



## Deliverable 5.1

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# Questionnaire on industrial and clinical key players and needs



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## Abbreviations, Participant short names

### Abbreviations

|       |                                   |
|-------|-----------------------------------|
| MR    | Magnetic resonance imaging        |
| NM    | Nuclear Medicine                  |
| PET   | Positron emission tomography      |
| RND   | Radionuclide                      |
| SPECT | Single-photon emission tomography |

### Participant short names

|            |   |
|------------|---|
| CERN       | European organization for nuclear research  |
| NPL        | National Physical Laboratory  |
| PSI        | Paul Scherrer Institut  |
| CEA        | Commissariat à l'énergie atomique et aux énergies alternatives                        |
| IST-ID     | Associação do Instituto Superior Técnico para a IST-ID Investigação e Desenvolvimento |
| DTU        | Danmarks Tekniske Universitet   |
| CHUV       | Centre hospitalier universitaire vaudois  |
| GANIL      | Grand Accélérateur National d'Ions Lourds   |
| SCK CEN    | Studiecentrum voor Kernenergie / Centre d'étude de l'énergie nucléaire                |
| ARRONAX    | Groupement d'intérêt public ARRONAX   |
| ESS        | European spallation source ERIC   |
| TUM        | Klinikum rechts der Isar der technischen Universität München                          |
| KULeuven   | Katholieke Universiteit Leuven  |
| MedAustron | Entwicklungs- und Betriebsgesellschaft MedAustron GmbH                                |
| SCIPROM    | SCIPROM Sàrl  |
| MUI        | Medizinische Universität Innsbruck  |
| ILL        | Institut Max von Laue - Paul Langevin   |
| JRC        | JRC -Joint Research Centre- European Commission                                       |
| NCBJ       | Narodowe Centrum Badań Jądrowych  |
| GSI        | GSI Helmholtzzentrum für Schwerionenforschung GmbH                                    |
| LU         | Latvijas Universitāte   |
| INFN       | Istituto Nazionale di Fisica Nucleare   |
| UiO        | Universitetet i Oslo  |

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## Summary

This document is a summary of responses received from the public known European industrial manufacturing and research institution and clinical facility representatives. The responses were given to the PRISMAP Consortium questionnaire disseminated in January-August 2022, approaching radionuclides and radiopharmaceutical **manufacturers**, research institutions and clinical end users in nuclear medicine, with the aim to identify potential stakeholders in the industrial and clinical communities interested by a coordinated approach in Europe such as PRISMAP.

The summary from PRISMAP questionnaire stratifies the feedback from 114 respondents: radionuclide and radiopharmaceutical producers, research facilities and preclinical/clinical end users. In addition, it gives an insight into the location and capabilities of the main isotope-producing cyclotron facilities, many of which are known from the IAEA cyclotron database [2]). The questionnaire was offered with an opportunity to make new research and international collaboration partners, where all parties could benefit from harmonised supply and legislation procedures, expanding network and distribution routes, and subsequently gain visibility within the PRISMAP User Forum map at [www.prismap.eu](http://www.prismap.eu). The questionnaire was focused on the radionuclide use in medicine with emphasis on future needs for specific radionuclides and possible research developments with awareness of legislation, logistics and involved personnel education challenges and future perspectives.

The data allow to draw a map with the presently collected data in the Europe. The majority of responses come from Western Europe, most notably the Benelux, France and Italy. More emphasis will be needed for reaching out to responders from South-East Europe regions.

The most often used emerging imaging technologies at respondent's institutions are SPECT/CT software advances (quantification, 3D dynamics etc.) and PET new generation cameras with extended axial field of view, optimised image and dose reduction. Advances in radionuclide therapy are also reported, where radionuclides that would be of interest for use in the research institutions within next 2-5 years are <sup>64</sup>Cu (50%), Terbium radionuclide "family" (37%) and alpha emitters, such as <sup>225</sup>Ac (67%).

The data also confirmed needed improvements for preclinical/clinical users - unified licensing and registration of available radionuclides and kits in Europe, specified equipment/technology (e.g., collimators etc.), database of available radionuclide suppliers with geographic location and information about transport and logistics networks in the Europe.

The data found common aspects from all producer-facility respondents: the biggest challenge for the producers is the availability of target materials, which goes hand-in-hand with their purity/enrichment grade. Increased demand and focus on higher isotopic purity, as well as current geopolitical developments strain the supply chain, leading to price increases and availability issues. Ultimately these factors can limit the future output of some of our novel products.

From the responses we can confirm the necessity of PRISMAP not only as a web-based entry platform for the production and dispatch of non-conventional radionuclides, but also as a long-term platform for aiding an advancement in, at the moment, emerging radionuclide distribution and their use in research and clinical nuclear medicine. 86% of the respondents expressed that the PRISMAP Consortium efforts would bring benefit in their research and development activities and elaborated on their needs for higher availability of radiopharmaceuticals, sharing the new research protocols across countries, to produce more reliable and stronger evidence data and speeding up the implementation of new radiotracers in clinical practice and collaboration with producers of emerging radionuclides.

This document also contains the existing portfolio and the list of the facilities involved in the production and research of the radionuclides and radiopharmaceuticals to develop access and collaboration pathways to translational research facilities for the industrial and clinical communities (see Appendix Nr. 2).

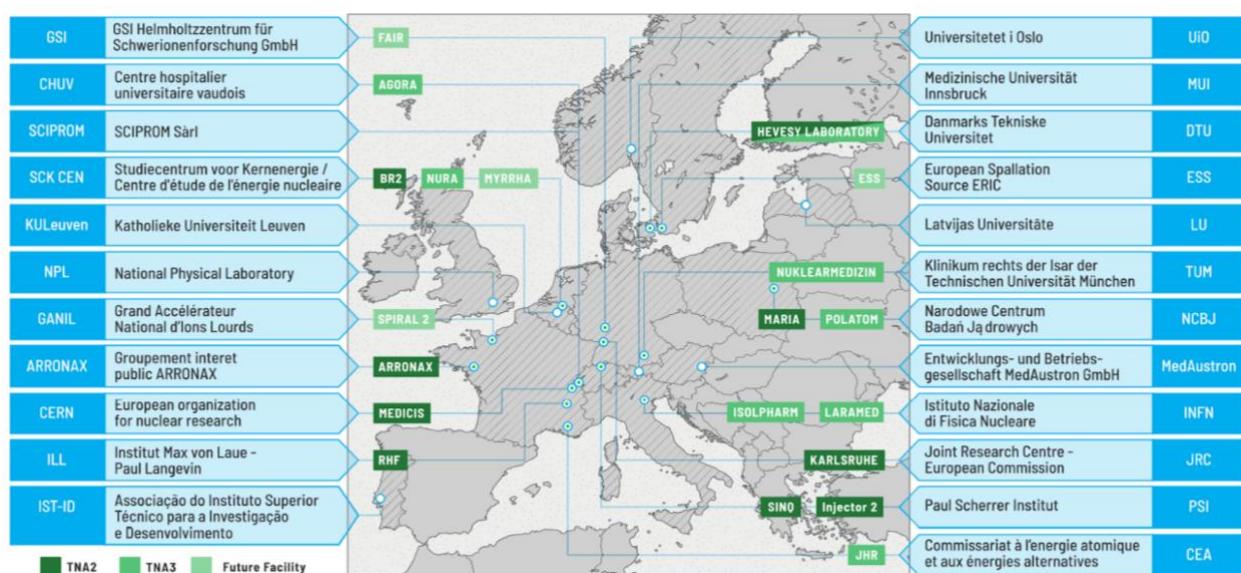
The information collected will be used to evolve the PRISMAP common interface WP1-TNA1 and it will naturally interface with WP2-TNA2 and WP3-TNA3 services to evolve the services to meet the industrial and

clinical researcher needs. The feedback for further development will be collected through the Industrial Board and the User Forum, to foster the industrial and clinical collaboration. Identified needs of industrial and clinical end-users will enrich and help to update the PRISMAP product and service portfolio accordingly with the aim to unify the currently scattered industrial and clinical landscape in nuclear medicine.

## 1. Introduction

PRISMAP – The European medical isotope programme: Production of high purity isotopes by mass separation proposes to federate a consortium of the key European intense neutron sources, isotope mass separation facilities and high-power accelerators and cyclotrons, with leading biomedical research institutes and hospitals active in the translation of the emerging radionuclides into medical diagnosis and treatment. PRISMAP will create a single-entry point for a fragmented user community distributed amongst universities, research centres, industry and hospitals, in a similar way as how the National Isotope Development Centre NIDC, supported by the Department of Energy (DOE), has provided radionuclide sources for users in the USA.

PRISMAP brings together a consortium of 23 beneficiaries from 13 countries, one European Research Laboratory and an International Organisation (see Figure 1). It further receives support from leading associations and institutions in the field such as the European Association of Nuclear Medicine (EANM) and the International Atomic Energy Agency (IAEA).



**Figure 1. PRISMAP Consortium**

The PRISMAP work package WP5-TNA2 takes care of the questionnaire on industrial and clinical key players and their needs. The PRISMAP Consortium questionnaire was disseminated in January-September 2022. The aim of the survey was to identify potential stakeholders in the industrial, research and clinical communities in the context of PRISMAP and investigate the needs of industrial, scientific and clinical end users in nuclear medicine and also analyse current facility profiles, geographic location, capabilities, licensing, logistics, future research and development perspectives, challenges and needs for collaboration and improvement.

## 2. The European medical radionuclides programme PRISMAP Questionnaire

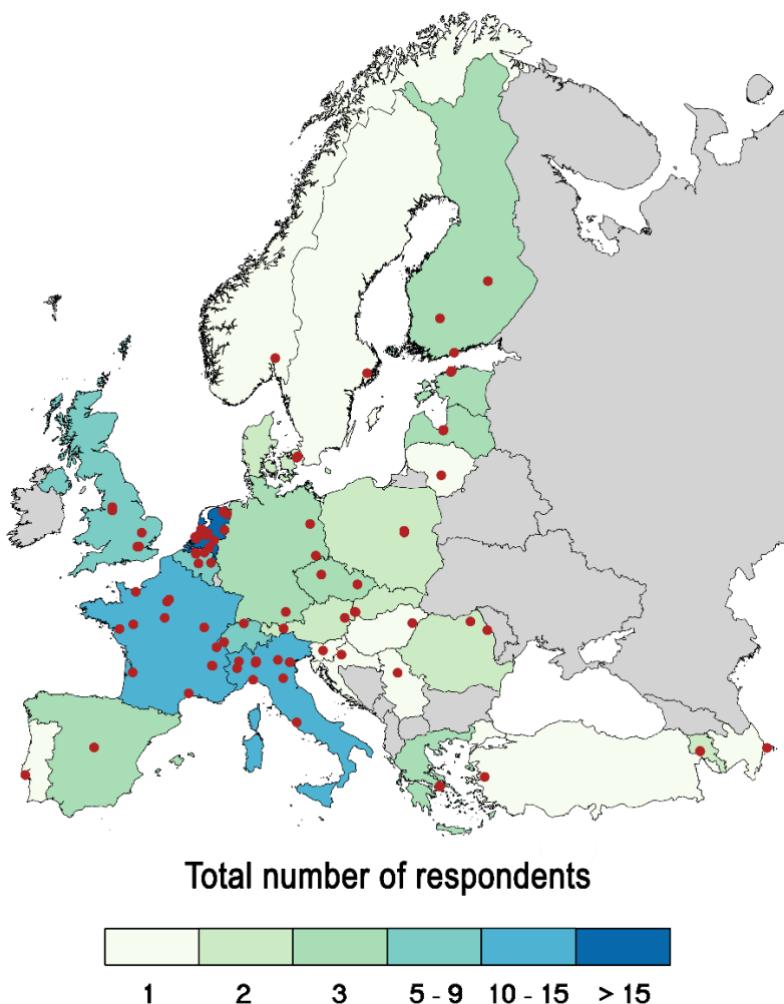
### 2.1 General aspects

#### 2.1.1 Respondents

A total of 114 respondents from 104 companies and institutions completed the survey. Respondent institutions were from 30 countries - 20 from Netherlands, 12 from France, 12 from Italy, 6 from United

Kingdom, 6 from Belgium, 5 from Switzerland, 3 each from Germany, Greece, Finland, Estonia, Czechia, Spain and Latvia, 2 each from Denmark, Austria, Romania, Armenia, Slovakia and Poland and 1 each from Sweden, Portugal, Turkey, Norway, Slovenia, Cyprus, Hungary, Azerbaijan, Croatia, Serbia, Lithuania and 1 from International Organisation across Switzerland-French border. The number of respondents may be amplified in some countries because several respondents filled the survey from the same institution, complementing the data or filling in different fields of interest - either as a manufacturer, researcher and end-user.

The survey responses covered most of the PRISMAP consortium member countries. The greatest activity comes from central Europe, but more emphasis is needed for reaching out to responders from South-East countries (see Figure 2)

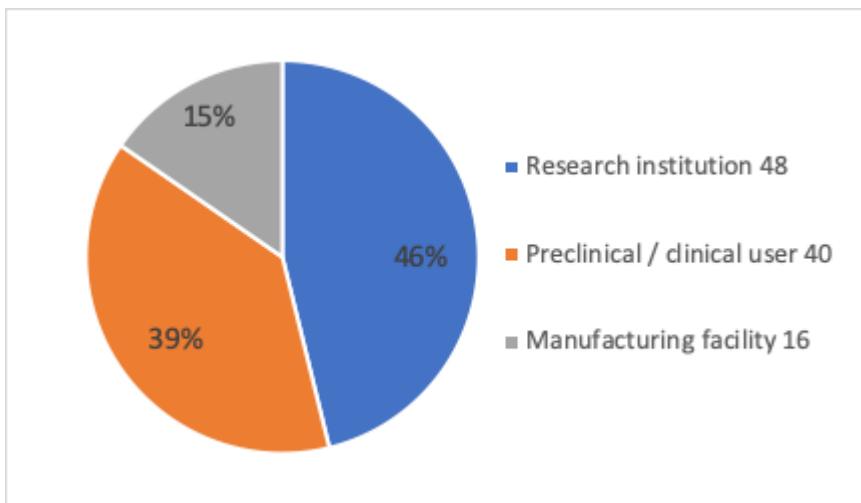


**Figure 2. Map of respondent countries**

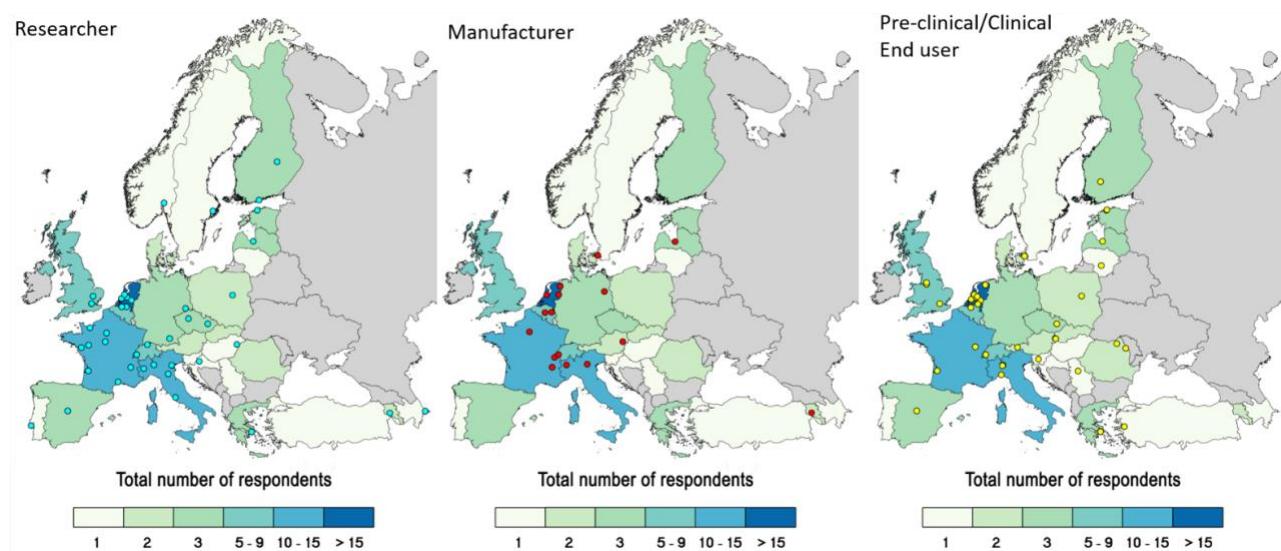
### 2.1.2 General profile

Forty-eight research institutions were represented (25 from universities, 15 from public laboratories other than universities, 1 from a private institution, 7 from other institutions - national public institution collaborations, University Medical Centre, Institute for Cancer Research, National Research Institution, etc.).

40 respondent institutions are preclinical/clinical users (22 from clinical hospitals, 10 from research institution-hospital collaborations, 4 from preclinical research institutions, 2 CRO companies, 1 private clinic and 1 manufacturer and ambulatory clinical nuclear medicine centre). 16 respondents represent manufacturing facilities (4 radionuclide production and 12 radionuclide/radiopharmaceutical production facilities), see Figure 3 and Figure 4.



**Figure 3. General profile of questionnaire respondents**



**Figure 4. Questionnaire respondent map with representation by institutional type**

### 2.1.3 Research field and interests

The main research areas of respondents were - radiopharmaceutical synthesis and development (40 respondents), pre-clinical studies (34 respondents), radiochemistry (32 respondents) radionuclide/radiopharmaceutical QC and analysis (26 respondents), radionuclide production (23 respondents), clinical trials and studies (19 respondents), radiopharmaceutical precursor development (16 respondents), radionuclide purification (15 respondents), radionuclide production target development (14 respondents) and radionuclide characterization and calibration (12 respondents).

Some other, more specific research interests were mentioned, such as neutron scattering and nuclear physics; radionuclide radiobiology; nanodosimetry; medical physics; synthesis of porous materials and characterization of solid materials by various tools (NMR, IR, Raman spectroscopy, DRX); biological effects of radionuclide therapies; policy-supporting research; studies for policy makers (availability of medical radionuclides); social sciences (patient perception); breast and vascular imaging and interventions; safety culture; clinical audit of medical exposures, dose measurements and modelling. Also included are a laboratory that has collaboration with the facility for Positron physics. A Pelletron low energy 3 MeV single-ended electrostatic accelerator plus a 1.5 MeV deuteron accelerator that can produce neutrons for material studies and radionuclide production was especially pointed out.

## 2.1.4 Research infrastructure

The most often mentioned equipment that respondents have for research purposes were - animal SPECT/CT or SPECT/MR (32 respondents), animal PET/CT or PET/MR (30 respondents), experimental long term animal facilities after radiation exposure (20 respondents), PET, PET/CT or PET/MR and SPECT, SPECT/CT or SPECT/MR (17 respondents each). Most popular SPECT, SPECT/CT and PET, PET/CT animal systems were Triumph, Siemens Simbya, Vetor 5 MILABS, Bruker and GE. In their practices, respondents also use planar scintigraphy (7 respondents), gamma spectrometers (4 respondents) but based on the research interest the actual users for such equipment must be higher. Alpha spectrometers (4 respondents) and autoradiography (3 respondents) were also mentioned.

Other equipment that participants mentioned were: LSC systems, detectors for ionising radiation measurements, dosimetry calculation systems, variable energy cyclotrons, hot-cells, high purity Germanium gamma detectors, e.g., for NAA and PGAA characterisation of samples or characterisation of radionuclides. Also identified was equipment for molecular and cell biology analysis, biochemistry, physico-chemistry, formulation, pharmaceutical sciences, ICP-MS/OES, dose calibrators and separation panels. More exotic equipment listed was the Vector 6\_IMB Versatile Emission Computed Tomography system (VECTor) that enables simultaneous sub-millimetre imaging of single-photon and positron-emitting radiolabelled molecules.

In addition, the need for and use of Radiochemical Laboratories; Physics measurements Laboratories; micro-SPECT-PET-CT, small animal SPECT-PET-CT, IBA Cyclotron, MRI 3T and 7T, Radiochemical Laboratory; Physics measurements Laboratories and Siemens CT/PET Flow; FlowMotion; Discovery MI PET CT system, which is state-of-the art 5 ring 2022 installation.

Animal imaging facility with PET/CT, small animal MR and dose calculation and modelling tools, small animal imaging and radionuclide therapy facility, precision X-ray irradiator for animals, radio-HPLCs, radio-TLCs, gamma counters, phosphor imager, synthetic chemistry labs, radiochemistry laboratories and QC labs. Equipment for in-vitro studies, Endoradiotherapy in small animals intended, MRI (7T, 3T, 1T), optical imager, hot ICPMS, hot TIMS, LSC counters, optical/fluorescent imaging, radiochemistry laboratories, tissue and cell culture labs, 68Ge/68Ga generator, digital autoradiography equipment (e.g., Fujifilm FLA-5100 and Ai4R BeaQuant), scintillation counters, gamma counters, such as (Wizard) for ex vivo biodistribution, Microbeta for autoradiography and NMR. Irradiation facilities with 60Co source and X-ray source, radiopharmaceutical production laboratories, animal optical imaging equipment and animal ultrasound were also indicated.

## 2.1.5 End user questionnaire

A total of 40 respondent institutions of this survey were preclinical/clinical users. 19 of the respondents conducted both preclinical and clinical studies, 15 respondents only clinical studies, 2 respondents - only preclinical studies and 4 respondents - other types of studies, such as medical physics, drug biodistribution, drug selection, fundamental (analytical methods), medical research. 15 respondents represent personal/individual assessments, 8 respondents - private institutions, 7 respondents - governmental institutions, 4 respondents - non-governmental, national society, 2 respondents - non-governmental, international society, 4 respondents - other (Medical Cluster (non-governmental non-profit organisation), University Medical Centre). 34 of respondents provide diagnostic, therapeutic and theranostic services, 2 respondents - both diagnostic, therapeutic services, but not theranostic. 4 respondents provide just diagnostic services and one respondent - just theranostic services.

