

Realizing the EUROPEAN Network of Biodosimetry

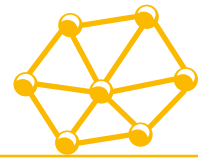


RENEB

Realising the European
Network of Biodosimetry

BULLETIN

NO 3 JUNE 2015



what is RENEb?

RENEb is a Coordination Action (CA) project funded within the seventh EU framework EURATOM Fission Programme. The project was launched in January 2012, and will continue until the end of the year 2015. The German Radiation Protection Authority – The Federal Office for Radiation Protection (BfS) coordinates the project.

The purpose of RENEb is to act as a sustainable European Network of Biodosimetry, capable of performing rapid biodosimetric dose estimation in large scale emergencies. The network infrastructure is based on well validated assays and techniques combined with high performance standards of the partners and inclusion of new promising biomarkers and methods. To enhance the visibility and viability of the network, existing European links will be extended so that RENEb will form part of the global Emergency Preparedness and Response systems.

More information of the project can be found on the project webpage: www.reneb.eu

Towards sustainable RENEb biodosimetry network

3 1/2 years after starting the EU funded project work, RENEb is preparing its transition to a self-sustainable network. To this end, the benefit and capabilities of RENEb for Emergency Preparedness and Response Systems were made public and co-operations have been initialised with national and international emergency and preparedness organisations such as IAEA and WHO.

To guarantee application of state of the art techniques, RENEb strongly promotes the introduction of new methods and further technical improvements of existing assays for individual dose estimation to support emergency preparedness.

After completion of the project, the network will be open to new member laboratories, providing that the labora-

tories are ready to fulfil the Quality Assurance (QA) and Quality Management requirements (QM) defined under the RENEb project.

RENEb, with its well organised and harmonised cooperative action between the laboratories, offers the realistic prospect for rapid and trustworthy provision of individualised dose assessment in a radiological large scale emergency situation. Additionally, the network has the potential to have a clear impact on the European radiation research area, through provision of highly trained individuals and extremely well validated biodosimetry research tools. In both regards, RENEb provides a unique infrastructure, high quality standards in application and validation of biomarkers and maintenance and advancement of scientific and technical competence.

As presented on the figure, the network is founded on three main pillars that are closely related to each other, which will ensure sustainability of the RENEb network.

Dissemination activities are carried out with the aim of strengthening awareness of the RENEb network amongst the biodosimetry community. Moreover, and even more importantly, such activities assist in strengthening awareness amongst stakeholders and decision makers within EU and worldwide radiological and nuclear emergency preparedness.

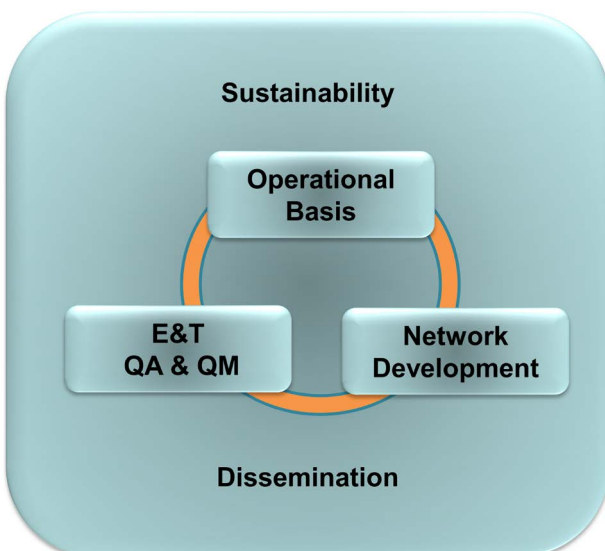
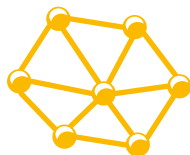


Fig. 1: RENEb network (drawing U.Kulka, BfS)



Operational basis of the network

The goal of the RENEb project is to ensure that the performance of the battery of five biological assays, and two physical retrospective assays of individual dose assessment can be harmonised in such a way that in the case of a radiological emergency, the partner laboratories can respond in a concerted way to provide efficient dose assessment in both large scale and/or complex exposure scenarios.

