For NMEU members only

Second International OECD Workshop on Medical Radioisotopes Supply Paris, 24-25 oct. 2024

Abstract

What was the objective ?

Co-organized by the **OECD-NEA**, US Department of Energy (**US-DOE**) and the European Commission's Joint Research Centre (**JRC**), the second edition workshop gathers physicians, governmental decision makers, private sector representatives, health organizations and researchers to chart the development of secure supply chains for conventional and innovative nuclear radioisotopes in the medical field.

The 2024 Workshop in Paris focused on the **Radioligand Therapy (RLT)** and the market potential of Lu-177, Ac-225, At-211 and other innovative medical radioisotopes (RI), strengthening the medical RI supply chain's resiliency.

All workshop presentations will be issued later on the OECD-NEA website.

The two-days meeting includes 8 sessions (see the program hereafter):

Session 1: Lu-177 and Ac-225 – RLT role in cancer treatment, demand scenarios and key enabling conditions

Session 2: Lu-177: Supply projections and enabling conditions

Session 3: Ac-225 and other innovative radioisotopes – Stage of development and emerging supply scenarios

Session 4: Lu-177 and Ac-225: The economic challenges related to their sufficient, responsible and fair production and supply

Session 5: National and regional program updates – Medical radioisotopes production

Session 6: Updates on innovative new builds and technologies for medical radionuclide research and production

Session 7: Monitoring supply and demand of medical radioisotopes

Session 8: Regulation of Lu-177 and Ac-225

The workshop offers a **very comprehensive scope of RLT** regarding clinical potential, best routes of production and regulatory challenges.

The workshop **attendance** was **much larger** than the previous ones showing high expectations for RLT.

Workshop main lessons:

- The potential and future of RLT for cancer therapy was clearly and positively presented by the physicians as a breakthrough for some cancers.

- The good news is that many options and methods for the RLT supply of beta radioisotopes show several reliable commercial solutions for future demand, including for stable isotopes as Ytterbium for non-carrier added Lu-177.
- Regarding RLT with alpha radionuclides as AC-225, At-211 or Pb-212, many teams show their R&D works showing a strong commitment for reliable supply solutions with different routes.

- A new opportunity has been introduced using commercial power reactor role for the irradiation of isotopes, in particular with Candu reactors for Lu-177. They could be a game changer in the competition with research reactors and accelerators that have been presented in the past OECD workshops.

- Regarding the regulatory definition of radioisotopes and radiopharmaceuticals, an important work has to be done to explain, to the authorities, the RLT specificities in comparison with conventional drugs.

- Regarding FCR (full cost recovery), a working group should be launched early 2025 for all radionuclides supply including Mo/Tc.

- In the presence of AIEA experts, the change of classification of type A packages with alpha emitters for AIEA transport regulations has been raised as a major concern as it involves the RLT drugs.

- Key hurdles or bottlenecks have not been addressed during the OECD workshop as the personnel shortage, the alpha RI waste management, the radioprotection for the medical staff, the need of dedicated patient rooms. All those aspects are key for patient equal opportunity in their path care.

NMEU action to consider and assess after the OECD workshop :

Regarding the novelty and complexity of RLT, a **NMEU initiative** to foster its diffusion among all stakeholders is currently under consideration. Following the OECD workshop, the following items should, at least, be included in the initiative:

- A comprehensive demonstration of the RLT potential for cancer treatment towards healthcare societies, the government decisions makers, the patient associations.
- Raising awareness and understanding of nuclear medicine's benefits with healthcare professionals, patients and the general public.

- Address the RLT-specific bottlenecks and hurdles for implementation. It starts from the manufacturer logistics, up to the hospital coordination between oncology, nuclear medicine and radiology departments, up to a dedicated workforce, up to the drug pricing/reimbursement and finally up to the hospital facilities.

- Support for innovation and technical development across the EU, through training and certification of healthcare professionals and equipment so all EU citizens can access the full benefits of nuclear medicine with equal opportunity.

- Adapt the regulations to the specificities of radiopharmaceuticals for marketing authorizations, product registration, preparation, transport/ delivery and radioprotection. As an example, the proposal of the new AIEA transport regulations could consider a new category of radioactive package, between type A and B, adapted for the RLT drug nuclear safety.

- Secure and reliable supply for current and future radioisotopes for both therapy and diagnosis, grounded in resilient European infrastructures.

- Involve the patient organizations for the quality of life of RLT treatment, when relevant, in comparison with other care modalities.

