International experts from irradiating reactors, other isotope producers, and direct users urgently call for a long-term strategy to prevent a critical shortage of research and production capacities. They jointly ask for a common framework that stimulates much needed policy changes and investments.

The high-level speakers unanimously highlighted the **crucial role medical radioisotopes play in beating cancer** and stressed the **necessity to secure a reliable, stable production and supply chain for the future**. Indeed, the challenges of technologies and increasing demands rise at the same pace as the importance of the sector.

Europe plays an essential role in the production of medical radioisotopes. Just consider that 4 neutron irradiation services suppliers on 6 and the 2 largest separation facilities for ^{99}Mo are located on our continent, where more than 1,500 nuclear medicine centres deliver about 10 million procedures to patients each year. At the European level, the Euratom Supply Agency (ESA) is co-chairing the European Observatory on the Supply of Medical Radioisotopes, which plays an important role in monitoring all the aspects related to this field.

Medical progress and innovation lead the radioisotopes market to a continuous evolution. Currently, promising therapeutic medical radioisotopes like lutetium-177 (^{177}Lu) or actinium-225 (^{225}Ac) are gaining their place in this market and others like terbium-161 (^{161}Tb) or copper-64 (^{64}Cu) are gaining attention. Therapies based on the use of these radioisotopes are recording positive results, saving thousands of lives with a limited number of non-invasive applications and a low level of toxicity.

The global demand of these and other radioisotopes is expected to increase dramatically in the coming years. The current European Research Reactor fleet is not sufficient to meet the future increasing demand for those radiopharmaceuticals requiring neutron irradiation for their production. This is certainly the case if some of the existing reactors would reach their end of life, so new and different facilities are necessary to avoid any shortages.

The successful cooperation between research reactors in Europe has already prevented the radioisotopes shortage on several occasions. The last one happened at the beginning of 2022 when a rescheduling of work at the MARIA research reactor in Poland and extending operating cycle of the BR-2 research reactor in Belgium prevented temporary shortages of medical molybdenum-99 (^{99}Mo) due to the temporary shutdown of HFR reactor in The Netherlands for one cycle. Panelists discussed the possibility of making up for the lack of research reactors in Eastern Europe by supporting the younger MARIA reactor (operating since 1974) to become a regional cooperation center. The development and building-up of the medical isotope production at traditionally beam-line type research reactors like FRM II in Germany and ILL in France is helpful to avoid such critical shortages in the future and to improve the European capacities.

Cyclotrons and other particle accelerators established themselves as part of the dynamic developments. In combination with Research Reactors and novel neutron sources, they can support the supply of medical isotopes for a part of the growing market. Such complementarity requires a strong cooperation between the different communities, as well as mutual, positive communication and efforts. Still, as clearly confirmed by the recently published SAMIRA and SMER reports, a stable supply of the full portfolio of medical isotopes will continue to also depend on the availability of Research Reactors – which will undoubtedly face significant challenges in keeping up with the dynamics.

An increasing number of **standards and regulations adopted in research reactors from nuclear power plants are rarely easily implemented in existing installations**, causing the increase of the resources needed for justification of continued operation.

And while life-time management operations currently allow for keeping up the lifesaving production of medical isotopes, the gap will inevitably increase if major isotope producing European research reactors shut down without available replacement. **A long-term strategy is urgently needed to prevent a critical shortage of research and production capacities.**

Many of the novel isotopes are based on irradiations of isotopically pure powders of non-radioactive material, a resource which is relatively rare for some of these. The stable isotopes supply situation depends on the production methods for each one individually, with some of the more crucial ones currently supplied by a single source. **As the development of additional production infrastructures is a capital-intensive endeavor, the business case tends to be unfavorable as long as the market forecasts are unclear. Oppositely, the successful development of new radio-pharmaceutical products will only be sponsored if there is a stable supply chain available**, which includes a reliable, diverse, and sustained supply of precursor material. **An issue where the supply of the precursor material would threaten the deployment of new radiopharmaceuticals, which has occurred in the past, should be avoided**, and fortunately current projections estimate that new players are expected to emerge in the stable isotope supply field over the coming years, as long as the positive forecasts for the development of the radiopharma field continue to be realised**. It remains to be seen to what extent some of these new players will be in Europe, which threatens the independency of the European isotope production chain.**

