

# HEALS Newsletter

Health and Environment-wide Associations based on Large population Surveys

Project No 603946 of the European Union's Seventh Framework Programme



## Contents

<b>Welcome Note</b> . . . . .	<b>1 Epi Meeting in Rome, Italy</b> . . . . .	<b>8</b>
<b>Introducing HEALS</b> . . . . .	<b>2 WHO is WHO</b> . . . . .	<b>9</b>
<b>HEALS background</b> . . . . .	<b>4 Press Releases</b> . . . . .	<b>10</b>
<b>HEALS perspectives</b> . . . . .	<b>5 Publications</b> . . . . .	<b>12</b>
<b>Kick-off Meeting in Paris, France</b> . . . . .	<b>6 Presentations at International Conferences</b> . . . . .	<b>12</b>
<b>HEALS Training Workshop in Munich, Germany</b> . . . . .	<b>7 Forthcoming Events</b> . . . . .	<b>13</b>

## Welcome Note

Welcome to the first newsletter of the HEALS Project!

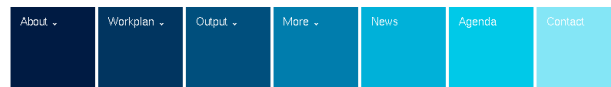
HEALS stands for Health and Environment-wide Associations based on Large population Surveys, a 60-month research project funded by the Seventh Framework Programme of the European Commission (starting in October 2013).

HEALS is carried out by a consortium composed of 29 partners from 15 countries. The objective of the project is to assess individual exposures to environmental stressors and predict health outcomes. The project also envisages to apply a pilot environment and health examination survey (EXHES Pilot Study), which will be mainly carried out in twins.

The HEALS Newsletter will be published twice yearly with the aim of provide details of the current activities, disseminate the research results and inform users about forthcoming events and other interesting information.

Furthermore, the HEALS website is now fully functional and provides useful information on the scientific activities of the project. Visit the website at:

[www.heals-eu.eu](http://www.heals-eu.eu)



Welcome to HEALS Health and Environment-wide Associations based on Large population Surveys

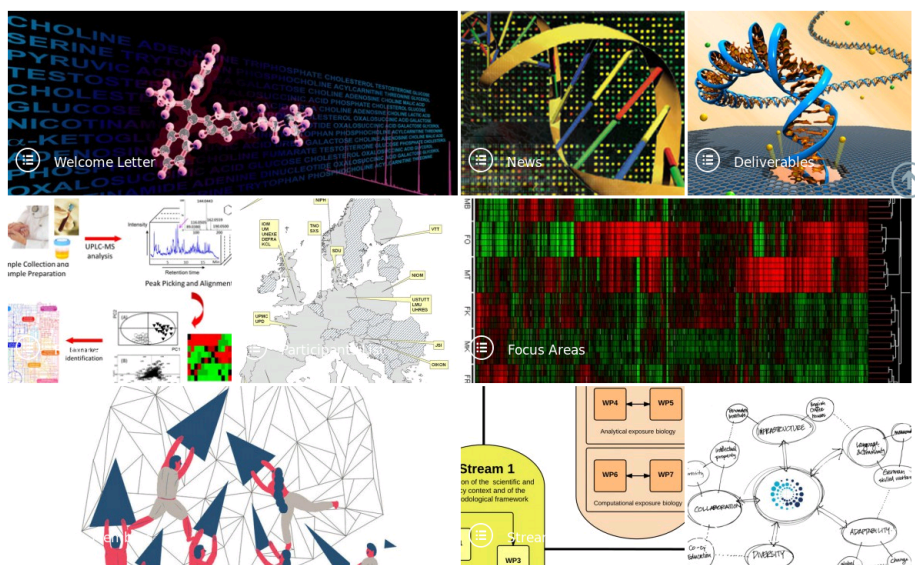
THE LARGEST RESEARCH PROJECT IN EUROPE ON ENVIRONMENT AND HEALTH

### HEALS Training workshop in Munich, Germany

16 - 17 DECEMBER 2013 || [CLICK HERE](#) FOR MORE INFORMATION.

### Kick-Off Meeting in Paris, France

23 - 25 OCTOBER 2013 || [CLICK HERE](#) FOR MORE INFORMATION.



HEALS is a Project, funded by the 7th Framework Programme of the European Commission

ASSESSING INDIVIDUAL EXPOSURE TO ENVIRONMENTAL STRESSORS AND PREDICTING HEALTH OUTCOMES - PAVING THE WAY FOR AN EU-WIDE ASSESSMENT

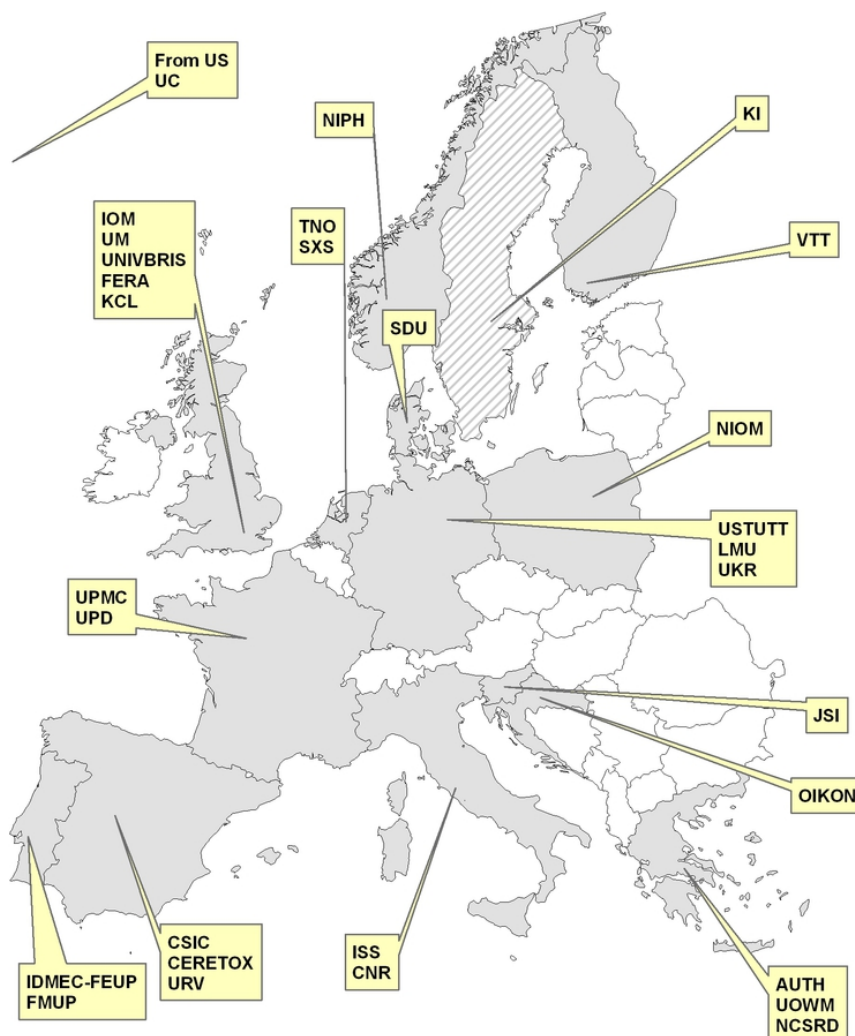
# Introducing HEALS

HEALS represents a comprehensive applied methodology focusing on the different aspects of individual assessment of exposure to conventional and emerging environmental stressors and on the prediction of the associated health outcomes. For the first time, HEALS will try to reverse the paradigm of "nature versus nurture" and adopt one defined by complex and dynamic interactions between DNA sequence, epigenetic DNA modifications, gene expression and environmental factors that all combine to influence disease phenotypes.

HEALS will start from analysis of data collected in on-going epidemiological EU studies involving mother/infant pairs, children, or adults including the elderly to evidence relevant environmental exposure/health outcome associations. These associations will aid in designing pilot surveys using an integrated approach, where the selection of biomarkers of exposure, effects and individual susceptibility results in integrated risk assessment. In the context of this new paradigm, a relevant contribution for a better understanding of the diseases comes also from twin studies. 🌐

## Partners in HEALS: 29 institutions from 15 countries

1. Université Pierre et Marie Curie - Paris 6 (UPMC, France)
2. Aristotle University of Thessaloniki (AUTH, Greece)
3. Institute of Occupational Medicine (IOM, United Kingdom)
4. Universität Stuttgart (USTUTT, Germany)
5. Institut Jožef Stefan (JSI, Slovenia)
6. Université Paris Descartes (UPD, France)
7. University of Bristol (UNIVBRIS, United Kingdom)
8. Istituto Superiore di Sanità (ISS, Italy)
9. Ludwig-Maximilians-Universität München (LMU, Germany)
10. Instytut Medycyny Pracy Nofera (NIOM, Poland)
11. Teknologian Tutkimuskeskus (VTT, Finland)
12. University of Manchester (UM, United Kingdom)
13. Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek (TNO, Netherlands)
14. Food and Environment Research Agency (FERA, United Kingdom)
15. Consejo Superior de Investigaciones Científicas (CSIC, Spain)
16. University of Western Macedonia (UOWM, Greece)



17. Centre de Recerca en Toxicologia (CERETOX, Spain)
18. Instituto de Engenharia Mecânica (IDMEC-FEUP, Portugal)
19. Oikon doo Institut Za Primijenjenu Ekologiju (OIKON, Croatia)
20. Consiglio Nazionale delle Ricerche (CNR, Italy)
21. Universidade do Porto (FMUP, Portugal)
22. National Center for Scientific Research Demokritos (NCSR, Greece)
23. Universitat Rovira i Virgili (URV, Spain)
24. Universitätsklinikum Regensburg (UKR, Germany)
25. ServiceXS (SXS, Netherlands)
26. King's College London (KCL, United Kingdom)
27. Norwegian Institute of Public Health (NIPH, Norway)
28. Syddansk Universitet (SDU, Denmark)
29. University of California Berkeley (UC, United States of America)

/// Karolinska Institutet (KI, Sweden)

## Organising the work: 6 streams and 20 work packages

**Stream 1** Definition of the scientific and policy context and of the methodological framework

**WP 1** Overview of scientific state of the art

**WP 2** Scientific networking

**WP 3** Definition of methodological framework

**Stream 2** Internal exposure assessment to define the exposome

**WP 4** Human biomonitoring

**WP 5** Omics and epigenetics analyses

**WP 6** Physiology based biokinetic modelling

**WP 7** Novel bioinformatics for predictive biomarker discovery

**Stream 3** Estimating external exposures to multiple health stressors

**WP 8** Environmental data mining

**WP 9** Exposure monitoring throughout lifetime - constructing the exposome

**WP 10** Taken account of socio-economic status when modelling external exposures

**WP 11** Integration of time- and spatially resolved data: Data and model synthesis

**Stream 4** Environment-wide associations between exposure and health effects

**WP 12** Exposure and health data management

**WP 13** Exposure and health association studies

**Stream 5** Population studies

**WP 14** Allergy and asthma - link with particulate matter (PM) and biologicals

**WP 15** Neurodevelopmental and neurodegenerative disorders

**WP 16** Obesity and childhood diabetes – link with endocrine disruptors

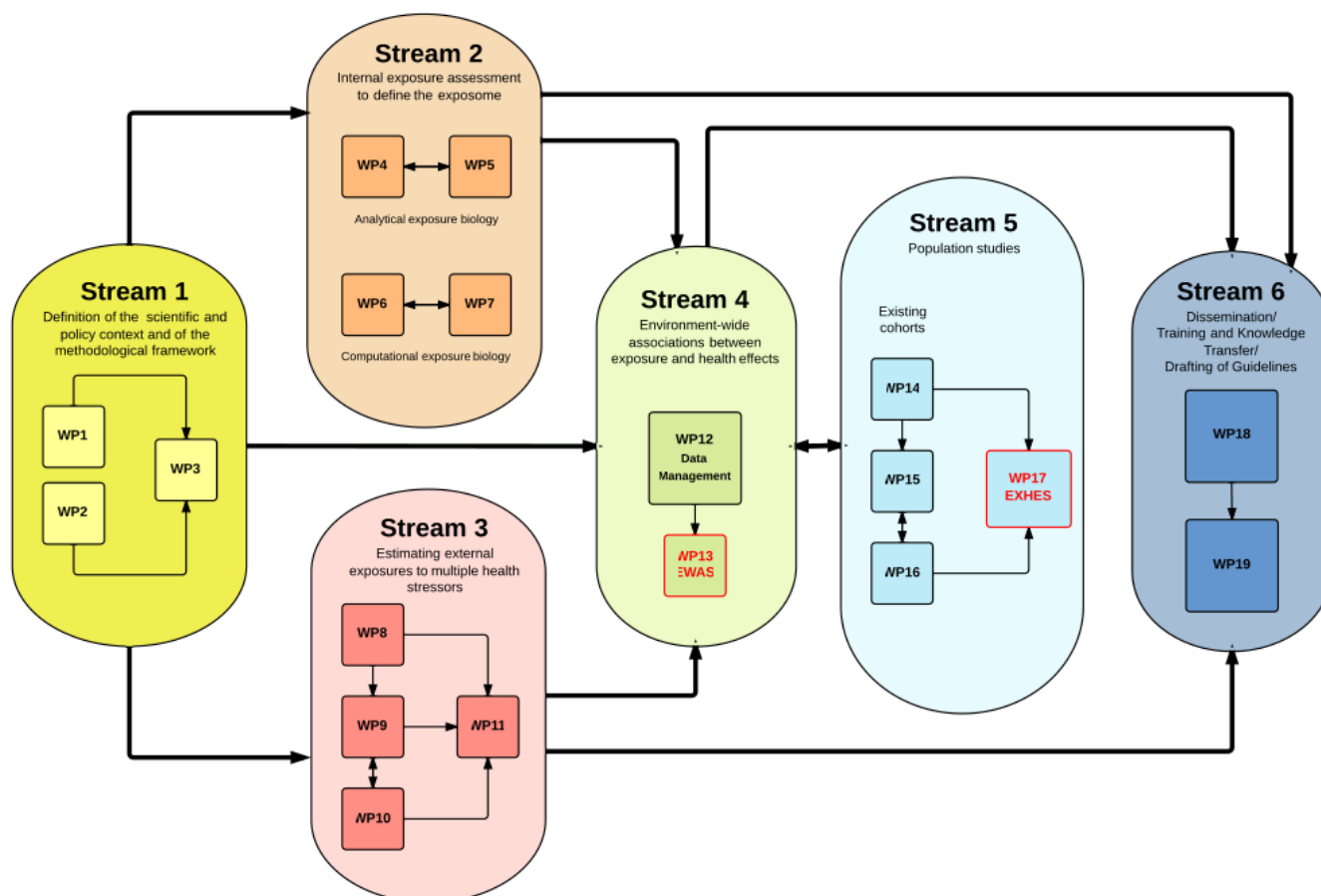
**WP 17** Pilot European Exposure and Health Examination Survey (EXHES)

