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PIANOFORTE Partnership

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D 5.3.1: Infrastructure Intercomparisons Review

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Abstract

We present here the review of methods for harmonisation and standardisation of most representative infrastructure classes within or related to radiation protection research.

Details on the definition, preparation, implementation, execution, and analysis of the outcomes are provided for intercomparison exercises covering different types of facilities/laboratories including dosimeter monitoring services, metrology, secondary standard dosimetry, centres of radiotherapy (comparable to research irradiation facilities), bio-analytical and simulation platforms.

The review is followed by the identification of some of the critical aspects that the current state of the art intercomparison initiatives are facing and the introduction of some hints towards possible improvements, that can likely stimulate proposals for more effective intercomparisons between critical and underserved facilities.

Content

1. Aim of the document

1.1. Introduction

A large proportion of radiation protection research needs diversifiable and qualified infrastructures characterised by detailed, accessible, reliable, and up-to-date information. On the other hand, infrastructures can benefit from well-defined, infrastructure and class specific, quality protocols and which will stimulate standardised intercomparisons to keep adequate level of quality standards, sharing and improving experiences and competences.

This document will continue and extend the CONCERT approach to infrastructures and harmonisation of their standard protocols and practices, taking into account the latest platforms and network communities (e.g., EURAMET) achievements and current activities in this direction.

The AIR2D2 database and documentations represents an extremely valuable reference, which is being expanded during PIANOFORTE. The recent OFFERR catalogue of infrastructures from SNETP is also a useful source of information, although only a sub-set of the OFFERR infrastructures are relevant for PIANOFORTE.

The document presents a schematic review of the available infrastructures and the analysis of existing systems of intercomparison.

1.2. Objectives

One of the main objectives of the WP5 is to promote harmonisation of quality standards, practices and protocols in all areas relevant to implementation of the research roadmap. In this broad framework, intercomparisons are an important tool for proper research harmonisation and standardisation.

1.3. Purpose and scope of this deliverable

This document reviews protocols and related quantification criteria on selected infrastructure classes; the first step towards the definition and development of a system for funding inter-comparisons to promote standardisation. Due to the large heterogeneity of the infrastructures (e.g., exposure facilities with different irradiation sources and related technologies, radioecology observatories, databases including biobanks, sample archives, cohorts, analytical platforms, modelling tools including recent advanced artificial intelligence based models), a review and an analysis of the existing systems of inter-comparisons as organised by international organisations, networks and platforms and their funding scheme (e.g., applied by funding agencies) represent a valuable guidance in identifying common protocols, practices, etc.

2. Infrastructures overview

Before presenting the details of the identified common protocols, the document offers a quick review of infrastructures classification and analysis of existing intercomparisons that can be related to radiation protection research. The review is focused on the relevant information which are expected to characterise the different classes of infrastructures for their best exploitation.

2.1. Classification

For radiation protection research, the following classes (and sub-classes) of platforms have been identified in AIR2D2 and integrated in the current analysis; minor improvements to the original AIR2D2 classification are proposed.

2.1.1. Exposure Platforms

Facility where organisms, samples or instruments may be irradiated under controlled conditions: dosimetric characteristics are quantitatively defined and subjected to quality control system/procedure and traceable. The traceability is guaranteed by a continuous chain of calibrations to the highest references available used for ionising radiation, built through the International System of Units (SI).

1. External Exposure Facilities: Facilities where organisms, samples or instruments may be irradiated by external radiation, under controlled conditions in which dosimetric characteristics are well known and under control and traceability.
2. Internal Exposure Facilities: Facilities where animals or plants are exposed to radiation via ingestion, inhalation or by wounds. Organisms are kept under controlled conditions.
3. Contaminated sites & Observatories: Natural sites contaminated by radionuclides (technology enhanced or anthropogenic radioactive materials) via industrial activities or accidental releases; this class includes the radioecological observatories, which are radioactively (and possibly chemically) contaminated large-scale field sites.

Some of these facilities are used for intercomparison of radiation protection devices and their calibration, as well as Monte Carlo simulation benchmarking; examples are represented by the CERN irradiation laboratories [Pozzi-2017] where standards such as the [ISO-17025], are applied.

There are different databases on irradiation facilities (in addition to the AIR2D2), including those below which are among the most populated:

- https://nucleus.iaea.org/sites/accelerators/Pages/default.aspx, theIAEA/NUCLEUS accelerators worldwide database
- https://irradiation-facilities.web.cern.ch/, which is operated within the AIDA2020 and RADNEXT networks

2.1.2. Collection (Archiving/Repository) Platforms

Organised collections of information, specific data, or samples:

1. Databases: An organised collection of data.
2. Sample Banks: Collection of biological samples (e.g., humans, animals, or plants samples…) and inert samples (soils, water, …) with a relation to radiation topics (e.g., nuclear workers, irradiation during childhood with low doses, irradiation/contamination during a radiological accident…) and generally associated/connected to databases. For research biobanks quality, the applicable UNI-ISO document 20387:2018 on “Biotechnology – biobanking – general requirements for biobanking” shall be considered as relevant reference.

3. Cohorts: Grouping of information and/or data about one particular population (e.g., person, plants…) in radiation research area (e.g., nuclear workers, irradiation during childhood with low doses, irradiation during a radiological accident…). Generally applied for epidemiological and/or health studies and can be linked to a sample bank.

An interesting source of information on radiation protection databases is also the review paper "Radiation databases and archives – examples and comparisons" [Zander-2019].

2.1.3. Processing Platforms

This class includes more heterogeneous facilities and their definitions vary, so the agreed definition is still to be identified.

1. Analytical Laboratories: infrastructures with measurement or analysis (e.g., omics) instruments and related services. Depending on the endpoints, dedicated analytical laboratory should be selected to investigate irradiated- or potentially irradiated- samples in order to define the received dose (e.g., Dicentric assay, PCC assay, EPR assay…: dosimetric laboratories) or to study biological alteration in the sample due to the irradiation (e.g., expression of proteins or genes, post-translational modification of proteins, activation/inactivation of regulatory and other biological pathways, DNA damage and repair 'omics platforms').
2. Model and Tools: Predictive or analytical softwares or processes, as well as biological model (such as animal or plant model).

2.2. Facility identification and characterisation data

For each facility, the following categories of information should be provided and collected in a database (and taken up to date), to adequately orient the potential users and, at the same time, promote the facility.

1. Facility General Information (name, address, class and sub-class, brief description, fields of application, …)
2. Contact Information
3. Access rules, including ethical/legal limitations, e.g., GDPR (General Data Protection Regulation) permission when applicable, proposal submission and evaluation procedure (link to examples can be useful)
4. User support (depending on facility type: instrumentation available during the irradiation, search interface for databases …)
5. Delivered Service Technical specifications (including quantitative specification of conditions of delivery, when applicable)
6. Mode of operation (e.g., experiment fully run by the facility, by facility material or equipment from user, by facility and user, run by user)
7. Link to required user training and safety procedures, when applicable
8. Applicable standards and regulations (including quality control procedures)
9. Service Costs

10. Facility specific details, e.g., for an irradiation facility: type of particles, energy spectrum, intensity range, time structure, mode of delivery, …; for a sample bank: type of organism, storage conditions, characteristics of the population, ...; for an analytical platform: input and output data type and formats, ...

The above, not exhaustive list, has been derived mainly from the AIR2D2 database and is now integrated in the OFFERR catalogue. OFFERR, the European User Facility Network within the Sustainable Nuclear Energy Technology Platform (SNETP) association, has recently defined and implemented a quite rich catalogue [OFFERR] oriented to Nuclear Energy Technology research which also includes several radiation protection research related infrastructures.

