

# ESA activities to support the secure supply of medical radioisotopes in the EU

Remigiusz Barańczyk, Stefano Ciccarello, Agnieszka Kaźmierczak Euratom Supply Agency https://euratom-supply.ec.europa.eu

## Contents

✓ Introduction

**Euratom Supply Agency** 

✓ Scene setter

Radioisotopes in medicine

## ✓ Core businesses

- European Observatory on the Supply of Medical Radioisotopes
- Nuclear raw materials for radioisotope production
- Impact of Russian aggression on Ukraine on the supply





## **Euratom Supply Agency (ESA)**

- Established by the Euratom Treaty (Art. 52) to ensure supply of nuclear materials on the principle of regular and equal access to sources of supply for power and non-power use by means of a common supply policy.
- Strategic objective the security of supply of nuclear materials for power and nonpower uses, by means of the common supply policy.

## **Medical radioisotopes**

- Vital role in diagnosing cancer, cardiac conditions and other diseases
- Increasingly used for cancer treatments



- Over 10 000 hospitals worldwide use radioisotopes in about 100 different nuclear medicine procedures totalling almost **49 million medical procedures** each year
- In the EU alone, more than **1500 nuclear medicine centres** deliver about **10 million procedures** to patients each year
- Up to 65% of nuclear medicine procedures are performed in oncology
- Molybdenum-99 (Mo-99) and its daughter product Technetium-99m (Tc-99m) used in 80% of all nuclear medicine diagnostic procedures



### Medical radioisotopes: use





## Medical radioisotopes: supply chain

- EU unique supply network innovative technology developments strong clinical research commitment -> a central role in the nuclear medicine domain
- The EU leading supplier of medical radioisotopes to the world market, with a market share of more than **60%** for some of the most widely used radioisotopes
- Main source of radioisotopes **research reactors**, with several other technologies that use cyclotrons or linear accelerators in use or under development
- The different radioisotopes and production technologies rely on highly specialised supply chains, which often extend across countries and continents and involve 24/7 "just-in-time" delivery



## **Medical radioisotopes: production**



- \* Various production routes for Mo-99 are being examined.
- \*\* The direct production of Tc-99m via accelerators is being examined.





Co-ordinated approach to the development and supply of radionuclides in the EU, Final report, 29/10/2021

## Medical radioisotopes: supply chain







**Euratom Supply Agency (ESA)** together with the industry association Nuclear Medicine Europe (NMEu) co-chairs the European Observatory on the Supply of Medical Radioisotopes, **set-up in 2012** 

#### With participation of

- Commission services (ENER, JRC, RTD, SANTE), European Medicines Agency (EMA)
- OECD Nuclear Energy Agency (NEA), International Atomic Energy Agency (IAEA)
- clinical end-users organization European Association of Nuclear Medicine (EANM)
- industry represented by the NMEu association





#### With objective to

- support secure and sustainable radioisotope supply across the EU
- ensure political visibility of the medical radioisotope supply issue
- identify any event likely to impact the radioisotope supply, including logistics and call relevant parties to take appropriate countermeasures
- promptly disseminate through agreed communication channels the enquired information regarding any possible supply disruptions
- establish periodic reviews of the radioisotope supply chain and capacities
- build a foresight overview of the supply and demand of radioisotopes at EU level
- to acquire the latest information on the development and implementation of new an alternative methods and technologies of medical radioisotope production





## **2021 Meeting of the Observatory**



#### Due to Covid-19 one e-meeting (29 June) instead of customary two face-to-face ones:

- Global Mo-99 producing research reactors scheduling
- Covid-19 impact on the supply
- Possible inclusion of Lutetium-177 in the scope of the Observatory
- Status of the EC projects connected with the supply of medical radioisotopes (SAMIRA, ERVI)
- Future supply outlook
- Updates from NMEu, OECD/NEA, IAEA and EANM

As of March 2021, the Observatory has an updated Mission Statement and new Terms of Reference to better define its way of operating



## 2022 Meeting of the Observatory 29 June, Brussels, 10-year anniversary

- Global Mo-99 producing research reactors scheduling
- Security of supply of medical radioisotopes in the current geo-political context (EMA, NMEu, EANM and ESA)
- Report of the ESA Advisory Committee Working Group on HALEU
- Stable isotopes production in EU (ORANO and URENCO)
  - Yb-176 (for Lu-177 production)
  - Mo-98, Mo-100 (for non-fission production of Mo-99/Tc-99m)
- Proposed Changes to IAEA A1/A2 Values impacting Nuclear Medicine
- Keynote speech on the outcomes of the Special Committee on Beating Cancer (BECA) by its Chair, MEP Bartosz Arłukowicz





## Coordination of the research reactor maintenance schedules to avoid and mitigate disruptions in the supply

- Voluntary participation of the operators
- Emergency Response Team (ERT) to monitor production and supply issues
  - research reactor operators
  - Mo-99 processors
  - Mo-99/Tc-99m generator manufacturers
- Continuous monitoring to identify potential shortages of Mo-99 and draw up mitigation action plans involving all stakeholders







## 2021/2022 Supply Challenges

#### • Covid-19 impact

- Contingency plans (alternative transport routes) developed by industry
- Close monitoring of the supply through ERT
- JCT communications to the stakeholders

#### Unplanned Outages

- OPAL Reactor (Australia) March-April
- IRE Mo-99 production line (Belgium) December – February
- HFR Reactor (Netherlands) January March 2022
  - ERT activated to address related disruptions