**Stream 6** Dissemination / Training and knowledge transfer / Drafting of Guidelines

**WP 18** Training on HEALS methodology and tools

**WP 19** Dissemination of results and knowledge transfer

**WP 20** Project management



# HEALS background

by DIMOSTHENIS A. SARIGIANNIS

Aristotle University of Thessaloniki (AUTH)  
Thessaloniki, Greece

Unraveling the exposome is daunting, particularly in the light of the enormous amount of information that needs to be integrated. As a result of dedicated actions and projects following the European Commission's (EC) Environment & Health Action Plan 2004–2010, various harmonization efforts have occurred. Projects such as COPHES (harmonization of HBM), EHES (harmonization of Health Surveys), EU-menu (harmonization of data collection on food consumption) or CHICOS (harmonization of child cohort studies) or U-BIOPRED (unbiased biomarkers in prediction of respiratory disease outcomes) all aim at providing common ground for the often disparate information which was scattered across Europe. In addition, European twin registries have collected biological material and longitudinal phenotypic and exposure data on tens of thousands of twins providing a valuable resource for investigating the development of complex phenotypes and their underlying biology.

A first attempt from our consortium to integrate these data in novel ways in order to produce new knowledge that would allow us to explore the early-life exposome was put together in the form of an integrated project proposal called EUREKA. The proposal, even though among the top three in Europe, did not receive funding in 2012. When the European Commission published the call for proposals on using the exposome for enhancing environment and health associations and risk assessment we felt that we were mature to move on with the integrative concept that was originally introduced in EUREKA and finally funded with HEALS. The HEALS project is a logical progression from much of the achievements of the EHAP 2004–2010.

Making optimal use of the availability of harmonized data across Europe, HEALS introduces significant advances to environmental and health data fusion, including assimilation of data from satellite remote sensing for direct measurement of environmental exposure to airborne pollutants such as particulate matter (PM) and for providing accurate spatially-resolved estimates of population exposed to environmental pollutants. Using data fusion techniques, traditional health and exposure data derived from fixed monitoring networks will be supplemented by a range of emerging novel techniques and technologies such as agent-based models (ABM), mobile phone apps, environmental sensor-webs, micro-sensors and satellite remote sensing. In addition we will considerably improve exposure modelling and phenotype identification using deterministic and probabilistic approaches, and applying new epidemiological and statistical methods to relate modelled exposure to health outcomes. ABM will be informed by data relating to an individual's behaviour within his/her environment (such as movement data within specific micro-environments) and between individuals exploring interactions around health related behaviours and issues such as low SES. Using these parameters and the evolution of agents, simulations will produce detailed information relating to the emulated systems, data that can

be used to fill in the gaps that exist in traditional datasets. This holistic approach takes the best from existing monitoring and sensor technology, but supplements it with computational modeling simulations where real-world data is unavailable at the spatial and temporal scales that the individual exposome requires. Although commonly used elsewhere, ABM and fusion methods have not been applied to our knowledge in environmental epidemiology. This array of novel technologies, coupled with state-of-the-art environmental monitoring of chemical health stressors will provide a complete and dynamic picture of external exposure to environmental chemicals.

HEALS also focuses on the main biological processes that govern the biological and physiological responses to toxicological insults from environmental xenobiotics. Thus, it introduces an integrated approach to health risk assessment, attempting to draw the maximum benefit from the exposure information related to the biomonitoring data collected throughout Europe. Biomonitoring studies performed so far in the EU indicate that children are exposed to several environmental contaminants/stressors but there is still limited or inadequate epidemiologic evidence to support clear associations between environmental exposures and health outcomes. HEALS intends to contribute to filling these knowledge gaps, by taking advantage of data collected in on-going EU epidemiological studies (including twin studies) to extract relevant information both for exposure and health effects in order to identify and validate predictive biomarkers to be applied in a pilot survey using cohorts across the EU. This will be attained through the use of -omics, primarily metabolomics and adductomics, supported by targeted transcriptomics and proteomics coupled with physiology-based biokinetic modeling for data interpretation. Advanced bioinformatics and multivariate statistical techniques developed for genome-wide associations will be used for environment-wide association studies to link environmental exposure and health status data collected and tested in population surveys tackling key health endpoints of SCALE and the Parma Declaration such as respiratory, neurodevelopmental and neurodegenerative disease, obesity, childhood and type II diabetes (T2D).

Finally, the tools brought to bear in HEALS will be put together in an integrated methodology that aims at optimally managing the knowledge base already available for twins cohorts in EU (including samples stored in dedicated biobanks) and to design and perform pilot surveys including twins (mother-child cohorts, starting from pregnancy up to 3 years of age) and matched singletons to be carried out in countries participating to HEALS. Thus, new methods for the estimation of the environmental burden of disease (EBD) will be developed, using novel data for predictive biological monitoring. The HEALS approach takes the temporal dimension into account, thus improving the study of latent and epigenetic effects of early life exposures. ☺



# HEALS perspectives

by ISABELLA ANNESI-MAESANO and DIMOSTHENIS A. SARIGIANNIS

Université Pierre et Marie Curie - Paris 6 (UPMC)  
Paris, France

Aristotle University of Thessaloniki (AUTH)  
Thessaloniki, Greece

To understand the development of a disease and its environmental causes in view of prevention, it is needed to characterize the human "exposome", which represents all the exposures to which people are exposed in their life from both endogenous (the "internal exposome") and exogenous (the "external exposome") sources including lifestyle factors. Advancing in the exposome assessment will require tight collaborations among epidemiologists, toxicologists, physicians, psychologists, sociologists, biostatisticians, experts in bioinformatics, exposure and laboratory scientists.

Assessing the exposome at its most complete degree in order to encompass life-course internal and external environmental exposures, from the preconception period onwards in order to explain the development of asthma and allergies, overweight, obesity and diabetes, as well as neurodevelopmental and neurodegenerative disorders is the first challenge taken up by HEALS. HEALS will disentangle the "internal exposome" by developing and validating biological markers using data from European pre-existing and new population-based studies and their bio-banks. This will allow detecting signals in body fluids through proteomics, metabolomics and transcriptomics permitting to characterize exposures to environmental contaminants and identify intermediate markers that lead to chronic diseases. To be exhaustive other "omics" technologies and measures in relation to external exposures (namely heavy metals, POPs...) as well as the assessment of DNA adducts in relation to a number of exposures will be conducted. Research on "external exposome" will include analysis of data from lifetime exposures to environmental pollutants in air, food, water, physical activity, medications, homes and daily stressors.

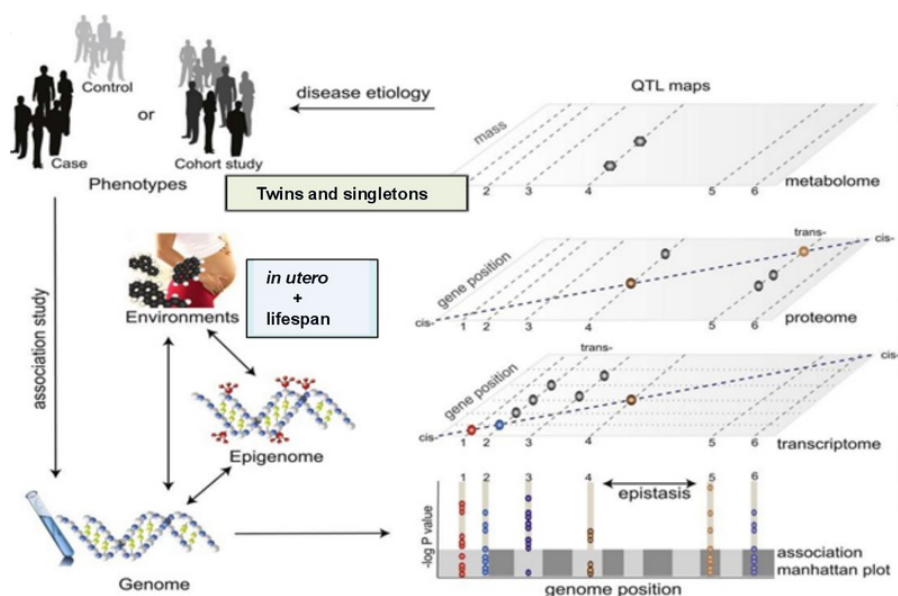
It is the prospective cohort study design through the new cohorts of singletons and twins that will be recruited since *in utero* life and followed-up for 3 years and of their parents (the Exposure and Health Examination Survey (EXHES)) that best suits the "expo-

somic" approach, providing the opportunities for collecting repeated sampling of questionnaires, clinical data and biological specimens to enable a large timeframe of exposure and diseases assessment, along with the avoidance of reverse causation by the collection of data prior to disease onset.

The insights HEALS will gain from studying twins from existing European twins registers and the EXHES will help to better understand how nature and nurture work together in the development of the diseases. Because monozygotic (identical) twins develop from a single fertilized egg, they have the same genome. So any differences between twins are due to their environments, not genetics. Recent studies have shown that many environmentally induced differences are reflected in the epigenome. The available large-scale epigenetic studies of monozygotic and dizygotic twins will provide data useful to the understanding of how genetic and environmental factors impact through lifespan upon epigenetics, and how epigenetics impacts on complex traits underlying diseases.

Developing reliable tools for assessing a complete exposure history is the second challenge taken up by HEALS. Such tools have to achieve very high precision and reliability in order to be applied in other investigations. And a data mining process will be used to extract information from the obtained huge data set, transform it into an understandable structure for further analyses and discover patterns in the environment-wide associations (EWAS) underlying diseases. The HEALS approach will be a mechanistic one, based not only on data associations but coupling bioinformatics analysis with mechanistic modeling to ensure that causal associations between exposures and health outcomes are highlighted.

The last daunting challenge for HEALS is to fully derive public health benefits from the expenditure in terms of energy, time or public money that have been allocated to the project. ☺



# Kick-off Meeting in Paris, France

(23–25 October 2013)

The HEALS kick-off meeting took place in Paris on October 23rd to 25th 2013, hosted by Université Pierre et Marie Curie (UPMC, France). The meeting was led by HEALS coordinators, Dr. Isabella Annesi-Maesano and Prof. Denis Sarigiannis, and was attended by all the project partners, a member from the European Commission (Dr. Tuomo Karjalainen), two members from the Project Advisory Board (Dr. Marco Martuzzi, Dr. David Balshaw), and some members from other European institutions and research projects.

The first session of the meeting was focused on setting the HEALS project in the context of the **EU exposome initiative**, which includes three major EU-funded projects, namely **Exposomics**, **HELIX** and **HEALS**. Dr. Tuomo Karjalainen pointed out the need of strong integration among the aforementioned projects because of the efforts of the European Commission in the Environment and Health research domain. The main expectations of the European Commission from the HEALS project are to contribute to the advancement of science/innovation and risk assessment and to integrate with the other projects and initiatives already running to maximize the synergies and to contribute to the building of a global virtual “centre of excellence” on the exposome concept.



Prof. Sarigiannis led a session on the HEALS implementation, presenting the project summary and outline. He indicated that the main aspect of the work is to have an integrated approach on the unraveling of the *exposome* that will significantly affect health risk assessment. Prof. Sarigiannis also presented the project website and the intranet, created by AUTH to manage all project information, the work plan and the following meetings in Munich, Thessaloniki, Ljubljana and another additional meeting to discuss the EXHES protocol.

