HELMHOLTZ ZENTRUM
DRESDEN ROSSENDORF

Advancements in Radiopharmaceutical and emerging guidance

CDDF Workshop - New Modalities in Cancer Drug Development

Institute of Radiopharmaceutical Cancer Research · Dr Oliver Kiß · o.kiss@hzdr.de · www.hzdr.de

DRESDEN concept

The Evolution of a Novel Radiopharmaceutical

„Cold“ chemistry / Design of target molecules/structures

Radionuclide production

Radiochemistry

Biological evaluation

Radiopharmacy GMP

Clinical trial(s)

Marketing authorization

Efficacy, toxicity and pharmacokinetics

Preclinical Phase

Pharmacokinetics

Phase 0

10

Phase 4

Surveillance

Safety

Phase 1

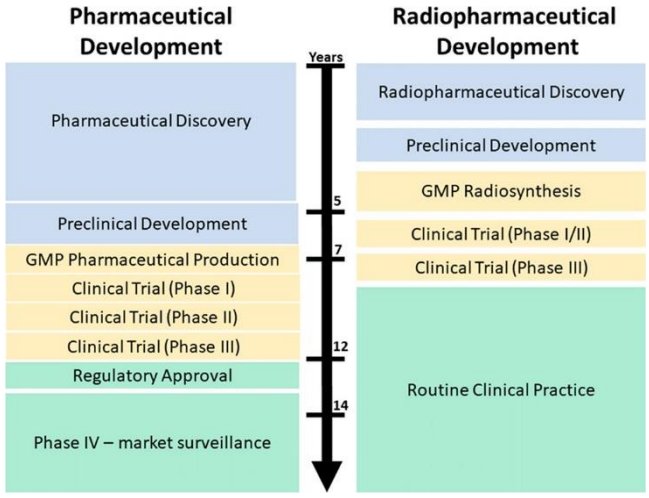
Efficacy and side effects

Phase 2

Efficacy, effectiveness and safety

Phase 3

300-3000



Allott and Aboagye, Mol Pharm 2020

[^{177}Lu]Lu-DOTATATE (Lutathera)

Int. J. Cancer: 92, 628–633 (2001)

UICC Publication of the International Union Against Cancer

[^{177}LU-DOTA^{0},TYR^{3}]OCTREOTATE FOR SOMATOSTATIN RECEPTOR-TARGETED RADIONUCLIDE THERAPY

Marion DE JONG[1]*, Wout A.P. BREEMAN[1], Bert F. BERNARD[1], Willem H. BAKKER[1], Michael SCHAAR[1], Arthur VAN GAMEREN[1], Joe E. BUGAJ[3], Jack ERION[3], Michelle SCHMIDT[3], Ananth SRINIVASAN[3] and Eric P. KRENNING[1,2]

[1]*Department of Nuclear Medicine, University Hospital and Erasmus University Rotterdam, Rotterdam, The Netherlands*
[2]*Department of Internal Medicine, University Hospital and Erasmus University Rotterdam, Rotterdam, The Netherlands*
[3]*Mallinckrodt Medical Inc., St. Louis, MO, USA*

2001

Preclinical to first-in-human 2001

Phase 3 trial (NETTER-1)
2012-2016

Original article

[^{177}Lu-DOTA^{0},Tyr^{3}]octreotate: comparison with [^{111}In-DTPA^{0}]octreotide in patients

Dik J. Kwekkeboom[1], Willem H. Bakker[1], Peter P. M. Kooij[1], Mark W. Konijnenberg[3], Ananth Srinivasan[4], Jack L. Erion[4], Michelle A. Schmidt[4], Joe L. Bugaj[4], Marion de Jong[1], Eric P. Krenning[1, 2]

[1] Department of Nuclear Medicine, University Hospital Rotterdam, Dr Molewaterplein 40, 3015 GD Rotterdam, the Netherlands
[2] Department of Internal Medicine, University Hospital Rotterdam, the Netherlands
[3] Mallinckrodt Medical, Petten, the Netherlands
[4] Mallinckrodt Medical, St. Louis, Missouri, USA

Received 26 February and in revised form 24 April 2001 / Published online: 4 July 2001

Abstract. The somatostatin analogue [DOTA^{0},Tyr^{3}]octreotate has a nine-fold higher affinity for the somatostatin receptor subtype 2 as compared with [DOTA^{0}, Tyr^{3}]octreotide. Also, labelled with the beta- and gamma-emitting radionuclide lutetium-177, this compound

Keywords: Somatostatin – Somatostatin receptor imaging – Octreotate – Peptide receptor radiotherapy

Eur J Nucl Med (2001) 28:1319–1325
DOI 10.1007/s002590100574

2001

Articles

The NEW ENGLAND JOURNAL of MEDICINE

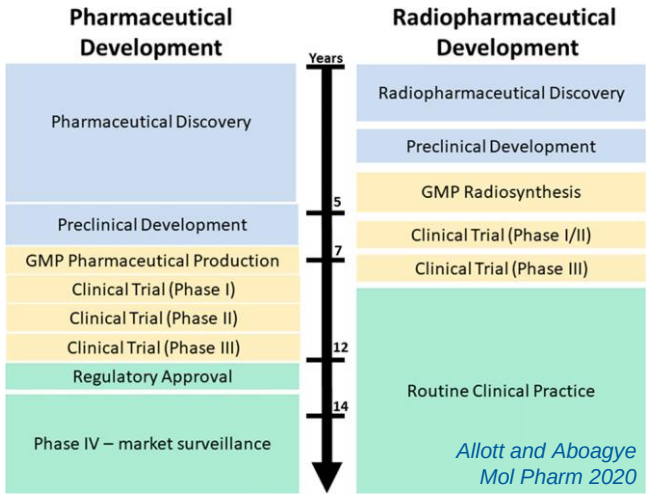
ORIGINAL ARTICLE

Phase 3 Trial of ^{177}Lu-Dotatate for Midgut Neuroendocrine Tumors

J. Strosberg, G. El-Haddad, E. Wolin, A. Hendifar, J. Yao, B. Chasen, E. Mittra, P.L. Kunz, M.H. Kulke, H. Jacene, D. Bushnell, T.M. O'Dorisio, R.P. Baum, H.R. Kulkarni, M. Caplin, R. Lebtahi, T. Hobday, E. Delpassand, E. Van Cutsem, A. Benson, R. Srirajaskanthan, M. Pavel, J. Mora, J. Berlin, E. Grande, N. Reed, E. Seregni, K. Öberg, M. Lopera Sierra, P. Santoro, T. Thevenet, J.L. Erion, P. Ruszniewski, D. Kwekkeboom, and E. Krenning, for the NETTER-1 Trial Investigators*

2017

Approval as Lutathera in 2017 (EMA)
Approval as Lutathera in 2018 (FDA)



^{177}Lu-Dotatate plus long-acting octreotide versus high-dose long-acting octreotide in patients with midgut neuroendocrine tumours (NETTER-1): final overall survival and long-term safety results from an open-label, randomised, controlled, phase 3 trial

*Jonathan R Strosberg, Martyn E Caplin, Pamela L Kunz, Philippe B Ruszniewski, Lisa Bodei, Andrew Hendifar, Erik Mittra, Edward M Wolin, James C Yao, Marianne E Pavel, Enrique Grande, Eric Van Cutsem, Ettore Seregni, Hugo Duarte, Germo Gericke, Amy Bartalotta, Maurizio F Mariani, Arnaud Demange, Sakir Mutevelic, Eric P Krenning, on behalf of the NETTER-1 investigators**

Lancet Oncol 2021; 22: 1752–63
Published Online November 15, 2021 https://doi.org/10.1016/S1470-2045(21)00572-6

Summary

Background The primary analysis of the phase 3 NETTER-1 trial showed significant improvement in progression-free survival with ^{177}Lu-Dotatate plus long-acting octreotide versus high-dose long-acting octreotide alone in patients with advanced midgut neuroendocrine tumours. Here, we report the prespecified final analysis of overall survival and long-term safety results.

