

Global Issues of Radiopharmaceutical Access and Availability: a Nuclear Medicine Global Initiative Project

Cathy S. Cutler¹, Elizabeth Bailey², Vijay Kumar³, Sally W. Schwarz⁴, Hee-Seung Bom⁵, Jun Hatazawa⁶, Diana Paez⁷, Pilar Orellana⁷, Lizette Louw⁸, Fernando Mut⁹, Hiroki Kato¹⁰, Arturo Chiti¹¹, Savvas Frangos¹², Frederic Fahey¹³, Gary Dillehay¹⁴, Seung J. Oh¹⁵, Dong S. Lee¹⁶, Sze-Ting Lee¹⁷, Rodolfo Nunez-Miller^{7,18}, Guru Bandhopadhyaya¹⁹, Prasanta K. Pradhan²⁰, Andrew M. Scott¹⁷.

¹ Brookhaven National Laboratory, Upton, NY, USA.

² Department of Nuclear Medicine, Royal North Shore Hospital, Sydney, NSW, Australia.

³ Department of Nuclear Medicine & PET, Westmead Hospital & The Children's Hospital at Westmead, and University of Sydney, NSW, Australia.

⁴ Washington University School of Medicine, St Louis, MO, USA.

⁵ Department of Nuclear Medicine, Chonnam National University Hwasun Hospital, Jeollanam, Korea.

⁶ Department of Quantum Cancer Therapy, Research Center for Nuclear Physics, Osaka University, Osaka, Japan.

⁷ Nuclear Medicine and Diagnostic Imaging Section, International Atomic Energy Agency, Vienna, Austria.

⁸ Department of Nuclear Medicine, Charlotte Maxeke Johannesburg Academic Hospital and University of Witwatersrand, Johannesburg, South Africa.

- ⁹ Nuclear Medicine Service, Italian Hospital, Montevideo, Uruguay.
- ¹⁰ Department of Nuclear Medicine and Tracer Kinetics, Osaka University Graduate School of Medicine, Osaka, Japan.
- ¹¹ Department of Biomedical Sciences, Humanitas University, and Nuclear Medicine Unit, Humanitas Research Hospital – IRCCS, Milan, Italy.
- ¹² Department of Nuclear Medicine, Bank of Cyprus Oncology Center, Nicosia, Cyprus.
- ¹³ Department of Radiology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA.
- ¹⁴ Department of Radiology, Division of Nuclear Medicine, The Robert H. Lurie Comprehensive Cancer Center, Northwestern University Feinberg School of Medicine, Chicago, IL, USA.
- ¹⁵ Department of Nuclear Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea.
- ¹⁶ Department of Nuclear Medicine, Seoul National University College of Medicine, Seoul, Korea.
- ¹⁷ Department of Molecular Imaging and Therapy, Austin Health; University of Melbourne; Olivia Newton-John Cancer Research Institute; and School of Cancer Medicine, La Trobe University, Melbourne, Australia.
- ¹⁸ Excel Diagnostics and Nuclear Oncology Center, Houston, TX, USA.
- ¹⁹ Department of Nuclear Medicine, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India.

²⁰ Department of Nuclear Medicine, Sanjay Gandhi Post Graduate Institute of Nuclear Medicine (SGPGIMS), Lucknow, India.

First Author: Cathy S. Cutler, Brookhaven National Laboratory, Upton, NY, USA. Tel: +1 6313443873 Fax: +1 6313445962 Email: ccutler@bnl.gov

Correspondence: Andrew M. Scott, Department of Molecular Imaging and Therapy, Austin Health, Studley Rd, Heidelberg, VIC, 3084, Australia. Tel: +613 94965876 Fax: +613 94965892 Email: andrew.scott@austin.org.au

Support for this project was provided by the Society of Nuclear Medicine and Molecular Imaging (SNMMI)

Word count: 4932

Short Running Title: Global Radiopharmaceutical Availability

ABSTRACT

The Nuclear Medicine Global Initiative (NMGI) was formed in 2012 by 13 international organizations to promote human health by advancing the field of nuclear medicine and molecular imaging by supporting the practice and application of nuclear medicine. The first project focused on standardization of administered activities in pediatric nuclear medicine and resulted in two manuscripts. For its second project the NMGI chose to explore issues impacting on access and availability of radiopharmaceuticals around the world. Methods. Information was obtained by survey responses from 35 countries on available radioisotopes, radiopharmaceuticals and kits for diagnostic and therapeutic use. Issues impacting on access and availability of radiopharmaceuticals in individual countries were also identified. Results. Detailed information on radiopharmaceuticals utilized in each country, and sources of supply, was evaluated. Responses highlighted problems in access particularly due to the reliance on a sole provider, regulatory issues and reimbursement, as well as issues of facilities and workforce particularly in low- and middle-income countries. Conclusions. Strategies to address access and availability of radiopharmaceuticals are outlined, to enable timely and equitable patient access to nuclear medicine procedures worldwide. In the face of disruptions to global supply chains by the COVID-19 outbreak, renewed focus on ensuring reliable supply of radiopharmaceuticals is a major priority for nuclear medicine practice globally.

Key Words: radiopharmaceuticals, access, global issues

INTRODUCTION

Every year more than 30 million patients are diagnosed and/or treated using nuclear medicine and molecular imaging techniques (1). Nuclear medicine comprises diagnostic and therapeutic techniques that use radiopharmaceuticals for applications like oncology, cardiovascular and neurological disorders to provide information at both the molecular and cellular level for probing, tracking tissue function, evaluating disease progression support treatment planning, guide tissue sampling, and assessing treatment responses (2,3). Nuclear medicine and molecular imaging procedures are among the most powerful analytic tools available today, providing physicians with critical patient information upon which important medical decisions are based (3,4). These procedures and therapies are a key component to personalized medicine; without which, patients may be required to undergo more invasive and more costly tests and even invasive surgeries (1,3). The International Atomic Energy Agency (IAEA), launched in September 2019 IMAGINE (the IAEA Medical imaging and Nuclear medicine global resources database), a comprehensive database on availability of nuclear medicine and diagnostic imaging equipment worldwide (5). According to IMAGINE over 140 countries have availability of SPECT or SPECT-CT with close to 27,000 systems installed, while 109 have PET-CT and over 5,200 systems. The utilization of nuclear medicine procedures varies between countries, in part due to costs, regulatory issues, training of workforce, and availability of radiopharmaceuticals, although the relative contributions of each of these factors is not well defined (6,7).

In 2014, the first Nuclear Medicine Global Initiative (NMGI) reported on the standardization of administered activities in pediatric patients (8,9). Based on the success

of this first project it was decided that the second project of the NMGI would be to assess the availability of diagnostic and therapeutic radiopharmaceuticals by country and region, to collate and analyze the data and develop a report outlining the current availability and issues preventing patient access to these resources. The aim of the project was to collate information regarding the availability of radiopharmaceuticals worldwide including the availability of the cold kits, generators and radionuclides, use of central pharmacies, listing of radiopharmaceuticals required but not available, and identification of issues impeding use of radiopharmaceuticals such as access, shipping, cost, regulatory requirements, facilities and training. This information could inform actions that could be taken to mitigate the identified barriers, ensure improved patient access, and encourage commercial interest, and research and development in the field.