During the meeting, a long session was dedicated to present the current state of the art and recent advances in the exposome

research area through the different EU-funded projects and also the activities on the exposome in the USA, as follows:

- Exposomics (EU), by Dr. Paolo Vineis
- COPHES/DEMOCOPHES (EU), by Dr. Dominique Aerts
- HELIX (EU), by Dr. Mark Nieuwenhuijsen
- SELMA (EU), by Dr. Carl Gustav Bornehag
- NIEHS and NIH (USA), by Dr. David Balshaw

The last session of the first day was dedicated to review the work packages (WPs) from Streams 1 and 6, specifically those related with the methodological framework and the dissemination and training of the HEALS project, respectively. The second day of the meeting was then dedicated to review the WPs related to Streams 2, 3, 4 and 5. For each work package, the WP leaders presented the aims and outlines, highlighting the most important aspects to be considered.

On the third day of the meeting the participants divided out into break-out sessions on the Streams 2 to 5 of the project. Finally, an additional session for WP17 (EXHES Pilot Study) was required. The session, led by Dr. Isabella Annesi-Maesano, focused on the inclusion and exclusion criteria and the design to be applied in the Pilot Study, which will include two stages. EXHES I is planned to be conducted in 10 countries, with singleton and twin cohorts, and a duration of a total of three years. EXHES II will include nested case-control studies, omics and geolocalisation techniques, and environmental assessments of air, water and noise exposures.

The last part of the meeting was dedicated to the coordination and networking of the HEALS project with other initiatives and projects, the administrative and financial issues within HEALS, which was led by Dr. Thomas Wiest, and finally, the Project Advisory Board meeting, which was led by Dr. Marco Martuzzi.







# HEALS Training Workshop in Munich, Germany

(16–17 December 2013)

by STEPHAN BÖSE-O'REILLY

Ludwig Maximilians Universitaet Muenchen (LMU)  
Munich, Germany

The first training workshop took place in Munich on December 16th and 17th 2013. It was hosted by the University Hospital Munich, Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine. The 33 participants came from 25 institutions. Prof. Dr. Dennis Nowak (LMU), Prof. Dr. Isabella Annesi-Maesano (UPMC), Prof. Dr. Dimosthenis Sarigiannis (AUTH) and PD Dr. Stephan Böse-O'Reilly (LMU) welcomed the participants. The aim of the training was to enhance the common understanding of HEALS.

At the beginning an our guest speaker, Johanna Hausmann (WECF – Women in Europe for a Common Future) gave a very clear and useful statement on "how to communicate scientific information to the interested public". The scientific results from HEALS need to be transported to the public. Important strategies in the communication of scientific information are awareness rising, choosing appropriate communication channels and preparing understandable questions. NGOs can be a partner for bringing the messages to the public. The presentation was intensively discussed, and the HEALS project will certainly put a special emphasis on communicating scientific results with relevant stakeholders, including the civil society.

The next presenter was the co-coordinator of HEALS; Prof. Dr. Dimosthenis Sarigiannis (AUTH). He presented an excellent update on "Integrated methodology and the application of the corresponding analytical and computational tools for performing environment-wide association". This update summarised the basis and the perspective of HEALS as a research project.

After these introductions the participants divided out into break-out sessions on the various streams of the project (stream 1 to 4). They discussed the existing conceptions of HEALS and discussed

also the misconceptions. The stream leaders encouraged the discussions to come to plausible and practical solutions for the future work and reported these results at the end of the day to all participants.

The interfaces between the different work packages were specially addressed. There is still a lot of misunderstanding on the concept of HEALS, especially in respect of the projected Epi-HEALS study (EWAS). It seems urgent that concrete and detailed protocols are developed to get the study started. Technically it is possible to analyse many specimens and many endpoints, but within HEALS it is not possible to analyse everything, it will be necessary to focus the analysis to the most important parameters. Needed are: define preliminary protocols for biomonitoring, omics, sample requirements, sample possibilities. As well, each HEALS partner should provide existing data or information for existing data. A preliminary list of substances that should be included was discussed:

- Indoor air quality: PM2.5, PM10, VOCs, NOx, SOx, ozone, humidity, temperature
- Metals: Selenium, lead, arsenic, manganese, mercury
- Noise

It will be essential to work across the streams and work packages. Stream 1 to 4 are developing the basis for the modelling and will interact with stream 5 (Epi HEALS) that is set up to confirm the model of lifelong exposure and health outcomes. Additional technical meetings are necessary. Research priorities need to be set very soon.

The second day was opened by a great presentation from Prof. Joachim Heinrich (Helmholtz Zentrum München – German Research Center for Environmental Health). He discussed very clearly and frankly the "The beauty of birth cohorts and potential pitfalls".

The essentials were:

- The scientific community considers birth cohorts as important.
- Data about the life prevalence might be biased.
- Birth cohorts do collect data with longitudinal character.
- Incidence and remission data are included in birth cohorts.
- Frozen samples are especially important if new biomarkers are developed.
- Participants with low socioeconomic status are underrepresented in birth cohorts.

Prof. Heinrichs take home message was that birth cohorts may solve the problem of reverse causality.

The next very valuable presentation was given by the coordinator of HEALS, Prof. Isabella Annesi-Maesano (UPMC), on the "Environment-wide association studies" (EWAS). She gave an overview on the intended HEALS epidemiological-study. A draft of the preliminary protocol was distributed to the participants and discussed. A lot of different protocols are necessary for the twin and singleton-study in order to respect local situations and resources. There will be a core protocol that will be compulsory for all centres, then an enlarged protocol and additionally several case-studies.

Later on that day the participants continued the breakout sessions to discuss once more common concepts and the misconceptions of HEALS, focusing on stream 5, population studies.

In the afternoon of the second day stream 6 (dissemination and training) was presented by Prof. Marta Schumacher (URV), Dr. Mercè Garí (CSIC), Prof. Joan Grimalt (CSIC), Dr. Julia Schoierer (LMU) and PD Dr. Stephan Böse-O'Reilly (LMU). Some conclusion were that, Moodle will be used for training as technical platform in HEALS. The details for the newsletter and the participation in scientific conferences were discussed.

Very important is that all scientific articles deriving from the HEALS project need to be published with open access (EU rule; EC-GA, Special Clause 39). The EU has an online store, where all scientific contributions of the HEALS project will be stored (<http://www.zenodo.org/collection/user-heals>).

The participants worked hard at the meeting but they also managed to have a good time in Munich. There was enough time and opportunities to get to know each other better which is important for such a multinational and interdisciplinary group. Two nice social events gave the participants the opportunity to learn more about Munich and its history, the traditional Munich food and beer, and some insides to Munich and its Christmas markets. ☺

## Epi Meeting in Rome, Italy

(4–5 February 2014)

by GEMMA CALAMANDREI

Instituto Superiore di Sanità (ISS)  
Rome, Italy

The second HEALS Workshop took place in Rome on February 4th and 5th 2014, hosted by the Istituto Superiore di Sanità (ISS; National Health Institute) in Rome. Dr. Gemma Calamandrei (ISS) in representation of the ISS, and then Prof. Dr. Isabella Annesi-Maesano (UPMC) and Prof. Dr. Dimosthenis Sarigiannis (AUTH) as co-coordinators, welcomed the participants.

The Workshop was dedicated to the preparation of the protocol of the Pilot European Exposure and Health Examination Survey (EXHES), and involved all the WPs based on epidemiological studies and other HEALS participants in charge of environmental exposure assessment, -omic analyses, human biomonitoring, ethical aspects.

The first session of the Workshop was focused on defining the EXHES design and the target population of the study. Prof. Annesi-Maesano presented the EXHES general schema, which include EXHES I –a population based sample– and EXHES II –the nested case control– where more targeted environmental and omic analyses will be performed. The main objective of the EXHES study will be to implement new birth cohorts of children including singletons and twins in order to collect new harmonized and standardized exposure and health data at the European level. EXHES will allow obtaining baseline measures for assessment of future trends in environmental exposures and major chronic diseases and provides a framework for further etiological research into lifestyle, environmental, epigenetic, genetic and medical care factors affecting health. Finally by applying the HEALS methodological framework to data

collected through EXHES the HEALS consortium will quantify the link between exposures with health outcomes, asthma and allergies, neurodevelopmental disorders and overweight, obesity and diabetes in particular. Such approach requires application of a standardised protocol to collect as many information as possible as for: mother and child general health, environmental exposure to chemicals, life stile and dietary habits of the parents and the child.

Collection of biological samples are foreseen during pregnancy, at birth and in the first three years of life: prenatal exposure to metals (chromium, cadmium), arsenic, POPs (PCB, PFC, organochlorine pesticides, brominated and fluorinated compounds) will be assessed in cord blood, early life exposure will be quantified using maternal milk (i.e. metals, arsenic and POPs) and at 2 years of age using child's urine metals, arsenic and phthalates and hair for mercury. Measures of exposure will be related to clinical outcomes as for asthma and allergies, obesity and diabetes, and neuropsychological maturation.

On the basis of Dr. Annesi-Maesano presentation, the leaders of the epidemiological WPs discussed both solved and unsolved issues she presented: among these, the feasibility of the recruitment process and of questionnaire administration, and the opportunity to have either a core and an enlarged protocol, this latter possibly answering to more specific research questions with the establishment of satellite case studies in the different countries. During Session 2, inputs from the epidemiological WPs contributed to define ex-



posures and outcomes of interest in EXHES. Chemicals of major relevance for the three groups of diseases were presented by Dr. Maesano (Obesity), Dr. Giovanni Viegi (Asthma and allergy) and Dr. Gemma Calamandrei (Neurodevelopmental disorders) in their respective fields, identifying common risk factors on which possibly focusing biomonitoring and measurement of external exposure. Outcomes of interest were also presented and feasibility of health assessment thoroughly discussed, in particular as for neuropsychological test batteries, which are extremely time-consuming and require adequate training and specific setting.

The second day of the workshop was dedicated to discuss exposures, human biomonitoring, omics and ethical issues. Specifically, the role of indoor environment and the methodology applied to measure exposures was presented by Prof. Eduardo Oliveira Fernandes (UP), while Prof. Sarigiannis and Dr. Alberto Gotti (AUTH) explained to the audience the methodological approach of exposomic analysis and fusion of exposure data from multiple remote sensors.

Dr. Milena Horvat (JSI) presented a detailed explanation of the technical problem associated with human biomonitoring and successfully identified criticalities to consider for feasibility of EXHES I and II, last but not least the number of chemical compounds to be assessed in biological samples, the need of linking biomonitoring to -omic analyses, the quality and quality of samples to be collected. In such framework Dr. Lorenza Nisticò (ISS) described the protocol applied to birth cohorts in order to collect and store samples for biobanking, underlying the need for specific operative procedures in the EXHES framework. The ethical issues related to birth cohorts were finally described in detail by Dr. Virginia Toccaceli (ISS).

In the final session of the two-day workshop, all participants chaired by Prof. Giovanni Viegi (CNR) and Prof. Fintan Hurley (IOM) discussed the questions to be included in questionnaires as well as the SOPs for collection of biosamples. There was general agreement on the detailed protocol to be delivered to get the study started. In this final discussion the interfaces between the different work packages were specially addressed and encouraged. ☺

## WHO is WHO

### HEALS senior scientists



HEALS Coordinator, Prof. **Isabella Annesi-Maesano** (Master, PhD, DSc, MD) is a respiratory epidemiologist by training, initially educated in physics and medicine (University Doctorates). She is research director at the French NIH (INSERM) and responsible of the EPAR (Epidemiology of Allergic and Respiratory Diseases) Department ([www.epar.fr](http://www.epar.fr)) at the Institute Pierre Louis of Epidemiology and Public Health (UMR-S 1136) of UPMC and INSERM in Paris. As PI or WP leader she has been or she is involved in several national and international projects targeting allergic and respiratory diseases in terms of exposure and mechanisms (among the EC-funded projects: HEALS, GERIE, SINPHONIE, PHASE, HESE, HESEINT, MED'HISS, MEDALL). She has just obtained the UPMC Foundation Excellence Chair that will last for 5 years. She is professor of environmental epidemiology. Prof. Annesi-Maesano is advisor to many international and national bodies, including the World Health Organisation (WHO). She is a member of several international and national advisory committees on respiratory medicine and environmental health (WHO, GARD, ARIA, ANSES, PRIMEQUAL, OQAI, RNSA...). Presently, Prof. Isabella Annesi-Maesano is member of the Environmental and Health Committee of the European Respiratory Society (ERS) and Head of the Interest Groups Aerobiology and Air Pollution of the European Academy of Allergology and Clinical Immunology (EAACI). Prof. Annesi-Maesano is Associate Editor and members of the Editorial Boards of several journals, including *European Respiratory Journal*, *International Journal of Tuberculosis and Lung Disease*, *BMC Public Health*, *European Respiratory Review*, *Therapeutic Advances in Respiratory Disease*, *Multidisciplinary Review* and the local journal *La lettre du pneumologue*. Prof. Annesi-Maesano is the author and co-author of 232 international and national peer-reviewed articles, without counting books and reports. Dr. Annesi-Maesano is the coordinator of the HEALS project, leader of Stream 5 and leader of WPs 13, 16 and 17. She is also involved in the other WPs.



