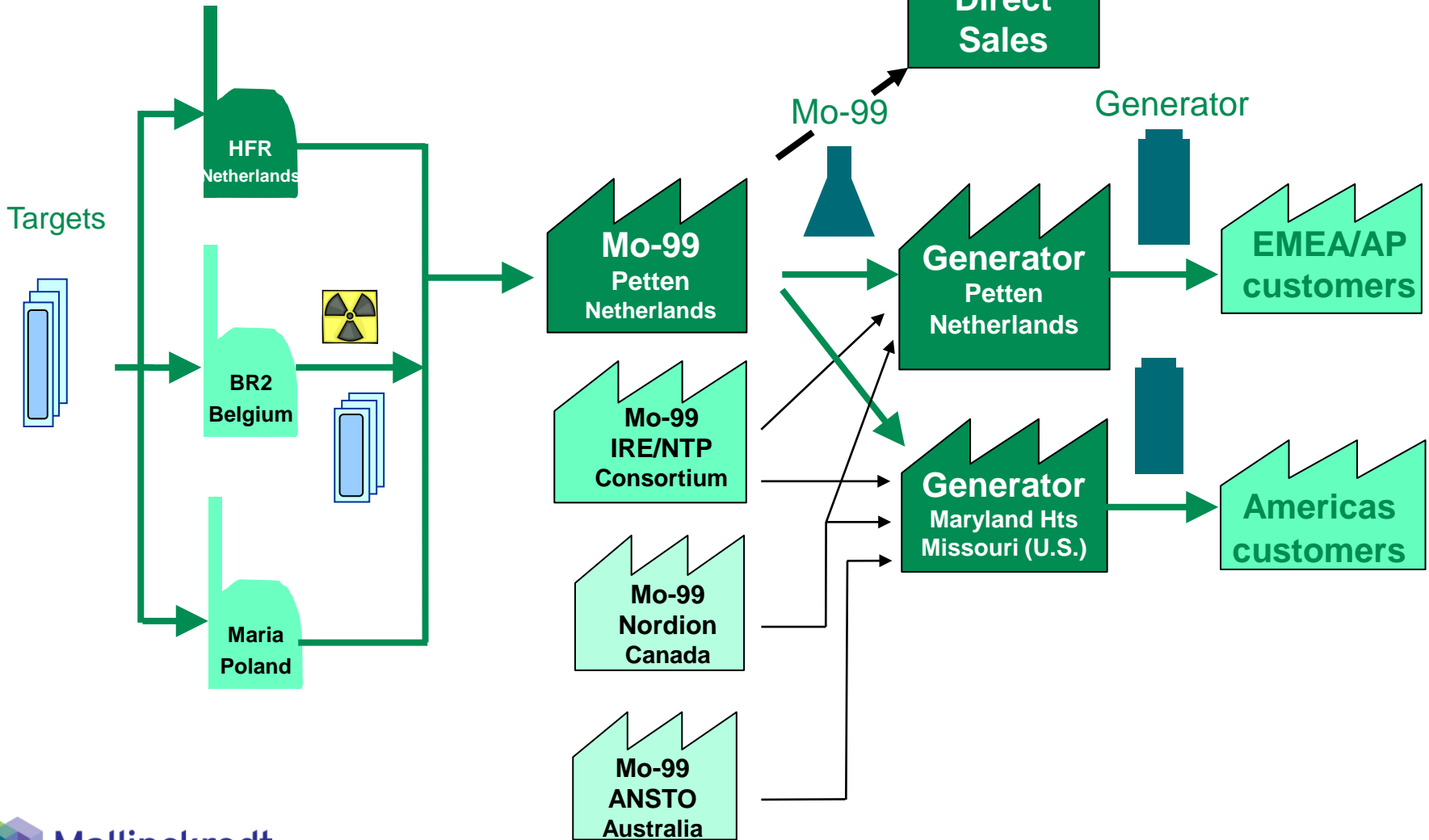


- ▶ We have operated two Mo-99 production lines in Petten four days a week since the 1990s.
- ▶ We continue to produce the majority of our Mo-99 needs utilizing the High Flux, BR2 and Maria reactors.
- ▶ We maintain the ability to purchase Mo-99 from the other four major global Mo-99 producers as part of our routine supply, and backup if needed.