- Regarding the cost of RLT drugs, a Health technology assessment (HTA) of RLT drugs should include a comprehensive calculation of the global cancer treatment including, for example, the hospital costs in comparison with other care modalities.

Overview

Welcome to the Second International Workshop on Medical Radioisotopes Supply co-organised by the Nuclear Energy Agency (NEA), United States Department of Energy (DOE) and the European Commission's Joint Research Centre (JRC) at the OECD Conference Centre in Paris on 24-25 October 2024. The event gathers governmental decision-makers, private sector representatives, health organisations and researchers to chart the development of secure supply chains for conventional and innovative nuclear radioisotopes in the medical field. The event builds on the success of the first workshop on medical radioisotopes supply organised by the NEA and on related events organised by the European Commission during 2023, which brought together a large number of expert attendees and online participants for engaged discussions.

Legacy of work on medical radioisotopes supply

Since 2009, the global community has been working diligently to ensure a reliable supply of medical radioisotopes, particularly Molybdenum-99 (Mo-99) and its decay product, Technetium-99m (Tc-99m) and this period, marked by significant shortages, led to the establishment of the High-Level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) at the NEA. Comprising experts from 18 countries, including non-NEA member countries, the Euratom Supply Agency (ESA) and the International Atomic Energy Agency (IAEA), the High-Level Group proved pivotal in informing policy decisions to stabilise supplies. However, challenges with Mo-99 shortages have since resurfaced. Additional organisations such as the European Observatory on the Supply of Medical Radioisotopes and Nuclear Medicine Europe (NMEU) have also proved pivotal to mitigating risk to the security of supply.

Workshop programme

The field of nuclear medicine continues to evolve rapidly, leading to significant shifts in the medical radioisotopes supply chain. Last year's events highlighted ongoing concerns about periodic supply disruptions and a growing optimism about the potential of a new generation of medical radioisotopes. However, the ageing of many production facilities and unexpected closures continue to pose challenges. The increasing use of innovative radioisotopes such as Lutetium-177 (Lu-177) and Actinium (Ac-225) further underscores the need for collaboration to build and maintain sustainable, and stable supply chains to ensure the availability, safety, and affordability of these life-saving applications.

Responding to a consensus among stakeholders, the 2024 event in Paris adds a focus on the market potential of Lu-177, Ac-225 and other innovative medical radioisotopes, strengthening the medical radioisotope supply chain's resiliency through monitoring supply and demand and critical infrastructure needs across medical systems.

Programme – 24 October (Day 1)

Room CC10

Arrival and check-in – 08:00-09:00 a.m.

Opening session

9:00 (25min)

Workshop opening

- Nick Sherman, Deputy Head of Division, Division of Nuclear Technology and Economics, NEA

Welcome remarks

- William D. Magwood, IV, Director-General, NEA
- Bernard Magenhann, Acting Director-General, European Commission Joint Research Centre (JRC)
- Ethan R. Balkin, Federal Program Manager for Radioisotope Production R&D, US Department of Energy, Office of Isotope R&D and Production

Global perspective

- Enobot Agboraw, Executive Secretary, African Commission on Nuclear Energy (AFCONE)

Session 1: Lu-177 and Ac-225 – Demand scenarios and key enabling conditions

9:25 (65 min)

Cancer is a leading cause of death worldwide and the leading cause in OECD member countries, accounting for nearly 10 million fatalities in 2020, with one in five people at risk of developing cancer in their lifetime. By 2040, these numbers are expected to reach 27.5 million new cancer cases and 16.3 million cancer deaths, solely due to the growth and ageing of the population. Current treatments such as surgery, chemotherapy, and immunotherapy continue to make significant progress in curing patients and extending lives. Today, the advent of novel radioisotopes and radioligand therapy (RLT) technologies promise to further revolutionise cancer diagnostics and therapeutics. Healthcare systems will need to adapt to significant gaps in specific infrastructure requirements for RLT technologies and workforce, regulatory, and healthcare system requirements. This session is dedicated to sharing the current and potential future medical applications of Lu-177, Ac-225 and other innovative radioisotopes to investigate present demand and enabling conditions for high-demand growth scenarios.