The biological assays currently part of RENEb are those based on formation of dicentric, micronuclei, premature chromosome condensation, fluorescence in situ hybridisation detection of translocations and gamma-H2AX foci in blood lymphocytes, and the physical methods: electron paramagnetic resonance and /optically stimulated luminescence in components of personnel electronic devices.

To fulfil the RENEb goals, the Consortium organised two full-scale inter-comparison exercises. In the second of these exercises, several non-RENEb laboratories have taken part (European laboratories that would like to join the

RENEb network as well as laboratories from Asia, America and South Africa, representing global biodosimetry networks). Depending on the assay, up to 23 EU and 24 Non-EU laboratories took part. During the exercises, technical proficiency of the laboratories was tested in addition to organisational and logistical challenges, for instance in EU trans-boundary and trans-continental sample transfer.

The third exercise – a 'table top' virtual accident simulation exercise - is currently in progress and will continue throughout summer 2015. This exercise has three aims: The first is to test the ability of every RENEb member to activate the network and to assess the capacity of the network at a given moment. The second is to train all participants in sorting of accident victims into dose and exposure scenario categories (homogeneous whole body, partial body, etc.). The third aim of this exercise is to evaluate the performance of the laboratory that activates the network (referred to as the Reference Laboratory). In addition to existing RENEb members, the Consortium invited RENEb candidate laboratories to participate in this exercise.

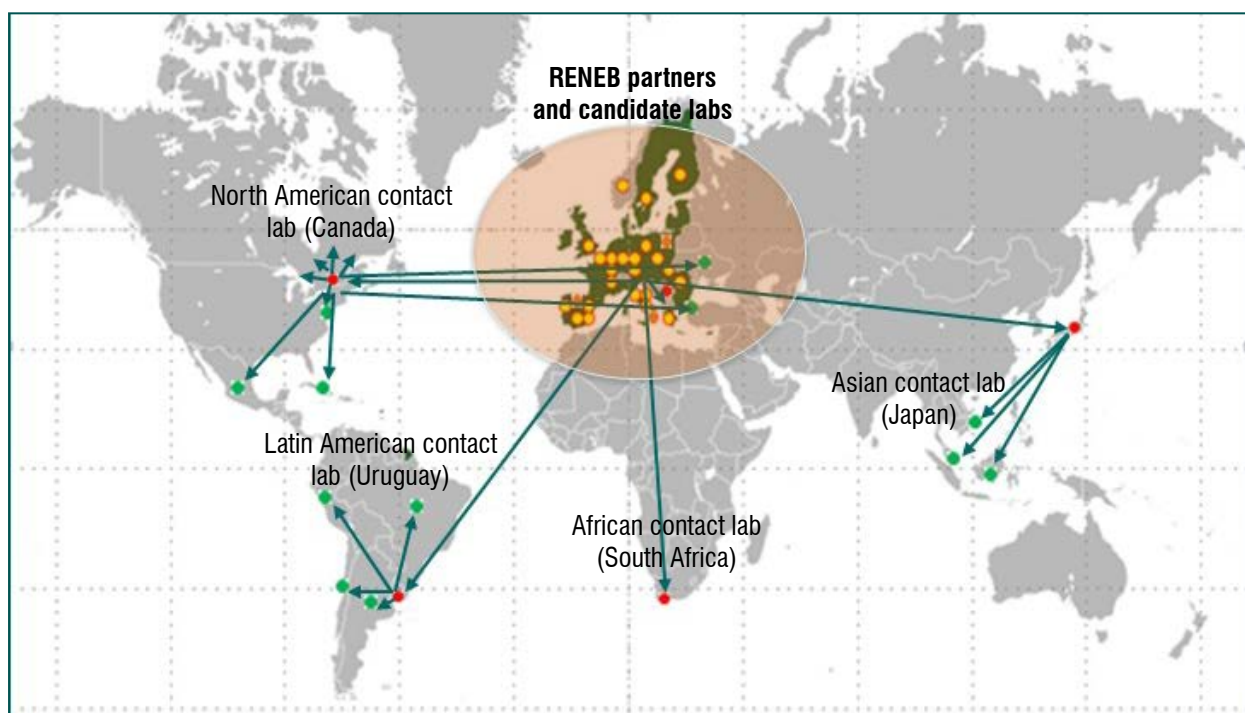
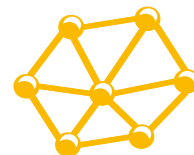


