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Radiopharmaceuticals

EU-IN Horizon Scanning Report

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Glossary

European Medicines Regulatory Network (EMRN): network comprised of the regulatory authorities for medicines in the Member States of the European Economic Area (EEA), the European Medicines Agency (EMA) and the European Commission.

Radiopharmaceuticals: medicinal products which, when ready for use, contain one or more radionuclides, or radioactive isotopes.

Radionuclide generator: Any system incorporating a fixed parent radionuclide from which is produced a daughter radionuclide which is to be obtained by elution or by any other method and used in a radiopharmaceutical.

Radionuclide kit: Any preparation to be reconstituted or combined with radionuclides in the final radiopharmaceutical prior to its administration.

Radionuclide precursor: Any other radionuclide produced for the radiolabelling of another substance prior to administration.

Executive summary

This horizon scanning report describes the current status and key emerging trends in the field of radiopharmaceuticals, explores challenges and opportunities related to their development and suggests recommendations to inform the work of medicines regulators and their stakeholders.

Radiopharmaceuticals are radioactive medicinal products used for both diagnostic and therapeutic purposes. Given their unique nature, radiopharmaceuticals require a regulatory framework and scientific guidelines that address their specific characteristics and challenges. In the European Union, industrially-prepared radiopharmaceuticals require a marketing authorisation and are regulated by the EU Directive 2001/83/EC relating to medicinal products for human use. This legal framework also applies to radionuclide precursors, radionuclide generators and radionuclide kits used for the in-house preparation of radiopharmaceuticals. In addition, radiopharmaceuticals are governed by the EU Directive 14 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation.

Scientific and regulatory guidance are being revised or developed to reflect the specific characteristics of radiopharmaceuticals and to keep pace with advances in the field. Harmonisation should further be ensured across EU legal and regulatory frameworks and between world regions. Radiopharmaceuticals require a broad range of expertise that varies depending on the stage of their lifecycle, whether they are used for diagnosis or therapy, or the targeted indications. Early and ongoing dialogue among stakeholders is crucial to ensure that standards and expectations for the development and approval of radiopharmaceuticals are understood from the outset. This collaboration will also help regulators appreciate the challenges industry faces in meeting these requirements. Supporting initiatives that promote knowledge exchange and shared databases, particularly for long-term safety studies, is needed. Finally, regulators and policy-makers should build on recommendations from expert groups focused on maintaining the supply of radiopharmaceuticals, in order to prevent potential shortages.

1. Rational and objectives of the report

Horizon scanning is the systematic examination of information to detect early signs of scientific and technological developments with previously unknown regulatory challenges or public health opportunities. It aims at enabling the European Medicines Regulatory Network (EMRN, a network comprised of over 50 regulatory authorities for medicines from the 30 European Economic Area countries, the European Medicines Agency and the European Commission), to proactively prepare for forthcoming challenges and opportunities. The European Medicines Agency (EMA) conducts horizon scanning in collaboration with experts and groups such as the EU-Innovation Network (EU-IN). Horizon scanning entails analysing and forecasting the future importance of selected topics and reporting their potential impact on the EMRN over the next 3 to 10 years. The reports include recommendations to adapt the EMRN to minimise regulatory bottlenecks, to support developers and to facilitate innovation reaching patients. Horizon scanning is an underlying action of the strategic goals in the European medicines agencies network strategy 2028[1]. Based on the continual screening of abstracts published by major scientific journals and following a consultation of EMA scientific coordination groups, the topic of radiopharmaceuticals was identified. Both diagnostic and therapeutic radiopharmaceuticals are in the scope of this report.

The report was shared for feedback on all aspects of the report with the EU-IN, the European Specialised Expert Community Oncology – Special interest area 'Radiopharmaceuticals', the drafting group of the guideline 'Clinical evaluation of therapeutic radiopharmaceuticals in Oncology', the Biologics Working Party (BWP), the drafting group of the guideline 'Antibody-based radiopharmaceuticals' and relevant experts of the EMRN.