Potential shortage of lodine-131 for nuclear medicine therapy in 2022

- In October 2021, ESA was informed about a potential shortage of Iodine-131 (I-131) for nuclear medicine therapy in the second half of 2022.
- The Agency promptly informed the EU HSC, which is mandated to improve the coordination and sharing of information on national preparedness activities, and the European Medicines Agency (EMA).
- The EMA subsequently presented the case to the Co-ordination group for Mutual Recognition and Decentralised Procedures – Human (CMDh) to raise awareness of the need to change the terms of a marketing authorisation of I-131 from HALEU targets.
- A work-sharing procedure was agreed to facilitate a coordinated approach and avoid multiple evaluations by individual competent authorities.
- In parallel, EMA asked the national single point of contact (SPOC) network to conduct the criticality assessment at nation to get a detailed view of the impact of the potential shortage



## Supply of High-Enriched Uranium (HEU) for European Research Reactors

- ESA continues cooperating with the US DoE/NNSA to ensure the supply of HEU for the use of European research reactors by means of transferring excess HEU to the US in exchange in order to minimize the amounts of HEU
- MoU between US DoE/NNSA and ESA
  - Signed in 2014
  - Review of balance of material annually
  - Revised and signed in February 2021 with agreement to
    - Take into account the withdrawal of UK from the EU
    - Maintain the material balance sheet
    - Continue annual reviews
    - Carry out the next review of MoU after three years
  - Last review meeting in May 2022





**SAMIRA** (Strategic Agenda for Medical Ionising Radiation Applications) Commission Action Plan to support Europe's fight against cancer



## Supply of High-Assay Low-Enriched Uranium (HALEU)

- ESA Advisory Committee's WG on European Supply of lowenriched (19.75%) uranium
  - 3<sup>rd</sup> mandate
    - April 2021 May 2022
    - to explore the necessary conditions, including European public and private sector and specific industrial and commercial options, and to facilitate preparation of the possible construction in Europe of a HALEU metal production capacity responding to the EU needs for the research reactors fuel and medial radioisotopes production.
  - Report endorsed at the May ESA Advisory Committee meeting and presented at the EU Council AQG in July 2022





## Supply of HALEU

- Report provides an updated view of HALEU needs, including potential EU and global demand and presents three options to provide (at different level of degree) a security of HALEU supply in the EU:
  - **Option 1.** The European Union relies on timely delivery by the US and Russia ('as is' scenario)
  - **Option 2.** A rolling reserve guaranteed by the ESA for 10 years of needs is maintained while competencies and capacities on relevant technologies are sustained
  - **Option 3.** A European Union production capability is built based on shared effort from EU, Member States concerned and commitments from all stakeholders.
- SWOT analyses performed for all options







#### **Option 1 is the least preferred**

• It would not address the security of supply risks

#### **Option 2 appears as a first intermediate step, keeping its weaknesses in mind**

• It requires to identify a suited instrument and pathway to: build up the initial stock, finance the rolling stock, manage the storage, define responsibilities and governance, define rules for prices and HALEU allocation

#### **Option 3 assures the EU sovereignty and strategic autonomy in the supply of HALEU**

- It provides an optimal long-term security of supply fully in EU control
- It requires integrating a complex setup of actions, commitments and/or financing from the relevant EU, Member States, industries and end users

## Impact of Russian aggression on Ukraine on the supply

#### NUCLEAR MEDICINE EUROPE

COMMUNICATION FROM NUCLEAR MEDICINE EUROPE TO WHOM IT MAY CONCERN

	Subject: Stable and radioactive isotopes imported from Russia	
In the context taken/to be ta the impact or the second pa NMEU wants medicinal pr pharmaceutic these medicin products. Bes considered as these radioiso Some stable i this is the cas document. It does not mea therefore not Furthermore, not be diagno estimation of per week for On behalf of i to be diagnos exemption as embargo. Brussels, 29 N C. Walley Erich Kollegge	<ul> <li>Free Construction of the construction</li></ul>	<u>sia</u> <u>tue source is Russia</u> <u>ue source is Russia</u> <u>a</u> <u>sia</u> -64, Zn-68, Cd-112 ,

#### **SANCTIONS**

In the EU Regulation dated 8 April concerning restrictive measures in view of Russia's actions destabilising the situation in Ukraine, art 5k and 5l include exception for the supply of precursor material for the production of medical radioisotopes and similar medical applications.

https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32022R0576



## Impact of Russian war

#### **DEPENDENCIES FROM RUSSIA**

- 1. The EU depends solely on Russia for the supply of some critically important isotopes, in particular Yb-176 needed for Lu-177 production. The EU is a large supplier of Lu-177, which has demonstrated spectacular growth in recent years, as new radiopharmaceuticals have got market approval.
- 2. Some EU research reactors producing vital medical radioisotopes are dependent on Russian fuel. Russia supplies up to 25% of the enriched uranium for EU research reactor fuels.
- 3. There is insufficient capacity in place to compensate for the loss of Russian supply of some key isotopes, which are also sourced from other countries. For instance, Ge-68 is the parent isotope for Ge-68/Ga-68 generators that are key for the diagnosis of neuro-endocrine tumors.
- 4. Some radioisotopes of lesser importance are sourced directly and exclusively from Russia. These are used in certain diagnostic procedures, as well as in some therapies.
- 5. Enriched isotopes currently sourced partly from Russia, will be needed in the longer term to develop non-fission alternatives of the most used radionuclide in nuclear medicine, Tc-99m. Non-fission routes will need to set up a large supply of enriched isotopes Mo-98 and Mo-100 that are sourced from Russia at present.

### For more information, studies and reports



https://energy.ec.europa.eu/topics/nuclear-energy/medical-uses-radiation\_en#documents





Euratom Supply Agency 1, rue Henri Schnadt L-2530 Luxembourg





- euratom-supply.ec.europa.eu@euratom\_supply
- in /euratom-supply-agency