Fig. 2: Participants of the second RENEb exercise (drawing U.Kulka BfS)

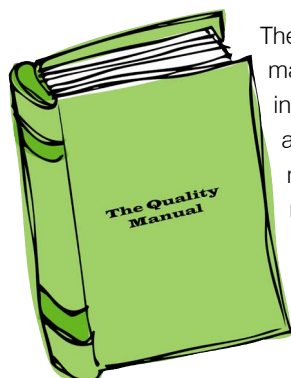
Education & training (E&T)

RENEb developed an E&T program with the aim of guaranteeing fast and reliable individual dose estimates and/or dose categorisation by the network partners in the case of a large scale accident.

The E&T program includes organisation of practical training courses and individual training for all the RENEb assays. The training needs were identified as a result of the performances of the laboratories in the RENEb exercises, described above. Additionally, classroom-based training courses in statistics, QA and QM as well as application of ISO standards were organised.



Quality Assurance and Quality Management (QA&QM)



The consortium developed a Quality manual of RENEb. This manual will insure that the present members as well as the potential new members of RENEb can deliver reliable dose estimations at a consistent high quality level.

RENEb Quality Manual addresses:

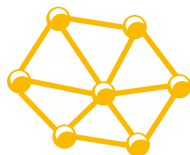
- Organisation of the network in case of emergency
- Confidentiality of personal customer information
- Laboratory safety requirements
- Guidance for establishing calibration curves
- Sample collection and analysis
- Estimation of dose, interpretation of the results and reporting
- Organisation of intercomparison exercises
- Criteria for enrolling new partners in RENEb
- Quality assurance and quality management of RENEb Laboratories

Legal status of the network as a guarantee for RENEb sustainability

The EU RENEb project will be completed by the end of 2015. It is pivotal to work for continuation of the network's activities to insure that high quality biodosimetry remains available to support EU emergency preparedness, the quality and efficiency of the network will be maintained, and that the future developments within biodosimetry are ensured. The RENEb project group performed a horizon scan, looking for a model for the organisation of the future European biodosimetry network that is possible and achievable. It was decided to take a step-by-step approach. The first step in this process is for each RENEb network member to sign the Memorandum of Understanding (MoU) between RENEb project organisations. The MoU was developed and legal representatives of RENEb organisations approved the text. RENEb project organisations and RENEb candidate organisations received the final MoU document for signing in May 2015.

The MoU document is not legally binding, but its signing will help to maintain the established European biodosimetry network and promote its recognition by emergency preparedness authorities. It will also facilitate the next steps towards a more legally binding organisation in the future.





Network developments

During the last two years of the RENEb project, there has been a growing interest from new laboratories to join RENEb. As of May 2015, seven new laboratories contacted the RENEb network to express an interest in joining in the future. The list of these laboratories, named RENEb candidates, can be found at the end of this bulletin. Some of the RENEb candidates participated already in RENEb activities, including the second RENEb inter-comparison exercises and attending the last annual meeting.

Improving the existing methodology

The French laboratory CEA successfully introduced fluorescent probes for centromeres and telomeres for the dicentric and premature chromosome condensation (PCC) assays. Use of this staining may facilitate an easier and more robust scoring process and may improve automation of the assays.