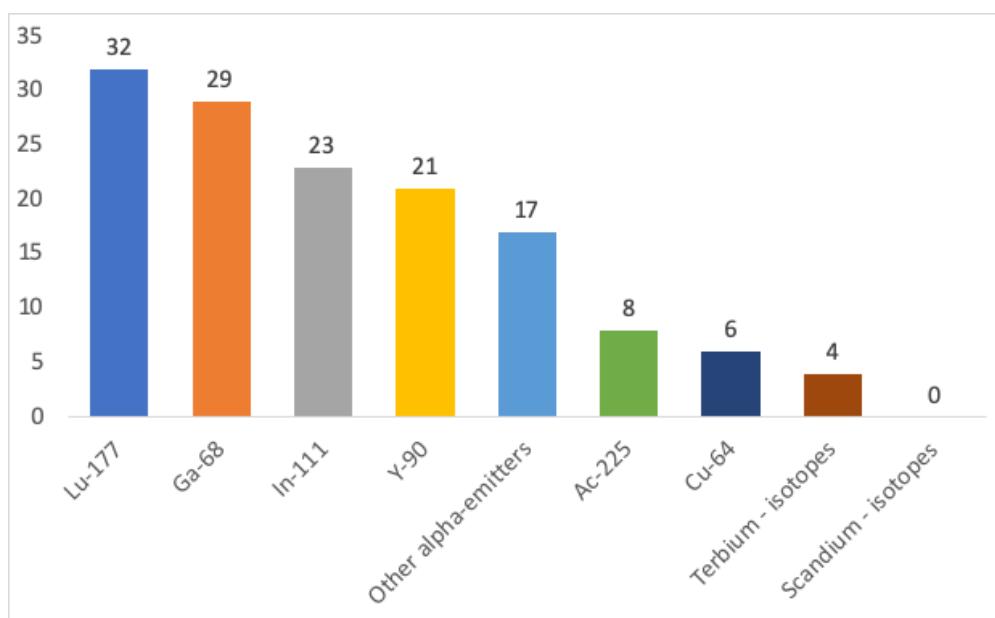
For routine clinical practice 36 respondents have PET, PET/CT or PET/MR, 33 respondents - SPECT, SPECT/CT or SPECT/MR, 28 respondents - planar scintigraphy, 16 respondents - animal PET/CT or PET/MR, 13 respondents - experimental long term animal facilities for radionuclide therapy studies and 12 respondents - animal SPECT or SPECT/CT. The most popular models were SIEMENS, GE-Healthcare, Philips Vereos, Siemens biograph mct flow PET/CT, GE DMI (2 scanner), GE discovery 860, GE discovery 830, Siemens Symbia T6 and Intevo Bold, PET/CT Biograph 64, Biograph Vision MILabs: Vector.

Frequently used emerging technologies that respondents' institutions have: SPECT/CT software advances (quantification, 3D dynamics etc.) (21 respondents), PET new generation cameras with extended axial field of view, optimised image and dose reduction (20 respondents). Respondents also mentioned Artificial Intelligence in Nuclear Medicine (7 respondents), Dedicated cardiac SPECT camera (6 respondents), and CZT cameras (4 respondents).

When questioned about emerging imaging technologies that respondents would like to work with in their facilities in 2-5 years, similar answers were obtained - Artificial Intelligence in Nuclear Medicine - 23 respondents, PET new generation camera with extended axial field of view, optimised image and dose reduction - 20 respondents, SPECT/CT software advances (quantification, 3D dynamics etc.) - 13 respondents, CZT camera - 8 respondents, dedicated cardiac SPECT camera - 3 respondents, PEM - positron emission mammography and Dedicated cardiac PET camera - 2 respondents each.

All respondents perform studies in oncology, while inflammation studies were reported from 32 respondents, cardiology - 31 respondents, neurology - 30 respondents, endocrinology - 29 respondents, nephrology - 24 respondents, pulmonology - 23 respondents, traumatology-orthopaedics - 22 respondents. A similar scene was seen about studies which respondent's facility plan to implement within the next 2-5 years. Most abundant answers were oncology (23 respondents), inflammation (20 respondents), neurology and cardiology (16 respondents each), endocrinology (13 respondents) and pulmonology and traumatology/orthopaedics (12 respondents each).

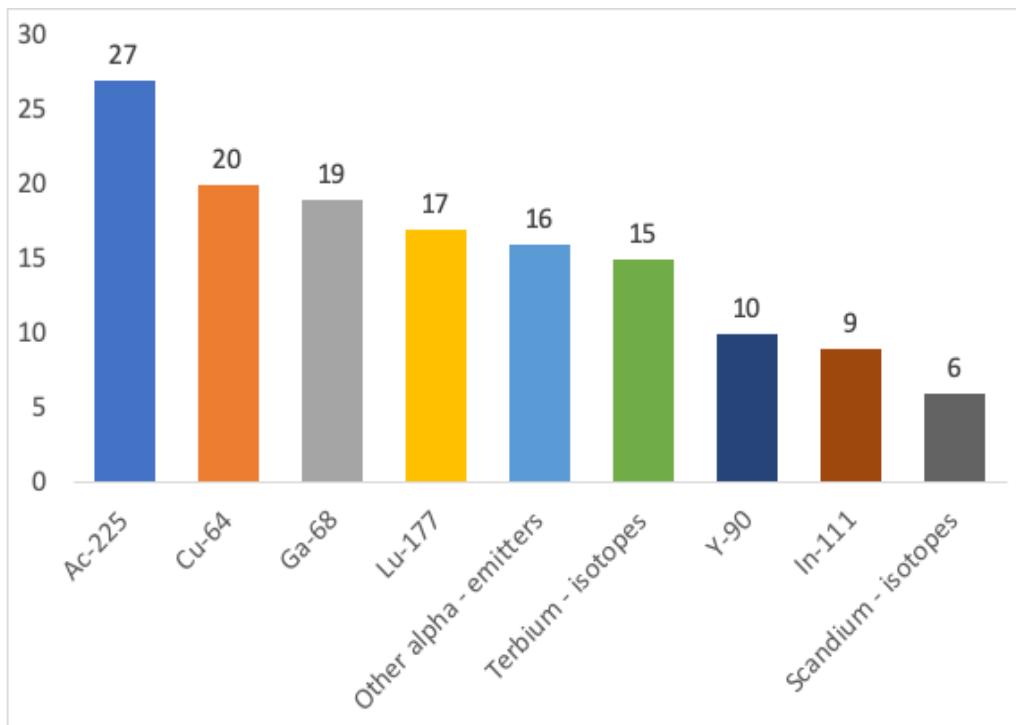
Nuclear medicine clinics, preclinical and clinical users currently use the following non-conventional radionuclides in their studies:  $^{177}\text{Lu}$  (32 respondents),  $^{68}\text{Ga}$  (29 respondents),  $^{111}\text{In}$  (23 respondents),  $^{90}\text{Y}$  (21 respondents), other alpha emitters (17 respondents),  $^{225}\text{Ac}$  (8 respondents),  $^{64}\text{Cu}$  (6 respondents) and Terbium isotopes (4 respondents) (see Figure 5). Other isotopes mentioned were  $^{223}\text{Ra}$ ,  $^{89}\text{Zr}$ ,  $^{166}\text{Ho}$ ,  $^{131}\text{I}$ ,  $^{123}\text{I}$ ,  $^{212}\text{Pb}$ ,  $^{89}\text{Sr}$  and  $^{153}\text{Sm}$ . Some of the radionuclides of terbium and scandium that are very promising, are not yet utilised in the clinical environment because of their poor availability at the time of the questionnaire.



**Figure 5. Novel radionuclides used by end users**

Novel radionuclides that respondents would be interested to use in the next 2-5 years were  $^{225}\text{Ac}$  (27 respondents),  $^{64}\text{Cu}$  (20 respondents),  $^{68}\text{Ga}$  (19 respondents),  $^{177}\text{Lu}$  (17 respondents), and other alpha emitters (16 respondents) and Terbium isotopes (15 respondents). See Figure 6 for other radionuclides that end users would be interested in. Here we can conclude that the demand for  $^{225}\text{Ac}$  and the terbium "family" from

research institutes will increase significantly in the following years. The foreseen application possibilities and an increasing demand for these radionuclides also point out the low availability of them at the moment, either by production capacity or required amounts or purity grade.



**Figure 6. Radionuclides that respondents would be interested to use in the next 2-5 years**

If we look at the current radionuclide use for theranostics, the most popular pairs were  $^{123}\text{I}$ - $^{131}\text{I}$  as Iodine (23 respondents),  $[^{68}\text{Ga}]$  Ga- DOTA-peptides -  $[^{177}\text{Lu}]$  Lu-DOTA-peptides (22 respondents),  $[^{64}\text{Cu}]$  Cu-peptides-  $[^{177}\text{Lu}]$  Lu-peptides (20 respondents),  $^{99}\text{mTc}$ - $^{223}\text{RaCl}_2$  for skeletal metastases (19 respondents),  $[^{18}\text{F}]$  PSMA -  $[^{177}\text{Lu}]$  Lu-PSMA (17 respondents) and  $[^{123}\text{I}]$  mIBG –  $[^{131}\text{I}]$ -mIBG (11 respondents).

Most often mentioned theranostic pairs that respondent would be willing to use in the future were  $[^{64}\text{Cu}]$  Cu-peptides- $[^{177}\text{Lu}]$  Lu-peptides (17 respondents),  $[^{18}\text{F}]$  PSMA -  $[^{177}\text{Lu}]$  Lu-PSMA (16 respondents),  $[^{68}\text{Ga}]$  Ga- DOTA-peptides -  $[^{177}\text{Lu}]$  Lu-DOTA-peptides (14 respondents),  $[^{68}\text{Ga}]$  Ga-PSMA -  $[^{177}\text{Lu}]$  Lu-PSMA (13 respondents) and  $[^{18}\text{F}]$  NaF –  $^{223}\text{RaCl}_2$  for skeletal metastases (8 respondents).

We observed that none (except for iodine radiopharmaceuticals) of the current responder institutions yet are interested in possibilities of “matched pair” from terbium and scandium radionuclides in the near future, this probably reflect the still insufficient pre-clinical data and/or availability of such radionuclides.

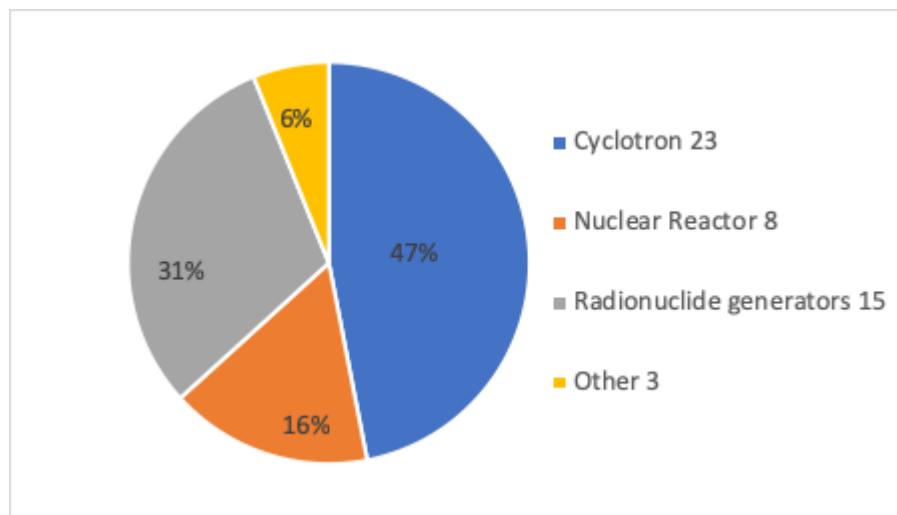
Improvements that preclinical/clinical users need for daily practice are unified licensing and registration of available radionuclides and kits in Europe (32 respondents), information about transport and logistics network in Europe (22 respondents), database of available radionuclides and the geographic location of the supply site (20 respondents), and some specified equipment/technologies (e.g., collimators etc.) (18 respondents). On-site training with the visit of international experts is also a wish (16 respondents) as is outsourced crucial training for technical personnel (13 respondents) and medical doctors (12 respondents).

There is a necessity to send patients to other countries for specified nuclear medicine examinations and/or treatment procedures due to unavailability of the specific radiopharmaceuticals (17 respondents), a lack of reimbursement by the national healthcare system (9 respondents) and unavailable radionuclide for radiopharmaceutical production (7 respondents).

## 2.2 Radionuclide production

Out of 64 respondents from research institutions and manufacturing facilities, 31 respondent companies or institutions produce radionuclides. Most respondents listed multiple methods and equipment of radionuclide production. For radionuclide production respondents mainly use cyclotrons (23 respondents), radionuclide generators (15 respondents) and nuclear reactors (8 respondents).

3 respondents indicated radionuclide production equipment, such as synchrotron high energy proton beam dump which in Europe is uniquely used by CERN-MEDICIS, natural thorium and accelerator driven subcritical neutron sources. None of the surveyed respondents indicated any other source for radionuclide production such as linear accelerators. See Figure 7.



**Figure 7. Radionuclide production source**

Main radionuclides produced by the respondents are  $^{68}\text{Ga}$  (15 respondents),  $^{64}\text{Cu}$  (8 respondents),  $^{99\text{m}}\text{Tc}$  (9 respondents),  $^{11}\text{C}$  (8 respondents),  $^{18}\text{F}$  (11 respondents),  $^{161}\text{Tb}$  (7 respondents),  $^{177}\text{Lu}$  (7 respondents),  $^{67}\text{Cu}$  (6 respondents),  $^{89}\text{Zr}$  (5 respondents),  $^{44}\text{Sc}$  (2 respondents),  $^{123}\text{I}$  (4 respondents),  $^{124}\text{I}$  (4 respondents),  $^{188}\text{Re}$  (4 respondents),  $^{90}\text{Y}$  (3 respondents),  $^{225}\text{Ac}$  (3 respondents),  $^{52}\text{Mn}$  (4 respondents),  $^{67}\text{Ga}$  (3 respondents),  $^{165}\text{Er}$  (3 respondents),  $^{223}\text{Ra}$  (2 respondents). See Table 1 for production of radionuclides by countries.

As it is proven by the end-user questionnaire there is amongst the research user community an increasing demand for the alpha emitting radionuclide  $^{225}\text{Ac}$ , which has been indicated as being produced by three of the survey respondents. PRISMAP consortium members offer  $^{225}\text{Ac}$  to the users from two sites - JRC Karlsruhe and CERN-MEDICIS. The aim to indicate more sites that would offer such increasing demand for radionuclides is still an open objective with high importance.

**Table 1. Production of radionuclides**

| Nr. | Respondent   | Radionuclides   |
|-----|--|---|
| 1   | Denmark Technical University (Denmark)                                 | $^{64}\text{Cu}$ , $^{67}\text{Cu}$ , $^{18}\text{F}$ , $^{52}\text{Mn}$ , $^{135}\text{Tc}$  |
| 2   | Sacro Cuore Hospital (Italy)   | $^{52}\text{Mn}$ , $^{53}\text{Mn}$ , $^{54}\text{Mn}$ , $^{64}\text{Cu}$ , $^{67}\text{Cu}$ , $^{68}\text{Ga}$ , $^{89}\text{Zr}$ , $^{99\text{m}}\text{Tc}$ , $^{123}\text{I}$ , $^{124}\text{I}$ , $^{155}\text{Tb}$ |
| 3   | Azienda Ospedaliero-Universitaria Policlinico S.Orsola Bologna (Italy) | $^{11}\text{C}$ , $^{18}\text{F}$ , $^{68}\text{Ga}$ , $^{99\text{m}}\text{Tc}$   |
| 4   | Eckert & Ziegler Radiopharma (Germany)                                 | $^{68}\text{Ga}$ , $^{90}\text{Y}$ , $^{177}\text{Lu}$  |

|    |   |  |
|----|---|--|
| 5  | GIP Arronax (France)  | $^{44}\text{Sc}$ , $^{64}\text{Cu}$ , $^{67}\text{Cu}$ , $^{68}\text{Ge}$ , $^{211}\text{At}$  |
| 6  | NUCLEO (Latvia)   | $^{11}\text{C}$ , $^{18}\text{F}$ , $^{68}\text{Ga}$   |
| 7  | ILL (France)  | $^{47}\text{Ca}$ / $^{47}\text{Sc}$ , $^{103}\text{Pd}$ , $^{103}\text{Ru}$ ,<br>$^{111}\text{Ag}$ , $^{129\text{m}}\text{Xe}$ , $^{131\text{m}}\text{Xe}$ , $^{143}\text{Pr}$ ,<br>$^{149}\text{Pm}$ , $^{161}\text{Tb}$ , $^{166}\text{Dy}$ / $^{166}\text{Ho}$ ,<br>$^{169}\text{Er}$ , $^{175}\text{Yb}$ , $^{177}\text{Lu}$ , $^{188}\text{W}$ ,<br>$^{195\text{m}}\text{Pt}$ |
| 8  | Cyceron (France)  | $^{11}\text{C}$ , $^{13}\text{N}$ , $^{15}\text{O}$ , $^{18}\text{F}$  |
| 9  | CEA (France)  | $^{67}\text{Cu}$ , $^{90}\text{Y}$ , $^{177}\text{Lu}$   |
| 10 | CERN-MEDICIS (Switzerland-France)                                   | $^{128}\text{Ba}$ , $^{153}\text{Sm}$ , $^{155}\text{Tb}$ , $^{165}\text{Er}$ ,<br>$^{169}\text{Er}$ , $^{225}\text{Ac}$   |
| 11 | Paul Scherrer Institute (Switzerland)                               | $^{44}\text{Sc}$ , $^{64}\text{Cu}$ , $^{161}\text{Tb}$ , $^{165}\text{Er}$  |
| 12 | Oslo University Hospital (Norway)                                   | $^{212}\text{Pb}$  |
| 13 | Fondazione Policlinico Universitario Agostino Gemelli IRCCS (Italy) | $^{64}\text{Cu}$ , $^{68}\text{Ga}$ , $^{89}\text{Zr}$   |
| 14 | University of Cambridge - Department of Radiology (United Kingdom)  | $^{68}\text{Ga}$ , $^{99\text{m}}\text{Tc}$  |
| 15 | King's College London (United Kingdom)                              | $^{44}\text{Sc}$ , $^{62}\text{Zn}$ , $^{62}\text{Cu}$ , $^{64}\text{Cu}$ , $^{67}\text{Ga}$ ,<br>$^{68}\text{Ga}$ , $^{99\text{m}}\text{Tc}$ , $^{111}\text{In}$ , $^{123}\text{I}$ , $^{124}\text{I}$ ,<br>$^{125}\text{I}$ , $^{131}\text{I}$ , $^{161}\text{Tb}$ , $^{177}\text{Lu}$ , $^{188}\text{Re}$ ,<br>$^{201}\text{TI}$  |
| 16 | University of Antwerp (Belgium)                                     | $^{68}\text{Ga}$ , $^{99\text{m}}\text{Tc}$ , $^{18}\text{F}$ , $^{11}\text{C}$ ,  |
| 17 | Helmholtz-Zentrum Dresden-Rossendorf (Germany)                      | $^{64}\text{Cu}$ , $^{67}\text{Cu}$ , $^{68}\text{Ga}$ , $^{123}\text{I}$ , $^{131}\text{Ba}$ ,<br>$^{133}\text{La}$ , $^{195}\text{Hg}$ , $^{197}\text{Hg}$   |
| 18 | KU Leuven (Belgium)   | $^{11}\text{C}$ , $^{13}\text{N}$ , $^{15}\text{O}$ , $^{18}\text{F}$ , $^{68}\text{Ga}$   |
| 19 | SCK CEN (Belgium)   | $^{90}\text{Y}$ , $^{99}\text{Mo}$ , $^{213}\text{Bi}$ , $^{223}\text{Ra}$ , $^{225}\text{Ac}$   |
| 20 | CNRS CEMHTI (France)  | $^{52}\text{Mn}$ , $^{165}\text{Er}$ , $^{166}\text{Ho}$   |
| 21 | Radboud University Medical Center (Netherlands)                     | $^{11}\text{C}$ , $^{18}\text{F}$ , $^{68}\text{Ga}$ , $^{99\text{m}}\text{Tc}$  |
| 22 | Institute for Nuclear Research (Hungary)                            | $^{48}\text{V}$ , $^{52}\text{Mn}$ , $^{55}\text{Co}$ , $^{56}\text{Co}$ , $^{64}\text{Cu}$ ,<br>$^{67}\text{Ga}$ , $^{68}\text{Ga}$ , $^{103}\text{Pd}$ , $^{123}\text{I}$ , $^{124}\text{I}$ ,<br>$^{155}\text{Tb}$ , $^{203}\text{Pb}$ , $^{209}\text{At}$  |
| 23 | University of Helsinki, Department of Chemistry (Finland)           | $^{11}\text{C}$ , $^{18}\text{F}$ , $^{68}\text{Ga}$   |
| 24 | Orano (France)  | $^{212}\text{Pb}$  |
| 25 | Karolinska Institute (Sweden)                                       | $^{11}\text{C}$ , $^{18}\text{F}$ , $^{45}\text{Ti}$ , $^{67}\text{Ga}$ , $^{68}\text{Ga}$ , $^{89}\text{Zr}$  |
| 26 | Delft University of Technology (Netherlands)                        | $^{64}\text{Cu}$ , $^{99\text{m}}\text{Tc}$ , $^{99}\text{Mo}$ , $^{153}\text{Sm}$ ,<br>$^{161}\text{Tb}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$ , $^{188}\text{W}$ ,<br>$^{188}\text{Re}$  |
| 27 | BV Cyclotron VU (Netherlands)                                       | $^{11}\text{C}$ , $^{18}\text{F}$ , $^{89}\text{Zr}$   |
| 28 | SHINE EUROPE (Netherlands)  | $^{177}\text{Lu}$  |
| 29 | The National Centre of Oncology (Azerbaijan)                        | $^{18}\text{F}$ , $^{68}\text{Ga}$ , $^{99\text{m}}\text{Tc}$  |

|    |  |  |
|----|--|--|
| 30 | Czech Technical University in Prague (Czechia) | $^{64}\text{Cu}$ , $^{67}\text{Cu}$ , $^{68}\text{Ga}$ , $^{99\text{m}}\text{Tc}$ ,<br>$^{161}\text{Tb}$ , $^{223}\text{Ra}$ |
| 31 | Radioisotope Production Center CSJC (Armenia)  | $^{18}\text{F}$  |

Thirteen of respondent's companies/institutions produce, develop or study radionuclide generators. Five of the surveyed respondents work with  $^{68}\text{Ge}/^{68}\text{Ga}$  generators, 3 institutions -  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ ,  $^{224}\text{Ra}/^{212}\text{Pb}$ ,  $^{225}\text{Ac}/^{213}\text{Bi}$  generators, 2 institutions -  $^{188}\text{W}/^{188}\text{Re}$  and  $^{82}\text{Sr}/^{82}\text{Rb}$  and one each  $^{62}\text{Zn}/^{62}\text{Cu}$ ,  $^{44}\text{Ti}/^{44}\text{Sc}$  generators (see Table 2).