2. Introduction

Radiopharmaceuticals are medicinal products which, when ready for use, contain one or more radionuclides[2]. Radionuclides, also called radioactive isotopes, dissipate excess energy by spontaneously emitting radiation in the form of alpha particles, beta particles, Auger electrons or gamma rays. Radiopharmaceuticals make use of this radiation to fulfil a diagnostic or therapeutic purpose. Over 50 million nuclear medicine procedures are delivered to patients each year worldwide and 10 million in the EU, 90% of which for diagnostic purposes[3,4]. Unlike radiotherapy which involves an external radiation source, radiopharmaceuticals are administered to the patients, delivering the radiation systemically or locally. Radionuclides used for diagnostic purposes emit gamma rays, a highly penetrating radiation that is detected by positron emission tomography (PET), single-photon emission computed tomography (SPECT) scans or scintigraphy. Radionuclides used for therapeutic purposes emit shorter range particles (alpha particles, beta particles or Auger electrons), resulting in DNA damage and cell death. A single vector molecule linked to a diagnostic radionuclide can also be used to image the therapeutic target before switching to the therapeutic radionuclide. This approach, referred to as 'radiotheranostics', allows for patient selection and dosing.

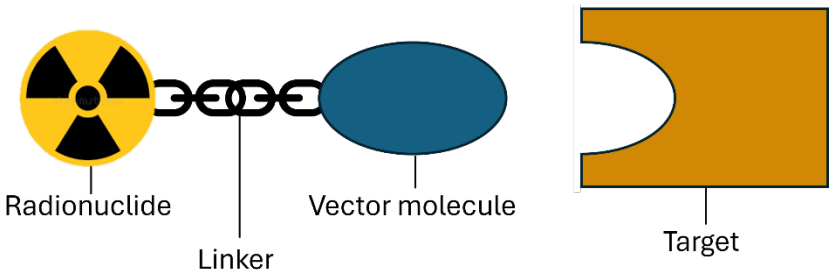

Figure 1: Schematic representation of a ready-to-use radiopharmaceutical

Ready-to-use radiopharmaceuticals are manufactured by linking a radionuclide precursor to a vector molecule, usually via a linker (Figure 1). The vector molecule delivers the radionuclide to the target. In some cases, the radionuclide itself is responsible for both targeting and irradiation. The radioactivity of radiopharmaceuticals decreases with time as a consequence of radioactive decay. Most radionuclides intended for diagnosis have a half-life of a few minutes to a few hours and the final preparation of radiopharmaceuticals must therefore be done shortly before being administered to patients. Therapeutic radiopharmaceuticals typically have a longer half-life and emit a radiation intended to damage tissue. Given their unique nature, radiopharmaceuticals require a regulatory framework that addresses their specific characteristics and challenges.

3. Current status and trends in radiopharmaceuticals development

The use of radiopharmaceuticals has significantly increased in the past two decades, reaching around 10 million diagnostic or treatment procedures per year in the EU in the past years. With continued scientific and technical innovations, the field of radiopharmaceuticals is expected to further expand. The following section exposes the current status of radiopharmaceuticals and upcoming developments.

3.1. Currently approved radiopharmaceuticals

Around 70 radiopharmaceuticals are approved by the Food and Drug Administration (FDA), 80% of which are intended for diagnostic use and 20% for therapeutic use[5]. When focusing on the EU, a total of 20 radiopharmaceuticals has been approved via the centralised procedure, among which five are approved for therapeutic use (oncology) and 15 for diagnostic use (oncology, neurodegenerative disorders and infectious diseases/inflammation). Among these 20 products, four are suitable for use as theranostic, namely edotreotide (after radiolabelling with gallium (^{68}Ga) chloride and lutetium (^{177}Lu) oxodotreotide for the diagnostic and treatment of gastro-entero-pancreatic neuroendocrine tumours, respectively) and gozetotide (after radiolabelling with gallium (^{68}Ga) or lutetium (^{177}Lu) vipivotide tetraxetan for the detection and treatment of castration-resistant prostate cancer, respectively). Other radiopharmaceuticals are approved via the national route and/or used outside the marketing authorisation route.

3.2. Upcoming developments: EMA forecast, clinical trials and early developers-EMA interactions

3.2.1. EMA forecast of upcoming centralised marketing authorisation to 2027

An EMA forecast of centralised marketing authorisation applications planned to be submitted until 2027 reports three applications for radiopharmaceuticals among which two antineoplastic and immunomodulating agents (ATC code L) and one product classified under ATC code V (various).

3.2.2. Clinical trial landscape

Research on radiopharmaceuticals is evolving significantly, with about 50 clinical trials initiated in 2015 versus more than 100 in 2024[6]. This trend is even clearer when focusing on therapeutic radiopharmaceuticals, with 3 planned or ongoing clinical trials in 2018 versus 80 by half 2025.