HEALS co-Coordinator, **Dimosthenis Sarigiannis** (MS, PhD) is Associate Professor at the Department of Chemical Engineering of the Aristotle University of Thessaloniki (AUTH), Adjunct Professor at the Master's Programme on Environmental Chemical Risk at the Institute for Advanced Studies of the University of Pavia and Senior Scientist at the Chemical Assessment and Testing unit of the Institute of Health and Consumer Protection (IHCP) at the European Commission's Joint Research Centre. At the European Commission, Prof. Sarigiannis has served as Scientific Coordinator of the IHCP, Action Leader for Consumer Product Safety and Quality and Community Reference Laboratory for Food Contact Materials, Action Leader for Human Exposure to Environmental Stressors and Health Effects and for Assessment of Chemicals at the European Chemicals Bureau, Scientific Assistant to the JRC Director General, Strategy Manager of the IHCP and as science advisor to the Greek Minister of the Environment. He is member of the international forum for evidence-based toxicology, has sat at the scientific committee for chronic risks of INERIS in France, and he currently is President of the Mediterranean Scientific Association for Environmental Protection (MESAEP), Vice-President of the Hellenic Society of Toxicology and of the Hellenic Chemical Engineering Association – Central and Western Macedonia Division. He is also member of the Air Quality committee of the Hellenic Ministry of Health and national expert at the Environment, Resources and Climate Change program committee of Horizon 2020. Since 2013 he serves as temporary advisor to the WHO on combined exposure to indoor health stressors, human biomonitoring and endocrine disruptors and he is member of the WHO Chemical Risk Network. Prof. Sarigiannis sits at the Editorial Board of the journals *Pharmacogenomics* and *Environmental Sciences*. His research focuses on the evaluation of the health and environmental impact of industrial and environmental toxicants, data/model fusion for environmental health monitoring and the direct and indirect effects of

climate change on public health. Since 2004, he has focused on setting up and using exposure biology-based computational models and toxicogenomics techniques for quantitative assessment of the risk from co-exposure to multiple chemical and physical/biological stressors through the environment and consumer products pose developing novel methods to explore the human exposome. He

has led several European projects on the above topics, including CROME, INTEGRA, TAGS, INTERA, CHEMTEST, ICAROS NET and ICAROS. Prof. Sarigiannis is the co-coordinator of the HEALS project, leader of Streams 2 and 4, and leader of WPs 3 and 7. He is also involved in the other WPs.

## HEALS young scientists



**Nadine Steckling** is a Ph.D. student of Public Health at Bielefeld University (Bielefeld, Germany). She holds a European Master of Science in Public Health and a Bachelor of Arts in Sports Science with a profile on Health and Management. Nadine worked for the School of Public Health of Bielefeld University (Bielefeld, Germany) in the projects VegAS, GEniUS, and DiWIn-tox. Now she works in the workgroup of Paediatric Environmental Epidemiology of the Institute and Outpatient Clinic for Occupational, Social, and Environmental Medicine of the University Hospital in Munich (Ludwig-Maximilians University, LMU, Germany). Her research is located in the public health area of environment and health with a special methodological focus on Environmental Burden of Disease assessments. Health effects of mercury exposed artisanal small-scale gold miners are an issue with highest priority in her research, while she is also focusing on other risk factors like cadmium and benzene. The analysis of primary health, exposure, human biomonitoring, and socio-economic data as well as merging and processing of secondary data belong to her expertise. Within the HEALS project, the LMU team around Stephan Böse-O'Reilly is involved in the work packages 4, 15, 17, 18, 19, 20, while Nadine is mainly involved in WP 4 (Human Biomonitoring) and WP 18 (Training on HEALS methodology and tools).



**Janja Snoj Tratnik** is a Ph.D. student at the Jozef Stefan International Postgraduate School (Ljubljana, Slovenia), under the mentorship of Prof. Dr. Milena Horvat. She studied Biology at the University of Ljubljana (Ljubljana, Slovenia). Janja is working on low-level mercury exposure in different population segments in Slovenia. Her areas of research are human biomonitoring

of metals, mercury analyses, analytical quality requirements and biostatistics. She has co-authored 15 papers in international peer-reviewed journals and has been involved in national and European projects such as PHIME, National Human Biomonitoring, COPHES and DEMOCOPHES. In the HEALS Project, Janja Snoj Tratnik is involved in several Work Packages (WPs 3, 4, 15, 16 and 17), in the JSI team together with Milena Horvat, Darja Mazej and Ingrid Falnoga. Specifically, she will work on metal environmental exposure, human biomarker data, link between metals and neurodevelopmental and neurodegenerative disorders, link between endocrine disruptors and obesity/childhood diabetes, and the Pilot European Exposure and Health Examination Survey (EXHES) for Slovenian population.



**Joaquim Rovira Solano** studied Chemistry and Biochemistry at Universitat Rovira i Virgili (URV, Tarragona, Catalonia, Spain). He obtained his Ph.D. degree on Environmental Monitoring and Human Health Risk Assessment at URV in March 2013. At the present, he works in the Centre of Environmental, Food and Toxicological Technology (TecnATox) of the URV as a post-doctoral researcher. His areas of research are Environmental Toxicity due to Heavy Metals and Persistent Organic Pollutants; Human Health Risk Assessment; and Optimization of Monitoring Methods through Active and Passive Sampling of Atmospheric Contaminants. He has co-authored 9 papers in international peer-reviewed journals and has been involved in national and European projects such as SCARCE, RISKCYCLE, and TDS-Exposure. In the HEALS Project, Joaquim Rovira is involved in several Work Packages (WPs 2, 4, 6, 7, 8, 12, 15, and 19), together with Marta Schuhmacher, José Luis Domingo, Martí Nadal, and Vikas Kumar. He will work on Physiology-based Biokinetic Modelling; Exposure and Health Data Management; and Dissemination and Knowledge Transfer Activities.

## Press Releases

© Press releases of the HEALS project in several Spanish Media (last updated: 10 March 2014):

- Newspaper Printed Editions: *Expansión*, *Diari Més* and *Diario Médico*
- Newspaper Digital Editions: *ABC*, *Agencia EFE*, *Agencia Europa Press*, *Deia*, *Diari de Barcelona*, *Diari de Tarragona*, *Diari de Lleida*, *Diario San Rafael*, *Diario Siglo XXI*, *El Economista*, *Diario de Madryd*,

*El Mundo*, *El Quiosco.net*, *Gente Digital*, *Lainformacion.com*, *La Vanguardia*, *La Razón*, *La Voz Libre*, *La Voz de Rusia*, *Noticias de Álava*, *Noticias de Guipúzcoa*, *Noticias de Navarra*, *Quo*, *Periòdic universitari 'Lo Campus Diari'*, *Tarragona 21*, *Te Interesa*, *PressPeople*, *Atención Primaria de Salud*, *Bioteecnologia al dia*, *ECOTicias*, *Ediciones Médicas*, *Farmanews*, *INNOVAticias*, *Medicina 21*, *Natural Zone*, *Portales Médicos*, *Redacción Médica* and *Teorema ambiental*.



– Corporate Webs: *Agencia de Noticias para la Difusión de la Ciencia y la Tecnología (Dycit)*, *Asociación Española de Bioempresas (ASEBIO)*, *Asociación de Parques Científicos y Tecnológicos de España (APTE)*, *Consejo Superior de Investigaciones Científicas (CSIC)*, *Instituto Superior del Medio Ambiente (ISM)*, *Observatorio de Salud y Medio Ambiente de Andalucía*

(*OSMAN*), *Parc Científic de Barcelona (PCB)*, *Servicio de Toxicología (Sertox)*, *Universitat de Barcelona (UB)*, *Universitat Rovira i Virgili (URV)* and *Xarxa de Parcs Científics i Tecnològics de Catalunya (XPCAT)*.

– Radio: *Radio Nacional de España (RNE)* – *Ràdio 4* <http://www.rtve.es/alacarta/audios/lobservatori/lobservatori-15-febrer-2014/2392862/>

- © Rob H. Stierum. Nederlandse Organisatie Voor Toegepast Natuurwetenschappelijk Onderzoek (TNO, Netherlands). 28th October 2013. *TNO participates in HEALS, the largest*

*European Union project to study health in relation to the environment* [Press release]. Retrieved from <https://www.tno.nl/>

The screenshot shows the TNO website with the headline "TNO PARTICIPATES IN HEALS, THE LARGEST EUROPEAN UNION PROJECT TO STUDY HEALTH IN RELATION TO THE ENVIRONMENT". The article mentions that the EU has decided to fund the 'Health and Environment-wide Associations based on Large population Surveys' (HEALS) project. It also includes a contact section for Dr R.H. (Rob) Stierum.

- © Mercè Fernández. Delegation of the Spanish Council for Scientific Research in Catalonia (CSIC, Spain). 29th January 2014. *HEALS, a European project for identifying lifetime*

*exposure to contaminants* [Press release]. Retrieved from <http://www.dicat.csic.es/>

The screenshot shows the CSIC website with the headline "HEALS, a European project for identifying lifetime exposure to contaminants". The article describes the objective of the HEALS project, which is to develop an integrated methodology for identifying and decoding an individual's exposome. It also lists the main health outcomes that will be assessed and the consortium of partners involved.



## Publications

Scientific contributions of the HEALS Project will be hosted on ZENODO, an open digital repository that enables researchers, scientists, EU projects and institutions to share and showcase multidisciplinary research results (data and publications) that are not part of the existing institutional or subject-based repositories of the research communities.

The collection of HEALS scientific papers on ZENODO can be found in the following website:

<https://zenodo.org/collection/user-heals>

At this stage of the project, there are the following publications:

- Vizcaino E, Grimalt JO, Fernández-Somoano A, Tardon A (2014) Transport of persistent organic pollutants across the human placenta. *Environment International* 65: 107-115.
- Visnjevec AM, Kocman D, Horvat M (2013) Human mercury exposure and effects in Europe. *Environmental Toxicology and Chemistry* (In press).
- Fort M, Grimalt JO, Casas M, Sunyer J (2014) Food sources of arsenic in pregnant Mediterranean women with high urine concentrations of this metalloid. *Environ Sci Pollut Res* (In press).
- Jerrett M, Reid CE, McKone TE, Koutrakis P. Participatory and Ubiquitous Sensing for Exposure Assessment in Spatial Epidemiology; In: Kanarolou P, Delmelle E, Gosh D, Páez A, editors. *Spatial Analysis in Health Geography*: Ashgate; 2014.
- Sarigiannis DA, Gotti A (2014) New methods for personal monitoring of air pollution through the use of passive sensors during childhood. *Pneumologia Pediatrica* 14 (54).



## Presentations of the HEALS Work at International Conferences

Dissemination and networking activities during the first 6 months of the project included the participation of several HEALS members at international workshops, conferences and scientific events hereinafter summarised:

- **Prof. Joan Grimalt (CSIC), Patrícia Freixas (Ph.D. Student, CSIC), Esther Marco (CSIC), Inmaculada Fernández (CSIC) and Roser Chaler (CSIC).** XIII Scientific Meeting of the Spanish Society of Chromatography and Related Techniques (SECyTA-2013), organized by the University of La Laguna (ULL) and the Spanish National Research Council (CSIC) Puerto de la Cruz, Tenerife, Canary Islands (Spain). 8-11 October 2013.
- **Prof. Joan Grimalt (CSIC), Marta Fort (Ph.D. Student, CSIC) and Patrícia Freixas (Ph.D. Student, CSIC).** INMA (Childhood and Environment) Research Network Annual Meeting, organised by the INMA Project in Donostia-San Sebastian (Spain). 14-15 November 2013.
- **Prof. Joan Grimalt (CSIC), Marta Fort (Ph.D. Student, CSIC) and Natalia Bravo (Ph.D. Student, CSIC).** Arctic Frontiers 2014 Annual Conference, on the topic 'Humans in the Arctic', in Tromsø (Norway). 19-24 January 2014.