MATERIALS AND METHODS

A detailed questionnaire on radiopharmaceuticals access, availability and issues relating to supply and access (Supplementary document) was sent to key contacts and the Nuclear Medicine Societies (where existing) of all countries listed in the IAEA database. This questionnaire was developed by the NMGI project members (Table 1), and was made available by SNMMI through a secure online portal or through direct correspondence with country Nuclear Medicine Societies. The information obtained was confirmed as applicable for the entire country and was based on country internal information gathering and data compilation. The responses were correlated into continental regions, and whether countries were of low, low-middle, high-middle and high-income countries, according to World Bank income classification (10). Data was compiled

and summarized, with verification of information if gaps in initial responses were identified.

RESULTS

A total of 35 countries provided complete data for the survey and are listed in Table 2. Of the country responders, 16 were from the Asia-Pacific region including Australia, 4 countries responded from Europe, 8 from Africa, 5 from Latin America, and both the United States and Canada. To facilitate the analysis, Mexico was included in Latin America. Based on data from the IMAGINE database (5) on individual country activity (numbers of SPECT and PET cameras), this cohort represents 76.4% of global SPECT camera sites, and 71.1% of global PET camera sites (Table 3).

For North America, Latin America and Australia the data represents 91.3% to 100.0% of nuclear medicine camera sites, while in Asia more than 73% of sites are represented. African country responses were more than 50% of nuclear medicine camera sites, with responses from both low income and middle income countries with nuclear medicine sites. Country responses from Europe were low, which reflected the challenges in obtaining accurate country-based data in this region for the purpose of this analysis.

^{99m}Tc generators

Responders were asked to name the manufacturer and supplier of ^{99m}Technetium (^{99m}Tc) generators (Table 4). There were 32 ^{99m}Tc generator suppliers globally, with 18 only supplying to a single country, leaving only 10 manufacturers that supply to multiple continents or countries, and 6 producers that supply to four or more countries. The US is

the major user of ^{99m}Tc representing approximately 50% of the global market even though it relies on only three suppliers of generators. The supply to Africa is the most limited with most countries reliant on a single generator supplier. The Asia-Pacific region has a large number of suppliers of generators, often imported from Europe, but also locally produced. It is probable that the data for Europe are not representative of the actual situation due to the limited number of respondents from European countries.

Cold kits

The concept of the "cold kit" which contains all the ingredients except the radionuclide was developed originally at Brookhaven National Laboratory (11,12) to simplify the production of radiopharmaceuticals and enable consistent formulation at multiple sites to support clinical trials and eventual drug development. Figure 1 shows the number of countries where the most commonly used cold kits for radiopharmaceuticals were available.

Table 5 lists the 53 companies indicated in the survey that sell cold kits for radiopharmaceutical preparation and the continents they supply. Over half of the 33 radiopharmaceutical kit manufacturers provide to only a single country, 8 provide cold kits to two countries, one manufacturer supplies to three countries, 5 manufacturers supply to four countries, and 6 distribute to five or more countries. The data for the US indicated only 8 suppliers for diagnostic kits and 5 suppliers of kits for therapeutics with local pharmacies supplying ^{131}I capsules and solutions.

Responders were further asked to state the radiopharmaceuticals they used by imaging category and their utility in each category. The responses were divided into three groups: SPECT imaging, PET imaging and Therapy.

SPECT Radiopharmaceuticals

Figure 2 shows the radiopharmaceuticals used for SPECT diagnostic imaging and the number of countries where they are available. SPECT imaging was dominated by ^{99m}Tc . For brain imaging a total of 13 different radiopharmaceuticals were listed, with the highest country use based on survey responses being ^{99m}Tc -HMPAO and ^{99m}Tc -DTPA at 74%, followed by ^{99m}Tc -ECD at 51%. For thyroid imaging the most commonly used was ^{99m}Tc -pertechnetate at 89% followed by ^{131}I at 86%. Parathyroid imaging had ^{99m}Tc -MIBI with the highest utilization at 97%, followed by ^{99m}Tc -pertechnetate at 80% for subtraction scanning, and ^{201}Tl at 23%. For pulmonary imaging the highest utilization was seen for ^{99m}Tc -MAA at 86% for perfusion scans followed by ^{99m}Tc -DTPA aerosol at 63%, and Technegas at 34% for ventilation scans. Cardiac myocardial perfusion imaging had ^{99m}Tc -MIBI with the highest utilization at 94%, and ^{201}Tl -chloride and ^{99m}Tc -Tetrofosmin having similar utilization at 45%.

The liver/biliary agent demonstrating the highest use is ^{99m}Tc -HIDA at 51% of countries followed by ^{99m}Tc -MAA at 43% (shunt studies), ^{99m}Tc -Mebrofenin at 40% and ^{99m}Tc -Sulfur colloid at 34%. For imaging the spleen and bone marrow the most highly used agents were ^{99m}Tc -denatured RBC at 43% (for spleen imaging) followed by ^{99m}Tc -sulfur colloid at 34%, and ^{99m}Tc -tin colloid at 31%. The agent with the highest utilization for renal imaging was ^{99m}Tc -DTPA at 94% followed by ^{99m}Tc -DMSA at 89%, and ^{99m}Tc -MAG3 at 83%. Adrenal imaging is performed predominantly with ^{131}I -MIBG at 60%

followed by ^{123}I -MIBG at 37%, ^{131}I -norcholesterol at 17% and ^{131}I -aldosterol at 11%. For bone scanning, $^{99\text{m}}\text{Tc}$ -MDP was the most common at 97%, followed by $^{99\text{m}}\text{Tc}$ -HMDP at 34%, and $^{99\text{m}}\text{Tc}$ -HDP at 29%. For gastrointestinal imaging the highest utilization was observed for $^{99\text{m}}\text{Tc}$ -pertechnetate at 71%, followed by $^{99\text{m}}\text{Tc}$ -sulfur colloid and $^{99\text{m}}\text{Tc}$ -RBC at 57%.

For SPECT tumor imaging, the highest utilization by responders was ^{131}I -MIBG at 60% followed by ^{67}Ga -citrate at 46%, ^{201}Tl -chloride at 43% and ^{123}I -MIBG at 34%. A total of 10 agents were supplied by responders as being used for infection and inflammation imaging. The most highly used was $^{99\text{m}}\text{Tc}$ -radiolabeled WBC at 57% followed by ^{67}Ga -citrate at 49% and Leukoscan (Sulesomab), and Ciprofloxacin at 11%.