3.2.3. Early EMA-developers interactions

To better map the current ongoing developments that are approaching marketing application readiness, a search was performed for five types of early-stage EMA-developers interactions held between January 2020 and December 2024 on the topic of radiopharmaceuticals: ITF briefing meetings (ITF BM), Portfolio Technology meetings (PTM, previously Business Pipeline meetings), Paediatric Investigation Plans (PIP) applications, PRIME and Scientific Advice (SA) procedures. The following EMA interactions on the development of radiopharmaceuticals were found:

- 1 ITF BM out of 168 held
- 2 PTM out of 94 PTMs held
- 1 PRIME granted
- 23 SA procedures out of 3181 initiated
- 0 PIP

Non-product-specific interactions (ITF BM and PTM) were used to discuss the production of novel radionuclides and the development of radiotheranostics pairs more than once. When focusing on the product-specific procedures SA and PRIME, 10 of those were dedicated to therapeutic applications, 13 to diagnostic applications, and one to theranostics. Indications were oncology (n=20), neurology (n=2), cardiovascular (n=1) and infectious diseases (n=1). Various radionuclides were incorporated in the final medicinal product, with a majority of ^{177}Lu (n=5), ^{68}Ga (n=4) and ^{18}F (n=4), but also ^{64}Cu(n=2), ^{89}Zr(n=2), ^{224}Ra (n=2), ^{225}Ac (n=1), ^{124}I (n=1), ^{131}I (n=1) and ^{99m}Tc (n=1).

3.2.4. Areas of innovation

Bibliography, white papers and other sources of information highlight a number of areas of innovation in the field of radiopharmaceuticals:

- **Expanding therapeutic indications beyond oncology,** e.g. inflammatory, neurodegenerative and cardiovascular diseases.

- **Novel radionuclides** are being developed for medical use. In particular, alpha-emitters are raising interest as they exhibit a limited range in tissue and a high linear energy transfer, allowing them to induce irreversible double DNA-strand breaks and limited damage to the surrounding tissue [7,8]. Among those, ^{225}Ac generates significant interest due to a high linear energy transfer and the four net alpha particles emitted per decay. Other novel radionuclides of interest include ^{64}Cu, ^{67}Cu and Terbium isotopes (^{149}Tb, ^{152}Tb, ^{155}Tb, ^{161}Tb)[9] .
- **Targeted radiotherapy** using new delivery mechanisms, e.g. cell-surface molecules and targets located in the tumour microenvironment, and subcellular targeting to reach intracellular molecules residing in organelles[10–12].
- **Development of conjugating tools or linkers** allowing to develop vector-agnostic radionuclides. E.g. linkers allowing to bind a variety of vector molecules (mAbs, small molecules or peptides) to a radionuclide.
- **Favorable pKpD properties and pretargeting approach** to increase uptake and retention of radiopharmaceuticals at the target site.
- **Combination of radiopharmaceuticals with other treatments**: A number of preclinical studies and early clinical trials include combinations with immunotherapies, chemotherapy and radiosensitisers [10,11].
- Growing availability of **novel hybrid imaging technologies** for better cancer detection and monitoring[10].
- **Increased production of radionuclides**. Novel methods are under investigation to improve the production and availability of radionuclides, such as electron beams to generate clinical-grade doses radionuclides [11].

4. Current regulatory status and initiatives

4.1. Regulatory framework

Radiopharmaceuticals are regulated by three European legislations:

1) The EU Directive 2001/83/EC relating to medicinal products for human use

The European pharmaceutical legislation requires a marketing authorisation to be obtained for industrially-prepared radiopharmaceuticals as well as for radionuclide precursors, radionuclide generators and radionuclide kits. In line with Article 7 of Directive 2001/83/EC, a marketing authorisation is not required for radiopharmaceuticals prepared at the time of use by an authorised person or establishment, in accordance with national legislation, exclusively from authorised radionuclide generators, radionuclide kits or radionuclide precursors and according to the manufacturer's instructions.

The use of approved radiopharmaceuticals should always be the first option in clinical practice. However due to the limited availability of approved radiopharmaceuticals for certain indications, radiopharmaceuticals are often produced in-house outside the marketing authorisation process[13]. These exemptions derive from the definitions in Art 3.1 and 3.2 of Directive 2001/83/ EC, the so-called "magistral" or "officinal" preparations, and from Article 5.1 of Directive 2001/83/ EC, which aims to meet specific needs. In these cases, they are regulated at the national level.

2) The EU Regulation No 536/2014 on clinical trials on medicinal products for human use

3) The EU Directive 14 2013/59/Euratom laying down basic safety standards for protection against the dangers arising from exposure to ionising radiation

The European legislation on radiation protection lays down the basic safety standards for the health protection of the general public, workers and patients. It also establishes the requirements for the addition of radioactive substances to medicinal products and for the importation of these medicinal products.