Chair: Paola A. Erba, President, EANM

Overview and focus points by the session chair

Current medical applications of Lu-177 and Ac-225 and their roles in cancer treatment

- Munir Ghesani, Associate Professor of Radiology, Mount Sinai Health System, Chief Medical Officer, United Theranostics
- Alfred Morgenstern, Senior Researcher, European Commission Joint Research Centre (JRC), Karlsruhe

Ongoing clinical developments of Lu-177 & Ac-225-based Pharmaceuticals and potential implications in clinical practice & Healthcare Systems

- Leonhard Schaetz, Global Head RLT HCS and Partnerships, Novartis

R&D on future Lu-177 and Ac-225-based pharmaceuticals, and their potential

- Mike Sathekge, Professor and Head of Nuclear Medicine Department, University of Pretoria, Steve Biko Academic Hospital, President and CEO, Nuclear Medicine Research Infrastructure.

Questions and answers

10:30 (10 min) Sponsor showcase – Novartis

10:40 (15 min) Coffee break and group photograph

Session 2: Lu-177: Supply projections and enabling conditions

10:55 (60 min)

Most Lu-177 is produced in a limited number of ageing multipurpose research reactors. However, innovative players in the field are exploring alternative neutron sources to reduce reliance on these traditional facilities. Key Lu-177 producers have significantly expanded their processing capacities in response to growing demand. This session will delve into various demand scenarios for Lu-177 production, addressing the critical challenges that impede its widespread medical application. Key topics will include potential supply chain chokepoints and capacity shortfalls in areas such as enrichment, irradiation, and processing.

Chair: Ira Goldman, Vice President, Global Public Policy and Government Relations, Lantheus

Overview and focus points by the session chair

Current situation and challenges of supply of Lu-177

- Roy W. Brown, Vice President, Government Affairs & Strategic Alliances, Curium
- Andrew Thiele, Executive Director, Canadian Nuclear Isotope Council
- Mark Harfensteller, COO, Isotope Technologies Munich SE, ITM.
- Harrie Buurlage, Managing Director SHINE Europe B.V. & VP of Strategic Alliances, SHINE

Questions and answers

11:55 (60 min)

Lunch break

Session 3: Ac-225 and other innovative radioisotopes – Stage of development and emerging supply scenarios

12:55 *(105 min)*

As Ac-225 and other innovative radioisotopes garner attention during medical trials with promising applications in targeted alpha therapy, understanding the outlook for production and utilisation will become increasingly critical. The current supply of Ac-225 is limited, relying heavily on a few specialised facilities. Key players are ramping up their production capabilities to meet the growing demand and exploring innovative methods to enhance availability. This session will explore the latest advancements in Ac-225 production, potential supply chain bottlenecks, and the strategies employed to ensure a steady supply for clinical trials and therapeutic use, including efforts to increase the availability of treatment rooms. Participants will place particular focus on the role of α-emitters such as Ac-225 and At-211 with an eye towards lessons learnt in resolving challenges related to transport and regulation.

Chair: Rachel Eloirdi, Head of Unit, European Commission Joint Research Centre (JRC), Karlsruhe

Overview and focus points by the session chair

Advancements in Ac-225 production and challenges

- Hamid Abderrahim, General Manager, Multi-purpose hYbrid Research Reactor for High-tech Applications, MYRRHA
- James T. Harvey, Senior Vice President & Chief Science Officer, Northstar
- Sven Van den Berghe, CEO of Pantera
- Frank Bruchertseifer, Senior Scientist, European Commission Joint Research Centre (JRC), Karlsruhe
- Norasalwa Zakaria, Section Head, Waste Technology Section, IAEA
- * Tatsuya Higashi, Division Head, Senior Principal Researcher, National Institutes for Quantum Science and Technology of Japan

** Remote participation*

Future of innovative medical radioisotopes

- Jean-Francois Gestin, Director of Research, INSERM
- Sunao Fujioka, CEO of Alpha Fusion

Questions and answers

14:40 (10 min) Sponsor showcase – Curium

14:50 (15 min) Coffee break

Session 4: Lu-177 and Ac-225: The economic challenges related to their sufficient, responsible and fair production and supply

15:05
(95 min)

Understanding the underlying economics of potential markets for the next generation of medical radioisotopes will help to avoid the challenges faced at times by Mo-99/Tc-99m and Iodine 131 (I-131) producers today. Comprehensive approaches, including healthcare system case studies, full cost recovery (FCR) models, and outage risk capacity (ORC) estimations at the onset of production, will provide investors with a financial return and ensure resilient supply chains to the risk of disruptions. This session will delve into appropriate investment levels in essential facilities and survey financing mechanisms that bolster the next generation of radioisotopes' production, availability, and affordability. Participants will share lessons learnt and best practices from various jurisdictions, exploring opportunities to enhance production and supply chain security co-operation, including planned mechanisms for FCR and ORC and competing reactor utilisation (e.g. Mo-99/Tc-99m, I-131 production). Differences between Lu-177 and Ac-225 in terms of FCR and ORC mechanisms will be investigated. Practical needs in terms of ensuring responsible supply and fair access across different countries other than pure market cases will be addressed and discussed.

