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<Date of submission>

Submission of comments on Concept paper on the revision of the Guideline on Clinical Evaluation of Diagnostic agents and its appendix 1 on imaging agents

(EMA/4366/2026)

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.
When completed, this form should be sent to the European Medicines Agency via the EU survey, in Excel format (not PDF).
Columns A to D should mandatorily be filled in prior to completing the columns "Comment and rationale" and/or "Proposed changes / recommendation". The "Outcome" column should not be completed.
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Name of organisation or	General or Specific	Line from* (line nr. or	Line to* (line nr. or	Comment and rationale (to go to next line within the same cell use Alt + Enter)	Proposed changes / recommendation (if applicable - to be used if you want to propose	Outcome (To be completed by the
European Association of Nuclear Medicine (EANM)	General	0	0	The EANM welcomes the initiative to revise the Guideline on the Clinical Evaluation of Diagnostic Agents and its Appendix 1 on Imaging Agents. EANM agrees that the current guideline, dating from 2009, no longer fully reflects the scientific, technological, and clinical developments that have taken place over the last decade. The concept paper appropriately identifies priority areas where clarification and updated guidance are needed, including theranostics and patient selection, longitudinal monitoring, quantitative and semi quantitative imaging, dose considerations, reproducibility, and the emergence of AI assisted diagnostic methods. EANM particularly welcomes the intention to improve readability, consistency of terminology, and alignment with contemporary regulatory and clinical practice. EANM encourages that the revised guideline remains proportionate to the specific characteristics and risk profile of diagnostic agents, especially radiopharmaceuticals, and sufficiently flexible to accommodate ongoing developments in imaging technology, clinical workflows, and personalised medicine, while ensuring robust evidence generation, patient safety, and data integrity.		
EANM	General	0	0	The Basic Safety Standards Directive (BSSD) contains several paragraphs on medical exposures explicitly mentioning diagnostics (Articles 55 – 64, eg. justification, optimisation etc.). We invite EMA to clarify with the European Commission Directorate for Energy the interlations between the BSSD and this guideline.		
EANM	General	0	0	EANM encourages EMA to include hyperpolarized MR agents in the scope of the guideline. These compounds will very likely gain significant importance in molecular imaging.		
EANM	Specific	19	22	**Scope of radiopharmaceuticals:** EANM notes that the overview of diagnostic agents includes radiopharmaceutical kits, generators, and precursors. To ensure completeness and clarity, EANM suggests explicitly including **cyclotron produced PET radiopharmaceuticals** within the scope of radiopharmaceuticals covered by the guideline, as these constitute a substantial part of current clinical and research practice in nuclear medicine.	"For clarity and completeness, the list of radiopharmaceuticals may explicitly include cyclotron-produced PET radiopharmaceuticals, in addition to generators, precursors, kits, and ready-to-use products."	
EANM	Specific	48	51	**Development framework proportionality:** EANM notes that diagnostic radiopharmaceuticals differ fundamentally from therapeutic products in terms of objectives, endpoints, and risk profile. The revision process offers an opportunity to ensure that development requirements are clearly aligned with the specific purpose of diagnostic agents, namely optimisation of image acquisition, diagnostic performance, and impact on clinical decision making, rather than default application of paradigms derived from therapeutic drug development. The same applies to line 75-88 and 97-103.		
EANM	Specific	57	59	**Theranostics and patient selection:** EANM welcomes the explicit recognition of theranostics and patient selection for targeted treatment as an area requiring dedicated guidance. The revised guideline would benefit from further clarification that diagnostic imaging agents are frequently used as **prerequisite tools** for therapy decision making, including patient selection for targeted and radionuclide therapies. Additional clarification would be valuable regarding: •Regulatory expectations for the evaluation of diagnostic–therapeutic pairs, including scenarios of co development or sequential development; •Acceptable approaches when diagnostic and therapeutic products are developed by different sponsors; •The level and type of evidence considered sufficient to support patient selection claims.		
EANM	Specific	75	80	**Posology, administered activity, and radiation dose:** EANM suggests that the revised guideline ensure **consistent and precise use of terminology**, clearly distinguishing between: •**Administered activity (MBq)** as the quantity given to the patient; and •**Radiation absorbed dose and effective dose** as derived dosimetric consequences dependent on biodistribution, patient characteristics, and imaging protocols. EANM also notes that administered activity required to achieve adequate diagnostic performance is highly dependent on imaging system performance (e.g. scanner sensitivity, acquisition time, and reconstruction methods). To support optimisation and future technological advances, the guideline may benefit from allowing **flexibility in activity specification** (e.g. activity ranges or protocol based approaches), provided diagnostic performance remains robust and radiation protection principles are respected.	"The guideline could consistently distinguish between administered activity (MBq) and absorbed or effective radiation dose, and allow appropriate flexibility in activity specification where justified by imaging performance and radiation protection principles."	