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

Mallinckrodt Has Diversified Mo-99 Supply Chain





Mallinckrodt's Conversion to LEU Production of Mo-99 in the Netherlands

Mallinckrodt LEU Conversion Update



- ▶ We remain committed to the conversion from HEU to LEU.
- ▶ Conversion to LEU will further non-proliferation goals and stabilize long-term supply of uranium for medical isotope production.
- ▶ Cold testing, R&D runs, and yield testing runs have already been completed.
- ▶ Process validation runs are in progress:
 - ▶ HFR began recently.
 - ▶ Maria and BR2 runs will commence later this month.
 - ▶ If needed, nuclear validation runs will be done in 2017.
 - ▶ Regulatory submissions are planned in early to mid 2017.
- ▶ Project completion is still anticipated by the end of 2017.



Support from National Nuclear Security Administration (NNSA) on Conversion Project

DOE NNSA Has Provided Financial and Technical Support on Conversion Project



- ▶ Mallinckrodt entered into a cost sharing agreement with DOE to assist with some of the conversion costs.
- ▶ This arrangement, administered by Pacific Northwest National Lab (PNNL), has helped to pay for some of the components of the costly conversion.
- ▶ PNNL has also provided technical assistance on methods development for Pu-239 measurements.
- ▶ DOE NNSA has also provided key assistance on several foreign governmental engagement challenges which have arisen during the conversion project.
- ▶ All of this DOE assistance has helped Mallinckrodt stay on schedule for a final conversion to LEU by December 31, 2017.



The Mallinckrodt Mo-99 Supply Outlook

Mo-99 Supply Outlook Remains Positive



- ▶ Mallinckrodt continues to increase its Mo-99 capacity
 - ▶ Successfully modified Maria target irradiation rigs and transport containers, increasing irradiation capacity substantially.
 - ▶ We are increasing the number of targets processed per Mo-99 production run as that capacity is needed.
 - ▶ Adding fifth weekly Mo-99 production run in advance of LEU conversion.

- ▶ NRCan¹ announced guidelines for the NRU “trigger mechanism²,” e.g., availability as backup supply post-2016 shutdown, based on:
 - ▶ Degree of global shortage
 - ▶ Availability of current producers, alternative technologies, other supply sources to compensate
 - ▶ Mitigation strategies

1. Natural Resources Canada

2. Presented at the Feb 17 2016 OECD High-Level Working Group Meeting

Work with EMA/CMDh is Yielding Results



- ▶ The European Medicines Agency (EMA) CMDh¹ has engaged on two topics of relevance to LEU conversion:
 - ▶ Active substance master files (ASMFs)²
 - ▶ Agreement reached that well-defined chemical precursors for radiopharmaceutical (RP) preparation are eligible for ASMF procedure
 - ▶ Analogous interpretation to approach for RP cold kits
 - ▶ AIPES members' LEU-variation applications have remained unapproved within EMA approval process, some for 2 years³
 - ▶ CMDh requested to aid in expediting approval process for these applications and national variation applications under which they are pending
 - ▶ Initial actions being taken by CMDh

1. Co-ordination Group for Mutual Recognition and Decentralized Procedures-Human
2. Referenced in letter to AIPES, Feb. 2016
3. Discussed at Mar. 2016 CMDh meeting

Summary



- ▶ Mallinckrodt's LEU conversion project remains on schedule.
- ▶ We have achieved major milestones with the completion of all cold runs, R&D runs and yield test runs.
- ▶ Cooperation with EMA/CMDh should aid LEU-related dossier approvals across Europe.
- ▶ LEU conversion completion expected by the end of 2017.
- ▶ Current Mo-99 supply outlook appears positive given currently available projections and supply chain contributors' status.