4.2. EU Guidelines

4.2.1. Main EMA guidelines

- **Guideline on the non-clinical requirements for radiopharmaceuticals (2018)**

Scope: Non-clinical testing required for the non-radioactive part of radiopharmaceuticals in the context of applications for marketing authorisations or clinical trials.

Status: Up-to-date.

- **Guideline on radiopharmaceuticals (2008)**

Scope: Specific quality requirements to be submitted in relation to radiopharmaceuticals, in the context of applications for marketing authorisation or variations to authorised medicinal products.

Status: revised Guideline on quality of radiopharmaceuticals open for public consultation until April 2026.

- **Guideline on radiopharmaceuticals based on monoclonal antibody (1992)**

Scope: Specific quality requirements to be submitted in relation to radiopharmaceuticals based on monoclonal antibodies, in the context of applications for marketing authorisation or variations to authorised medicinal products.

Status: Under revision, finalization of the revision planned for Q4 2026[14].

- **Guideline on the clinical evaluation of therapeutic radiopharmaceuticals in Oncology (upcoming)**

Scope: specific guidance on how the key concepts from the pharmaceutical legislation (2001/83/EC) and the radiation protection legislation (Directive 14 2013/59/Euratom) should be applied to the clinical development of therapeutic radiopharmaceuticals for marketing authorisation applications. This guideline will complement the more general guideline on the clinical evaluation of anticancer medicinal products.

Status: Consultation of the Concept paper on clinical evaluation of therapeutic radiopharmaceuticals in Oncology ended in January 2025. The concept paper aims to identify aspects that are specific for therapeutic radiopharmaceuticals and that are not addressed in the revised guideline on the clinical evaluation of anticancer medicinal products.

- **Guideline on clinical evaluation of diagnostic agents and its appendix 1 (2009)**

Scope: Principles for the clinical evaluation of diagnostic agents administered *in vivo*, including diagnostic radiopharmaceuticals. The appendix 1 is to be read in conjunction with the general part. Imaging agents refer to both radiopharmaceuticals and contrast agents.

Status: Revision planned, Concept paper on the revision of the guideline on clinical evaluation of diagnostic agents and its appendix 1 on imaging agents open for consultation until April 2026.

4.2.2. Main EU and international guidelines and regulatory documents beyond EMA guidelines:

- **Ph. Eur. 11.8, 0125 (07/2025) on "Radiopharmaceutical preparations"**
- **Ph. Eur. 11.0, 2902 (07/2022) on "Chemical precursors for radiopharmaceutical preparations"**
- **Ph. Eur. 11.0, 51900 (04/2022) on "Extemporaneous preparation of radiopharmaceuticals"**
- **Volume 4 Good manufacturing practice (GMP) Guidelines, Annex 3: Manufacture of radiopharmaceuticals (2008)**

  Status: Revision planned, Concept Paper on the revision of Annex 3 of the guidelines on Good Manufacturing Practice for Radiopharmaceuticals (public consultation closed on February 2026).

- **PIC/S Annex 3: Good practices for the manufacture of radiopharmaceuticals**

  Status: Revision planned, Concept Paper on the revision of Annex 3 of the guidelines on Good Manufacturing Practice for Radiopharmaceuticals (public consultation closed on February 2026).

- **TRS 1025 - Annex 2: IAEA - WHO good manufacturing practices for radiopharmaceutical products**

4.3. EU policies and initiatives

Below are listed the main initiatives and working groups established at the EU level:

- **EU Observatory for the Supply of Medicinal Radioisotopes** - established in 2012 by the European Commission and the industry organisation for Europe, it aims to monitor, assess and support the supply of medical radioisotopes in the EU with a particular focus on Molybdenum-99/Technetium-99m, a radioisotope used in 80% of nuclear medicine diagnostics[15].
- **Euratom Supply Agency** – One of the Agency's missions is to facilitate the continued and equitable supply of medical radioisotopes. Annual work programmes and activity reports are publicly available: Planning and reporting - European Commission.
- **Strategic Agenda for Medical Ionising Radiation Applications (SAMIRA) action plan** - EU initiative adopted in 2021 under the Europe's Beating Cancer Plan as a response to the EU Council's conclusion from 24 May 2019 on non-power nuclear and radiological technologies and applications. The SAMIRA action plan defines 3 priority actions:

  - Ensuring medical radioisotope supply security through the European Radioisotope Valley Initiative;

- Advancing quality and safety in medical ionising radiation applications through the European Initiative on Quality and Safety of Medical Applications;

- Fostering innovation and technology development by establishing a research roadmap for medical applications involving ionising radiation.