There are additional databases within the community which will also need to be explored as this work continues, e.g. the Nuclear Energy Agency (NEA) Data Bank at https://www.oecd-nea.org/jcms/rni_6530/jportal-data-bank-workspace which is the international reference centre for computer codes, nuclear and thermochemical data (more nuclear safety-oriented) and the Global Register on low dose research projects which is the reference online database of ongoing and planned low-dose and low-dose rate research projects around the world accessible at https://www.oecd-nea.org/ldr/bo/login.

3. Existing intercomparison related initiatives

In this section some of the most relevant initiatives related to radiological intercomparisons, and likely reasonably comprehensive for the PIANOFORTE activities, are reviewed.

3.1. EURADOS

The European Radiation Dosimetry Group (EURADOS) is a network of 86 European institutions (Voting Members) and more than 650 scientists working in the field of dosimetry of ionising radiation. EURADOS e. V. is registered in the German Register of Societies as a non-profit association for promoting research and development and European cooperation in the field of the dosimetry of ionising radiation.

One of the aims of EURADOS is to contribute to the compatibility of the dosimetric procedures used within the EU and their conformance with international practices. This aim is realised in form of intercomparisons organised since more than 30 years.

Intercomparisons are organised on regular basis. 33 intercomparison exercises were organised up to 2022.

3.1.1. Intercomparisons for Individual Monitoring Services

Intercomparison is one of the EURADOS major product offered to the stakeholders, in particular to the Individual Monitoring Services (IMS) in Europe. For IMS EURADOS organises self-sustained intercomparison exercises where personal dosimeters in suitable fields are irradiated and compared.

The programme aims at providing intercomparisons to services, which enables IMS to:

- Show: compliance with their quality management system, particularly for those working according to ISO 17025;
- Compare: their results with those from other participants;
- Develop: action plans for improvement of their systems.

In order to meet the main aims of the programme, the association aims to meet the following essential criteria:

- intercomparisons are organised at regular intervals. Compliance to ISO 17025 and exercise organised at regular intervals are particularly important because the positive results of intercomparisons are frequently required by the accreditation procedure. In particular, an interval of two years for intercomparisons of whole-body dosimeters in photon fields turned out to be feasible.
- confidentiality with respect to irradiation plans and results of individual participants. All members of the Organisation Group (OG) signed a confidentiality clause. Details of the irradiation plans were known to all members of the OG, but only one person (the coordinator) and the irradiating laboratory knew the exact values of the doses delivered to each dosimeter. Only the coordinator has access to the data which link the results to individual participants.
- accessibility for all IMS interested. The main limiting factor for the accessibility of intercomparison for all interested IMS was the throughput of the irradiation laboratories i.e. the maximum time period, which could be given to the irradiating institute to perform the

irradiations. In order to accept all IMS, the programme of irradiation was finalised after collection of all requests from IMS and the number of systems (dosimeters) accepted from a single IMS was limited. The fees have been calculated on a non-profit basis and any surplus money is used to support harmonisation of individual monitoring and other EURADOS activities.

- reliability of reference dose values was assured by selection of the irradiation sites only among accredited laboratories.

The intercomparison procedure for IMS usually consists of the following steps:

a. Announcement of the intercomparison procedure and the time schedule are published.
b. IMS wishing to participate completes an application form accessible also after registration.
c. The participating IMS is informed when the applications have been accepted.
d. On acceptance of the application, the participants will receive an invoice from EURADOS and instructions for dosimeter labeling and dispatch.
e. The number of dosimeters (including transit/spare) per laboratory is defined.
f. After the irradiations have been carried out, the co-ordinating laboratory will return the dosimeters to the participants for readout.
g. Within one month of receiving the dosimeters the participants will submit the results.
h. After the deadline for submitting results to the co-ordinating laboratory has passed, participants will receive details of their response values.
i. After confirmation of the results, EURADOS provides the participants with a “Certificate of Participation”.
j. The organisation Group will prepare a report summarising the results of the intercomparison. The report includes the names of the IMS that have participated. The results will be presented anonymously.
k. Meeting with IMSes is organised to discuss results.
l. EURADOS Report is published.

An example of the EURADOS report on the results of the intercomparison for IMS is the EURADOS Report 2020-03 [Stadtmann-2020]. In the IC2016 for whole body dosimeters in photon and beta fields participated 103 participating dosimetry systems from 86 institutes and participants from 36 countries around the world. The systems tested during this exercise included 68 TLD, 8 Film, 17 OSL and 10 dosimeter systems based on other techniques (Other), i.e. radiophotoluminescence (RPL), direct ion storage (DIS) or active personal dosimeters (APD). A total of 3090 dosimeters were handled by the coordinator of which 2266 dosimeters were irradiated. All irradiations were carried out by selected metrology laboratories, VSL and Seibersdorf Labor GmbH, accredited to EN ISO/IEC 17025. Out of the total of 103 systems, 85 reported both HP(10) and HP(0.07) and 18 reported HP(10) results only. In general, the participants showed a satisfactory performance with only 6% outliers for the dose quantity. HP(10) from the total reported values 55% systems had no outliers from the “trumpet curve” criteria. 87% of the systems fulfilled the ISO 14146 performance criteria (max. 2 outliers are allowed).

3.1.2. Special Intercomparisons

In addition to the regular (every 2 years) photon whole body dosimetry intercomparisons for IMS, several intercomparisons for passive area dosimeters, calibration methods in passive dosimetry, extremity dosimeters in photon and beta fields, whole-body dosimeters in neutron fields,

environmental monitoring systems, Monte Carlo modeling, Early warning Dosimetry Network Systems and on internal dosimetry have been organised only infrequently.

The organisational scheme of the intercomparisons of extremity dosimeters in photon and beta fields, or the whole-body dosimeters in neutron fields are very similar to the procedure described in the previous section. In short: (i) the participants (IMS) send their dosimeters to the organizers, dosimeters are sent to accredited calibration laboratory, which (ii) returns them to IMS with the irradiation certificate. Organisers sent back the irradiated dosimeters (iii), informing IMS on the irradiation date and sometimes, in special cases, on some important irradiation conditions (iv). An important element of the entire intercomparison is the final meeting with participating IMS (v), where organisers present details of the irradiation and anonymised results of all participants are presented. Such a discussion is intended to help IMS to improve their performance. The final step (vi) of the EURADOS intercomparison is the publication of results, which allows, e.g. to document the performance of the dosimetric systems over longer periods of time. The major difference in the intercomparison of the passive area dosimetry systems performed by EURADOS in 2021 was that all dosimeters were irradiated simultaneously, in two specially prepared irradiation fields: outside and in the normal office. However, all other key elements of the system, remained similar.

3.1.2.1. Facility Intercomparisons

Most of the intercomparisons organised by EURADOS was directed towards Individual Monitoring Services (IMS) to allow them for an independent quality assurance of their dosimetric systems. Only recently EURADOS organised, in collaboration with IRSN, BfS, CIEMAT, a unique intercomparison of performance of whole-body counters (WBC) in Europe. Whole Body Counters are instruments (facilities) used to identify and measure the radioactive material, primarily gamma-ray emitters in the body of humans. It was organised between October 2019 and June 2022 and dedicated to whole-body measurement of gamma emitters in several tasks selected that cover the range of such possible measurements associated to different intake scenarios. One of the objectives of the intercomparison was to simulate measurements that are relevant for the occupational monitoring program of individuals exposed to intakes of gamma emitters at the workplace. In total, 43 WBC installations from 21 countries took part in the intercomparison exercise.

