

GUIDANCE

EARL

THERANOSTICS

VERSION 1.0

01 JULY 2024

This guidance provides the background of the EARL Theranostics certification for centers to become a EARL Qualified theranostic center of excellence (level 1), with a short description of the context and detailed instructions for submitting the required information.

For support contact EARL via e-mail: earl@eanm.org



TABLE OF CONTENTS

INTRODUCTION	4
THERANOSTIC PROCEDURES	6
Neuroendocrine tumors	6
Prostate cancer	6
Liver disease	7
Bone metastases.....	7
EU REGULATIONS	7
ADMINISTRATION OF RADIOPHARMACEUTICALS	8
RADIATION PROTECTION	8
STORAGE OF RADIOPHARMACEUTICALS	9
RADIOACTIVE WASTE	9
EARL THERANOSTICS CERTIFICATION ENROLLMENT AND CRITERIA	9
EARL FEEDBACK	13
ENROLLMENT SUBMISSION TIMELINES	13
CERTIFICATION ON HOLD	13
CERTIFICATION FEE	13

REVISIONS

Date	Version	Description of changes
01Jul2024	1.0	Initial release

INTRODUCTION

The EANM establishes a Theranostics Center of Excellence (CoE) network with the main goal to ensure a harmonized theranostic approach of the highest possible quality across a network of centers. As such, specialized theranostics centers dedicated to a high quality personalized theranostic procedures are inventoried at the benefit of first and foremost our patients but also of other stakeholders, including industry and regulatory authorities.

Providing the best possible care for patients is a mandatory aspect of improving personalized health care. However, all changes and evaluation in medical applications need to be tested and validated by suitable experts with suitable roles in certified centers according to certain quality standards. Thus, high quality clinical service including a comprehensive clinical set of treatment options and quality care, with sufficient possibilities of different services and variants in technology are necessary criteria for a CoE structure.

The theranostics concept – i.e. using the same target for both imaging and therapy – has been the cornerstone of nuclear medicine since the introduction for treatment of thyroid disease in the early 1940s. Even though iodine-131 (^{131}I) and yttrium-90 (^{90}Y) radiolabeled anti-CD20 antibodies showed excellent long term clinical outcomes in low- grade Non-Hodgkin Lymphomas^{1,2,3}, these agents have largely been replaced by non- radioactive therapies, mainly due to market forces and the relative ease of delivering non- radioactive treatments.

The success story of iodine theranostics in thyroid diseases as well as the recent approval of [^{177}Lu]Lu-DOTATATE for treating patients with gastroenteropancreatic neuroendocrine tumours (GEP-NETs) following the landmark NETTER-11 trial have increased the applications of targeted radionuclide therapies (tRNT). The expansion of the theranostics concept beyond thyroid cancer and neuroendocrine tumours towards higher-incidence diseases like prostate cancer (and subsequently to other tumours) shifts nuclear medicine and radionuclide therapy into the spotlight of modern cancer therapies. The TheraP and VISION trial^{4,5} showed that in prostate cancer, the most common and second most fatal cancer in men, [^{177}Lu]Lu-PSMA-617 therapy significantly increased the median overall survival² in patients with metastatic castration- resistant prostate cancer (mCRPC), resulting in the approval of [^{177}Lu]Lu-PSMA-617 by FDA and EMA.

In addition, although the above-described trials show promising results using ^{177}Lu for tRNT, there is still room for improving response rates and patient outcome, while maintaining a good quality-of-life for the patient. Over the last years, a promising new generation of tRNT-radiopharmaceuticals is emerging with the entrance of α -emitters in the tRNT-scene. Several studies^{6,7,8,9,10,11,12} have reported promising results with Targeted Alpha Therapy (TAT). TAT has been shown to overcome resistance to β -emitters in clinical applications. More specifically, preliminary results have demonstrated the efficacy of [^{225}Ac]Ac-DOTATATE and [^{225}Ac]Ac-DOTATOC^{13,14} for treatment of β -radiation–refractory NET patients, especially when the maximal prescribed doses with ^{177}Lu -ligands therapy have been reached. Therefore, it could be considered as adjuvant to β -emitting [^{177}Lu]Lu-DOTATATE¹⁵ as it has been shown that 18–32% of the patients are resistant to β -emitting [^{177}Lu]Lu-DOTATATE therapy¹⁶. Also for treatment of metastatic castration-resistant prostate cancer (mCRPC), recent clinical studies have demonstrated high efficacy of [^{225}Ac]Ac-PSMA^{17, 18, 19, 20, 21, 22, 23, 24}. These studies reported good tumour response for patients with advanced stage prostate cancer, who were heavily pre-treated (e.g. prostatectomy, EBRT, androgen deprivation therapy, chemotherapy, [^{177}Lu]Lu-PSMA-targeted radioligand monotherapy, etc.) and developed resistance to those treatments.