2021

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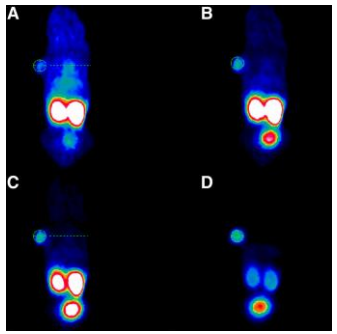
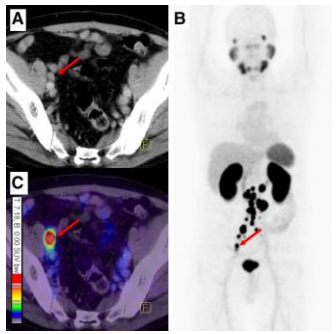
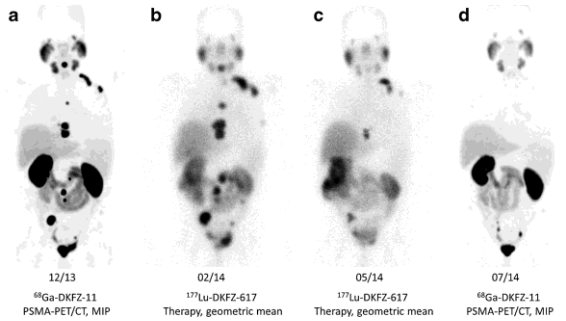
[^{177}Lu]Lu-PSMA-617 (Pluvicto)

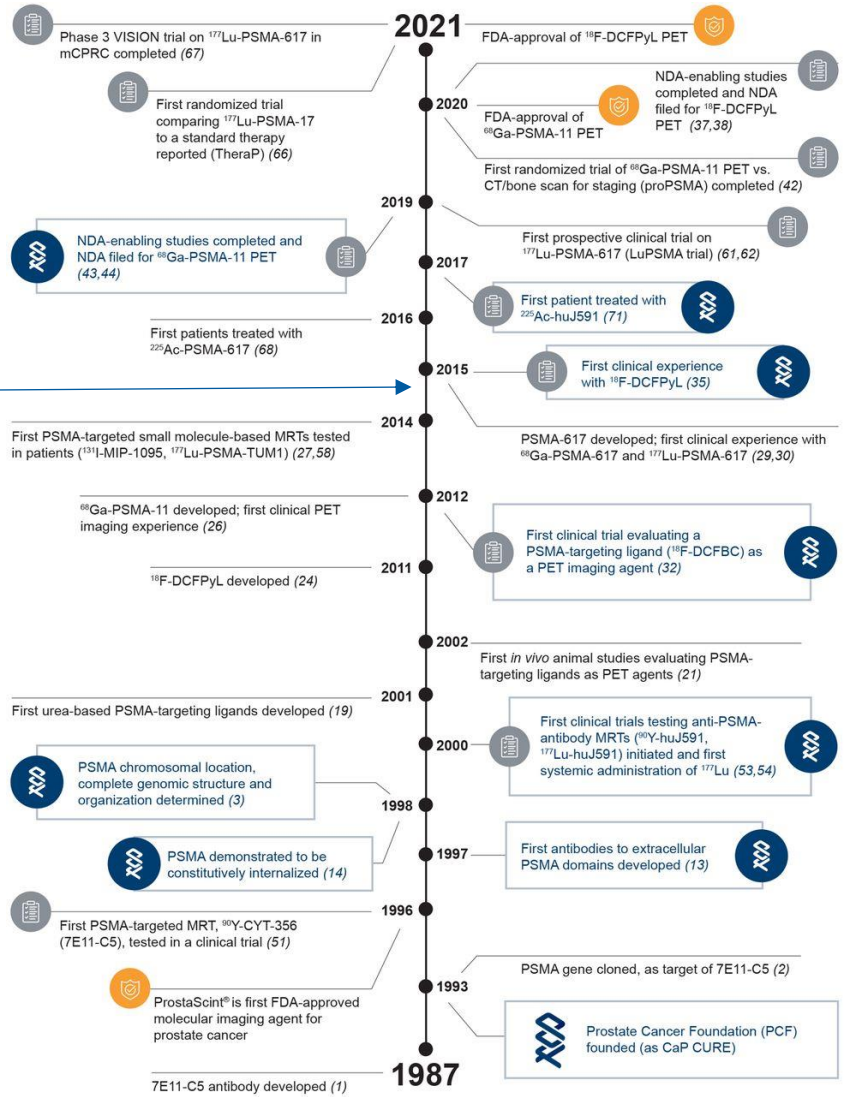




Benešová et al., J Nucl Med 2015



Kratochwil et al., Eur J Nucl Med Mol Imaging 2015



Miyahara and Soule, J Nucl Med 2022

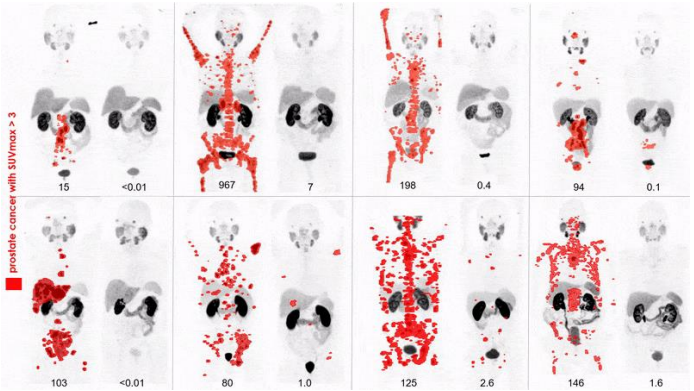
Letter | Letters to the Editor

Determining PSMA-617 Mass and Molar Activity in Pluvicto Doses

Ivan E. Wang, Allen F. Brooks, Peter J. Scott and Benjamin L. Viglianti

Journal of Nuclear Medicine March 2025, jnumed.124.269111; DOI: https://doi.org/10.2967/jnumed.124.269111

No information is given on mass and molar activity of Pluvicto neither in the VISION trial data nor in the FDA approved package insert.



Hofman et al., J Nucl Med 2018

Luurtsema et al. EJNMMI radiopharm. chem. (2021) 6:34
https://doi.org/10.1186/s41181-021-00149-6

EJNMMI Radiopharmacy and Chemistry

GUIDELINE ARTICLE Open Access

EANM guideline for harmonisation on molar activity or specific activity of radiopharmaceuticals: impact on safety and imaging quality

Gert Luurtsema[1], Andrew Pichler[2], Salvatore Bongarzone[3], Yann Seimbille[4], Philip Elsinga[1], Antony Gee[1] and Johnny Vercouillie[1]

Major drawbacks:

- Optimizing the therapy dosage becomes difficult
- Optimizing the therapy frequency becomes difficult
- Increased potential of poor treatment efficacy

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PLUVICTO safely and effectively. See full prescribing information for PLUVICTO.