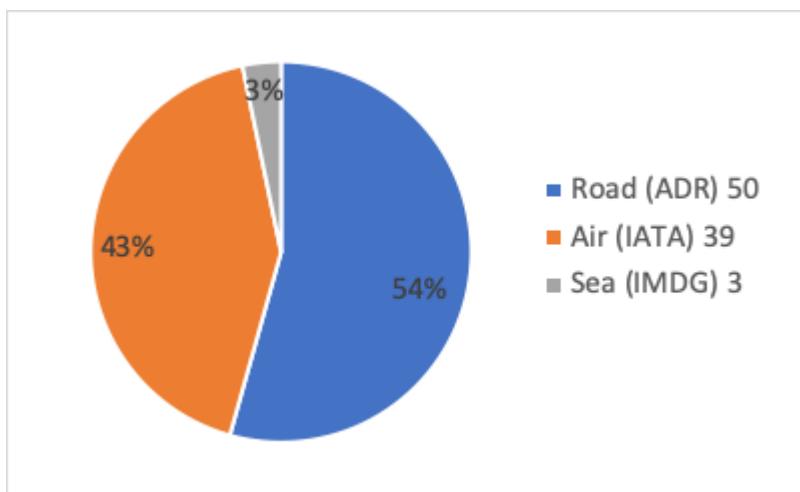
**Table 2. List of radionuclide generators produced used or studied by respondent institutions**

| Nr. | Respondent   | Generators   |
|-----|--|--|
| 1   | Denmark Technical University (Denmark)   | $^{68}\text{Ge}/^{68}\text{Ga}$  |
| 2   | Eckert & Ziegler Radiopharma (Germany)   | $^{68}\text{Ge}/^{68}\text{Ga}$  |
| 3   | GIP Arronax (France)   | $^{82}\text{Sr}/^{82}\text{Rb}$  |
| 4   | Oslo University Hospital (Norway)  | $^{224}\text{Ra}/^{212}\text{Pb}$  |
| 5   | King's College London (United Kingdom)   | $^{62}\text{Zn}/^{62}\text{Cu}$ , $^{68}\text{Ge}/^{68}\text{Ga}$ ,<br>$^{82}\text{Sr}/^{82}\text{Rb}$ , $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ ,<br>$^{188}\text{W}/^{188}\text{Re}$ |
| 6   | Institute of Nuclear Chemistry and Technology (Poland)   | $^{225}\text{Ac}/^{213}\text{Bi}$ , $^{224}\text{Ra}/^{212}\text{Pb}$ ,<br>$^{103}\text{Pd}/^{103\text{m}}\text{Rh}$   |
| 7   | Lausanne University Hospital (Switzerland)   | $^{44}\text{Ti}/^{44}\text{Sc}$  |
| 8   | SCK CEN (Belgium)  | $^{225}\text{Ac}/^{213}\text{Bi}$  |
| 9   | CNRS CEMHTI (France)   | $^{165}\text{Tm}/^{165}\text{Er}$  |
| 10  | Orano (France)   | $^{224}\text{Ra}/^{212}\text{Pb}$  |
| 11  | Delft University of Technology (Netherlands)   | $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ , $^{188}\text{W}/^{188}\text{Re}$ ,<br>$^{47}\text{Ca}/^{47}\text{Sc}$ , $^{166}\text{Dy}/^{166}\text{Ho}$                                    |
| 12  | Radboud University Medical Center (Netherlands)  | $^{68}\text{Ge}/^{68}\text{Ga}$ , $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  |
| 13  | Czech Technical University in Prague, Faculty of Nuclear Sciences and Physical Engineering, Department of nuclear chemistry (Czech Republic) | $^{68}\text{Ge}/^{68}\text{Ga}$ , $^{225}\text{Ac}/^{213}\text{Bi}$ ,<br>$^{227}\text{Ac}/^{227}\text{Th}/^{223}\text{Ra}$   |

## 2.3 Logistics and distribution

The most often used transportation types that respondents or their distributor/supplier use for radioactive material transport are by road (50 respondents) and air (39 respondents), see Figure 8. Transportation types. Only 3 of the respondents used transportation through the sea, possibly due to less time effective logistic chains. Such sea transportation would only become effective if it would be between 2 ports of short distance as, for example, countries around the Baltic Sea or in the middle of some more complex supply chains.

Here we see that the most common and less constrained type is road transport on a national, less frequent international level for short distance distribution. For large distance or short-lived radionuclide transportation, the most effective transport is by air.

**Figure 8. Transportation types**

Nearest airports which respondents use for radioactive material transport - AMS, BLQ, BRU, BHX GVA, CDG, CPH, LIS, HAJ, HEL, LEJ, LIS, RIX, MAD, BLQ, ZRH, OSL, FCA, Heathrow, PRG, TLL, VNC, VCE, USA, etc. These airports support radioactive package shipment. Such information is important for establishing supply chains, by identifying airports and commercial airline companies that accept radioactive materials for shipment. Respondents also mention that some airports are close, but in neighbouring countries, therefore are used due to additional border crossing.

Thirty-one of respondents subcontract radioactive material (class 7) transport companies – see Table 3.

**Table 3. Subcontracted radioactive material (class 7) transport companies of various institutes/companies**

| Nr. | Respondent   | Company  |
|-----|--|--|
| 1   | Università degli Studi di Milano - UNIMI (Italy)                               | Gamma Servizi, Italy   |
| 2   | Denmark Technical University (Denmark)   | Junge Spedition, K.Sand Andersen Transport, Lorrys Eft.            |
| 3   | University of Milan, Department of Physics (Italy)                             | Gamma Servizi srl,   |
| 4   | CHUV (Switzerland)   | SAR transport  |
| 5   | IBA (Belgium)  | N/A  |
| 6   | Eckert & Ziegler Radiopharma (Germany)   | Information can only be disclosed with a confidentiality agreement |
| 7   | GIP Arronax (France)   | Isolife, Forestier   |
| 8   | NUCLEO, Ltd. (Latvia)  | KOLL (road)<br>AirBaltic (Air)                                     |
| 9   | ILL(France)  | Company depends on the destination,<br>e.g. SAR for Switzerland.   |
| 10  | Cyceron (France)   | Not disclosed (French national company)                            |
| 11  | CEA (France)   | N/A  |
| 12  | LRB (Laboratoire Radiopharmaceutiques Biocliniques, UGA, INSERM 1039) (France) | Transrad (IRE)<br>PME Express (Arronax)                            |
| 13  | CERN-MEDICIS (Switzerland-France)  | Not disclosed  |
| 14  | Paul Scherrer Institute (Switzerland)  | SAR  |

|    |  |   |
|----|--|---|
| 15 | Oslo University Hospital (Norway)  | Jekra AS, Norway  |
| 16 | King's College London (United Kingdom)   | N/A   |
| 17 | University of Antwerp (Belgium)  | ISI ( <a href="http://www.isotopes.be">www.isotopes.be</a> )                            |
| 18 | Helmholtz-Zentrum Dresden-Rossendorf (Germany)   | ADR (Road)  |
| 19 | Institute of Nuclear & Radiological Sciences & Bollore Transport Technology, Energy & Safety,<br>National Center for Scientific Research "Demokritos" (Greece) |   |
| 20 | Fundación para la Investigación Biomédica del Fedex Hospital Gregorio Marañón (Spain)  |   |
| 21 | Fundación de investigación Gregorio Marañón Fedex (Spain)  |   |
| 22 | University of Turin (Italy)  | Crisago Trasporti   |
| 23 | CNRS CEMHTI (France)   | Isolife, Dangxpress ("Capelle"), Ulysse (CNRS internal structure to organize transport) |
| 24 | Advanced Accelerator Applications (Italy)  | Crisago MIT   |
| 25 | Institute for Nuclear Research (Hungary)   | Eötvös Lóránd University, ADR   |
| 26 | Orano (France)   | N/A   |
| 27 | Karolinska Institute (Sweden)  | N/A   |
| 28 | BV Cyclotron VU (Netherlands)  | Fiege   |
| 29 | Antoni van Leeuwenhoek/Netherlands Cancer Institute (Netherlands)  | Fiege (Road)<br>AAA (Air)   |
| 30 | The National Centre of Oncology (Azerbaijan)   | Turkish Airline, Lufthansa  |
| 31 | SCK CEN (Belgium)  | N/A   |

11 respondents expressed that there are restrictions on the availability or logistics and distribution of radionuclides/radiopharmaceuticals after 1st march, 2022, mostly indicating the shutdown of partner institutes that supply them with radionuclides. This should be noted as an important matter with increasing radionuclide demand across users.

A key element for radionuclide production is choice of appropriate target material. The most common issues with the enriched material supply/stock that companies/institutions experienced was availability (28 respondents), delivery time (15 respondents), purity/enrichment grade (13 respondents), quantity (11 respondents) and price (7 respondents).

The biggest bottleneck for the producers is the stable isotope availability, which goes in correlation with purity/enrichment grade and delivery time. With higher isotopic purity, the availability of the desired material decreases drastically. Availability is limited by the abundance of desired target material or companies that provide them for specific radionuclide production, therefore suggesting alternative desired radionuclide obtaining options, for example by utilising different production approach and supply from other institutions within reasonable distances and optimized supply routes.

The majority of respondents did not indicate the price as the main bottleneck, therefore suggesting that the cost of high purity target materials for certain radionuclide production is justified based on their availability and the product radionuclide necessity.

Out of 64 respondents from research institutions and manufacturing facilities, 24 respondent companies/institutions distribute radionuclides to national external research institutes, radiopharmaceutical producers or users. Twelve of the respondent institutions distribute radionuclides to international recipients (see Table 4).

The results show that half of respondents that supply institutes externally already have international distribution routes established. The longer distance distribution routes, such as between different continents are especially noteworthy, as they require more logistics and legal issues.

**Table 4. Radionuclide distribution to international recipients**

| Nr. | Respondent                                     | Radionuclides  | International recipient   |
|-----|--|--|---|
| 1   | Sacro Cuore Hospital (Italy)                   | $^{52}\text{Mn}$ , $^{53}\text{Mn}$ , $^{54}\text{Mn}$ , $^{64}\text{Cu}$ , $^{67}\text{Cu}$ , NL<br>$^{68}\text{Ga}$ , $^{89}\text{Zr}$ , $^{99\text{m}}\text{Tc}$ , $^{123}\text{I}$ , $^{124}\text{I}$ , $^{155}\text{Tb}$  |   |
| 2   | Eckert & Ziegler Radiopharma (Germany)         | $^{90}\text{Y}$  | USA, EU   |
| 3   | GIP Arronax (France)                           | $^{64}\text{Cu}$ , $^{82}\text{Sr}$  | CH, NL, USA   |
| 4   | ILL (France)                                   | $^{47}\text{Ca}/^{47}\text{Sc}$ , $^{103}\text{Pd}$ , $^{103}\text{Ru}$ , $^{111}\text{Ag}$ , AT, CH, DE, DK, FR, PL<br>$^{129\text{m}}\text{Xe}$ , $^{131\text{m}}\text{Xe}$ , $^{143}\text{Pr}$ , $^{149}\text{Pm}$ , $^{161}\text{Tb}$ ,<br>$^{166}\text{Dy}/^{166}\text{Ho}$ , $^{169}\text{Er}$ , $^{175}\text{Yb}$ , $^{177}\text{Lu}$ ,<br>$^{188}\text{W}$ , $^{195\text{m}}\text{Pt}$ |   |
| 5   | CERN-MEDICIS (Switzerland-France)              | $^{128}\text{Ba}$ , $^{153}\text{Sm}$ , $^{155}\text{Tb}$ , $^{165}\text{Er}$ , $^{169}\text{Er}$ , BE, CH, FR, LV, PK, UK<br>$^{225}\text{Ac}$  |   |
| 6   | Paul Scherrer Institute (Switzerland)          | $^{64}\text{Cu}$   | CH, DE  |
| 7   | Helmholtz-Zentrum Dresden-Rossendorf (Germany) | $^{64}\text{Cu}$   | HU  |
| 8   | Institute for Nuclear Research (Hungary)       | $^{103}\text{Pd}$  | South Africa  |
| 9   | Orano (France)                                 | Not disclosed  | US  |
| 10  | BV Cyclotron VU (Netherlands)                  | $^{89}\text{Zr}$   | Europe: NL, BE, GB, FR, SP, IT, NO, SW, GE USA, CA<br>Distribution worldwide.<br>Australia, Asia, China and Singapore |
| 11  | SHINE EUROPE (Netherlands)                     | Not disclosed  | Not disclosed   |
| 12  | SCK CEN (Belgium)                              | Not disclosed  | Not disclosed   |

It is confirmed by the survey responses that main limitations are fragmented and unharmonized procedures for import/export legislation of radionuclides across Europe and beyond (9 respondents each), complex supply chains (6 respondents) and licensing (5 respondents). Nine respondents indicated that they do not face any of the issues. Two respondents indicated they have other constraints, such as cost. Harmonized legislation therefore is one of main issues already indicated, discussed and therefore targeted by the PRISMAP consortium. For longer international radionuclide shipments also customs clearance was mentioned and due to some radionuclide short half-life, such delays must be mitigated.

Some of the information about logistics and distribution was not available to be disclosed due to company policies.

Out of 24 respondents that export the produced radionuclides, generators or radiopharmaceuticals 10 respondent institutions use an external company as distributor (see Table 5). Tendency for larger radionuclide manufacturing facilities to sub-contract external distributors is observed. Such approach eases the acquisition of radionuclides by the users and operations by the manufacturers.

**Table 5. National radionuclide distribution by external companies**

| Nr. | Respondent                                   | Radionuclides   | External company   |
|-----|--|---|--|
| 1   | University of Padua (Italy)                  | Not indicated   | Curium, GE   |
| 2   | Eckert & Ziegler Radiopharma (Germany)       | <sup>68</sup> Ga, <sup>90</sup> Y, <sup>177</sup> Lu  | Information can only be disclosed with a confidentiality agreement |
| 3   | ILL (France)                                 | <sup>177</sup> Lu   | ITM in Garching  |
| 4   | CEA (France)                                 | <sup>90</sup> Y, <sup>67</sup> Cu, <sup>177</sup> Lu  | Novartis   |
| 5   | CERN-MEDICIS (Switzerland-France)            | <sup>128</sup> Ba, <sup>153</sup> Sm, <sup>155</sup> Tb, <sup>165</sup> Er, <sup>169</sup> Er, <sup>225</sup> Ac, | Isovital, SAR, Asept   |
| 6   | Oslo University Hospital (Norway)            | <sup>212</sup> Pb   | Oncoinvent AS, Norway<br>Nucligen AS, Norway                       |
| 7   | University of Antwerp (Belgium)              | N/A   | Curium, Cyclotron BV, Perkin Elmer                                 |
| 8   | Delft University of Technology (Netherlands) | <sup>166</sup> Ho microspheres  | Terumo NL  |
| 9   | BV Cyclotron VU (Netherlands)                | <sup>89</sup> Zr  | PerkinElmer  |
| 10  | SCK CEN (Belgium)                            | N/A   | IRE, Fleurus   |

It should be noted that ITM Isotopen Technologien München AG is also a key n.c.a. <sup>177</sup>Lu radionuclide supplier and the <sup>68</sup>Ge/<sup>68</sup>Ga generator supplier in Europe.

Four of the above-mentioned 10 respondents subcontract with an external company to pack and/or do the Dangerous Goods Declaration (see Table 6).

**Table 6. Respondents and their subcontracting with external companies (Dangerous Goods Declaration)**

| Nr. | Respondent                             | External company   |
|-----|--|--|
| 1   | Eckert & Ziegler Radiopharma (Germany) | Information can only be disclosed with a confidentiality agreement |
| 2   | CEA (France)                           | Novartis   |
| 3   | BV Cyclotron VU (Netherlands)          | PerkinElmer and SDG  |
| 4   | SCK CEN (Belgium)                      | Not Disclosed  |

Out of 64 respondents from research institutions and manufacturing facilities, 19 respondent companies/institutions plan to export or extend the already existing export region of produced radionuclides in following years. Only 8 respondents were interested in both regions - within Europe and outside of Europe, 10 respondents - within Europe only and 1 respondent - outside Europe only. Involvement in an early stage

of establishing these routes may help foster the radionuclide distribution as well as give the ability for users to gain access to desired radionuclides in a more foreseeable timeframe.

Main limitations that respondents face or foresee are lack of harmonised import/export legislation (10 respondents), complex supply chains (9 respondents), regulatory limitations (6 respondents) and licensing (5 respondents). Four respondents do not foresee any of the limitations. Respondents also indicate the main problems with air cargo transport, which are limitations due to the dose rate of the radiation, shielding of the radioactive source and packaging. Another issue is already mentioned - slow and bureaucratic administrative procedures such as customs clearance.

Furthermore, 30 respondent companies/institutions plan to increase manufactured volume of radionuclides in following years. Even without plans to expand, main limitations that respondents face or foresee are limitations in infrastructure (15 respondents), shortage of staff, expertise (15 respondents), "beam time" or production capacity and target material supply (11 respondents each) and other financial or managerial issues (3 respondents). Possibilities to teach and train students, staff and to transfer knowledge, as indicated by responders as one of the main limitations, can be addressed through more open communication between the institutions. As such, this is one of PRISMAP objectives that is already being addressed. Some respondents do not foresee any issues yet due to low or manageable demand at the moment.

Fifty respondents are involved in radiopharmaceutical synthesis, production and/or research. Out of these 50 respondents, 20 companies/institutions distribute radiopharmaceuticals to external research institutes or users (pre-clinical and clinical research/applications). Four from these 20 respondents distributed radiopharmaceuticals to international recipients within EU and outside EU borders.

In general radiopharmaceutical distribution is more even more demanding in terms of legal compliance than radionuclide or radiopharmaceutical precursor distribution. Often, radiopharmaceuticals for pre-clinical and clinical applications are produced "in-house". Therefore, we can conclude that the radiopharmaceuticals distributed at national and international level are labelled mainly with radionuclides outside the scope of PRISMAP. Nevertheless, the existing distribution routes and expertise in legislation and regulations are of great interest for the emerging radiopharmaceuticals coming into clinical trial phase.

Out of 64 respondents, 41 of respondent's companies or institutions obtained radionuclides from external suppliers for their radionuclide precursor, radiopharmaceutical production and/or research and development activities (see Table 7).

