

EANM Position Paper

Nuclear Medicine

What it is. Where it goes. What it needs.

Nuclear Medicine provides a multitude of highly effective pathways for medical diagnosis and treatment.

It is used successfully in the detection, evaluation and treatment of many diseases, including cancer.

Every year, more than 10 million patients in Europe benefit from Nuclear Medicine in the diagnosis and treatment of illnesses.

No matter the current disruptions and the Covid-19 pandemic, Nuclear Medicine services should remain accessible and available to all European patients.

The European Association of Nuclear Medicine (EANM) believes that fostering advances in science and education will support impactful policy change.

Who are we?

The European Association of Nuclear Medicine (EANM) is the largest organisation dedicated to Nuclear Medicine in Europe. As an umbrella organisation of individuals and national societies, representing more than 9,000 specialists, and aiming at advancing science and education in Nuclear Medicine for the benefit of public health, we advocate for better recognition and support for Nuclear Medicine at the European level.

Guidelines, educational activities and scientific sessions represent our core contributions to the Nuclear Medicine community, developed and validated by our volunteering experts who are the core of our association.

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Executive summary

Nuclear Medicine is a medical specialisation that involves the administration of radioactive substances (radiopharmaceuticals) for the diagnosis and treatment of diseases in patients of every age group.

With already 100 different Nuclear Medicine procedures approved by regulators, every year, more than 10 million patients in Europe benefit from Nuclear Medicine in the diagnosis and treatment of e.g.:

- cancers,
- endocrinological diseases,
- cardiovascular diseases,
- neurovascular diseases,
- musculoskeletal diseases,
- infections and inflammations.

The European Association of Nuclear Medicine is advocating for easier access to Nuclear Medicine services for all patients. In the 2022 political context and the political attention given to cancer, this statement sparks a specific interest in policy initiatives related to oncology.

Nuclear Medicine applications have an excellent safety profile; given their physical and clinical particularities, radiopharmaceuticals are an exceptional class of medicines which require specific considerations.

Despite broad acceptance and widespread application in clinical medicine, Nuclear Medicine is still facing significant challenges for optimal scientific, clinical and commercial development across Europe¹, related to:

- The lack of harmonised high-quality standards for the education of healthcare professionals on the delivery of high-quality Nuclear Medicine services and unharmonised training curricula throughout Europe, as well as Nuclear Medicine professionals' shortages.
- Insufficient healthcare infrastructure to accommodate Nuclear Medicine facilities, in terms of medical equipment, configurations of supply chains and ageing research reactors producing medical isotopes.
- Non-optimal regulatory frameworks that do not consider the specificities of the sector.

In this respect, the European Association of Nuclear Medicine is committed to ensure that all patients in Europe have equal access to high-quality Nuclear Medicine services. This should be fulfilled by:



- Achieving full recognition of Nuclear Medicine as a core individual medical speciality by all national and international stakeholders and institutions.
- Upholding and advancing a common high standard of Nuclear Medicine professionals' education and training in all European countries.
- Creating a supportive regulatory environment for Nuclear Medicine that recognises and understands the specific characteristics of the field.
- Ensuring that health systems have in place robust and sustainable supply chains and state of the art infrastructure to guarantee sustained contribution of Nuclear Medicine to patient care.

¹ This paper mainly tackles the clinical aspects of Nuclear Medicine, rather than the pre-clinical aspects.

Glossary

- **Nuclear Medicine:** Nuclear Medicine is a medical speciality that utilises the application of radioactive substances for diagnosis and treatment of disease.
- **Ionising Radiation:** Ionising radiation is a type of energy released by atoms that travels in the form of electromagnetic waves (gamma or X-rays) or particles (neutrons, beta or alpha). Ionising radiation is used in the medical field for diagnostic and treatment. Today, the most common human-made sources of ionising radiation are medical devices, including X-ray machines².
- **Radionuclide therapy:** Radionuclide therapy (also called: radiopharmaceutical therapy, molecular radiotherapy or endoradiotherapy) is a systemic and targeted therapy which uses unsealed radioactive sources.
- **Radioligand therapy:** Radioligand therapies are made up of a ligand, which can target and bind to cancer cells, and a radioisotope, which emits therapeutic radiation to kill these cells. It can be applied to many cancers, such as neuroendocrine tumours, including thyroid and prostate cancer and lymphoma.
- **Theranostics:** Theranostics is a term derived from a combination of therapeutics and diagnostics. It is used in Nuclear Medicine to describe the possibility of both diagnosing and treating a disease with the same chemical structure to ensure best patient outcome.
- **SPECT:** Single photon emission computed tomography (SPECT) is a Nuclear Medicine procedure using single photons to depict body-internal biological processes – the imaging procedure resulting in the so-called SPECT scan of the patient. Also, commonly used to refer to the device/machine that is employed to produce these scans.
- **PET:** Positron emission tomography (PET) is a Nuclear Medicine procedure utilising positrons to depict body-internal biological processes – the imaging procedure resulting in the so-called PET scan of the patient. Also, commonly referring to the device/machine that is used to produce these scans. The use of PET and SPECT depends on the kind of particle/radiation emitted by the radioisotope.
- **Hybrid imaging:** Hybrid imaging describes Nuclear Medicine imaging modalities that are based on SPECT or PET machines that are combined with other imaging modalities' scanners (such as computed tomography CT or magnetic resonance MR) to enrich the functional imaging properties of Nuclear Medicine with the anatomical information of those modalities in one scan procedure for the patient. Similarly to the above, expressions like PET/CT, PET/MR, SPECT/CT, etc. describe both the hybrid imaging procedure as well as the equipment that is needed to obtain the patient scans.
- **Radiopharmaceutical:** A drug that contains a radioactive substance and is used to diagnose or treat disease, including cancer.

