ADDRESSING SOCIETAL CHALLENGES THROUGH ADVANCING THE MEDICAL, INDUSTRIAL AND RESEARCH APPLICATIONS OF NUCLEAR AND RADIATION TECHNOLOGY

20 – 21 March 2018, Brussels

Conference Summary

The material below represents the rapporteurs' summaries of the main topics presented and discussed in the different conference sessions. No reference is made to the specific presentations or other interventions by individual speakers. The views expressed have not been adopted or in any way approved by the European Commission and should not be relied upon as a statement of the Commission's views.

Proceedings of the conference, including the opening address, the conference slide and written statements of panellists are available at: https://ec.europa.eu/info/events/addressing-societal-challenges-through-advancing-medical-industrial-and-research-applications-nuclear-and-radiation-technology-2018-mar-20_en. The conference webpage also contains full video recording of the meeting.

CONFERENCE OPENING

Miguel Arias Cañete, European Commissioner for Climate Action and Energy, and Vytenis Andriukaitis, European Commissioner for Health and Food Safety, opened the conference. They welcomed the opportunity to discuss the important topic, and set the scene for the conference from the Commission's perspective.

They were followed by Yukiya Amano, Director General, International Atomic Energy Agency, and Maria Neira, Director Public Health, Environment and Social Determinants, at the World Health Organisation, who provided the international perspective in this area.

SESSION 1

Health: Ensuring security of supply of medical radioisotopes to deliver diagnosis and treatment

This session discussed the current and future supply of medical radioisotopes, globally and in Europe, and sought to identify any actions that need to be taken to ensure a secure and continuous supply. The ageing of existing research reactors as well as the transition to low enriched uranium (LEU) targets for radioisotope production will have implications for the future. Europe's research reactors currently provide about 60% of global demand and we need to ensure that supply is secured through adequate infrastructure investments, while considering viable alternative methods of production.
Session summary
The session commenced with keynote speeches from Kevin Charlton from OECD NEA, and Andre Kolmeyer from NucAdvisor who are conducting an EC study to support the evidence base for the medical, industrial and research applications. The panel discussion included insight from Richard Zimmerman of the Association of Imaging Producers & Equipment Suppliers (AIPES); Kristoff Muylle, President of the European Association of Nuclear Medicine (EANM), Roy Brown from Curium; and Sally W. Schwarz of the US Society of Nuclear Medicine and Molecular Imaging (SNMMI). The session was chaired by Marian O'Leary, Director General of the Euratom Supply Agency.

The main messages of this session are summarised below:

- The medical radioisotopes market is global and ensuring secure and economically sustainable supply is essential. The medical radioisotopes are utilised in a wide range of diagnostic procedures, must be produced almost continuously and any disruption to the supply chain can cause immediate disruption to patient services leading to sub-optimal care. As medical radioisotopes move from diagnosis towards therapy with the development of so-called theranostics pairs, security of supply will be even more important.

- At present the supply is stabilised as a result of the actions of existing supply chain participants and the co-ordination activities of the Association of Isotope Producers and Equipment Suppliers (AIPES), but challenges remain. The conversion from high enriched uranium (HEU) to low enriched uranium (LEU) targets used to produce radioisotopes in research reactors presents technical challenges; it is less efficient, produces more waste and has a higher unit cost for the product. For more than 70% of the global market, the conversion to LEU has been recently achieved.

- The main imaging radioisotopes are today produced in nuclear research reactors – Mo-99/Tc-99m for single-photon emission computed tomography (SPECT) – or cyclotrons – F-18, and likely Ga-68 in the next future, for positron emission tomography (PET). However, the main therapeutic radioisotopes and brachytherapy compounds are only produced in research reactors. European research reactors, among them HFR (The Netherlands), BR2 (Belgium), Maria (Poland) and LVR-15 (Czech Republic), are producing around 60% of the global needs for Mo-99/Tc-99m, which is the nuclear imaging workhorse (around 80% of the annual 10 million nuclear medicine imaging procedures in Europe). Most of the European reactors are ageing, periodically subject to revamping operations in order to ensure their continuous safe use, but their life cannot be indefinitely extended, jeopardizing the mass supply of radioisotopes.

