Low Dose Risk Research: The MELODI European Platform Project

MELODI Document n°1

Framework for the MELODI Platform

October 2009

Overview

There is a wide consensus in the specialised community on the opinion that the current international radiation protection system, as founded by ICRP's radiation protection philosophy and its recommendations, is in general robust to adequately protect people against the various modes of exposure to radionuclides. However, during recent discussions with the wider scientific community some questions came up, which were not settled by the recent recommendations of ICRP, which are for example uncertainties in risk assessment of chronic low dose and low dose rate exposures, the issue of individual differences for the carcinogenic effects at low and protracted exposures, and uncertainties in risk assessment related to incorporated radionuclides.

Additional factors related to risk perception increasingly contribute to undermine the societal trust in the validity of the current radiation protection system:

- On one hand, there is a growing apprehension in society that the potential health risks posed by complex protracted low level exposure to various chemical substances (pesticides, heavy metals, NOx, …) or physical agents (ionising or non ionising radiation) and their possible interaction may have been underestimated and therefore insufficiently regulated. For ionising radiation, in a paradoxical way, because the risk assessment doctrine is based on a no threshold linear dose-effect relationship benefiting from a wide consensus among the scientific community, this societal concern seems to be particularly in evidence.

- On the other hand there is a weakness in the approach to the radiation protection system for low doses, which is based mainly on epidemiological evidence from acute exposure situations and derived from modelling work and expert consensus conclusions based on experimental and additional epidemiological data. There is now growing evidence from epidemiology that radiation risk after chronic low dose exposure may not differ significantly from that after acute exposure. This situation of open scientific questions provides leverage to controversies, with a high potential of outreach to public opinion because it may send an unclear message to the public.

- Up to now, the risk estimates are based on cancer risk only. The question whether or not non cancer risks have to be included in the detriment is subject to scientific discussions based on new evidence.

There is increasing awareness that a situation of still existing scientific uncertainties in a highly controversially discussed field may pose greater problems in the future. The European Commission, and EU Member States within the CCE Fission Euratom Committee in 2008 set up a "high level and expert group" (HLEG) in order to investigate the ways to take advantage of scientific progress in biology. A renovated Europe wide education and training (R&T) strategy could lead to new breakthroughs in the reduction of scientific uncertainties in risk assessment in the wider area of radiation protection.

The HLEG report (www.hleg.de) was published in the spring 2009, after a period of public consultation through an internet procedure. This report:

- Identifies the five overarching scientific questions which are at the heart of the main uncertainties about the risks associated with low dose exposures.

- Suggests that a multidisciplinary R&T approach, associating scientists in advanced cellular biology, toxicology, epidemiology and modelling to a shared ambitious objective, may provide opportunities to breaking new ground in the understanding of low dose effects, relating to cancer as well as non cancer risks.

- Analyses, in the light of the complexity of the scientific challenge, the relatively high costs and regulatory constraints associated with experimental work aiming at studying the biological effects resulting from a low dose exposure to a wide range of radionuclides. This has gradually led to the current situation in Europe, where R&T capability has been reduced, and survives through "niche oriented" strategies, where the EURATOM fission R&T programme is almost the only instrument to promote trans-national cooperation.

- Argues that any significant progress may only be obtained through the federation of national and EU R&T strategies, mobilising as widely as possible a wide scientific community towards a concerted and integrated effort to implement such a multidisciplinary effort.

- Concludes that the questions raised, the stakes in play, and the lasting scientific and technical complexity of the challenge justify that the EU sets up a dedicated R&T Platform, in accordance with the 7th EU R&T Framework Programme orientations.

Five national organisations: BfS (Germany), CEA (France), IRSN (France), ISS (Italy), STUK (Finland), have decided, with the support of their governments and of the European Commission, to work together towards this challenge, and propose to initiate the creation of a new EU Platform called for in the HLEG report. This Platform, named MELODI (Multidisciplinary European Low Dose Initiative), will be open to all scientific organizations and scientists wishing and able to contribute to the implementation of the scientific strategy proposed by the HLEG report, and supported by the EC and EU CCE Fission governmental community.

