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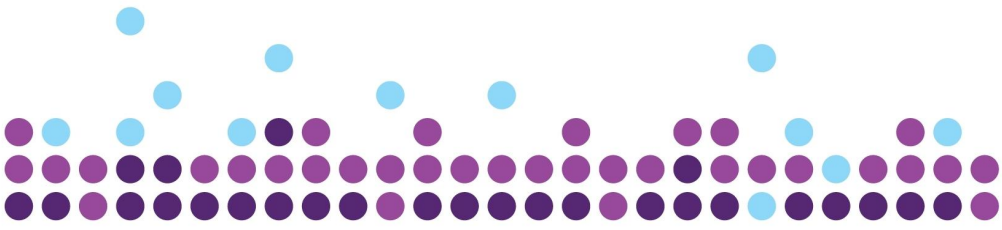

EURAMED ROCC-N-ROLL
European Medical Application and Radiation Protection Concept

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D2.4 Identification and prioritisation of ALLIANCE and NERIS SRA topics relevant to medical radiation protection research

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Abbreviations

AI	Artificial intelligence
ALLIANCE	European platform for radioecological research
DSS	Decision support system
EURAMED	European platform for research activities in medical radiation protection
HEU	Highly-enriched uranium
Rocc-n-roll	Radiation prOteCtion Concept: strategic research agenda aNd ROadmap interLinking to heaLth and digitisation aspects
NERIS	European Platform on preparedness for nuclear and radiological emergency response and recovery
SRA	Strategic research agenda

Disclaimer

The opinions stated in this report reflect the opinions of the authors and not the opinion of the European Commission.

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1. EXECUTIVE SUMMARY

The goal of the EURAMED rocc-n-roll Project is to propose an integrated and coordinated European approach to research and innovation in medical applications (including veterinary ones) of ionising radiation and related radiation protection, based on stakeholder consensus and existing research agendas of radiation protection platforms and related activities. As part of this endeavour, a joint EURAMED rocc-n-roll panel of ALLIANCE and NERIS members were appointed under Task 2.4 of this project to identify and prioritise ALLIANCE and NERIS SRA topics relevant to EURAMED rocc-n-roll.

The panel performed a review and discussion of relevant topics. From the ALLIANCE SRA viewpoint, the different stages of the life cycle of radionuclides used in nuclear medicine were considered to be relevant to EURAMED rocc-n-roll, and priority areas of research were evaluated with focus on the environment: radionuclide production, radiopharmaceutical manufacturing, post-medical application, and final disposal of related radioactive waste. For NERIS, the areas relevant to rocc-n-roll included aspects of emergency management and preparedness in radiological emergencies related to specific nuclear medicine life-cycle stages.

The subjects identified from the ALLIANCE SRA for consideration as EURAMED rocc-n-roll priority areas include:

- A compilation of radionuclides used in medicine including decay products and associated long-lived impurities.
- Identification of data gaps for these radionuclides including missing environmental parameter values.
- Studies on the speciation of medical radionuclides and compounds formed in the environment following their release, encompassing releases arising from manufacturing and those following radiopharmaceutical use.
- Methods to address data gaps in assessment model parameters.
- Identification and systematic description of environmental exposure pathways for people and environment.
- Identification of the most common exposure situations for demonstration of dose assessment procedures involving medical facilities for both the general public and wildlife.

The topics identified from the NERIS SRA for consideration as EURAMED rocc-n-roll priority areas include:

- Possible two-way collaboration with EURAMED on countermeasures.
- Governance of preparedness.
- Stakeholder engagement and communication.
- Decision making under uncertainties.
- Health surveillance and artificial intelligence in simulation models as well as decision support systems (DSS).
- Societal and ethical aspects for holistic emergency management.

2. INTRODUCTION

In this deliverable, we elaborate on the ideas of the joint panel of the European radiation protection research platforms ALLIANCE and NERIS dealing with radioecology and preparedness for radiological accidents, respectively. The goals were (1) to identify and prioritise research needs relating to the radiation protection of members of public and wildlife arising from releases due to the production and use of radionuclides for medical applications,

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including emergencies, and (2) to provide EURAMED rocc-n-roll with a concise statement on these priority R&D domains to be considered for inclusion in their SRA.

