

Workshop on Infrastructures for Radiation Biology Research – Preparing for the Transfer from DoReMi to CONCERT

Meeting Venue: Port Sitges Hotel (Barcelona), Spain

Date: April 27-28

Meeting Organizers: Laure Sabatier, William Hempel, Jean-Michel Dolo: CEA

Steering Committee: MELODI Infrastructures Working Group

Summary

The goal of the workshop was to bring together members of DoReMi, OPERRA and CONCERT along with experts on various types of infrastructures to help assess the current state of research infrastructures for low dose radiation biology research and to work towards creating a roadmap to take into account future research needs and how to meet them, potential gaps, and ways to improve access to research infrastructures including funding strategies.

This was accomplished by first having a series of presentations on the first day so that different research platforms including those that received support from DoReMi as well as others within and outside the radiation biology field, including ESFRI platforms, could share their experiences. With these presentations in mind, this was followed on the second day by 3 parallel breakout sessions divided by infrastructure type. In each session, participants were provided with an initial list of technical and selection criteria appropriate to the type of research platform that has been developed by the MELODI infrastructures working group. They were asked to complete or modify the list to arrive to a final list of criteria and asked to identify any unmet infrastructure needs. Participants in each session were also asked to provide ideas for financing strategies and ways to improve infrastructures access. The results from the 3 breakout sessions were then presented in a common session before a final wrap-up was presented by Laure Sabatier.

Introduction to the Workshop – Laure Sabatier

Laure Sabatier presented an overview of the evolution of integration activities in Euratom starting with an overview of the High Level Expert Group HLEG report and the question of how robust is the system of radiation protection and risk assessment. This was followed by the mention of the different radioprotection platforms: MELODI for low dose, NERIS for emergency

preparedness and remediation, ALLIANCE for Radioecology, EURADOS for dosimetry, and their mission to produce a Strategic Research Agenda (SRA), stressing that these organizations receive no EU funding. Brief mention was then made of the funded Networks of Excellence (NoE) and preparatory programs for the integration of radiation protection research including the DoReMi NoE for low dose research, the STAR NoE for radioecology and the preparatory programs NERIS-TP for emergency preparedness and remediation, COMET for radioecology, and OPERRA for the integration of radioprotection research. A brief introduction to the ESFRI platforms was also made stressing those that could be of interest to radiation biology research. This was followed by a description of the infrastructure related activities within DoReMi and OPERRA, concluding with a brief description of the EJP-CONCERT and activities within CONCERT to promote the visibility of selected infrastructures for R&D, harmonize practices and protocols, and the development of strategies for facilitating access to infrastructure.

Session 1 – Improved Access to Infrastructures (physical access, supporting facilities and management, financial strategies)

Session 1 was chaired by Antonella Tabocchini of the ISS and focused on presentations by irradiation facilities that were made available to DoReMi partners following identification of specific gaps via financing through open calls as an example of how DoReMi has provided access to infrastructures. These included the FIGARO facility for low dose/dose rate gamma irradiation of cells and small animals which was upgraded using DoReMi funds, the IES irradiation facility in Rokasho, Japan for low dose/dose rate gamma irradiation of rodents which was a partner in a DoReMi funded research project to study the effects of low dose chronic exposure in the development of brain cancer in mice, the low dose gamma radiation facility at Stockholm University which was made available to DoReMi partners and which received financing through ad hoc funding, and finally the SNAKE ion microbeam facility in Munich which provided beam time financed by DoReMi.

Session 2 – Infrastructures for data sharing and biobanks

This session chaired by Fieke Dekkers of the RIVM focused on infrastructures for data sharing and biobanks, including a general presentation of the databases/biobanks, their use, accessing data and samples, their management, their sustainability, etc. These included presentations of the STORE database for data and samples from radiobiology experiments, the FREDERICA database of published data in the field of radioecology, the Janus and NURA archives of data and samples from studies carried out in the US at the Argonne National Laboratory, and the BBMRI Large Population Cohorts project run under the auspices of the ESFRI, BBPRI-ERIC.

Session 3 - The experience of National and European level distributed platforms (harmonization, choice of partners, criteria, intra-laboratory comparisons, financing, and sustainability)

This session chaired by Rafi Benotmane of the SCK-CEN focused on national and distributed infrastructures from within and outside the radiation research field where the presentation included an overview of the platforms, their history, current status, management, and future directions. These included 3 ESFRI platforms consisting of BBMRI-ERIC for biobanking of samples for biomedical research, Euro-BioImaging for biomedical imaging, and ELIXIR, the European life science infrastructure for biological data. These were followed by a presentation of the French national metabolomics laboratory Metabohub. To conclude a presentation was made on the European organization EURADOS which supports activities in radiation dosimetry including harmonization exercises and RENEB, a project to develop a network of biodosimetry laboratories throughout Europe using harmonized protocols to respond to radiological emergencies, but which could also be used for large retrospective epidemiology studies.

