Frequently Asked Questions (FAQs): New/Hybrid Radiopharmaceutical Products

Note: This FAQ supplements Drug Registration Guidance Document (DRGD) Appendix 3 for radiopharmaceutical products under the New Drug Product (NDP) category.

1. How are radionuclide-containing and related products classified for regulation?

Regulatory classification depends on the primary mode of action and intended use. For example:

Product	Primary Mode of Action	Classification / Authority
Yttrium-90 microspheres for selective internal radiation therapy (SIRT) in liver tumour	Radiological (localised radiation)	Medical device / Medical Device Authority
Yttrium-90 solution for radiolabelling (radionuclide precursor)	Pharmacological	Radiopharmaceutical / NPRA
Carbon-14 urea breath test	Pharmacological	Radiopharmaceutical (radioactive isotope) / NPRA
Carbon-13 urea breath test	Pharmacological	Pharmaceutical (stable isotope) / NPRA

It is recommended to seek classification service via a classification application.

2. What radiopharmaceutical substance is considered a New Chemical Entity (NCE)?

A registrable new radiopharmaceutical substance is a radionuclide or a ligand that has not been registered in any radiopharmaceutical product*; or a coupling mechanism to link the molecule and the radionuclide that has not been registered (DRGD Appendix 3), including[1]:

Category	Product	Description
Ready for use	Radiopharmaceutical, including Positron Emission Tomography (PET) radiopharmaceutical	Any radiopharmaceutical product ready for direct administration as registered, as such or after a simple dilution
Special types of substances or preparations	Radionuclide generator	Any system incorporating a fixed parent radionuclide from which a daughter radionuclide is produced by elution or other method and used in a radiopharmaceutical
	Radionuclide precursor	Any other radionuclide produced for the radiolabelling of another substance prior to administration
	Kit for radiopharmaceutical preparation	Any preparation to be reconstituted or combined with radionuclides in the final radiopharmaceutical, usually prior to its administration

Since alternative manufacturing processes usually result in preparations of differing radiochemical quality, including in respect of impurities, only one synthesis route can be registered for an individual preparation[2].

**Under the Control of Drugs and Cosmetics Regulations (CDCR) 1984, Regulation 2, "product" means:*

(a) a drug[a] in a dosage unit or otherwise, for use wholly or mainly by being administered to one or more human beings or animals for a medicinal purpose[b]; or

(b) a drug[a] to be used as an ingredient of a preparation for a medicinal purpose[b]

Under Sales of Drug Act 1952, Section 2:

[a] "drug" includes any substance, product or article intended to be used or capable, or purported or claimed to be capable, of being used on humans or any animal, whether internally or externally, for a medicinal purpose.

[b] "medicinal purpose" means any of the following purposes:

(a) alleviating, treating, curing or preventing a disease or a pathological condition or symptoms of a disease;

(b) diagnosing a disease or ascertaining the existence, degree or extent of a physiological or pathological condition;

(c) contraception;

(d) inducing anaesthesia;

(e) maintaining, modifying, preventing, restoring, or interfering with, the normal operation of a physiological function;

(f) controlling body weight;

(g) general maintenance or promotion of health or wellbeing.

3. What radiopharmaceutical substances are considered hybrid radiopharmaceutical products?

According to DRGD Appendix 3, any new radiopharmaceutical product containing registrable radiopharmaceutical substances that do not fall under the NCE category.

Examples include radiopharmaceutical products containing registered radiopharmaceutical substances in a new chemical or new dosage form; with a change in posology; for use by a new route of administration; for a new indication or patient population; in a radiopharmaceutical product whose innovator has never been registered by the DCA; or a second-source or replacement radiopharmaceutical product.

It is recommended to seek classification service via a classification application.

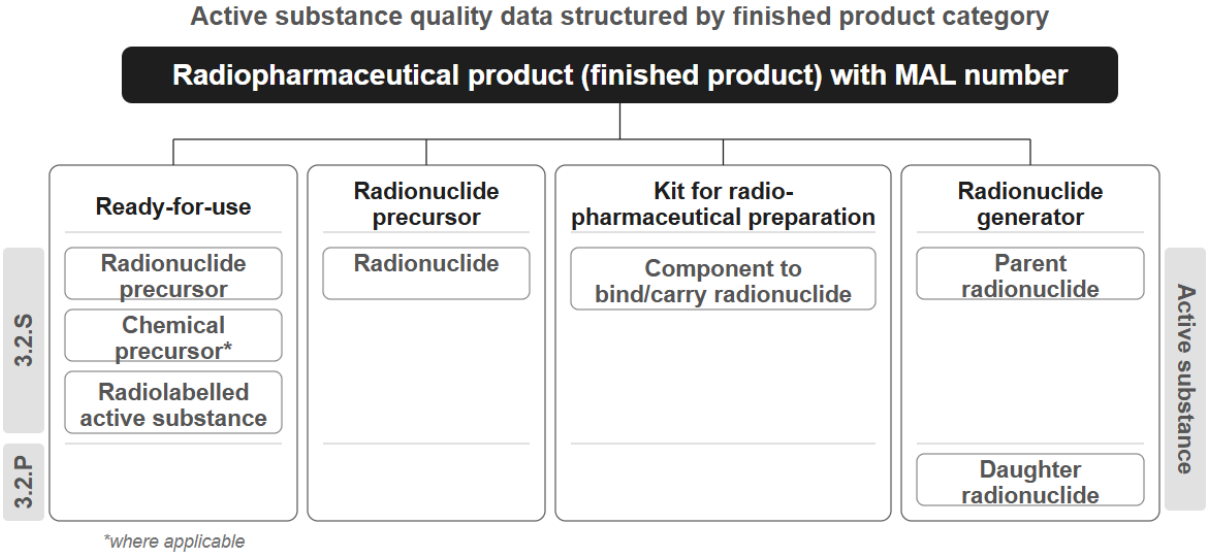
4. What quality data is required for radiopharmaceutical products?