For EURAMED rocc-n-roll, the ALLIANCE's focus is on prioritisation of predicting human and wildlife exposure and on the need for improved radiation protection by integrating radioecology and radiological emergency planning. Ongoing improvements in the medical field have resulted in an expansion of the use of radionuclides for diagnostic and therapeutic purposes. This has led to an increasing demand for and an increasing number of radionuclides (e.g. ^{177}Lu and the α-emitting ^{223}Ra and ^{227}Th which has previously not been used for medical purposes). The production of radiopharmaceuticals for diagnostic and therapeutic applications is rising to cope with this demand. This increased medical radionuclide production and their use in medicine leads to potential releases of radioactive substances into the environment.

In the case of routine authorised releases, radionuclides can reach the environment as planned discharges from production facilities. Usually, activities released from production facilities comply with regulations, although exceedances of discharge limits can happen occasionally for a variety of reasons. Moreover, for some radionuclides (most notably ^{131}I from ^{99}Mo production), authorisation limits held by medical isotope production facilities are actually higher than those of nuclear reactors.

Incidental releases from either radiopharmaceutical manufacturing plants or hospitals have occurred in Europe in the past decade. New medical radioisotopes and production routes (such as ^{225}Ac production from ^{226}Ra targets) may potentially increase such incidences.

In hospitals, there are protocols to limit the releases after inpatient treatments. Of the various routes possible, the most relevant releases would occur after radionuclides leave the patient's body via excretion. Excreta wastes are placed in dedicated sewage tanks with a decay storage before being released into the sewage system. However, the procedure depends on the local regulations. In many cases, urines are stored for decay in dedicated tanks, but faeces are drained out without significant decay because of the nosocomial hazard that has to be avoided within hospitals. Outpatient treatment, on the other hand, may result in radionuclides leaving the patient's body and entering directly the sewage system outside of hospitals, inevitably omitting the tank storage step. For both situations, additional releases can take place if the patient dies soon after treatment and if their body is cremated.

The need for medical radioisotope/radiopharmaceutical production plants and medical facilities to monitor and to assess the impact of their releases is not uniformly authorised in all European countries. In some states, facilities may be exempted from authority control if they can demonstrate that agreed dose limits are not exceeded. In other countries there are requirements to prove that such radionuclides are not liable to affect the quality of drinking water or otherwise impact people and the environment. Overall, impact assessments for planned and emergency releases in radionuclide production, diagnostic and treatment uses are difficult to find, and few data are available for input in assessment models for many of the medical radionuclides released. There is growing interest on this topic from international organisations such as the EU and e.g. the OSPAR Commission[1], and in several member states there is a growing demand for a more transparent assessment of releases of medical radioisotopes and associated impact.

The main challenges in hazard characterisation relate to current as well as future radionuclides arising from medical use are missing environmental transfer data for

[1] OSPAR is the mechanism by which 15 Governments & the EU cooperate to protect the marine environment of the North-East Atlantic. OSPAR is so named because of the original Oslo (1972) and Paris (1974) Conventions ("OS" for Oslo and "PAR" for Paris)

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radionuclides uncommon in current databases (e.g. ^{225}Ac), either because they are part of new treatments and are radioisotopes of elements not considered for other uses of radioactivity, or because of the different physical form or speciation of radioisotopes as used in medical therapy compared to industrial applications.

In general, most releases of radionuclides after therapy are limited and their radiological impact will likely be lower than that of releases from the production of radioisotopes or radiopharmaceuticals. However, environmental parameters for short-lived radionuclides are by their very nature more difficult to obtain, leading to assessment uncertainty. Unusual exposure pathways may need to be considered, such as the transfer of radionuclides to land. This may occur through sewage sludge incineration, application of sewage sludge to agricultural fields or through use of irrigation waters downstream from the treatment plant. Nevertheless, levels of short-lived radionuclides in the environment will be limited due to dilution processes and radioactive decay during environmental transport.