Chair: Nick Sherman, Deputy Head of Division, Division of Nuclear Technology and Economics, NEA

Overview and focus points by the session chair and progress of FCR discussion, application for Lu-177, estimate of ORC cost needs and differences of Lu-177 and Ac-225 in terms of FCR and ORC

Case study of cost recovery and health care system

- Ethan R. Balkin, Federal Program Manager for Radioisotope Production R&D, Office of Isotope R&D and Production, US Department of Energy
- Joanie Dix, Office Director, National Nuclear Security Administration (NNSA)
- Eric Schutt, Chief of Staff, Vice President Government Affairs, Mo-99 Project Director, SHINE
- Marieke van Dok, Programme Director for Medical Isotopes, Dutch Ministry for Health, Welfare and Sport and Ronald Schram, Director of Strategic Alliances, NRG PALLAS

Questions and answers

Discussion of cost recovery and health care system for Lu-177 and Ac-225 (All workshop participants)

Discussion of competing reactor utilisations for the production of Lu-177 and other purposes, including producing other medical radioisotopes (e.g. Mo-99/Tc-99m, I-131) (All workshop participants)

Closing remarks	
16:40 *(15 min)*	• Nick Sherman, Deputy Head of Division, Division of Nuclear Technology and Economics, NEA • Ulla Engelmann, Director for Nuclear Safety and Security, European Commission, JRC • Ethan R. Balkin, Federal Program Manager for Radioisotope Production R&D, DOE
18:00 (90 min)	Cocktail reception Roger Ockrent Room, Château de la Muette

Programme – 25 October (Day 2)

Room CC10

Arrival and check-in – 08:00-09:00 a.m.

Session 5: National and regional programme updates – Medical radioisotopes production

9:00 (105 min)

OECD and NEA countries are actively updating their national programmes to support robust and healthy supply chains for medical radioisotope production, which are crucial for diagnostics and therapy. This session provides an opportunity for countries to update the medical radioisotope community on efforts to enhance the resiliency of supply chains for both the production of Mo-99 as a cornerstone in medical imaging as well as the development of next-generation therapeutic radioisotopes. Such efforts are designed to meet the increasing demand from the healthcare sector, ensure patient access to essential diagnostic and treatment options, and drive medical innovation.

Chair: Nick Sherman, Deputy Head of Division, Division of Nuclear Technology Development and Economics, NEA

Progress of medical radioisotopes production and R&D activities

- Ethan R. Balkin, Federal Program Manager for Radioisotope Production R&D, US Department of Energy Office of Isotope R&D and Production, United States
- Georgi Simeonov, Policy Officer, Directorate for Energy (DG ENER), European Commission
- Alberto Fernandez Fernandez, Director/Nuclear Applications, Belgian Ministry of Economy and Energy (Belgium)
- Ronald Schram, Director Strategic Alliances, NRG PALLAS (The Netherlands)
- Renata Mikołajczak, Director's Plenipotentiary for Research and Cooperation at the Radioisotope Centre, National Centre for Nuclear Research, POLATOM, Poland
- Thabo Tselane, Group Managing Director, NTP Radioisotopes SOC Ltd (South Africa)
- Jun Hatazawa, Special Advisor, Japan Atomic Energy Commission (Japan)
- Daniel Cestau, Radioisotopes Production Manager, National Commission of Atomic Energy (Argentina)

Questions and answers

10:45 (15 min) Coffee break

Session 6: Updates on innovative new builds and technologies for medical radionuclide research and production

11:00 (85 min)

Currently, most Lu-177 production depends on a relatively limited number of multipurpose research reactors – many of which are over 60 years old, much like with the production of Mo-99. Although upgrades, improvements and optimisations have been made for them to enhance their production capacities for pharmaceutical use, new production facilities are required to ensure the security of supply to meet not only growing Lu-177 demand but also the needs of conventional medical radioisotopes such as Mo-99 and I-131. This session will survey the ongoing progress in developing new production facilities and technologies for both conventional and innovative medical radioisotopes, including ongoing challenges faced by the public and private sectors regarding full cost recovery and return on investment.