² <https://www.who.int/news-room/fact-sheets/detail/ionizing-radiation-health-effects-and-protective-measures>

- **Radioisotopes:** Radioisotopes are radioactive isotopes of a chemical element, i.e. ‘versions’ of an atom which share the same number of protons, but not of neutrons, as their stable, non-radioactive counterparts, thereby providing them with the capacity to lose their energy by radiation (radioactivity). Radioisotopes are produced in nuclear reactors, cyclotrons or generators. They are used to produce radiopharmaceuticals: the most common radioisotope used in Nuclear Medicine is technetium-99m (Tc-99m).
- **Radiopharmacy:** Within a hospital, radiopharmacy requires a dedicated space, respecting radiation protection requirements, where Nuclear Medicine specialists prepare radioactive materials for patient administration.
- **Nuclear Medicine specialists:** Appropriate delivery of Nuclear Medicine services requires multidisciplinary with the involvement of various professionals, including Nuclear Medicine physicians, Nuclear Medicine physicists, radio pharmacists, radio chemists and Nuclear Medicine technologists as well as others.
-  **Nuclear Medicine is not radiology!** It is a common misperception that radiology incorporates Nuclear Medicine. In fact, while both specialities share the delivery of diagnostic imaging services, Nuclear Medicine also offers treatment options. In addition, Nuclear Medicine scans differ from radiological scans, as the emphasis is not on imaging *anatomy*, but on cell *function*. Hence, Nuclear Medicine obtains images of **how the body is working** as compared to showing that there is a tissue structure or organ, but also what it is doing. Moreover, Nuclear Medicine uses internal radiation from the body emitted by incorporated radiopharmaceuticals while radiology uses external radiation sources (e.g. X-ray tubes) outside of the body.
-  **Nuclear Medicine is not radiation oncology!** Radiation oncology and Nuclear Medicine are separate medical specialities. Radiation oncology is generally a cancer treatment modality. While there are some overlaps (e.g. the local use of sealed radioactive substances), radiation oncology normally uses external high-energy radiation sources to treat localised diseases.

I. Nuclear Medicine – a unique paradigm in patient care

As a medical application of nuclear technology, Nuclear Medicine uses radioactive **isotopes** for applications in diagnosis and treatment of patients.

Indeed, Nuclear Medicine contributes to the diagnostic and treatment of **numerous severe diseases, including cardiological, endocrinological and neurological diseases**, with a specific focus on cancer as **more than 80% of all Nuclear Medicine procedures are related to cancer treatment**³.

Every year, more than 10 million patients in Europe benefit from Nuclear Medicine through the diagnosis and treatment of illnesses such as cancer, but also cardiovascular and neurovascular diseases, with 100 different Nuclear Medicine procedures already approved by regulators⁴.

Nuclear Medicine procedures are used in three different ways:

- **Diagnostic applications**
- **Therapeutic applications**
- **Theranostics applications**

1. Nuclear Medicine diagnostics

Nuclear Medicine uses radiation for diagnostic purposes. Accounting for 90% of Nuclear Medicine procedures⁵, Nuclear Medicine diagnostics allow the diagnosis of various types of disease and assess patients' health status in the post-treatment phase, particularly in oncology where it can play a key role in tumour staging or monitoring of suspected tumour relapse. In addition, the importance of Nuclear Medicine in early detection impacts positively the quality of life and survivorship.

- Images of tissues at the cellular level can be obtained through the detection of radioactivity and converting this into images: radiopharmaceuticals that have the property to recognise and therefore remain in targeted cells (e.g. tumour cells) are administered to the patient, allowing for radioactive substances to concentrate in these specific cells and to therefore localise these cells thanks to the emitted radioactivity (cells undertaking transformation – such as tumours – can easily be differentiated from normal neighbouring cells).
- Special imaging devices, such as SPECT or PET scanners⁶ (using gamma rays), are then able to detect the radiation that is emitted from these zones where the drug is concentrated. Imaging methods in

³ Filipe Boccato Payolla, Radiopharmaceuticals for diagnosis in nuclear medicine: a short review. Eclética Química, vol. 44, no. 3, pp. 11-19, 2019: <https://doi.org/10.26850/1678-4618eqj.v44.3.2019.p11-19>

⁴ https://ec.europa.eu/energy/topics/nuclear-energy/medical-uses-of-radiation_en

⁵ Ibid.

⁶ Single photon emission computed tomography (SPECT) and positron emission tomography (PET) are nuclear medicine imaging techniques which provide detailed metabolic and functional information than cannot be provided with other imaging techniques.

Nuclear Medicine are ideal to identify, localise and evaluate tumours and metastases. Due to its high sensitivity, Nuclear Medicine can detect very limited sources of radioactivity corresponding to very specific biological elements; it is therefore ideal for early detection of a disease and can also be used to follow the efficacy of a therapy.

2. Nuclear Medicine therapeutics

Diseased tissues, cells and organs can also be treated with radiopharmaceuticals, accounting for 10% of Nuclear Medicine procedures, although this share is growing through the latest research resulting in the development of new radiopharmaceuticals⁷.

- Therapeutic applications of Nuclear Medicine can target and kill diseased cells, thanks to the radiation emitted by medical isotopes. The emission of particles kills these cells with a high level of specificity due to strong, but very local and focussed irradiation.
- Thus, the Nuclear Medicine sector offers established and promising opportunities for cancer care and personalised medicine without the side effects of other traditional, non-targeted therapies, like chemotherapy.

3. Nuclear Medicine theranostics

The combination of diagnostic with therapeutic radiopharmaceuticals using the same chemical structure has paved the way for targeted treatments in oncology in the so-called “**theranostic**” approach, which is becoming a gold standard in terms of personalised medicine.

While the concept of theranostics has been successfully applied by Nuclear Medicine physicians in the past decades mainly in the treatment of thyroid disease, recent innovations expanded the potential of theranostics for other applications in the area of neuroendocrine and other cancers (e.g. prostate).