The intercomparison consisted of the 3 main steps:

- Preparation of the phantoms and radioactive sources
- Organisation of the phantoms transport to WBC installations
- Evaluation of results

The intercomparison has been carried out using anthropomorphic Saint-Petersburg brick phantom equipped with sealed radioactive sources. The use of such phantoms is a common method for the calibration of whole-body counters and the examination of their proficiency. These phantoms are an unofficial de-facto standard that is used worldwide by many laboratories for their calibrations and that is considered an appropriate method for calibration also by ICRU [ICRU 1992, ICRU 2003]. The key element for setting up the intercomparison was preparation of a set of sealed radioactive sources with well -known activities. In the intercomparison the following sources were applied: ^{60}Co ^{68}Ge ^{88}Y ^{133}Ba ^{134}Cs ^{137}Cs ^{152}Eu ^{40}K. All the sources underwent a strict quality control involving measurement of each single radioactive rod with an HPGe gamma-spectroscopy but also measurement of phantoms equipped with a whole set of sources in whole-body counters of the organisers of the project.

The transport of phantoms took place in two ways: supervised transport (25 WBC) and the remaining phantoms transported by shipment. Principal point for the decision between attended transport or shipment were: the distance, prospective traveling time, the accessibility (possibly also of nearby facilities), temporal availability and an in-line connection of the institutions in one of the tours. An additional factor, which had to be taken into account by organizing the transport, was the custom formalities since some of the participants were outside the EU.

The final step of the intercomparison was the evaluation of results. The quality of most of the participating laboratories was found independent from the metrological and organisational characteristics. The dispersion of the results within each investigated property, e.g. determined activity, was stronger than the difference between different properties. Therefore, attributable differences of these properties were found small. WBC with NaI(Tl) detectors reported results that did not differ significantly from those with HPGe detectors, showing that the use of NaI(Tl) detectors is still justified despite the trend of the last years to use HPGe detectors.

3.1.2.2. Simulation Intercomparison Exercise

The recent EURADOS intercomparison exercise [EURADOS-2024] on simulation of gold nanoparticles irradiated by kV x-rays has evaluated the variability of the results of the different MC codes used by the participants. Seven different MC codes have been adopted for the (conceptually simple) simulation of one gold nanoparticle (GNP) irradiated in water by kV x-rays, in a simple well-defined geometry.

The GNP represents an interesting material to assisted radiation therapy thanks to their combined properties of biocompatibility, strong photoelectric absorption coefficient and emission of Auger electrons. Experiments on GNP have shown rather ambiguous results due to the different assumptions, competing processes (physical, chemical and biological) and variability of simulations.

Given well-defined geometries (far from realistic clinical conditions) and x-ray spectra, the participants had to determine by their simulators of each combination of geometry and photon spectrum the dose enhancement ratio on specific water shells (mimicking cellular targets) around the GNP, and to report the electron spectra emitted by the GNP and the electron depositions in water shells around it.

The results of the different simulations were compared showing a significant variability; some of this variability was partially mitigated by fixing geometry deviations and wrong simulation settings. However, the remaining large variability in the low-energy electrons region confirmed the critical impact of different physics models, cross sections, cut-off energies and other simulation choices, despite the simple geometric conditions.

The conclusions of the exercise pointed out the importance of a quality assurance of Monte-Carlo simulators and the gained experience suggests that: description of exercise shall be clear and well written by a team of experts and expected quantities to be reported clearly defined, including units; pre-testing the exercise setup is essential to identify potential ambiguities; for efficient analysis a reporting template (or reporting format) shall be provided to the participants; define criteria for the analysis of the delivered results.

3.2. EURAMET/Metrology

EURAMET is the Regional Metrology Organisation (RMO) of Europe (EURAMET - European Association of National Metrology Inst). It brings together institutes in Europe who maintain national measurement standards.

Therefore, National Metrology Institutes (NMIs) of the member states of European Union and of the European Free Trade Association are members or associates of the EURAMET network.

The other NMIs non-EU states included in EURAMET shall fulfil the following requirements:

- *traceability routes to the SI identified and in operation for the last three years*
- *participation in international comparisons*
- *participation in EURAMET projects*

EURAMET mission is "*to develop and disseminate an integrated, cost effective and internationally competitive measurement infrastructure for Europe. Always taking into account the needs of industry, business and governments. With the services EURAMET supports its members to meet their national requirements and to establish a balanced European measurement infrastructure. To enhance benefits of metrology to society is one of the highest priorities for EURAMET and its members*". In this respect the EURAMET comparison initiatives represent an essential reference, especially in terms of structure, preparation, execution and outcome exploitation and are therefore described in more details in the present document.

EURAMET works to this mission through several tools, the main of which are research programmes and scientific and technical cooperation.

Research programmes are co-funded by the Member States and the European Union. They are: European Metrology Research Programmes (EMRP, 2009-2013), Metrology Programme for Innovation and Research (EMPIR, 2014-2020), and Metrology Partnership (2021-2027). The last research tool aims to *support accelerating the transition towards a green, climate neutral and digital Europe, as well as strengthening the resilience, competitiveness, and economic growth of the European industry*.

The scientific and technical cooperation activity carried out by EURAMET, is organised through Technical Committees (TCs). 10 TCs on specific topics and 2 TCs deal with the overall topics concerning Quality and Interdisciplinary Metrology are active. The areas/fields in which the 10 TCs operate/work are:

- Acoustics, Ultrasound and Vibration
- Electricity and Magnetism
- Flow
- Ionising Radiation
- Length
- Mass and Related Quantities
- Metrology in Chemistry
- Photometry and Radiometry
- Thermometry
- Time and Frequency

The activities of the TCs are organised/structured in TC projects that involve:

- Cooperation in research: projects between EURAMET members, which are not funded by the European Metrology Research Programmes.
- Comparison in measurement standards: comparisons can be Key Comparisons (KC), Supplementary Comparisons (SC) or Pilot Studies.
- Traceability: documentation of agreements between EURAMET members (formal or informal) for provision of metrological traceability. There is no standard procedure describing this type of collaboration.
- Consultation on facilities: consultation projects are knowledge transfer activities between EURAMET members. This project type comprises, among others, direct consultation among NMIs/DIs, expert meetings, training courses and workshops, peer reviews of Quality Management Systems within TC-Q, studies, preparation of guidance documents, drafting and revision of calibration guides.

EURAMET does not provide funding for TC projects; each partner has to provide their own resources. Project partners may search for third-party funding or make other financial arrangements between them.

3.2.1. Technical Committees objective and Scope

As a duty of RMO, EURAMET conducts its activities for the fulfilment of the Mutual Recognition Arrangement of the International Committee of Weights and Measures (CIPM-MRA). This activity comprises:

- Intra-RMO review and submission of the Calibration and Measurement Capabilities (CMCs) of EURAMET Members and Associates
- Inter-RMO review of CMCs of other RMOs Proposal of RMO Key and Supplementary Comparisons and support of their conduct
- In the case of TC-Q, review and providing formal acknowledgement of the Quality Systems of EURAMET Members and Associates
- In the case of TC-IM, development of a EURAMET position regarding issues related to the CIPM-MRA

In addition, the TCs contribute to the Research Programmes (EMRP, EMPIR, Metrology Partnership)

3.2.2. EURAMET Comparisons

In the following, we will focus on EURAMET comparisons, considering the various categories and types of comparisons and their purpose.