In the forthcoming years, the MELODI platform will play a key role in close coordination with ongoing and future R&T initiatives addressing the issue of low dose risk:

- for the definition of R&T targets in the field of low dose risk and the necessary means to achieve them, particularly in terms of infrastructure, education and training,
- for the enlargement of the scientific community involved in the research programmes and for the development of multidisciplinary R&T programmes in coherence with the road map defining the different steps to reach the implementation of a clear and widely accepted long term strategic research agenda (SRA),
- for the assessment of results, and their transfer to the international expert community responsible for the development of the international radiation protection system (UNSCEAR, ICRP),
- for the facilitation of a science based dialogue between stakeholders on the issues of health risks associated with low dose ionising radiation.

This document presents the current thinking of the MELODI founding partners towards the implementation of the strategy, scientific and organisational, that underpins the HLEG Report to the European Commission. It is meant as a supporting document for further discussions, since the success of MELODI and of the above mentioned strategy implies the involvement in this initiative of all competent bodies and interested parties across Europe.

1. Background and rationale

Although much is known about the quantitative effects of exposure to ionising radiation, considerable uncertainties and divergent views remain about the health effects for low doses. Outside Europe, the USA and Japan have established major programmes of low dose risk research. Many of the larger Member States of the EU have also considerable research activities in low dose risk. However, little has been done so far to integrate these programmes. There has been a decline in scientific and regulatory expertise in radiobiology and radiotoxicology during the last decades, but the renaissance of the nuclear industry in some countries as well as the increasing application of ionising radiation in medicine accentuate more and more the need to revitalise the research capacity in low dose risk.

The HLEG, set up to consider these issues, has concluded that there were a number of open scientific questions which should be resolved in order to consolidate the European radiation protection framework in the area of low dose exposure to ionising radiation. The HLEG report also points out the complexity and interrelation of these issues, which require a multidisciplinary and carefully coordinated approach. The report recognizes also that several scientific bodies in Europe are willing to set up together a platform in order to implement together such the recommendations of the HLEG. The report finally states that only a sustainable integration of European research in this area would be able to achieve this goal. Indeed, the HLEG consensus provides a sound conceptual basis on which to proceed but, alone, it is not sufficient. It needs to be complemented by more strategic and practical considerations, in particular how to translate the concept in practice in the light of a number of important impediments to its realisation. As a result, there is a clear need for:

- A trans-national organisation capable of ensuring appropriate governance of research in low dose risk research, in the pursuit of a long term shared vision.

- A scientific strategy in order to structure the research programmes in the most effective way, taking into account the available resources.

In order to initiate an integration process, the five MELODI founding partners have signed in the early 2009 a letter of intent in which they mark jointly their intention to progressively integrate their low dose risk research programmes, starting with the creation of the platform MELODI, as proposed in the HLEG report. Complementary to the emergence of this global network, the EC has included in the EURATOM call for proposals FP7-Fission-2009 to create a network of excellence (NoE) in low dose risk research, making explicit reference to the conclusions and proposals of the HLEG report.

Under the co-ordination of STUK and together with the signatories of the letter of intent and other European organisations playing a key role in radiation protection and radiation research, a proposal for a NoE (see MELODI Document No 2) has been submitted in response to the above call. The proposed network, called DoReMi (Low Dose Research towards Mutidisciplinary Integration), consistently with the proposals made in the HLEG report, aims to address the issues of the shape of dose response curve for cancer, individual sensitivity for cancer, non cancer effects, infrastructures, and education and training. This NoE is meant to be a transitory initiative the EC will support to:

- Facilitate and accelerate the integration process within the MELODI platform, including the establishment of a SRA in the field of low dose risk research.

- Better define the more promising research lines upon which the SRA will be built.

- Ensure the continued performance of R&T work in a few identified priority areas, involving R&T teams across Europe in an open manner, subject to independent evaluation according to EU procedures.

2. MELODI objectives

a. Scope

The MELODI platform will integrate in a step by step approach and with a view of sustainability funding bodies and research organisations in Europe with significant programmes in low dose risk research program. The platform will be open to other organisations and scientists that are willing and able to contribute to its goals.