PLUVICTO™ (lutetium Lu 177 vipivotide tetraxetan) injection, for intravenous use
Initial U.S. Approval: 2022

——————INDICATIONS AND USAGE——————
PLUVICTO is a radioligand therapeutic agent indicated for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy. (1)

——————DOSAGE AND ADMINISTRATION——————
- Select patients for treatment using LOCAMETZ® or an approved PSMA-11 imaging agent based on PSMA expression in tumors. (2.2)
- Recommended Dosage: Administer 7.4 GBq (200 mCi) every 6 weeks for up to 6 doses. (2.3)
- Dose interruption, reduction, or permanent discontinuation may be required due to adverse reactions. (2.4)

——————DOSAGE FORMS AND STRENGTHS——————
Injection: 1,000 MBq/mL (27 mCi/mL) in a single-dose vial. (3)

——————CONTRAINDICATIONS——————
None. (4)

——————WARNINGS AND PRECAUTIONS——————
- Risk From Radiation Exposure: Minimize radiation exposure during and after treatment with PLUVICTO consistent with institutional good radiation safety practices and patient treatment procedures. Ensure patients increase oral fluid intake and advise patients to void as often as possible to reduce bladder radiation. (5.1)
- Myelosuppression: Perform complete blood counts. Withhold, reduce dose, or permanently discontinue PLUVICTO and clinically treat based on severity. (2.4, 5.2)
- Renal Toxicity: Advise patients to remain well hydrated and to urinate frequently. Perform kidney function laboratory tests. Withhold, reduce dose, or permanently discontinue PLUVICTO based on severity. (2.4, 5.3)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise male patients with female partners of reproductive potential to use effective contraception. (5.4, 8.1, 8.3)
- Infertility: PLUVICTO may cause temporary or permanent infertility. (5.5, 8.3)

——————ADVERSE REACTIONS——————
Most common adverse reactions (≥ 20%) are fatigue, dry mouth, nausea, anemia, decreased appetite, and constipation. (6.1)
Most common laboratory abnormalities (≥ 30%) are decreased lymphocytes, decreased hemoglobin, decreased leukocytes, decreased platelets, decreased calcium, and decreased sodium. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novartis Pharmaceuticals Corporation at 1-888-669-6682 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 3/2022

FDA Marketing Authorization Pluvicto 2022
EMA Marketing Authorization Pluvicto 2023

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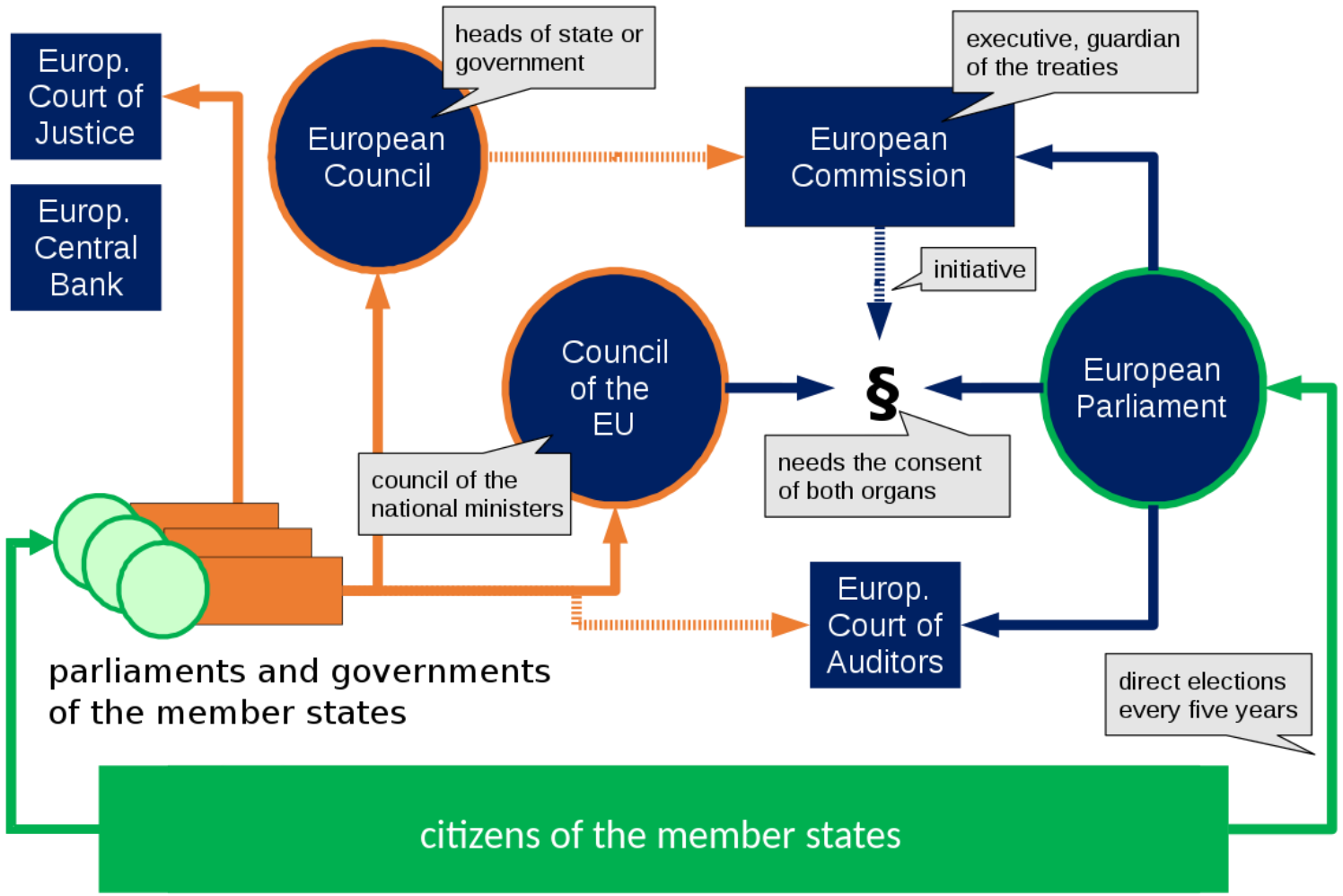
Political system of the European Union



Picture taken from wikipedia.org

Legislation in Europe

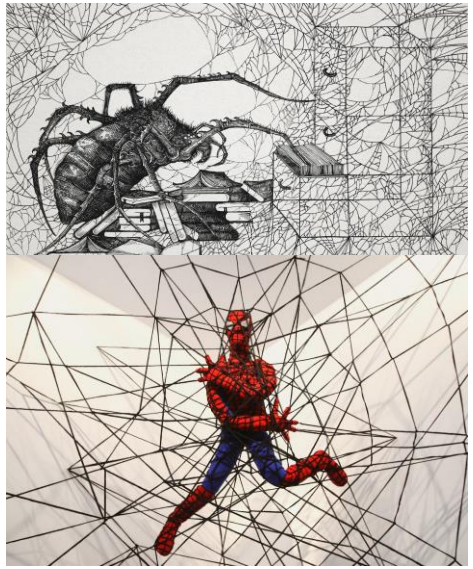
28 member states

A **directive** is a legal act of the European Union which *requires member states to achieve a particular result without dictating the means of achieving that result*.