**Table 7. Respondents and their obtained radionuclides by external suppliers**

| Nr. | Respondent                         | Radionuclides   | External supplier  |
|-----|------------------------------------|---|--|
| 1   | Denmark<br>(Denmark)               | Technical University<br><sup>68</sup> Ge/ <sup>68</sup> Ga<br><sup>103</sup> Pd, <sup>199</sup> Au, | generator, Not disclosed                                 |
| 2   | CHUV (Switzerland)                 | Not disclosed   | ITM in Garching<br>Eckert&Ziegler<br>Curium              |
| 3   | IST-ID (Portugal)                  | Not disclosed   | Mallinckrodt<br>Polatom<br>SCK-CEN                       |
| 4   | Istituto Oncologico Veneto (Italy) | Not disclosed   | IRCCS Ospedale Sacro Cuore don Calabria di Negar (Italy) |
| 5   | University of Padua (Italy)        | <sup>44</sup> Sc, <sup>64</sup> Cu, <sup>67</sup> Cu, <sup>68</sup> Ge, <sup>211</sup> At           | Curium and GE  |
| 6   | GIP Arronax (France)               | <sup>177</sup> Lu   | Not disclosed supplier from Germany                      |

|    |  |  |  |
|----|--|--|--|
|    |  | <sup>111</sup> In                            | Not disclosed supplier from Netherlands                |
| 7  | NUCLEO (Latvia)  | <sup>68</sup> Ge/ <sup>68</sup> Ga generator | Eckert & Ziegler                                       |
|    |  | <sup>177</sup> Lu                            | ITM in Garching  |
| 8  | Cyceron (France)   | <sup>64</sup> Co, <sup>177</sup> Lu          | Arronax  |
| 9  | CEA (France)   | Not disclosed                                | Novartis   |
| 10 | Laboratoire Radiopharmaceutiques Biocliniques, LRB (France)              | <sup>68</sup> Ge/ <sup>68</sup> Ga generator | IRE, Belgium   |
|    |  | <sup>177</sup> Lu                            | ITG, Germany   |
|    |  | <sup>177</sup> Lu                            | IDB (AAA-Novartis), Netherlands                        |
|    |  | <sup>99m</sup> Tc generator                  | charged with Grenoble Hospital                         |
|    |  | <sup>125</sup> I                             | Perkin-Elmer, USA                                      |
|    |  | <sup>111</sup> In                            | Mallinckrodt, Netherlands                              |
|    |  | <sup>123</sup> I                             | IBA, Belgium   |
|    |  | <sup>64</sup> Cu                             | Arronax, France  |
|    |  | <sup>201</sup> Tl                            | Curium pharma, France                                  |
| 11 | Oslo University Hospital (Norway)  | <sup>177</sup> Lu                            | ITG, Germany   |
|    |  | <sup>223</sup> Ra                            | Bayer  |
|    |  | <sup>224</sup> Ra                            | OncoInvent   |
| 12 | Fondazione Policlinico Universitario Agostino Gemelli IRCCS (Italy)      | <sup>68</sup> Ge/ <sup>68</sup> Ga generator | ITM (DE)   |
| 13 | INSERM (France)  | Not disclosed                                | ORANO, ORANO MED, ITU                                  |
| 14 | Department of Radiology, University of Cambridge (United Kingdom)        | <sup>89</sup> Zr                             | VUMC, Amsterdam, Netherlands                           |
| 15 | Barts Cancer Institute, Queen Mary University of London (United Kingdom) | <sup>18</sup> F ([ <sup>18</sup> F]-FDG)     | etNet, Alliance Medical UK                             |
|    |  | <sup>64</sup> Cu                             | King's College London, UK                              |
|    |  | <sup>68</sup> Ge/ <sup>68</sup> Ga generator | Curium, IRE, and other various generator suppliers     |
|    |  | <sup>89</sup> Zr                             | Perkin Elmer   |
|    |  | <sup>111</sup> In                            | Local - via hospital generators                        |
|    |  | <sup>99m</sup> Tc                            | Local radiopharmacy, generators                        |
|    |  | <sup>177</sup> Lu                            | ITM in Garching  |
|    |  | <sup>188</sup> Re                            | Oncobeta   |
|    |  | <sup>225</sup> Ac                            | ITM in Garching  |
| 16 | Helmholtz-Zentrum Rossendorf (Germany)                                   | Dresden-                                     | Not disclosed  |
| 17 | Lausanne University (Switzerland)  | Hospital                                     | <sup>99m</sup> Tc, <sup>68</sup> Ga, <sup>177</sup> Lu |
|    |  |  | Not disclosed  |

|    |  |   |   |
|----|--|---|---|
| 18 | KU Leuven (Belgium)  | Not disclosed   | Karlsruhe, SCK-CEN  |
| 19 | Institute of Nuclear & Radiological Sciences & Technology, Energy & Safety,<br>National Center for Scientific Research "Demokritos" (Greece) | Not disclosed   | POLATOM, ITM  |
| 20 | Fundación para la Investigación Biomédica del Hospital Gregorio Marañón (Spain)  | <sup>89</sup> Zr<br><sup>18</sup> F and <sup>99m</sup> Tc<br><sup>68</sup> Ge/ <sup>68</sup> Ga generator                       | Perkin Elmer, Netherlands<br>CuriumPharma, Spain<br>France  |
| 21 | Fundación de investigación Gregorio Marañón (Spain)  | <sup>89</sup> Zr<br><sup>18</sup> F, <sup>99m</sup> Tc<br><sup>68</sup> Ge/ <sup>68</sup> Ga generator                          | Perkin Elmer, Netherlands<br>CuriumPharma, Spain<br>France  |
| 22 | University of Turin (Italy)  | <sup>18</sup> F ([ <sup>18</sup> F]-FDG)  | AAA   |
| 23 | SCK CEN (Belgium)  | <sup>177</sup> Lu, <sup>188</sup> W, <sup>225</sup> Ac  | Not disclosed   |
| 24 | CNRS CEMHTI (France)   | <sup>52</sup> Mn, <sup>165</sup> Er (from irradiation)  | DTU, Denmark  |
| 25 | Radboud University Medical Center (Netherlands)  | <sup>89</sup> Zr<br><sup>111</sup> In<br><sup>177</sup> Lu<br><sup>212</sup> Zr<br><sup>225</sup> Ac                            | Cyclotron BV, NL<br>Curium, NL<br>ITM, Germany<br>NRG Petten, NL<br>ITU Karlsruhe GE, van Overeem nuclear BV, NL            |
| 26 | King's College London (United Kingdom)   | <sup>67</sup> Ga<br><sup>89</sup> Zr<br><sup>111</sup> In<br><sup>201</sup> Tl<br><sup>188</sup> W/ <sup>188</sup> Re generator | Not disclosed<br>Perkin Elmer<br>Not disclosed<br>Not disclosed<br>Various - Not disclosed                                  |
| 27 | Advanced Accelerator Applications (Italy)  | Not disclosed   | Not disclosed   |
| 28 | University of Helsinki, Department of Chemistry (Finland)  | <sup>99m</sup> Tc<br><sup>89</sup> Zr<br><sup>111</sup> In<br><sup>123</sup> I<br><sup>125</sup> I<br><sup>177</sup> Lu         | Curium Pharma, BE<br>Perkin Elmer, NL<br>Curium Pharma, BE<br>GE Healthcare, NL?<br>GE Healthcare, NL?<br>Curium Pharma, BE |
| 29 | University of Bordeaux (France)  | <sup>89</sup> Zr, <sup>177</sup> Lu, <sup>64</sup> Cu   | Not disclosed   |
| 30 | Charles River / Discovery (Finland)  | <sup>18</sup> F, <sup>68</sup> Ga<br><sup>89</sup> Zr<br><sup>177</sup> Lu  | Finland<br>Perkin Elmer, Netherland<br>ITM, Germany   |

|    |   |   |  |
|----|---|---|--|
| 31 | Karolinska Institute (Sweden)   | $^{125}\text{I}$<br>$^{89}\text{Zr}$  | PerkinElmer - NL<br>BV Cyclotron - NL  |
| 32 | Delft University of Technology (Netherlands)  | Not disclosed   | Perkin Elmer, ITU (JRC, Germany), van Overeem Nuclear (the Netherlands), Oak Ridge (USA), Center for Energy Research (Hungary) |
| 33 | BV Cyclotron VU (Netherlands)   | $^{81}\text{Rb}$  | Curium, Petten, NL   |
| 34 | Antoni van Leeuwenhoek hospital/ Dutch Cancer Institute (Netherlands)   | $^{18}\text{F}$ ([ $^{18}\text{F}$ ]-FPSMA, [ $^{18}\text{F}$ ]-FAPI)   | Cyclotron Noordwest, Noordwest Ziekenhuisgroep, Netherlands  |
| 35 | OLVG (Netherlands)  | $^{89}\text{Zr}$<br>$^{177}\text{Lu}$   | Netherlands<br>IDB, NL   |
| 36 | Antoni van Leeuwenhoek/Netherlands Cancer Institute (Netherlands)   | $^{68}\text{Ga}$<br>$^{177}\text{Lu}$<br>$^{18}\text{F}$ , $^{89}\text{Zr}$<br>$^{99\text{m}}\text{Tc}$                           | IRE, Belgium<br>ITM, Germany<br>Cyclotron BV, Netherlands<br>Curium, Netherlands   |
| 37 | The National Centre of Oncology (Azerbaijan)  | $^{68}\text{Ge}/^{68}\text{Ga}$ generator, $^{177}\text{Lu}$<br>$^{99}\text{Mo}$ generator, $^{131}\text{I}$<br>$^{225}\text{Ac}$ | ITM Germany<br>Monrol Turkey<br>Oak Ridge National Laboratory  |
| 38 | University of Zagreb School of Medicine (Croatia)   | $^{18}\text{F}$ ([ $^{18}\text{F}$ ]-FDG)   | Not disclosed  |
| 39 | Palacky University (Czechia)  | Not disclosed   | NPI Rez (CZ), UJV Rez (CZ), MGP Zlin (CZ), KC Solid (CZ), HZDR (Germany)   |
| 40 | Czech Technical University in Prague, Faculty of Nuclear Sciences and Physical Engineering, Department of nuclear chemistry (Czechia) | $^{225}\text{Ac}$   | JRC ITU, Karlsruhe, Germany  |
| 41 | Paul Scherrer Institute (Switzerland)   | $^{67}\text{Ga}$ , $^{99\text{m}}\text{Tc}$ , $^{111}\text{In}$<br>$^{177}\text{Lu}$  | Curium<br>ITM in Garching  |

The main issues of obtaining/importing the radionuclides the respondents face are transport limitations (13 respondents), regulatory limitations (11 respondents), licensing and lack of harmonized import/export legislation (8 respondents each). Sixteen respondents did not face or indicate any of the limitations. Some respondents had already solved their constraints of regulatory and transport limitations. There are also limitations on the amount of radioactivity (activity cap) to be imported, both for regulatory reasons and because of supply restrictions.

Respondents of 44 institutions mentioned additional radionuclides they consider producing or obtaining in following years by external suppliers for any of their research and development activities. Most often mentioned radionuclides are -  $^{149}\text{Tb}$ ,  $^{152}\text{Tb}$ ,  $^{155}\text{Tb}$ ,  $^{149}\text{Tb}$ ,  $^{161}\text{Tb}$ ,  $^{225}\text{Ac}$ ,  $^{89}\text{Zr}$ ,  $^{67}\text{Cu}$ ,  $^{64}\text{Cu}$ ,  $^{165}\text{Er}/^{169}\text{Er}$ ,  $^{47}\text{Sc}$ ,  $^{44}\text{Sc}$ ,  $^{177}\text{Lu}$ ,  $^{211}\text{At}$ ,  $^{188}\text{Re}$ ; The main limitations that respondents face again are regulatory limitations (15 respondents), lack of harmonised import/export legislation (13 respondents), licensing (11 respondents), transport limitations (10 respondents) and availability and sources (6 respondents). After Brexit, there are additional

constraints with import/export involving the UK. A limitation often mentioned was also the amount of activity supplied.

In recent years, the Tb radionuclide “family” and  $^{211}\text{At}$ ,  $^{177}\text{Lu}$ ,  $^{89}\text{Zr}$ ,  $^{67}\text{Cu}$ ,  $^{64}\text{Cu}$ ,  $^{47}\text{Sc}/^{44}\text{Sc}$  and others have become the main research topics towards theranostic/therapeutic use. Also identified as important is  $^{225}\text{Ac}$  as alpha emitter in radionuclide therapy and radiopharmaceutical development, and the interest for such is only increasing, therefore supply of these radionuclides should address the demand.

From responses of the respondents, we can conclude the necessity of PRISMAP not only as a web-based entry platform for the production and dispatch of non-conventional radionuclides, but also as a long-term platform for aiding an advancement in, at the moment, emerging radionuclide distribution and use in research, translational research, pre-clinical/clinical research and nuclear medicine.

## 2.4 Research and development activities

Out of all respondents, 80% (90 respondents) indicated that their R&D activities would benefit from collaboration/cooperation in obtaining emerging radionuclides with centralised and harmonised procedures and legislation, offered by efforts of the PRISMAP consortium.

More than a third of the responders indicated the interest in novel radionuclides either for radiopharmaceutical development and labelling studies, for already ongoing projects or for new project applications and even new preclinical study equipment optimization with the novel radionuclides.

Twenty respondents indicated the interest in collaborating with PRISMAP consortium members to foster or use radionuclides and expertise offered for pre-clinical and clinical applications and studies.

Fifteen respondents expressed the need to collaborate with PRISMAP consortium members to have contacts and supporters of their future activities.

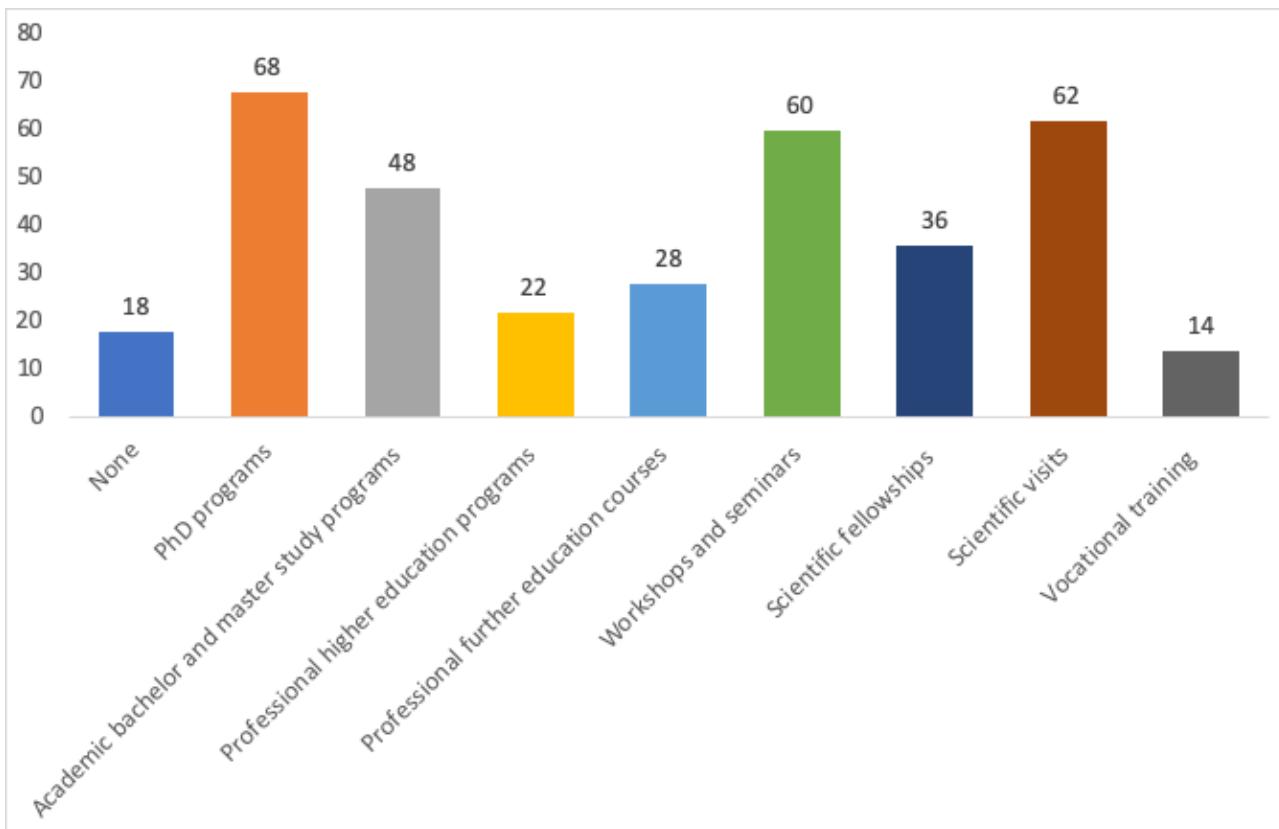
Members of PRISMAP consortium also mentioned the benefit of additional collaborating institutes, as additional sites to carry out research activities related to radionuclide production and purification.

Main emphasis on R&D activities in collaboration with PRISMAP is the availability of emerging medical radionuclides, workflow and access to mass-separated, pure medical isotopes.

## 2.5 Training and capacity building

83% of all the institutions (86 respondents) in this survey are involved in the training of industry experts, technicians, students and researchers at various expertise levels, considering that the respondents of this survey are almost equally from clinical, research and manufacturing fields (accelerator and particle physics, radionuclide production, synthesis and development, purification, calibration and characterization, quality control, analysis and radiochemistry).

Out of all respondents, 86 of respondent's companies/institutions provide training in nuclear physics, radiochemistry and radiopharmacy. The most often mentioned answers about training level were - PhD programmes (68 respondents), scientific visits (62 respondents) and workshops and seminars (60 responses). See Figure 9. Types of provided training in nuclear physics, radiochemistry and radiopharmacy for other types of provided training.

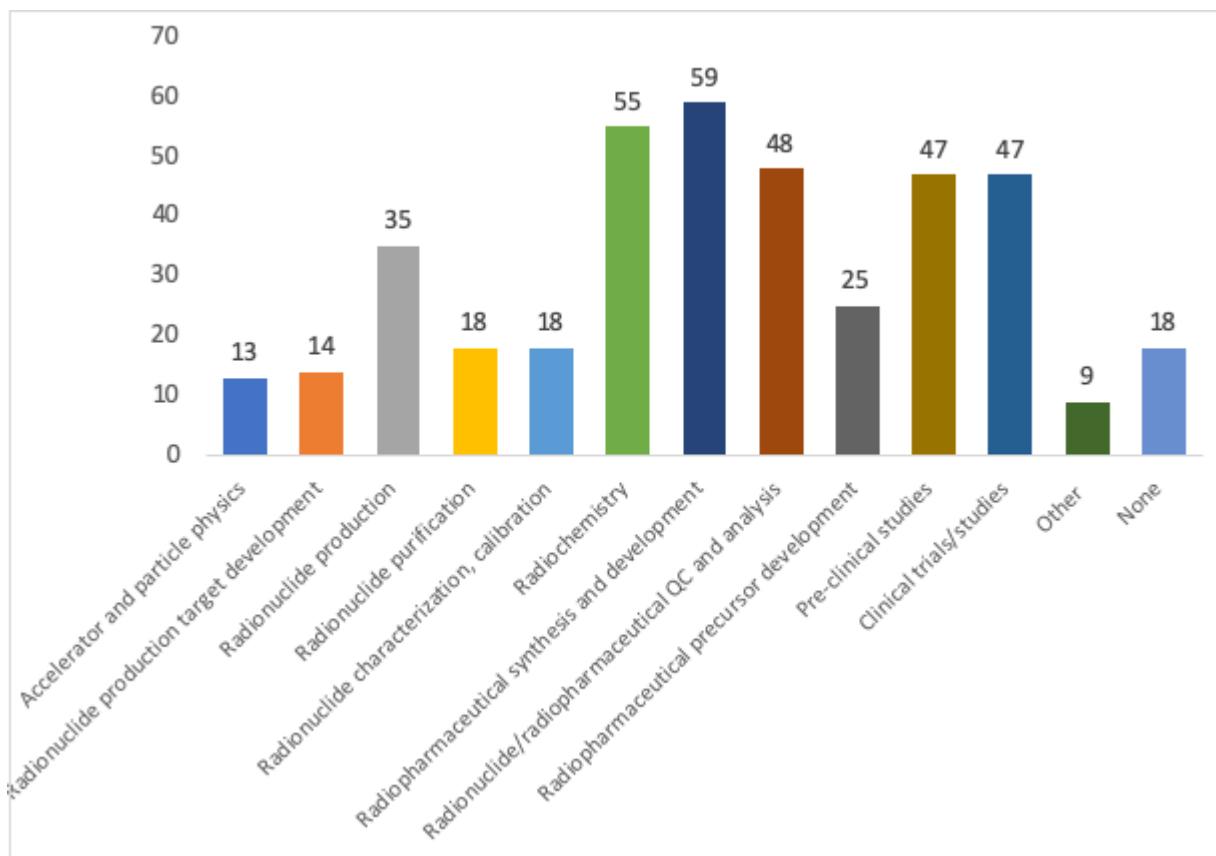


**Figure 9. Types of provided training in nuclear physics, radiochemistry and radiopharmacy**

The most popular training fields are radiopharmaceutical synthesis and development (59 respondents), radiochemistry (55 respondents), radionuclide/radiopharmaceutical QC and analysis (48 respondents), pre-clinical studies (47 respondents) and clinical trials/studies (47 respondents). See Figure 10 for provided training fields.

The target audience for training provided at respondent institutions are students (83 respondents), early-stage researchers (79 respondents), technologists (49 respondents), experienced researchers (44 respondents), nurses (23 respondents) and industry professionals (14 respondents).

Eighty percent of the respondents provide education for students, 76 % for early-stage researchers, 47% provide training for technologists/technicians and 42 % are training experienced researchers, although there were mentioned some limitations, such as capacity limitation to 2 persons or short training time periods, including funding and infrastructure limitation.



**Figure 10. Training and knowledge transfer fields**

The main limitations in the training process were unavailability for full hands-on training, access to infrastructure (e.g., accelerators), low funding, difficulties in recruiting students and above all the lack of technical staff; lack of integrating radiopharmaceutical research in faculty courses and student curricula. In some cases, the number of participants was too low to organise training courses.

Respondents also mention lack of teaching staff and even revisions in the educational programmes of the universities. However, an equal number of respondents indicate no issues in the training process itself.

It has also been indicated that there exists insufficient access to radioisotopes, no dedicated programme for nuclear medicine physicians, technologists and radiochemists in the universities; lack of trained pre-clinical scientists with a global view from radiochemistry to pharmacology. Often there is a lack of fundamental background knowledge on nuclear physics and the associated technology (reactors, accelerators) when candidates come from university.

## 2.6 Portfolio of radionuclide and radiopharmaceutical production in Europe

Through the survey already identified potential stakeholders in the industry and scientific community were asked to share their expertise in radionuclide production. Out of 64 respondents from research institutions and manufacturing facilities, 31 of respondent's companies/institutions indicated to produce radionuclides. 23 respondents indicated to use of cyclotrons and 8 respondents indicated the use of a research reactor.

It has been identified that there are at least 358 cyclotrons in Europe, with accelerated particle energies ranging from 3 MeV (for deuterons) up to 590 MeV for protons (in proton-synchrotrons). Most dominant are cyclotrons in the proton energy range of 16-18 MeV dedicated for conventional medical radionuclide production of F-18, O-15, C-11, Ga-68 and other standard PET radionuclides. Main cyclotron manufacturers mentioned are IBA, GE, Siemens and NIIIEFA.

From the identified accelerators with indicated accelerated particle energy, 40 accelerators have the capability to produce beams of 30 MeV protons or higher, making them suitable for non-conventional radionuclide production and supply.

Seventeen cyclotrons are identified that can produce proton beams from 60-100 MeV, making them suitable for more exotic radionuclide production that require higher incident particle energies. PSI (Switzerland) operates a high energy proton accelerator with proton energy of up to 590 MeV. Here it is worth noting that high energy accelerators such as synchrotrons like the PSB operated at 1.4GeV at CERN are not covered in this survey.

Countries with the most proton accelerators in Europe are France, Germany, Italy, United Kingdom, Denmark, Sweden, Spain and Netherlands [1,2].

### 2.6.1 Cyclotron portfolio for radionuclide production

According to the available public data form IAEA about cyclotron facilities, we have grouped the sites depending on their proton energy and radionuclide production type (PET and SPECT), see Appendix 1 with the list of the facilities according to the official publicly available IAEA data [2].