The majority of radionuclides applied today in nuclear medicine are sourced by decay of their long-lived precursors. To date, the radiation hazard at the level of acquiring or production of such precursors has not been considered as a part of the medical application of radionuclides, although some operators may choose to consider their usage in impact assessments. Issues related to the generation of radioactive waste due to medical radionuclide production include, for example, short-lived isotope ingrowth generation from a long-lived precursor prepared for transmutation (e.g. ^{226}Ra) or the long-lived radionuclides remaining after target radionuclide separation (e.g. after ^{99}Mo separation from irradiated HEU).

The EURAMED SRA does not currently consider research priorities related to the impact of radiopharmaceuticals outside medical facilities, both before and after use. Yet, such research is advised to enable better understanding of the environmental behaviour of radionuclides used in novel nuclear medicine applications, imparting confidence in the required hazard characterisation and risk assessments. The need for assessments of radionuclides released from nuclear facilities is mentioned in the ALLIANCE SRA, which states that parameter data for some recently emerging medical radioisotopes data are missing. However, it is necessary to put this need into perspective: scoping calculations related to potential dose contribution are required before setting off any complex assessment modelling.

Nuclear and radiation emergencies in the past have demonstrated the need for preparedness at all levels, from local to national and transnational. The NERIS Platform has developed a strategic research agenda that addresses these needs. One key topic identified therein is the application of a holistic approach or framework in emergency management and recovery preparedness. Such a holistic approach requires interaction with all relevant stakeholders. In the case of nuclear medicine, the involvement of medical doctors and physicists is crucial. Early and late countermeasures and countermeasure strategies cannot focus on radiation effects alone but require balancing of different needs and constraints of the affected population. Medical is one key attribute that requires consideration when developing sustainable countermeasure strategies. In this respect, the NERIS community is lacking in valuable expertise that is available in EURAMED. Both platforms can develop realistic scenarios for different types of emergencies from local ones (e.g. hospitals) to large scale ones involving nuclear reactors.

Governance of preparedness, social and ethical aspects are important for a holistic emergency management framework. In both the emergency and recovery phases, sustainable strategies require consideration also of medical risks and their possible impact on the strategies. Integrating medical, societal, and ethical considerations requires that

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several research platforms work together and therefore EURAMED rocc-n-roll should consider such a challenge in its SRA.

Radiation Protection research comprises many areas that are of interest to many platforms, but the perspective and type of approach is different. For example, NERIS is much interested in stakeholder engagement and communication, decision making under uncertainties, health surveillance and use of artificial intelligence (AI). NERIS assumes that similar topics are on the agenda of EURAMED and proposes to interact in exploring common methodologies.

For example, medical applications use AI more and more intensively (e.g. use of AI algorithms to improve readability of CT-scans). NERIS is also investing effort in using AI for simulation models and decision support systems. The latter, however, requires a so called “explanatory” layer as decision makers might have some objections against results from AI without understanding the rationale behind. We assume that such an explanatory layer might be also important for medical applications as there is the need for both doctors and patients to understand and trust the outcome of AI. Similar examples can be found for the other topics where platforms may exchange perspectives on methods and approaches.

3. RESEARCH NEEDS FROM AN ALLIANCE AND NERIS PERSPECTIVE

From the perspective of ALLIANCE, the research needs are linked to the fact that there are novel sources of radioactivity involved in radionuclide and radiopharmaceutical manufacturing, medical use, and waste disposal. Radiological impact assessments are being conducted for some of these sources even though data are lacking, which likely leads to overly conservative assessments. This is deemed to be acceptable if the resulting predicted doses are insignificant, but likely increases assessment uncertainty. For many medical radionuclides, there are no or few data for environmental parameter values. For novel medical radionuclides, there is a need to obtain migration and accumulation pathways, transfer factors, and K_d values and, given the need to assess the impact of radionuclides not only on humans but also on wildlife; biological half-lives for biota are also required for the dynamic assessment of non-continuous releases. The physico-chemical form may be very different than for radionuclides conventionally released from nuclear industry, changing mobility and bioavailability and finally impact. The ALLIANCE SRA implies that these research needs to be guided by a fitness-for-purpose approach, in the sense of conducting preliminary projects rather than launching directly into too complex investigations.