As a result, a tremendous increase in the demand for theranostics procedures can be expected, and this projected surge in demand for both theranostics infrastructure and appropriately skilled professional staff will pose a challenge and opportunity for healthcare systems. Even in countries with a strong track record in radionuclide theranostics, the existing infrastructure may be insufficient to meet the growing demand^{25,26}. Therefore, theranostics and radionuclide therapy need to get ready for the expected surge in demand from cancer patients, referring physicians and society. Here we provide an enabling guide for stakeholders interested in registering their theranostics centre with EARL's Theranostics Center of Excellence network.

The EARL Theranostics certification programme has three distinguished levels of certification: Qualified, Advanced and Educational Center. At the start of the programme only the Qualified Theranostics CoE will be launched, referred to as level 1, which will be followed by the other two levels at a later stage.

This manual covers level 1 which mainly consists of a questionnaire to generate an overview of the current theranostic capacity within and beyond Europa. This inventory will serve as baseline where special attention is given to current infrastructure and technical challenges, medical considerations including collaboration with clinical partners and treatment indications, staffing and their training levels as well as regulatory considerations and requirements.

Essentially every center that performs theranostic procedures is eligible for level 1 if procedures comply with minimal quality and safety standards including patient stratification, storage and administration of radiopharmaceuticals, radioprotection, and waste management. To cover all these aspects of theranostics, centers can work together to provide both diagnostic and therapeutic services. However, as this certification program is complementary to other running and starting certification programs on Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT), this certification program focusses on tRNT. Therefore, tRNT procedures should be performed in-house while diagnostic procedures can be performed at a different site. This also implies that centers who only perform diagnostic procedures will not be considered eligible for a level 1 EARL Qualified theranostic center of excellence certification.

Level 1 will not inquire about the specific requirements associated with the in-house production of radiopharmaceuticals since there is no global harmonization, and national laws differ considerably. If, based on the information you have provided through the questionnaire, your center is not deemed eligible for level 1 certification, EANM will reach out via email to ask for additional information or clarifications that would still be needed to become a level 1 EARL Qualified theranostic center of excellence.

Partially based on the level 1 inventory, EANM will define quality and safety requirements for level 2 which will be more stringent and rely on other ongoing EARL PET and SPECT certification programmes. In addition, expertise on different theranostic procedures needs to be demonstrated with a minimal number of specific procedures performed each year. A multidisciplinary approach involving nuclear medicine physicians, radiopharmacist/chemists, medical physicists and dedicated technologists also needs to be in place together with minimal staffing levels and training requirements to support more advanced theranostic procedures. The questionnaire for level 1 certification will already enquire whether a center would apply for a level 2 EARL advanced theranostic center of excellence as a next step such that these centers can be identified and briefed in time about the additional requirements for level 2 certification. Eventually, EARL can reach out to some of these centers and ask them to get involved as pilot centers for setting up the level 2 certification programme.

Finally, the level three certification for EARL educational theranostic center of excellence will be rolled out. This level three certification is meant for centers that help the field of theranostics moving forward. These centers are actively developing new theranostics procedures (diagnostic and/or therapeutic radiopharmaceuticals), considering current theranostic procedures in new patient groups or optimizing existing theranostic procedures to improve efficacy or to make these procedures more accessible for a larger number of patients. These centers should also have the knowledge to conduct multicenter or phase 1 clinical trials and the capacity to disseminate their expertise by providing training to other theranostic centers.