# Forthcoming Events

## HEALS meetings

- **HEALS Internal Meeting: *Internal Exposome Markers in HEALS* (Stream 2: WP4 and WP5).**  
26–28 May 2014, Ljubljana (Slovenia)  
[www.heals-eu.eu](http://www.heals-eu.eu)
- **HEALS Internal and External Meeting: *Recent advances in the environmental pressure and health outcomes.***  
15–17 September 2014, Edinburgh (United Kingdom)  
[www.heals-eu.eu](http://www.heals-eu.eu)

## Other related meetings

- **SETAC Europe 24th Annual Meeting: *Science across bridges, borders and boundaries***  
11–15 May 2014, Basel (Switzerland)  
<http://basel.setac.eu>
- **European Academy of Allergy and Clinical Immunology Congress 2014 (EAACI)**  
7–11 June 2014, Copenhagen (Denmark)  
<http://www.eaaci2014.com/>
- **Biomaterials 2014: *A conference exploring metals in biology, medicine and the environment***  
13–18 July 2014, Durham (NC, USA)  
<http://biomaterials2014.chem.duke.edu>
- **IEA World Congress of Epidemiology: *Global epidemiology in a changing environment: The circumpolar perspective***  
17–21 August 2014, Anchorage (Alaska, USA)  
<http://www.epidemiology2014.com>
- **26th Annual International Society for Environmental Epidemiology Conference (ISEE): *From Local to Global: Advancing Science for Policy in Environmental Health***  
24–28 August 2014, Seattle (WA, USA)  
<http://depts.washington.edu/uwconf/isee2014>
- **34th International Symposium on Halogenated Persistent Organic Pollutants (Dioxin 2014)**  
31 August – 5 September 2014, Madrid (Spain)  
<http://www.dioxin2014.org>
- **European Respiratory Society (ERS) International Congress**  
6–10 September 2014, Munich (Germany)  
<http://www.erscongress.org/>
- **50th Congress of the European Societies of Toxicology (Eurotox)**  
7–10 September 2014, Edinburgh (Scotland, UK)  
<http://www.eurotox2014.com>
- **International Environmental Omics Synthesis Conference (iEOS 2014)**  
15–19 September 2014, Liverpool (United Kingdom)  
<http://environmentalomics.org/ieos2014-announcement/>
- **6th International Conference on Metals and Genetics (ICMG)**  
22–25 September 2014, Huelva (Spain)  
<http://www.uhu.es/6thICMG>
- **14ava Jornadas de Análisis Instrumental (JAI-2014)**  
1–3 October 2014, Barcelona (Catalonia, Spain)  
<http://www.secyta.org/secyta/>
- **International Society of Exposure Science 24th Annual Meeting (ISES): *Exposure Science Integration to Protect Ecological Systems, Human Well-Being, and Occupational Health***  
12–16 October 2014, Cincinnati (Ohio, USA)  
<http://www.ises2014.org>
- **The 5th Congress of the European Academy of Paediatric Societies (EAPS)**  
17–21 October 2014, Barcelona (Spain)  
<http://www2.kenes.com/eaps/pages/home.aspx>

## Editorial Board

Prof. Joan O. Grimalt Dr. Mercè Garí



## Editorial Information

If you wish to contribute to the *Newsletter* or share any information for publication, please contact Mercè Garí:

[merce.gari@idaea.csic.es](mailto:merce.gari@idaea.csic.es)

This project has received funding from the European Union's Seventh Programme for research, technological development and demonstration under grant agreement No 603946



# HEALS Newsletter

Health and Environment-wide Associations based on Large population Surveys

Project No 603946 of the European  
Union's Seventh Framework Programme



## Contents

Editorial Note . . . . .	1	First Annual meeting of the HEALS Project . . . . .	8
The complexity of HEALS from an ethical and legal perspective . . . . .	2	WHO is WHO . . . . .	10
Critical life events and stages: when to measure the exposome? . . . . .	3	Press Releases . . . . .	11
HEALS Concept and Methodology Workshop . . . . .	5	Publications . . . . .	11
Workshop on Internal Exposome Markers in HEALS . . . . .	7	Presentations at International Meetings and Workshops . . . . .	12
		Forthcoming Events . . . . .	13

## Editorial Note

Welcome to the second issue of the HEALS Newsletter!

This issue reports progress in developing the HEALS project after the first year of implementation. It also includes two articles. One by Virgilia Toccaceli and Ludwine Casteleyn that addresses ethical concerns in research using confidential health information. The other by Nour Baiz and Isabella Annesi-Maesano describes the critical life stages for exposome assessment and health outcomes need to be studied in priority.

The Newsletter also describes three of the most important meetings organized within HEALS during 2014: the *HEALS Concept and Methodology Workshop* held in Thessaloniki, Greece, in March (article written by Dimosthenis Sarigiannis); the *Workshop on Internal Exposome Markers in HEALS* held in Ljubljana, Slovenia,

in May (article written by Milena Horvat); and the *First Annual Meeting of the HEALS Project* in Edinburgh, UK, conducted in September (article written by John Cherrie).

The *Who is Who* section shows the professional profiles of John Cherrie and Marta Schuhmacher, two Stream Leaders, and Joana Madureira and Juha Parkka, two leading young researchers involved in several WPs.

The issue also lists the scientific publications, presentations at meetings, workshops and conferences, and other dissemination activities (e.g. press releases) performed by HEALS researchers after March 2014. Interesting forthcoming events for HEALS participants and exposome researchers are also announced.

Our best wishes for a happy and productive 2015!



HEALS

wishes you a

2 1 5 HAPPY NEW YEAR



# The complexity of HEALS from an ethical and legal perspective

by VIRILIA TOCCACELI and LUDWINE CASTELEYN

Instituto Superiore di Sanità (ISS)    SPF Health, Food chain safety and Environment  
Rome, Italy    Brussels, Belgium

HEALS aims at being a forefront project, whose underlying hypothesis of complex and dynamic interactions between DNA sequence, epigenetic DNA modifications, gene expression and environmental factors that all combine to influence disease phenotypes, implies investigations of sensitive data that raise ethical concerns and require adequate protection of privacy. HEALS will not only produce knowledge for advancements in public health, but will also generate procedures, data and information significant at individual level that need to be carefully dealt with from the start. The implications and consequences which might derive from the "actions" taken within HEALS have to be assessed and addressed as early as possible.

First of all, the right for information of the study subjects requires clear communication procedures at several stages of the study, from recruitment till dissemination of results. Informed consent procedures need to guarantee accurate and relevant information to participants. Moreover, the biomarker results will need to be clarified with respect to their significance (or lack of significance) at individual level and the eventual implications for health. Another central issue relates to the potential psychological and/or social vulnerability of subgroups of participants that may necessitate adapted procedures.

Finally, data sharing issues are of major concern in a project like HEALS and, above all, a harmonized treatment of sensitive data is required despite differences in legal context across Europe. Furthermore, taking into account advancements in the field of IT and data networking, it will be essential to define also the extent to which privacy and confidentiality can be really guaranteed.

## A focus on the ethics of communication for the Exposome

Biomonitoring programmes conducted in many countries are increasingly using new methods and technology that allow the detection of ever lower levels of concentration of substances, chemicals and pollutants for which both animal and cell studies show troubling biological effects. However, harmful concentration levels, sources of exposure, potential health effects are often not yet fully understood and exposure reduction strategies not available. This "lack" of knowledge brings a series of ethical concerns regarding, most of all, the reporting of results to individuals. What is more, when human biomarkers are used within a research framework, these concerns become even more serious being the experimental aspect of the monitoring enhanced.

Fundamental questions arise: "*when*" is it right to report? "*How*" is it efficient and effective to report? There is a strong need to relate to a widely agreed framework addressing policies for communication both to the participants as a group (or subgroups) and to each individual.

There are cornerstone documents like the Belmont Report, the Helsinki Declaration, and more specifically at the EU level, the Oviedo Convention and the Privacy Directives '95 and 2002 which provide guidelines and ethical principles to be applied. Respect for persons (and their human dignity and autonomy), beneficence and no maleficence, social justice, the right "not to know" and the right "to be forgotten", etc. are some of the main principles to consider. Nevertheless, what researchers continuously discover is that principles cannot be unproblematically applied, they cannot be prescriptive but only critically weighed with several rights and duties at stake. For example, while the respect for individual autonomy could favor a clear-cut reporting of individual results, the no maleficence principle obliges to consider that reporting might in some cases result in harmful experiences such as undue anxiety, stigmatization, or legal constraints. Moreover, the costs of customizing results reports might be high in terms of efforts and finances considered by some a waste of "limited resources" that could be used for other goals.

Other relevant questions relate to: *What should be the extent of the information given? What kind of results/findings should be disclosed? When should such information be communicated? How should the right to know be applied regarding children?* Large-scale, high-throughput 'omics studies like those in HEALS complicate this particular context by raising these questions at a larger scale.

Different reference models for disclosure of results can be outlined and some of them are already widely recognized by experts. They relate to the responsibility of the research group and to the adoption of decisions on the basis of the clinical significance of the results (i.e. results are communicated to individuals whenever they indicate, for experts, an adverse health outcome or they trigger an intervention. If the health effect is not known it is considered not cautious to communicate), or they involve a dynamic model with the participation of different stakeholders in all decision making processes. All these models contain positive aspects as well as specific weak points.

The study methods, the potential social impact of the results, the biological material collected, the significance of the "omics", the huge amount of phenotypic data and the sharing of these make of HEALS an original ethical challenge, addressing a series of ethical, social and legal issues that can be tackled only if the work begins "near to the bench", with an early commitment of the research group. What, nowadays, seems to be urgent for the development of both science and research, for a new culture of respect for human dignity, and for motivating individuals to participate in research is an "Ethics of responsibility" which leaves out paternalistic attitudes by researchers and, at the same time, takes into account the needs at both individual and collective levels. A research project like HEALS should adopt an approach that eases the dialogue between researchers and participants. ☺

# Critical life events and stages: when to measure the exposome?

by NOUR BAÏZ and ISABELLA ANNESI-MAESANO

Université Pierre et Marie Curie - Paris 6 (UPMC)  
Paris, France

The exposome can be defined as the measure of all the exposures of an individual in her/his lifetime, from conception throughout the lifespan (Wild, 2005).

The individual exposome has to be intended as dynamic and continually changing. Indeed, all exposures and their determinants and modifiers can vary over the course of a day, not to mention over the weeks, months, and years that make up a lifetime, as our bodies, diets, risk factors and lifestyles change. Because sources and levels of exposure change over time, and because capturing all these changes verges on the impossible in the impracticality of "high-resolution real-time" monitoring of all the exposures for the entire lifetime, the exposome has to be constructed by assessing the exposures at the critical life periods of life through representative snapshots that act as demonstrative measures of these critical periods. In particular, for the comprehension of the mechanisms underlying the development of the diseases, the assessments of the internal chemical environment in biological specimens at critical life stages is mandatory. The major challenge consists then in identifying critical life stages that are informative at most as well as the snapshots reflecting the exposures and the downstream consequences at the individual level.

So, the main question that needs to be answered is "in which period of life is it important to monitor the exposome?". This question implies one further consideration: "When are data collections of exposure and health outcomes respectively, and when in the case of biomarkers of exposure, effect and disease and omics..., is human biomonitoring (HBM) most informative?". Literature shows that the answer depends on the type of health event and related endotypes, phenotypes and sub-phenotypes, the target organ, the type of agent (diet, pollutant, toxicants...), its action, and the individual's characteristics. Theoretical knowledge on individual development was retrieved for the entire lifespan from the literature and findings from population-based data were investigated.

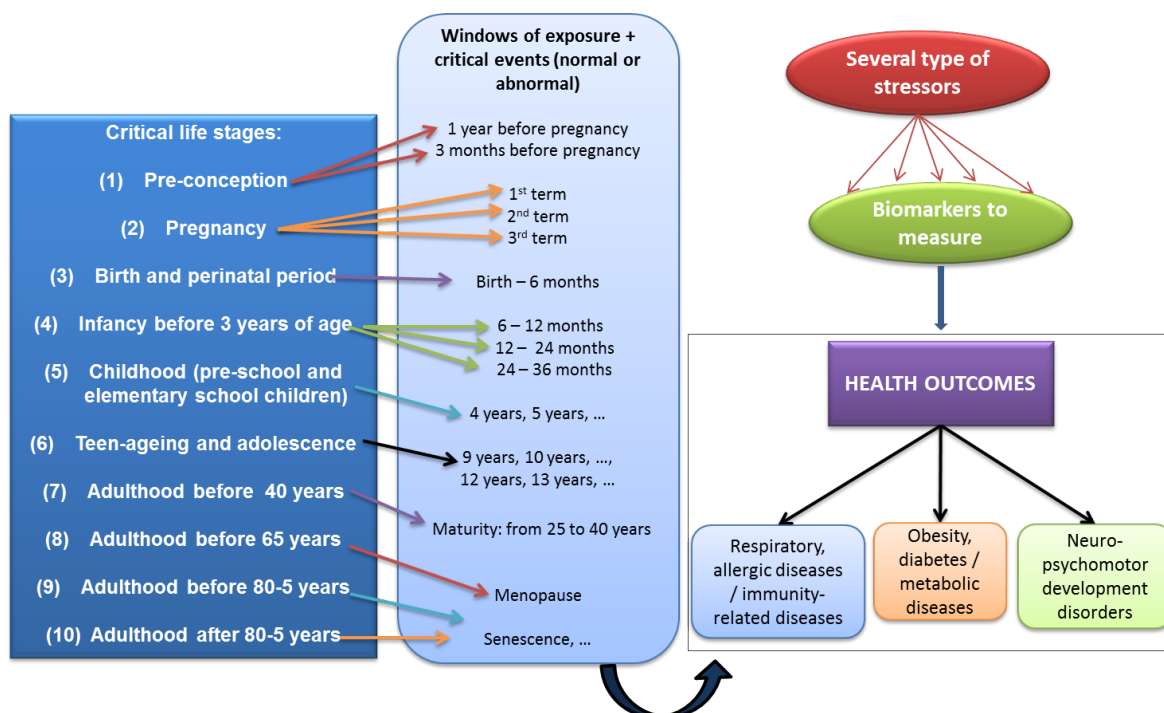
As a result, in spite of the heterogeneity of existing findings that precludes comparisons and the lack of convincing evidence from population data, the following facts emerged:

- i Onset of age-dependent diseases such as asthma and allergic diseases, diabetes, Parkinson disease and of subclinical phenotypes as allergic sensitization, overweight and neurodevelopmental troubles is strongly dependent on multifactorial interactions with other features such as: Presence of specific susceptibility genes/alleles; Vulnerability increasing the exposure; Methylation status; Environmental insults; and among adults, pre-existing health status and comorbidities.
- ii Preconception is a crucial period for making change to the lifestyle and diet that can both help increase the chances of getting pregnant and birthing a healthy baby.