### 2.6.2 Major research reactors in the Europe

Similarly, the main active research reactors producing radionuclides located in the European Union are listed in Table 8. There have been identified 7 research reactors. According to IAEA nuclear reactor database [3], main radionuclides produced by the reactors are listed below:

**Table 8. Major research reactors in the Europe**

| Nr | Reactor | Country        | Operator                       | Produced therapeutic radionuclides  |
|----|---------|----------------|--------------------------------|---|
| 1  | MARIA   | Poland         | POLATOM                        | $^{32}\text{P}$ , $^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{188}\text{Re}$ |
| 2  | HFR     | Netherlands    | NRG                            | $^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{166}\text{Ho}$ , $^{169}\text{Er}$ , $^{177}\text{Lu}$ , $^{212}\text{Pb}$  |
| 3  | BR2     | Belgium        | SCK-CEN                        | $^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{188}\text{Re}$                                       |
| 4  | FRMII   | Germany        | Technical University of Munich | $^{166}\text{Ho}$ , $^{177}\text{Lu}$   |
| 5  | ILL     | France         | Institut Laue-Langevin         | $^{47}\text{Sc}$ , $^{111}\text{Ag}$ , $^{161}\text{Tb}$ , $^{169}\text{Er}$ , $^{175}\text{Yb}$ , $^{177}\text{Lu}$ , $^{188}\text{Re}$                                    |
| 6  | LVR-15  | Czech Republic | CVŘ Řež                        | $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{188}\text{Re}$  |
| 7  | BRR     | Hungary        | BNC/AEKI                       | $^{32}\text{P}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$  |

### 2.6.3 Therapeutic radionuclides and radiopharmaceuticals

As for diagnostic radionuclide production, there is a wide range of radionuclides for therapeutic use. Recently a survey study was carried out by JRC [4] to indicate the main therapeutic radionuclides and their use in Europe. Below is given a list of currently produced radionuclides and radiopharmaceuticals in Europe based on JRC published data (Ligtvoet et al, 2021) [4] in the Table 9 and Appendix Nr. 2.

It contains the list of Radionuclides and Radiopharmaceuticals, type of emission, production facility, indications for use (in Europe), available price per dose (euros), producer, supplier, supply issues and suggested solutions.

**Table 9. Therapeutic radionuclide and radiopharmaceutical use in the European countries**

| Nr | Country | Radionuclides in use: | Radiopharmaceuticals in compassionate use: |
|----|---------|-----------------------|--|
|----|---------|-----------------------|--|

|    |                |  |
|----|----------------|--|
| 1  | Austria        | $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{169}\text{Er}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{223}\text{Ra}$ , $^{225}\text{Ac}$ , $^{90}\text{Y}$   |
| 2  | Belgium        | $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{223}\text{Ra}$ , $^{213}\text{Bi}$   |
| 3  | Bulgaria       | $^{131}\text{I}$ , $^{223}\text{Ra}$ , $^{153}\text{Sm}$   |
| 4  | Croatia        | $^{131}\text{I}$ , $^{177}\text{Lu}$ , $^{223}\text{Ra}$ , $^{90}\text{Y}$   |
| 5  | Cyprus         | $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{177}\text{Lu}$ , $^{223}\text{Ra}$ , $^{225}\text{Ac}$   |
| 6  | Czech Republic | $^{131}\text{I}$ , $^{90}\text{Y}$ , $^{153}\text{Sm}$ , $^{89}\text{Sr}$ , $^{223}\text{Ra}$ , $^{186}\text{Re}$ , $^{169}\text{Er}$ , $^{177}\text{Lu}$  |
| 7  | Denmark        | $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{177}\text{Lu}$ , $^{223}\text{Ra}$   |
| 8  | Estonia        | $^{131}\text{I}$ , $^{32}\text{P}$ , $^{223}\text{Ra}$ , $^{186}\text{Re}$ , $^{169}\text{Er}$ , $^{153}\text{Sm}$ , $[^{177}\text{Lu}]$ Lu-DOTATATE<br>$^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{177}\text{Lu}$   |
| 9  | Finland        | $^{131}\text{I}$ , $^{177}\text{Lu}$ , $^{90}\text{Y}$ , $^{186}\text{Re}$ $[^{131}\text{I}]\text{-NaI}$ , $[^{177}\text{Lu}]$ Lu-DOTATATE, $^{90}\text{Y}$ -glass microspheres, $[^{131}\text{I}]$ I-mIBG, $^{186}\text{Re}$ -colloids  |
| 10 | France         | $^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{169}\text{Er}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{223}\text{Ra}$  |
| 11 | Germany        | $^{32}\text{P}$ , $^{67}\text{Cu}$ , $^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{169}\text{Er}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{188}\text{Re}$ , $^{211}\text{At}$ , $^{213}\text{Bi}$ , $^{223}\text{Ra}$ , $^{225}\text{Ac}$ , $^{227}\text{Th}$   |
| 12 | Greece         | $^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{169}\text{Er}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{188}\text{Re}$ , $^{223}\text{Ra}$  |
| 13 | Hungary        | $^{32}\text{P}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{223}\text{Ra}$   |
| 14 | Ireland        | $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{223}\text{Ra}$ , $^{153}\text{Sm}$ , $[^{177}\text{Lu}]$ Lu-PSMA-617, $[^{177}\text{Lu}]$ Lu-DOTATATE<br>$^{169}\text{Er}$ , $^{32}\text{P}$   |
| 15 | Italy          | $^{131}\text{I}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$ , $^{169}\text{Er}$ , $^{188}\text{Re}$ , $^{223}\text{Ra}$ , $^{89}\text{Sr}$ , $^{90}\text{Y}$  |
| 16 | Latvia         | $^{11}\text{C}$ , $^{18}\text{F}$ , $^{68}\text{Ga}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{177}\text{Lu}$ , $^{223}\text{Ra}$ $[^{18}\text{F}]\text{-FDG}$ , $[^{18}\text{F}]$ F-PSMA, $[^{68}\text{Ga}]$ Ga-PSMA, $[^{177}\text{Lu}]$ Lu-PSMA   |
| 17 | Lithuania      | $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{166}\text{Ho}$ , $^{223}\text{Ra}$   |
| 18 | Luxembourg     | $^{32}\text{P}$ , $^{90}\text{Y}$ , $^{131}\text{I}$ , $^{153}\text{Sm}$ , $^{169}\text{Er}$ , $^{186}\text{Re}$ , $^{211}\text{At}$ , $^{213}\text{Bi}$ , $^{223}\text{Ra}$ , $^{225}\text{Ac}$ , $^{227}\text{Th}$   |
| 19 | Malta          | $^{131}\text{I}$ , $^{90}\text{Y}$   |
| 20 | Netherlands    | $^{32}\text{P}$ , $^{89}\text{Sr}$ , $^{90}\text{Y}$ , $^{103}\text{Pd}$ , $^{125}\text{I}$ , $^{131}\text{I}$ , $^{152}\text{Eu}$ , $[^{177}\text{Lu}]$ Lu-DOTATATE, $[^{225}\text{Ac}]$ Ac-PSMA<br>$^{154}\text{Eu}$ , $^{153}\text{Sm}$ , $^{166}\text{Ho}$ , $^{169}\text{Er}$ , $^{177}\text{Lu}$ , $^{186}\text{Re}$ , $^{188}\text{Re}$ , $^{213}\text{Bi}$ , $^{223}\text{Ra}$ , $^{225}\text{Ac}$ , $^{227}\text{Ac}$ , $^{227}\text{Th}$ |
| 21 | Poland         | $^{153}\text{Sm}$ , $^{89}\text{Sr}$ , $^{223}\text{Ra}$ , $^{90}\text{Y}$ , $^{169}\text{Er}$ , $^{186}\text{Re}$ , $^{131}\text{I}$ , $^{177}\text{Lu}$  |
| 22 | Portugal       | $^{131}\text{I}$ , $^{166}\text{Ho}$ , $^{177}\text{Lu}$ , $^{223}\text{Ra}$ , $^{90}\text{Y}$ , $^{32}\text{P}$ , $^{89}\text{Sr}$ $[^{177}\text{Lu}]$ Lu-DOTATATE  |

|    |          |   |
|----|----------|---|
| 23 | Romania  | <sup>89</sup> Sr, <sup>90</sup> Y, <sup>131</sup> I, <sup>153</sup> Sm, <sup>177</sup> Lu, <sup>188</sup> Re  |
| 24 | Slovakia | <sup>131</sup> I, <sup>223</sup> Ra, <sup>177</sup> Lu, <sup>89</sup> Sr, <sup>90</sup> Y   |
| 25 | Slovenia | <sup>131</sup> I, <sup>177</sup> Lu, <sup>90</sup> Y, <sup>223</sup> Ra, <sup>186</sup> Re, <sup>64</sup> Cu  |
| 26 | Spain    | <sup>32</sup> P, <sup>89</sup> Sr, <sup>90</sup> Y, <sup>131</sup> I, <sup>153</sup> Sm, <sup>166</sup> Ho, <sup>169</sup> Er, <sup>177</sup> Lu, <sup>186</sup> Re, <sup>188</sup> Re, <sup>223</sup> Ra |
| 27 | Sweden   | <sup>131</sup> I, <sup>90</sup> Y, <sup>223</sup> Ra, <sup>153</sup> Sm, <sup>32</sup> P, <sup>177</sup> Lu   |
| 28 | UK       | <sup>90</sup> Y, <sup>131</sup> I, <sup>177</sup> Lu, <sup>223</sup> Ra [ <sup>177</sup> Lu] Lu-PSMA  |

### 3. Needs

80 % respondents expressed that PRISMAP Consortium efforts would bring benefit in their research and development activities and elaborated on their needs: higher availability for radiopharmaceuticals, sharing the new research protocols across countries, to produce more reliable and stronger evidence data, speeding up the implementation of new radiotracers in clinical practice. It was also expressed that there is a need for multicentric trial facilitation (both preclinical and clinical), extension of portfolio, theranostic advancements, access to radio-lanthanides and Auger emitters and options to collaborate with producers of emerging radionuclides. Some respondents expressed they were self-sufficient in terms of production and would not benefit from PRISMAP consortium efforts yet.

Few respondents directly indicated the need to use isotope mass-separator both for research and optimization of method itself as well as use of the mass-separator for already produced radionuclide purification.

### 4. Conclusions

From a first overview, some companies and research centres active in the field of radionuclide/radiopharmaceutical production, research and nuclear medicine are already self-sufficient and do not require additional access. A clear majority of respondents (80 %), however, indicated to gain benefit and foster their research and development from the PRISMAP consortium already at this stage. Either it is availability of the novel radionuclides, mass-separated isotopes, research partnerships or a platform for uniform educational capacities.

**Manufacturing.** The data confirmed common aspects in all respondents: the biggest challenge for the manufacturers is the availability of target materials. Respondents did indicate the most common issues with the enriched material supply/stock that companies/institutions experienced – availability, delivery time, purity/enrichment grade, quantity and price as well as transport and regulatory limitations, including lack of harmonized import/export legislation and complexity of supply chains.

The results show that there are sufficient national >38% or international >18% distribution routes and methods established, although having reported challenges due to legislation constraints, especially for novel radionuclides. For longer international radionuclide shipments - the customs clearance was indicated as obstacle due to medical radionuclide short half-life, obviously such delays must be mitigated. Some of the information about logistics and distribution matters were not available to be disclosed due to company policies. Furthermore, 30 respondent companies/institutions plan to increase manufactured volume of radionuclides in following years with certain limitations in infrastructure, shortage of staff and expertise, "beam time" or production capacity, target material supply and other financial or managerial issues.

Main novel radionuclides that would be of interest for this user community in the next 2-5 years are <sup>225</sup>Ac, <sup>149</sup>Tb, <sup>152</sup>Tb, <sup>155</sup>Tb, <sup>161</sup>Tb, <sup>89</sup>Zr, <sup>67</sup>Cu, <sup>64</sup>Cu, <sup>165</sup>Er/<sup>169</sup>Er, <sup>47</sup>Sc, <sup>44</sup>Sc, <sup>177</sup>Lu, <sup>211</sup>At, <sup>188</sup>Re. Quite interestingly, there is

not yet in the responses expressed interest in other PRISMAP portfolio radionuclides from respondents such as:  $^{111}\text{Ag}$ ,  $^{135}\text{La}$ ,  $^{153}\text{Sm}$ ,  $^{213}\text{Bi}$ . We can therefore expect even more demand for  $^{225}\text{Ac}$ , terbium radionuclides and  $^{67}\text{Cu}$  production in the following years, while other radionuclides should be elaborated within the PRISMAP user forum. We must stress that none (except for iodine radiopharmaceuticals) of the current responder institutions are interested in possibilities of “matched pair” from Terbium and Scandium radionuclides in the near future, this reflects still insufficient pre-clinical data and/or availability of the forementioned radionuclides.

The main limitations that respondents foresee to face again are regulatory limitations and transport limitations, including activity limits of radionuclides. The elaboration of a list of potential transport companies able to deal with the transnational transport of non-conventional radionuclides on the web access platform, together with efforts from PRISMAP to provide data towards regulation authorities would address some of these findings.

**Clinical use.** Radiopharmaceuticals for pre-clinical and clinical applications are mainly produced on site. The existing and established import or distribution routes can reduce decay losses during transportation and foster translational research to bring emerging radiopharmaceuticals into clinical trial phase. Respondents expressed that PRISMAP consortium efforts would enhance their research and development activities towards higher availability for radiopharmaceuticals, sharing the new research protocols across countries, to produce more reliable and stronger evidence data and speeding up the implementation of new radiotracers in clinical practice and collaboration with producers of emerging radionuclides. All respondents from the nuclear medicine/user section perform studies in oncology, fewer in cardiology, inflammation, endocrinology, neurology, traumatology/orthopaedics, nephrology and pulmonology.

Necessity to transfer patients to other countries for specified Nuclear Medicine examinations and/or treatment procedures were required in up to 70 % of end user respondents for the following reasons - unavailable radiopharmaceutical access, unavailable radionuclide or no reimbursement by the national healthcare system.

The data also confirmed needed improvements for preclinical/clinical users such as unified licensing and registration of available radionuclides and kits in Europe, specified equipment/technology (e.g., collimators etc.) and information about transport and logistics networks in Europe.

The most often emerging technologies at respondents' institutions are the following - SPECT/CT software advances (quantification, 3D dynamics etc.) and PET new generation camera with extended axial field of view, optimised image and dose reduction. End users are interested not only in new radionuclides and pharmaceuticals for research and preclinical/clinical purposes, but also in technology advancements that shows their interest in development but first of all is responsibility of individual centres and not the purpose of this consortium.

**Training.** 83% of all the institutions in this survey are involved in the training of industry experts, technicians, students and researchers at various expertise levels in nuclear physics, radiochemistry and radiopharmacy. The most often offered training levels are PhD programmes, scientific visits, workshops and seminars. Main limitations in the training process are unavailability for full hands-on training, access to infrastructure (e.g., accelerator), low funding, difficulties in recruiting students and above all the lack of technical staff and pre-clinical scientists with a global view from radiochemistry to pharmacology. Often there is a lack of fundamental background knowledge on nuclear physics and research reactors due to non-existent dedicated programmes for trainees in the universities. To conclude, there is a need for hands-on and targeted trainings.

From the survey results, we can conclude that there is evident necessity of PRISMAP not only as a web-based entry platform for the production and dispatch of non-conventional radionuclides, but also as a long-term network for aiding an advancement in emerging radionuclide distribution. With centralised and harmonised procedures and legislation and their use in translational research, pre-clinical/clinical research and nuclear medicine, offered by efforts of the PRISMAP consortium and future initiatives. Hands-on and targeted trainings should also become an integral part of the PRISMAP activities to match the needs of the community.

Even though respondent activity has been considered optimal, there is still a need for reaching out to more responders from South-East regions (e.g., Balkan countries). Therefore, it would be advised to continue gathering the data from respondents even after the deliverable 5.1. term and to have a continuous update of the available facilities and their activities and include them in the PRISMAP map project supporting WP6 and WP7 concepts. The continuous data acquisition is crucial to maintain actual radionuclide map across Europe, therefore aiding radionuclide producer and user communities.

The information collected will be used to evolve the PRISMAP common interface WP1-TNA1 and it will naturally interface with WP2-TNA2 and WP3-TNA3 to evolve the services to meet the industrial and clinical research further needs.

## References

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4. The IAEA Research Reactor Database (RRDB)" <https://nucleus.iaea.org/rrdb/#/home>
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## Appendices

### Appendix 1: Cyclotrons for radionuclide production in Europe<sup>1</sup>

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<sup>1</sup> Database of Cyclotrons used for Radionuclide production: <https://nucleus-new.iaea.org/sites/accelerators/Pages/Cyclotron.aspx>

**Appendix 1 - Deliverable 5.1 - WP5-TNA2 - Questionnaire on industrial and clinical key players and needs**  
**Cyclotrons for radionuclide production in Europe [1]**

| Nr | Facility   | Country             | City                       | Manufacturer | Model           | Proton energy (MeV) | PET RND | SPECT RND |
|----|--|---------------------|----------------------------|--------------|-----------------|---------------------|---------|-----------|
| 1  | Alikhanyan Science (Yerevan Institute) Laboratory Physics      | Armenia             | Yerevan                    | IBA          | CYCLONE 18      | 18                  | Yes     | No        |
| 2  | Argos Klagenfurt   | Zyklotron Austria   | Klagenfurt                 | GE           | PETtrace        | 16                  | Yes     | No        |
| 3  | Argos Zyklotron Linz   | Austria             | Linz                       | GE           | PETtrace        | 16                  | Yes     | No        |
| 4  | Seibersdorf Laboratories                                       | Austria             | Seibersdorf                | GE           | PETtrace        | 16                  | Yes     | No        |
| 5  | AKH Wien   | Austria             | Wien                       | GE           | PETtrace        | 16                  | Yes     | No        |
| 6  | Azerbaijan Centre of Oncology                                  | National Azerbaijan | Baku                       | IBA          | CYCLONE 18/9    | 18                  | Yes     | No        |
| 7  | NUCLEAR CENTRE MEDICINE  | Azerbaijan          | Baku                       | IBA          | CYCLONE 18      | 18                  | Yes     | No        |
| 8  | N.N. Alexandrov National Cancer Centre of Belarus              | Belarus             | Lesnoy                     | IBA          | CYCLONE 18/9 HC | 18                  | Yes     | No        |
| 9  | Molecular Imaging Center Antwerp (MICA), University of Antwerp | Belgium             | Antwerp                    | Siemens      | ECLIPSE         | 11                  | Yes     | No        |
| 10 | University Hospital UZ Brussels                                | Belgium             | Brussel                    | IBA          | CYCLONE KIUBE   | 18                  | Yes     | No        |
| 11 | BetaPlus Pharma  | Belgium             | Bruxelles                  | IBA          | CYCLONE 18      | 18                  | Yes     | No        |
| 12 | Université Libre de Bruxelles, Hospital Erasme                 | Belgium             | Brussels                   | IBA          | CYCLONE 30      | 30                  | Yes     | Yes       |
| 13 | IRE  | Belgium             | Fleurus                    | IBA          | CYCLONE 14      | 14                  | Yes     | No        |
| 14 | University Hospital Gent                                       | Belgium             | Gent                       | IBA          | Cyclone 18      | 18                  | Yes     | No        |
| 15 | Cyclotron UZGent   | Belgium             | Gent                       | IBA          | CYCLONE 18      | 18                  | Yes     | No        |
| 16 | University Hopital KU Leuven                                   | Belgium             | Leuven                     | IBA          | CYCLONE 18      | 18                  | Yes     | No        |
| 17 | Research University Liege Center                               | Belgium             | Liège                      | IBA          | CYCLONE 18      | 18                  | Yes     | No        |
| 18 | University Hospital CHU Liege                                  | Belgium             | Liège                      | IBA          | CYCLONE KIUBE   | 18                  | Yes     | No        |
| 19 | UCL, Centre de Recherches du Cyclotron                         | Belgium             | Ottignies-Louvain-la-Neuve | IBA          | CYCLONE 30      | 30                  | No      | Yes       |

|    |  |                |            |              |            |       |     |     |
|----|--|----------------|------------|--------------|------------|-------|-----|-----|
| 20 | Alexandrovksa-University Multiprofile Hospital for Active Treatment        | Bulgaria       | Sofia      | ABT          | BG-75      | 7.5   | Yes | No  |
| 21 | The Institute for Nuclear Research and Nuclear Energy (INRNE)              | Bulgaria       | Sofia      | ACSI         | TR-24      | 24    | Yes | Yes |
| 22 | ECZACIBASI-MONROL BULGARIA   | Bulgaria       | Sofia      | IBA          | CYCLONE 18 | 18    | Yes | No  |
| 23 | St. Marina - University Multiprofile Hospital for Active Treatment         | Bulgaria       | Varna      | ABT          | BG-75      | 7.5   | Yes | No  |
| 24 | Rudjer Boskovic Institute  | Croatia        | Zagreb     | IBA          | CYCLONE 18 | 18    | Yes | No  |
| 25 | Oncology Centre  | Cyprus         | Limassol   | ABT          | BG-75      | 7.5   | Yes | No  |
| 26 | Masaryk Memorial Cancer Institute, PET Center                              | Czech Republic | Brno       | IBA          | CYCLONE 18 | 18    | Yes | No  |
| 27 | unspecified  | Czech Republic | Prague     | IBA          | CYCLONE 18 | 18    | No  | No  |
| 28 | Nuclear Physics Institute of the Academy of Sciences of the Czech Republic | Czech Republic | Prague     | NIIIFA       | U-120      | 36    | No  | No  |
| 29 | unspecified  | Czech Republic | Peč        | IBA          | CYCLONE 18 | 18    | No  | No  |
| 30 | unspecified  | Czech Republic | Řež        | IBA          | CYCLONE 18 | 18    | No  | No  |
| 31 | Nuclear Physics Institute of the Academy of Sciences of the Czech Republic | Czech Republic | Řež        | ACSI         | TR-24      | 18-24 | Yes | Yes |
| 32 | Aarhus Sygehus   | Denmark        | Aarhus     | GE           | PETtrace   | 16    |     |     |
| 33 | unspecified  | Denmark        | Aarhus     | GE           | PETtrace   | 16    | No  | No  |
| 34 | unspecified  | Denmark        | Aarhus     | IBA          | CYCLONE 18 | 18    | No  | No  |
| 35 | University Hospital of Copenhagen  | Denmark        | Copenhagen | Scanditronix | MC 32NI    | 32    |     |     |
| 36 | unspecified  | Denmark        | Copenhagen | Siemens      | ECLIPSE    | 11    | No  | No  |
| 37 | Bispebjerg Hospital  | Denmark        | Copenhagen | GE           | GENtrace   | 7.8   |     |     |
| 38 | unspecified  | Denmark        | Herlev     | IBA          | CYCLONE 18 | 18    | No  | No  |
| 39 | Odense Universitetshospital  | Denmark        | Odense     | GE           | PETtrace   | 16    |     |     |
| 40 | unspecified  | Denmark        | Odense     | GE           | PETtrace   | 16    | No  | No  |
| 41 | Forskningscenter Riso  | Denmark        | Roskilde   | GE           | PETtrace   | 16    |     |     |