- **Regulation (EU) 2022/123 of the European Parliament and of the Council on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices**[16] – Entered into force beginning of 2022, it reinforces the role of the EMA in crisis preparedness and management for medicinal products and medical devices and set the monitoring of medicine shortages under EMA's remit. In order to ensure a robust and coordinated response to major events and public health emergencies, the legislation established an Executive Steering Group on Shortages and Safety of Medicinal Products, also known as the Medicines Shortages Steering Group (MSSG, see bullet point below).

- **Medicines Shortages Steering Group (MSSG)** - Established in 2022 by EMA, in line with EMA's extended mandate to ensure preparedness and action related to the EU supply of medicinal products during crises. In March 2025, the MSSG adopted multistakeholder recommendations to address the vulnerabilities in the supply chain of radiopharmaceuticals[17]. The MSSG role in the coordination and management of supply and availability challenges will be further extended in the **proposed revised EU pharmaceutical legislation** and **proposed Critical Medicines Act.**

- **Union list of critical medicines** – The first version of the Union list of critical medicines was published by EMA, Heads of Medicines Agencies and the European Commission in December 2023, and first updated in December 2024. An annual review process is ongoing. The list contains active substances of medicines for human use considered critical for the smooth functioning of healthcare systems across the EU/ European Economic Area, for which continuity of supply is a priority and shortages should be avoided. Certain radiopharmaceuticals are included on the list: Union list of critical medicines | European Medicines Agency (EMA) The MSSG is developing a methodology to identify vulnerabilities in the supply chains of medicines on the Union list, in anticipation of the proposed pharmaceutical legislation. Once identified, MSSG may issue recommendations to address those vulnerabilities and support the secure supply of those medicines. This may also be complemented by certain provisions of the proposed Critical Medicines Act.

- **Medicine Shortages Single Point of Contact (SPOC) Working Party** – Formally established in 2022 by EMA, this group monitors and reports events, including shortages, that could affect the supply of medicines in EU. The SPOC Working Party also provides recommendations to the MSSG on all matters related to the monitoring and management of medicines shortages and other medicine availability issues affecting human and veterinary medicines: Medicine Shortages Single Point of Contact (SPOC) Working Party | European Medicines Agency (EMA)

- **Council conclusions on the security of supply of radioisotopes for medical use** - drafted in 2024, call for 5 key priority actions aimed at the EC and the EMRN:

  - Ensuring EU's global leadership role in the supply of medical radioisotopes;

- Monitoring and forecasting the demand and supply for all relevant medical radioisotopes;

- Fostering research and innovation on topics related to medical radioisotopes and other medical radiological technologies;

- Assessing and developing critical skills;

- Assessing the framework for transporting radioisotopes for medical use in the EU member states.

- **The Critical Medicines Alliance** – consultative mechanism set up in 2024 to bring together stakeholders from EU Member States (national competent authorities and ministers of health), industry, civil society and the scientific community to strengthen the supply of critical medicines in the EU, including radiopharmaceuticals. A Strategic Report, published in 2025, outlines key findings and recommendations to enhance the security and resilience of the EU's Critical Medicines supply chains[18].
- **Critical Medicines Act** – EU Regulation on a framework for strengthening the availability and security of supply of critical medicinal products and accessibility of, medicinal products of common interest, proposed by the European Commission in March 2025[19]. This includes the possibility for designation of **Strategic Projects** for critical medicines or their ingredients so that they benefit from easier access to funding and fast-tracked procedures.
- **SPARC-Europe** - Launched in 2020, this European policy initiative aims to build a comprehensive policy framework for radioligand therapies[20].

4.4. Key fundings and tenders

Fundings on radiopharmaceuticals include but are not limited to:

- Preparatory activities to support Implementation of quality and Safety of Medical ionising radiation Applications (PrISMA) is a joint action that aims to support and sustain developments addressing quality and safety issues related to medical applications of ionising radiation across all EU Member States.
- SIMPLERAD | EIBIR aims to harmonise EU regulatory requirements on the therapeutic use of radiopharmaceuticals, with a focus on dosimetry-based treatment optimisation, patient release, education and training.
- Radioligand Therapy Academy aims to promote education on radioligand therapies in Europe and to bridge the educational gap among healthcare professionals.
- CLAUD-IT focuses on organising clinical audit campaigns as a tool to improve quality and safety of medical applications of ionising radiation, bringing together 13 beneficiaries and one affiliated entity from 10 EU Member States.
- MARLIN: Harmonising incident learning systems for enhanced patient safety in radiology
- EU-REST aims to collect and analyse data on workforce availability, education, and training needs to ensure quality and safety of medical applications involving ionising radiation in the EU
- IHI fundings on the development of radiotheranostics (e.g. Thera4Care, Illuminate, Accelerate)

5. Challenges

5.1. Regulatory and guidance gaps

- **Compartmentalisation of the European pharmaceutical legislation and the European legislation on radiation protection**

  The two legislations need alignment, e.g. in terms of terminology and on the need of a dosimetry-based treatment for all patients.

