European Partnership on Metrology
Call 2024 –Digital Transformation, Green Deal, Normative and Research Potential

Selected Research Topic number: **SRT-r05**
Version: 1.0

Title: Establishing traceability routes in nuclear medicine

Abstract

Accurate measurement of radioactivity forms the basis for medical exposure assessment in nuclear medicine (NM). Increased desire for quantitative imaging, alongside advancements in dosimetry techniques in molecular radiotherapy has changed the landscape in NM, adding quantitative measurement to the existing qualitative assessments. Whilst the clinical practice is advancing, not all countries have the capability to provide traceable calibration services to hospitals leading to discord when it comes to measurement of radioactivity across Europe. Proposals addressing this SRT should focus on establishing traceability routes in nuclear medicine for key clinical radionuclides and improve uncertainty assessment in the clinical sites.

Keywords

Nuclear medicine, radionuclide calibrator, targeted/molecular therapy

Background to the Metrological Challenges

Over 9 million patients receive injections of radiopharmaceuticals each year across Europe. The global nuclear medicine market is currently valued at around 9 billion € and is anticipated to grow to 26.5 billion € by 2032. The lack of metrology input to nuclear medicine service delivery is a common theme across Europe and partly stems from the origins of nuclear medicine as a qualitative or palliative technique. This lack of metrology has led to poor knowledge of the dose effect relationships for many treatments leading to under treatment of tumours and unsuccessful clinical trials.

In nuclear medicine, the injected activity is a fundamental quantity, and at present, the accuracy in the measurement of intended activity injected to patients varies, even within the same country and can be 10 % or more from the prescribed value. This leads to variability in the diagnostic images produced (leading to an inability to compare the images) and variability in the accuracy of absorbed doses delivered to tumours. Whilst legislation varies between countries, there is generally a requirement for the devices (typically radionuclide calibrators) used to measure activity administered to be calibrated in a manner traceable to national standards. In addition, article 56.1 of EU BSS Council Directive 2013/59/EURATOM states that *"For all medical exposure of patients for radiotherapeutic purposes, exposures of target volumes shall be individually planned, and their delivery appropriately verified taking into account that doses to non-target volumes and tissues shall be as low as reasonably achievable and consistent with the intended radiotherapeutic purpose of the exposure."* The same directive also states that absorbed doses should be calculated in a traceable manner.

This requirement can be fulfilled in multiple ways, with the most accurate method being the use of the specific radionuclide in question in a relevant geometry. However, there are over 20 radionuclides used for diagnosis and therapy; each of these requires its own primary standard and there are a variety of techniques employed to realise these standards. Due to operational, administrative, or financial reasons, calibration services to ensure traceability by use of the specific radionuclide are not available in every country and therefore the accuracy and traceability of these devices varies significantly across Europe. The quantitative imaging is used for the classification and diagnosis of disease alongside determination of absorbed dose to target tumours and healthy organs. Without traceable calibration processes, patients may be mis-diagnosed (or wrongly classified) and calculated absorbed doses for radionuclide therapy are not traceable. The latest advancements in so-called 'theragnostics', whereby therapeutic-diagnostic radionuclide pairs are used to tailor treatment, further increase the need for traceability. Creating traceability routes can improve the accuracy of both measured activity prior to injection and the activity derived from imaging techniques.

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Besides, it is necessary to validate effectiveness of calibration routes and to assess measurement capability by performing comparison exercises among users of newly established routes for clinical radionuclides of interest.

A common theme throughout the nuclear medicine community is the lack of consideration of uncertainties. This not only makes statistical comparisons difficult to perform, but it also demonstrates a gap in the traceability chain through to quantitative imaging and dosimetry which needs to be addressed to comply with legislation and improve patient outcomes. By analysing uncertainty components, clinicians can have greater confidence in their decision making based on images or calculated absorbed dose. Providing the guidance documents on the calibration services for key clinical radionuclides, validation of measurements and uncertainty assessment can further improve the accessibility of traceable calibration routes in Europe.

Objectives

Proposers should address the objectives stated below, which are based on the PRT submissions. Proposers may identify amendments to the objectives or choose to address a subset of them in order to maximise the overall impact, or address budgetary or scientific / technical constraints, but the reasons for this should be clearly stated in the protocol.