- iii Early-life influences, beginning with the intrauterine environment and continuing through the first few years of life, shape the trajectory of the various organs throughout the life course and are responsible for health outcomes. Prenatal and early-life environmental insults ranging from malnutrition to toxic exposures can tilt the odds toward development of adverse health effects decades later. These effects likely occur, at least in part, through alterations in an individual's genetic potential to thrive in the environment in which he or she will live. These early challenges set the bar for what's "normal", and the foetus and infant adapt for a less-than-optimal environment in ways that may contribute to adult-onset disease. Vulnerability to chemical toxicity after birth may be highest during the first 6 months and continue for years before maturation.
- iv Both puberty and menopause and the pre-existing periods constitute essential steps in asthma, weight and behaviour changes and downstream health conditions, through significant changes in endocrine system and hormonal status.
- v Old age relates to a multidimensional process of physical, psychological and social change and seems to be an especially vulnerable period. From existing data (The GERIE study, ERJ 2015, *in press*) two old ages deserve to be considered, before and after 80 years.

As a main result, based on existing knowledge and findings, ten critical life stages were identified as of interest for the exposome of the major health outcomes considered in HEALS, namely asthma and allergies, overweight and diabetes and neurodevelopmental troubles (see figure).

1. Pre-conception
2. Pregnancy
3. Birth and the period from the perinatal (28 days after birth) period up to 6 months
4. Infancy between 6 months and 3 years of age
5. Childhood (school children)
6. Teen-ageing and adolescence
7. Adulthood before 40 years
8. Adulthood before 65 years (in the 50s)
9. Adulthood before 80-5 years (according to the gender, 85 years in women)
10. Adulthood after 80-5 years



HEALS targets both existing datasets of individuals and twins having participated in epidemiological, toxicological and HBM surveys which allow covering the entire life time as well as forthcoming dataset in the frame of the European Exposure and Health Examination Survey (EXHES), where children (both singleton and twins) are recruited since *in utero* life, with their siblings, parents and other relatives, thus constituting a transgenerational study including almost the entire lifespan. Therefore, critical life stages and the specific feature identified as of interest for HEALS are:

- **Preconception** that has to be target in terms of lifestyle, diet and other exposures.
- The **three trimesters of pregnancy** have to be monitored for organs' development as a function of environmental exposures according to the event of interest.
- **Before and after 3 years** of age constitute also important periods for individual normal and pathological growth and development.
- **Puberty** with hormones changes is crucial for asthma, weight and behaviour variations.
- **Middle age** (after the age of 30) lifestyle parameters (nutrition, exercise, smoking...), environmental exposures (air pollution, water content, other toxicants...), health status (lung function, hypertension, metabolic disorders, cognitive problems...) and use of drugs are determinant for the onset and the progress of several diseases. Lifestyle changes are related to professional advancement for most individuals, altering significantly their daily time-activity patterns leaning towards relatively higher caloric intake, more sedentary life spent indoors and thus exposure to xenobiotics. Gene-environment interactions worsen asthma and allergies, overall in women due to changes in hormonal factors. Stress and obesity can also be at the origin of asthma in adulthood.

• There is sufficient evidence that **menopause** in women (between the age of **45** years and **55** years) is a period of significant changes in the hormonal status, impacting a cascade of health outcomes: asthma, increasing susceptibility metabolic disorders, as well as to neuro-inflammation. At the age of **50** years, significant changes in gene expression related to brain related function seem to be determinant for the onset of neurodegenerative disorders.

- **After 65** years both males and females are more susceptible to environmental insults, due to reduced detoxification capacity, as well as reduced capacity of maintaining homeostasis.
- At **80** and **85** years, normal ageing is accompanied by pathological ageing.

In HEALS, data on the relationships between exposome and the targeted health outcomes will be drawn from questionnaires, HBM, omics (genomics, epigenomics, metabolomics, proteomics...) and clinical tests in singletons, twins and parents. The investigation of the interrelationships among the three considered health outcomes and their exposome as well as the underlying mechanisms will pave the way to better understand the development of these chronic diseases.

## Some definitions

**Critical life stages.** Critical life stages are defined as the periods of time in an individual's lifespan in which critical life events occur characterized by changes of the organism status, because some quality, property or phenomenon suffers a definitive modification. Examples of critical life events include, for instance, foetus development according to the stage of growth, immune system maturation, organs development, puberty, menopause... These changes can be normal or abnormal as result of either reshaping of the ordinary pattern (for instance: anticipation of puberty) or modification of the event (for instance: event amplification, increase in severity...) (see figure), the latter because of external or internal influences. Vice



versa, changes in exposures may be present as a consequence of developmental changes or altered patterns of behaviour.

**Windows of exposures.** Windows of exposures are the periods of time in an organism's lifespan in which the organism is the most susceptible or vulnerable (see the definitions below) to the adverse effects caused by exposure to stressors including toxicants at the origin of abnormal and pathophysiological changes. It is important to underline here that a same critical life event can be observed at different life stages.

**Susceptibility.** Refers to the degree to which individuals or groups may respond to a given exposure to a hazard. Susceptibility can be subdivided into innate and acquired susceptibility. Innate susceptibility is to a large extent due to genetic predisposition or to incomplete development of normal (adult) physiological functions. For example, a young child may be susceptible to a given pollutant because detoxification processes are not yet fully developed. Such susceptibility is transient and disappears with age and growth. Acquired susceptibility may be due to disease or age.

**Vulnerability.** Refers to the variations in exposure between individuals or groups –and thus to the potential for health effects. This is likely to be due to variations in the hazards themselves as well as to the fact that exposure is also a function of where people live, how (and where) they spend their time, and their more general lifestyle. In the case of pesticides, living close to areas where crops are sprayed or eating foodstuffs that have been heavily treated during production, storage or processing likewise acts to increase exposure, and thus vulnerability.

## References

**Wild C.P.** Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiol Biomarkers Prev* 2005, 14(8): 1847-1850.

**Annesi-Maesano I. et al.** Indoor air quality, ventilation and respiratory health in elderly from EU Nursing Homes. *ERJ* 2015, In press.

# HEALS Concept and Methodology Workshop

Thessaloniki, Greece (17–20 March 2014)

by DIMOSTHENIS SARIGIANNIS and ALBERTO GOTTI

Aristotle University of Thessaloniki (AUTH)  
Thessaloniki, Greece

The *HEALS Concepts and Methodology Workshop* took place at the Aristotle University of Thessaloniki from Monday 17th to Wednesday 19th March 2014. The workshop was a successful opportunity to create a common understanding of the exposome concepts and to share and discuss the HEALS approach to unravel the exposome.

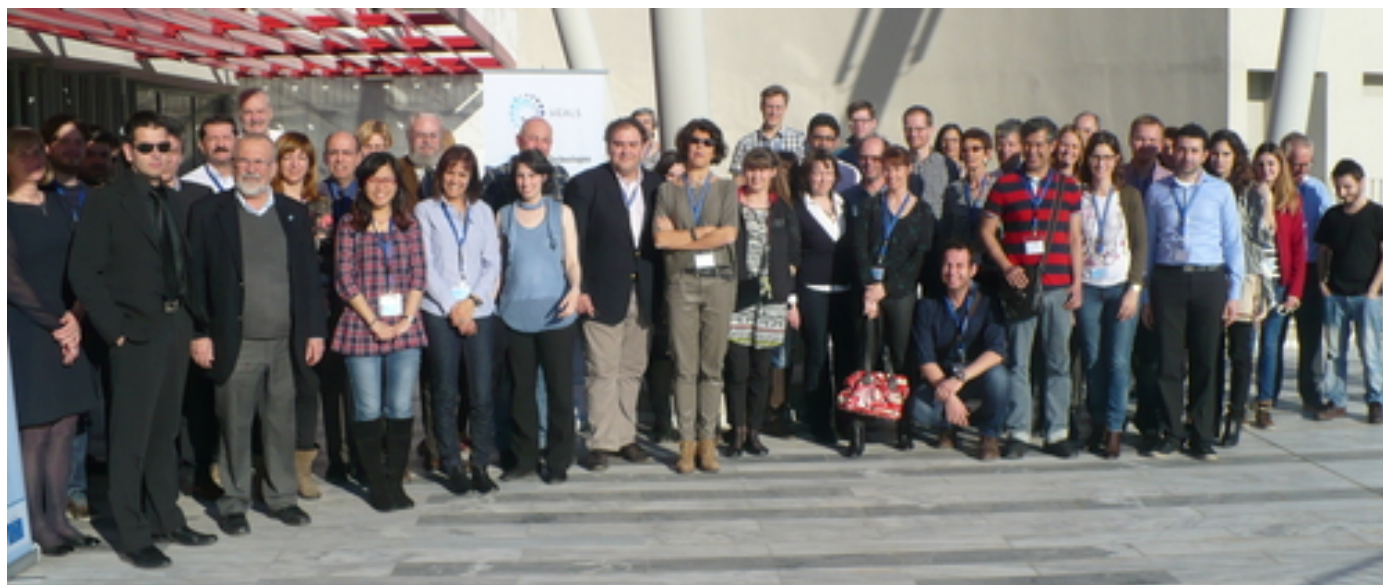
The workshop was led by Prof. Denis Sarigiannis. Around 70 delegates from the 29 HEALS Partners took part and delivered a number of presentations on the different facets of the exposome concept. The event consisted of one day Technical meeting (17 March) on the project workpackages, which was followed by an one and a half day scientific workshop (HEALS concepts and methodology – 18 and the morning of 19 March). In addition to presentations from the project team, from the afternoon of March 19 until lunch time of March 20, Agilent Technologies co-hosted a dedicated event on the Agilent exposomics workflows with external high-level expert discussion on the use of advanced analytical and -omics technologies for exposome research both in the EU and the USA and demonstration of Agilent technology and data analysis tools. Both the HEALS workshop and the Agilent seminar were held at the Research Dissemination Center of Aristotle University of Thessaloniki (KE.D.E.A).

Prof. S. Kouidou-Andreou Vice-Rector of the Aristotle University of Thessaloniki opened the meeting and Profs Denis Sarigiannis and Isabella Annesi-Maesano highlighted that the aims of the workshop were to discuss, understand and expand the conceptual framework of HEALS and to bring all disciplines together in a coherent and harmonized framework.

During the first day of the workshop every work-package leader reported on work progress, current status, next steps and timeplan. The scientific workshop started on the second day and it was organized in three sessions: external exposome, internal exposome and data management and modeling for EWAS.

In the first session Prof. J. Bartzis presented the concept of the external exposome in the context of HEALS and proposed first suggestions on how to proceed. Although the exposome represents the totality of exposure over an individual's lifetime the HEALS approach will need to take into account 'critical' exposure periods and the varying spatial and temporal accuracy and availability of the input data sources.





In this light for each pollutant and each population subgroup, a combination of methods ('pathways to exposure') has to be chosen in order to transform the available information/data into external exposures. This approach will be applied and tested in Stream 5 on regional studies supporting the analysis of existing cohort studies and it will provide an EU-wide estimation for the EXHES pilot study.

Prof. J. Cherrie presented how personal sensors can support external exposome studies at the individual level. He provided examples of personal sensors that can be used for babies and for adults to track position and physical activities. Due to the large amount of information which can be collected as well as the ethical hurdles involved in collecting real individual space-time movement data for whole populations he pointed out how post-processing and integration with models are critical in retrieving the required information at the individual level. On this subject Prof. C. Sable presented the role of agent-based modelling (ABM) in constructing the exposome. These models can simulate individuals (agents) and their interactions with other agents and their environments informed by sensor technologies. In this light the use of ABM will enable us to better understand the behavior of individuals and populations in social and evolutionary settings, and to 'fill-in' the gaps in the exposome currently not available from real-world monitoring and sensor data. In order to derive estimates of external exposures of individuals and of vulnerable population subgroups all the data collected and modelled have to be merged through data fusion techniques. To this aim Prof. R. Friedrich proposed a conceptual framework to be applied for estimating the individual external exposures to multiple stressors via different exposure routes. Big data analysis techniques combining different data and methods including those developed in the previous WPs. This framework will be applied and will support the HEALS population studies. The morning session ended with a general discussion about the methodological approach to follow to unravel the external exposome. It was pointed out that untargeted-agnostic individual exposome derivation approaches have to be the main thrust of the project with regard to both the external and internal exposome.