Several types of comparisons can be carried out in the framework of the TC activities:

- Key Comparison
- Supplementary Comparison
- Pilot Study
- Hybrid Comparison

Key comparisons are selected by a Consultative Committee (CC) of the CIPM to test the principal techniques and methods in the specific CC field. This kind of comparisons results in a key comparison reference value (KCRV) that represents the reference value for a KC carried out by an RMO; it must follow the same protocol as a preceding CC-KC and will provide the link to the respective KCRV for the participants from the RMO (or other RMOs). It must be approved in advance as KC by the corresponding CC or CC Working Group. An RMO-KC may be launched while the corresponding CC-KC is still running.

Supplementary comparisons are comparisons, usually carried out by CCs and RMOs to meet specific needs not covered by a KC, for instance measurement of specific artefacts, quantities, or measurements of parameters not within the "usual" scope of the CC.

Pilot studies are a third category of comparisons normally undertaken in the CIPM framework to establish confidence in measurement for a new field or instrument, or as a training exercise.

The pilot study is used in EURAMET for all type of comparisons not being KCs or SCs.

Specific purposes of a pilot study may be:

- Testing of new instruments
- Testing of new methods or methods at an early stage
- Preparation of a KC
- Training for emerging NMIs
- Benchmarking of an NMI, in particular if it has never participated in a KC or SC before
- New metrology fields or quantities, where no CMCs are to be supported now or in near future.

Hybrid Comparisons can be used when the time interval between a KC or SC is very long or in the case of some simple calibration services where no KC or SC has ever been conducted. In the case of an HC the difference between the measurement result obtained by the NMI/DI submitting a CMC claim and the result of a routine calibration provided by the other NMI/DI can be used as supporting evidence in a similar way to the use of the degree of equivalence (DoE) from a comparison. These comparisons are not registered in the KCDB.

Participation in EURAMET comparisons is open, in principle, to all members of EURAMET, National Metrology Institutes (NMI) or associated Designated Institutes (DI), provided the technical competence of the institute is appropriate for the particular comparison.

In the case of EURAMET KCs and SCs, the participation should, in general, be restricted to NMIs and DIs, in line with CIPM rules. For EURAMET Pilot Studies more flexibility is given.

In exceptional circumstances and in particular for PS, participation of expert guest laboratories may be appropriate. Their participation should not conflict with the national interest of the corresponding NMI or DI participating in the TC.

3.2.3. Ionising Radiation Technical Committee

In this section we focus on the activities of the IONISING RADIATION TC (TC-IR)

Technical Committee for ionising radiation

The Technical Committee for Ionising Radiation (TC-IR) is concerned with the metrology of ionising radiation related to medical, industrial, environmental, scientific and radiation protection applications. According to the type and nature of ionising particles and quantities required to measure, radiation dosimetry and radionuclide-/neutron measurements are the main subfields.

The fundamental SI quantities and units are the

- Particle Fluence, Φ (m^{-2})
- Activity, (Bq)
- Kerma, K, (Gy)
- Absorbed Dose D, (Gy)
- Dose Equivalent, H, (Sv)

74 projects (since 1988) are reported as activity of the TC-IR on the EURAMET website (https://www.euramet.org/technical-committees/tc-ir/projects), 47 of which concern comparison projects.

The following documents describe how the TC comparison activity has to be conducted, the rules to be followed and the requirements to be fulfilled to participate. They are common for all TCs.

- EURAMET Guide No. 4: Guide on Comparisons
- Eligibility Criteria for the Participation in EURAMET TC Projects
- EURAMET Guidelines for TC Projects

It is worth to highlight that the relevant rules for TC comparisons are those defined in the CIPM-MRA-G-11 “Measurement comparisons in the CIPM MRA” [CIPM-2021] that represents the master document which EURAMET TCs follow. The other documents can be more detailed and specific for a given topic.

All pieces of information here reported have been extracted from the cited documents.

Roles and responsibilities in the TC comparisons

In the preparation of comparisons, roles and responsibilities should be assigned in a way, that an effective implementation of the comparison is ensured, and that workload is shared among participants in a fair and the best viable way.

Technical Committees, Subcommittees, TC Chair

The TCs have the responsibility to identify the needs for comparisons through consultation of the EURAMET members or by other means. They shall discuss relevance, priorities and modalities of the proposed comparisons and decide on those to be carried out and on their time schedule.

The TC Chair has the responsibility to coordinate and oversee the whole process and to ensure that the comparison is in line with EURAMET policies and properly agreed with the TC.

The TC Chair might delegate part of his/her responsibilities to a Subcommittee Convenor or another TC contact person, ensuring, however, their proper conductance. Registration of a comparison and submission of reports to a CC or a CC working group should in any case be done by the TC Chair. In the

case on HCs, the TC Chair could act as the Third Party or delegate this role to another TC/SC contact person not belonging to the applicant NMI or the issuing NMI.

Pilot laboratory

When agreeing on a comparison, one of the participant laboratories must be assigned the role of coordinator, called pilot laboratory.

The pilot laboratory has the principal responsibility for:

- specifying the group of participants,
- drafting the technical protocol in consultation with the participants and the TC Chair,
- the registration of the comparison in the EURAMET TC database and in the KC database (KCDB) (if applies), by filling the templates, and providing them to the TC Chair,
- organising the preparation of the transfer standard(s) and its/their circulation among the participants,
- collating the measurement results of the participants,
- giving follow-up at all stages and reminding delayed participants on their outstanding duties,
- consulting the TC Chair in case of major issues like significant delays, damage or loss of a standard, etc.,
- preparing annual progress reports for the TC meetings and the TC project database,
- evaluation of the comparison results,
- link of the results to the KCRV (in case of a KC),
- preparing the subsequent reports after concluding the measurements (Draft A, Draft B, Final Report, Executive Report if needed).
- uploading the final report of the comparison onto KCDB once this has been approved by the body in charge.

Link laboratories

In case of a EURAMET KC, at least two of the participants, where possible, should have participated in the preceding CC KC, in order to allow a proper link of the comparison results to the KCRV.

Participants

Before agreeing to participate in a EURAMET comparison, the laboratory must make sure that

- it has the technical competence to handle the transfer standard and to do the measurements as described in the protocol,
- it has the capacity to carry out the measurements within the foreseen time schedule,
- resources are available for a proper transport of the transfer standard to the next laboratory.

A laboratory is expected to participate in a EURAMET KC (or alternatively in the corresponding CC KC), in case it has published CMCs (calibration measurement capabilities) related to this KC.

The participating laboratory must accept that their results are published in the final report of the comparison, even if they are not satisfactory for the laboratory.

The participants confirm that they accept these conditions by signing the corresponding EURAMET form.

Initiation of a comparison

EURAMET TCs set up and maintain a long-term plan of the KCs and SCs of their area, in line with the guide on “Strategic planning of comparisons in EURAMET TCs”.

It is recommended to propose new comparisons in advance to the meeting of the TC, as this will enable the contact persons to consult the management of their institute prior to this meeting. This consultation is important to reach agreement about the involvement of the institute in the comparison and, if so, to guarantee that the required resources and time needed to undertake the work will be made available.

At their annual meetings, the TCs shall discuss and examine the actual needs for comparisons and priorities.

The decision on the comparisons as such and on their modalities is taken by the TC, normally at its plenary meeting. In exceptional cases and in particular for Pilot Studies, it might also be discussed and decided in between annual meetings by correspondence.

The status of comparisons is defined as:

- ‘in progress’: when a project was agreed by the respective TC and has started
- ‘ongoing’: project with continuous or periodic activities, without a fixed end
- ‘completed’: when the work programme has been carried out and results have been
- achieved
- ‘concluded’: when the project was terminated without being completed

To avoid workload of the participants and pilot labs in general the comparisons do not exceed three years from the start to their completion.