Effective links and a continuous dialogue will also need to be established with key stakeholders, in particular regulatory bodies and users of radiation and radioactive material in industry and medicine who will be the ultimate end-users of the research outcomes, as well as with the public who is more and more concerned with the possible health effects resulting from the use of ionising radiation. One of the aims of such a dialogue is to increase awareness of the current knowledge of low dose risks with ultimate goals of further developing public trust and promote safety culture at all levels of operation. Such a dialogue will provide also feedback to and from the researchers on their practical needs and questions arising during their daily use of ionising radiation. In addition, a potentially more important consideration is to raise awareness among users and producers of radioactive material and/or ionising radiation in industry and medicine of the need for and importance of low dose risk research and for them to make a more significant contribution to its funding.

b. Strategic objectives

The current understanding and quantification of risk at low doses is limited by the uncertainties of the available scientific methods and by a lack of understanding of the basic biological mechanisms. This situation can only be improved by a long term commitment of all scientific disciplines involved, a shared view on the roles of these disciplines within a research strategy and a common vision among the research community. To interact in a most effective way with the broader scientific and health communities, the MELODI platform will establish effective and timely links with broader biological research communities, in particular to take advantage of emerging developments elsewhere.

Thus, a comprehensive and systematic understanding of the biological processes that lead to cancer, and other relevant diseases, and also the identification and quantification of the particular roles played by radiation in the processes can only be achieved within the context of the broad advances in biological and medical knowledge through basic and applied research. This requires an intensive scientific exchange with disciplines outside the classical areas of radiobiology, nuclear physics, radioecology, and (molecular) epidemiology, such as with cancer research, genetics and biomedical research more generally. The current understanding and quantification of risk at low doses can only be

improved by a long term commitment of all scientific disciplines involved, a shared view on the roles of these disciplines within a research strategy and a common vision among the research community at national and European level and beyond.

In addition to the need of identifying appropriate mechanisms to be put in place to ensure effective dialogue with key stakeholders, and with the view of implementing a long term research strategic agenda (SRA), three other key concepts have been identified that will be incorporated into the scientific strategy for multidisciplinary low dose initiative to become viable:

- Holistic approach: recognizing that there is a particular need to move away from or rise above the more traditional “organ pipe” structure where scientists of a given area are in charge of defining their own research objectives and related actions, the SRA will aim to overcome the failure to fully integrate the many disciplines involved within a coherent vision and programme, in particular between the experimental and theoretical scientific communities. The SRA will engineer programmes that will take on board the most recent paradigms developed in radiation biology and in fundamental biology, and solicit the most recent investigative techniques. This will require the development of closer links between the radiobiology and epidemiology communities and other disciplines involved in fundamental biology.

- Periodic review of objectives and dissemination of outcomes: given the complexity of the policy issues to be resolved, the SRA will need to span a relatively long period during which adjustments to the research strategy will need to be kept under continuous review and adjustments made at intervals. In addition, given that many EU Member States have lost key competences and are no longer capable of independently retaining their current research activities in radiation sciences, MELODI will pay special attention to the implementation of programmes aiming at knowledge management across generations designed in a way that such programmes achieve sustainable results. Indeed, scientific programmes have to address questions which are attractive for both young scientists and universities or the management of research organizations.

- Ensuring that key prerequisites are met: the SRA will identify impediments or barriers that must be overcome before further progress can be made. As a result, the programming and funding system to be set up under MELODI will be conceived and implemented so as to ensure that, where necessary, resources will be directed to “barrier solving” before “barrier dependant” programmes are initiated. In addition, recognizing that research infrastructures are essential for low dose risk research, since they could represent a key prerequisite to be met, one of the early priorities of the MELODI platform will be to establish an inventory of European infrastructures and future needs of radiation facilities, data bases and tissue banks, large experimental facilities, and trans-national cohorts, in order to achieve the SRA goals.

c. MELODI Development Process

The MELODI platform implementation was initiated in April 2009 with the signature of a letter of intent (LoI) by the first five partners. Since then several Organizations have expressed their intent to join the MELODI development process. To continue its development process, the platform will:

- Consolidate its structure, providing an adequate legal status, and its capacity to achieve the full integration of research in Europe.

- Become a broadly recognized forum for all stakeholders in the field of low dose risk, producing qualified and trusted recommendations on science and policy.

- Develop appropriate links to other key partners across the world.

- Promote the MELODI approach and results at the international level through appropriate scientific and general media communication.

To achieve these objectives, the following actions will be launched:

- Creation of a MELODI Executive Board, constituted of the designated representatives of the signatory bodies.

- Development of the "internal rules" for the operation of MELODI. This will include the procedures for the operational management: admission of members (current and future LoI signatories, members from the scientific community, stakeholders), finance, relations to the EC, deontology, scientific management conditions (development and review of implementation of the SRA, dialogue with the scientific community beyond the membership of the platform).

- Setting up of a MELODI website (using resources in conjunction with those used to set up the NoE's own website).

- Creation of a scientific committee to oversee the implementation of the SRA.