- At the current stage many technical problems around the production of medical radioisotopes in research reactors have been solved and a range of alternative production technologies have been demonstrated (the first alternative technology is now being introduced into the US market – in February 2018 FDA approved NorthStar Medical Radioisotopes' RadioGenix System for use to produce Tc-99m from non-uranium based Mo-99). Notwithstanding these developments some challenges remain:
- Full cost recovery (FCR) pricing levels for reactor produced medical radioisotopes have not yet been achieved;
- Paid outage reserve capacity (ORC) remains underutilised by the supply chain;
- Reimbursement levels remain unchanged in many markets.

- The market remains economically unsustainable and there are some risks of delay or cancellation of new investments. Further work is needed on healthcare economics.

- Despite the increase in PET imaging, there is no sign that the massive use of Mo-99 will decline in the near future. Its use could even increase if theranostics develop as predicted. However, a key prerequisite for radiotherapeutics development is the active new imaging vector-payload compound development. To this aim, molecular imaging research must remain very active and affordable, which is not the case today. A solution for this situation could be “in-house labelling” in universities, hospitals or medicine schools, to foster the first phases of development until large companies can take over the Phase II/III clinical trials. In-house labelling of radiopharmaceuticals can be performed in safe conditions, meeting high quality standards under adequate supervision.

- Given the development costs, the market for radiotherapeutics compounds must be global. This means that the compound production (especially the radioisotopes) must be based on a cost-efficient, good manufacturing practice (GMP) proven, reliable, versatile and mass-production supply chain, which today can only be ensured with multi-radioisotope-production reactors. A number of stakeholders should work closely together, namely, irradiators and processors, researchers, universities and labs, imaging equipment manufacturers, financiers, large pharmaceutical companies. Strategic investments in this domain should be supported. This suggests that the EU could foster European centres of excellence, created around new radioisotope production facilities, gathering all the stakeholders required for achieving efficient imaging and therapy compounds development. New approaches should involve experts in applied nuclear physics and chemistry as well as nuclear engineering, radiopharmacists, nuclear physicians, medical physicists, and experts in molecular imaging and targeted radionuclide therapy, and business stakeholders. This is a typical example of the interdisciplinary R&D needed in ionizing radiation applications.

- When discussing innovation in the use of radionuclides for medical applications, one should consider the full cycle of research, production infrastructures, including the irradiation targets, full market circuit, clinical use and waste management. In this context, the supply chain for radioisotopes should be secured up to the supply of LEU for irradiation targets. Even if LEU irradiation targets lead to increased radioisotope costs and waste, they are preferred over HEU, the use of which raises nuclear proliferation and security concerns. Neither HEU nor LEU are produced in the EU. The supply of medical radioisotopes depends on securing an adequate supply of LEU required for their production.
SESSION 2

Health: Novel nuclear medicine to advance patient care

This session sought to highlight examples of the recent developments and innovations with regards to radiopharmaceuticals and their expected contribution to the personalised cancer treatments of the future. The discussion sought to identify any potential barriers to the introduction of new treatments, technologies and applications, and the structures required to support their successful development and implementation in Europe.

Session Summary

The session was opened by Vladimir Sucha, Director General of the Joint Research Centre (JRC), followed by keynote speeches from Stefano Buono, Advisor to Advance Accelerator Applications; Julien Dodet, CEO of Orano Med; and Kristoff Muylle, President of the European Association of Nuclear Medicine (EANM). The panel discussion included thoughts from Sally W. Schwarz of the US Society of Nuclear Medicine and Molecular Imaging (SNMMI), Francesco Giammarile from the International Atomic Energy Agency (IAEA), Riccardo Schiavo from the Italian Medicines Agency; Paul M. Parizel from the European Society of Radiology (ESR); and Maria Betti from JRC. The session was chaired by John Ryan, Director of Public health, country knowledge, crisis management in DG Health and Food Safety (SANTE).

The main messages of this session are summarised below:

- The Joint Research Centre (JRC) carries out several activities relating to the medical uses of nuclear technology. Alfa-immunotherapy and targeted cancer therapy are being studied with the view of identifying their potential to treat cancer patients. Member States have recently asked JRC to investigate the landscape of radioisotopes for medical use in the EU and, as part of the EU Security Union process, identify possible measures to secure their sustainable supply in the future. JRC further coordinates the European Network of Cancer Registries and the development of the European Cancer Information System, now freely available on the web, contributing to the high quality of cancer screening and management enjoyed by the European citizens.