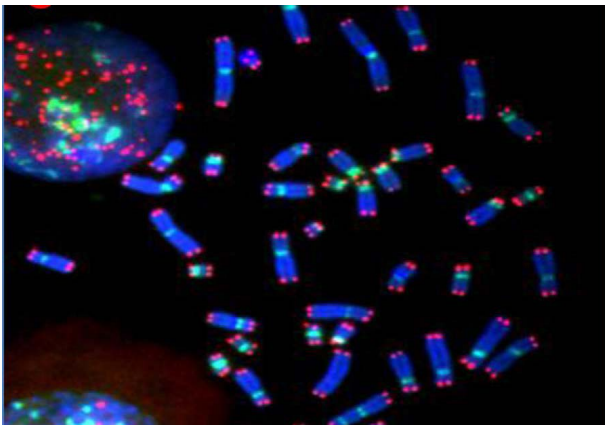


Fig. 3: Use of florescent probes for centromeres (cyan blue) and telomeres (pink) for easier scoring of dicentric chromosomes (photo: M'kacher R)

RENEb consortium members have been building on work done under the MULTIBIDOSE project to define and validate approaches to uncertainty characterisation in dose assessment. This includes assessing the importance of including uncertainty estimates in triage categorisation using the RENEb table-top exercise data.

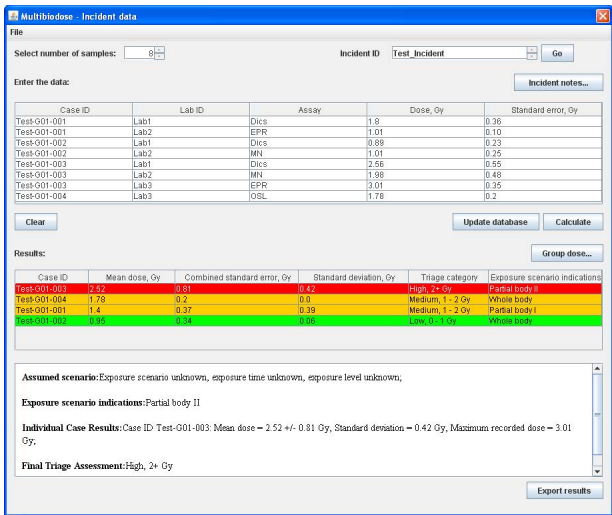
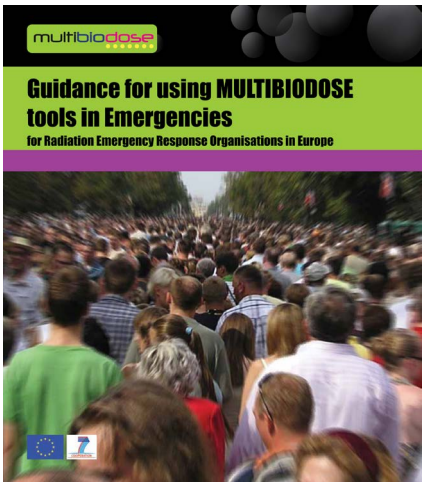


Fig. 4: The Multibiodose automated triage categorisation software tool, which is being tested and extended under recent RENEb activities

Introduction of novel assays

Several laboratories of RENEb and some non-RENEb laboratories have been working together to introduce the gene expression assay for biological dose assessment. Recent developments and the results of the second RENEb exercise proved that it might be possible to fully integrate this assay into the battery of established biodosimetry techniques in the near future.

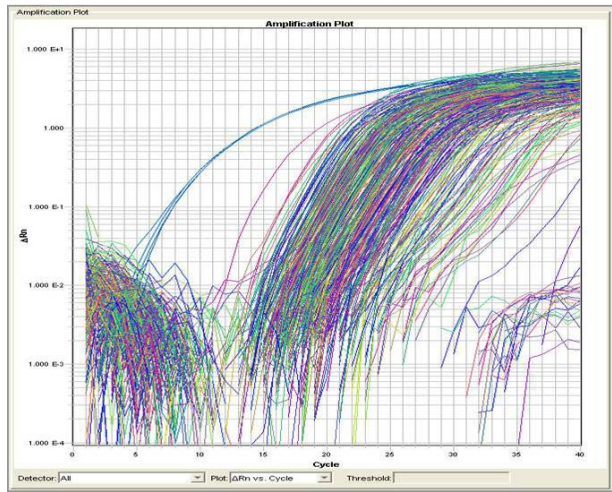
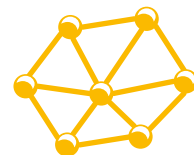


Fig. 5: Gene expression (Microarray / qRT-PCR): amplification plots of 384-qRT-PCR reactions (photo: Michael Abend)

A small number of laboratories in the network have been working towards introducing the physical techniques of individual dose assessment: thermoluminescence (TL) assay and RAMAN spectroscopy – work is ongoing here.