All Nuclear Medicine applications have an excellent safety profile. Indeed, due to the extreme sensitivity of the scanners and the high efficiency of radionuclides, radiopharmaceuticals are applied in tracer amounts, only once or a few times in a patient’s lifetime and are always administered in a controlled environment by a Nuclear Medicine physician. As stated by the European [Directive on Basic Safety Standards](#), the physician always needs to justify its use and remains fully responsible for the procedure. In this respect, thanks to dosimetry principles, Nuclear Medicine is opening the way toward **personalised medicine**.

⁷ Johannes Czernin and Jeremie Calais, 177Lu-PSMA617 and the VISION Trial: One of the Greatest Success Stories in the History of Nuclear Medicine, Journal of Nuclear Medicine June 2021, jnumed.121.262710; DOI: <https://doi.org/10.2967/jnumed.121.262710>

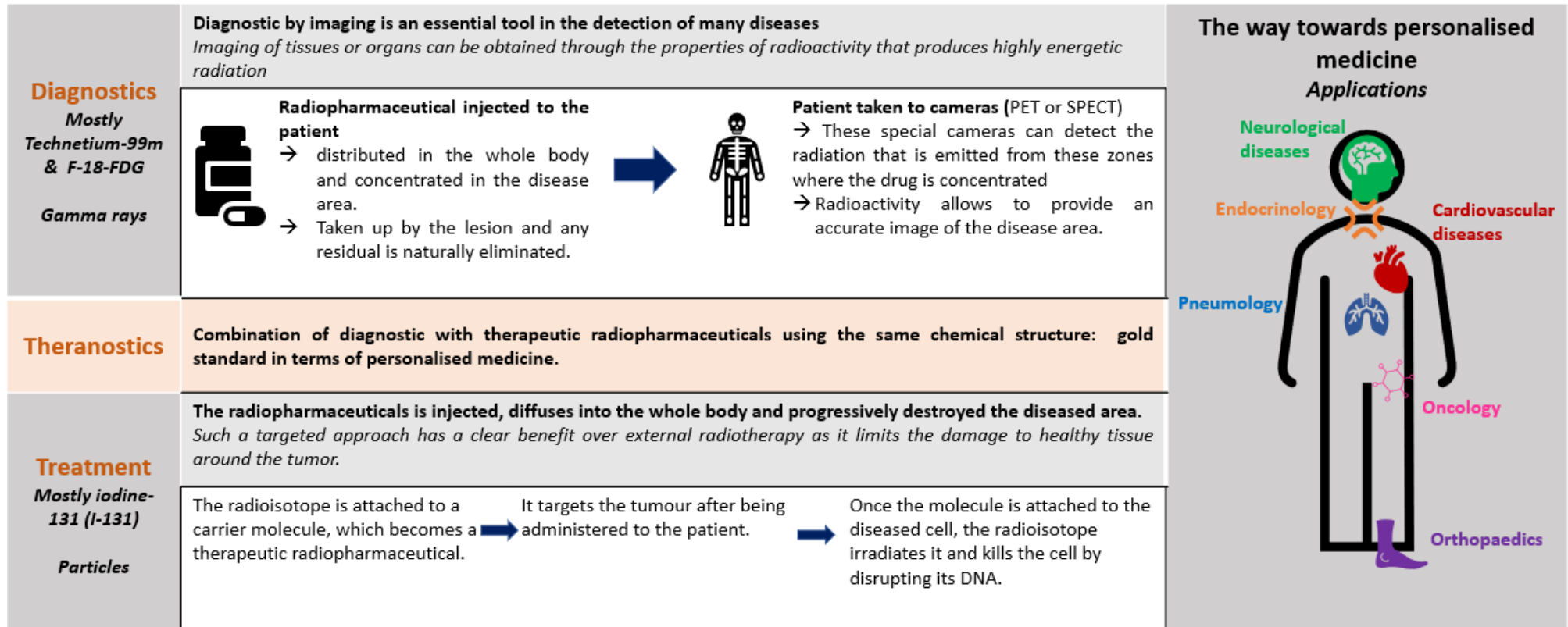


Figure 1 – Applications of Nuclear Medicine

II. Nuclear Medicine in Europe & activities at the European level

1. European production and supply of radiopharmaceuticals

The European Nuclear Medicine sector benefits from a **strong competitive advantage**. Indeed, the major nuclear facilities are based in Europe, ensuring **100% self-sufficiency in the production of medical isotopes in research reactors at present**⁸.

Europe plays a leading role in the supply of medical radioisotopes worldwide because it currently hosts the **largest, most coherent and coordinated supply chain from target manufacturing to medical applications**.

Europe has also an essential role in international research and development efforts and is **helping 30 million patients worldwide every year**⁹, with a long and strong tradition in Nuclear Medicine, being home to some of the biggest radiopharmaceutical companies and benefiting from strong academic and medical centres. **Most Nuclear Medicine research & development comes from European academic centres and research hubs**. Practically all recent major clinical breakthroughs in Nuclear Medicine over the last decade, exemplified by the success of theranostics with Somatostatin analogues for the treatment of neuroendocrine tumours and prostate cancer applications¹⁰, were based on the European inventions, developed with in-house preparations of these innovative products.

2. Nuclear Medicine policy landscape

For a few years, the European Union has increased its involvement in Nuclear Medicine facilities through many projects and policy initiatives. In addition to several funding schemes available, the medical applications of nuclear technology are currently being highly monitored by the European institutions through [SMER programmes](#), [EURATOM supply agency](#) and the [European Observatory on the supply of Medical Radioisotopes](#).