Agreement on participants

In principle, participation in a EURAMET comparison is open to all member NMIs of EURAMET and associated DIs, provided the technical competence of the institute is appropriate for the particular comparison.

If a member of EURAMET or an external laboratory expresses interest in participating in a comparison that has already started, the pilot laboratory must consider the effect of this participation on the time schedule. The a priori assumption should be that the additional participant should not extend considerably the duration of the comparison. If all the participants agree, then the new participants’ entry can be accepted.

Otherwise, it is left to the pilot laboratory or to any other interested participant to go to a bilateral comparison with this laboratory once the comparison is completed.

Technical protocol and preparation of the comparison

The pilot laboratory has the responsibility to submit the technical protocol, which can be drafted by a member of the coordinating group in consultation with the participants and the TC Chair and supported by the coordinating group.

The technical protocol has to be drawn up in line with [CIPM-2021] sections 3 and 4. It must contain at least the following information (when applicable):

a) Introduction on the subject and exact definition of the measurand(s) of the comparison
b) Description of the scheme/topology of the comparison (A comparison may range from the simple circulation of a single transfer standard around all the participants to the sending of an individual transfer standard directly to each participant from the pilot institute, or from each participant to the pilot institute or any combination of these ([CIPM-2021] sec. 4. & 4.1)
c) Stability / homogeneity check of the transfer standard, i.e., via measuring the standard at least in the beginning and the end by the same laboratory (In case of "Certified Reference Materials" (CRMs) in some fields, "standard" may refer to "sample", "solution", "material" or "source").
d) Time schedule, in particular starting date and envisaged date of completion.
e) Description of the transfer standard(s): make, type, serial number, technical data needed for operation, stability statement, etc. In the case of a HC the transfer standard is chosen to assure that the applicant NMI/DI (i.e., the NMI/DI seeking for CMC evidence) has no previous information about its performance.
f) Advice on handling and organising the transport of the transfer standard.
g) Tests to be carried out before measurements.
h) Handling precautions of the transfer standard(s) at receipt and during measurements.
i) Description of the used calibration method, measurement conditions and calibration points.
j) Indications for the presentation of the results (e.g., format, conformity with published CMCs)
k) List of the principal components of the uncertainty budget with indication of the final combined uncertainty.
l) Timetable for communicating the results.
m) Principle of evaluation of the results and linkage mechanism to the corresponding KCRV, if applicable. For HC in which the applicant NMI/DI has traceability to the issuing NMI/DI (the NMI/DI which performs the comparison based on its routine calibration service) a study of the correlations between measurements should be performed.
n) Financial aspects, e.g., transportation or costs for transfer standard if applicable.
o) Reference to useful documents.

Furthermore, possible custom issues should be discussed before starting a comparison and custom documents to accompany the transfer standard should be described in the protocol, if applicable.

A EURAMET key comparison must basically follow the same protocol as a preceding CC key comparison. A restricted scope for individual participants is admissible, if the participant is not able to deliver all measurement points of the protocol.

The circulation time of transfer standards or transfer instruments must be fixed and may exceed eighteen months only in exceptional circumstances. Options to cope with a large group of participants in case of round-robin comparisons should be analysed, for example organising two or multiple parallel loops with linking laboratories measuring the transfer standards of both loops.

In case of key and supplementary comparisons to be registered in the KCDB, the pilot laboratory shall send the draft protocol via the TC Chair to the appropriate CC working group for approval (in case of KC) or information (in case of SC). The KC must be compatible and linkable to the parent CC comparison.

The pilot laboratory sends a formal invitation to all members of the TC and concerned Subcommittees and the envisaged external participants, with a deadline for confirmation of the participation, using the proper template. Having received the confirmations from the participating laboratories, the pilot laboratory draws up the final circulation scheme for the transfer standards and the time schedule.

In the case of comparisons not registered in the KCDB, the comparison protocol should be reviewed by the TC Chair.

Registration of each comparison always will be done in the TC database.

Only KCs and SCs can be registered in the KCDB.

The nomenclature for KCs and SCs registered in the KCDB is described in [CIPM-2021] sec. 5.1; EURAMET Pilot Studies for the cases described in Section 2.1 are not registered in the KCDB. Once a comparison has started as PS, it cannot be "upgraded" to a KC or SC.

Comparison Toolbox

A EURAMET web portal is available to support TCs and pilot laboratories in the organisation and management of measurement comparisons.

3.2.4. Conducting a Comparison

Performing the measurements

The pilot laboratory is responsible for organising the transport of the transfer standards or instruments and has to ensure that the participants make proper arrangements for local customs formalities. This includes also handling instructions for the equipment at the customs office.

For circulating the transfer standard, there are several options, for example:

a) Each participant organises the transport to the next participant on his own responsibility and costs.
b) A company is hired to organise the circulation centrally. A corresponding fee should be paid by the participants to cover the costs. Hence, in this way administrative complications are avoided for the participants.

Participants must strictly follow the technical protocol. In case of problems, they have to consult the pilot lab before the measurements are carried out.

If the lab is not able to carry out the measurements in the due time, according to the pilot lab and comparison participants the schedule can be rearranged without change in the comparison timeframe. Otherwise, a bilateral comparison with pilot lab or other participant can be considered after the main comparison is completed.

For complete transparency, the pilot laboratory may consider submitting their results to some independent party, e.g., the Secretariat, ahead of receiving results from other participants.

Dealing with delays and other issues

The following table from EURAMET Guide [EURAMET-N4], pg 15, summarises the corrective measures taken in case of specific issues.

Issue	Corrective measures
Measurements are not performed properly, but issue is reported by the laboratory	- Laboratory gets the opportunity to repeat measurements at the end of the loop, if feasible and if all other participants agree. - Exclusion of the laboratory from the comparison, if issue cannot be resolved.
Measurements are not performed within time schedule / transfer standard is not sent to the next participant	- Pilot lab sends reminder. - If laboratory is not responding, it will be excluded from the comparison after a final alert to laboratory and Delegate.
Transfer standard is damaged or shows stability issues	- Replacement and linkage to original standard, if possible. - Replacement of standard and repetition of all measurements.
Measurement results are not sent to the pilot lab within deadline	- Pilot laboratory sends reminder. - If laboratory is not responding, it will be excluded from the comparison after a final alert to laboratory and Delegate.
Pilot lab is delayed in preparing the report	- Support group offers support to pilot laboratory. - TC-Chair consults TC if a further participant can support. - TC-Chair suggests, after consultation of the participants, to pass the responsibility for preparing the report to another participant.

3.3. IAEA

The International Atomic Energy Agency is the intergovernmental organisation for scientific and technical cooperation in the nuclear field, promoting safe, secure and peaceful use of the nuclear energy and technology worldwide. IAEA is involved in several intercomparisons exercises which aim to promote harmonisation and standardisation, in particular for internal dosimetry.

3.3.1. Dosimetry Audits

Since 1969 IAEA and WHO collaborate to provide dosimetry intercomparisons (called more generally audits) for the validation of radiotherapy beam calibration in developing countries.

The IAEA is responsible for the technical aspects while the WHO selects and coordinates the participation of the hospitals and the distribution of the dosimeters; participation to the audit is cost free. Other international and national institutions and networks are also involved in the audits preparation and running.

Audits are organised annually into 8 irradiation runs; by 2000 the audit program has served more than 3300 radiotherapy beams world-wide [Izekwsa-2000].

The quality audits consist in the postal distribution of Thermoluminescence Dosimeters (TLD) to radiotherapy centers (initially ^{60}Co, then high energy photons beams); the dosimeters are capsules (black polyethylene cylinder of about 20 mm inner length and 3 mm inner diameter, 1 mm wall) of lithium fluoride powder properly annealed.