The proposal shall focus on the development of metrology capability in measurement of radioactivity for nuclear medicine.

The specific objectives are

1. To establish traceability routes in order to provide traceable calibration services for key clinical radionuclides with an uncertainty (at k = 1) of 2 % or better. The services will be developed in collaboration with the local responsible NMI/DI and partner hospitals to ensure a functional service that will operate effectively within the legislative requirements of the host country.
2. To assess and develop uncertainty evaluation techniques used by calibration laboratories and users in order to provide practical support for end-to-end uncertainty evaluation from activity determination at the calibration laboratory to quantitative imaging and patient treatment optimisation.
3. To validate effectiveness of calibration routes and to assess measurement capability by performing comparison exercises among users for key clinical radionuclides. The target would be for 80 % or more of participants from countries with emerging metrology capabilities in this field to be able to measure activity to within 10 % of the reference value. A supplementary target would be to receive uncertainty budgets from 70 % or more of participants.
4. To provide a guidance document on the calibration for key clinical radionuclides, validation of measurements and uncertainty assessment to further improve the accessibility of traceable calibration routes in Europe.
5. To facilitate the take up and long-term operation of the capabilities, technology and measurement infrastructure for nuclear medicine measurements developed in the project, by the measurement supply chain (NMIs/DIs, calibration and testing laboratories), and end users (e.g. industry, instrument manufacturers, regulators). The approach should be discussed within the consortium and with other EURAMET NMIs/DIs, e.g. via EURAMET TC-Ionising Radiation (IR) and EMN for Radiation Protection, to ensure that a coordinated and optimised approach to the development of traceability in this field is developed for Europe as a whole.

Joint Research Proposals submitted against this SRT should identify

- the particular metrology needs of stakeholders in the region,
- the research capabilities that should be developed (as clear technical objectives),
- the area for which the capabilities will be built (Green Deal, Digital Transformation, Health, Integrated European Metrology, Industry, Normative or Fundamental Metrology) and in which future main call the developed research capabilities are planned to be employed,
- the impact the developed research capabilities will have on the industrial competitiveness and societal needs of the region,
- how the research capability will be sustained and further developed after the project ends.

Proposers should establish the current state of the art and explain how their proposed research goes beyond this.

The development of the research potential should be to a level that would enable participation in other TPs.

Proposers should note that the programme funds the activity of researchers to develop the capability, not the required infrastructure and capital equipment, which must be provided from other sources.

EURAMET expects the average EU Contribution for the selected JRPs in this TP to be 0.7 M€ and has defined an upper limit of 0.9 M€ for this proposal.

EURAMET also expects the EU Contribution to the external funded beneficiaries to not exceed 20 % of the total EU Contribution across all selected projects in this TP.

Any industrial beneficiaries that will receive significant benefit from the results of the proposed project are expected to be beneficiaries without receiving funding or associated partners.

Potential Impact

Proposals must demonstrate adequate and appropriate participation/links to the 'end user' community, describing how the project partners will engage with relevant communities during the project to facilitate knowledge transfer and accelerate the uptake of project outputs. Evidence of support from the "end user" community (e.g. letters of support) is also encouraged.

You should detail how your proposal's results are going to:

- Address the SRT objectives and deliver solutions to the documented needs,
- Provide a lasting improvement in the European metrological capability and infrastructure beyond the lifetime of the project,
- Facilitate improved industrial capability or improved quality of life for European citizens in terms of personal health, protection of the environment and the climate, or energy security,
- Transfer knowledge to the radiopharmaceutical sector and the metrology community.

You should detail other impacts of your proposed JRP as specified in the document "Guide 4: Writing Joint Research Projects (JRPs)"

You should also detail how your approach to realising the objectives will further the aim of the Metrology Partnership to develop a coherent approach at the European level in the field of metrology and include the best available contributions from across the metrology community. Specifically, the opportunities for:

- improvement of the efficiency of use of available resources to better meet metrological needs and to assure the traceability of national standards
- the metrology capacity of EURAMET Member States whose metrology programmes are at an early stage of development to be increased
- organisations other than NMIs and DIs to be involved in the work.

Timescale

The project should be of up to 3 years duration.