Towards applications of RENEb in Radiation Research

In addition to provision of retrospective dosimetry techniques for accident management, the RENEb network with its established strategies to guarantee consistently high performance on the existing techniques between the partner laboratories, has the ability and capacity to contribute to large-scale research. Furthermore, the critical identification and integration of new and upcoming technologies could have a positive impact on European radiation research, particularly for large-scale health surveillance and radiation risk assessment. In this regard, links to leading European Platforms including NERIS, MELODI, EURADOS and ALLIANCE have been initiated and the benefits of the RENEb approach have been promoted for large scale research approaches such as molecular-epidemiology. In this context, RENEb will have the ability to act as an analy-

sis infrastructure for research projects, offer E&T activities to assure the maintenance of competence and provide a QA&QM concept that will help to actively identify, verify and integrate new techniques and biomarkers of exposure and effect.

A Strategic Research Agenda (SRA) for RENEb is under development. The aim of the SRA is to identify the priorities in further networks developments and to outline the benefits to European radiation research that can be expected from this high quality scientific network with outstanding technical expertise from over 20 European countries with experience in biological dose assessment. Such expertise is presently not available in the operated European Research platforms to such an extent.

Recent and forthcoming events

The Annual Meetings in Valencia (February 2014) and Rome (March 2015)

At the third annual RENEb meeting in Valencia in February 2014, the Consortium reviewed progress in the project and discussed the way forward for the RENEb network. Details of training events (e.g. exchange of partners, organisation of seminars) and the organisation of the second inter-comparison exercise were presented. Participants discussed possible communication structures as well as the future legal status of the network.

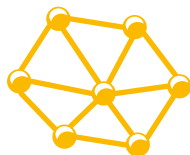
The Advisory Board recommended the development of a Strategic Research Agenda (SRA), and a SRA working

group was established. The Consortium concluded that besides networking in biological dosimetry for emergency preparedness, RENEb should set up a service infrastructure, for biomarkers of exposure, in order to contribute to mechanistic, and long- term studies in radiation research.

The fourth Annual RENEb meeting in Rome, in March 2015, gathered not only Consortium members, but also representatives from laboratories that have expressed an interest to join the RENEb network in the future (i.e. RENEb network candidates). Representatives from non-RENEb laboratories introduced their laboratories to the network and/or presented novel methods for biological dose assessments which are not yet established within RENEb.



Fig. 6: Participants of the 4th Annual Meeting of RENEb (photo ENEA)



On the first day of the meeting, RENEB participants presented the results of the second RENEB exercise. The sustainability of RENEB network as a whole, and its future status, after completion of the funded project at the end of 2015, was further discussed.

Representatives of the STORE database of biological data (www.storedb.org) discussed with the Consortium the potential use of this database for storage of biodosimetry images.

Open public RENEB events

In connection to the last two annual meetings of RENEB, in 2014 and 2015, the Spanish and Italian hosts organised open public events. The aim of these events was to present the importance of biodosimetry in the wider context of emergency response.

On the 26th of February 2014, during the 3rd Annual RENEB meeting, the Hospital Universitario y Politécnico La Fe in Valencia hosted the public session. This session was entitled “ARE WE PREPARED FOR A LARGE SCALE RADIOLOGICAL ACCIDENT IN EUROPE?” The Minister of Health from the province Valencia and the Director General of the Hospital had opened the session. The experts from the International Atomic Energy Agency (IAEA), World Health Organization (WHO), the European Emergency Preparedness Platform NERIS and European projects on emergency preparedness and dose assessments presented their approaches. At the end of this session, a press conference was organized.