A **regulation** is a legal act of the European Union that becomes *immediately enforceable as law in all member states simultaneously*.

National laws of EU member states

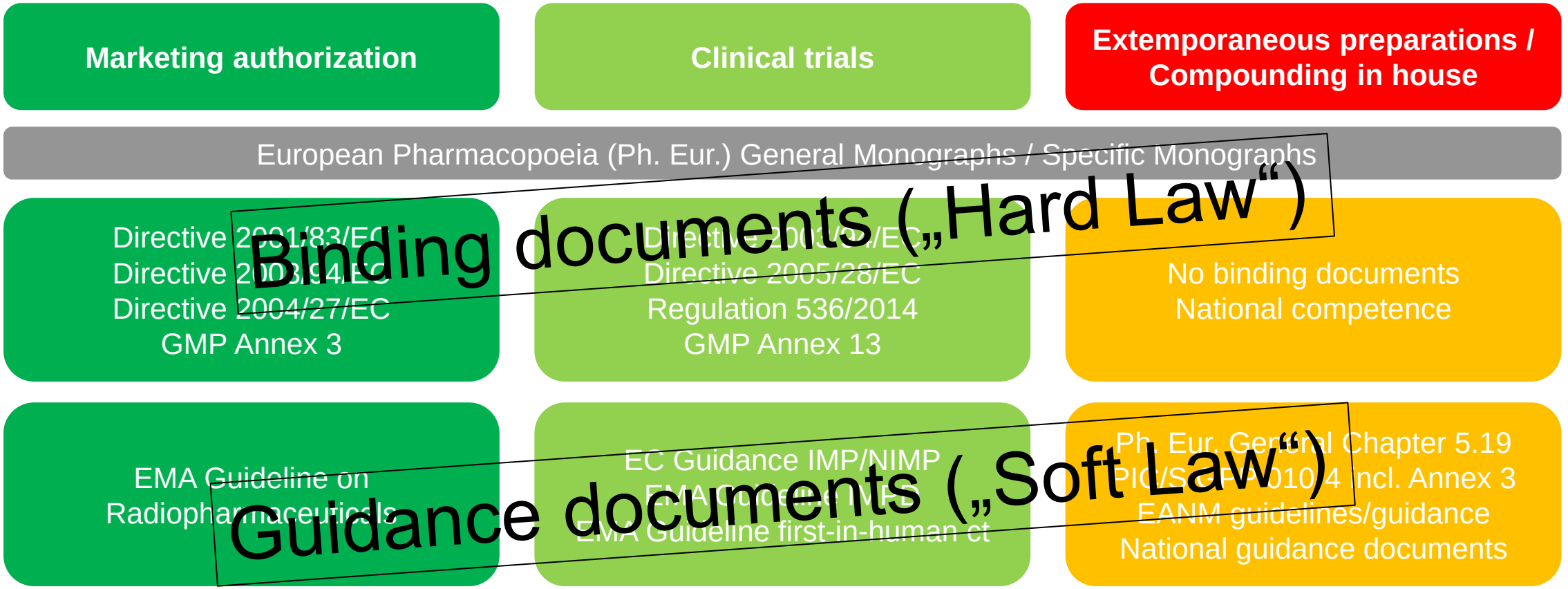
Spinning the web of European regulations



47 member states

EDQM contributes to the basic **human right of access to good quality medicines and healthcare**, and promotes and protects human and animal health by establishing and providing official ***standards for the manufacture and quality control of medicines*** in all the signatory states of the Convention on the Elaboration of a **European Pharmacopoeia** and beyond.

Regulatory basis for the use of radiopharmaceuticals



Lange et al., Nucl Med Commun 2015
Decristoforo et al., Front Med 2021

Regulatory basis for the use of radiopharmaceuticals

Marketing authorization

Clinical trials

Extemporaneous preparations / Compounding in house

European Pharmacopoeia (Ph. Eur.) General Monographs / Specific Monographs

Located in Strasbourg, France

3 Sessions per year

More than 70 Working Parties and Groups of Experts

Group of Experts 14 (Radiopharmaceutical preparations)

Working Party PRP (Precursors for radiopharmaceutical preparations)

edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

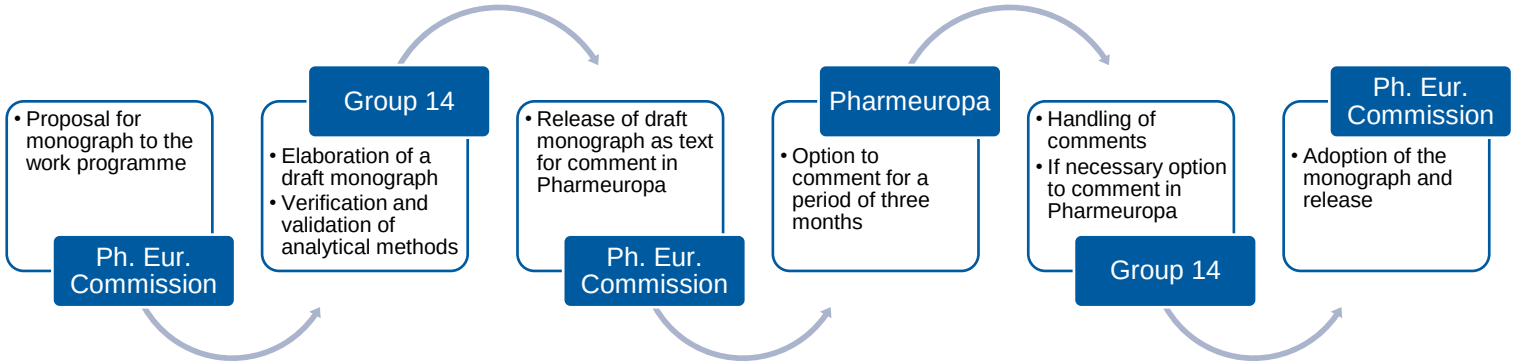
DRESDEN concept
SCIENCE AND INNOVATION CAMPUS

HZDR

Regulatory basis for the use of radiopharmaceuticals

Marketing authorization | **Clinical trials** | **Extemporaneous preparations / Compounding in house**

European Pharmacopoeia (Ph. Eur.) General Monographs / Specific Monographs



edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Is the pharmacopoeia „hard“ or „soft“ law?

Monographs are legally binding

General chapters are only legally binding if cited in a monograph

Upcoming: general text on Ac-225 for radiolabelling

DRESDEN concept SCIENCE AND INNOVATION CAMPUS

HZDR

Regulatory basis for the use of radiopharmaceuticals

Marketing authorization

Directive 2001/83/EC (on the Community code relating to **medicinal products** for human use)
→ **Currently under revision!**
European Association of Nuclear Medicine (EANM) and Nuclear Medicine Europe (NMEU) have been strongly advocating for improvement for the field of Nuclear Medicine

Directive 2003/94/EC (laying down the principles and guidelines of **good manufacturing practice** in respect of medicinal products for human use and investigational medicinal products for human use)
Directive 2004/27/EC (amending Directive 2001/83/EC on the Community code relating to medicinal products for human use)

Directive 2001/83/EC - Definitions

Impact for radiopharmaceuticals:

Definitions:

- *Medicinal product*:
  - (a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or
  - (b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.
- *Radiopharmaceutical*: Any medicinal product which, when ready for use, contains one or more radionuclides (radioactive isotopes) included for a medicinal purpose.
- *Radionuclide generator*: Any system incorporating a fixed parent radionuclide from which is produced a daughter radionuclide which is to be obtained by elution or by any other method and used in a radiopharmaceutical.
- *Kit*: Any preparation to be reconstituted or combined with radionuclides in the final radiopharmaceutical, usually prior to its administration.
- *Radionuclide precursor*: Any other radionuclide produced for the radio-labelling of another substance prior to administration.