The centres that receive the TLDs (together with instructions) are required to irradiate the dosimeter in a water phantom using the same procedure for a patient irradiated during clinical practice.

The TLDs (with information on the absorbed doses to water) are sent back to the IAEA Dosimetry Laboratory where they are read out by a reference automatic reader.

Results of the measured doses are analysed taking into account all sources of uncertainties and correction factors (e.g. powder homogeneity, fading, ...). disseminated to solve discrepancies and improve the quality of the radiotherapy beams.

The acceptance limit between measured and hospital stated doses is +/- 5% (compatible with the dosimetry uncertainty). A value outside this limit triggers an investigation procedure: the hospital is informed of the discrepancy (but the actual value not reported) and asked to identify the source of the discrepancy, providing a second TLD check. If the problem persists an IAEA expert is available to support the hospital in solving the discrepancy.

In 2017 the TLD has been replaced by Radio-photoluminescence dosimeter (RPLD), which is expected to provide improved reading efficiency, sensitivity and re-usability. The RPLD with a dedicated holder that simplifies the correct position at the reference depth in the water tank phantom for electron beam irradiation [Dimitriadis-2023].

Remote beam quality audits are carried on also by other national and international organisations as described in the review [Kry-2018] where 0.63% of the analysed 210167 audits results have been found outside the 5% tolerance. The study confirms that the calibration of an electron beam is more critical than a photon beam and depends on the beam energy. Moreover, the reduction of the out of tolerance cases with time and therefore better beam calibrations are supposedly associated with improvement of the medical physicists training since calibration protocols have not significantly changed during the same period.

3.3.2. Network of Secondary Standards Dosimetry Laboratories (SSDL)

Since 1981 the above dosimetry audits have been extended within the SSDL network [IAEA-SSDL]; the IAEA offers to their members a service of intercomparison, related to radiation protection, external beam radiation therapy and diagnostic radiology.
In bilateral comparisons, IAEA send a calibrated transfer ionization chamber which is recalibrated by the participating laboratory according to their specific procedure. IAEA dosimetry laboratory evaluates the comparison results and prepares a report. If the result is not within the acceptance limits, the IAEA works with the participating laboratory to resolve any discrepancies.
The IAEA Dosimetry Laboratory participates also in intercomparisons organized by regional metrology organisations, to qualify the calibration and measurement capabilities of the IAEA Laboratory.

Information on intercomparison and related activity of the IAEA Dosimetry Laboratory and SSDL networks are available on the SSDL web site [IAEA-SSDL] (see also the newsletter section).

3.4. Radioecology related inter-comparisons

Two classes of intercomparisons are generally considered within the radioecology initiatives such as STAR (STrategy for Allied Radiecology), COMET projects on the ALLIANCE platform [ALLIANCE]: the proficiency test exercises to quantify the anthropogenic, natural radionuclides in water, soil and simulated contaminated samples and the comparisons of radioecological models which describe the transfer of radionuclides, dose to humans and/or biota.
Annual proficiency test exercises are organised by the IAEA Terrestrial Environmental Radiochemistry Laboratory within the ALMERA (Analytical Laboratories for the Measurement of Environmental Radioactivity) Network which consists of 200 laboratories (in 2023) from 90 countries. As coordinator IAEA supports also the development of standardised methods for sample collection and analysis and organisation of periodic interlaboratory comparison exercises [IAEA-ALMERA]. The tests and intercomparisons are designed to evaluate performance and analytical capabilities of the participating laboratories and identify potential, problematic areas where improvement is needed.

The typical proficiency test for the determination of radionuclides in sea water consists of (see [IAEA-RML-2016] for details):

1. distribution of sample water (5L) spiked by IAEA with specific radionuclides (e.g. 3H, 90Sr, 134Cs and 137Cs) whose massed activities (from fraction to slightly above 1 Bq/kg) are traceable to a standard provided by a certified Metrology Institute;
2. participants quantify the massic activities of the specific radionuclides including uncertainties;
3. participants are required to submit the quantification results together with description of the analytical method used for the sample analysis, type of calibration and software used for gamma spectroscopy, nuclear data used;
4. performance analysis by IAEA following predefined criteria.

Other main intercomparison line on Radioecological models have been organized under different IAEA programmes; typical number of participants (from all around the world) around 10-15; participation is free, no funding for meeting attendance.

Within the environmental radioprotection context, it is worth mentioning the intercomparisons organized by the Nordic Nuclear Safety Research forum and networking organisation (www,nks.org) on laboratory analyses of radionuclides in environmental samples and food. In the exercise published in 2006 [Nielsen-2006] samples of different type and origin (with one certified reference material from IAEA), with gamma emitting radionuclides homogeneously distributed with statistical counting uncertainty between 1 and 6%, where delivered to the laboratories for the measurement of the relative activities of the different radionuclides. The evaluation of the exercise considered as basic quantity the relative deviation from the median across all laboratories for each radionuclide (z-score) with a target of 10% standard deviation. The intercomparison results showed margin of improvement for the analytical quality of most laboratories and poor agreement for total alpha and beta radioactivity in lake water (impacting on drinking water screening).

Intercomparisons of models that estimate radionuclide activity concentrations in non-human biota have been conducted before and after the Fukushima accident, by IAEA and other organisations, in different scenarios, e.g. using transfer parameters [Beresford-2008] or complex metabolic dynamic models [VivesIBatlle-2016], which seem to represent the most critical factors affecting the variability of the comparison results.

3.5. RENEB and biodosimetry

The "Realising the European Network for Biodosimetry and Retrospective Physical Dosimetry" European network and the next related association "Running the European Network of Biological and retrospective Physical dosimetry" (RENEB) aim to provide a "rapid, comprehensive and standardised methodology for individual dose estimation" in case for large scale radiological emergency events. This goal requires to ensure an high quality of biodosimetry services across the associated laboratories, following international standards and organizing inter-laboratory comparisons.

Since 2013 RENEB has organized several inter-laboratory comparisons essentially based on the (blind) analysis of ad-hoc exposed reference sample essays for the identification and quantification of biological, molecular or physical changes induced by the radiation, with prevalent (but not exclusive) focus on detection of cytogenetic changes, where the Dicentric Chromosomes analysis (DCA) represents a sort of "gold-standard" of biodosimetry technique [RENEB-2023].

Therefore, the RENEB intercomparisons specifically involve the Processing Platforms that have the possibility to perform biological, molecular or physical analyses on samples.

Once the intercomparison has been designed in detail, the laboratories have been recruited and the plan consolidated, the typical intra-laboratory intercomparison essentially runs through the following steps:

1. Preparation of samples
2. Timely shipment and shipment perturbation
3. Laboratories measurement of the delivered samples
4. Laboratories (statistical) analysis of the measured quantities
5. Collection of the results by RENEB, including ancillary data such as quantitative information on the calibration curves used by each laboratory and procedure of analysis of the data
6. Analysis of the collected results by RENEB
7. Distribution of the results
8. Feedback from laboratories
9. Interpretation of the results

In the recent inter-laboratory comparison [RENEB-2023], some unique approaches have been adopted, which present rather general relevance and may have positive impact in the organisation of the future PIANOFORTE intercomparisons:

1. In parallel comparisons of different dosimetric technologies for cytogenetic assays, molecular biology and physical dosimetry assays;
2. opportunity to participate by laboratories external to the RENEB association;

3. samples were delivered to the participating laboratories and the same time providing the possibility of improvements when inconsistencies where identified (similar to the NKS-RESINA evaluation described in the next session);
4. consider simulation also of worst-case situations which can suggest possible improvements.