Sentinel lymph node imaging was reported to be performed with 7 agents, three of which are restricted to use in a single country. Those used in multiple countries are $^{99\text{m}}\text{Tc}$ -nanocolloid with a utilization of 74%, $^{99\text{m}}\text{Tc}$ -sulfur colloid with a utilization of 20%, $^{99\text{m}}\text{Tc}$ -antimony colloid 11% and $^{99\text{m}}\text{Tc}$ -Phytate at 9%. South Africa was the sole user of ^{131}I -sunflower oil for confirmation and localization of a lymphatic leak. *In vitro* studies were performed using only four agents: ^{14}C -urea at 26% utilization, ^{51}Cr -chromate at 17%, ^{51}Cr -EDTA at 9% and ^{125}I -HSA at 6%. These agents see limited use due to restricted availability.

PET Radiopharmaceuticals

Of the 35 countries that provided responses to the survey only 28 indicated they provided PET services. Low and low-middle income countries had the lowest numbers of PET sites. Survey responders indicated they used a total of 34 PET agents, and five

radiometal radionuclides $^{82}\text{Sr}/^{82}\text{Rb}$, ^{64}Cu , ^{89}Zr , ^{68}Ga and ^{44}Sc were listed (Figure 3). The most highly used PET agent is ^{18}F -FDG (Figure 3A). Eleven other ^{18}F -labeled PET agents were listed (Figure 3B).

Gallium-68 has experienced significant growth due to its availability via a long-lived generator that now sees wide availability. The most highly utilized ^{68}Ga tracer was ^{68}Ga -PSMA which is at 50% utilization, followed by ^{68}Ga -DOTATATE (also known as NETSPOT™) at 46% and ^{68}Ga -DOTATOC at 25% utilization (Figure 3C).

Several radiopharmaceutical agents have been developed with ^{11}C , and the two most highly used were ^{11}C -methionine and ^{11}C -Choline at 32% followed by ^{11}C -PIB which is utilized at 25% (Figure 3D).

Therapeutic Radiopharmaceuticals

The use of radiopharmaceuticals for therapeutic applications is shown in Figure 4, and for ^{131}I (imaging and also therapeutic use) in Figure 2. The responses indicated limited use other than ^{131}I , mainly due to limited access and high cost. The utilization of ^{131}I for hyperthyroidism was 94% and for thyroid cancer in 91% of countries. A total of 16 radiopharmaceuticals were provided by responders as being utilized for therapy, with the next most prevalently used was ^{153}Sm -EDTMP for bone pain palliation at 51% utilization, and ^{131}I -MIBG was utilized in 51% of countries. ^{177}Lu -DOTATATE was reported to have 29% utilization, ^{177}Lu -DOTATOC at 11% and ^{90}Y -DOTATATE at 11% utilization. ^{177}Lu -PSMA was mainly under research use at the time of the survey. Restricted availability of ^{32}P was noted, with a number of countries indicating they would use ^{32}P if it was available.

Training and Education

All countries noted a lack of trained and qualified staff to perform certain tasks including radiopharmaceutical quality assurance (QA) and quality control (QC), cell labeling, production, manufacturing and final dispensing. Low and Low-middle income countries in particular identified the lack of education and training of staff, including clinicians, physicists, radiochemists and radiopharmacists, as a barrier to providing certain services. This resulted in them being unable to offer complex procedures such as cell labeling, radionuclide therapy such as ^{177}Lu -targeted therapies, and other new radiopharmaceutical tracers that required in-house QC and QA. Even in some high-income countries, a lack of training in QC/QA and GMP, as well as drug release and radiation safety personnel were noted as inhibiting growth and patient access.

DISCUSSION

This project has highlighted a number of important issues regarding radiopharmaceutical access and availability at a global level. As with the first NMGI project there was variability in response among countries and regions, however the survey obtained country-based responses that covered approximately 75% of global nuclear medicine sites. Moreover, the data obtained spanned all geographical regions, and country income status (Table 3). While there was limited data available from European countries, the results from comparable socio-economic countries with similar nuclear medicine infrastructure (IMAGINE database) in our cohort suggests that our data still provides a valuable portrayal of the current availability and use of nuclear medicine and the challenges that restrict its use and future growth.

Despite multiple efforts including the IAEA, the US Department of Energy, Nuclear Medicine Europe and high-level working groups to ensure sustainable supply of $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator supplies, our survey showed a lack of availability of generators as an ongoing issue with many countries only having a single supplier, limited deliveries to once a week or once a fortnight, and problems with reliability of supply. This was identified as an issue particularly in low- and middle-income countries. This problem of supply chains has also been highlighted in the recent COVID-19 pandemic, where generator supplies to many countries have been markedly reduced due to flight restrictions (14-17).

The survey data highlights the dependency of the nuclear medicine field and individual countries on single source manufacturers or distributors of their radiopharmaceutical cold kits. There were a number of cold kits that are no longer available especially in developing countries, including HIDA, Sulphur colloid, antimony

colloid, MAA, MAG3, brain perfusion agents both HMPAO and ECD, HDP, and PYP. This was reported to be due to the high costs to import the products, only having a single sole supplier of cold kits with limited product availability, and regulatory factors (preventing importation). Surprisingly, many countries do not have any access to ventilation agents for performing a V/Q scan and commonly perform perfusion only imaging.

Non-FDG PET tracers had limited availability in most countries, predominantly due to barriers such as high cost, no access to a cyclotron, regulatory restrictions, studies not being funded by health care providers, and lack of suppliers. ^{68}Ga generator supply in particular has been identified as restricted in many countries, and likely to have increased demand in the future with more widespread clinical use of ^{68}Ga -peptide studies.

Many therapeutic tracers were not available due to their high cost, as well as no available supplier or distributor, and lack of regulatory approval. Over the past 10 years there have been significant changes and increases in the regulatory burden regarding production, handling and transportation of radiopharmaceuticals (13). Most countries did not use or have access to ^{123}I , ^{123}I -MIBG and ^{131}I -MIBG mainly due to cost. This is especially true for low- and middle-income countries. PRRT and PRLT therapeutics including ^{177}Lu -Lutathera® had limited utilization across all countries, although it should be mentioned that this field is rapidly changing, and many more sites and countries will have access to these therapeutic radiopharmaceuticals since the survey was completed.

Strategies for addressing access and availability of radiopharmaceuticals

The data obtained in this survey project clearly shows that all countries have issues of radiopharmaceutical access and availability, although the capability to address these

issues varies according to the size of the country, funding and nuclear medicine infrastructure (including workforce). Interestingly, the problems of limited suppliers of cold kits, and many diagnostic SPECT radiopharmaceuticals, were seen in low-, middle- and high-income countries globally, indicating the problem is not just restricted to countries with challenges in funding of nuclear medicine studies. Many of the workforce issues can be addressed in part by coordinated efforts to enhance training of physicians, technologists and scientists in nuclear medicine, regional (eg SNMMI, EANM, AOFNMB) as well as IAEA programs all play a part in supporting direct training, as well as documentation and position papers on protocols and infrastructure requirements. The ability of nuclear medicine societies to identify access issues and work with regional societies/associations to identify sources of radioisotopes and kits and facilitate local regulatory approvals may play a role. It is also important for companies and professional organizations (eg Nuclear Medicine Europe) to be involved in provision of supplies and stability of supply chains. Regional initiatives through IAEA and WHO may have a role in supporting access programs, particularly in low- and middle-income countries. In the context of personalized medicine and targeted therapies, and particularly in theranostics, strategic initiatives aimed at promoting the use and funding of SPECT and PET radiopharmaceuticals should align with drug development and approvals in countries. This would also benefit from cooperation and sharing of health technology assessments between countries, thus improving time to approvals and economic justification of new studies. While global efforts to enhance access and availability of radiopharmaceuticals will also be subject to major industry-wide events such as ^{99}Mo - $^{99\text{m}}\text{Tc}$ shortages, and more recently the COVID-19 pandemic which is impacting on global supply chains (14-

18), the importance of nuclear medicine in routine patient care should be a key driver of any approach.