Directive 2001/83/EC - Exemptions

Impact for radiopharmaceuticals:

- *Article 2*:
  - 1. This Directive shall apply to *medicinal products for human use* *intended to be placed on the market* in Member States and either prepared industrially or manufactured by a method involving an industrial process.
- *Article 3*:
  - This Directive shall not apply to:
  - 1. Any medicinal product prepared in a pharmacy in accordance with a *medical prescription for an **individual** patient* (commonly known as the magistral formula).
  - 2. Any medicinal product which is prepared in a pharmacy in accordance with the *prescriptions of a pharmacopoeia* and is *intended to be supplied directly to the patients* served by the pharmacy in question (commonly known as the officinal formula).

Radionuclide precursors in Directive 2001/83/EC

Impact for radiopharmaceuticals:

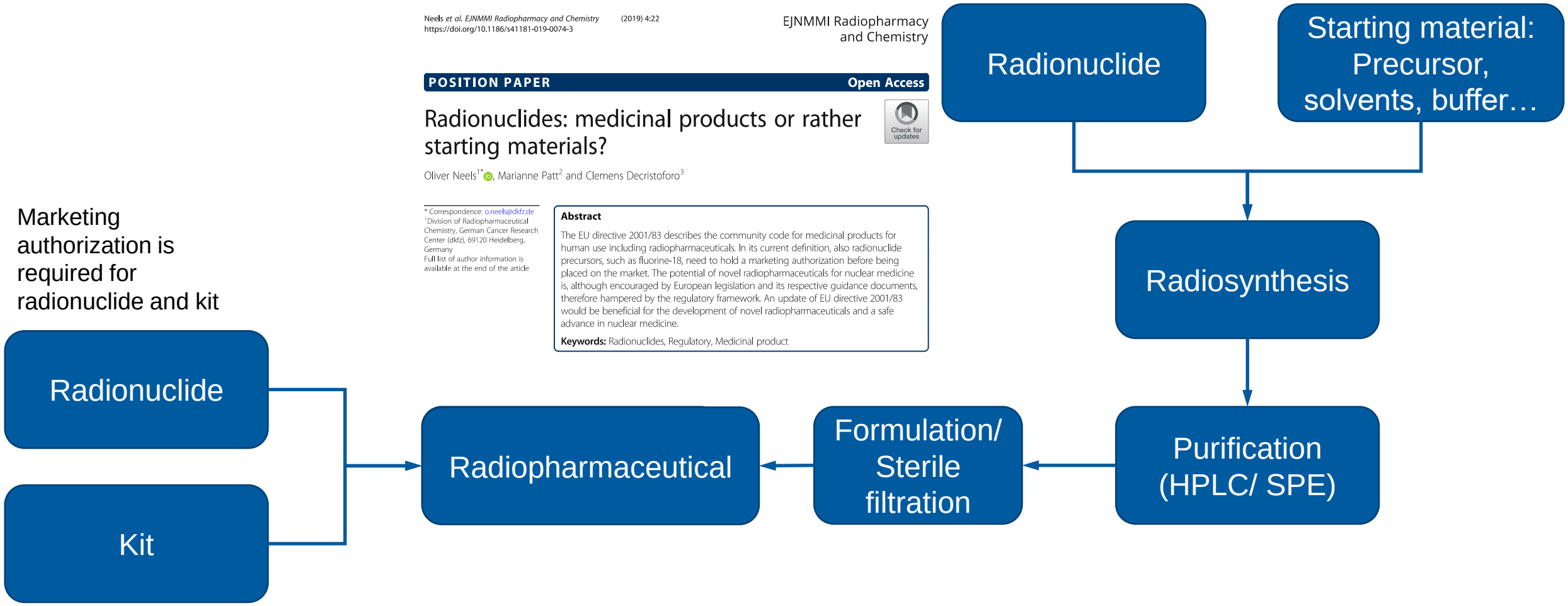
- Marketing authorization
- *Article 6*:
  - 1. No medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued by the competent authorities of that Member State in accordance with this Directive…
  - 2. The authorisation referred to in paragraph 1 shall also be required for radionuclide generators, kits, *radionuclide precursor* radiopharmaceuticals and industrially prepared radiopharmaceuticals.

Def.: Radionuclide precursor: Any other radionuclide produced for the radio-labelling of another substance prior to administration.

→ Radiometals for theranostic applications but also F-18 or C-11

Kits vs. Radiosynthesis

Marketing authorization is required if the radionuclide is obtained from an off-site location



Marketing authorization is required for radionuclide and kit

Neels *et al. EJNMMI Radiopharmacy and Chemistry* (2019) 4:22
https://doi.org/10.1186/s41181-019-0074-3

EJNMMI Radiopharmacy and Chemistry

POSITION PAPER Open Access

Radionuclides: medicinal products or rather starting materials?

Oliver Neels[1*], Marianne Patt[2] and Clemens Decristoforo[3]

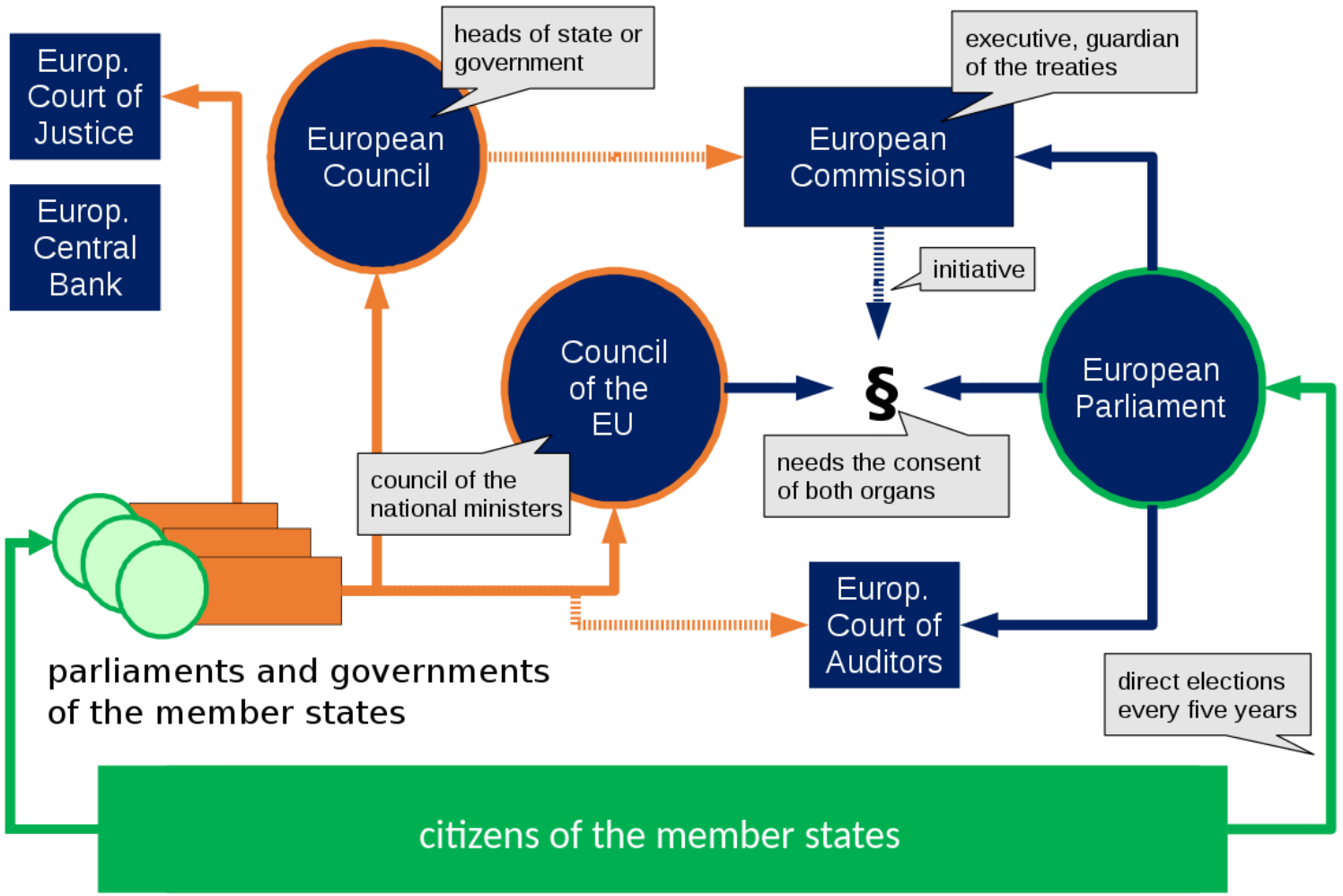
* Correspondence: o.neels@dkfz.de
[1]Division of Radiopharmaceutical Chemistry, German Cancer Research Center (dkfz), 69120 Heidelberg, Germany
Full list of author information is available at the end of the article