The afternoon session was focused on the internal exposome. Prof. M. Horvat gave a presentation on the role of human biomonitoring in the context of HEALS and its links with -omics technologies. She pointed out the key role of human biomonitoring in the

HEALS methodology stressing the importance of a harmonized approach built on the outcomes of the DEMOCOPHES study. Within HEALS biological samples are available in bio-banks from previous population studies (WP14, WP15 and WP16) and they will be further analyzed. A further important issue is the identification of the laboratories for different analysis. On this point it was suggested to centralize the analyses in few laboratories so as to improve comparability and reduced inter-laboratory error. Dr. R. Stierum gave an overview of the several -omics technologies and infrastructure components available in HEALS and of the interdisciplinary omics data integration possibilities to bridge human clinical information and mechanistic toxicological information towards the exposome concept. A discussion followed on the minimum omics/biomarker requirements and feasibility in order for them to be applied on the already existing cohort samples and the samples collected through the pilot exposure and health examination (EXHES) survey foreseen in HEALS.

Prof. Sarigiannis illustrated the role of Internal dose modeling using physiology-based biokinetic (PBBK) models in the HEALS methodology to bridge the external and internal exposome. In HEALS PBBK models play a central role as they are a powerful tool to assess the time history of internal exposure, focusing on susceptible developmental stages. Furthermore, PBBK models link external exposure to target tissue dosimetry relevant to in vitro testing responses and support integrative bioinformatics and systems toxicology modelling to allow for reverse dosimetry assessment. In this way PBBK models will serve for linking exposure biomarkers to external exposures and biomonitoring data to internal concentration of xenobiotics and their metabolites in target tissues and the associated health effects.

The next session took started with a presentation on the HEALS GeoDatabase provided by Dr. Nousiainen. This will be a publicly available platform, which will systematically support the collection of and access to all datasets collected/developed for HEALS. Through the platform the users can manage and explore spatial data, process and visualize them.

The subsequent discussion focused on the functionalities the platform has to incorporate, the available IT solutions as well as the compatibility with existing platform such as the IPCheM platform of the European Commission.

The platform will be linked to the Environmental Data Man-



agement System (EDMS) of HEALS, which was presented by Dr. Karagiannis. He illustrated the main functionalities of the EDMS pointing out that it will accommodate geo-referenced environmental data retrieved data from existing Databases. The EDMS will be a module of the HEALS Geodatabase platform. The session continued with the presentation given by Prof. Papaloukas on bioinformatics strategies for biomarker prediction. He provided an overview of the current techniques for descriptive data mining, predictive data mining and model integration, which represent the methodological tools for integrating multiple biomarkers into a mechanistic description aiming at understanding the biological functions of toxicity pathway interactions in relation to external/internal exposure and confirming the causative effect between exposure and disease endpoints. The

session ended with an overview of the bio-statistical methods for Environment-Wide Association Studies given by Dr. Banerjee who illustrated the different statistical methods applied in environmental health sciences pointing out the advantage and limitations of each of them.

There was a general agreement that the workshop was a successful step toward the development of a common agreed methodology to unravel the exposome. The final discussion reflected this collective understanding as witnessed by the very active participation of all delegates. A number of issues were discussed and clarified reinforcing the energy needed to face the great challenges we will need to address in the next years.®

## Workshop on Internal Exposome Markers in HEALS

Ljubljana, Slovenia (26–28 May 2014)

by MILENA HORVAT

Institut Jozef Stefan (JSI)  
Ljubljana, Slovenia

The workshop *Internal Exposome Markers in HEALS* was organised by Stream 2 (WP4 and WP5 leaders, JSI and TNO respectively) and took place in Ljubljana, Slovenia from May 26 to 28, 2014.

The meeting consisted of a two days workshop (Internal Exposome Markers in HEALS – 26 and 27 May) and one day



Technical meeting (28 May) for WPs 4 and 5. The meeting was organized in the Conference Center MONS and was attended by 39 participants.

The morning session of the first day provided the general understanding of what is needed in terms of biomarker and -omics research to support the construction of the exposome (D. Sarigiannis and I. Annesi-Maesano). The selection of exposure, susceptibility and effect biomarkers have been addressed for metals, metalloids and other elements (I. Falnoga), organic contaminants and their metabolites (J. Grimalt and L. Leondiadis) and other stressors related to health impacts: obesity, neurodevelopment and asthma (G. Calamandrei, G. Viegi and I. Annesi-Maesano).

The session on "omics" and biomarkers dealt with technology, concepts, possibilities, challenges and final suggestion & decision for inclusion in HEALS. This session covered presentations on Metabolomics at FERA and AUTH (M. Dickinson); Adductomics, exposure and susceptibility to endogenous and exogenous alkylating agents (A. Povey); SNP profiling: SNP genotyping, different platforms for different questions (W. van Workum); DNA methylation and epigenetics (S. Koudou); miRNA profiling technologies (G.

Viegi); Transcriptomics providing the mechanistic basis for causality in EWAS (D. Sarigiannis); and DNA repair functional assays within the HEALS project (E. Dogliotti). This session provided good background for further discussion on pre-selected biomarkers and -omics methodologies, taking into account the state of the art knowledge and recent practices.

The session on "phenotyping/endotyping in the HEALS paradigm" was chaired by I. Annesi-Maesano and included topics related to phenotyping/endotyping in asthma and allergies (I. Annesi-Maesano), diabetes and overweight (E. Ramos), neurodevelopmental troubles (G. Calamandrei) and the methodology for phenotyping/endotyping (S. Banerjee). The session provided background for further discussion on phenotyping/endotyping in relation with -omics and biomonitoring in view of EWAS, taking into account the state of the art knowledge and recent practices.

The following session was concentrated on existing cohorts of significance for the HEALS project (G. Calamandrei, G. Viegi and I. Annesi-Maesano). The following cohorts have been presented: REPRO\_PL cohort from Poland (K. Polanska), PHIME Mediterranean (J. Snoj Tratnik), Slovenian DEMOCOPHES cohort (D. Mazej), Spanish INMA cohort (J. Grimalt), and the Italian twin study (L. Nistico).







This session provided scientific rationale of the existing HEALS cohorts, including practicalities of implemented protocols in existing exposome like studies performed so far, including truly available samples/study designs for HEALS from WPs 14, 15 and 16.

Round table discussion addressed urgent questions related to the use of existing data and samples and several questions were addressed related to comparability of data between cohorts, availability of samples, usefulness of existing exposure, effects, and susceptibility biomarkers. Moreover, gaps were identified and plans for future research were made between the partners. Most importantly, the suitability of -omics analysis/technologies on existing and new

samples were discussed in detail.

The workshop represented an important step forward in the implementation of the EWAS and EXHES protocols in HEALS. Active participation of HEALS participants resolved numerous issues related to the use of existing HBM samples available in cohorts as part of EWAS. Harmonization of approaches for the analysis of exposure and -omics markers has also reached and concrete planning of actions were set up.

Apart from reach discussion, participants were taken to the tour visit of old Ljubljana with a dinner entertainment at Ljubljana Castle.®

## First Annual meeting of the HEALS Project

Edinburgh, UK (15-17 September 2014)

by JOHN CHERRIE

Institute of Occupational Medicine (IOM)  
Edinburgh, UK

The first HEALS annual meeting, hosted by the IOM, took place in Edinburgh between the 15th and the 17th September 2014. The meeting was organized as a three days workshop on recent advances in understanding links between environmental pressures and health outcomes. In addition to presentations for the project team and the HEALS advisors, the agenda included a public lecture given by Dr. David Balshaw, from the National Institute for Environmental Health Sciences (NIEHS).



Over fifty delegates from 28 partners attended the meeting, which was held at the COSLA Conference Centre in the Haymarket area of the city. In addition, a number of people participated via the telephone/web connection. The whole meeting took place against the backdrop of the referendum on Scottish independence, which ultimately (the day after the workshop ended) resulted in a vote in favour of Scotland remaining part of the United Kingdom. The campaign and discussions provided a memorable aspect to the meeting.

The first day kicked off with introductory lectures by Prof. Isabella Annesi-Maesano and Prof. Denis Sarigiannis. Specifically for this workshop we aimed to discuss:

- How to build the exposome into studies of asthma/allergies, overweight/diabetes and neurodevelopmental troubles.
- How best to utilize both existing and prospectively collected data
- To respond to specific questions in order to investigate *ad hoc* environment stressors and health phenotypes/endotypes.
- To build the EXHES study in the most efficient way.



Dr. Nour Baiz from UPMC presented the outcome of one of the key literature reviews being undertaken within HEALS, which was to consider "Critical life events in defining when and how frequently biological samples should be collected to define the exposome". She described the work and outlined ten critical life stages that are recommended for characterizing the exposome: from pre-conception to old age.

The meeting then went on to discuss studies of exposure to particulate matter and biological agents in relation to asthma, and gene-environment interactions for asthma and allergies. Dr. Gemma Calamandrei spoke on studies of neurodevelopmental and neurodegenerative disorders in relation to exposure to metals and pesticides, which highlighted some of the challenges involved in undertaking exposome assessments within existing cohorts. This session was followed by a more general discussion about common causal mechanisms for the diseases of interest in the HEALS project.

During the 1st day we also reflected upon the conclusions of the HEALS workshop on internal exposome markers, which had been held in Ljubljana. The output from this meeting provided a very helpful introduction to the biomarker discussions on the second day.

During the evening, HEALS delegates along with local scientists and policy makers listened to David Balshaw's public lecture, organised by the IOMs Centre for Human Exposure Science (CHES). David gave a very interesting and informative talk about "The Exposome Concept and its Implementation". He concluded with key questions, including what are the bounds of the exposome, how should we try to implement exposome projects and what should be the key "deliverables" from such projects. The questions prompted a lively discussion with the audience, which continued into the evening reception.

Day 2 began with a series of presentations and discussions about the internal exposome, including "Guidelines for Exposure Biomarkers in HEALS", including descriptions of the 51 Fact Sheets on specific stressors and associated biomarkers being prepared by WP 4. We then discussed the practicalities around using "omics" technologies in the HEALS study.

The meeting continued with joint presentations from Andy Povey and Michael Dickinson on sample optimization for metabolomics/adductomics in agnostic analyses. As part of the work it was agreed that the two labs doing this work should undertake inter-laboratory comparisons. Then Dr. van Workum spoke on genomic profiling – the HEALS SNP array. A number of suggestions were made to help improve this aspect of the work and the team agreed to consider these.

The morning concluded with a discussion on biomarker data integration and systems biology, led by Prof. Sarigannis.

After lunch we switched to talk about the external exposome with presentations by John Bartzis, Miranda Loh and Michael Jerrett. It was clear that although the sensor technologies available to measure the environment have developed rapidly they are probably still fairly immature and unsuitable for wide-scale deployment in the EXHES study as personal monitors. What emerged from the discussions were proposals to combine together low-cost sensors to track subject location and activity, with fixed location monitors sensor data and modeling approaches to synthesize estimates of exposure. Prof. Friedrich spoke about the planned work on exposure data assimilation to integrate the various data being generated, and Sami Nousiainen described the plans for the HEALS Geodatabase platform, which will incorporate public data and data generated in the EXHES.

We also discussed the availability of European data on air pollution (both outdoor and indoor) and data on water contamination. These data will provide an important resource for exposure estimation in both the existing cohorts studied in WPs 14, 15 and 16, and in the EXHES. The potential effect of socio-economic status on the external exposome was described by Dr. Smith.

The delegates continued their discussions over dinner at the Hilton Hotel, close to the meeting venue.

The final day, which included the project General Assembly, a discussion of ethical issues and practical arrangements for the EXHES, plus dissemination and training activities within HEALS. The HEALS data exchange policy was discussed and it was agreed that delegates would comment on the text.

Dr. Balshaw, who is a member of the HEALS Project Advisory Board, summarized the Board's opinions of the progress of the study. He recognized the good work that has been undertaken to date, but encouraged the HEALS team to identify the best practical way forward for the use of sensor technologies and the sample/data acquisition procedures for the EXHES.

He also recognized that the team should focus efforts on linking data across temporal and spatial domains. He highlighted issues around agreeing semantics, ontology and metadata terminology as being important for HEALS, to help ensure clear and efficient communication across this very large project. Dr. Balshaw finished by encouraging the HEALS team to organise a workshop on modeling and data integration within the exposome paradigm.

The final discussion offered an opportunity for delegates to ask further questions and to discuss the future plans for the project. There was general agreement that the meeting had been a successful milestone in the HEALS journey and the delegates left reinvigorated to address the upcoming challenges.©





## WHO is WHO



Professor **John Cherrie** is currently Research Director at the Institute of Occupational Medicine (IOM) in Edinburgh, and Honorary Professor at the University of Aberdeen, UK. He originally trained as a physicist and then completed his PhD at the University of Aberdeen, working on retrospective occupational exposure assessment for epidemiological studies. He has a wide range of research interests including exposure assessment for environmental and occupational epidemiology, chemical risk assessment, dermal exposure assessment, inadvertent ingestion of chemicals and several other topics. He has been involved in a number of health impact assessment studies, including an evaluation of the socioeconomic, health and environmental impacts of changes to the EU Carcinogens Directive on behalf of the European Commission. He is leading Stream 1 and WP9 in HEALS, with a particular focus on developing methods to characterize the external exposome. The IOM is a not for profit research and consulting organization based in Scotland with three offices in England and one in Singapore. It employs over 140 staff, mostly scientists and technicians. Typically IOM is involved with 30 to 40 research projects at any one time, covering risks from chemicals, environment and health, nanotechnology, human sciences and other topics. John is a member of the Editorial Board of the *Annals of Occupational Hygiene and Particle and Fibre Toxicology*. He is also an Assistant Editor on the journal *BMC Public Health*. He is a Past President of the British Occupational Hygiene Society (BOHS), and in 2013 he won the Bedford Medal for outstanding contributions to occupational hygiene. At the start of 2015, John will take up a new part-time post as Professor of Human Exposure Science and Health at Heriot Watt University in Edinburgh. In this post he aims to develop new research involving the exposome and sensor technologies. He will continue to work on the HEALS project as part of the IOM team.