Introduction to day 2 – William Hempel

Day 2 started with an introduction which first chronicled the growth of DoReMi WP4 from 4 to 10 tasks to respond to the infrastructure needs in low dose radiation biology research. This was followed by a brief presentation of the results of a DoReMi survey on the use of external facilities. The conclusions of the survey were that there is a high interest in using certain external irradiation, 'omics, and imaging facilities as well as archived data/samples if sufficient funding is available. It was also felt that all of the necessary facilities already exist, but that there remain significant barriers to access including financing, complicated logistics, the presence of appropriate on-site staff, and the availability of supporting laboratories. The need to identify and promote high quality infrastructures best suited to serve the needs of radiation biology research was then presented. This includes improving access by focusing on selected infrastructures and facilities, the better rationalization of the use of existing infrastructures and available financial resources, improving reproducibility by supporting infrastructures that meet necessary quality criteria (ex. 'omics), and improve sustainability of rare but essential infrastructures (ex. internal contamination facilities (radon)). A potential strategy to identify qualifying facilities using technical and selection criteria was then presented along with the elements of a roadmap which included listing of the selected facilities/infrastructures, a description of the process (and criteria) used to select the infrastructures, proposed funding strategies to promote their use and support research projects that use the qualifying

facilities/infrastructures, and procedures for the inclusion of additional facilities/infrastructures to the list of qualifying facilities/infrastructure. Finally a brief discussion of the importance of harmonization and inter-laboratory comparisons was presented including discussion points for the following sessions.

Session 4 - Irradiation platforms: Chair - Kevin Prise (QUB)

The list of technical and selection criteria for external and internal irradiation platforms presented to session 4 by the MELODI research infrastructures WG was already quite detailed and extensive. A number of relevant additions were made to the criteria and additional potential facilities were added to the list. Concerning potential gaps, it was felt that most needs were well-met. It was felt that there is a lack of fast Neutron facilities in Europe, while mixed exposure facilities (alpha/X-ray, gamma/neutron) exist, but need to be identified and listed. Proposed funding models included providing funds for external beam time, for short-term visits, and within integrated projects. It was felt that both investigators and facilities needed to be funded in parallel. Finally, the preference was for a bottom up approach based on scientific value, followed by an evaluation of the feasibility.

Session 5 - Data sharing platforms, cohorts and biobanks: Chair - Bernd Grosche (BfS)

The conclusion from this session was that the criteria for cohorts, databases and biobanks are not the same, but for all there needs to be “as much information as possible”. For cohorts, a comprehensive survey has already been performed within DoReMi generating an extensive information set. For databases, it was felt that a priority needs to be that it is user-friendly with easy searchability. For animal information it was proposed that a minimum information set should be defined. In the case of biobanks, it was felt that information on how the samples have been prepared and stored should be a priority. For STORE, potential links with ELIXIR were discussed, but further discussion will be necessary before any conclusions can be made.

Concerning funding and sustainability, the question of making STORE an ERIC was discussed but it was decided that an ERIC would be too big a solution for the radiation protection community. Other possibilities discussed included seeking money from government agencies, setting aside a portion of funds from accepted projects for biobanking/data archiving, or linking databases/biobanks to E&T activities.

Elements of the roadmap should include the development of a searchable database of all infrastructures. In addition, the use the same metadata for archived data as well as access

through one portal should be considered. Before creating new cohorts, BBMRI should be asked for advice. Finally, financial strategies to guarantee sustainability should be integrated into the roadmap. The first steps should be to develop an exhaustive list of infrastructures followed by the development of quality criteria that could change over time.

As we move towards CONCERT, it would be nice to put all the information from the DoReMi projects in STORE (either the data or the link to the data). In addition, technically STORE could be an umbrella for all the databases created in the different platforms (EURADOS, ALLIANCE, NERIS). A possible project could be to “Integrate all the existing databases”. The question remains as how to motivate/oblige scientists to include the data in STORE or other databases although this may be integrated as a requirement to obtain CONCERT funding.

Session 6 - ‘omics and analytical platforms: Chair - Soile Tapio (HMGU)

The list of criteria for ‘omics facilities provided to the session participants had a number of proposed selection criteria as well as suggested platforms based on existing EC funded networks in genomics and proteomics and the MERIL database, but the technical criteria remained to be completed. A main conclusion from this session was that it will be very difficult to define specific facilities in the ‘omics realm because of the vast number of available facilities as they serve all of biomedical science and not just radiation protection research. Furthermore, the available number of varying technologies, and the complexity of the methodologies also present significant challenges in assessing which facilities may be the most appropriate.

Nonetheless, a number of possible criteria were considered. For proteomics and metabolomics platforms, the sensitivity as measured by the number of analytes or peptides identified per samples should be considered. The use of “old fashioned” techniques such as spotted arrays for transcriptomics and 2D gels for proteomics should be avoided. For certain standardized techniques, should outsourcing to private companies be considered? Furthermore, core-labs facilities, large institutes and/or private companies offer high quality service, as they already comply with strict quality control processes to become certified as such. In addition, depending on the approach, NGS could be an affordable alternative provided by private companies, whereas proteomics and metabolomics are more complex and are better performed at large institutes (core labs). Throughput could also be used as a selection criterion along with the technology used and associated publications.