Abstract

The EU directive 2001/83 describes the community code for medicinal products for human use including radiopharmaceuticals. In its current definition, also radionuclide precursors, such as fluorine-18, need to hold a marketing authorization before being placed on the market. The potential of novel radiopharmaceuticals for nuclear medicine is, although encouraged by European legislation and its respective guidance documents, therefore hampered by the regulatory framework. An update of EU directive 2001/83 would be beneficial for the development of novel radiopharmaceuticals and a safe advance in nuclear medicine.

Keywords: Radionuclides, Regulatory, Medicinal product

Current status of Directive 2001/83/EC revision



- EANM/NMEU have proposed amendments for a revised Directive
- All amendments have been positively voted by EU Commission's Committee on the Environment, Public Health and Food Safety (ENVI)
- Surprisingly, all tabled amendments of EANM/NMEU have been taken out of the revised version four weeks prior to the vote in the European Parliament which took place on 10th April 2024
- The Council of the EU has to vote, likely by end of 2025
- EANM is asking for transparency on the process to understand decisionmaking

Picture taken from wikipedia.org

Directive 2003/94/EC

Impact for radiopharmaceuticals:

„Full“ GMP:

- Pharmaceutical Quality System
- Personnel
- Premises and Equipment
- Documentation
- Production
- Quality Control
- Outsourced activities
- Complaints and product recalls
- Self Inspection

as described in EudraLex Volume 4 Good Manufacturing Practice (GMP) Guidelines

Regulatory basis for the use of radiopharmaceuticals

Clinical trials

Directive 2001/20/EC (on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of **good clinical practice** in the conduct of **clinical trials** on medicinal products for human use)
Directive 2003/94/EC (laying down the principles and guidelines of **good manufacturing practice** in respect of medicinal products for human use and investigational medicinal products for human use)
Directive 2005/28/EC (laying down principles and detailed guidelines for **good clinical practice** as regards **investigational medicinal products** for human use, as well as the requirements for authorisation of the manufacturing or importation of such products)
Regulation 536/2014 (on clinical trials on medicinal products for human use, and **repealing Directive 2001/20/EC**)

Regulation 536/2014

Clinical trials

Regulation 536/2014 (on clinical trials on medicinal products for human use, and **repealing Directive 2001/20/EC**)

Key features:

- More harmonization in the submission process, transparency and higher safety standards of clinical trials
- Into force since 16th June 2014
- Entry into application 31st January 2022
- Transition period until 31st January 2025
- (Electronic) application for clinical trials will change from National to European level

Regulation 536/2014 - Radiopharmaceuticals

Therapeutic radiopharmaceuticals???

Impact for radiopharmaceuticals:

- *Article 61 (Authorisation of manufacturing and import)*
  - 1. The manufacturing and import of investigational medicinal Products in the Union shall be subject to the holding of an authorisation.
  - 5. Paragraph 1 shall **not** apply to any of the following processes:
    - (b) preparation of radiopharmaceuticals used as diagnostic investigational medicinal products where this process is carried out in hospitals, health centres or clinics, by pharmacists or other persons legally authorised in the Member State concerned to carry out such process, and if the investigational medicinal products are intended to be used exclusively in hospitals, health centres or clinics taking part in the same clinical trial in the same Member State;
- *Article 63 (Manufacturing and import)*
  - 1. Investigational medicinal products shall be manufactured by applying manufacturing practice which ensures the quality of such medicinal products in order to safeguard the safety of the subject and the reliability and robustness of clinical data generated in the clinical trial ('good manufacturing practice'). …
  - 2. Paragraph 1 shall not apply to the processes referred to in Article 61(5).

Specific considerations underlying in-house preparations of radiopharmaceuticals (compared to „classical“ drugs)

Extemporaneous preparations / Compounding in house

European Pharmacopoeia (Ph. Eur.) General Monographs / Specific Monographs

- **No pharmacological effect** due to tracer amounts of drug substance resulting in low toxicological risk
- **Highly skilled/specialised staff** due to radiation safety aspects next to radiopharmaceutical sciences aspects
- **Small-scale preparation produced extemporaneously** within nuclear medicine or radiopharmacy departments
  - For individual patient or few patients only
  - In single-dose containers or syringes
  - Small, insufficient volume to perform extensive testing
- **Short interval between preparation and administration** (minutes to hours) reducing the risk of microbial contamination
- Radiopharmaceuticals are **released to trained nuclear medicine specialists and never to patients** themselves with administration in a controlled environment
- Due to radioactive decay **full testing** (e.g. sterility testing) and storage over longer periods is in most circumstances **not possible**

No binding documents
National competence

Ph. Eur. General Chapter 5.19
PIC/S GPP 010-4 incl. Annex 3
EANM guidelines/guidance
National guidance documents

Hendrikse et al., Eur J Nucl Med Mol Imaging 2022

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Increased importance of in-house preparations of radiopharmaceuticals

Extemporaneous preparations / Compounding in house

European Pharmacopoeia (Ph. Eur.) General Monographs / Specific Monographs

- **Theranostics**
- PET (F-18, C-11)
- Antibodies (Zr-89)
- “Novel” radionuclides, e.g. Cu-64, Sc-44, Tb-161…
- Alpha therapy: Ac-225, …
- Novel targets: FAPI, CXCR4, Integrins…
- Technology developments (automation of radiosyntheses)

No binding documents
National competence

Ph. Eur. General Chapter 5.19
PIC/S GPP 010-4 incl. Annex 3
EANM guidelines/guidance
National guidance documents

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National Regulations for in-house preparation (exemplified)

Moya et al. EJNMMI Radiopharmacy and Chemistry (2024) 9:64
https://doi.org/10.1186/s41181-024-00281-z

EJNMMI Radiopharmacy and Chemistry

REVIEW Open Access

Radiopharmaceutical small-scale preparation in Europe: will we be able to harmonize the situation?