The required ACTD quality data for radiopharmaceutical products is based on the finished product type. For details, refer to the EMA Guideline on the quality of radiopharmaceuticals[1].

The table and diagram below outline the structure of quality data for **active substance(s)**, defined under "radiopharmaceutical substance" in DRGD Appendix 3, according to category:

Finished product type	Structure of quality data for active substance[1]
Ready for use	The active substance presented in the finished product and administered to the patient is a **radiolabelled active substance**. In cases where it can be isolated, characterised and tested, it will be the subject of a **complete module 3.2.S**. Even in cases where it is not isolated, a **reduced module**

	3.2.S (or Part II-S) containing the minimum required information should be provided. The **radionuclide precursor** (e.g., in solution form containing the radionuclide in a suitable form for the radiolabelling process) which, if it can be isolated, characterised, and tested, should be the subject of a complete specific **module 3.2.S**. Where applicable, information on the **chemical precursor** (a non-radioactive chemical substance intended to bind or carry the radionuclide) should be presented in a separate **module 3.2.S**, including those for synthesis of PET radiopharmaceuticals. For details, refer to DRGD Appendix 11.
Radionuclide generator (e.g., shielded column elution system)	Both parent and daughter radionuclides are to be considered as active substances. The **parent radionuclide** is always in equilibrium with the daughter radionuclide and should be the subject of **module 3.2.S.** The quality of the **daughter radionuclide**, once separated from the parent, should be dealt with in **module 3.2.P** (or Part II-P).
Radionuclide precursor (e.g., solution in vials)	The subject of **module 3.2.S** is the **radionuclide** prior to its final formulation into the finished product. Registration is required when intended to be sold or supplied for use by the end user (e.g., distributed beyond the facility).
Kit for radiopharmaceutical preparation (e.g., lyophilised powder in vials)	The active substance, subject of **module 3.2.S,** is **that component** of the formulation **intended to bind or carry** the radionuclide. Registration is required when intended to be sold or supplied for use by the end user (e.g., distributed beyond the facility).



Note: The table and diagram above provides an outline of active substance quality required data. For complete finished product documentation requirements (module 3.2.P), refer to the EMA Guideline on the quality of radiopharmaceuticals[1].

5. What non-clinical and clinical data are required for NCE radiopharmaceutical products?

Full non-clinical and clinical data are required (refer to DRGD Appendix 3) based on the intended use and radiopharmaceutical product type, according to the relevant ICH (e.g., M3(R2) and S9) and European Medicines Agency (EMA) guidelines (e.g., first-in-human clinical trials,[3] radiopharmaceutical non-clinical requirements,[4] and clinical evaluation of new diagnostic radiopharmaceuticals[5]).

For new diagnostic radiopharmaceuticals administered in small quantities without expected pharmacodynamic effect, simplifications to non-clinical requirements may be possible based on a justified risk analysis.[4] For new therapeutic radiopharmaceuticals, efficacy should be demonstrated on the basis of randomised clinical trials,[6],[7] taking into account emerging guidance on clinical evaluation of therapeutic radiopharmaceuticals in oncology.[8]

6. What non-clinical and clinical data is required for hybrid radiopharmaceutical products?

Even the smallest variations in radiopharmaceutical quality (e.g. isotope impurities), synthesis or radiolabelling can have far-reaching clinical consequences. It is also particularly difficult to show evidence of bioequivalence for composite molecules (radionuclide and ligand). Therefore, apart from comprehensive quality documentation, the following additional data should be submitted:

- **Diagnostic radiopharmaceuticals:** Results of imaging procedures, including data on distribution in the body and dosimetry as well as literature data on biodistribution
- **Therapeutic radiopharmaceuticals:** Biodistribution data and clinical studies of therapeutic equivalence with the reference product

Deviations from the reference product should be documented comprehensively in respect of their effects on the quality, efficacy and safety of the product.[9]

7. Does a radiopharmaceutical substance require its own MAL registration?

Any radiopharmaceutical product that is sold or supplied requires a MAL registration (Reg 7(1), CDCR 1984). This includes radionuclide generators, radionuclide precursors, and kits for radiopharmaceutical preparation when placed on the market for distribution. The required quality data for any substance used in the manufacture of radiopharmaceutical products must be included in the registration application (see Q4).

Key References

[1] EMA Guideline on the quality of radiopharmaceuticals (EMA/CHMP/QWP/363827/2025, draft Revision 2)
[2] Sec. 5.4.4, Swissmedic Radiopharmaceutical Guidance, Swissmedic ZL000_00_034, Version 2.2, 2025
[3] EMA Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials
[4] EMA Guideline on Non-Clinical Requirements for Radiopharmaceuticals
[5] EMA Guidelines on Clinical efficacy and safety: radiopharmaceuticals and diagnostic agents
[6] EMA Guideline on Evaluation of anticancer medicinal products
[7] Sec. 5.4.6.4, Swissmedic Radiopharmaceutical Guidance, Swissmedic ZL000_00_034, Version 2.2, 2025
[8] EMA Guideline on Clinical evaluation of therapeutic radiopharmaceuticals in oncology
[9] Sec. 5.1.4.3; Table 1, Swissmedic Radiopharmaceutical Guidance, Swissmedic ZL000_00_034, Version 2.2, 2025