- Theranostics provides unique opportunities for joining the nuclear medicine's diagnostics and therapeutic capabilities to provide personalised treatment of cancer patients. Notwithstanding its great potential, theranostics faces major challenges with respect to the administration of therapeutic radiopharmaceuticals to outpatients, the reimbursement of diagnostic drugs and the regulation of institutional 'home-brew' drug formulation. The multiple regulatory authorities, both on the health and nuclear side, and logistics (delivery, transport and distribution of products) issues pose a challenge for the smooth functioning of the EU internal market.

- Nuclear medicine fast innovation in the past decades delivered new diagnostic instruments, new molecular imaging applications and the possibility to treat patients with targeted therapies. These innovations opened the door to an increased impact of nuclear medicine on patient's management and revived the interest in radionuclide therapy. The next decades are expected to bring further improvements in the sensitivity of the
instrumentation leading to a reduction of the radiation dose to patients and faster imaging. New targeted therapy treatments will go hand-in-hand with better selection of patients in order to avoid or reduce toxicity and reduce treatment costs.

- However, innovation may be hampered by regulatory issues, such as the Euratom radiotherapy requirements which are not adapted for radionuclide therapy, and the treatment of radiopharmaceuticals and their precursors as pharmaceuticals by the EU legislation. It has been suggested that a specific nuclear medicine framework may be needed to achieve the main goal of helping patient access to these innovations while maintaining high quality standards.

- Continued dialogue and collaboration of all involved stakeholders is needed to address the above issues. Collaboration among different specialities – radiology, nuclear medicine, oncology – would improve a shared decision making process concerning patients diagnosis and treatment and has to be translated into university curricula following the successful examples of several Member States. Finally, patients and patients’ organisations have to be fully involved in the overall path of new technological and product development.

SESSION 3

Quality and safety: improving medical practice

This session discussed the key quality and safety challenges associated with diagnostic and therapeutic applications of nuclear and radiation technologies. The various issues were approached from the perspective of public health bodies, regulators, equipment manufacturers and medical specialties using these technologies. The discussion covered different elements of European policy, e.g. in the fields of radiation protection, medical devices and public health, and possible actions that the Commission can take to address the identified challenges.

Session Summary

The session was opened by John Ryan, Director, DG SANTE, followed by keynote speeches from Dominique Le Guludec, President, High Authority of Health, France; Yolande Lievens, President of the European Society for Radiotherapy and Oncology (ESTRO); and Paul M. Parizel of the European Society of Radiology (ESR). The panel discussion included thoughts from Sakari Karjalainen from the European Cancer League (ECL)), Lionel Hadjadjeba from the European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry (COCIR), Sandra Gomez from the French Hospital Federation, Mette Øhlenschlaeger from the Heads of the European Radiological Protection Competent Authorities (HERCA). The session was chaired by Carlo Pettinelli, Director at DG Internal Market, Industry, Entrepreneurship and SMEs (GROW).

The main messages of this session are summarised below:

- Recent developments in several areas of European policy have direct influence on quality and safety aspects of the diagnostic and therapeutic applications of nuclear and radiation
technologies. In the Health domain, a number of specific actions have been undertaken to deliver on the policy objectives of complementing the work of health authorities and exploring opportunities for cooperation across the EU. Recent revisions of the EU legal framework for medical devices and the Euratom radiation protection legislation aim to ensure high level of patient safety and stimulate innovation. Nevertheless, there is a need to close the gaps between the regulatory framework and its practical implementation, e.g. in the area of radiation protection of patients.

- Adequate medical education, training and continuous professional development play a central role in guaranteeing quality of care and patient safety. Ageing population and rapid technological innovation are challenging the resilience of the health workforce and increasing the need to forecast future skills and competences and mitigate the gaps between supply and demand of medical staff. Efforts need to be stepped up to ensure cross-sector networking of specialists, better integrate the specificities of different sectors and provide patients with appropriate information.

- High level of quality and patient safety should be ensured through the integration of these aspects in good practice guidance and quality standards covering the key steps of disease prevention, diagnosis, treatment and post-treatment care. Such guidance and standards should be based on high-quality information and solid evidence, best gathered through co-ordinated European (or international) action. Good examples, such as the European Initiative on Breast Cancer, can be used as a blueprint for other areas.

- Recent technological developments have brought numerous advantages in terms of more efficient and safer radiotherapy as well as lower radiation and better quality medical imaging. Yet, significant differences exist among the EU Member States in terms of access to modern equipment. Suggestions have been made that national plans may be needed for the timely replacement of old and obsolete radio-diagnostic equipment. With respect to radiotherapy equipment and treatments – which are more complex, higher-risk and costlier – a more cautious approach have been advocated. A co-ordinated EU action, e.g. within the Health Technology Assessment framework, may bring added value.