- Achievement of the first steps of operational integration of existing programmes between the members of the platform.

- Propose a legal status for the incorporation of the MELODI Platform as an Association of all its members.

d. Activities and deliverables

The main activities of the MELODI platform will consist of conducting the following actions:

- Development and maintenance of a strategic research agenda: it is anticipated that the first edition of a comprehensive overall SRA for European low dose research will be developed by the spring of 2011, taking on board the preparatory work

developed in the DoReMi NoE's respective WP's; this jointly formulated SRA will guide the orientations of EU R&T in the field of low dose risk.

- Ensuring the extension of the policy of scientific cooperation and integration at the European level: to enlarge the MELODI platform to further members, whilst retaining the momentum for further integration, a category of "associate member" will be created in order to include in the platform all the partners involved in the DoReMi NoE operations, as well as the partners that are not able to be engaged in a long term commitment, but who could contribute for a short term period to the objectives of the MELODI platform. The internal rules will be reviewed to specify the role of associated members in the governance of MELODI.

- Organisation of large public MELODI conferences and workshops: in addition to the continuous review that will be put in place to ensure the SRA remains fully responsive in addressing policy issues, emerging needs and scientific progress, periodic review and dissemination meetings will be organized under the framework of MELODI. Fully open to all the concerned R&T community, the radiation protection community and to other stakeholders, these meetings should result in an assessment of the progress in implementing the SRA, and of the perspective for strengthening, at the operational and policy levels, the radiation protection system. Such strengthening could result either from validation of existing radiation protection policy or practice, thereby reinforcing the societal robustness of the system, or from identifying the need or desirability for change in order to reflect new scientific findings. Such a process would enhance Europe's position in the further development of radiation protection policy and practice internationally.

- Organisation of institutional relations with the regulatory bodies in the field of radiation protection, and with the EU (EC, EP, relevant official committee structures), as well as with organisations outside Europe involved in significant low dose R&T programmes (USA/DOE, Japan,…) in order to seek scientific cooperation and coherence wherever possible.

In term of deliverables, the Platform will also produce the following, on a mostly yearly basis:

- A report to the EC and to the governments in the participating countries in order to enable the preparation of successive national planning as well as EURATOM calls in support of the progressive implementation of the SRA. This report will in particular trace the progress of the integration of national programmes.

- On a yearly basis (possibly every two years at a later stage), an assembly of the platform, during which the results of the SRA implementation will be promoted, the representatives of the organisations involved will be nominated to the governance structures, and the SRA will be reviewed in the light of the achieved results. During the operation of the NoE, this will be organised in conjunction with the DoReMi NoE WP operators. These assemblies will also serve to ensure that the widest scientific community continues to adhere, and to contribute to the implementation of the SRA. Continued financial support from the EU/EURATOM programmes will obviously be instrumental for achieving such a goal.

3. Structure

a. MELODI Members

MELODI will be an open, autonomous forum, associating as Members all organisations, such as R&T bodies, existing cooperation networks or structures, radiation protection institutions, industry, and stakeholder organisations, which are based in Europe, and committed to promote and implement the HLEG scientific strategy. It will aim to achieve a balanced representation of interests, of expert knowledge and of R&T disciplines. It will develop its own governance structure, and ensure its independence from any single one (or subgroup) of its member entities, from the European Commission and from EU member States. It will develop its own methods of working, and establish interfaces with appropriate institutions and organisations in Europe and beyond.

Participation in MELODI, beyond the general commitment to support its objectives and to abide by its rules of procedure, will require an adequate level of contribution to its working structures, since each member will be required to bear the costs of their participation in the governance and working group structure of the Platform.

Once a sufficient consensus is established within the "MELODI community" about the organisation of its general governance, legal statutes will be prepared, most likely in the form of an international non profit association under the legislative system of the EU member states.

These Statutes of MELODI should provide that access to membership will be granted by the Governing board, on the basis of an expression of interest by a candidate organisation, supported by a formal letter (*to be developed*) addressed to the Chairperson of the Governing Board, explaining its motivation, and how it intends to contribute to the achievements of the objectives of MELODI.

b. Organisation

i. Governing Board

The Governing Board (GB) is a relatively small group, able to meet as frequently as necessary (possibly via videoconference) in order to steer the activities of the Platform in accordance with its general policy as agreed in the Assembly of members, with the support of the Scientific Committee. The GB evaluates and decides on the candidature of new members to MELODI. It is responsible for the management of external relations of the Platform, in particular with EC, EU member states structures, and international institutions and partner organisations.
It is made up of:

- One representative of each of the initial Founding institutions, signatories of the LOI
- The Chair and Vice-Chair(s) of the Scientific Committee
- The Chair of the SRA WG
- One representative of the EC services (DGRTD)
- Three representatives appointed by the Assembly of members, including representation from stakeholder organisations.