Conclusions

This NMGI has revealed an interesting portrayal of the issues related to the supply, availability, cost, regulatory barriers and other factors related to the use of radiopharmaceuticals internationally. Particularly surprising was the limited availability of standard diagnostic radiopharmaceuticals in many countries, particularly low and middle income countries. There are a number of strategic initiatives required to address the varied causes of reduced supply, ideally linking major industry and health organizations. Nuclear medicine is widely used and is expanding worldwide and addressing the issues of access and availability of radiopharmaceuticals is a key strategy for ensuring patients can benefit from these vital imaging and therapeutic procedures.

Disclosures

Support for this project was provided by the Society of Nuclear Medicine and Molecular Imaging (SNMMI). The authors do not have any conflicts of interest to disclose. AMS is supported by NHMRC Senior Investigator Fellowship No. 1177837.

ACKNOWLEDGEMENTS

The authors would like to thank the leadership of the countries that contributed data for this project, as well as Virginia Pappas, Nikki Wenzel-Lamb, Bonnie Clarke and

Teresa Ellmer of the SNMMI for their support of this Nuclear Medicine Global Initiative. We also acknowledge the input of Dr Ravi Kashyap and Prof. Lin Li in the project.

KEY POINTS

This Nuclear Medicine Global Initiative (NMGI) project aimed to survey and identify issues impacting on access and availability of radiopharmaceuticals at a global level. The project identified limited sources of radiopharmaceuticals and kits, supply chains, regulatory and reimbursement issues, and workforce as limitations to access. Strategic action to address these issues are required to ensure optimal availability of radiopharmaceuticals for patients in all countries.

REFERENCES

1. OECD/NEA (2019), The Supply of Medical Isotopes: An Economic Diagnosis and Possible Solutions, OECD Publishing, Paris, 2019.
<https://doi.org/10.1787/9b326195-en>. Accessed April 9 2020.
2. National Research Council (US) and Institute of Medicine (US) Committee on State of the Science of Nuclear Medicine. Nuclear Medicine Imaging in Diagnosis and Treatment. In: Advancing Nuclear Medicine Through Innovation. Washington (DC): National Academies Press (US) 2007;3.
3. Wu M, Shu J. Multimodal molecular imaging: current status and future directions. *Contrast Media Mol Imaging*. 2018; Article ID 1382183.
4. Cutler CS. Economics of new molecular targeted personalized radiopharmaceuticals. *Seminars in Nucl Med*. 2019;49:450-457.
5. <https://humanhealth.iaea.org/HHW/DBStatistics/IMAGINE.html> Accessed April 9, 2020.
6. Adedapo KS, Onimode YA, Ejeh JE, Adepoju AO. Avoidable challenges of a nuclear medicine facility in a developing nation. *Indian J Nucl Med*. 2013;28:194-199.
7. Dondi M, Kashyap R., Paez D, Pascual T., Zaknun J, Bastos FM, Pynda Y. Trends in nuclear medicine in developing countries. *J Nucl Med*. 2011;52 supplement 2:16S-23S.
8. Fahey FH, Bom HH, Chiti, et al. Standardization of administered activities in pediatric nuclear medicine: a report of the first nuclear medicine global initiative

project, part 1-statement of the issue and a review of available resources. *J Nucl Med.* 2015; 56:646-51.

9. Fahey FH, Bom HH, Chiti A, et al. Standardization of administered activities in pediatric nuclear medicine: a report of the first nuclear medicine global initiative project, part 2-current standards and the path toward global standardization. *J Nucl Med.* 2016;57:1148-57.
10. <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>. Accessed April 9 2020.
11. Eckelman W, Richards P, Hauser W, Atkins H. Technetium-labeled red blood cell. *J Nucl Med.* 1971;12:22-24.
12. Eckelman W. Instant ^{99m}Tc -DTPA. *J Nucl Med.* 1970;11:761.
13. Decristoforo C, Lyashchenko SK. Recommendations for Conducting Clinical Trials with Radiopharmaceuticals. In: Volterrani D., Erba P., Carrió I., Strauss H., Mariani G. (eds) *Nuclear Medicine Textbook*. Springer, 2019:1039-1050.
14. Communication from the NMEu Emergency Response Team (ERT) to the European Observatory for the supply of Radioisotopes for Medical Use. Subject: Possible impact of COVID-19 on global supply of Mo-99.
https://cdn.ymaws.com/www.bnms.org.uk/resource/resmgr/radioisotope_supplies/aipes_or_oecd/ert_communication_9march_202.pdf. Accessed April 9 2020.
15. IAEA webinar: 'Coronavirus disease (COVID-19) Pandemic: Challenges for the Nuclear Medicine Departments'
<https://humanhealth.iaea.org/HHW/covid19/webinars.html> Accessed April 9, 2020.

16. Lam WW, Loke KS, Wong, WY, et al. Facing a disruptive threat: how can a nuclear medicine service be prepared for the coronavirus outbreak 2020. *Eur J Nucl Med Mol Imaging*. 2020 doi.org/10.1007/s00259-020-04790-2
17. Czernin J, Fanti S, Meyer PT, et al. Nuclear Medicine Operations in the Times of COVID-19: Strategies, Precautions, and Experiences. *J Nucl Med*. 2020;61:626-629.
18. Paez, D., Gnanasegaran, G., Fanti, S. et al. COVID-19 pandemic: guidance for nuclear medicine departments. *Eur J Nucl Med Mol Imaging* (2020). doi.org/10.1007/s00259-020-04825-8

Table 1. List of NMGI Organizations and Representatives

Organization	Representatives
SNMMI (Society of Nuclear Medicine and Molecular Imaging)	Cathy S. Cutler Sally Schwarz Fred Fahey Gary Dillehay
WFNMB (World Federation of Nuclear Medicine and Biology)	Andrew Scott Sze Ting Lee
ALASBINM (Latin American Association of Societies of Biology and Nuclear Medicine)	Fernando Mut
ANZSNM (Australian and New Zealand Society of Nuclear Medicine)	Vijay Kumar Elizabeth Bailey
AOFNMB (Asia Oceania Federation of Nuclear Medicine and Biology)	Henry Hee-Seung Bom
ARCCNM (Asian Regional Cooperative Council for Nuclear Medicine)	Jun Hatazawa
CSNM (China Society of Nuclear Medicine)	Lin Li
EANM (European Association of Nuclear Medicine)	Arturo Chiti Savvas Frangos
IAEA (International Atomic Energy Agency)	Ravi Kashyap Rodolfo Nunez-Miller Pilar Orellana Diana Paez
JSNM (Japan Society of Nuclear Medicine)	Hiroki Kato
KSNM (Korea Society of Nuclear Medicine)	Seung Jun Oh Dong Soo Lee
SASNM (South African Society of Nuclear Medicine)	Lizette Louw
SNM, India	Guru Bandhopadhyaya Prasanta K. Pradhan