The next section gives an overview of current theranostic procedures that can be covered by a level 1 EARL Qualified theranostic center of excellence. The following section will shortly describe the current legal EU framework. Next, the safety and quality required for level 1 certification will be shortly discussed starting with patient stratification,

Theranostic Procedures

Below are listed most established, new, and emerging theranostic procedures which can be covered by an EARL Qualified theranostic center of excellence.

Thyroid disease

[¹³¹I]-based treatment for managing and treating benign thyroid disease and thyroid cancer^{27,28}

- Therapeutic radiopharmaceutical: [¹³¹I]NaI
- Diagnostic procedure: [^{99m}Tc]Tc- or [¹²³I]I-scintigraphy or [¹²⁴I]I-PET

Neuroendocrine tumors

- [¹³¹I]-based treatment for managing unresectable, locally advanced or metastatic²⁹ pheochromocytoma, paraganglioma or neuroblastoma requiring systemic anticancer therapy, with the suitability for treatment confirmed
 - Therapeutic radiopharmaceutical: [¹³¹I]mIBG
 - Diagnostic procedure: [¹³¹I]I-SPECT/CT
- Peptide Receptor Radionuclide Therapy (PRRT)³⁰ targeting the somatostatin type 2 receptor (SSTR2), which is overexpressed on the membrane of neuroendocrine tumor (NET) cells
 - Therapeutic radiopharmaceutical: [¹⁷⁷Lu]Lu-DOTATATE (Lutathera, Novartis), which has been approved by the European Medicines Agency (EMA, 2017) and American Food and Drug Administration (FDA, 2018) as PRRT for patients with gastroenteropancreatic neuroendocrine tumours (GEP-NETs) overexpressing SSTR2 who have metastatic disease and therefore are not eligible for surgery or other SSTR targeting ligands for the same indication (e.g. [¹⁷⁷Lu]Lu-DOTATOC, [¹⁷⁷Lu]Lu-DOTANOC). Additionally, other SSTR2 agonists and antagonists being employed for PRRT, labeled with other beta emitters like ¹⁶¹Tb or ⁹⁰Y or with alpha emitters like ²²⁵Ac.
 - Diagnostic procedure: PET imaging with the corresponding ⁶⁸Ga or ¹⁸F labeled SSTR2 (ant)agonist

Prostate cancer

PSMA (prostate-specific membrane antigen) radioligand therapy (PRLT)³¹ targeting PSMA that is overexpressed on the membrane of prostate cancer cells.

- Therapeutic radiopharmaceutical: [¹⁷⁷Lu]Lu-PSMA-617 (Pluvicto, Novartis), which has been approved by the FDA (2022) and EMA (2022) as PRLT for patients with progressive, PSMA positive metastatic castration-resistant prostate cancer (mCRPC) or other PSMA targeting radioligands (e.g. PSMA-I&T) for the same indications. Additionally, PSMA labeled with other beta emitters like ¹⁶¹Tb or alpha emitters like ²²⁵Ac is employed for PRLT

- **Diagnostic procedure:** PET imaging with the corresponding ^{68}Ga - or ^{18}F -labeled PSMA ligands.

Liver disease

Radioembolization treatment with intra-arterial radioactive compounds of liver cancer and liver metastases, including hepatocellular carcinoma and liver metastatic colorectal cancer.

- **Therapeutic radiopharmaceutical:** Resin or glass microspheres labeled with ^{90}Y or alternatively ^{166}Ho -microspheres.
- **Diagnostic procedure:** pre-treatment intra-arterial $^{99\text{m}}\text{Tc}$ -labelled albumin macroaggregated albumin1 ($^{99\text{m}}\text{Tc}$ -MAA) scintigraphy to quantify potential liver-lung shunting and exclude reflux to bowel, stomach or pancreas. For ^{166}Ho -microspheres radioembolization, administration of a scout dose of ^{166}Ho -microspheres can be considered as it is safe and more accurate for the calculation of the lung shunt fraction when compared to $^{99\text{m}}\text{Tc}$ -MAA