The GB proposes to the assembly of members the appointment of its Chair and Vice Chairs.

The GB may, if it appears pertinent to do so in the course of time, wish to delegate some tasks to a Bureau, in order to expedite efficiently managerial tasks, with the support of the Secretariat.

The length of the first mandate to participate in the MELODI governance structures should be designed to ensure continuity of action and policy over time.

The GB deliberates on the basis of consensus between its members. If needed, a voting procedure may be requested by the GB Chair, in which case decisions are taken with a two third majority of votes.

ii. Scientific Committee

The Scientific Committee is responsible for the scientific supervision of the initial elaboration of the SRA, of its subsequent maintenance and implementation in accordance with the vision proposed by the HLEG Report and the strategic guidance provided by the GB. It reports **to** the GB, and presents an activity report to the Assembly of Members.

It is composed of up to 20 representatives of the MELODI related scientific community, chosen for their professional ability to contribute to the mission of MELODI and taking into account the need for a balanced representation of:

- the participating EU member states (the Scientific Committee should however include some members from outside the EU),

- the type of expertise: radiation protection, international system, scientific disciplines of interest for radiation protection research (radiobiology, epidemiology, dosimetry, …), other academic disciplines of interest for low dose risk research (cellular biology, toxicology, …).

A list of members of the Scientific Committee, including nominations of the chair and vice chair(s), is proposed by GB to the Assembly for approval. It deliberates on the basis of consensus between its members. If needed, a voting procedure may be requested by the Committee Chair, in which case decisions are taken with a two third majority of votes.

iii. Working groups

The technical operations of MELODI are based on the processing of information provided on a voluntary basis by its member organisations, in order to develop the foreseen deliverables, such as the Low Dose Risk Strategic Research Agenda (SRA), and MELODI Technical Reports (MTR). These MTR will aim to foster appropriate initiatives for the enhancement of cooperation between MELODI member organisations, and to make proposals to the EC and EU Member States towards the implementation of the HLEG strategy. They will contribute to the monitoring of progress in the various cooperation areas, and to the dissemination of information on low dose risk research.

For this purpose, the GB of MELODI will set up Working Groups (WGs), to which members of the Platform will be invited to contribute. In all cases, the exchange of information within

the WG's will be governed by the existing Intellectual Property Rules (IPR) pertaining to the contributor organisations, or to their cooperative networks.

The SRA WG will be of particular importance to the operation of MELODI. It will need to liaise with other consortia/organisations involved in the implementation of R&T projects in the field of competence of MELODI.

In some cases, the GB may initiate specific Integrated Research Projects, where existing cooperative arrangements may prove inappropriate, for example for sharing important experimental infrastructures, and for organising funding schemes for such projects.

iv. Secretariat

For the first years of operation of the Platform, and until the Governing board decides otherwise, the secretariat will be operated by one of the MELODI Funding Members, on a rotating voluntary arrangement basis among those members able to provide strong professional management expertise, and solid financial background.
The Secretariat provides support for:

- Administrative, logistical and IT support for the Governing Board, Scientific Committee, and where needed of Working Groups.

- The Platform Internet information exchange service.

- External relations of the Platform Bodies with the European Commission, and other European, International or other partner institutions.

MELODI may elect, in consultation with the European Commission, to seek some financial support from the EURATOM R&T budget for the first years of operation.

v. Plenary Assembly

The assembly of members meets periodically (once a year initially) in a formal plenary meeting, generally in conjunction with MELODI Workshops, in order to, inter alia:

- Approve the formal constitution of a legal association named MELODI.

- Approve the report of the GB and Scientific Committee on the management and scientific achievements of MELODI.

- Approve the key orientations for the MELODI development of activities.

- Appoint the Chair (and Vice Chairs) of the GB, who also chairs the assembly of members.

- Appoint members and Chair, Vice Chairs of the Scientific Committee.

Each member holds one vote when formal deliberation by vote is required. Decisions are taken by consensus, or by a majority of expressed votes in case a ballot is necessary.