Within PIANOFORTE, the possibility to exploit the effort of intercomparisons to improve potentially discordant situations or other kind of issues shall be considered as one of the main goals, providing appealing opportunities for platforms to enhance the quality of the offered services.

The RENEB experience on intra-laboratory intercomparisons has also shown the limits on the existing approaches [RENEB-2021], in particular related to the adopted statistical tools for laboratories results evaluation; these tools do not seem to be capable of taking advantage of the heterogeneous results of large intercomparisons (and different ways of harmonisation) and actually the two adopted statistical methods can lead to misinterpretations. Another issues, more directly related to radioprotection, is the use of laboratory-specific dose-effect curves whose robustness requires dedicated considerations and assessment, as part of the intercomparisons definition.

For further details refer to the RENEB web site [RENEB-Web], publications pages.

3.6. NKS – decommissioning radioactive waste examples

The Nordic Nuclear Safety Research forum and networking organisation (www,nks.org) has recently reported on intercomparison exercise on difficult to measure alpha radionuclides in radioactive waste sample (spent ion exchange resin) within the RESINA project [RESINA-2023], a continuation of previous radiochemical analysis-based exercises on beta and gamma emitters from the same type of sample. These intercomparisons require a preliminary efficient purification of the radionuclide of interest since other interfering radionuclides may impact the alpha spectra analysis and a careful preparation of the sample where the radionuclides are deposed on thin layer.

The evaluation in RESINA has been carried on following the recent ISO 13528:2022 “Statistical methods for use in proficiency testing by interlaboratory comparison" and assessed using the z-score as in other comparisons. The radionuclides to be measured were selected by the participants in a kick-off meeting. In an intermediate meeting the preliminary results and encountered difficulties were discussed. This offered the opportunity to the participants to apply corrections, tune their methods, and carry-on new measurements before the final evaluation.

3.7. Bio Banks

In the context of radioprotection research, and more generally research on medical application of ionising radiation, biobanks represent an important sub-class of facilities; harmonisation of quality procedures in these facilities are generally guaranteed by the application of specific standards.

Cross-validation initiatives where reproducibility of new findings is validated using samples from different biobanks, somehow replace the intercomparisons approaches described above which are not easily transferable to biobanks; this section does not describe biobank intercomparisons (which was not found on the consulted literature) but try to summarise the main aspects of biobanks and their peculiarities.

A research biobank is a repository dedicated to storing and handling of samples (biospecimens) of various kinds (e.g., plant, microbe, and biological materials, usually human) for use in research (and medical purposes).

In recent years, biobanks have become a valuable resource especially for preclinical and clinical research, supporting areas such as genomics and personalised medicine. For this reason, structural and management organisation has become increasingly defined and organised; in fact quality biological material is an essential prerequisite for reliable biological research.

In other areas, such as in radiation protection, however, biobanks may require further consolidation and improved structure. An initial attempt to collect various types of infrastructures of interest in the area of low dose and low dose rate research was made by the three working groups formed within WP6 of CONCERT.

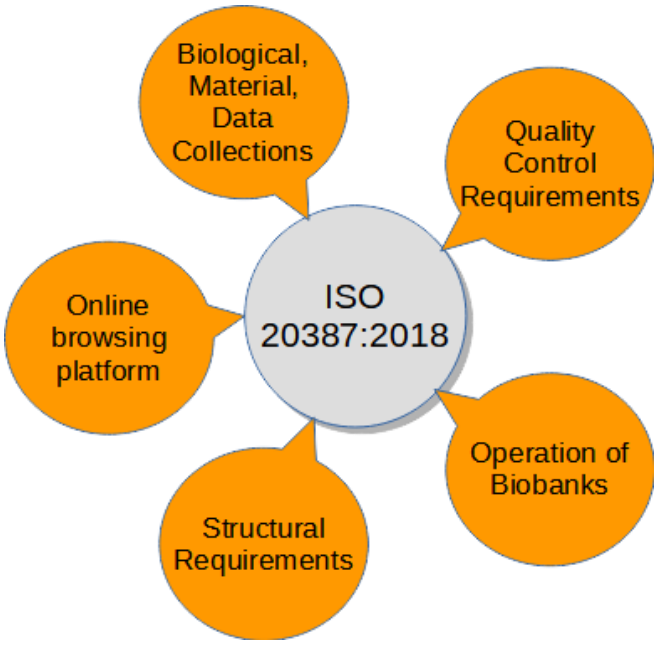
The typical activities of a biobank involve the collection, preparation, handling of samples, analysis, quality control, conservation and distribution, management and preservation of the data associated with them.

Some of the key information that characterise a biobank are identified by:

- exposure scenario
- type and method of sample storage and preservation
- quality control protocols
- data associated to the samples (e.g., dosimetric data)
- availability of a user guide for requesting/accessing samples
- name of the biobank manager and contact details

One aspect that biobanks shall face is related to the GDPR regulations that may restrict fruition of samples; in fact, there is an urgent need to solve problems related to privacy and research ethics. Instruments should be found at the regulatory level to enable biological samples deposited in a biobank to be used for purposes other than those for which they were stored and in the event of the death of the person who authorised their storage.

The UNI-ISO standard [UNI-ISO-20387] represents the main standard on Biotechnology – Biobanking for human, veterinary and environmental research biobanks with no specific considerations on radiation-related biobanks; the standard has benefited of the integration of the existing heterogeneous guidelines on the biobank sector. The document [ISO-TR2020] is a guide to the implementation of the UNI-ISO 20387 standard whose content is sketched in the following scheme. The standard includes specific requirements for validation and verification of the processing procedures.



Radiation protection research related biobanks shall maximise samples integrity which can be facilitated by the following quality assurance technical aspects:

- sample collection and handling: should be defined by appropriate and detailed protocols for sample collection, processing, storage and retrieval;
- traceability: Samples shall be tracked in all above steps and adequate metadata on sample including exposure history, collection, processing and storage conditions, taking into account any applicable regulation on data privacy.
- environmental stability: optimise environmental condition (e.g., temperature and humidity) for preserving (radiobiological) samples (common to any biobank), minimizing at the same time the exposure to additional radiation of the stored samples.

Any (hypothetical) biobank intercomparison should take into account the ISO 20387 standard.

4. Fostering harmonisation protocols between infrastructures

The above review suggests that several intercomparisons related to radiation protection research are adequately covered by existing networks, organisations, platforms …; most of the approaches adopted by these intercomparisons either have several common general aspects that can be considered as the benchmark standard for intercomparison protocols or use consolidated standards.

PIANOFORTE shall continue to co-operate with the above organisations and networks to foster regular, periodic (depending on the type) intercomparisons. Furthermore, PIANOFORTE WP5 is developing a plan for PIANOFORTE to collaborate with various organisations/owners of facilities/infrastructures to conduct periodic intercomparison and harmonisation activities to assess and compare their performance, protocols and capabilities, so that such infrastructure network can support RP research. The ultimate aim will be to identify approaches that will make those intercomparisons sustainable beyond the PIANOFORTE partnership. Specific calls could be implemented to gather new ideas on these aspects.

On the other hand, the recently organised WP5 workshop (Jan/2024, https://agenda.infn.it/event/39062/) has pointed out or reiterated some critical aspects (most of them emerging also from the above review) that may affect intercomparisons/harmonised protocols (paper under preparation):

Dose and dose rate: low and very-low dose experiments shall generally consider the level of background, its composition and energy distribution during the exposure and transportation of samples. This aspect is particularly relevant in cases of exposures to dose levels comparable to the natural background radiation. Indeed, the transport of the sample in terms of dose cumulated during the travel to and from the facility could largely affect the results, just as the waiting period, after exposure, before the sample analysis must be considered for proper investigation and in the comparison with other data.