Bone metastases

- **Alpha therapy** of bone metastases in patients with metastatic castration-resistant prostate cancer and no known visceral metastatic disease
 - **Therapeutic radiopharmaceutical:** [^{223}Ra]Radiumdichloride
 - **Diagnostic procedure:** $^{99\text{m}}\text{Tc}$ -labeled radiopharmaceuticals for bone scan, or [^{18}F]-Fluoride-PET/CT with evidence of bone metastases and cross sectional imaging of thorax and abdomen, e.g. with CT/MR or hybrid PET/CT or PET/MR (possible tracers: [^{18}F]-Fluorethylcholine, [^{11}C]-Choline, and [^{68}Ga]-PSMA)
- **Beta therapy** of bone metastases in cancer patients
 - **Therapeutic radiopharmaceutical:** bone-seeking beta emitting radiopharmaceuticals such as strontium-89 (^{89}Sr) or samarium-153 (^{153}Sm) lexidronam (^{153}Sm -EDTMP), both approved in EU and US and phosphorus-32 (^{32}P) sodium phosphate, only approved in US.
 - **Diagnostic procedure:** bone scan or [^{18}F]-Fluoride-PET/CT

EU REGULATIONS

Foremost, institutions wishing to apply for the EARL Theranostics registration, must comply with all relevant local country regulations. If this is not covered by national regulations, therapeutic procedures should adhere as much as possible to the International Basic Safety Standards (BSS)³² by the International Atomic Energy Agency (IAEA) that sets a consensus requirements derived from knowledge of radiation biology and radiation protection, respectively³³. The recommendations and requirements of the BSS and ICRP were established by the European Commission Directive 2013/59/EURATOM³⁴ for EU countries. This legal act has been transposed into national law by the Member States with specific requirements that apply to all existing and planned exposure situations and must be considered when establishing and operating a theranostic centre.

More specifically, chapter VII on medical exposure emphasis the sufficient net benefit, where the potential diagnostic or therapeutic benefits to health of an individual and to society, should be weighed against the individual detriment that the exposure might cause, while also taking into account the efficacy, benefits and risks of available alternative techniques having the same objective but involving no or less exposure to ionizing radiation (Article 55). In addition, medical exposure of patients for radiotherapeutic purposes, including nuclear medicine for therapeutic purposes, should be optimized with exposures of target volumes individually planned and their delivery appropriately verified while doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure (Article 56). Also, the different levels of involvement by a medical physics expert (MPE) are described (Article 58) with MPE involvement required for standardized therapeutical nuclear medicine practices and even close MPE involvement needed for radiotherapeutic practices other than standardized therapeutic nuclear medicine practices.

Based on BSS, the regulatory basis for operating a theranostics centre requires that the legal entity apply to the regulatory authority for a license, in accordance with the national regulations and laws governing the handling of radioactive materials for medical applications, as defined in ICRP Publication 105³⁵. This radioactive material license (RAM) must cover all aspects of both diagnostic and therapeutic use of radiopharmaceuticals. Prerequisites for applying for a RAM license include the existence of adequate infrastructure, sufficient personnel (including trained physicians, technologists, nursing staff, a radiation safety officer (RSO), MPE involvement, sufficient means of radiation protection and processes for discharge management of treated patients and handling of radioactive waste and sewage. To this end, several requirements must be met, depending on the respective spectrum of diagnostics and therapies applied and the radiopharmaceuticals used.

ADMINISTRATION OF RADIOPHARMACEUTICALS

Accurate quantification of the radioactivity administered to the patient is the first step of the radiopharmaceutical administration and traceability chain. A radionuclide calibrator measures the activity and cross-calibrates other equipment. It is therefore essential to ensure that calibration is traceable to primary standards when these are available^{36,37,38}.

A well-documented programme for quality assurance (QA) and quality control (QC) is essential to ensure the dependable performance of safe, accurate and reproducible equipment operation and the appropriate clinical administration of radiopharmaceuticals^{9,39,40}. Following installation of any new instrument, acceptance testing must confirm that the system meets the performance specifications and provides a baseline for comparison during routine QC. The type and frequency of QC tests should follow national guidelines.