Table 2. Countries Responding to the Survey

Countries	Region	Income Category
United States	North America	HIC
Canada	North America	HIC
Brazil	Latin America	UMIC
Chile	Latin America	HIC
Mexico	Latin America	UMIC
Colombia	Latin America	UMIC
Uruguay	Latin America	HIC
Australia	Australia	HIC
Japan	Asia	HIC
Korea	Asia	HIC
Bangladesh	Asia	LMIC
India	Asia	LMIC
Indonesia	Asia	LMIC
Iran	Asia	UMIC
Israel	Asia	HIC
Jordan	Asia	UMIC
Malaysia	Asia	UMIC
Mongolia	Asia	LMIC
Pakistan	Asia	LMIC
Philippines	Asia	LMIC
Singapore	Asia	HIC
Taiwan	Asia	UMIC
Thailand	Asia	UMIC
Algeria	Africa	UMIC
Ghana	Africa	LMIC
Morocco	Africa	LMIC
Niger	Africa	LIC
South Africa	Africa	UMIC
Tanzania	Africa	LIC
Uganda	Africa	LIC
Zambia	Africa	LMIC
Austria	Europe	HIC
Cyprus	Europe	HIC
Estonia	Europe	HIC
Poland	Europe	HIC

HIC: High-Income Country; UMIC: Upper Middle-Income Country; LMIC: Lower Middle-Income Country; LIC: Low-Income Country; Data from World Bank (10).

Table 3. Survey Countries Representation of Regional Nuclear Medicine Activity

Region	SPECT Cameras (%)*	PET Cameras (%)*
North America	100.0	100.0
Latin America	94.9	91.3
Europe	5.1	5.0
Africa	53.9	57.9
Asia	73.5	74.3
Australia	100.0	100.0
Global	76.4	71.1

* SPECT and PET camera numbers based on IMAGINE database (5)

Table 4: Technetium Generator Suppliers

Supplier	Total number countries	US / Canada	Europe	Asia-Pacific	Africa
GE	7	1	3	2	1
IBA / CIS Bio France	10		1	8	1
Monrol	4			3	1
Polatom	5		1	2	2
ANSTO	2			2	
BAEC (Bangladesh)	1			1	
IPEN	3	2	1		
Mallinckrodt/Covidien	6	1	1	4	
Amersham	4				4
Parsisotope (Iran)	3			3	
Sam Young Unitech (Korea)	1			1	
Pinstech (Pakistan)	1			1	
BRIT (India)	1			1	
Jubilant DraxImage	1			1	
Saxons Healthcare	1			1	
SDS Life Sciences	1			1	
Vishat Diagnostic Priv Ltd	1			1	
Polatom	2		1	1	
NTP South Africa	2				2
Lantheus	3	2		1	
Rotop	2	1		1	
BSM	1	1			
Nihon Medi-Physics Co Ltd (Japan)	1				1
Fujifilm RI Pharma (Japan)	3			2	1
CGM Nuclear	1	1			
Positronpharma (Chile)	1	1			
Comision Chilena Energia Nuclear (Chile)	1	1			
Elumatac	1			1	
Quantarad Priv Ltd	1			1	
Pinstech	1			1	
MDS Nordion (Canada)	1	1			
Alumina chrom column	1	1			

Table 5: Commercial Radiopharmaceutical Kit Suppliers

Supplier	Total no. countries	US / Canada	Europe	Asia-Pacific	Africa
BRIT (India)	1			1	
Jubilant DraxImage	1			1	
Saxons Healthcare	1			1	
SDS Life Sciences	1			1	
Vishat Diagnostic Pvt Ltd	1			1	
Sanlar Imex Service Pvt Ltd	1			1	
GE	13	1	4	6	2
Polatom	11		4	5	2
TINT	1			1	
GMS	2			2	
Biogenetech	1			1	
IBA / CIS Bio	11	1	2	6	2
Mallinckrodt / Covidien	8	1	3	3	1
Monrol	4			3	1
Izotope	4			3	1
JPT/IDB	1			1	
Bristol-Myers (Hungary & Canada)	1				1
Amersham	2				2
DRAXImage	4	1		1	2
AAA	5	1	3		
Bayer	6	1	2	3	1
Nihon Medi-Physics Co Ltd (Japan)	1			1	
Fujifilm RI Pharma (Japan)	1			1	
CGM Nuclear (Chile)	1	1			
Positronpharma (Chile)	1	1			
Coimision Chilena Energia Nuclear (Chile)	1	1			
Rotop	3		1	2	1
Atomic High Tech China	1			1	
Medi-Radiopharma	4			3	1
Immunomedics	4		2	1	1
San Yung Tosh	2			1	
Kibion	1			1	
Pinstech	1			1	
Lantheus	2	1		1	
Pharmalucence	2	1		1	
Bracco	1	1			
Ayto Pharma	1	1			
Spectrum	2	1	1		
Radpharm	1			1	
Ansto	1			1	
Sirtex	2			2	
Perkin Elmer	1			1	
BAEC	1			1	
Institute of Isotope Co Ltd	1			1	
China Isotope Company	1			1	
Gipharma	2			1	1
Sanofi	1				1
NTP	1				1
Ithema Labs	1				1
Shin Jin (Indonesia)	1			1	
Kimia Farma (Indonesia)	1			1	
Parsisotope (Iran)	1			1	
IPEN	1	1			