The von der Leyen Commission's specific commitment to health, and especially cancer, offers new opportunities for engagement and support for the Nuclear Medicine sector. In the current political context, the EANM welcomes:

- [The Europe's Beating Cancer Plan](#) and its recognition of Nuclear Medicine as an efficient way to tackle the disease.
- [The SAMIRA Action Plan](#) is a dedicated plan for medical applications of ionising radiation, responding to the need for a more coordinated approach and more dedicated policy attention.
- [The review of the general pharmaceutical legislation](#) will hopefully bring appropriate solutions for the regulatory challenges faced by Nuclear Medicine.

⁸ OECD/NEA (2019), *The Supply of Medical Isotopes: An Economic Diagnosis and Possible Solutions*, OECD Publishing, Paris, <https://doi.org/10.1787/9b326195-en>.

⁹ Ibid.

¹⁰ Gomes Marin JF, Nunes RF, Coutinho AM, Zaniboni EC, Costa LB, Barbosa FG, Queiroz MA, Cerri GG, Buchpiguel CA. Theranostics in Nuclear Medicine: Emerging and Re-emerging Integrated Imaging and Therapies in the Era of Precision Oncology. *Radiographics*. 2020 Oct;40(6):1715-1740. doi: 10.1148/rg.2020200021. PMID: 33001789.

- [EU Roadmap on NCDs](#), focussing on 5 key areas: cardiovascular diseases, diabetes, chronic respiratory diseases, mental health and neurological disorders, health determinants, this initiative will hopefully unlock some opportunities for Nuclear Medicine in these areas.

III. The specificities of Nuclear Medicine & the need for dedicated policy attention

Because of their unique radioactive features, radiopharmaceuticals are a **very special class of medicines** that require specific considerations within regulatory frameworks. Three of the most impactful features of radiopharmaceuticals are related to:

- **Preparation**
- **Availability**
- **Production**

1. **Preparation:** Due to radioactive decay, the vast majority of radiopharmaceuticals used for medical applications have a **very short half-life**: they need to be prepared extemporaneously *in-house*, e.g. in the institution where they are used normally within minutes after preparation, for them not to lose their radioactive potentials. The radioactive nature of the products requires handling and preparation in dedicated facilities complying with radiation protection standards (e.g. Clinical Nuclear Medicine Departments, PET centres) and not in standard hospital pharmacies.
2. **Availability:** The high diversity of radiopharmaceuticals, combined with very patient-specific indications resulting in lower patient volumes, is responsible for the **lack of commercial interest** and, therefore, bottlenecks in the supply chains for some radiopharmaceuticals, which may lead to inequalities in access across European countries.
3. **Production:** It is important to remind that the **Nuclear Medicine sector is not involved in any power applications of nuclear energy**. Many radioisotopes used in Nuclear Medicine are produced in **research reactors**, which are quite different from traditional nuclear reactors: they generate neutrons rather than power and are only used to produce medical radioisotopes used for research. Research reactors are simpler than power reactors and operate at lower temperatures, needing far less fuel. **These are very small-scale installations, and the Nuclear Medicine sector is currently facing regular disturbances of supplies due to the ageing of research reactors. This aging equipment will also negatively affect Europe's leading role as a global supplier and put its self-sustainability at considerable risk.**

IV. Challenges & opportunities for Nuclear Medicine

While the Nuclear Medicine sector is doing its utmost to provide European patients with optimal medical services, harnessing its tremendous potential to tackle diseases such as cancer, Nuclear Medicine still faces several cross-sectoral barriers, leading to **inequalities of access to Nuclear Medicine facilities**.

1. **Challenges in education:** knowledge gaps among healthcare professionals.
2. **Challenges in healthcare infrastructure:** unadopted healthcare systems and hospital infrastructure necessary to deliver Nuclear Medicine services to the patients and supply chain issues.
3. **Regulatory challenges:** not fit for purpose regulations at EU and national level.

1. HEALTHCARE PROFESSIONALS' EDUCATION TO DELIVER HIGH-QUALITY NUCLEAR MEDICINE SERVICES

An **adequately sized and well-trained workforce** is essential to bring Nuclear Medicine to the patients and to ensure the safe and correct implementation of radioactivity-based procedures. Indeed, the preparation and delivery of radiopharmaceuticals in clinical settings requires in-depth knowledge of radiochemistry, imaging technology, radiation safety and automated procedures.

Nuclear Medicine is a **multi-disciplinary medical specialisation** that not only requires a broad level of knowledge in various fields (e.g. anatomy, pathophysiology, (radio)biology, (radio)chemistry, radiation protection etc.) but also a well-educated team of specialists involved in the optimal delivery of Nuclear Medicine services to patients. These include:

- Physicians
- Medical Physics Experts, specialised in various fields e.g. image technologies, radiation protection, dosimetry, data analysis etc.
- Radiopharmacists/radiochemists
- Technologists
- Nurses

a. **Common challenge – a rapidly evolving specialisation**

While Nuclear Medicine professionals are doing their best to ensure safe and efficient delivery of services to patients, common challenges to all specialities involved in Nuclear Medicine might be highlighted.

As the **Nuclear Medicine speciality is highly based on technological advances and is, therefore, a rapidly evolving speciality, lifelong learning is a prerequisite to delivering state-of-the-art care for patients**.

Recent technologic and radiopharmaceutical developments have contributed to tremendous progress in the field of Nuclear Medicine, creating the **need for changes in Nuclear Medicine training programmes**. For example, the introduction of hybrid imaging has justified some adaptations to the Nuclear Medicine training programme to provide sufficient expertise.¹¹ However, Continuing Professional Development¹² schemes for Nuclear Medicine specialists are not yet a reality in most European countries and are not harmonised¹³.

The same holds true for the non-medical specialities working in Nuclear Medicine.

¹¹ Kristoff Muylle and Lorenzo Maffioli, *opt.cit.*

¹² Continuing Professional Development (CPD) is similar to Continuing Medical Education (CME): the purpose is to keep physicians current in their medical practice as part of a life learning commitment.