The theranostic compounds can be administered in several ways: adequate shielding must be ascertained to avoid undesirable beta and gamma irradiation and to minimise the risk of contamination, e.g., by using hybrid shielding consisting of layers of PMMA (polymethyl metacrylate) and lead/tungsten, which results in attenuation of both beta and gamma radiation and minimizes the occurrence of bremsstrahlung. A syringe is prepared with the therapeutic agent, and the qualified operator administers the drug via correctly placed and patent intravenous access. This is followed by flushing with saline. This method is particularly used for drugs such as PSMA ligands, which do not require specific administration as a bolus. Alternatively, the syringe content can be administered via perfusor or injection pump. To minimize staff radiation exposure it is recommended to use an automatic dispensing and semi- or fully automated infusion pumps for the administration of the radiopharmaceuticals.

RADIATION PROTECTION

Long lived radioactive contaminants may require specific regulatory attention for patients' release after therapy administration. Shielding of syringes and vials, as well as in some jurisdictions, waste and storage containers, is an important aspect of reducing external exposure among staff, the public and patients. After administration of the radiopharmaceutical, it may be necessary (mainly in Europe) to isolate the patient from other persons, either within the hospital or in the public domain. The type of radiation emitted from the theranostics compound will dictate the extent of shielding required. This can vary from PMMA storage boxes for vials and waste containers, lead pots and tungsten syringe shields, to concrete waste bunkers or lead-lined treatment rooms. This infrastructure must be prepared according to local regulation and must be in place before any activity involving radiation is carried out. Appropriateness of the control measures must also be demonstrated, usually in the form of a written radiation risk assessment that considers radiation protection of both employees and patients. Established risk analysis methods such as Failure Mode and Effects Analysis (FMEA) or Fault Tree Analysis (FTA) should be used for this purpose. Compliance with NRC and/or state radiation safety regulations is required in the US.

^{177}Lu is one of the main isotopes of the element lutetium, and is also the most used emerging theranostic radionuclide. ^{177}Lu emits beta particles with half-life of 6.7 days. With ^{177}Lu , attention must be paid to the underlying manufacturing pathway, which may result in unwanted small quantities of metastable lutetium-177 ($^{177\text{m}}\text{Lu}$) with a half-life of 161 days. In this case, $^{177\text{m}}\text{Lu}$ may account for approximately 0.02% of the total amount of ^{177}Lu in the final radiopharmaceutical. This requires special consideration in terms of storage and disposal of waste depending on local regulations.

STORAGE OF RADIOPHARMACEUTICALS

Radiopharmaceuticals must be stored in a safe, secure, and environmentally appropriate (such as refrigerated or frozen) place to which only the licensee and appropriate staff may have access. In addition, provisions for the safe storage and custody of radioactive materials must be in place, including protection against theft, fire, and chemicals. Transport and movement of radioactive materials to, from, and within the hospital must be carefully documented so that any radioactive material can be tracked from source to final use and disposal.

RADIOACTIVE WASTE

Storage for decay is essential for the clearance of radioactive waste containing short lived radioisotopes, with a half-life of less than 100 days. "Clearance is the removal of radioactive material from regulatory control provided that the radionuclide concentrations are below specific clearance levels"⁴¹.

EARL THERANOSTICS CERTIFICATION ENROLLMENT AND CRITERIA

The enrollment form is submitted via the EARL web site: <https://earl.eanm.org/theranostics>. Prior to starting to complete the enrollment form, review the details online to ensure you have all relevant information available.

After initial certification, a renewal will be required every year.

Contact information

- Full name and email of person completing the enrollment form & contact e-mail
- Institution & Department name in English (will be displayed on the accreditation certificate)
- Address of institution in English: street & number, city, post code, country
- EU VAT number (if applicable)
- Billing details
 - Billing entity name in English
 - EU VAT number
 - Street & number, city, post code, country
- Head of Department title & full name, email, phone
- Primary contact full name, email, phone
- Additional department contacts full name, email

Staff & Training

- Theranostics personnel - provide the number of theranostics trained personnel as follows:
 - Nuclear medicine physicians.
 - Nuclear medicine physicists
 - Nuclear medicine radiochemists / pharmacists
 - Nuclear medicine technologists
 - Nurses
 - Residents

- Others (specify)
- Is your staff up to date with local continued education units requirements: Yes/No
- Do you run a CME program? Yes/No
- Do you run other internal training programs? Yes/No, if Yes, specific topic