It is therefore clear that a sustainable framework for the European supply of medical isotopes will need to consider the entire chain of production, including the availability of suitable source materials, which also means the fissile materials required for isotope production routes relying on fission, either as a target or as a fuel for the neutron source in which they are produced. With finite resources of Highly Enriched Uranium (HEU) used for down-blending to High Assay Low Enriched Uranium (HA-LEU), a similar issue as with the isotope precursor materials will arise if action is not taken. Currently, no HA-LEU can be sourced anywhere in Europe and all non-European actors benefit from very strong political and financial government support in their own country. Equally, diversification of fuel element manufacturing is recommendable, and the qualification of suppliers should be supported. Although the ESA is preparing some activities needed to resolve these problems[1], **the sector would benefit from innovations and commitments for the security of fuel supply.**

[1] https://euratom-supply.ec.europa.eu/document/download/f639d7d8-1447-4834-bf27-861b860662c1_en?filename=HALEU%20report%20May%202022%20print.pdf

For the production of radioisotopes based on research reactor irradiations to be sustainable, it is required that reactors can recover their costs directly and indirectly linked to the production activities and generate a margin capable of managing their dismantling provisions, as well as the preparation of a construction of a replacement reactor. Historically, this sustainability was never created as isotope production was a small by-product of research reactors and pricing was never adopted to secure sustainability as public funding was flowing thanks to the other missions of those research reactors. Alternative missions of the existing research reactors are often less and less supported by the countries in which they operate and cannot be commercially offered at prices which cover the costs, let alone to allow margins to be created. At the same time, projected dismantling costs continue to rise, all of which reduces the support to use public funding supplied by the taxpayers of those host countries to continue to operate the reactors. Because the production of the radio-isotope is at the beginning of the value chain, it requires an evolution throughout the value chain to allow it to increase. For pharmaceutical products, this is further complicated by the reimbursement policies in healthcare. **It is vital for Europe to consider decoupling the reimbursement of the radioisotope from the rest of the reimbursement of the nuclear medicine procedure, as is already the case in Belgium and a few other member states. In that way, these tariffs can be individually managed and evolve with the true evolution of the production cost. The impact on the healthcare budgets of individual member states is minute, while the impact on the sustainability of the reactors in the host countries and therefore of the radioisotope supply chain, is a game changer.**

All experts welcomed the **European Radioisotope Valley Initiative (ERVI)**, planned under the European Commission's SAMIRA Action Plan[2], as a first step into the right direction. **Expectations are for a framework that stimulates much needed policy changes, as well as investments in new research reactors, novel neutron sources, accelerators and stable isotopes enrichment centers**. The COVID pandemic and the Russian invasion on Ukraine have shown the risks of a dependence on outside suppliers and the US is strongly investing in indigenous supply of different medical radioisotopes. This indicates the necessity to retain and develop the skills and the facilities for supporting the whole chain domestically in Europe as well. It would reduce the dependency and allow Europe to remain a global leader in nuclear medicine.

All speakers recognised the global good situation regarding the technology aspects and the partnership in international scale, but further efforts in terms of harmonization

[2] https://energy.ec.europa.eu/topics/nuclear-energy/radiological-and-nuclear-technology-health/samira-action-plan_en

of both medical procedures' requirements and the transport of radioactive materials are always desirable.

The European Research Reactor Conference (RRFM) is the annual gathering of the Research Reactor Community. It regularly brings together more than 200 experts from over 40 countries worldwide. At this years' edition, a Panel of experts from irradiating reactors and other isotope producers as well as direct users discussed the situation and prospects for the security of supply of medical isotopes.

Participants: Mr Jean Bonnet (IRE, Belgium – attended online), Dr Sven Van Den Berghe (SCK CEN – BR2, Belgium), Dr Frodo Klaasen (NRG - HFR Petten and Pallas, The Netherlands), Mr Maciej Lipka (National Centre for Nuclear Research – MARIA Research Reactor, Poland), Dr Richard Henkelmann (ITM Isotope Technologies Munich SE, Germany), Mr Harrie Buurlage (ShineMED, The Netherlands/USA), Mr Laurent Bigot (Orano, France), Dr Gilles Bignan (CEA – JHR, France).

Moderators: Remigiusz Barańczyk, Euratom Supply Agency (ESA), and Steven Van Dyck (SCK CEN)