|    |  |           |                      |           |               |       |     |     |
|----|--|-----------|----------------------|-----------|---------------|-------|-----|-----|
| 42 | HUS Medical Imaging Center Cyclotron unit                                | Finland   | Helsinki             | IBA       | Cyclone KIUBE | 18    | Yes | No  |
| 43 | Docrates Facility  | Finland   | Helsinki             | GE        | PETtrace      | 16    | Yes | No  |
| 44 | University of Helsinki   | Finland   | Helsinki             | IBA       | Cyclone 10/5  | 10    | Yes | No  |
| 45 | University of Jyväskylä (JYFL)   | Jyväskylä | NIIefa               | MCC-30/15 | 18-30         | Yes   | Yes |     |
| 46 | KYS  | Finland   | Kuopio               | GE        | PETtrace      | 16    |     |     |
| 47 | Turku PET Center   | Finland   | Turku                | ACSI      | TR-19         | 14-19 | Yes | No  |
| 48 | Turku PET Center   | Finland   | Turku                | IBA       | CYCLONE 3D    | 3     | Yes | No  |
| 49 | Turku PET Center   | Finland   | Turku                | NIIefa    | MGC-20        | 3-20  | Yes | No  |
| 50 | Turku PET Center   | Finland   | Turku                | NIIefa    | CC-18/9       | 18    | Yes | No  |
| 51 | unspecified  | France    | Caen                 | IBA       | CYCLONE 18    | 18    | No  | No  |
| 52 | Cyclopharma Laboratories   | France    | Dijon                | GE        | PETtrace      | 16    |     |     |
| 53 | unspecified  | France    | Fontenay aux Roses   | IBA       | CYCLONE 18    | 18    | No  | No  |
| 54 | unspecified  | France    | Gif sur Yvette Cedex | IBA       | CYCLONE 30    | 30    | No  | No  |
| 55 | Laboratoires Cyclopharma Amiens  | France    | Glisy                | GE        | PETtrace      | 16    |     |     |
| 56 | University of Strasbourg/CNRS, Institut Pluridisciplinaire Hubert Curien | France    | Strasbourg           | ACSI      | TR-24         | 24    |     |     |
| 57 | Laboratoires Cyclopharma Lyon  | France    | Janneyrias           | GE        | PETtrace      | 16    |     |     |
| 58 | CERMEP - Imagerie du Vivant  | France    | BRON (LYON)          | IBA       | CYCLONE 18    | 18    | Yes | No  |
| 59 | CIMGUA   | France    | Les Abymes           | PMB       | ISOTRACE      | 12    | Yes | No  |
| 60 | TECHNOPOLE CHATEAU GOMBERT   | DE France | Marseille            | GE        | PETtrace      | 16    |     |     |
| 61 | Cerimed  | France    | Marseille            | GE        | PETtrace      | 16    |     |     |
| 62 | Arronax  | France    | Saint Herblain       | IBA       | CYCLONE 70    | 70    | Yes | Yes |
| 63 | Cis Bio International  | France    | Nimes                | GE        | PETtrace      | 16    |     |     |
| 64 | CEA - SHFJ   | France    | Orsay                | PMB       | ISOTRACE      | 12    | Yes | No  |
| 65 | unspecified  | France    | Orsay                | IBA       | CYCLONE 18    | 18    | No  | No  |
| 66 | unspecified  | France    | Paris                | IBA       | CYCLONE 18    | 18    | No  | No  |
| 67 | unspecified  | France    | Paris                | Siemens   | ECLIPSE       | 11    | No  | No  |

|    |   |         |                           |         |            |      |     |     |
|----|---|---------|---------------------------|---------|------------|------|-----|-----|
| 68 | Hopital Xavier Arnozan  | France  | Pessac                    | GE      | PETtrace   | 16   |     |     |
| 69 | IBA RENNES  | France  | Rennes                    | GE      | PETtrace   | 16   |     |     |
| 70 | unspecified   | France  | Saint Genis- Pouilly      | IBA     | CYCLONE 18 | 18   | No  | No  |
| 71 | Institut Curie's René Huguenin                                      | France  | Saint-Cloud               | GE      | PETtrace   | 16   |     |     |
| 72 | GIP CYROI   | France  | Sainte Clotilde - Reunion | GE      | PETtrace   | 16   |     |     |
| 73 | Réseau de Soins Cancérologie Onconord, Positron                     | France  | Sarcelles                 | GE      | PETtrace   | 16   |     |     |
| 74 | unspecified   | France  | Sarcelles                 | IBA     | CYCLONE 18 | 18   | No  | No  |
| 75 | Advanced Accelerator Applications, St Genis Pouilly                 | France  | Saint Genis- Pouilly      | GE      | PETtrace   | 16   |     |     |
| 76 | Laboratoires Cyclopharma Toulouse                                   | France  | Toulouse                  | GE      | PETtrace   | 16   |     |     |
| 77 | unspecified   | France  | Toulouse                  | IBA     | CYCLONE 10 | 10   | No  | No  |
| 78 | Cyclopharma Laboratories  | France  | Tours                     | GE      | PETtrace   | 16   |     |     |
| 79 | Advanced Accelerator Application                                    | France  | Troyes                    | GE      | PETtrace   | 16   |     |     |
| 80 | CSBIO Nancy Chu Brabois   | France  | Vandœuvre les Nancy       | GE      | PETtrace   | 16   |     |     |
| 81 | University Hospital Aachen  | Germany | Aachen                    | GE      | PETtrace   | 16.5 | Yes | No  |
| 82 | unspecified   | Germany | Aachen                    | Siemens | ECLIPSE    | 11   | No  | No  |
| 83 | unspecified   | Germany | Bad Berka                 | GE      | PETtrace   | 16   | No  | No  |
| 84 | unspecified   | Germany | Bad Berka                 | Siemens | ECLIPSE    | 11   | No  | No  |
| 85 | Hertz-Diabeteszentrum NRW   | Germany | Bad Oeynhausen            | GE      | PETtrace   | 16   |     |     |
| 86 | unspecified   | Germany | Bad Oeynhausen            | IBA     | CYCLONE 18 | 18   | No  | No  |
| 87 | Diagnostisch Therapeutisches Zentrum Radiochemie am Frankfurter Tor | Germany | Berlin                    | GE      | MiniTrace  | 10   |     |     |
| 88 | EUROPET BERLIN ZYKLOTRON GMBH                                       | Germany | Berlin                    | GE      | PETtrace   | 16   |     |     |
| 89 | Charité – Berlin  | Germany | Berlin                    | IBA     | CYCLONE 3  | 3    | Yes | No  |
| 90 | Umbra Medical AG  | Germany | Bonn                      | GE      | PETtrace   | 16   |     |     |
| 91 | unspecified   | Germany | Bonn                      | Siemens | RDS112     | 11   | No  | No  |
| 92 | Helmholtz-Zentrum Dresden-Rossendorf,                               | Germany | Dresden                   | ACSI    | TR-FLEX    | 24   | Yes | Yes |

| Institute of Radiopharmacy |  |         |                          |                           |                     |    |     |    |
|----------------------------|--|---------|--------------------------|---------------------------|---------------------|----|-----|----|
| 93                         | unspecified  | Germany | Dresden                  | NIIefa                    | U-120               | 36 | No  | No |
| 94                         | ZAG Zyklotron AG   | Germany | Eggenstein-Leopoldshafen | ACSI                      | TR-19/9             | 19 |     |    |
| 95                         | unspecified  | Germany | Essen                    | IBA                       | CYCLONE 18          | 18 | No  | No |
| 96                         | Institute for Medical Radiation Physics  | Germany | Essen                    | TCC                       | CV 28               | 28 |     |    |
| 97                         | EURO PET GMBH  | Germany | Freiburg                 | GE                        | PETtrace            | 16 |     |    |
| 98                         | Universitätsklinikum Hamburg-Eppendorf   | Germany | Hamburg                  | Philips                   | 140/IV              | 25 |     |    |
| 99                         | Medizinische Hochschule Hannover (MHH)   | Germany | Hannover                 | Scanditronix              | MC 35               | 35 |     |    |
| 100                        | German Cancer Research Centre (DKFZ)   | Germany | Heidelberg               | Scanditronix-Negative-Ion | MC 32- Negative-Ion | 32 | Yes | No |
| 101                        | Forschungszentrum Jülich GMBH - Institute of Neuroscience and Medicine Nuclear Chemistry (INM-5) | Germany | Jülich                   | IBA                       | CYCLONE 18          | 18 | Yes | No |
| 102                        | Forschungszentrum Jülich GMBH - Institute of Neuroscience and Medicine Nuclear Chemistry (INM-5) | Germany | Jülich                   | GE                        | PETtrace            | 16 |     |    |
| 103                        | Forschungszentrum Jülich GMBH - Institute of Neuroscience and Medicine Nuclear Chemistry (INM-5) | Germany | Jülich                   | IBA                       | CYCLONE 30          | 30 | No  | No |
| 104                        | Forschungszentrum Jülich GMBH -Institute of Neuroscience and Medicine Nuclear Chemistry (INM-5)  | Germany | Jülich                   | Japan Works               | Steel BC 1710       | 40 | No  | No |
| 105                        | ZAG Zyklotron AG   | Germany | Karlsruhe                | ACSI                      | TR-19/9             | 19 |     |    |
| 106                        | ZAG Zyklotron AG   | Germany | Karlsruhe                | TCC                       | CP-42               | 42 |     |    |
| 107                        | unspecified  | Germany | Kiel                     | Siemens                   | ECLIPSE             | 11 | No  | No |
| 108                        | Max-Planck-Institut fuer Neurologische Forschung   | Germany | Koln                     | Scanditronix              | MC 16               | 16 |     |    |
| 109                        | Universität Leipzig N.M.   | Germany | Leipzig                  | GE                        | PETtrace            | 16 |     |    |
| 110                        | unspecified  | Germany | leipzig                  | IBA                       | CYCLONE 18          | 18 | No  | No |
| 111                        | Johannes Gutenberg-Universität Mainz   | Germany | Mainz                    | GE                        | MiniTrace           | 10 |     |    |

|     |   |                          |             |                        |                        |                  |          |     |     |
|-----|---|--------------------------|-------------|------------------------|------------------------|------------------|----------|-----|-----|
| 112 | University Muenster   | Hospital                 | Germany     | Muenster               | IBA                    | Cyclone KIUBE 18 | 18       | Yes | No  |
| 113 | unspecified   |                          | Germany     | Muenster               | Siemens                | ECLIPSE          | 11       | Yes | No  |
| 114 | Klinikum Rechts der Isar AOER   |                          | Germany     | Munich                 | GE                     | PETtrace         | 16       |     |     |
| 115 | Ludwig-Maximilians Universitat   |                          | Germany     | Munich                 | GE                     | PETtrace         | 16       |     |     |
| 116 | unspecified   |                          | Germany     | Munich                 | Siemens                | RDS112           | 11       | No  | No  |
| 117 | ABX GmbH  |                          | Germany     | Radeberg               | GE                     | MiniTrace        | 10       |     |     |
| 118 | University Regensburg   | Hospital                 | Germany     | Regensburg             | Siemens                | RDS111           | 11       | Yes | No  |
| 119 | unspecified   |                          | Germany     | Rossendorf bei Dresden | IBA                    | CYCLONE 18       | 18       | No  | No  |
| 120 | Universitatsklinikum Rostock AR, Klinik und Poliklinik fr Nuklearmedizin                       |                          | Germany     | Rostock                | GE                     | MiniTrace        | 10       |     |     |
| 121 | Eberhard Karls University of Tubingen  |                          | Germany     | Tubingen              | GE                     | PETtrace         | 16       |     |     |
| 122 | Uni. Ulm - Eselsberg  |                          | Germany     | Ulm                    | GE                     | PETtrace         | 16       |     |     |
| 123 | unspecified   |                          | Germany     | Ulm                    | IBA                    | CYCLONE 18       | 18       | No  | No  |
| 124 | Universitatsklinikum   |                          | Germany     | Wurzburg              | GE                     | PETtrace         | 16       |     |     |
| 125 | BIOKOSMOS S.A.  |                          | Greece      | Lavrion                | GE                     | PETtrace         | 16.4     |     |     |
| 126 | BIOKOSMOS SA  |                          | Greece      | Thessaloniki           | GE                     | PETtrace 890     | 16.4     | Yes | No  |
| 127 | unspecified   |                          | Hungary     | Budapest               | Siemens                | ECLIPSE          | 11       | No  | No  |
| 128 | University of Debrecen Clinical Center  | Hungary Nuclear Medicine | Hungary     | Debrecen               | GE                     | PETtrace 800     | 16.5     | Yes | No  |
| 129 | Dept Applied Nuclear Physics, Institute for Nuclear Research of the Hungarian Academy of Sciences |                          | Hungary     | Debrecen               | Rossatom (Sovietunion) | MGC-20E          | 18       | Yes | Yes |
| 130 | IMC-Debreceni Orvosi Egyetem  |                          | Hungary     | Debrecen               | GE                     | PETtrace         | 16       |     |     |
| 131 | ATOMKI  |                          | Hungary     | Debrecen               | NIIEFA                 | MGC-20           | 20       | No  | No  |
| 132 | Medicopus Nonprofit Ltd.  |                          | Hungary     | Kaposvar              | Siemens                | Eclipse          | 11       | Yes | No  |
| 133 | Landspitali   |                          | Iceland     | Reykjavik              | GE                     | MiniTrace        | 10       |     |     |
| 134 | M2i Limited   |                          | Ireland     | Dublin                 | GE                     | PETtrace         | 16.5     |     |     |
| 135 | S. Gaetano Nuclear Medicine Center  |                          | Italy       | Bagheria               | IBA                    | CYCLONE 18/9     | 18       | Yes | No  |
| 136 | Policlinico Malpighi  |                          | Sant'Orsola | Italy                  | Bologna                | GE               | PETtrace | 16  |     |

|     |  |                         |              |              |                 |    |     |    |
|-----|--|-------------------------|--------------|--------------|-----------------|----|-----|----|
| 137 | A.O. Spedali Civili-Brescia  | Italy                   | Brescia      | GE           | PETtrace        | 16 |     |    |
| 138 | A.O. Brotzu, Centro PET  | Italy                   | Cagliari     | GE           | MiniTrace       | 10 |     |    |
| 139 | SPARKLE  | Italy                   | Casarano     | IBA          | CYCLONE<br>18/9 | 18 | Yes | No |
| 140 | Castelfranco<br>Radiopharmacy-<br>Cyclotron Unit                                   | Veneto Italy            | Castelfranco | Siemens      | RDS112          | 11 | Yes | No |
| 141 | Castelfranco<br>Radiopharmacy-<br>Cyclotron Unit                                   | Veneto Italy            | Castelfranco | Siemens      | ECLIPSE         | 11 | No  | No |
| 142 | AZIENDA OSPEDALIERA CANNIZZIRO   | Italy                   | Catania      | IBA          | CYCLONE<br>18   | 18 | Yes | No |
| 143 | Azienda Sanitaria Ospedaliera S. Croce E Carle                                     | Italy                   | Cuneo        | GE           | MiniTrace       | 10 |     |    |
| 144 | Ospedale Careggi   | Italy                   | Florence     | GE           | MiniTrace       | 10 |     |    |
| 145 | AZIENDA OSPEDALIERA SAN MARTINO  | Italy                   | Genova       | Siemens      | ECLIPSE         | 11 | Yes | No |
| 146 | Joint Research Centre (European Commission)  | Italy                   | Ispra        | Scanditronix | MC-40           | 40 |     |    |
| 147 | AAA Colleretto Giacosa   | Italy                   | Ivrea        | GE           | PETtrace        | 16 |     |    |
| 148 | Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (I.R.S.T.) S.r.l | Italy                   | Meldola      | GE           | PETtrace        | 16 |     |    |
| 149 | AZIENDA OSPEDALIERA POLICLINICO UNIVERSITARIO "G. MARTINO"                         | Italy                   | Messina      | Siemens      | ECLIPSE         | 11 | Yes | No |
| 150 | Policlinico Maggiare   | Ospedale Italy          | Milan        | GE           | PETtrace        | 16 |     |    |
| 151 | IEO  | Italy                   | Milan        | GE           | PETtrace        | 16 |     |    |
| 152 | San Raffaele Hospital  | Italy                   | Milan        | IBA          | CYCLONE<br>18/9 | 18 | Yes | No |
| 153 | IRCSS OSPEDALE SAN RAFFAELE  | Italy                   | Milan        | IBA          | CYCLONE<br>18   | 18 | Yes | No |
| 154 | CURIUM PHARMA c/o EUROPEAN INSTITUTE OF ONCOLOGY (IEO)                             | Italy                   | Milan        | IBA          | CYCLONE<br>18   | 18 | Yes | No |
| 155 | Istituto Nazionale per lo Studio e la Cura dei Tumori                              | Italy                   | Milan        | Scanditronix | MC 17E          | 17 |     |    |
| 156 | A.C.O.M. CENTER MACERATA S.r.l   | ADVANCED ONCOLOGY Italy | Montecosaro  | IBA          | CYCLONE<br>18   | 18 | Yes | No |
| 157 | S.D.N. SPA   | Italy                   | Naples       | GE           | MiniTrace       | 10 |     |    |

|     |  |            |                 |  |            |     |     |    |
|-----|--|------------|-----------------|--|------------|-----|-----|----|
| 158 | AZIENDA OSPEDALIERA UNIVERSITARIA FEDERICO II                    | Italy      | Naples          | GE                                       | MiniTrace  | 10  |     |    |
| 159 | CROM   | Italy      | Avellino        | GE                                       | MiniTrace  | 10  |     |    |
| 160 | INSTITUTO NAZIONALE TUMORI - IRCSS FONDAZIONE PASCALE            | Italy      | Naples          | IBA                                      | CYCLONE 18 | 18  | Yes | No |
| 161 | Consiglio Nazionale delle Ricerche Institute Pascale (CNR)       | Italy      | Naples          | Scanditronix                             | MC 17      | 17  |     |    |
| 162 | Azienda Ospedaliera Villa Sofia CTO                              | Italy      | Palermo         | GE                                       | PETtrace   | 16  |     |    |
| 163 | LA MADDALENA S.p.A. (private oncology center)                    | Italy      | Palermo         | IBA                                      | CYCLONE 18 | 18  | Yes | No |
| 164 | LABORATORY OF APPLIED NUCLEAR ENERGY (LENA), UNIVERSITY OF PAVIA | Italy      | Pavia           | IBA                                      | CYCLONE 18 | 18  | Yes | No |
| 165 | AZIENDA OSPEDALIERA DI PERUGIA                                   | Italy      | Perugia         | GE                                       | MiniTrace  | 10  |     |    |
| 166 | AREA DELLA RICERCA DI PISA C.N.R.                                | Italy      | Pisa            | GE                                       | PETtrace   | 16  |     |    |
| 167 | ARCISPEDALE S. MARIA NUOVA                                       | Italy      | Reggio Emilia   | GE                                       | MiniTrace  | 10  | Yes | No |
| 168 | CURIUM PHARMA c/o POLICLINICO TOR VERGATA                        | Italy      | Rome            | IBA                                      | CYCLONE 18 | 18  | Yes | No |
| 169 | Radius / Policlinico Gemelli Hospital                            | Italy      | Rome            | ACSI                                     | TR-19      | 19  |     |    |
| 170 | Iason S.R.L.   | Italy      | Rome            | GE                                       | MiniTrace  | 10  |     |    |
| 171 | NSA S.R.L.   | Italy      | Rome            | GE                                       | PETtrace   | 16  |     |    |
| 172 | ROZZANO  | Italy      | Milan           | IBA                                      | CYCLONE 18 | 18  | Yes | No |
| 173 | ITEL TELECOMUNICAZ.S.R.L   | Italy      | Ruvo di Puglia  | GE                                       | PETtrace   | 16  |     |    |
| 174 | Ospedale San Raffaele  | Italy      | Milan           | Siemens                                  | ECLIPSE    | 11  |     |    |
| 175 | Ospedale Molinette   | Italy      | Turin           | GE                                       | PETtrace   | 16  |     |    |
| 176 | CURIUM PHARMA  | Italy      | Udine           | IBA                                      | CYCLONE 18 | 18  | Yes | No |
| 177 | AAA Venafro  | Italy      | Venafro         | GE                                       | PETtrace   | 16  |     |    |
| 178 | IRCSS Ospedale Sacro Cuore Don Calabria                          | Italy      | Negrar (Verona) | ACSI (Advanced Accelerator Applications) | TR-19      | 19  | Yes | No |
| 179 | unspecified  | Kazakhstan | Almaty          | ABT                                      | BG-75      | 7.5 | No  | No |
| 180 | The Institute of Nuclear Physics                                 | Kazakhstan | Almaty          | IBA                                      | CYCLONE 30 | 30  | Yes | No |