Imaging infrastructure

- Available equipment at your site:
 - SPECT only gamma camera: Yes/No; make & model (you will need to list each SPECT camera in this section)
 - SPECT/CT gamma camera: Yes/No; make & model (you will need to list each SPECT/CT camera in this section)
 - PET/CT: Yes/No; make & model (you will need to list each PET/CT in this section)
 - PET/MR: Yes/No; make & model (you will need to list each PET/MR in this section)
 - If not do you have a SPECT system, specify which center you are cooperating with for SPECT imaging
 - If not do you have a PET system, specify which center you are cooperating with for PET imaging
- Are (or is one of) the PET scanners EARL accredited? Yes/No
- Do you consider Diagnostic Reference Levels (DRLs) for the diagnostic procedures that you perform in the context of Theranostics? Yes/No
- Are you interested in accrediting your SPECT/CT system via EARL? Yes/No

Radiopharmaceuticals (RF)

- Do you have a cyclotron?
 - At your site
 - In cooperation
 - No, we only use commercially approved and available RF
- Do you have in-house radiolabelling facility?
 - For diagnostics only
 - For therapeutics only
 - Both
- Do you use a 68Ga-generator? Yes/No
- Do you perform immunoPET in the context of theranostics? Yes/No, if Yes, please specify the radionuclide
- If relevant, who is your supplier for?
 - Iodine
 - ¹³¹I MIBG
 - ¹⁷⁷Lu
- Select all available theranostic procedures at your institution:

Y/N	Therapeutic	Specify diagnostic	Nr of pts/year
	[¹³¹ I]NaI		
	[¹³¹ I]mIBG		
	¹³¹ I-labelled Apamistamab		
	[¹⁷⁷ Lu]Lu-PSMA-ligant		
	[¹⁷⁷ Lu]Lu- SSTR2-ligand		
	[⁹⁰ Y]Yttrium citrate		
	[¹⁸⁶ Re]Rhenium sulfide		
	[¹⁶⁹ Er]Erbium citrate		
	[⁹⁰ Y]Y-Ibritumomab tiuxetan		
	⁹⁰ Y- spheres		
	¹⁶⁶ Ho- spheres		

	[²²³ Ra]Radichloride		
	Others to be entered		

Radioprotection

- Do you have probe measuring station for uptake measurements?: Yes/No
- Do you have dose rate meter?: Yes/No
- Do you have activity meter with CE certificate and dedicated QA programme in place?: Yes/No
- Do you have radiation protection equipment (e.g. contamination monitor)?: Yes/No
 - If yes, please describe radiation protection equipment:
- Do you have well counter (or equivalent)?: Yes/No
- Do you have QM system for radionuclide therapies (therapy SOPs, etc.)? Yes/No
 - If no, provide a reason
 - If yes, briefly describe the QM system
 - or upload a file with the details:
- Do you have a waste management system?:
 - If no, provide a reason
 - If yes, upload a file with the details

BSS compliance

- What is the level of involvement of the MPE in theranostic procedures?
 - Reachable by phone during procedures
 - Present on site during procedures but not actively involved
 - Actively involved in the therapy planning and verification of procedures
 - Closely involved in the decision making on the activities to be administered for the procedures
- Are you performing dosimetry on a routine basis? Yes/No,
 - Yes
 - No, do you have the expertise and capacity to perform dosimetry for specific study purposes?
 - Yes
 - No

Therapies

- How many Out-pts/month?
- How many Hospitalized-pts/month?
- How long is the hospitalization for

Therapy	Threshold activity (when applicable)	Duration (days)	Release criteria (Y/N, if Y specify)
Iodine-131 low activity			
Iodine-131 high activity			
Lutetium-177			
Actinium-225			
Other			

- How many beds for treatment are available at your site?
- Which clinical trials are you performing?
 - Phase I
 - Phase II-III
 - None but interested in conducting clinical trials
 - None

EARL FEEDBACK

Information about the theranostics certification acceptance or rejection is provided via email. If the certification is granted your site's name, address and department head and primary contacts will be listed on EARL's website in the Theranostics Centres of Excellence network. You will receive via email a certificate and signet. The certificate contains your institution name, the department, therapies provided for the respective year.