Estrella Moya[1], Celia Cerrato[1], Luis Miguel Bedoya[2,3] and José Antonio Guerra[2*]

Extemporaneous preparations / Compounding in house

European Pharmacopoeia (Ph. Eur.) General Monographs / Specific Monographs

Exemptions for preparations under the direct responsibility of the physician

Exempting Nuclear Medicine Institutions from manufacturing authorisation

Radiopharmaceuticals in hospitals under the responsibility of hospitals (radio)pharmacist, Radiopharmacist's specialisation

New regulation for kit based preparations

Specific guideline and exemptions for public health system only for diagnostics

Swiss Regulations for in-house preparations

No binding documents
National competence

Ph. Eur. General Chapter 5.19
PIC/S GPP 010-4 incl. Annex 3
EANM guidelines/guidance
National guidance documents

High variability, complex interpretation and heterogenous implementation

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Who is playing and how can we take part?

European Union

National authorities

National regulations
Licensing
Inspection
National Pharmacopeia
Control laboratories

Council of Europe

COUNCIL OF EUROPE

CONSEIL DE L'EUROPE

edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

European Commission

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Directives
Regulations

Medicinal Products
- Evaluation
- Supervision
- Pharmacovigilance

European Pharmacopoeia
Official Medicines Control Laboratory (OMCL)

Professional organisations

PIC/S
NUCLEAR MEDICINE EUROPE
EANM
IAEA

Quality
Good Manufacturing Practice (GMP)
Marketing Authorization

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What else…further questions to be considered

- *Who are the stakeholders and what is their goal?*
- *Potential route(s) of translation?*
- *When is a translation successful?*
- *How important is intellectual property (IP)?*
- *Ethical aspects*

van Leeuwen *et al. EJNMMI Research* (2022) 12:31
https://doi.org/10.1186/s13550-022-00903-0

EJNMMI Research

EDUCATIONAL Open Access

Perspectives on translational molecular imaging and therapy: an overview of key questions to be addressed

Fijs W. B. van Leeuwen[1*], Margret Schottelius[2], Felix M. Mottaghy[3,4], Fabien Hyafil[5,6], Mark Lubberink[7,8], Gabriela Kramer-Marek[9] and Wim J. G. Oyen[10,11,12]

Advanced Drug Delivery Reviews 181 (2022) 114086

Contents lists available at ScienceDirect

Advanced Drug Delivery Reviews

journal homepage: www.elsevier.com/locate/adr

Translating a radiolabeled imaging agent to the clinic

Gary L. Griffiths[a], Crystal Vasquez[b], Freddy Escorcia[b], Jeff Clanton[c], Liza Lindenberg[b], Esther Mena[b], Peter L. Choyke[b,*]

[a] Clinical Research Directorate, Frederick National Laboratory for Cancer Research, Leidos Biomedical Research, Frederick, MD, United States
[b] Molecular Imaging Branch, National Cancer Institute, Bethesda, MD, United States
[c] Independent Consultant, Nashville, TN, United States

What else…further questions to be considered

European Journal of Nuclear Medicine and Molecular Imaging (2025) 52:796–800
https://doi.org/10.1007/s00259-024-07020-1

EDITORIAL

Identifying and navigating bottlenecks in the translation of novel radiopharmaceuticals: a perspective

Margret Schottelius[1,2]

Published online: 20 December 2024

Clinical Relevance: aligning scientific curiosity with clinical need

"Me-Too" tracers: differentiating incremental changes from true innovation

Novelty and Originality: setting transparent criteria for advancement

Target Validation: ensuring relevance and translational potential

Ethical and Effective Use of Animal Models: Moving towards scalable dosimetry

Data Transparency and Integrity: setting higher standards

Navigating Systemic Constraints: Regulatory and logistical challenges

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International harmonisation… a topic on its own

ELSEVIER

Drug Discovery Today: Technologies

Vol. 8, No. 2-4 2011

Editors-in-Chief
Kelvin Lam – Blue Sky Biotech Inc., USA
Henk Timmerman – Vrije Universiteit, The Netherlands

TODAY TECHNOLOGIES

Imaging techniques

Radiopharmacy: regulations and legislations in relation to human applications

Clemens Decristoforo[1,*], Sally W. Schwarz[2]

[1]Department of Nuclear Medicine, Innsbruck Medical University, Innsbruck, Austria
[2]Department of Radiology, Division of Radiological Sciences, Washington University School of Medicine, St. Louis, MO, USA

CONTINUING EDUCATION

Harmonization of U.S., European Union, and Canadian First-in-Human Regulatory Requirements for Radiopharmaceuticals: Is This Possible?

Sally W. Schwarz[1], Clemens Decristoforo[2], Anne E. Goodbody[3], Nikhita Singhal[4], Sarah Saliba[4], Patrick S. Ruddock[3], Katherine Zukotynski[4], and Andrew A. Ross[5]

[1]Washington University School of Medicine, St. Louis Missouri; [2]Department of Nuclear Medicine, Medical University Insbruck, Innsbruck, Austria; [3]Center for Probe Development and Commercialization, Hamilton, Ontario, Canada; [4]McMaster University, Hamilton, Ontario, Canada; and [5]Department of Diagnostic Imaging, Queen Elizabeth Health Sciences Center, Halifax, Nova Scotia

Learning Objectives: On successful completion of this activity, participants should be able to (1) understand the requirements for first-in-human radiopharmaceutical applications for the United States, European Union, and Canada; (2) realize the overall need for reduction of the human-use requirements due to lack of toxicity and the need to facilitate patient access; and (3) recognize that harmonization efforts between the U.S. Food and Drug Administration, Health Canada, and the European Medical Authority would streamline efforts in moving new radiopharmaceuticals forward for clinical care.

Schwarz and Decristoforo *EJNMMI Radiopharmacy and Chemistry* (2019) 4:10
https://doi.org/10.1186/s41181-019-0059-2

EJNMMI Radiopharmacy and Chemistry

DEBATE Open Access

US and EU radiopharmaceutical diagnostic and therapeutic nonclinical study requirements for clinical trials authorizations and marketing authorizations

Sally W. Schwarz[1] and Clemens Decristoforo[2*]

Korde *et al.*
EJNMMI Radiopharmacy and Chemistry (2024) 9:2
https://doi.org/10.1186/s41181-023-00230-2

EJNMMI Radiopharmacy and Chemistry

POSITION PAPER Open Access

Position paper to facilitate patient access to radiopharmaceuticals: considerations for a suitable pharmaceutical regulatory framework

Aruna Korde[1], Marianne Patt[2], Svetlana V. Selivanova[3,4], Andrew M. Scott[5,6], Rolf Hesselmann[7], Oliver Kiss[8], Natesan Ramamoorthy[9], Sergio Todde[10], Sietske M. Rubow[11], Luther Gwaza[12], Serge Lyashchenko[13], Jan Andersson[14,15], Brian Hockley[16], Ravindra Kasliwal[17] and Clemens Decristoforo[18*]