|     |  |               |             |           |                   |            |     |     |    |
|-----|--|---------------|-------------|-----------|-------------------|------------|-----|-----|----|
| 181 | The Institute of Nuclear Physics   | Kazakhstan    | Almaty      | NIIIFA    | U-150M            | 60         | No  | No  |    |
| 182 | unspecified  | Kazakhstan    | Astana      | IBA       | CYCLONE 18        | 18         | No  | No  |    |
| 183 | unspecified  | Kazakhstan    | Semey       | IBA       | CYCLONE 18        | 18         | No  | No  |    |
| 184 | NUCLEO   | Latvia        | Riga        | IBA       | CYCLONE 18        | 18         | YES | No  |    |
| 185 | University Institution for positron emission tomography of Republic of Macedonia | Macedonia     | Skopje      | GE        | PET 860           | Trace 16.5 | Yes | No  |    |
| 186 | unspecified  | Netherlands   | Alkmaar     | IBA       | CYCLONE 18        | 18         | No  | No  |    |
| 187 | BV Cyclotron VU (1)  | Netherlands   | Amsterdam   | IBA       | CYCLONE 18        | 18         | Yes | No  |    |
| 188 | BV Cyclotron VU (2)  | Netherlands   | Amsterdam   | IBA       | Cyclone® KIUBE18  | 18         | Yes | No  |    |
| 189 | BV Cyclotron VU (3)  | Netherlands   | Amsterdam   | IBA       | Cyclone® KIUBE 18 | 18         | Yes | No  |    |
| 190 | unspecified  | Netherlands   | Amsterdam   | IBA       | CYCLONE 3         | 3          | No  | No  |    |
| 191 | unspecified  | Netherlands   | Amsterdam   | Siemens   | ECLIPSE           | 11         | No  | No  |    |
| 192 | unspecified  | Netherlands   | Eindhoven   | IBA       | CYCLONE 30        | 30         | No  | No  |    |
| 193 | unspecified  | Netherlands   | Groningen   | IBA       | CYCLONE 18        | 18         | No  | No  |    |
| 194 | Groningen Hospital   | University    | Netherlands | Groningen | Scanditronix      | MC 17F     | 17  |     |    |
| 195 | Radboud Medicine   | Translational | Netherlands | Nijmegen  | Siemens           | Eclipse HP | 11  | Yes | No |
| 196 | unspecified  | Netherlands   | Petten      | IBA       | CYCLONE 30        | 30         | No  | No  |    |
| 197 | Mallinckrodt Medical   |               | Netherlands | Petten    | Philips           | AVF        | 25  |     |    |
| 198 | Cyclotron Rotterdam B.V (Erasmus MC)   |               | Netherlands | Rotterdam | GE                | PETtrace   | 16  |     |    |
| 199 | Haukeland Hospital   | University    | Norway      | Bergen    | GE                | PETtrace   | 16  | Yes | No |
| 200 | Oslo Univ. Rikshosp.   | Sykehus       | Norway      | Oslo      | GE                | PETtrace   | 16  |     |    |
| 201 | University of Oslo   |               | Norway      | Oslo      | Scanditronix      | MC 35      | 35  |     |    |
| 202 | unspecified  |               | Norway      | Tromso    | GE                | PETtrace   | 16  | No  | No |
| 203 | unspecified  |               | Norway      | Trondheim | GE                | PETtrace   | 16  | No  | No |
| 204 | Maria Sklodowska-Curie memorial Cancer Center and Institute of Oncology          | Poland        |             | Gliwice   | IBA               | CYCLONE 18 | 18  | Yes | No |

|     |   |                     |                 |         |                  |              |      |     |    |
|-----|---|---------------------|-----------------|---------|------------------|--------------|------|-----|----|
| 205 | Swietokrzyskie Center at Kielce                         | Oncology            | Poland          | Kielce  | Siemens          | ECLIPSE      | 11   | Yes | No |
| 206 | Voxel SZPITAL KLINICZNY Z POLIKLINIKA                   | 5 WOJSKOWY          | Poland          | Krakow  | GE               | PETtrace 860 | 16.5 | Yes | No |
| 207 | Kopernik Oncology Center                                | Regional            | Poland          | Lodz    | Siemens          | ECLIPSE      | 11   | Yes | No |
| 208 | Monrol Poland   | Poland              | Mszczonow       | IBA     | CYCLONE 18       | 18           | Yes  | No  |    |
| 209 | SRODOWISKOWE LABOLATORIUM CIEZKI (Heavy Ion Laboratory) | Poland              | Warsaw          | GE      | PETtrace         | 16           | Yes  | No  |    |
| 210 | Military Institute of Medicine                          | Institute of Poland | Warsaw          | Siemens | ECLIPSE          | 11           | Yes  | No  |    |
| 211 | Eckert & Ziegler PET                                    | EURO- Poland        | Warsaw          | Siemens | ECLIPSE          | 11           | Yes  | No  |    |
| 212 | University of Coimbra- ICNAS (1)                        | Portugal            | Coimbra         | IBA     | CYCLONE 18       | 18           | Yes  | No  |    |
| 213 | University of Coimbra- ICNAS (2)                        | Portugal            | Coimbra         | IBA     | Cyclone KIUBE 18 | 18           | Yes  | No  |    |
| 214 | Hospital da Boavista                                    | Portugal            | Porto           | GE      | PETtrace         | 16           |      |     |    |
| 215 | Radiopharmaceutical Research Centre                     | Romania             | Magurele Ilfov  | ACSI    | TR-19            | 19           | Yes  | Yes |    |
| 216 | ECZACIBASI-MONROL ROMANIA                               | Romania             | Bucharest       | IBA     | CYCLONE 18       | 18           | Yes  | No  |    |
| 217 | unspecified   | Romania             | Bucharest       | NIIefa  | U-120            | 36           | No   | No  |    |
| 218 | INSTITUTUL REGIONAL DE ONCOLOGIE IASI                   | Romania             | Iasi            | GE      | MiniTrace        | 10           |      |     |    |
| 219 | unspecified   | Russia              | Ekaterinburg    | NIIefa  | P-7              |              | No   | No  |    |
| 220 | unspecified   | Russia              | Cheljabinsk     | Siemens | ECLIPSE          | 11           | No   | No  |    |
| 221 | unspecified   | Russia              | Dubna           | NIIefa  | U-120            | 36           | No   | No  |    |
| 222 | unspecified   | Russia              | Dubna           | NIIefa  | U-150            | 60           | No   | No  |    |
| 223 | unspecified   | Russia              | Dubna           | NIIefa  | U-300            | 10 MeV/n     | No   | No  |    |
| 224 | unspecified   | Russia              | Dubna           | NIIefa  | Cytrack          | 2,5 MeV/n    | No   | No  |    |
| 225 | Ural Federal University                                 | Russia              | Ekaterinburg    | ACSI    | TR-24            | 24           |      |     |    |
| 226 | Cancer Center   | Russia              | Elets           | GE      | PETtrace         | 16           |      |     |    |
| 227 | GUZ REPUBLICAN CLINICAL ONCOLOGICAL DISPENSARY          | Russia              | Kazan           | GE      | PETtrace         | 16           |      |     |    |
| 228 | Pet Center  | Russia              | Khabarovsk      | GE      | PETtrace         | 16           |      |     |    |
| 229 | unspecified   | Russia              | Khanti-Mansiysk | GE      | MiniTrace        | 10           | Yes  | No  |    |

|     |  |        |                |              |                     |     |     |    |
|-----|--|--------|----------------|--------------|---------------------|-----|-----|----|
| 230 | unspecified  | Russia | Krasnoyarsk    | IBA          | CYCLONE<br>18       | 18  | No  | No |
| 231 | unspecified  | Russia | Magnitogorsk   | Siemens      | ECLIPSE             | 11  | No  | No |
| 232 | Federal Medical Biophysics Centre                      | Russia | Moscow         | ACSI         | TR-24               | 24  |     |    |
| 233 | RONC   | Russia | Moscow         | GE           | PETtrace            | 16  |     |    |
| 234 | RONC   | Russia | Moscow         | GE           | PETtrace            | 16  |     |    |
| 235 | unspecified  | Russia | Moscow         | IBA          | CYCLONE<br>18       | 18  | No  | No |
| 236 | unspecified  | Russia | Moscow         | IBA          | CYCLONE<br>18       | 18  | No  | No |
| 237 | unspecified  | Russia | Moscow         | IBA          | CYCLONE<br>70       | 70  | No  | No |
| 238 | unspecified  | Russia | Moscow         | NIIefa       | M-1                 |     | No  | No |
| 239 | unspecified  | Russia | Moscow         | NIIefa       | M-C                 |     | No  | No |
| 240 | unspecified  | Russia | Moscow         | NIIefa       | P-7                 |     | No  | No |
| 241 | unspecified  | Russia | Moscow         | NIIefa       | MGC-20              | 20  | No  | No |
| 242 | unspecified  | Russia | Moscow         | NIIefa       | DC-3                |     | No  | No |
| 243 | Center for high-tech diagnostics                       | Russia | Moscow         | NIIefa       | CC-18/9M            | 18  | Yes | No |
| 244 | unspecified  | Russia | Moscow         | Siemens      | ECLIPSE             | 11  | No  | No |
| 245 | unspecified  | Russia | Moscow         | Siemens      | ECLIPSE             | 11  | No  | No |
| 246 | unspecified  | Russia | Moscow         | Siemens      | ECLIPSE             | 11  | No  | No |
| 247 | GVKG IM.BURDENKO                                       | Russia | Moscow         | GE           | MiniTrace           | 10  | Yes | No |
| 248 | unspecified  | Russia | Obninsk        | NIIefa       | U-150               | 60  | No  | No |
| 249 | unspecified  | Russia | Obninsk        | NIIefa       | RIC-14              |     | No  | No |
| 250 | unspecified  | Russia | Petrusko       | GE           | PETtrace            | 16  | No  | No |
| 251 | Cancer Center  | Russia | Novosibirsk    | IBA          | CYCLONE<br>Kiube 18 | 18  | Yes | No |
| 252 | JSC Nuclear Medical Technologies – Snezhinsk           | Russia | Snezhinsk      | NIIefa       | CC-18/9             | 18  | Yes | No |
| 253 | unspecified  | Russia | St Petersburg  | ABT          | BG-75               | 7,5 | No  | No |
| 254 | Medical Institute Berezin Sergey (MIBS)                | Russia | St Petersburg  | IBA          | CYCLONE<br>KIUBE    | 18  | Yes | No |
| 255 | Institute of Human Brain RAS                           | Russia | St Petersburg  | Scanditronix | MC-17               | 17  |     |    |
| 256 | unspecified  | Russia | St Petersburg  | Siemens      | ECLIPSE             | 11  | No  | No |
| 257 | unspecified  | Russia | St Petersburg  | Siemens      | ECLIPSE             | 11  | No  | No |
| 258 | St Petersburg State University (Human Brain Institute) | Russia | St. Petersburg | GE           | PETtrace            | 16  |     |    |

|                  |                                      |              |                |                   |         |            |    |     |    |
|------------------|--------------------------------------|--------------|----------------|-------------------|---------|------------|----|-----|----|
| 259              | NII                                  | KARDIOLOGII  | Russia         | St. Petersburg    | GE      | PETtrace   | 16 |     |    |
| IM.ALMAZOVA      |                                      |              |                |                   |         |            |    |     |    |
| 260              | unspecified                          |              | Russia         | St. Petersburg    | GE      | PETtrace   | 16 | No  | No |
| 261              | unspecified                          |              | Russia         | St. Petersburg    | NIIIEFA | РИ         |    | No  | No |
| 262              | unspecified                          |              | Russia         | St. Petersburg    | NIIIEFA | ФТИ        |    | No  | No |
| 263              | unspecified                          |              | Russia         | St. Petersburg    | NIIIEFA | U-120      | 36 | No  | No |
| 264              | unspecified                          |              | Russia         | St. Petersburg    | NIIIEFA | MGC-20     | 20 | No  | No |
| 265              | unspecified                          |              | Russia         | St. Petersburg    | NIIIEFA | CC-18/9    | 18 | No  | No |
| 266              | unspecified                          |              | Russia         | St. Petersburg    | NIIIEFA | CC-12      | 12 | No  | No |
| 267              | unspecified                          |              | Russia         | St. Petersburg    | NIIIEFA | C-80       | 80 | No  | No |
| 268              | unspecified                          |              | Russia         | Stavropol         | GE      | PETtrace   | 16 | No  | No |
| 269              | unspecified                          |              | Russia         | Tomsk             | NIIIEFA | P-7        |    | No  | No |
| 270              | unspecified                          |              | Russia         | Tver              | NIIIEFA | RIC-30     | 30 | No  | No |
| 271              | unspecified                          |              | Russia         | Tyumen            | Siemens | ECLIPSE    | 11 | No  | No |
| 272              | unspecified                          |              | Russia         | Ufa               | GE      | PETtrace   | 16 | No  | No |
| 273              | unspecified                          |              | Russia         | Voronezh          | Siemens | ECLIPSE    | 11 | No  | No |
| 274              | FEDERAL                              | PROTON       | Russia         | Dimitrovgrad      | GE      | MiniTrace  | 10 |     |    |
|                  | THERAPY CENTRE                       |              |                |                   |         |            |    |     |    |
| 275              | John Mallard                         | Scottish PET | United Kingdom | Aberdeen          | Siemens | RDS 111    | 11 | Yes | No |
| Centre           |                                      |              |                |                   |         |            |    |     |    |
| 276              | unspecified                          |              | Serbia         | Belgrade          | NIIIEFA | CC-1-3     |    | No  | No |
| 277              | HOSPITAL                             | INFANTA      | Spain          | Badajoz           | GE      | MiniTrace  | 10 |     |    |
| CRISTINA         | SERVISION DE                         |              |                |                   |         |            |    |     |    |
| MEDICINA NUCLEAR |                                      |              |                |                   |         |            |    |     |    |
| 278              | HOSPITAL                             | VIRGEN DE LA | Spain          | Barcelona         | GE      | PETtrace   | 16 |     |    |
| ARRIXACA         |                                      |              |                |                   |         |            |    |     |    |
| 279              | unspecified                          |              | Spain          | Barcelona         | IBA     | CYCLONE 18 |    | No  | No |
| 280              | unspecified                          |              | Spain          | Barcelona         | IBA     | CYCLONE 18 |    | No  | No |
| 281              | BARNATRON SA                         |              | Spain          | El Palmar, Murcia | GE      | PETtrace   | 16 |     |    |
|                  |                                      |              |                |                   |         |            |    |     |    |
| 282              | Molypharma S.A. / Clinica Lopez Ibor |              | Spain          | Madrid            | GE      | MiniTrace  | 10 |     |    |
|                  |                                      |              |                |                   |         |            |    |     |    |
| 283              | unspecified                          |              | Spain          | Madrid            | IBA     | CYCLONE 18 |    | No  | No |
| 284              | unspecified                          |              | Spain          | Madrid            | IBA     | CYCLONE 18 |    | No  | No |
| 285              | Centro PET Complutense (CPC)         |              | Spain          | Madrid            | Oxford  | OSCAR 12   | 12 |     |    |
|                  |                                      |              |                |                   |         |            |    |     |    |
| 286              | unspecified                          |              | Spain          | Madrid            | Siemens | ECLIPSE    | 11 | No  | No |
| 287              | unspecified                          |              | Spain          | Madrid            | Siemens | ECLIPSE    | 11 | No  | No |

|     |  |                   |                        |              |                     |    |     |    |
|-----|--|-------------------|------------------------|--------------|---------------------|----|-----|----|
| 288 | Universidad de Malaga  | Spain             | Malaga                 | GE           | PETtrace            | 16 |     |    |
| 289 | unspecified  | Spain             | Pamplona               | IBA          | CYCLONE<br>18       | 18 | No  | No |
| 290 | unspecified  | Spain             | San Sebastian          | IBA          | CYCLONE<br>18       | 18 | No  | No |
| 291 | Hospital Universitario Marques de Valdecilla                             | Spain             | Santander              | GE           | PETtrace            | 16 |     |    |
| 292 | Instituto Galego de Medicina Tecnica S.a.<br>(Galaria)                   | Spain             | Santiago de Compostela | GE           | PETtrace            | 16 |     |    |
| 293 | Centro Andaluz de Diagnostico Pet  | Spain             | Sevilla                | GE           | PETtrace            | 16 |     |    |
| 294 | unspecified  | Spain             | Sevilla                | IBA          | CYCLONE<br>18       | 18 | No  | No |
| 295 | unspecified  | Spain             | Tenerife               | IBA          | CYCLONE<br>11       | 11 | No  | No |
| 296 | unspecified  | Spain             | Valencia               | Siemens      | ECLIPSE             | 11 | No  | No |
| 297 | AAA Zaragoza   | Spain             | Zaragoza               | GE           | PETtrace            | 16 |     |    |
| 298 | Sahlgrenska Universitetssjukhus  | Sweden            | Göteborg               | GE           | PETtrace            | 16 |     |    |
| 299 | CORPUS   | Sweden            | Linköping              | GE           | MiniTrace           | 10 | Yes | No |
| 300 | Skånes Universitetssjukhus, Lund   | Sweden            | Lund                   | GE           | PETtrace            | 16 |     |    |
| 301 | Skånes Universitetssjukhus, Lund   | Sweden            | Lund                   | GE           | PETtrace            | 16 |     |    |
| 302 | Karolinska Solna   | Sjukhuset, Sweden | Solna                  | GE           | PETtrace            | 16 |     |    |
| 303 | Karolinska Solna   | Sjukhuset, Sweden | Solna                  | GE           | PETtrace            | 16 |     |    |
| 304 | Karolinska Sjukhuset   | Sweden            | Stockholm              | GE           | PETtrace            | 16 |     |    |
| 305 | Norrlands Universitetssjukhus  | Sweden            | Umeå                   | GE           | PETtrace            | 16 |     |    |
| 306 | Uppsala Universitet  | Sweden            | Uppsala                | Scanditronix | MC 17               | 17 |     |    |
| 307 | SWAN / Uni. Bern   | Switzerland       | Bern                   | IBA          | CYCLONE<br>18/18 HC | 18 | Yes | No |
| 308 | unspecified  | Switzerland       | Genève                 | IBA          | CYCLONE<br>18       | 18 | No  | No |
| 309 | Universitätsspital Zuerich, Labor Schlieren, Klinik für Onkologie (Wagi) | Switzerland       | Schlieren              | GE           | PETtrace            | 16 |     |    |
| 310 | Paul Scherrer Institute  | Switzerland       | Villigen               | PSI          | 72 MeV              | 72 |     |    |
| 311 | Universitätsspital Zürich  | Switzerland       | Zürich                 | GE           | PETtrace            | 16 |     |    |

|     |   |          |                  |         |  |          |     |     |
|-----|---|----------|------------------|---------|--|----------|-----|-----|
| 312 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. Adana Tesisi                  | Turkey   | Adana            | GE      | PETtrace                                 | 16.5     | Yes | No  |
| 313 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. Ankara<br>Üniversitesi Tesisi | Turkey   | Ankara           | GE      | PETtrace<br>880                          | 16.5     | Yes | No  |
| 314 | HACETTEPE UNIVERSITY<br>RECTORATE   | Turkey   | Ankara           | GE      | MiniTrace                                | 10       | Yes | No  |
| 315 | Sarayköy Nuclear<br>Research and Training<br>Center                                     | Turkey   | Ankara           | IBA     | CYCLONE<br>30                            | 30       | Yes | Yes |
| 316 | Eczacıbaşı-Monrol Ankara  | Turkey   | Ankara           | IBA     | CYCLONE<br>18                            | 18       | Yes | No  |
| 317 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. Gebze Tesisi<br>(1)           | Turkey   | Kocaeli          | IBA     | CYCLONE<br>18/9                          | 18       | Yes | No  |
| 318 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. Gebze Tesisi<br>(2)           | Turkey   | Kocaeli          | IBA     | Cyclone<br>Twin                          | 18 18    | Yes | No  |
| 319 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. İstanbul Tesisi<br>(2)        | Turkey   | Istanbul         | IBA     | Cyclone<br>Twin                          | 18 18    | Yes | No  |
| 320 | Eczacıbaşı-Monrol Gebze   | Turkey   | Gebze<br>Kocaeli | - IBA   | CYCLONE<br>18                            | 18       | Yes | No  |
| 321 | Moltek  | Turkey   | Gebze<br>Kocaeli | - ACSI  | TR-19                                    | 19       |     |     |
| 322 | MEDICHECK -1  | Turkey   | Istanbul         | GE      | PET TRACE<br>890                         | 16.5     | Yes | No  |
| 323 | MEDICHECK-2   | Turkey   | Istanbul         | GE      | PET TRACE<br>890                         | 16.5     | Yes | No  |
| 324 | MEDICHECK -3  | Turkey   | Istanbul         | GE      | PET TRACE<br>890                         | 16.5     | Yes | No  |
| 325 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. İstanbul Tesisi<br>(1)        | Turkey   | Istanbul         | IBA     | Cyclone<br>18/9<br>(Upgraded<br>to twin) | 18       | Yes | Yes |
| 326 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. İzmir Tesisi (1)              | Turkey   | Izmir            | Siemens | CTI RDS-<br>111 Eclipse<br>S/N :DV26     | 11       | Yes | No  |
| 327 | ECZACIBAŞI-MONROL<br>NÜKLEER ÜRÜNLER SAN.<br>VE TİC. A.Ş. İzmir Tesisi (2)              | Turkey   | Izmir            | Siemens | CTI RDS-<br>111 Eclipse<br>S/N<br>:DV108 | 11       | Yes | No  |
| 328 | Kiev City Hospital  | Oncology | Ukraine          | Kiev    | GE                                       | PETtrace | 16  |     |