- Working together is a prerequisite to reach a high standard of quality and patient safety, and a number of European co-operation mechanisms and options already exist. Examples of good co-operation between national health and radiation protection authorities as well as among different professional groups have been highlighted. European and national actions should be further explored to improve governance through stakeholder co-operation and policy co-ordination in areas, such as education and training, safety culture, introduction of new technology, clinical audit and regulatory control of practices.
SESSION 4

Quality and Safety: challenges for the management of non-energy radioactive waste and spent fuel

This session sought to identify challenges and potential actions in the area of safety of radioactive waste and spent fuel management for non-energy use of nuclear and radiation technology. Predisposal and disposal of radioactive waste and spent fuel, legacy waste and 'exotic waste' for which there is no clear disposal option to date were discussed. The discussion explored how well advanced Member States can assist other Member States in developing approaches for the management of radioactive waste and spent fuel from non-energy use of nuclear and radiation technology.

Session Summary

The session was opened by Michèle Rivasi, Member of the European Parliament, followed by keynote speeches from Fabien Hubert, Head of Service Solutions for Non-Electronuclear Producers, ANDRA, France; Andrej Stritar, Director, Nuclear Safety Administration, Slovenia; and Michalis Tzortzis, Radiation Inspection and Control Service, Cyprus. Joining them for the panel discussion were Gerard Bruno of the IAEA; Johan Swahn of the Nuclear Transparency Watch, Sweden; and Andreas Vesely, Austrian Nuclear Engineering Seibersdorf. The session was chaired by Massimo Garribba, Director, DG Energy (ENER).

The main messages of this session are summarised below:

• All EU Member States using sources of radiation generate radioactive waste; and some Member States also generate and store spent fuel. All Member States are legally responsible for the safe management of these materials. Member States need to develop a national policy, framework, programme and an overall systemic approach for the management of radioactive waste and spent fuel from their generation to disposal, including post-closure of disposal facilities.

• Although the principles for safe management of radioactive waste and spent fuel are the same for nuclear energy and non-power applications, there are a number of challenges specific to the latter. Yet, there appears to be insufficient recognition of these challenges, stemming mostly from the relatively limited amounts of spent fuel and radioactive waste involved. Small non-nuclear Member States, in particular, face significant challenges related to securing the human and financial resources needed for the safe management of their limited inventories. Moreover, there is a need to strengthen spent fuel and radioactive waste management safety culture and staff training outside the nuclear fuel cycle, which may not be at the same level as for nuclear facilities.

• Although management routes exist for most radioactive waste and spent fuel, some radioactive waste streams – such as waste containing tritium, metal waste, orphan waste, legacy waste and waste from the clean-up of contaminated sites from past activities – require further work. Governments need to take responsibility for all this radioactive waste until disposal. There is also a need to address the point of "decommissioning" of
disused sealed sources, which have been generated from use around the world. Different technical solutions – including borehole disposal developed by the IAEA for small non-nuclear countries – exist internationally.

• Co-operation between countries is important for the implementation of safe disposal solutions in practice, and shared disposal is seen by some Member States as a safe and secure option that should be pursued on a European and/or international level. It was suggested that the Commission could be given a mandate to take specific action (possibly together with the IAEA) to support and examine options for the implementation of shared disposal solutions that would contribute to safe and secure disposal of radioactive waste from non-power applications without compromising Member States ultimate responsibilities for safe management of this material. It should be emphasized that developments in this area should not prevent the progress of national disposal projects.

• The Commission has a key role in ensuring the implementation of the EURATOM law in Member States. The Commission has to ensure that Directive 2011/70/Euratom\(^1\) is fully implemented in Member States, including that mechanisms are in place to safely manage all spent fuel and radioactive waste and that established criteria for predisposal and disposal (including clearance) are respected. Furthermore, the peer review mechanisms under Directive 2011/70/Euratom could be used to support the maintenance of safety culture and technical and professional capacity of the generators and managers of non-nuclear waste. The Commission could also support further work towards the minimisation and clearance of radioactive waste and should encourage cooperation between Member States and with international organisations as well as information sharing and engagement with the civil society.