Figure 1

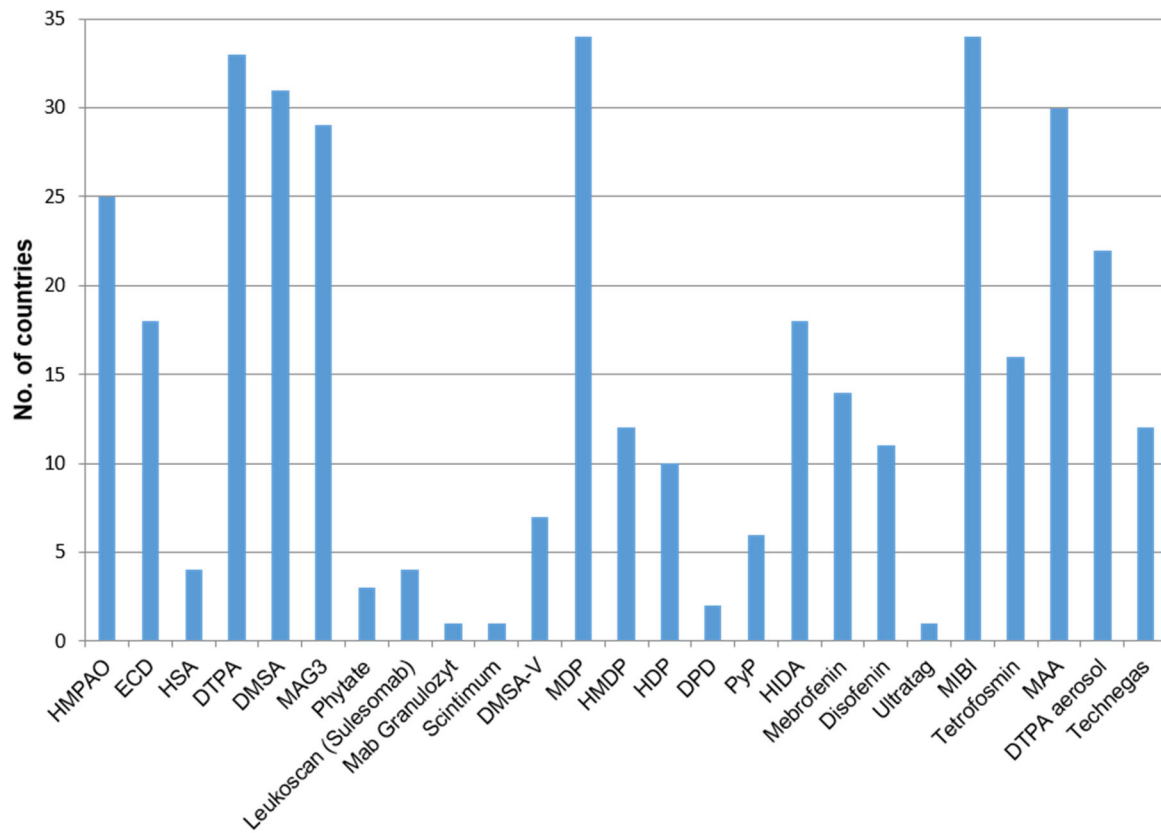


Figure 1. Range of most commonly available cold kits and ventilation agents in countries surveyed.

Figure 2

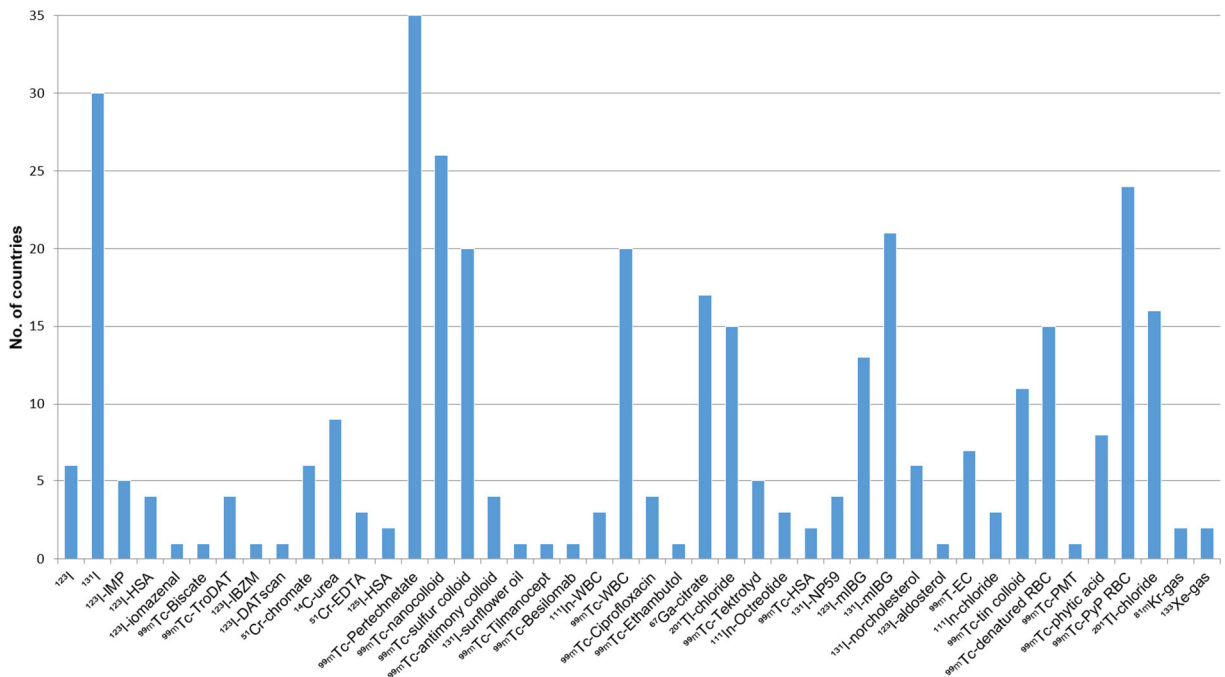


Figure 2. SPECT radionuclides and radiopharmaceuticals available in countries surveyed.