|     |  |                  |                     |              |              |      |     |     |
|-----|--|------------------|---------------------|--------------|--------------|------|-----|-----|
| 329 | unspecified                                      | Ukraine          | Kiev                | NIIefa       | P-7          |      | No  | No  |
| 330 | unspecified                                      | Ukraine          | Kiev                | NIIefa       | U-240        | 80   | No  | No  |
| 331 | unspecified                                      | Ukraine          | Kiev                | Siemens      | ECLIPSE      | 11   | No  | No  |
| 332 | AMERSHAM INTERNATIONAL PLC                       | United Kingdom   | Amersham            | GE           | PETtrace     | 16   |     |     |
| 333 | Douglas Cyclotron Centre                         | United Kingdom   | Bebington           | Scanditronix | MC-62        | 62   | No  | No  |
| 334 | Belfast Health and Social Care Trust             | Northern Ireland | Belfast             | GE           | PETtrace     | 16   | Yes | No  |
| 335 | unspecified                                      | United Kingdom   | Birmingham          | Scanditronix | MC-40        | 40   | Yes | No  |
| 336 | WOLFSON BRAIN IMAGING CENTRE                     | United Kingdom   | Cambridge           | GE           | PETtrace     | 16   |     |     |
| 337 | Wales Research and Diagnostic PET Imaging Centre | United Kingdom   | Cardiff             | IBA          | CYCLONE 18/9 | 18   | Yes | Yes |
| 338 | Edinburgh Imaging / University of Edinburgh      | United Kingdom   | Edinburgh           | GE           | PETtrace8    | 16.5 | Yes | Yes |
| 339 | Gartnaval Hospital                               | United Kingdom   | Glasgow             | GE           | PETtrace     | 16   |     |     |
| 340 | unspecified                                      | United Kingdom   | Guilford            | IBA          | CYCLONE 18   | 18   | No  | No  |
| 341 | unspecified                                      | United Kingdom   | Hammersmith         | Siemens      | ECLIPSE      | 11   | No  | No  |
| 342 | unspecified                                      | United Kingdom   | Hammersmith         | Siemens      | ECLIPSE      | 11   | No  | No  |
| 343 | University of Hull PET Research Centre           | United Kingdom   | Hull                | ABT          | BG-75        | 7.5  | Yes | No  |
| 344 | Keele University Science Park                    | United Kingdom   | Keele Staffordshire | GE           | PETtrace     | 16   |     |     |
| 345 | King's College London-1                          | United Kingdom   | London              | GE           | PETtrace     | 16.5 | Yes | No  |
| 346 | King's College London-2                          | United Kingdom   | London              | Siemens      | RDS 112      | 11   | Yes | No  |
| 347 | St. Thomas Hospital, Pet Centre                  | United Kingdom   | London              | GE           | PETtrace     | 16   |     |     |
| 348 | unspecified                                      | United Kingdom   | London              | IBA          | CYCLONE 3    | 3    | No  | No  |
| 349 | unspecified                                      | United Kingdom   | London              | IBA          | CYCLONE 3    | 3    | No  | No  |
| 350 | WOLFSON MOLECULAR IMAGING CENTRE                 | United Kingdom   | Manchester          | GE           | PETtrace     | 16   |     |     |
| 351 | unspecified                                      | United Kingdom   | Middlesex           | Siemens      | ECLIPSE      | 11   | No  | No  |
| 352 | unspecified                                      | United Kingdom   | Newcastle           | ABT          | BG-75        | 7.5  | No  | No  |

|     |                                    |                |               |         |            |     |    |    |
|-----|------------------------------------|----------------|---------------|---------|------------|-----|----|----|
| 353 | unspecified                        | United Kingdom | Nottingham    | Siemens | ECLIPSE    | 11  | No | No |
| 354 | Royal Preston Hospital             | United Kingdom | Preston       | GE      | PETtrace   | 16  |    |    |
| 355 | unspecified                        | United Kingdom | Sheffield     | IBA     | CYCLONE 18 | 18  | No | No |
| 356 | Alliance Medical                   | United Kingdom | Sheffield     | ACSI    | TR-24      | 24  |    |    |
| 357 | Royal Marsden NHS Foundation Trust | United Kingdom | Sutton Surrey | GE      | PETtrace   | 16  |    |    |
| 358 | Castle Hill Hospital               | United Kingdom | Yorkshire     | GE      | GENtrace   | 7.8 |    |    |

References:

1. Database of Cyclotrons used for Radionuclide production:  
<https://nucleus-new.iaea.org/sites/accelerators/Pages/Cyclotron.aspx>  
 Updated 11.04.2022.

## Appendix 2: Radioisotopes in EU<sup>2</sup>

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<sup>2</sup> Ligvoet, A., Scholten, C., Dave, A., King, R., Petrosova, L. and Chiti, A., Study on sustainable and resilient supply of medical radioisotopes in the EU, Goulart De Medeiros, M. and Joerger, A. editor(s), EUR 30690 EN, Publications Office of the European Union, Luxembourg, 2021, ISBN 978-92-76-37422-0, doi:10.2760/642561, JRC124565.

<https://publications.jrc.ec.europa.eu/repository/handle/JRC124565>

Appendix 2 - Deliverable 5.1 - WP5-TNA2 - Questionnaire on industrial and clinical key players and needs  
Radioisotopes in EU [1]

|       |              |   |   |   |                        |   |       |                             |   |   |   |   |
|-------|--------------|---|---|---|------------------------|---|-------|-----------------------------|---|---|---|---|
|       |              |   |   | Hodgkin lymphoma<br>90Y-somatostatin is used for treatment of neuroendocrine tumours  |                        |   | 11923 | [90Y]Y-ibritumomab-tiuxetan |   | Bayer; Curium Pharma; Eckert & Ziegler; IBA |   |   |
|       |              |   |   |   |                        |   | 9,214 | 90Y-resin microspheres      |   | Sirtex Medical Curium Pharma                |   |   |
| 131I  | Iodine-131   | β | Nuclear reactor: CA: extraction of 131I from 235U fission product (by-product from 99Mo production, similar processing); CA: irradiation of (enriched) 130Te target   | [131I]-NaI is used in benign thyroid diseases, thyroid remnant ablation and thyroid cancer and adult neuroendocrine tumours [131I]I-mIBG (IOBENGUANE) is used in neuroblastoma  | Generics and Theracap® | One of the most important and widely used radionuclides for thyroid diseases. | 2150  | [131I]I-mIBG                | POLATOM (PL); SCK-CEN (BE); IRE (BE) BRR/IZOTOP (HU) CVR Řež (CZ) | GE Healthcare, Curium Pharma POLATOM        | • Product failed quality control<br>• Reactor maintenance or outage<br>• Shipping delayed (esp. air travel) | • Improve quality control throughout value chain<br>• Better anticipation of demand/orders  |
| 153Sm | Samarium-153 | β | Nuclear reactor:CA: irradiation of enriched 152Sm targets   | Bone metastases   | Quadramet®             |   | 1426  | [153Sm]Sm-EDTMP             | POLATOM (PL) SCK-CEN (BE) BBR/IZOTOP (HU) CVR Řež (CZ)            | Curium Pharma/CIS Bio; GE Healthcare        | • Reactor maintenance or outage   |   |
| 166Ho | Holmium-166  | β | Nuclear reactor: CA: Irradiation of 165Ho (100% abundant) target (common route); NCA: elution of 166Dy/166Ho generator, with 166Dy produced by irradiation of enriched 164Dy with high flux (experimental, not yet available) | 166Ho-microspheres are used in intra-arterial treatment in the liver and against recurrences of head and neck squamous cell carcinoma [166Ho]Ho-chitosan is used in hepatocellular carcinoma (HCC) [166Ho]Ho-DOTMP is used in bone metastasis | QuiremSpheres®         |   |       | [166Ho]Ho-chitosan          | NRG (NL) ITM/FRMII (DE) POLATOM (PL) BRR/IZOTOP (HU) CVR Řež (CZ) | Unknown                                     | • Reactor maintenance or outage<br>• Product failed quality control   | • Increase the number of suppliers/sources for the radionuclide   |
| 169Er | Erbium-169   | β | Nuclear reactor: CA: irradiation of (enriched) 168Er target (fairly scarce)   | 169Er-colloids are used in radiation synovectomy  | n/a                    |   | 431   | 169Er-colloids              | NRG (NL) CVR Řež (CZ); Institut Laue-Langevin (FR)                | Curium Pharma                               | • Reactor maintenance or outage<br>• Product failed quality control   | • As demand is low, supply is less (frequent), which makes supply chain weaker. Higher demand could solve these issues, but depends on needs. |

|       |              |         |  |  |   |   |                                |   |   |  |  |  |
|-------|--------------|---------|--|--|---|---|--------------------------------|---|---|--|--|--|
| 177Lu | Lutetium-177 | $\beta$ | <p>Nuclear reactor: CA: irradiation of highly enriched 176Lu targets (direct route, efficient, but contains long-lived 177mLu impurity); NCA: irradiation of 176Yb targets (indirect route, requires elaborate processing)</p> <p>[177Lu]Lu-PSMA is used in therapy of castration resistant prostate cancer (pc) and pc-metastases [177Lu]Lu-somatostatin is used in neuroendocrine tumours (NETs)</p> | <p>177Lu-antibodies (Betalutin®) are used in non-Hodgkin lymphoma [177Lu]Lu-DOTATATE (Lutathera®) is used in gastroentero-pancreatic neuroendocrine tumours (GEP-NETs)</p> | <p>Betalutin® Lutathera® EndolucinBeta®</p> | <p>Lutetium-177 is a therapeutic radioisotope of rapidly increasing importance.</p> | <p>2200<br/>18056<br/>3050</p> | <p>177Lu-antibodies<br/>[177Lu]Lu-DOTATATE<br/>177Lu-peptides</p> | <p>POLATOM (PL) – CA, precursor; NRG (NL); Eckert &amp; Ziegler (DE, GMP in 2021); CVR Řež Institut Laue-Langevin (FR) SCK-CEN (BE) FRMII/ITM (DE) – NCA BRR/IZOTOP (HU);</p> | <p>ITM; Nordic Nanovector<br/>AAA/Novartis<br/>ITM</p> | <ul style="list-style-type: none"> <li>Problems with labelling (PSMA/DOTATATE)</li> <li>Reactor maintenance or outage</li> <li>Shipping delayed (esp. air travel – flight activity limit reached)</li> <li>Miscommunication with supplier</li> </ul> | <ul style="list-style-type: none"> <li>Expand the network of suppliers/sources for the radionuclide</li> <li>Optimising transport/flight bookings by better monitoring flight activity limits</li> </ul> |
|       |              |         |  |  |   |   |                                |   |   |  |  |  |
|       |              |         |  |  |   |   |                                |   |   |  |  |  |
|       |              |         |  |  |   |   |                                |   |   |  |  |  |
| 186Re | Rhenium-186  | $\beta$ | Nuclear reactor (commonly used); CA: Irradiation of metallic enriched 185Re target;<br>Accelerator/cyclotron: NCA: proton or deuteron irradiation of 186W target (arising)   | Radiation synovectomy  |   |   | 661                            | 186Re-colloids  | POLATOM (PL)<br>SCK-CEN (BE)<br>CVR Řež (CZ)<br>NRG (NL)  | Curium Pharma/CIS BIO                                  | <ul style="list-style-type: none"> <li>Changes in production schedule</li> <li>Product failed quality control</li> </ul>   | Better coordination within supply chain<br><ul style="list-style-type: none"> <li>Increase number of suppliers/sources for the radionuclide</li> </ul>   |
| 188Re | Rhenium-188  | $\beta$ | <p>Nuclear reactor: CA: irradiation of (highly) enriched 187Re target; NCA: elution of 188W/188Re generator, with 188W produced by irradiation of enriched 186W in (very) high flux reactors</p>   | <p>Treatment of non-melanoma skin cancer<br/>[188Re]Re-HEDP used in painful bone metastases</p>  | Rhenium-SCT®                                |   |                                | 188Re   | <p>POLATOM (generator) (PL);<br/>SCK-CEN (generator) (BE);<br/>CVR Řež (generator) (CZ)</p>   | Curium Pharma  |  |  |
|       |              |         |  |  |   |   |                                | [188Re]Re-HEDP  |   | Curium Pharma  |  |  |

|              |                  |                 |   |  |         |  |      |  |  |  |  |  |
|--------------|------------------|-----------------|---|--|---------|--|------|--|--|--|--|--|
| <b>211At</b> | Astatine-211     | $\alpha$        | Accelerator/cyclotron:<br>Alpha particle irradiation of<br>natural 209Bi (100%<br>abundant) targets   | Under investigation<br>for a range of<br>tumours   |         |  |      | NPI Řež cyclotron<br>(CZ); University<br>Hospital<br>Copenhagen (DK);<br>CNRS/CERI (FR);<br>Forschungszentrum<br>Karlsruhe<br>cyclotron (DE);<br>Medizinische<br>Hochschule<br>Hannover<br>cyclotron (DE);<br>JRC IHCP Ispra<br>cyclotron (IT);<br>HNIP cyclotron<br>Krakow (PL) | Unknown: likely<br>hospital preparation as<br>still experimental   |  |  |  |
| <b>212Pb</b> | Lead-212         | $\beta$         | Generator: Elution from<br>224Ra/212Pb generator  | Under investigation<br>for a range of<br>tumours   |         |  |      | NRG (NL) –<br>production; Orano<br>Med (FR)  | Orano Med/Roche  |  |  |  |
| <b>213Bi</b> | Bismuth-213      | $\alpha, \beta$ | Generator: Elution from<br>225Ac/213Bi generator<br>(limited availability, high<br>costs, see also 225Ac<br>production)   | Under investigation<br>for a range of<br>tumours   |         |  |      | JRC Karlsruhe<br>(DE)  | Unknown: likely<br>hospital preparation as<br>still experimental and<br>very short half-life                     |  |  |  |
| <b>223Ra</b> | Radium-223       | $\alpha, \beta$ | Nuclear reactor: NCA:<br>Irradiation (high flux) of<br>226Ra target, resulting in<br>227Ac which decays into<br>223Ra (industrial generator);<br>Accelerator/cyclotron: Proton<br>irradiation of 232Th<br>(naturally abundant) target<br>(not yet industrialised) | Castration-resistant<br>prostate cancer<br>Symptomatic bone<br>metastases and no<br>known visceral<br>metastases | Xofigo® |  | 4041 | [223Ra]RaCl2   | IFE (NO); Supply<br>from abroad, only<br>disclosed source:<br>Oakridge National<br>Laboratory, part of<br>US DOE | Bayer (NO)   | <ul style="list-style-type: none"> <li>• Long delivery times</li> <li>• Reactor maintenance or outage (for parent radionuclide)</li> <li>• Shipping delayed (esp. air travel)</li> </ul> | • Increase number<br>of<br>suppliers/sources<br>for the<br>radionuclide<br>(capacity has<br>increased after<br>long delivery<br>times) |
| <b>225Ac</b> | Actinium-<br>225 | $\alpha, \beta$ | Nuclear reactor: Extraction<br>from natural decay of<br>229Th, obtained from fissile<br>233U, originally reactor  | [225Ac]Ac-PSMA<br>is used for<br>metastatic castration<br>resistant prostate                                     |         |  |      | [225Ac]Ac-<br>Lintuzumab   | JRC Karlsruhe<br>(DE)<br>Eckert&Ziegler<br>(DE), Rest of   | Unknown: likely<br>hospital preparation as<br>still experimental |  |  |

|              |             |          |   |  |  |  |  |                              |  |  |  |
|--------------|-------------|----------|---|--|--|--|--|------------------------------|--|--|--|
|              |             |          | produced by irradiation of natural $^{232}\text{Th}$ targets (limited, too small amounts to serve market); Extraction from natural decay of $^{229}\text{Th}$ , obtained from $^{233}\text{U}$ legacy waste from US weapon programme (limited, inefficient, costly, long half-life); Accelerator/cyclotron:Proton irradiation of $^{226}\text{Ra}$ target (few producers) | cancer<br>[ $^{225}\text{Ac}$ ]Ac-Lintuzumab is used for acute myeloid leukemia (AML)  |  |  |  | [ $^{225}\text{Ac}$ ]Ac-PSMA | suppliers abroad in US and Russia                        |  |  |
| <b>227Th</b> | Thorium-227 | $\alpha$ | Nuclear reactor: Irradiation of $^{226}\text{Ra}$ target  | 227Th-conjugate is used for (CD22 positive) non-Hodgkin lymphoma<br>227Th-antibody is used for ovarian cancer and mesothelioma<br>[ $^{227}\text{Th}$ ]Th-PSMA is used for metastatic castration resistant prostate cancer |  |  |  | 227Th-antibody               | Irradiator unknown Eckert&Ziegler (DE)<br><br>Bayer (NO) |  |  |
|              |             |          |   |  |  |  |  | 227Th-conjugate              |  |  |  |
|              |             |          |   |  |  |  |  | [ $^{227}\text{Th}$ ]Th-PSMA |  |  |  |

### Main research reactors in EU [1]

| Nr | Reactor | Country               | Operator                             | Produced therapeutic radionuclides                            |
|----|---------|-----------------------|--------------------------------------|---|
| 1  | MARIA   | Poland                | POLATOM                              | 32P, 89Sr, 90Y, 131I,<br>153Sm, 166Ho, 177Lu,<br>186Re, 188Re |
| 2  | HFR     | the<br>Netherlands    | NRG                                  | 89Sr, 90Y, 166Ho, 169Er,<br>177Lu, 212Pb                      |
| 3  | BR2     | Belgium               | SCK-CEN                              | 89Sr, 90Y, 131I, 153Sm,<br>177Lu, 186Re, 188Re                |
| 4  | FRMII   | Germany               | Technical<br>University of<br>Munich | 166Ho, 177Lu  |
| 5  | ILL     | France                | Institute Laue-<br>Langevin          | 47Sc, 169Er, 177Lu, 188Re                                     |
| 6  | LVR-15  | the Czech<br>Republic | CVŘ Řež                              | 131I, 153Sm, 166Ho, 169Er,<br>177Lu, 186Re, 188Re             |
| 7  | BRR     | Hungary               | BNC/AEKI                             | 32P, 90Y, 131I, 153Sm,<br>166Ho, 177Lu                        |

### Radionuclides and radiopharmaceuticals used in EU [1]

| Nr | Country        | Radionuclides in use:   | Radiopharmaceuticals in compassionate use: |
|----|----------------|---|--|
| 1  | Austria        | 131I, 153Sm, 169Er, 177Lu, 186Re, 223Ra, 225Ac, 90Y   |  |
| 2  | Belgium        | 90Y, 131I, 153Sm, 166Ho, 177Lu, 186Re, 223Ra, 213Bi   |  |
| 3  | Bulgaria       | 131I, 223Ra, 153Sm  |  |
| 4  | Croatia        | 131I, 177Lu, 223Ra, 90Y   |  |
| 5  | Cyprus         | 131I, 153Sm, 177Lu, 223Ra, 225Ac  | 153Sm                                      |
| 6  | Czech Republic | 131I, 90Y, 153Sm, 89Sr, 223Ra, 186Re, 169Er, 177Lu  |  |
| 7  | Denmark        | 90Y, 131I, 177Lu, 223Ra   |  |
| 8  | Estonia        | 131I, 32P, 223Ra, 186Re, 169Er, 153Sm, 89, 90Y, 177Lu   | [177Lu]Lu-DOTATATE                         |
| 9  | Finland        | [131I]-NaI, [177Lu]Lu-DOTATATE, 90Y-glass microspheres, [131I]I-mIBG, 186Re-colloids.                   |  |
| 10 | France         | 89Sr, 90Y, 131I, 153Sm, 166Ho, 169Er, 177Lu, 186Re, 223Ra   |  |
| 11 | Germany        | 32P, 67Cu, 89Sr, 90Y, 131I, 153Sm, 166Ho, 169Er, 177Lu, 186Re, 188Re, 211At, 213Bi, 223Ra, 225Ac, 227Th |  |

|    |             |  |  |
|----|-------------|--|--|
| 12 | Greece      | 89Sr, 90Y, 131I, 153Sm, 169Er, 177Lu, 186Re, 188Re, 223Ra  |  |
| 13 | Hungary     | 32P, 90Y, 131I, 153Sm, 166Ho, 177Lu, 186Re, 223Ra  |  |
| 14 | Ireland     | 90Y, 131I, 177Lu, 186Re, 223Ra, 153Sm, 169Er, 32P  | [177Lu]Lu-PSMA-617, [177Lu]Lu-DOTATATE |
| 15 | Italy       | 131I, 166Ho, 177Lu, 169Er, 188Re, 223Ra, 89Sr, 90Y,  |  |
| 16 | Latvia      | 18F, 68Ga, 90Y, 131I, 177Lu 223Ra  |  |
| 17 | Lithuania   | 90Y, 131I, 166Ho, 223Ra  |  |
| 18 | Luxembourg  | 32P, 90Y, 131I, 153Sm, 169Er, 186Re, 211At, 213Bi, 223Ra, 225Ac, 227Th   |  |
| 19 | Malta       | 131I, 90Y  |  |
| 20 | Netherlands | 32P, 89Sr, 90Y, 103Pd, 125I, 131I, 152Eu, 154Eu, 153Sm, 166Ho, 169Er, 177Lu, 186Re, 188Re, 213Bi, 223Ra, 225Ac, 227Ac, 227Th | [177Lu]Lu-DOTATATE, [225Ac]Ac-PSMA     |
| 21 | Poland      | 153Sm, 89Sr, 223Ra, 90Y, 169Er, 186Re, 131I, 177Lu   |  |
| 22 | Portugal    | 131I, 166Ho, 177Lu, 223Ra, 90Y, 32P, 89Sr,   | [177Lu]Lu-DOTATATE                     |
| 23 | Romania     | 89Sr, 90Y, 131I, 153Sm, 177Lu, 188Re   |  |
| 24 | Slovakia    | 131I, 223Ra, 177Lu, 89Sr, 90Y  |  |
| 25 | Slovenia    | 131I, 177Lu, 90Y, 223Ra, 186Re, 64Cu   |  |
| 26 | Spain       | 32P, 89Sr, 90Y, 131I, 153Sm, 166Ho, 169Er, 177Lu, 186Re, 188Re, 223Ra  |  |

|    |        |  |             |
|----|--------|--|-------------|
| 27 | Sweden | 131I, 90Y, 223Ra, 153Sm,<br>32P, 177Lu |             |
| 28 | UK     | 90Y, 131I, 177Lu, 223Ra                | Lu-177 PSMA |

Reference:

1. Ligtvoet, A., Scholten, C., Dave, A., King, R., Petrosova, L. and Chiti, A., Study on sustainable and resilient supply of medical radioisotopes in the EU, Goulart De Medeiros, M. and Joerger, A. editor(s), EUR 30690 EN, Publications Office of the European Union, Luxembourg, 2021, ISBN 978-92-76-37422-0, doi:10.2760/642561, JRC124565. <https://publications.jrc.ec.europa.eu/repository/handle/JRC124565>

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