¹³ A.P. Stefanoyiannis, Structured intercomparison of nuclear medicine physicians' education and training programmes in 12 EANM member-affiliated member countries.

b. Specific challenge for physicians – heterogeneity of training

At present there is **huge heterogeneity amongst training pathways available for physicians, practising Nuclear Medicine ranging from a three-month rotation as part of radiology speciality training to 4 to 5 years under Nuclear Medicine specialist training, leading to significant differences in scope of practices and competencies among Nuclear Medicine physicians**¹⁴.

The advantage of a dedicated training programme is that it covers the entire range of Nuclear Medicine's aspects such as pathophysiology and biology of diseases, therapy-related radiobiology and dosimetry, integration of functional and molecular imaging in the clinical context and patient management¹⁵. When Nuclear Medicine is taught as part of other medical specialities or as an optional subject¹⁶, this will prevent that the next-generation Nuclear Medicine physicians, will have the necessary skills and competence to shape the best conditions for the further development of molecular imaging and radionuclide therapy¹⁷.

This wide diversity of training across Europe can be explained by the many differences with respect to national law on professional activities (the use of unsealed radioactive sources is in most EU countries restricted to Nuclear Medicine physicians, whereas in other countries its use is authorised for other specialities; a double specialisation is allowed in one EU country and prohibited in another).

Consequently, there is a **need to define and harmonise the recommended basic minimum training requirements for Nuclear Medicine as a medical speciality**, to ensure the safety and quality of clinical practice¹⁸.

Similar observations are also true for the non-medical specialities, e.g., radiopharmacists, radiochemists, or medical physics experts, working in Nuclear Medicine.

Without an adequately trained workforce, the healthcare systems might not be able to fully harness the potential of Nuclear Medicine. In this respect, Nuclear Medicine should be recognised as a dedicated speciality in a harmonised way in all European curriculums.

The European Union of Medical Specialists (UEMS) provides **specialisation-based recommendations** for decision makers at the national and European levels to comply with the European Directive (2005/36/EC) establishing the mechanism of automatic mutual recognition of qualifications for medical doctors. The training requirements for Nuclear Medicine, officially endorsed by the Nuclear Medicine community, defined competencies and procedures. These requirements should be regarded as a model and be implemented in all Member States.

Given the wide diversity of national Nuclear Medicine training programmes across Europe and the changing educational needs of the Nuclear Medicine community, the EANM offers a multitude of educational offers for the Nuclear Medicine community through its **European School of Multimodality Imaging and Therapy (ESMIT)**.

¹⁴ Matos, Ana & Massa, Raquel & Lucena, Filipa & Vaz, Tania. (2015). Nuclear medicine technologist education and training in Europe. *Nuclear medicine communications*. 36.

¹⁵ Kristoff Muylle and Lorenzo Maffioli, Nuclear Medicine Training in Europe: "All for One, One for All": *Journal of Nuclear Medicine* December 2017, 58 (12) 1904-1905; DOI: <https://doi.org/10.2967/jnumed.117.201012>

¹⁶ Grammaticos P. Problems especially for nuclear medicine: better to prevent than to treat. *Hell J Nucl Med*. 2005 May-Aug;8(2):93-4. PMID: 16142249.

¹⁷ Kristoff Muylle and Lorenzo Maffioli, *opt.cit*.

¹⁸ IAEA, Training Curriculum for Nuclear Medicine Physicians (2019): <https://www-pub.iaea.org/MTCD/Publications/PDF/TE-1883web.pdf>

Our policy recommendations: The EANM supports:

- **The inclusion of the medical specialisation of Nuclear Medicine**, alongside other medical specialities involved in cancer diagnosis and treatment, **into the Inter-Speciality Cancer Training Programme.**
- **The improvement of Nuclear Medicine education and training standards** through Europe's Beating Cancer Plan and EU4Health Programme. Sharing of best practices through platforms such as European Reference Networks should be supported.
- **The inclusion of Nuclear Medicine into the professional qualification directive** (Directive 2005/36/EC).

2. HEALTHCARE INFRASTRUCTURES TO ACCOMMODATE NUCLEAR MEDICINE FACILITIES

Due to the specific nature of Nuclear Medicine, **particular settings are necessary for the adequate delivery of Nuclear Medicine.**

- **Infrastructure requirements**
- **Supply chains configurations**
- **Radioisotope's shortages**

a. **Infrastructure requirements**

Specific infrastructures are required for Nuclear Medicine departments such as state-of-the art equipment, good manufacturing practise requirements, adequate radiation protection and sufficient storage capacity for nuclear waste. Therefore, Nuclear Medicine services require innovative, comprehensive and well-equipped facilities, leading to significant discrepancies across the Member States in terms of infrastructures and facilities.

Within the European Union, there is currently a **need for improved healthcare infrastructure to accommodate and effectively deliver Nuclear Medicine services.**

b. **Supply chains configurations**

Moreover, Nuclear Medicine procedures require specific **supply chain configurations both in-house as well as externally.**

Indeed, due to the short life of products, the production of radioisotopes requires continuous processing and complex logistics as they cannot be stockpiled. After irradiation in nuclear facilities, radioisotopes undergo a series of processing (separation and purification) in laboratories.

Between irradiation, transformation and delivery to the patients, the timeframe should be as short as possible, and transportation should comply with radioactive requirements. **Therefore, the management of supply chains for radioisotopes is a complex task.** Time constraints in the production and transport of

isotopes and having access to transportation hubs that understand the need for quick and swift handling and processing is key.

Annex 1 – figure 1 represents the complex supply chain for industrial production, while *annex 1 – figure 2* represents the supply chain for in-house production. No matter the production site, **common challenges might be highlighted such as radioactive storage and timeliness**. In addition to these challenges, in-house production also raises the issue of Good Manufacturing practice in small-scale radiopharmacies and marketing authorisations for direct use.

c. Radioisotope's shortages

Finally, as presented in *Annex 2*, the **Nuclear Medicine community is concerned with the Europe-wide issue of aging research reactors**.