Radiation quality: in radiation exposure, and especially for radiobiological experiments, the quality of radiation should be carefully considered, at least in terms of type and energy spectrum of the radiation field. Indeed, sensitivity of samples under investigations can be affected by radiation quality and comparison between data obtained by different beam qualities could be critical or not applicable.

Interplay between radiations (ionising and non-ionising): simultaneous exploitation of ionising and non-ionising radiation devices are becoming more and more frequent. The lack of systematic biological investigations on effects of combined non-ionising and ionising radiation may likely trigger new studies in this field, that in turn shall require to take into appropriate consideration different, interfering aspects (e.g., magnetic field versus radiation shielding).

Regularity of intercomparisons: frequency of suitable quality validation depends on the type and complexity of intercomparisons, the class of infrastructure where the intercomparison is applied, the effort that the organiser and participants can spend on them. Ideally a high frequency of intercomparison should guarantee a high-quality standard but may result in an unaffordable task.

Missing intercomparisons: quality standards of the infrastructure should provide to the researcher the appropriate parameters affecting the experimental activities, somehow mitigating the different sensitivity, cultural background and derived potential biases of the researchers. Examples are represented by reproducibility issues in ions and X-ray biological irradiation due to the missing

information on beam quality or the difficulty of comparing radiobiological results obtained on radiation with different Relative Biological Effectiveness (RBE). In fact, the correct evaluation of RBE remains challenging in intercomparisons because dedicated experiments are needed where conditions are well controlled.

Biodosimetry Intercomparisons: Emerging biodosimetry techniques, like analysing chromosomal aberrations in lymphocytes, should be compared for accuracy in measuring radiation exposure. These studies may involve irradiating biological samples with known doses and comparing the results obtained by different laboratories using the same biodosimetry technique. The multiscale approach mentioned above can be introduced to further assist the definition and analysis of this type of intercomparisons.

The next two sections try to provide some initial hints towards the improvement of these critical aspects, driven by an interdisciplinary view, which will be further addressed by PIANOFORTE during the remainder of the partnership.

4.1. Multiscale Approach

Radiation protection is intrinsically related to the physical, chemical and biological processes caused by radiation that occur at different spatial and temporal scales (several order of magnitudes involved); the descriptions, models and experimental results at different scales are and need to be interconnected [Solovyov-2024]. This multiscale approach has gained widespread consideration in the latest decades; it is becoming a key research topic (not only in radioprotection) also thanks to the availability of performant computation resources and it is expected to be impacted by the Artificial Intelligence (AI) methods in the coming years.

The Multiscale approach requires integration of competences (theoretical and experimental) from different disciplines which are mandatory for a comprehensive description of the relevant radiation protection aspects; such description can ultimately provide more accurate predictions of the effects of radiation in biological systems and materials (e.g., shielding).

Convergence towards a common multiscale framework, taking into account the uncertainties and limitations of each model adopted, may facilitate the validation and interpretation of the research findings and therefore improving their reliability and consistency.

This approach should be supported by adequate extended intercomparisons at different scales and between scale interfaces and probably require some new perspectives for intercomparisons definition, organisation, running and reporting.

In the multiscale approach for radiation protection, Artificial Intelligence may play a crucial role by enhancing data analysis, predictive modelling, real-time monitoring, and personalised protection where relevant. Intercomparisons of hardware (e.g., irradiation facilities or detectors), software (e.g. simulation), biomaterials response (e.g. biodosimeters), in the multiscale context shall begin to consider the application of AI and other new technologies – indeed it is crucial that activities in support

of harmonisation and standardisation keep pace with technological development in this and other areas.

On the other hand, the multiscale modelling can support the definition and implementation of the intercomparison by appropriate preliminary simulations and related analysis to define the more appropriate statistical tools and any other aspects that may impact in the intercomparison, and that simulation can bring to light.

4.2. Low dose harmonisation exercise

Epidemiological analyses have limits to detect risk at doses and dose-rates below 100 mSv and 0.1 mSv/min respectively and need to be complemented by radiobiological experiments. Reliable exposure infrastructures delivering low dose/dose rates are therefore needed. As already mentioned, in the framework of CONCERT many European low dose/dose-rate irradiation facilities have been described in AIR2 Bulletins and AIR2D2 data base.

In order to improve the harmonisation of low-dose research platforms and procedures, it is important to conduct intercomparisons between low-dose irradiation facilities, evaluating the effects on different types of biosamples. To extend the investigation to the effects of extremely low doses/dose rates, such as in underground facilities where very- or ultra-low doses/dose rates of radiation are naturally occurring or can be artificially controlled, can provide additional information relevant for improving the understanding of effects on living organisms and/or validating health risk models.

The aim of such intercomparisons is to verify if the results coming from different facilities can be pooled and all of them used in multi-centric studies. From a mechanistic point of view, possible differences in the results obtained can be used to investigate the role of their different physical characteristics (filtering, absorbers, …) on the biological response.

As reported in the introduction to this chapter, low and very- or ultra-low dose experiments have to take into account several factors that may impact on the reproducibility of the experiments.

Low dose radiobiological intercomparison requires the selection of robust (tested and validated in relevant scenarios) model system(s) (e.g., human primary fibroblasts or whole blood cells) and robust endpoint(s). Furthermore, minimisation of the biological variability (culture conditions, incubator parameters, …) is fundamental in the attempt to keep all the experimental conditions under adequate control.

These aspects are fundamental considering that small variations respect to the background levels are expected in the biological effects.

Acute exposure can be used as reference for model systems and endpoints. An adaptive response irradiation scheme could also be applied to influence the biological response.

5. Conclusions and next steps

The above discussion summarises the state of the art in terms of intercomparisons involving uses of ionising radiation in different types of facilities/laboratories including dosimetry monitoring services, metrology, secondary standard dosimetry, centres of radiotherapy (comparable to research irradiation facilities), bio-analytical and simulation platforms. It can represent the starting point for the identification and implementation of effective facility intercomparisons for the radioprotection research within PIANOFORTE.

The discussion presented in the previous chapter presented some of the main critical, and clearly challenging aspects that have emerged from the intercomparisons review and the discussions within the WP5 meetings and workshop, and that need to be considered in initiatives aimed at improving harmonisation through intercomparisons.

Some tentative suggestions are also proposed for the identification of the best approaches for improved infrastructure qualifications. This will be used to define a call for proposals devoted to the implementation of intercomparisons (or use-cases) which shall address one or more of the above critical aspects.

6. Glossary

APD	Active Personal Dosimeter
BoD	Board of Directors
CC	Consultative Committee of the Metre Convention
CC-KC	Key comparison organised by a Consultative Committee
CC-WGKC	Key Comparison Working Group organised by a Consultative Committee
CIPM	International Committee for Weights and Measures of the Metre Convention
MRA	Mutual Recognition Agreement
DI	Designated Institute
DIS	Direct Ion Storage
DoE	Degree of Equivalence
GNP	Gold Nanoparticle
ILC	Inter-laboratory comparison
IMS	Individual Monitoring Services
KC	Key Comparison
KCDB	Key Comparison Data Base
KCRV	Key Comparison Reference Value
MSM	Member Service Manager
NEA	Nuclear Energy Agency
NMI	National Metrology Institute
OG	organisation Group
PS	Pilot Study
PT	Proficiency test
RPLD	Radio-photoluminescence dosimeter
RMO	Regional Metrology Organisation
SC	Supplementary Comparisons
TLD	Thermoluminescence Dosimeter
WBC	Whole-Body Counters

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