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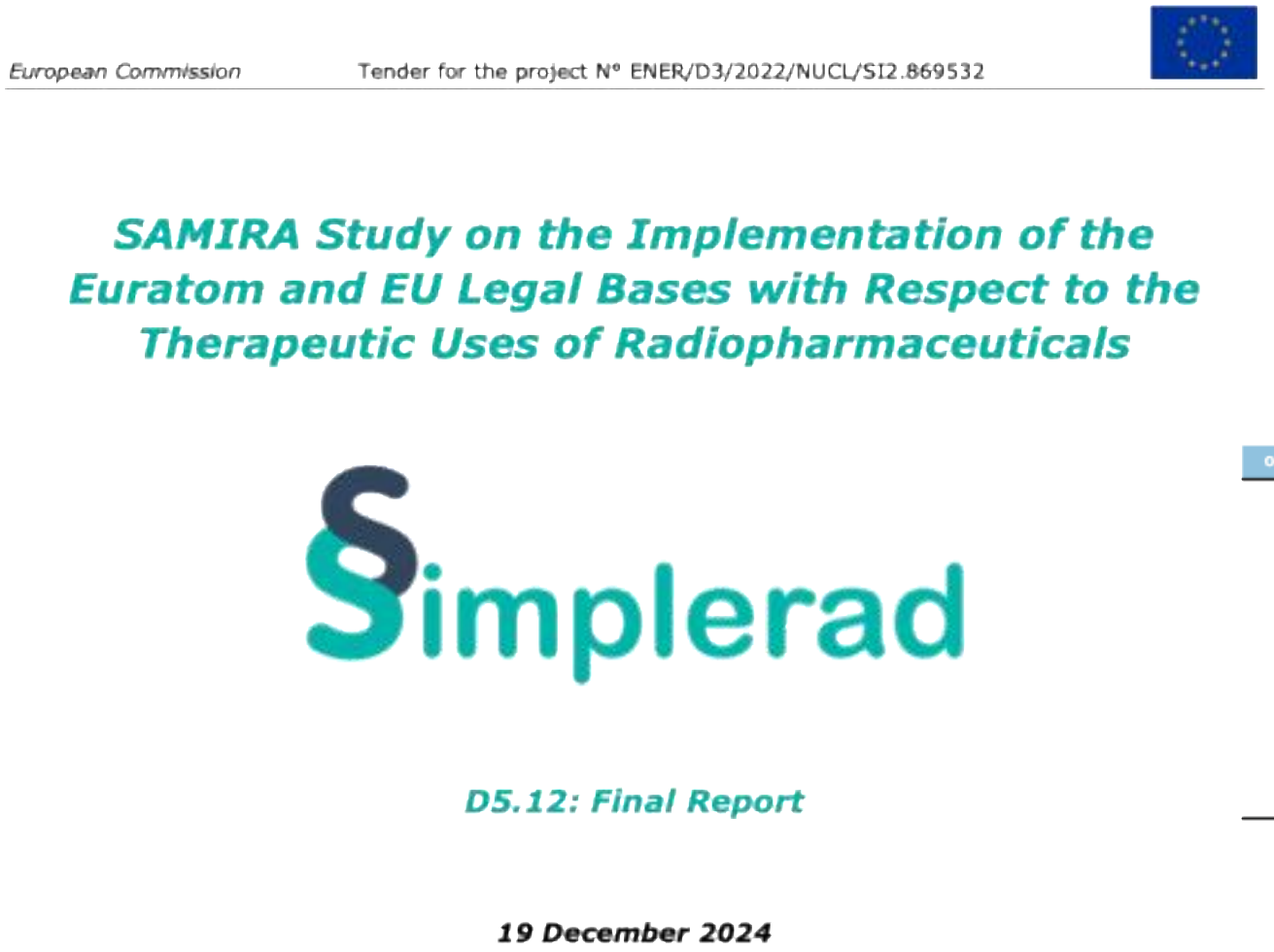
Potential dosimetry and infrastructural challenges



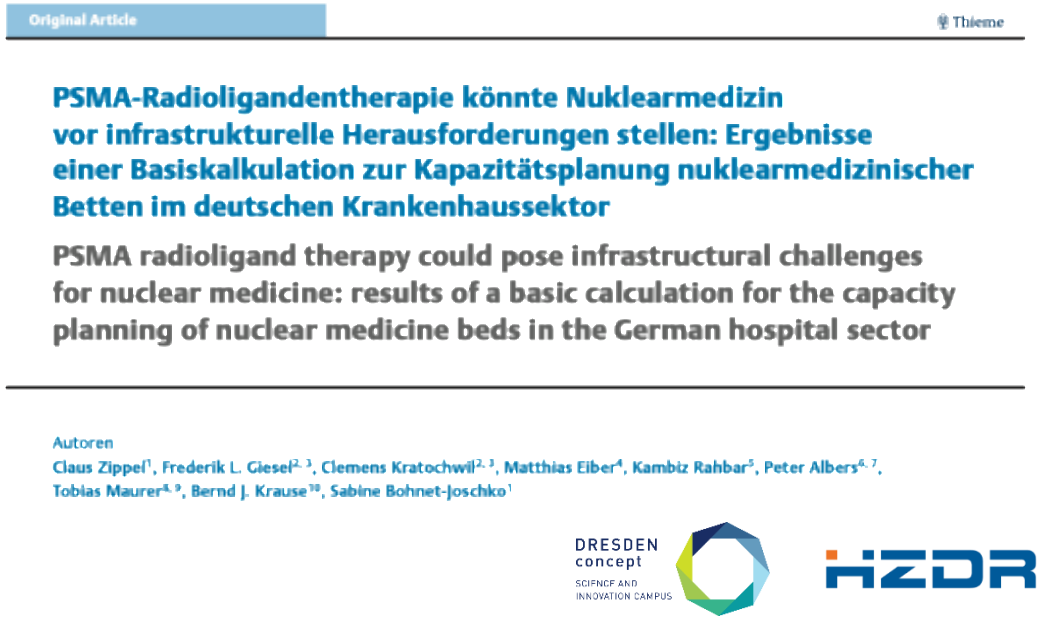
European Commission Tender for the project N° ENER/D3/2022/NUCL/SI2.869532

SAMIRA Study on the Implementation of the Euratom and EU Legal Bases with Respect to the Therapeutic Uses of Radiopharmaceuticals

Simplerad

D5.12: Final Report

19 December 2024



Original Article Thieme

PSMA-Radioligandentherapie könnte Nuklearmedizin vor infrastrukturelle Herausforderungen stellen: Ergebnisse einer Basiskalkulation zur Kapazitätsplanung nuklearmedizinischer Betten im deutschen Krankenhaussektor

PSMA radioligand therapy could pose infrastructural challenges for nuclear medicine: results of a basic calculation for the capacity planning of nuclear medicine beds in the German hospital sector

Autoren
Claus Zippel[1], Frederik L. Giesel[2, 3], Clemens Kratochwil[2, 3], Matthias Eiber[4], Kambiz Rahbar[5], Peter Albers[6, 7], Tobias Maurer[8, 9], Bernd J. Krause[10], Sabine Bohnet-Joschko[1]

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What can we do?

- *Communicate*
- *Discuss*
- *Participate*
- *Publish*
- *Get visible*
- *Interact*
- *Exchange*
- *Take Action*

Image courtesy of Peitl, Rangger et al., J Labelled Comp Radiopharm 2019