While the number of accelerators, i.e. cyclotrons for the production of medical radioisotopes, is increasing, the supply of reactor-produced medical radioisotopes relies on a limited number of research reactors. In the next decade, it is expected that several research reactors will shut down in Europe.

Current research reactors are ageing, expensive to replace and – due to safety and financial issues – a continuing source of public and political debate. Indeed, as **over two thirds of the world's operating research reactors are now over 30 years old**, a crucial need of refurbishing and modernising reactors to ensure a continuous and safe supply of medical radioisotopes has been identified.

Some European countries, such as the Netherlands, are looking for long-term solutions. Indeed, the PALLAS initiative envisions a new medical isotopes reactor to replace the old High Flux Reactor (HFR) in Petten, currently too old for reliable coverage of the radioisotopes supply needs. The arrival of the PALLAS-reactor will enable the Netherlands and the EU to continue to help millions of people and even save lives for the next 50 years, as PALLAS will start in the future with activities to produce medical isotopes for diagnosis, therapy and medical nuclear research. In cooperation with other European initiatives, the PALLAS-project could play an important role in ensuring a European cooperation in securing the security of supply of medical radioisotopes in Europe.

In this respect, the European Association of Nuclear Medicine supports the European Commission's "European Radioisotopes Valley Initiative", aiming at maintaining the EU's position in the supply of medical radioisotopes and helping accelerate the development and introduction of new radioisotopes and production methods.

Our policy recommendations :

- **Healthcare infrastructures should be built, renewed, or maintained**, in order for all European patients to have equal access to dedicated centres with Nuclear Medicine facilities. **The increase in hospital readiness for the delivery of Nuclear Medicine services is fundamental for scaling up their full treatment potential.**
- **Investment in Nuclear Medicine state-of-the-art equipment** should be reinforced when developing the EU Network of National Comprehensive Care Centre and through EU funding schemes (Cohesion Funds).
- **The inclusion of Nuclear Medicine into the Cancer Inequalities Registry** should be supported to have a clear picture of EU discrepancies in terms of Nuclear Medicine facilities.
- The EU needs to develop a **robust supply chain which goes from the research reactor to the patients** and includes the supply of starting materials as well as processing materials.
- The EU should promote **new research reactor capacity**.

3. DESIGNING AN OPTIMAL AND EFFICIENT REGULATORY FRAMEWORK FOR EFFECTIVE AND EQUAL ACCESS TO NUCLEAR MEDICINE

Current European regulations and standards are considering various medical specialities under the same umbrella and therefore do not fit the specific needs of Nuclear Medicine. In this respect, radiopharmaceuticals' development and delivery are hampered by a **complicated and fragmented regulatory environment**.

a. **Challenges with regards to the European Pharmaceutical Legislation (Directive 2001/83)**

Within the European Union, radiopharmaceuticals are mainly regulated under the [Directive 2001/83 EC](#), i.e. the general pharmaceutical legislation. Since the introduction of this directive in 2001, the technological advances and the immense progress in research and development of new radiopharmaceuticals have changed most practices of preparations and delivery. By not fully considering their specificities, the requirements under the Directive 2001/83 EC pose a direct threat to the future availability of radiopharmaceuticals.

Moreover, as the interpretation of the Directive varies widely throughout the European Union, an urgent need for standardisation is required.

In the context of the review of the Directive 2001/83, several issues have been identified by the Nuclear Medicine community:

- ✓ **Marketing Authorisation:** While radiopharmaceuticals can either be prepared through a kit-type procedure or complex preparation, the Directive 2001/83 does not make a clear distinction between both, leading to **the unintended effect that all (radioactive) starting materials for the in-house preparation of radiopharmaceuticals, regardless of the type of preparation they are used in, need a marketing authorisation to be distributed.** Strict interpretation and a lack of commercial interest to provide the necessary radioisotopes and starting materials, **negatively impacts the supply of these starting materials.**
 - ➔ **Revision of existing definitions and a clear distinction between kit-based preparations and complex preparations are to be welcomed.**
- ✓ **Good Manufacturing Practice:** Because radiopharmaceuticals have a very short life and present a low market interest, they often need to be prepared extemporaneously in-house, meaning in the hospital where they are often used within minutes after preparation. However, the same standards of **Good Manufacturing Practice (GMP)** apply for industrial large-scale production and small-scale preparation in hospital or academic settings in some member states, posing important challenges to the delivery of Nuclear Medicine services to patients: this disproportional increase of quality assurance processes which are not fit-for-purpose, is slowing down and hindering innovation. A clear statement that **no industrial GMP** and **no manufacturing authorization** is needed for extemporaneous preparation of radiopharmaceuticals is strongly encouraged.
 - ➔ **Specific provisions** concerning radiopharmaceuticals that are prepared **in-house, noncommercially** outside the usual marketing authorisation track are to be welcomed, defining a dedicated **quality framework for this practice.**

b. Challenges with regards to dosimetry and radiation protection

- ✓ **Dosimetry:** While the [Basic Safety Standards Directive](#) (2013/59/Euratom) rightly states that radiotherapeutic exposure volumes should be patient-centric, personalised and as limited as possible, the European Medicines Agency's marketing authorisations schemes for radiopharmaceuticals most often follow traditional posologies, similar to the ones for chemotherapies. **This discrepancy between both frameworks is leading to complex clinical practices and triggers liability challenges.**
 - ➔ The EANM would welcome **reconciliation between these differing requirements** and would support the establishment of a close working relationship between DG Energy and DG SANTE and the respective European agencies for improved harmonising requirements and regulations for therapeutically used radiopharmaceuticals.
- ✓ **Concentration & dosage:** Similarly, the [European Medicines Agency's guideline on radiopharmaceuticals](#) requests the definition of a single radioactivity concentration. For radiopharmaceuticals with very short half-lives, the adjustment to a defined radioactivity concentration is not relevant since the adjusted concentration value will be valid only for a specific time point. The dosage for the individual patient should exclusively be based on radioactivity measurement at the time of application and not based on the activity concentration declared by the manufacturer.
 - ➔ The EANM, therefore, suggests the **definition of a concentration range instead.**