The certification signet will be provided via email as soon as the certification has been granted. You are allowed to use the certification signet (see an example below) on your correspondence and website.



If the certification is not granted for the respective level, our team will discuss with you the reasons and provide detailed feedback on the necessary steps to achieve the certification.

ENROLLMENT SUBMISSION TIMELINES

The timelines for certification enrollment:

Quarter 1: 02Jan – 15Jan

Quarter 2: 01Apr – 15Apr

Quarter 3: 01Jul – 15Jul

Quarter 4: 01Oct – 15Oct

Initial feedback on the enrollment status is provided within one month of the full data submission, and a notification that the application process has started.

Yearly renewal is required. The above timelines are applicable to renew your institution's EARL Theranostics certification. Delinquency to submit the renewal form will result in suspension of the certification.

CERTIFICATION ON HOLD

Please submit enrollment/renewal form on time as noted above in the timelines section. If the deadlines are disregarded, your certification is no longer active. Re-entry into the certification programme is possible as soon as you are able to fulfil these requirements again in the next respective quarter as defined above. At the start of each quarter EARL updates the Theranostics Centers of Excellence network on the web site. If your certification is not active at the time of this update, your institution will not be listed. It will be listed when your certification is reactivated but no earlier than the next quarter when again the list updated (start of the 3rd month of each quarter).

CERTIFICATION FEE

The fee for the theranostics certification programme is per calendar year per site (regardless of when the process starts within the calendar year), covering the costs for the initial certification procedure and maintaining the status of an EARL Theranostics Center of Excellence. For Level 1 there is no fee. For up-to-date information of the fee, please check the EARL web site under Theranostics certification fees. EARL will send you an invoice via email specifying an invoice number. Please reference the invoice number when transferring the payment.

The accreditation fee needs to be transferred to the following account:

ERSTE Bank

Bank code: 20111

IBAN: AT90 2011 1828 5173 8400

BIC: GIBAATWWXXX

¹Mark S. Kaminski, Kenneth R. Zasadny, Isaac R. Francis, Adam W. Milik, Charles W. Ross, Scott D. Moon, Shelley M. Crawford, Jeanne M. Burgess, Neil A. Petry, Gregory M. Butchko, Stephan D. Glenn, and Richard L. Wahl. Radioimmunotherapy of B-cell lymphoma with [131I]anti-B1 (anti-CD20) antibody. *N Engl J Med* 1993; 329(7): 459-65

²Franck Morschhauser 1, John Radford, Achiel Van Hoof, Barbara Botto, Ama Z S Rohatiner, Gilles Salles, Pierre Soubeyran, Herve Tilly, Angelika Bischof-Delaloye, Wim L J van Putten, Jelle W Kylstra, Anton Hagenbeek. ⁹⁰Yttrium-ibritumomab tiuxetan consolidation of first remission in advanced-stage follicular non-Hodgkin lymphoma: updated results after a median follow-up of 7.3 years from the International, Randomized, Phase III First-Line Indolent trial. *J Clin Oncol* 2013; 31(16): 1977-83

³Mazyar Shadman, Hongli Li, Lisa Rimsza, John P. Leonard, Mark S. Kaminski, Rita M. Braziel, Catherine M. Spier, Ajay K. Gopal, David G. Maloney, Bruce D. Cheson, Shaker Dakhil, Michael LeBlanc, Sonali M. Smith, Richard I. Fisher, Jonathan W. Friedberg, and Oliver W. Press, Continued Excellent Outcomes in Previously Untreated Patients With Follicular Lymphoma After Treatment With CHOP Plus Rituximab or CHOP Plus (131)I-Tositumomab: Long-Term Follow-Up of Phase III Randomized Study SWOG-S0016. *J Clin Oncol* 2018; 36(7): 697-703

⁴Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt, Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, Andrew D Redfern, William Macdonald, Alex Guminski, Edward Hsiao, Wei Chua, Peter Lin, Alison Y Zhang, Margaret M McJannett, Martin R Stockler, John A Violet, Scott G Williams, Andrew J Martin, Ian D Davis “[¹⁷⁷Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial,” *The Lancet*, vol. 397, no. 10276, pp. 797–804, Feb. 2021, doi: 10.1016/S0140-6736(21)00237-3.

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