There is a need for improved transfer and assessment models so that they include new exposure pathways to workers, public and environment requiring appropriate modelling approaches. The exposure pathways to be represented include the novel ones brought into existence by radiopharmaceutical use. They comprise patient excretion (outpatient treatment) with wastes being routed to sewage treatment plants, patient burial after inpatient and outpatient treatment, and radionuclide emissions into the atmosphere from incinerators including those before radiopharmaceutical use, such as treatment and disposal of radioactive residues created at the relevant radionuclide production stage. Moreover, there is a need to adapt assessment models to obtain practical tools for end users leading to improved guidance to regulators in terms of highlighting what information they need in order to carry out an assessment of this type. These modelling needs should also follow a fit-for-purpose development.

From the perspective of NERIS, which has developed a strategic research agenda that addresses emergency management and preparedness in radiological emergencies, the research needs concern the medical aspects of sustainable countermeasure strategies. There is a need to develop realistic scenarios for different types of emergencies from local

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e.g. hospitals to large scale e.g. nuclear reactors. On the topic of countermeasures, governance of preparedness, societal and ethical aspects for holistic emergency management, NERIS may attain an advisory role for EURAMED to consider such a challenge in their research activities. Stakeholder engagement and communication, decision making under uncertainties, health surveillance and Artificial Intelligence in simulation models and DSSs, also provide the potential to explore common methodologies and approaches between NERIS and EURAMED.

4. PROPOSED RESEARCH TOPICS IN ORDER OF RANKING ACCORDING TO ALLIANCE AND NERIS

The ranking of the research topics proposed by the ALLIANCE/NERIS joint panel as part of Task 2.4 for the EURAMED rocc-n-roll project is given in Tables 1 and 2. The ranking number is obtained by averaging over the level of priority set by each contributor involved in ALLIANCE and NERIS (see Section 5 below for the limitations of this approach). The project partners and involved external advisory experts evaluated the research topics, leading to the conclusions presented below.

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Table 1: Proposed ALLIANCE SRA research topics relevant to rocc-n-roll in order of ranking

Topic	Rank: high (10) to low (5)
Methodological guide on what radionuclides are relevant and requirements for assessment to people and wildlife.	9.3
European survey on the extent of use of radiopharmaceuticals from production to patient use to waste disposal.	8
Physical and chemical speciation of the most environmentally-relevant, longer-lived medical radionuclides, highlighting the environmental interactions.	7.8
Identification and systematic description of environmental exposure pathways for people (workers and the public) and wildlife.	7.7
Methods to address data gaps in assessment model parameters (mathematical evaluation and communication of uncertainties).	7.5
Compilation of terrestrial and freshwater transfer parameter values (CR, K_d, $T_{B1/2}$, etc.) and identification of data gaps for medical radionuclides.	7.4
Generic assessment software modelling system for release/processing of releases from hospitals and radionuclide production facilities.	7.2
General approach to define scenarios (atmospheric, coastal, river, terrestrial, urban) for transfer to humans and biota in clinical treatments and the radiopharmaceutical industry.	6.8
Estimation of dose to the general public from routine and accidental releases for demonstration of dose assessment procedures involving medical facilities	6.8
Improved radio-ecological dispersion models for use in discharges impact assessment.	6.7
Lifecycle analysis “radionuclide factsheets” from a human and environmental safety perspective.	5.8
Demonstration scenarios for wildlife dose rates arising from routine and accidental releases for medical facilities.	5.7

Table 2: Proposed NERIS SRA research topics relevant to rocc-n-roll in order of ranking

Topic	Rank: high (10) to low (5)
Countermeasures & countermeasure strategies: Develop with EURAMED realistic scenarios for nuclear accidents, “dirty bombs” and accidental medical exposures, analysing relevant individual countermeasures and complementary actions (i.e. victim triage, biodosimetry, use of radioprotector/radiomitigator drugs, management guidelines, resource optimisation, etc.).	10.0
Governance of preparedness, societal and ethical aspects: Improve guidance framework and tools to support sustainable strategies of preparedness to the management of post-accident situations including risk for evacuees and patients.	8.3