Figure 3

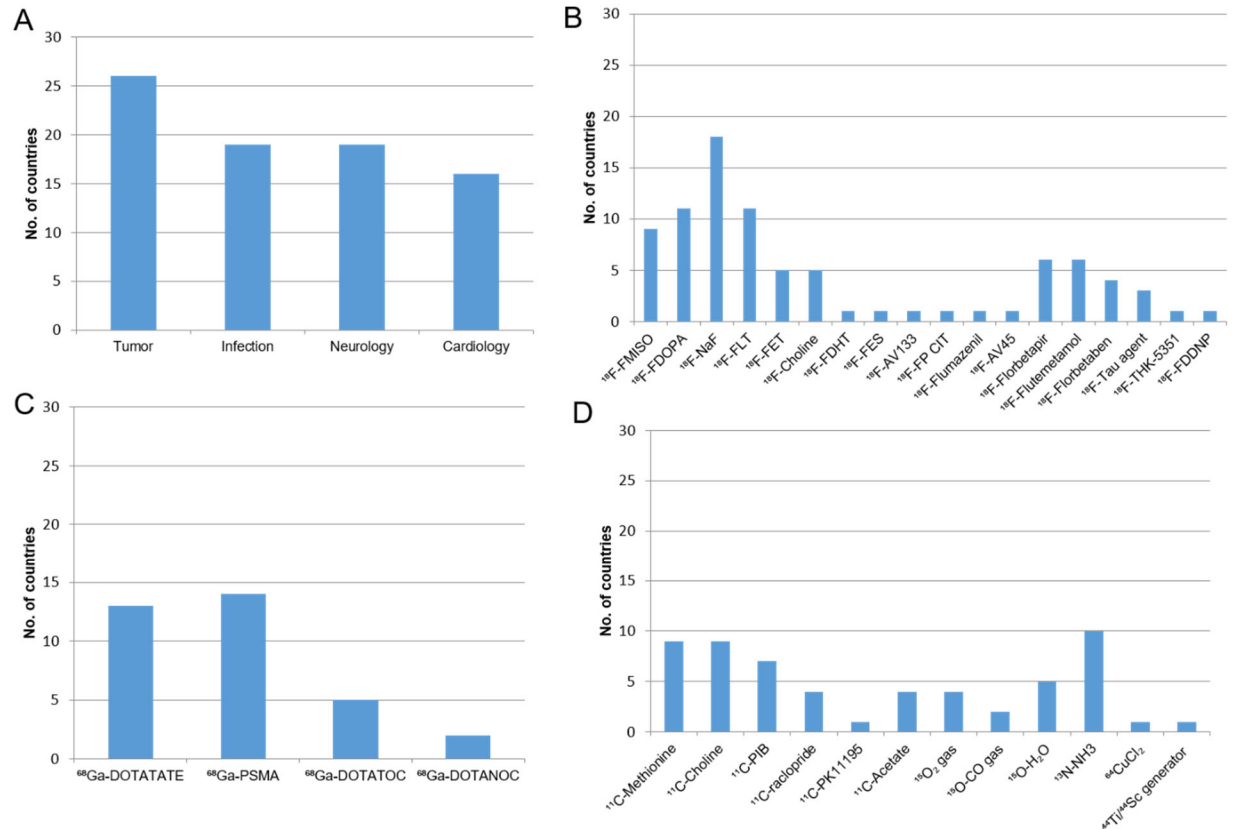


Figure 3. Number of countries with access to PET radiopharmaceuticals, (A) showing ^{18}F -FDG clinical utilization, (B) available ^{18}F -labeled PET tracers, (C) commonly used ^{68}Ga -labeled tracers and (D) other PET tracers.

Figure 4

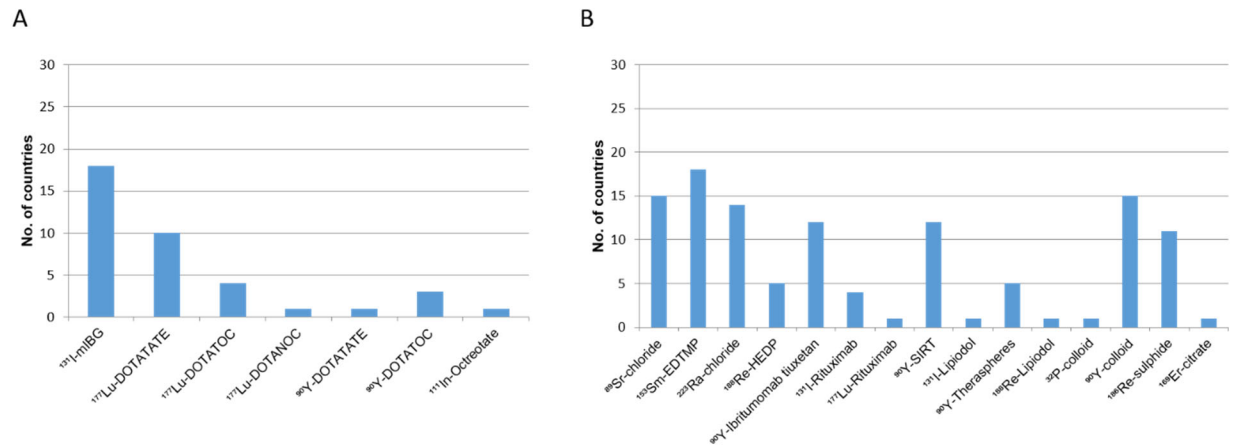


Figure 4. Number of countries with access to a range of radionuclide therapies, (A) targeted therapy and (B) radionuclide therapies currently used other than ^{131}I .

Radiopharmaceutical Access and Availability
Nuclear Medicine Global Initiative

Information of answering person (Country, affiliation, name, phone, email, address)

Nuclear Medicine Status in Country

Number of Nuclear Medicine Sites in Country:

Nuclear Medicine Sites - Government, Public:

Nuclear Medicine Sites - Private:

Nuclear Medicine Sites – Mobile Cameras:

Manufacturers / Suppliers of ^{99m}Tc -generators:

Manufacturers / Suppliers of kits:

Manufacturers / Suppliers of Therapeutic Radiopharmaceuticals:

Commercial Radiopharmacies:

Radiopharmaceuticals

Diagnostic Radiopharmaceuticals

Please confirm availability of the following radiopharmaceuticals, source and dose

^{99m}Tc -generators

Indicate number of sites that use in-house, or access via external radiopharmacies

Indicate source of ^{99m}Tc -generators, size of generators

Indicate issues relating to access or availability of ^{99m}Tc -generators

In vivo examinations

Brain imaging, CSF studies

- eg ^{123}I IMP, ^{99m}Tc HMPAO, ^{99m}Tc ECD, ^{99m}Tc HSA, ^{99m}Tc DTPA, ^{133}Xe gas, ^{123}I iomazenil, ^{99m}Tc RBC
- Indicate which tracers are available, which tracers are used for brain imaging and CSF studies, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Salivary gland

- eg ^{99m}Tc pertechnetate
- Indicate which tracers are available, which tracers are used salivary gland imaging, and source of tracer or doses)
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Thyroid gland (including thyroid carcinoma, medullary thyroid carcinoma)

- eg ^{99m}Tc pertechnetate, ^{123}I , ^{131}I , ^{124}I , ^{123}I -MIBG, ^{131}I -MIBG
- Indicate which tracers are available, which tracers are used for thyroid imaging, and source of tracer or doses
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Parathyroid gland

- eg $^{201}\text{Tl-Cl}$, $^{99\text{m}}\text{Tc-99m}$ pertechnetate, ^{123}I , $^{99\text{m}}\text{Tc-MIBI}$
- Indicate which tracers are available, which tracers are used for parathyroid imaging, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Lung

- eg $^{99\text{m}}\text{Tc-DTPA}$, ^{81}Kr gas, ^{133}Xe gas, $^{99\text{m}}\text{Tc MAA}$, $^{99\text{m}}\text{Tc-Technegas}$
- Indicate which tracers are available, which tracers are used for lung scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Heart (myocardial scintigraphy, blood-pool scintigraphy, first-pass)

- eg $^{201}\text{Tl-Cl}$, $^{99\text{m}}\text{Tc MIBI}$, $^{99\text{m}}\text{Tc tetrofosmin}$, $^{99\text{m}}\text{Tc-RBC}$
- Indicate which tracers are available, which tracers are used for heart scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Liver, Biliary tract

- eg $^{99\text{m}}\text{Tc phytic acid}$, $^{99\text{m}}\text{Tc sulphur colloid}$, $^{99\text{m}}\text{Tc PMT}$, $^{99\text{m}}\text{Tc HIDA}$ (DISIDA, Mebrofenin), $^{99\text{m}}\text{Tc-MAA}$
- Indicate which tracers are available, which tracers are used for liver and biliary scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Spleen, Bone marrow

- eg ^{99m}Tc phytic acid, ^{99m}Tc tin colloid, ^{111}In chloride, ^{99m}Tc -denatured RBCs
- Indicate which tracers are available, which tracers are used for spleen and bone marrow scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Kidney, Urinary system