EANM	Specific	81	83	**AI assisted diagnostic methods:** EANM welcomes the inclusion of AI assisted diagnostic methods as an area for further guidance. Given the rapidly expanding use of AI in image reconstruction, segmentation, quantification, and decision support, the revised guideline would benefit from additional clarification on: •The scope of AI tools covered; •Validation expectations when AI contributes to primary endpoints, image interpretation, or patient selection; •Considerations where AI tools are integrated into theranostic workflows.	"Additional guidance could be provided on the scope and validation of AI-assisted diagnostic methods, particularly where such tools contribute to image interpretation, quantitative endpoints, or patient selection."	
EANM	Specific	89	96	**Reproducibility and operational considerations:** EANM agrees with the emphasis on reproducibility and reliability of diagnostic imaging. In addition to methodological considerations, EANM notes that reproducibility is strongly influenced by **operational factors**, including radiopharmaceutical preparation, administration techniques, and imaging acquisition, all of which require standardised procedures and appropriate training. Explicit acknowledgment that reproducibility is both a methodological and operational aspect may help ensure that clinical development programmes and multicentre trials adequately address sources of variability.		
EANM	Specific	122	129	**Individualised dosing and special patient populations:** EANM notes that, in routine clinical practice, administered activity is often adapted to patient specific factors such as body weight, altered excretory function, or repeated imaging. Practical guidance acknowledging these considerations would be helpful. EANM further suggests that the revised guideline explicitly highlight the importance of optimisation strategies for **paediatric patients** and for patients requiring **repeated imaging**, given the particular relevance of radiation protection in these populations. The guideline may also benefit from acknowledging the routine use of concomitant medicinal products administered alongside diagnostic agents and the importance of considering potential interactions in the clinical evaluation. The same applies to lines 75-80.	"The guideline could acknowledge the need for individualised activity administration based on patient-specific factors, and highlight optimisation strategies for paediatric and repeat-imaging populations, as well as consideration of concomitant medicinal products where relevant."	
EANM	Specific	122	129	**Role of qualified professionals:** EANM suggests that the revised guideline explicitly acknowledge the importance of appropriately qualified professionals in the preparation, quality control, administration, and imaging of radiopharmaceutical diagnostic agents. These roles are integral to ensuring patient safety, radiation protection, dose accuracy, image quality, and data integrity in both clinical practice and clinical trials. The same applies to lines 75-77.		
EANM	Specific	122	129	**Extravasation:** EANM notes that extravasation is a clinically relevant and relatively frequent event in the administration of radiopharmaceuticals. Extravasation may affect patient safety, image quality, and the quantitative reliability of imaging endpoints. Consideration of extravasation, including its prevention, recognition, documentation, and management, within the scope of safety and methodological guidance would therefore be valuable.	"Consideration could be given to addressing extravasation, including its prevention, recognition, documentation, and potential impact on image quality and quantitative endpoints, within safety and methodological guidance."	
EANM	Specific	122	129	**Safety assessment and repeated use**: EANM supports the continued emphasis on safety and radiation protection. With regard to repeated use of diagnostic radiopharmaceuticals, EANM suggests that guidance be framed in a **risk proportionate manner,** reflecting the extensive historical experience with diagnostic radiopharmaceuticals administered at microdose levels, and focusing on substance specific characteristics and radiation exposure where relevant.		