  Opportunities:

  - Ensure dialogue and collaboration between radiation protection authorities and medicines agencies;

  - Provide guidance on the implementation of the European legislation on radiation protection and on interdependencies between the EU pharmaceutical legislations and the EU radiation protection legislation to ensure that both regulatory areas are respected.

- **Lack of harmonisation in the interpretation and implementation of EU Regulations for radiopharmaceuticals across Member States**

  This lack of harmonisation firstly affects small scale production of radiopharmaceuticals. When prepared extemporaneously to meet specific needs or patients, radiopharmaceuticals, in particular PET radiopharmaceuticals, can be administered as magistral preparations, officinal preparations or via the compassionate use route depending on the EU Member State. These different legal routes can lead to the administration of radiopharmaceuticals produced using non-authorised kits, generators and radionuclide precursors, and to various degrees of compliance with the Good Manufacturing Practices across EU Member States [13]. Other EU-wide variations include inconsistent criteria for patient release and radioactive waste management.

  Opportunities:

  - Continue working towards a harmonised regulation of the radiopharmaceutical small-scale preparations and the implementation of Good Manufacturing Practices. Special attention should be given to PET radiopharmaceuticals.

  - Ensure consistency in the assessment of radiopharmaceuticals across the EU Member States via the ongoing revision of the guidelines on diagnostic and therapeutic radiopharmaceuticals.

  - Provide guidance on the implementation of the EU radiation protection legislation.

5.2. Scientific

- **Limited experience in therapeutic radiopharmaceuticals and radiotheranostics**

  There is limited experience with the development and marketing authorisation of therapeutic radiopharmaceuticals, and even less with theranostic pairs, and regulatory guidance on the required clinical data is missing.

  Opportunities:

  - Engage with developers to capture and address, if possible, the challenges in preparing an adequate clinical dossier for therapeutic radiopharmaceuticals and theranostic pairs.

- Include guidance on the development of theranostic pairs within the framework of the ongoing revision of the EMA guideline on clinical evaluation of diagnostic agents (including the Appendix 1 on diagnostic imaging).

- **Therapeutic radiopharmaceuticals remain second- or third-line therapies, resulting in poor understanding of their long-term toxicity**

  Therapeutic radiopharmaceuticals generally remain a second- or third-line therapy in clinical practice, the first choice remaining chemotherapy or radiotherapy for treatment. Long-term toxicity is being investigated in first-line treatments, when patients have a relatively long life expectancy. For later-line therapies administered to patients with limited survival expectancy, tumour shrinkage and symptom control might be prioritised above the risk of long-term toxicity. As a result, the long-term toxicity of radiopharmaceuticals is under-evaluated or not understood. In particular, the long-term toxicity of radiopharmaceuticals in the organs receiving the highest radiation dose is lacking, preventing the establishment of the maximal absorbed dose limit. Other important data include mutagenicity and long-term carcinogenicity studies, which are usually omitted despite the carcinogen and mutagen potential of radiation.

  Opportunities:

  - The conduction of long-term toxicity studies in the development and post-approval of therapeutic radiopharmaceuticals has been integrated in the Concept paper on clinical evaluation of therapeutic radiopharmaceuticals in Oncology. As it appears that, similar to other cancer treatments, the long term toxicity of radiopharmaceuticals depends on the previous lines of treatments, a correlation between previous therapies and toxicity should also be investigated.

  - Work towards the establishment of databases gathering both dosimetry data and long-term toxicity in order to assess the toxicity associated with each radiation dose.

- **Difficulty for novel radionuclides to meet regulatory requirements in terms of purity specifications**

  For certain novel radionuclides, impurity levels need to be balanced with radiation exposure. Besides, definition of purity levels of some novel radionuclides can be challenging due to complex decay chain.

  Opportunity:

  Adopt a risk-based approach depending on the radionuclide, the prescribed indication and the radioactive dose.