On 6th March 2015 an open public RENEB Event took place at Agenzia Nazionale per le Nuove Tecnologie, L'Energia e lo Sviluppo Economico Sostenibile (ENEA)



Fig. 7: Panel of international experts during the open event in Valencia in 2014 (photo LAFE)

headquarters in Rome. ENEA organised this meeting jointly and Istituto Superiore di Sanità (ISS). Representatives from IAEA, WHO, and EURADOS organisations gave presentations. The event was entitled “THE BIODOSIMETRY NETWORKS FOR THE PREPAREDNESS OF A LARGE SCALE RADIOLOGICAL EMERGENCY”.

Both events were well attended and well received.

Dissemination event in Brussels, 26th November 2015 (participation by invitation)

This event will demonstrate progress made under the RENEB network project over the last 3 years to international and national stakeholders and decision makers in radiation and public health emergency preparedness. The RENEB Consortium will invite speakers from EU, HERCA and representatives from the medical emergency preparedness and radiation protection related public health communities from European countries. It is envisaged that this will be an interactive event with feedback from the participants, which should aid the formation of plans for the future of the RENEB network.

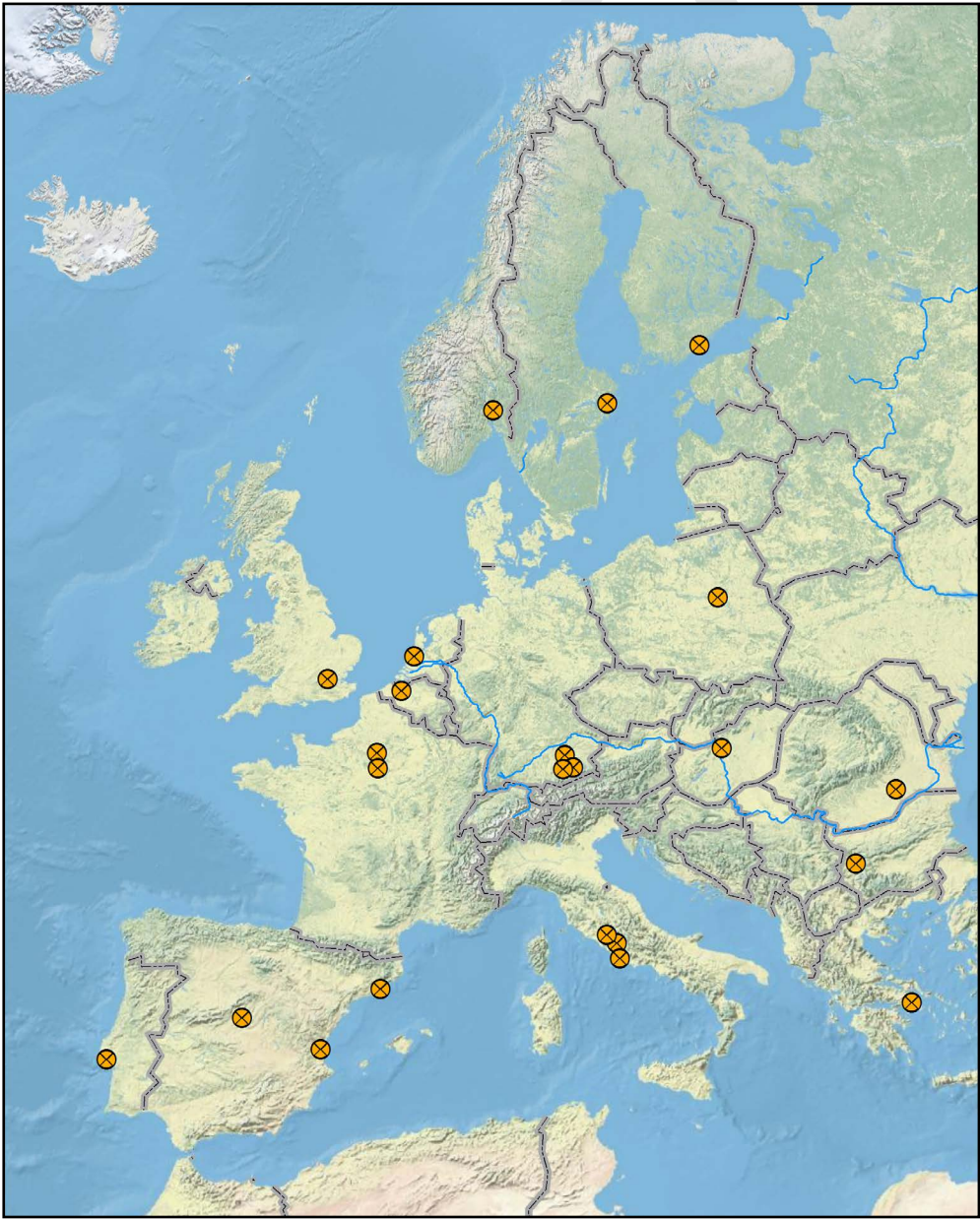
RENEB Publications as for April 2015

- Kulka U et al. Realising the European network of biodosimetry: RENEB - status quo. Radiation protection dosimetry. 2014;ncu266.
- Barnard S et al. The first gamma-H2AX biodosimetry inter-comparison exercise of the developing European biodosimetry network RENEB. Radiation protection dosimetry. 2014;ncu259.
- M'kacher R et al. New tool for biological dosimetry: Reevaluation and automation of the gold standard method following telomere and centromere staining. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis. 2014;770:45.
- M'kacher R et al. Automated Scoring of Dicentric Chromosomes in Nonstimulated Lymphocyte Prematurely Condensed Chromosomes After Telomere and Centromere Staining. International Journal of Radiation Oncology* Biology* Physics. 2015.

- Kulka et al. RENEB-Realizing the European Network of Biodosimetry. IRPA 13, Glasgow 2012. Conference paper.
- Voisin et al. RENEB-Realising European Network in Biological Dosimetry. NATO Science and Technology Organisation Report 10/2012.
- Kulka et al. Realising the European Network of Biodosimetry (RENEB). Radiat Prot Dosimetry 2012; 151(4):621.