• Transparency is very important aspect and, public perception and acceptability of spent fuel and radioactive waste management remain critical to successfully manage and dispose of these materials. For example, the discussions showed that it would be necessary to further study and understand the public attitudes to date, and to find ways to present evidence of the benefits of the safe management of spent fuel and radioactive waste from non-nuclear fuel cycle facilities and activities.

SESSION 5

Innovation: the potential of nuclear and radiation technology to deliver societal benefits in the future

Technological advances have the potential to bring forward further beneficial uses of non-energy nuclear and radiation technologies. This session discussed how research and development can realise these benefits while controlling radiation exposures. The session sought to identify actions to support the evolution of technology whilst achieving the highest level of quality and safety.

\(^{1}\) COUNCIL DIRECTIVE 2011/70/EURATOM of 19 July 2011 establishing a Community framework for the responsible and safe management of spent fuel and radioactive waste
Session Summary

The session was opened by Patrick Child, Deputy Director General of DG Research and Innovation (RTD) [replaced by RTD Head of Unit, Rita Lecbychova after he was called away], followed by keynote speeches from Angeles Faus-Golfe, Applications of Particle Accelerators in Europe; and Winfried Petry, Scientific Director of the Research Neutron Source Heinz Maier-Leibnitz. The panel discussion included thoughts from Caterina Petrillo of Perugia University; Erik Briers of the Patient Advisory Group of ESR; Maurizio Vretenar of CERN/Eucard2; and Luca Cozzi representing COCIR. The session was chaired by Charlina Vitcheva, Deputy Director General, DG JRC.

The main messages of this session are summarised below:

- Many examples of how nuclear and radiation technologies assist in addressing societal challenges were presented. The variety and scale of these technologies and their uses in the EU is staggering – from world-leading research reactors and high-energy particle accelerators used in fundamental and applied research to everyday uses of radioactive sources, x-ray machines and smaller accelerators in health, security and various industrial processes. The markets in many areas (e.g. medical equipment) are characterised by fierce competition, high investment in research and innovation and rapid technological development.

- Neutrons, which are produced in research reactors or spallation sources, are used in various applications and have some unique capabilities. Research reactors are the main source of radioisotopes for medicine and various industrial applications and are also used for silicon doping and material testing. Neutrons enable researchers to see at the nanoscale and study issues like bacterial antibiotic resistance, bipolar disorder or cultural heritage as well as develop better data storage, batteries and silicon chips. Therefore, continuous support for neutron research was seen as crucial. However, recent ESFRI projections show that by 2025 Europe will remain with only 5 neutron sources, which could lead to a neutron shortage. It was therefore strongly suggested that nuclear research infrastructures should be managed in a European collaboration perspective.

- Linear accelerators are a versatile and readily available technology for driving innovation in nuclear science applications. They provide for example alternative methods for the production of radionuclides of interest, with the advantages of a more robust supply (from many potential suppliers), flexibility in terms of working conditions and low waste management and decommissioning cost compared to classic approaches. The accelerator applications are vast and open up new opportunities in terms of novel products, industrial processes, and techniques addressing different societal challenges. To accomplish its full benefit, a linear accelerator strategy should take into consideration long term investment vision, strong cooperation and adequate public communication, all areas in which the EU provide crucial support.

- There is room for improvement on technology transfer from concept to application and for better cooperation between the research community and the industry. The time it takes to getting products to market could be improved. The process of market
authorisation, for instance of medical technologies, should also be streamlined to make them more equally available across Member States. The Commission could help addressing these challenges.

- From the patients’ perspective, radiation is present in every step, from diagnosis through treatment and monitoring of long term outcomes. Ensuring the adequate radiation protection of patients is extremely important, and EU initiatives such as projects to identify patients that are sensitive to radiation, should continue to be supported. Researchers should be encouraged to engage with patients in all steps of their research. Enhancing the networking of hospitals and researchers to share data, improve learning and identify patterns is highly recommended. Benefits and potential risks of radiation should be better communicated to the public.

- Radiation technology can offer solutions to some of today’s most pressing needs, for instance in crop production to feed the world’s growing population. To realise these benefits, further work is needed on developing multi-disciplinary projects and improving the public perception of radiation. Education and training is also a key part of ensuring that Europe remains a leader in this field. There is widespread support for more cooperation within the EU and with international partners in these areas.

**CONFERENCE CLOSING**

The conference was closed by Gerassimos Thomas, Deputy Director General, DG ENER. Mr Thomas thanked all speakers, panellists, attendees and organisers for their valuable contributions to make it an interesting conference with rich discussion.