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Artificial intelligence and knowledge databases: Explore AI and Deep Learning methods for improving simulation models and to develop new generation of decision support systems applicable in medicine for image recognition.	6.7
Health surveillance: This includes risk assessment and general aspects of treatment of affected people, including reflections on the well-being of vulnerable people, justifying medical procedures and ethical aspects.	6.7
Decision making including under uncertainties: Improve decision making by testing formal decision aiding tools and improving methods in frame of personalised medical treatments.	5.0
Stakeholder engagement and communication: Stakeholder engagement and communication to patients. In particular the basis/modalities/approaches of communication on risk-benefits related to the faced choices/decisions.	5.0

5. DISCUSSION AND LIMITATIONS OF THE EXERCISE

The research topics were listed by the rocc-n-roll Task 2.4 panel members and then ranked according to the perceived order of relevance by the participating specialists. Some involvement of external advisory experts took place to verify the conclusions obtained. The results are issued with the caveat that the ranking cannot be absolute, as it is based on the perspectives and research orientations of each expert. In other words, it could be said that the potential weak point of the applied methodology for prioritisation is an opinion built upon the experience and duties of the responders. It is for this reason that the recommendations were discussed at ALLIANCE and NERIS meetings, leading to the aforesaid further advice beyond the ranking as given below.

The EURAMED rocc-n-roll Task 2.4 ALLIANCE/NERIS joint panel presented the research prioritisation results to the meeting of the ALIANCE Board of Directors on 26th May 2021 for discussion. The main feedback received from the ALLIANCE perspective was that panel ranking should be balanced with dose criteria (i.e. to consider the likely potential to contribute to dose) since dose estimation is the crucial assessment step. However, this should include not only the level of dose as a generic criterion but also the need to demonstrate sufficient protection against uncommon exposure pathways (e.g. outpatient releases, deceased patient cremation, wastewater treatment) For example, radionuclides which have a relatively short half-live do not warrant detailed speciation or other type of mechanistic studies as they will in all likelihood decay before they reach humans and the environment. However, it would be justified to demonstrate protection for uncommon pathways for these radionuclides by conducting a screening (i.e. first tier) assessment under simplified and conservative conditions (though even for this one would need transfer parameters or an agreed approach to extrapolate them).

On the advice of the ALLIANCE bureau, it was agreed to bring this analysis to further scrutiny by the ALLIANCE SRA Working Group in search of additional opinions. One proposal was the production of recommendations and advice for practical assessment – methodological guide (listed as one of the research topics) which would build upon results from the listed research activities.

The EURAMED rocc-n-roll Task 2.4 joint panel also presented the results at the General Assembly of NERIS on 9th June 2021. Participants of the meeting had time to provide comments in the aftermath, however, the proposed wording was accepted as is.

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In the future, additional topics may need to be considered as further knowledge and awareness arise around the increasing use of radionuclides in medical applications.

6. CONCLUDING STATEMENT

The established Task 2.4 panel recommends that EURAMED rocc-n-roll extends the EURAMED's SRA based on the justification that radionuclides from use of radiopharmaceuticals eventually enter the environment and that, currently, assessments are difficult to make due to gaps in data and modelling approaches for the relevant radionuclides. In addition, there is a need to link the medical community to emergency planning and countermeasures for the various accident situations that may arise.

EURAMED rocc-n-roll Task 2.4 has identified from the ALLIANCE SRA the need to establish the relevant radionuclides' lifecycle from production to disposal and generating methodological guidance, followed by studying processes and pathways leading to improved models for dose assessment not only for members of the public but also for wildlife.

EURAMED rocc-n-roll Task 2.4 has identified from the NERIS SRA the need to develop (jointly with EURAMED) countermeasures and strategies for accidental exposures, governance of preparedness, societal and ethical aspects and improving models with artificial intelligence and better knowledge databases. Next in order of priority are health surveillance, improving decision making including under uncertainties, and stakeholder engagement and communication.

The above prioritisation has an inevitable degree of subjectivity, hence it should be pragmatically balanced in a sensible and realistic way, taking into account practical rather than theoretical considerations specific to the medical use of radiation and radionuclides in order to minimise unnecessary complexity in the assessment process. Important balancing factors to consider are the need to demonstrate protection for uncommon pathways, the need to achieve a consistency of approach between protection of people and protection of the environment and the need to maintain a meaningful stakeholder dialogue about the risks of both routine and potential accidental exposures involving medical radionuclides.

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