- **Limited access to approved radiopharmaceuticals**

  The characteristics of radiopharmaceuticals, in particular the short shelf life of diagnostic radiopharmaceuticals, explain that only a limited number of ready-to-use radiopharmaceuticals are commercialised.

  Opportunity:

  - Incentivise companies to develop kits for diagnostic radiopharmaceutical preparation. While there are many radionuclide precursors and generators authorised, kits allowing radiolabelling could improve access in regions far away from manufacturing facilities.

5.3. Lack of availability, capacity and capabilities

- **Radionuclide supply shortage**

  As reflected in the MSSG recommendations mentioned above, the use of radiopharmaceuticals is steadily increasing while the manufacturing capacity remains limited. Disruption in the supply of radionuclides, in particular of α-particle-emitting radionuclides and rare earth radionuclides, represent the main vulnerability in the manufacturing of radiopharmaceuticals and can severely impact patient care and clinical outcomes[17].

  Opportunities:

  - Ensure communication and collaboration between the actors of the supply chain (healthcare professionals, wholesalers, manufacturers and regulators) to monitor and anticipate potential shortages through the SPOC WP, as recommended by the MSSG.

  - Ensure a reliable supply of source materials for radionuclide production that allows to meet patients' demand as recommended by the MSSG.

  - Promote research on isotope production methods to improve the availability of radionuclides.

- **Production of radiopharmaceuticals is concentrated in only a few member states**

  In addition to the lack of harmonisation on the small-scale production of radiopharmaceuticals highlighted above, important variations exist in the availability of medical cyclotrons. This is problematic in view of the short half-life of diagnostic radionuclides.

  Opportunities:

  - Develop reliable transportation and distribution networks capable of ensuring the safe and timely delivery of these agents.

  - Promoting the decentralised production of radionuclides, for instance establishing and using cyclotrons within hospitals, would be particularly beneficial as it would yield a higher radioactivity per radionuclide produced and would reduce unwanted exposure of workers and the public.

  - Promote research on manufacturing methods to improve the local production and availability of radionuclides.

- **Lack of expertise and multidisciplinary collaboration**

  On the regulatory side, expertise varies across EU Member States due to limited in-house expertise in some national competent authorities and challenges in accessing external expertise, often stemming from conflicts of interest for academic practitioners. Nuclear medicines physicians and treatment facilities to administer the radiopharmaceuticals are also limited in some EU Member States[21]. In particular, many nuclear medicine centres face a shortage of medical physics expertise for therapy planning and response assessment and limited physician knowledge of dosimetry. Finally, multidisciplinary knowledge is needed to develop, regulate and use radiopharmaceuticals, allying pharmacists and radiopharmacists, chemists, nuclear physicians, medical physicists, oncologists, radiobiologists and metrology experts. Another issue lays on the limited regulatory knowledge of certain developers, which hampers the development of regulatory-compliant radiopharmaceuticals.

Opportunities:

- Ensure access to training to regulators on diagnostic radiopharmaceuticals, therapeutic radiopharmaceuticals and theranostic approaches.

- Ensure cross-domain expertise on radiopharmaceuticals on the regulatory side, e.g. by establishing a European Specialised Expert Community (ESEC) or Special Interest Area (SIA) group with specialists in radiopharmacy, medical physics, clinical nuclear medicine and with clinical assessors experienced in the assessment of diagnostic and therapeutic radiopharmaceuticals.

- Increase multidisciplinary collaboration to gain expertise from oncologists, nuclear medicine doctors, medical physics, radiopharmacists, etc. For instance, collaboration between academic, clinical centers and professional societies to foster the establishment of clinical data registries and databases would be beneficial.

- Train researchers and developers, in particular academics, to ensure awareness on the need to follow regulatory requirements, and increase the visibility of early advice mechanisms at both the national and EMA levels.

- The resources are limited for radiopharmacist and facilitating the release process may be useful, especially for preparations occurring early in mornings and at multi sites. Leverage regarding remote release may be envisaged.

6. Recommendations

6.1. Changes to the regulatory framework

- Update or create guidance where necessary. In particular, in view of the recent scientific developments in the field of biomarkers and diagnostics and evolved regulatory thinking, the need to create guidance on diagnostic radiopharmaceuticals is needed.

- Consider the establishment of a EU-wide working group to develop a harmonised approach to the regulation of in-house radiopharmaceuticals and to the implementation of Good Manufacturing Practices.

- Promote bilateral dialogue with other international regulatory agencies to share knowledge and ensure harmonisation.