- ✓ **Radiation protection: Ionising radiation protection requirements**, as already included within the BSS Directive, are a prerequisite but may make Nuclear Medicine services overregulated. As mentioned previously, Nuclear Medicine shows an excellent safety profile: current measures are sufficient, and the further restrictions would ultimately affect the delivery to patients.

c. Challenges with regards to Accessibility & Affordability of Nuclear Medicine services

Differences in market access conditions of Nuclear Medicine services across the European Member States impose a massive access inequality for patients.

- ✓ **Research:** The development of innovative RPs often takes place in radiopharmacies or research centres. In case a new radiopharmaceutical has the potential to be produced and distributed commercially, it then makes its way from there to pharmaceutical companies, taking over from academia and providing funding for further clinical trials. **It is of the utmost importance that specific incentives target academic research and hospital preparations.**
- ✓ **Market access:** Patient access to novel radiopharmaceuticals is limited because of a **lack of commercial interest for many types of radiopharmaceuticals**. Enabling different types of marketing schemes such as standard authorizations provided by EMA will improve access.
- ✓ **Reimbursement policies: Reimbursement and pricing strategies of radiopharmaceuticals** in Europe vary significantly between the Member States. Further studies on appropriate reimbursement as well as European guidelines on reimbursement schemes for radiopharmaceuticals are to be welcomed.

Our policy recommendations:

- **The *Pharma legislation* should be reviewed to be adapted to today's standards**, including non-industrial standards for small scale preparations, marketing authorisations for radiopharmaceuticals and common framework for drugs and radiations.
- Applications of legal requirements between **EMA and EURATOM should be harmonised** to support an easy delivery of Nuclear Medicine to the patients.
- Market access conditions for radiopharmaceuticals should be harmonised across the European Union.

ANNEXES

Annex 1

- Figure 1: Radiopharmaceuticals' supply chain in industrial/large scale preparations
- Figure 2: Radiopharmaceuticals' supply chain for in-house small-scale preparations

Annex 2 – Figure: Contribution to international production of radioisotopes and age of research reactors – comparison between European and the rest of the world.

Radiopharmaceuticals' supply chain in industrial/large-scale preparations (with distribution)

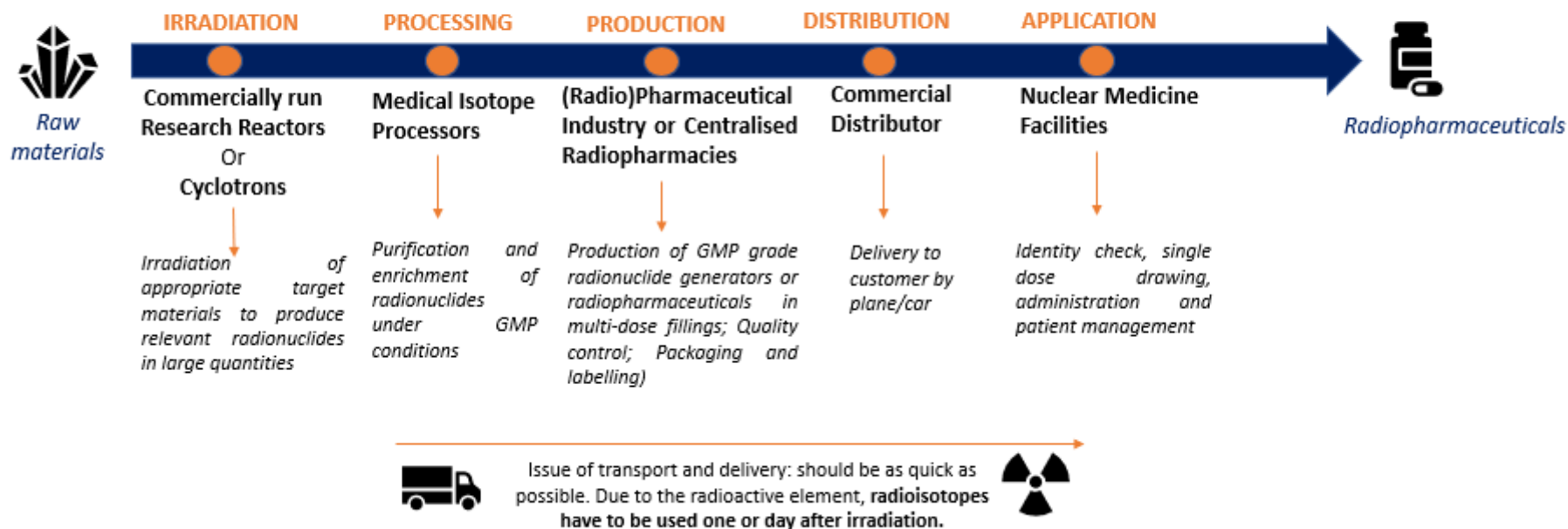


Figure 1: Radiopharmaceuticals' supply chain in industrial/large scale preparations

Radiopharmaceuticals' supply chain for in-house small-scale preparations (without distribution)