RENEB presentations:

From the start of the project until the time this bulletin was issued, the RENEB project has been presented in about 30 oral presentations and posters at European and international scientific meetings, and also additionally at numerous national meetings in the consortium members' countries. During this period, as described earlier in this bulletin, the Consortium presented RENEB during a number of public events. The need for a biodosimetry network has been presented to the audience of these meetings from the point of view of international organisations dealing with radiation protection and public health such as WHO and IAEA.



consortium members institutions:

Bundesamt für Strahlenschutz (BfS), Germany (Project Coordinator)	Institute of Nuclear Chemistry and Technology (INCT), Poland
Bundeswehr Institut für Radiologie in Verbindung mit der Universität Ulm (BIR), Germany	Stockholm University (SU), Sweden
National Center for Radiobiology and Radiation Protection (NCRRP), Bulgaria	Institutul National de Sanatate Publica (INSP), Romania
Commissariat a l'Energie Atomique (CEA), France	Universitat Autònoma de Barcelona (UAB), Spain
National Centre for Scientific Research «Demokritos» (NCSR), Greece	Institut de Radioprotection et de Sûreté Nucléaire (IRSN), France
Agenzia Nazionale per le Nuove Tecnologie, L'Energia e lo Sviluppo Economico Sostenibile (ENEA), Italy	Universiteit Gent (UGent), Belgium
National Research Institute for Radiobiology & Radiohygiene (NRIR), Hungary	Istituto Superiore di Sanità (ISS), Italy University of Tuscia (UNITUS), Italy
Helmholtz Zentrum München (HMGU), Germany	Instituto Superior Técnico, Universidade de Lisboa (IST/CTN), Portugal
Norwegian Radiation Protection Authority (NRPA), Norway	Servicio Madrileño de Salud - Hospital General Universitario Gregorio Marañón (HGUGM), Spain
Public Health England (PHE), United Kingdom	Hospital Universitario y Politécnico La Fe (LAFE), Spain
Radiation and Nuclear Safety Protection (STUK), Finland	

RENEb candidate institutions:

Radiation Protection Centre, Lithuania
Belgian Nuclear Research Center (SCK•CEN), Belgium
Laboratori Nazionali di Legnano (INFN), Italy
Army Medical and Veterinary Research Centre, Italy
Forschungszentrum Jülich, Germany
University of Sevilla, Spain
Dublin Institute of Technology, Ireland

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