- eg ^{99m}Tc DTPA, ^{99m}Tc DMSA, ^{99m}Tc MAG3
- Indicate which tracers are available, which tracers are used for kidney and urinary system scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Adrenal gland

- eg ^{131}I adosterol, ^{131}I MIBG, ^{123}I MIBG
- Indicate which tracers are available, which tracers are used for lung scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Bone, joints

- eg $^{99\text{m}}\text{Tc}$ MDP, $^{99\text{m}}\text{Tc}$ HMDP, $^{99\text{m}}\text{Tc}$ pyrophosphoric acid (PYP)
- Indicate which tracers are available, which tracers are used for bone and joint scans, and source of tracer or doses
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Digestive tract

- eg ^{99m}Tc pertechnetate, ^{99m}Tc RBC, ^{99m}Tc sulphur colloid (gastric emptying)
- Indicate which tracers are available, which tracers are used for GI tract scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Tumor

- eg ^{67}Ga citrate, ^{201}Tl chloride, ^{99m}Tc -(V) DMSA, ^{123}I -MIBG, ^{131}I -MIBG
- Indicate which tracers are available, which tracers are used for tumor scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Inflammation

- eg ^{67}Ga citrate, ^{111}In WBC, $^{99\text{m}}\text{Tc}$ WBC
- Indicate which tracers are available, which tracers are used for inflammation scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Lymph nodes, sentinel lymph nodes

- eg $^{99\text{m}}\text{Tc}$ HSA, $^{99\text{m}}\text{Tc}$ antimony sulphur colloid, $^{99\text{m}}\text{Tc}$ phytic acid, $^{99\text{m}}\text{Tc}$ -nanocolloid
- Indicate which tracers are available, which tracers are used for lung scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

In-vitro studies

- eg ^{51}Cr chromate, $^{99\text{m}}\text{Tc}$ DTPA, ^{14}C urea
- Indicate which tracers are available, which tracers are used for in vitro studies, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Other examinations

- Indicate which tracers are available, which tracers are used for different scans, and source of tracer or doses and kits
- Typical administered dose (MBq) for each tracer
- Are there any issues that impact on access and availability of these tracers

Please identify any diagnostic radiopharmaceuticals required but not available in your country, and indicate issues that prevent use eg access, shipping, cost, regulatory, facilities, training etc.

Therapy by unsealed Radiopharmaceuticals

Hyperthyroidism

- eg ^{131}I - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Thyroid Carcinoma

- eg ^{131}I - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Phaeochromocytoma

- eg ^{131}I MIBG - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Neuroblastoma

- eg ^{131}I MIBG - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Bone pain

- eg ^{89}Sr choride, ^{153}Sm EDTMP, ^{223}Ra chloride - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Neuroendocrine Tumors

- eg ^{177}Lu DOTATATE, ^{177}Lu DOTATOC - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Lymphomas

- eg ^{131}I Tositumumab, ^{90}Y Ibritumomab tiuxetan - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Liver Tumors

- eg ^{90}Y SIRspheres, ^{90}Y glass spheres, ^{188}Re spheres - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Polycythemia Rubra Vera

- eg ^{32}P - indicate if used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Joint Therapy

- eg ^{90}Y , ^{188}Re - indicate which therapeutic radiopharmaceuticals are used, and source
- Typical administered dose (MBq) for each therapy
- Are there any issues that impact on access and availability of these therapeutic tracers

Please identify any therapeutic radiopharmaceuticals required but not available in your country, and indicate issues that prevent use eg access, shipping, cost, regulatory, facilities, training etc.

PET Studies

Diagnostic PET Radiopharmaceuticals

Please confirm availability of the following radiopharmaceuticals, source and dose

^{18}F -FDG

- indicate number of sites that use in-house produced ^{18}F -FDG, or access via external radiopharmacies

- Typical administered dose (MBq) for ^{18}F -FDG

- Clinical Indications funded for ^{18}F -FDG PET

- Are there any issues that impact on access and availability of ^{18}F -FDG

¹⁸F- other PET tracers (non-dementia)

- eg ¹⁸F-FLT, ¹⁸F-FMISO, ¹⁸F-DOPA, ¹⁸F-NaF, ¹⁸F-FET
- indicate number of sites that use other ¹⁸F-tracers (non-dementia)

- Indicate which tracers are available, and indications

- Typical administered dose (MBq) for other ¹⁸F-PET tracers

- Clinical Indications funded for other ¹⁸F-PET tracers

- Are there any issues that impact on access and availability of other ¹⁸F-PET tracers

¹⁸F- other PET tracers (dementia)

- eg ¹⁸F-Florbetapir, ¹⁸F-Flutemetamol, ¹⁸F-Florbetaben, ¹⁸F-Tau agents
- indicate number of sites that use other ¹⁸F-tracers (dementia)

- Indicate which tracers are available

- Typical administered dose (MBq) for dementia ¹⁸F-PET tracers

- Clinical Indications funded for ¹⁸F-PET tracers in dementia

- Are there any issues that impact on access and availability of ¹⁸F-PET tracers in dementia

^{11}C -PET tracers

- eg ^{11}C -PIB, ^{11}C -methionine, ^{11}C -choline, ^{11}C -flumazenil, ^{11}C -raclopride
- indicate number of sites that use ^{11}C -tracers

- Indicate which tracers are available, and indications

- Typical administered dose (MBq) for ^{11}C -PET tracers

- Clinical Indications funded for ^{11}C -PET tracers

- Are there any issues that impact on access and availability of ^{11}C -PET tracers

^{68}Ga -PET tracers

- eg ^{68}Ga -DOTATATE, ^{68}Ga -PSMA
- indicate number of sites that use ^{68}Ga -tracers

- Indicate which tracers are available, and indications

- Typical administered dose (MBq) for ^{68}Ga -PET tracers

- Clinical Indications funded for ^{68}Ga -PET tracers

- Are there any issues that impact on access and availability of ^{68}Ga -PET tracers

^{15}O -PET tracers

- eg ^{15}O -O₂ gas, ^{15}O -CO gas, ^{15}O -H₂O
- indicate number of sites that use ^{15}O -tracers

- Indicate which tracers are available, and indications

- Typical administered dose (MBq) for ^{15}O -PET tracers

- Clinical Indications funded for ^{15}O -PET tracers

- Are there any issues that impact on access and availability of ^{15}O -PET tracers

^{13}N -PET tracers

- eg ^{13}N - NH_3 , ^{13}N -other tracer
- indicate number of sites that use ^{13}N -tracers
- Indicate which tracers are available, and indications
- Typical administered dose (MBq) for ^{13}N -PET tracers
- Clinical Indications funded for ^{13}N -PET tracers
- Are there any issues that impact on access and availability of ^{13}N -PET tracers

other PET tracers

- Indicate which other PET tracers are available, which clinical indications they are used for, and source of tracer or doses and kits

- Typical administered dose (MBq) for each tracer

- Are there any issues that impact on access and availability of these tracers

Please identify any PET tracers required, but not available in your country, and indicate issues that prevent use eg access, shipping, cost, regulatory, facilities, training etc.