- Consider the creation of a working group with EU medicines regulators and radiological protection regulators to provide aligned guidance on radiation safety and pharmaceutical regulations in the EU. While the risk acceptability between workers and patients are distinct, guidance to define the need for patient-specific dosimetry is required.

6.2. Knowledge exchange with stakeholders

- Engage with pharmaceutical industry to exchange on our standards and expectations for radiopharmaceuticals approval, and understand the challenges faced by industry in meeting these expectations.

- Build joint groups bringing together pharmaceutical industry, academia and health care professionals to discuss how to fast track the development of diagnostic and therapeutic radiopharmaceuticals applied to new diseases or conditions.
- Promote the creation of databases to gather data generated by clinicians, researchers and companies to access long term safety data on therapeutic radiopharmaceuticals. Consider leveraging DARWIN-EU to run a feasibility assessment and possibly conduct long-term safety studies.

6.3. Need for development of additional knowledge / expertise within the regulatory network or access to such knowledge / expertise via external experts

- Build an EU-wide community of experts for radiopharmaceuticals with multidisciplinary backgrounds and across topic expertise to share knowledge, provide training and facilitate the implementation and application of the regulatory framework and provide inputs on the draft guidelines. Expertise in both therapeutic and diagnostic radiopharmaceuticals is needed.

6.4. Secure manufacturing and supply chain of radiopharmaceuticals

- Follow those recommendations set out in the Recommendations of the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) and by the SPOC WP to ensure a robust response to the supply of radiopharmaceuticals in the EU[17,22].

Bibliography

1. *Seizing Opportunities in a Changing Medicines Landscape: The European Medicines Agencies Network Strategy 2028*. (Publications Office, Luxembourg, 2025). doi:10.2809/8994389.
2. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use.
3. World Nuclear Association. Radioisotopes in Medicine.
4. Results of the targeted consultation on European Radioisotope Valley Initiative (ERVI).
5. Zhang, S. *et al.* Radiopharmaceuticals and their applications in medicine. *Signal Transduct Target Ther* **10**, 1 (2025).
6. Kinley, A. Clinical Trial Trends: Radiopharmaceuticals.
7. Baidoo, K. E., Yong, K. & Brechbiel, M. W. Molecular pathways: targeted α-particle radiation therapy. *Clin Cancer Res* **19**, 530–537 (2013).
8. Harrison, C. Biopharma dives into tumor-seeking radioactive drugs. *Nat Biotechnol* **43**, 653–656 (2025).
9. Radzina, M. *et al.* Questionnaire on industrial and clinical key players and needs. (2022).
10. Bodei, L., Herrmann, K., Schöder, H., Scott, A. M. & Lewis, J. S. Radiotheranostics in oncology: current challenges and emerging opportunities. *Nat Rev Clin Oncol* **19**, 534–550 (2022).
11. Lapi, S. E. *et al.* Recent advances and impending challenges for the radiopharmaceutical sciences in oncology. *Lancet Oncol* **25**, e236–e249 (2024).
12. Bavelaar, B. M., Lee, B. Q., Gill, M. R., Falzone, N. & Vallis, K. A. Subcellular Targeting of Theranostic Radionuclides. *Front Pharmacol* **9**, 996 (2018).
13. Moya, E., Cerrato, C., Bedoya, L. M. & Guerra, J. A. Radiopharmaceutical small-scale preparation in Europe: will we be able to harmonize the situation? *EJNMMI Radiopharm Chem* **9**, 64 (2024).
14. European Medicines Agency. 3-year work plan for the Biologics Working Party. (2025).
15. European Observatory on the supply of medical radioisotopes: mission statement.
16. European Commission. REGULATION (EU) 2022/123 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 25 January 2022 on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices. (2022).
17. European Medicines Agency. Recommendations of the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG) to address vulnerabilities in the supply chain of radiopharmaceuticals. (2025).
18. Critical Medicines Alliance. STRATEGIC REPORT OF THE CRITICAL MEDICINES ALLIANCE.
19. Proposal for a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL laying a framework for strengthening the availability and security of supply of critical medicinal products as well as the availability of, and accessibility of, medicinal products of common interest, and amending Regulation (EU) 2024/795.

20. SPARC EUROPE - Stakeholder Political Alliance For Radioligand Cancer Therapies. https://sparc-europe.com/.

21. Hricak, H. *et al.* Medical imaging and nuclear medicine: a Lancet Oncology Commission. *Lancet Oncol* **22**, e136–e172 (2021).

22. European Medicines Agency. MSSG recommendations to strengthen supply chains of critical medicinal products.