Concerning the question of and performing intercomparisons, they have been carried out in the past in transcriptomics and proteomics. An intercomparison exercise may be needed in the field of metabolomics as the methodology is evolving and this has successfully been carried out in France and Germany. One of the great challenges is the vast number of ‘omics platforms to

run intercomparisons as is done for dosimetry or other fields. In addition, it is not clear how to motivate these platforms, as the projects coming from radioprotection research would represent a small fraction of their overall work. Furthermore, the technologies in the 'omics fields are rapidly evolving. A further challenge is the complex bioinformatics and data analysis and the question of whether these can be standardized. It is thus felt that the harmonization of proteomics and genomics is not feasible, although this may be possible for metabolomics as the number of facilities are limited, so it may be possible to identify a reference lab for each country and guide radiation biologists to these facilities.

Education and training should play an important role in the use of 'omics technologies as good experimental design is crucial to ensure reliable results in the 'omics fields. In order to ensure the optimum use of available 'omics facilities it is necessary to have a minimum understanding about omics experimental design, data analysis and interpretation. For example, EMBO/EBI offers a good panel of omics training courses.

Finally, sustainability was not considered to be an issue as the 'omics platforms are well outside the relatively limited scope of radiation biology as compared to the whole of biomedical research.

General Conclusion from the workshop and Proposition for CONCERT

It is clear from the workshop that not one solution fits all concerning improving access to the best facilities for the different types of infrastructure. The simplest way to provide access to infrastructures is through the provision of financing for their use within each project proposal. Two possible mechanisms that could be used for future CONCERT calls are the following:

- (1) Provide a list of selected facilities to be used for CONCERT funded projects based on the technical and selection criteria. Anyone proposing to use another facility must provide a scientifically valid reason which will be considered by the external proposal reviewers. This process may be more appropriate for irradiation facilities
- (2) Leave the choice of the facility to be used up to the scientists, but require that they test a standardized sample set that will be provided by WP6 of CONCERT on their selected platform. This sample set will have already been independently validated on 3 national level platforms. The results obtained using this sample set must be incorporated into a go/no go decision for the use of the selected facility to ensure that the chosen facility meets the necessary technical standards to ensure that the project obtains meaningful results. This solution may be more appropriate for transcriptomic, proteomic, or metabolomics facilities.

The performance of intercomparison exercises is difficult to carry out and will only be considered for specific cases.

AGENDA

Monday, April 27

8:15 – 8:45 Arrival of workshop participants

9:00 Introduction to the workshop – *Laure Sabatier (CEA)*

Session 1 – Chair: Antonella Tabocchini (ISS)

Improved Access to Infrastructures (physical access, supporting facilities and management, financial strategies)

9:10 FIGARO – *Dag Anders Brede (NMBU)*

9:30 IES – *Ignacia Tanaka (IES)*

9:50 Low dose gamma radiation facility – *Siamak Haghdoost (SU)*

10:10 SNAKE – *Günther Dollinger (UBWM)*

10:30 Discussion/Roundtable

11:00 Coffee Break

Session 2 – Chair: Fieke Dekkers (RIVM)

Infrastructures for data sharing and biobanks

11:30 STORE – *Bernd Grosche (Bfs)*

11:50 FREDERICA and other radio ecology databases – *Almudena Réal (CIEMAT)*

12:10 Janus Archives – *Gayle Woloschak (Northwestern University)*

12:30 BBMRI-LPC – *Outi Törnwall (THL)*

12:50 Discussion/Roundtable

13:20 Lunch

Session 3 – Chair: Rafi Benotmane (SCK-CEN)

The experience of National and European level distributed platforms (harmonization, choice of partners, criteria, intra-laboratory comparisons, financing, and sustainability)

14:30 BBMRI-ERIC – *Andrea Wutte (BBMRI-ERIC)*

15:00 EURO-BIOIMAGING – *Pamela Zolda (EIBIR)*

15:30 ELIXIR – *Andrew Smith (ELIXIR)*

16:00 Coffee break
16:30 METABOHUB – *Christophe Juno (CEA)*
17:00 RENEb – *Ulrike Kulka (BfS)*
17:30 EURADOS – *Jean François Bottollier-Depois (IRSN)*
18:00 Discussion/Roundtable
18:30 End of Day 1

Tuesday, April 28

9:00 Introduction to Day 2 – *William Hempel (CEA)*

DoReMi WP4 – The path from 4 to 10 tasks to respond to the needs of the low dose radiation research community and the way forward

9:30 Parallel Sessions

Session 4 - Irradiation platforms: Chair - Kevin Prise (QUB)

Session 5 - Data sharing platforms, cohorts and biobanks: Chair - Bernd Grosche (BfS)

Session 6 - 'omics and analytical platforms: Chair - Soile Tapio (HMGU)

12:30 Lunch

Session 7 – Chair: Laure Sabatier (CEA)

14:00

Construction of a roadmap - Each parallel session leader will be asked to give a presentation summarizing the conclusions of the session which will be used to develop a roadmap.

- a. Establishment of a template and definition of major themes
- b. Distribution of tasks for the filling in of details after the workshop

17:00 Concluding remarks

17:15 Closure of the workshop