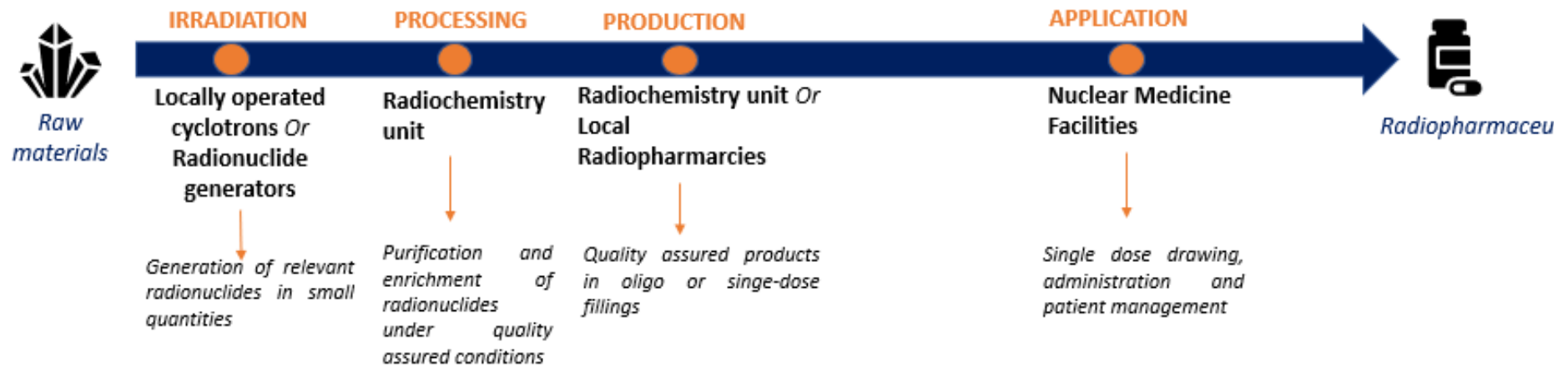
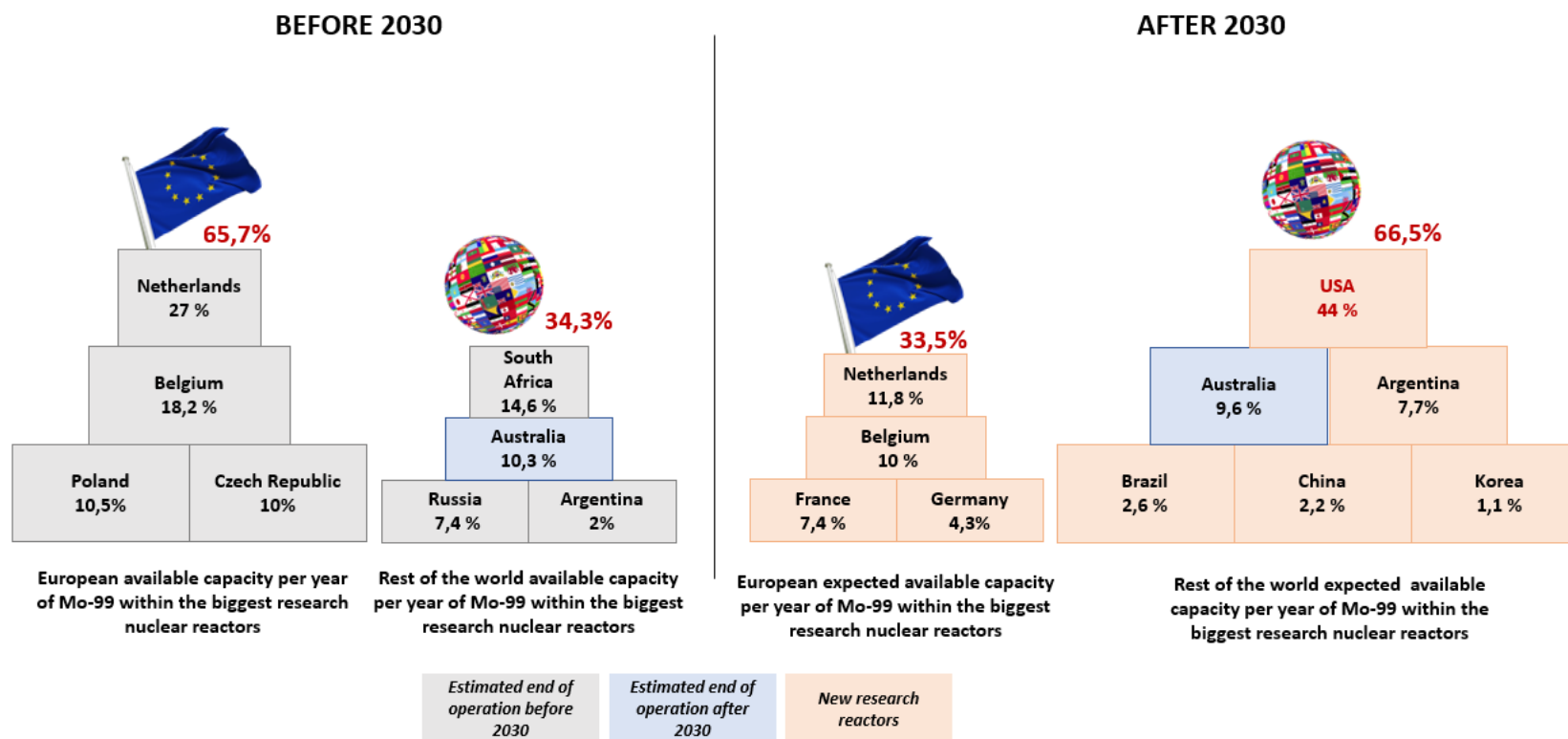


Figure 2: Radiopharmaceuticals' supply chain for in-house small-scale preparations

Shift from a European competitive advantage in radioisotope production to the rest of the world due to aging research reactors in Europe



Source: Technopolis & NucAdvisor, European study on medical, industrial and research applications of nuclear and radiation technology, 2018

Annex 2 – Contribution to international production of radioisotopes and age of research reactors – comparison between Europe and the rest of the world