Chair: Bernard Ponsard, SCK CEN, EU Observatory on the Supply of Medical Radionuclides (Belgium)

Overview and focus points by the session chair

Plans for new radioisotope production reactors

- Florian Jeschke, Deputy Technical Director, Technical University of Munich, FRM II (Germany)
- Marion Libessart, Business Development Manager, Jules Horowitz Reactor Project Client and Consortium Directorate, Alternative Energies and Atomic Energy Commission, CEA (France)
- Chad MacLean, Senior Director, Business Development & Energy Innovation, Bruce Power (Canada)
- Curtis Van Cleve, President and CEO, Framatome Canada, and Yousef Yacoob, Director of Medical Isotope Production & Projects at Kinectrics (Canada)
- Bertrand Morel, R&D Director, Orano (France)
- Naoyuki Takaki, Professor, Tokyo City University (Japan)

Questions and answers

12:25 (60 min)

Lunch break

Session 7: Monitoring supply and demand of medical radioisotopes

13:25 (70 min)

Considerable efforts have been made to maintain a stable supply of Mo-99/Tc-99m through monitoring, forecasting, and co-ordinating supply and demand. Similar efforts are essential for ensuring the stable supply of Lu-177. Understanding demand trends, facility operations, and investments remains crucial in this effort, based on accurate data and analysis when forecasting supply and demand balances. Policymakers and private sector investors can apply lessons learnt from the evolution of Mo-99/Tc-99m markets to ensure an effective market for novel radioisotopes such as Lu-177 and Ac-225. This session will seek to build consensus on potential market design and monitoring approaches as demand for the full range of medical radioisotopes grows in the coming years.

Chair: Ethan R. Balkin, Federal Program Manager for Radioisotope Production R&D, DOE Office of Isotope R&D and Production

Overview and focus points by the session chair

Landscape and challenges for medical radionuclide supply and monitoring facility capabilities and utilisation of medical radioisotopes

- Bernard Ponsard, Chair, EU Observatory on the Supply of Medical Radionuclides
- Remigiusz Baranczyk, Head of Sector, European Supply Agency, ESA
- Maria Alcaraz, Senior Medicines and Medical Devices Shortages Specialist, European Medicines Agency, EMA
- Jun Hatazawa, Senior Managing Director, Japan Radioisotope Association
- Nicolas Mario, Senior Consultant, NucAdvisor
- Nick Sherman, Deputy Head of Division, Division of Nuclear Technology and Economics, NEA

Questions and answers

14:35 (15 min)

Coffee break

Session 8: Regulation of Lu-177 and Ac-225

14:50 (80 min)

Effective regulation for the production and distribution of Lu-177 and Ac-225 will be crucial in accelerating R&D activities and enhancing the utilisation of radiopharmaceuticals such as Lu-177, Ac-225, and other new and emerging radiotherapeutics – spanning fundamental research, clinical trials, applications, production, distribution, and treatment. This session aims to identify key regulatory obstacles and opportunities to foster co-operation to create the enabling conditions necessary to incentivise a healthy market for medical radioisotope production and use.

Chair: Margarida Goulart, Head of Unit of Euratom Coordination, JRC

Overview and focus points by the session chair

Key current challenges of Lu-177 and Ac-225

- Jasminka Taleska, Director, RLT Healthcare System Readiness & Policy, Novartis
- Ekaterina Dadachova, Professor, University of Saskatchewan
- Sven Van den Berghe, CEO of Pantera

Aligning standards for safety, quality control, and manufacturing process requirements

- * Ravindra Kasliwal, Office of New Drug Products DNDP-3, Branch-6 Office of Pharmaceutical Quality, U.S. Food and Drug Administration (FDA)
- * Rolf Hesselmann, Scientific Advisor, the Swiss Federal Office of Public Health
- Estrella Moya Sánchez, Radiopharmacy Specialist and Pharmacist, Spanish Medicine Agency
- Aruna Korde, Radiopharmaceutical Scientist, IAEA

**Remote participation*

Questions and answers

Closing remarks

16:10
(15 min)

- Diane Cameron, Head of Division, Division of Nuclear Technology Development and Economics (NEA)
- Rachel Eloirdi, Head of Unit, European Commission Joint Research Centre (JRC)
- Ethan R. Balkin, Federal Program Manager for Radioisotope Production R&D, DOE Office of Isotope R&D and Production