**Juha Parkka** received the Master of Science (Tech) and Doctor of Science (Tech) degrees in information technology (digital signal processing) from Tampere University of Technology, Tampere, Finland, in 1997 and 2011, respectively. Since 1997, he is working as a Senior Scientist at VTT Technical Research Centre of Finland, in Tampere. His daily work includes ICT for Health research and development as well as project management. His research interests include biomedical signal processing, data analysis, classification, software development and quality assurance. In 2010, he received the VTT Certificate of Recognition for active and high-level scientific publishing. He has (co-) authored more than 50 scientific publications. In HEALS, his main interest is to find new ways to study how different exposures (the exposome) affect health. His work focuses on data analysis and management as well as on data collection using wearable and other sensors (WPs 9, 12 and 13).



**Marta Schuhmacher** is Professor of Environmental Engineering at the University Rovira i Virgili (URV) (Catalonia, Spain). She is the head of the Laboratory of Environmental Engineering research group (AGA) (<http://www.etseq.urv.es/aga>) and the Technical Director of TecnATox ([www.tecnatox.cat](http://www.tecnatox.cat)) both in URV. In HEALS context, Marta Schuhmacher is leader of the stream on dissemination, training and knowledge transfer, and drafting guidelines stream (Stream 6). Her principal research interests are, among others, environment monitoring and risk assessment, human biomonitoring, environmental modelling and simulation, PBPK modelling, environmental indicators, data mining, multicriteria analysis, and environmental decision making. As a result of the work in these areas, Dr. Schuhmacher has published more than 180 papers in top scientific journals (h index of 30). She has contributed with more than 220 studies to international scientific meetings, 21 of which were invited keynote lectures. She has been the member of three congress organizing committees and plenary lecturer in 6 international conferences. She has supervised 40 master theses and 19 Doctoral theses (plus 3 ongoing). She is member of the Editorial board of *Environmental Toxicology and Chemistry* (ET&C) and *Integrated Environmental Assessment and Management* (IEAM). She is member of the network on "Contaminated sites and Health" coordinated by WHO Regional Office for Europe, the Society of Environmental Toxicology and Chemistry (SETAC) and The Society for Risk Analysis (SRA). She has participated in other European Funded projects: The Use of Life Cycle Assessment Tools for the development of integrated Waste Management Strategies for Cities and Regions with Rapid Growing Economies (LCA-IWM), Integrated Multiscale Process Units with Locally Structured Elements (IMPULSE), A Neuro-Fuzzy Model for the Ecological Risk Assessment in Wetlands and Risk-based management of chemical and products in a circular economy at a global scale (RISKCYCLE).



**Joana Madureira** holds a PhD on Occupational Safety and Health from the Faculty of Engineering of the University of Porto (FEUP). She integrated the Institute of Mechanical Engineering – FEUP since 2007 attached to the R&D Unit UEAEAC (Unit of Advanced Studies on the Urban Environment). Since that date she has been participating in research projects related to air pollution in different indoor micro-environments and co-related basic risk management strategies. She is author and co-author of some publications in international journals, conference proceedings, posters and scientific reports in environment and environmental health. In the HEALS project, Joana Madureira is involved in several Work Packages (WPs 1, 2, 3, 8, 12, 13, 17, 18 and 19), together with professor Eduardo de Oliveira Fernandes.



## Press Releases

- OIKON (Croatia). Promotion of the HEALS project at various web sites and occasions/meetings/panels (in Croatian). Further information in:

- <http://www.simet.unizg.hr/dokumenti/Vijesti/novi-eu-projekt-fp7-heals?searchterm=heals>
- <http://www.hrpsor.hr/hrpsor/>



- NIOM (Poland). Presentation of HEALS at the 60 Anniversary of NIOM. The audience was composed of health professionals, stakeholders and scientists.



## Publications

Scientific contributions of the HEALS Project are hosted on ZENODO, an open digital repository that enables researchers, scientists, EU projects and institutions to share and showcase multidisciplinary research results (data and publications) that are not part of the existing institutional or subject-based repositories of the research communities.

The collection of HEALS scientific papers on ZENODO can be found in the following website:

<https://zenodo.org/collection/user-heals>

Papers published from March 2014:

- Fort M, Grimalt JO, Casas M *et al.* (2014) Food sources of arsenic in pregnant Mediterranean women with high urine concentrations of this metalloid. *Environmental Science and Pollution Research* 21: 11689-11698.
- Linšak DT, Linšak Ž, Špirić Z *et al.* (2014) Influence of cadmium on metallothionein expression and products of lipid peroxidation in the organs of hares (*Lepus europaeus* Pallas). *Journal of Applied Toxicology* 34(3): 289-295.
- Vizcaino E, Grimalt JO, Glomstad B *et al.* (2014) Gestational weight gain and exposure of newborns to persistent organic pollutants. *Environmental Health Perspectives* 122(8): 873-879.
- Grgurić S, Križan J, Gašparac G *et al.* (2014) Relationship between MODIS AOD (Aerosol Optical Depth) and PM10 over Croatia. *Central European Journal of Geosciences* 6(1): 2-16.
- Špirić Z, Vučković I, Stafilov T *et al.* (2014) Biomonitoring of air pollution with mercury in Croatia by using moss species and CV-AAS. *Environmental Monitoring and Assessment* 186(7): 4357-4366.
- Fort M, Grimalt JO, Casas M *et al.* (2014) Interdependence between urinary cobalt concentrations and hemoglobin levels in pregnant women. *Environmental Research* 136: 148-154.
- Grimalt JO, Torrent M and Sunyer J (2014) The influence of organochlorine compound exposure on the physiological development of children. *Medicina Balear* 29(3): 25-36.

## Presentations at International Meetings and Workshops

Dissemination and networking activities since March 2014 included the participation of several HEALS members at international workshops, conferences and scientific events hereinafter summarised:

- **Joan O. Grimalt (CSIC).** *Inverse age-dependent accumulation of decabromodiphenyl ether and other PBDEs in serum from a general adult population* (platform presentation) and *The HEALS approach to health and environment-wide associations* (poster). SETAC Europe 24th Annual Meeting. Basel, Switzerland. 11-15 May 2014.
- **Mercè Gari (CSIC).** *Impacts of atmospheric chlor-alkali factory emissions in surrounding populations* (lecture). CREAL Seminars. Barcelona, Catalonia, Spain. 20 May 2014.
- **Kinga Polanska (NIOM).** *Environmental and occupational exposures and population health* (lecture) and *The HEALS approach to health and environment-wide associations* (poster). 60 Anniversary of NIOM. Poland. 3-6 June 2014.
- **Dimosthenis Sarigiannis (AUTH).** *The HEALS approach to health and environment-wide associations* (oral presentation). Workshop "Modeling from external exposure dose down to internal doses – bridging the gap" organized by ICCA-LRI & JRC 2014. Lugano, Switzerland. 17-18 June 2014.
- **Dimosthenis Sarigiannis (AUTH).** *Health and Environment-wide Associations via Large population Surveys to unravel the Exposome* (lecture). NIEHS Exposure Science and the Exposome Webinar. 14 July 2014.
- **Joan O. Grimalt (CSIC).** *Determinants of the accumulation of polybromodiphenyl ethers in general adult population from Catalonia and other European Countries* (oral presentation). 26th Annual Conference of the International Society for Environmental Epidemiology (ISEE). Seattle, Washington, USA. 24-28 August 2014.
- **Jutta Lindert and Dimosthenis Sarigiannis (AUTH).** *Air Pollution Impacts on Pregnancy Occurrence and Outcome* (oral presentation). 26th Annual Conference of the International Society for Environmental Epidemiology (ISEE). Seattle, Washington, USA. 24-28 August 2014.
- **Dimosthenis Sarigiannis (AUTH).** *Exposome Ethics: An Important Dimension in Individual, Lifelong Exposure Characterization* (oral presentation). Symposium on International Collaboration on the Exposome at the ISEE Annual Conference. Seattle, Washington, USA. 24-28 August 2014.
- **Joan O. Grimalt (CSIC).** *Impacts and potential effects of DDT reintroduction against malaria in African populations* (Opening Plenary Lecture) and *Health and environment-wide associations based on large population surveys* (oral presentation). 34th International Symposium on Halogenated Persistent Organic Pollutants (Dioxin 2014). Madrid, Spain. 31 August – 5 September 2014.
- **Marta Fort (CSIC).** *Association between metal body burden in pregnant women and atmospheric traffic pollution and Assessment of exposure to trace metals in a cohort of pregnant women from an urban center by urine analysis in the first and third trimesters of pregnancy* (oral presentations). 17th International Conference on Heavy Metals in Environment (ICHMET 2014). Guiyang, China. 22-25 September 2014.
- **Janja S. Tratnik (JSI).** *Toxic and potentially toxic microelements in EXPOSOME* (oral presentation). 17th International Conference on Heavy Metals in Environment (ICHMET 2014). Guiyang, China. 22-25 September 2014.
- **Janja S. Tratnik (JSI) and Alessandro Alimonti (ISS).** *Toxic metal exposure and effects – the EXPOSOME approach* (session chairs). 17th International Conference on Heavy Metals in Environment (ICHMET 2014). Guiyang, China. 22-25 September 2014.
- **Dimosthenis Sarigiannis (AUTH).** *Radiological exposome: lifelong ionising and non-ionizing radiation exposure and human health* (lecture). ENMF International Workshop "Expanding Nuclear Medicine Frontiers". Thessaloniki, Greece. 27 September 2014.
- **Marta Fort (CSIC).** *Interdependence between urinary cobalt concentrations and hemoglobin levels in pregnant women* (poster). 1st Young Researchers Conference on Environmental Epidemiology (ISEE). Barcelona, Catalonia, Spain. 20-21 October 2014.
- **Mercè Gari (CSIC)** *Impacts of atmospheric chlor-alkali factory emissions in surrounding populations* (oral presentation) and *Inverse age-dependent accumulation of decabromodiphenyl ether and other PBDEs in serum from a general adult population* (poster). 1st Young Researchers Conference on Environmental Epidemiology (ISEE). Barcelona, Catalonia, Spain. 20-21 October 2014.

## Forthcoming Events

- **ICEPPHI 2015: XIII International Conference on Environmental Pollution, Public Health and Impacts**  
26–27 January 2015, Istanbul (Turkey)  
<https://www.waset.org/conference/2015/01/istanbul/ICEPPHI>
- **Children's Environmental Health Network (CEHN) 2015 Research Conference. Children: Food and Environment**  
4–6 February 2015, Austin, Texas (USA)  
[http://www.cehn.org/2015\\_research\\_conference](http://www.cehn.org/2015_research_conference)
- **ICAPC 2015: XIII International Conference on Air Pollution and Control**  
23–24 February 2015, Paris (France)  
<http://www.waset.org/conference/2015/02/paris/ICAPC>
- **SETAC Europe 25th Annual Meeting. Environmental Protection in a Multi-Stressed World: Challenges for Science, Industry and Regulators.**  
3–7 May 2015, Barcelona (Catalonia, Spain)  
<http://barcelona.setac.eu/>
- **ICCBES 2015: International Congress on Chemical, Biological and Environmental Sciences**  
7–9 May 2015, Kyoto (Japan)  
<http://www.iccbes.org>
- **Healthy Buildings Europe 2015. Stepping beyond traditional boundaries, (re)creating healthy buildings.**  
18–20 May 2015, Eindhoven (The Netherlands)  
<http://www.hb2015-europe.org>
- **ICACI 2015: XIII International Conference on Allergy and Clinical Immunology**  
25–26 May 2015, London (UK)  
<https://www.waset.org/conference/2015/05/london/ICACI>
- **EAACI 2015 Annual Congress: European Academy of Allergy and Clinical Immunology.**  
6–10 June 2015, Barcelona (Catalonia, Spain)  
<http://www.eaaci2015.com>
- **DIOXIN 2015**  
23–28 August 2015, Sao Paulo (Brazil)  
<http://www.dioxin20xx.org>
- **ISEE 2015. 27th Conference on the International Society for Environmental Epidemiology. Addressing Environmental Health Inequalities.**  
30 August – 3 September 2015, Sao Paulo (Brazil)  
<http://www.isee2015.org>
- **Eurotox 2015. 51st Congress of the European Societies of Toxicology. Bridging Sciences for Safety.**  
13–16 September 2015, Porto (Portugal)  
<http://www.eurotox2015.com>
- **European Academy of Paediatrics. Congress and Master-Course 2015.**  
17–20 September 2015, Oslo (Norway)  
<http://www.eapcongress.com>
- **25th Annual ISES Conference. International Society of Exposure Science. Exposures in an Evolving Environment.**  
18–22 October 2015, Las Vegas, Nevada (USA)  
[http://www.isesweb.org/Meetings/mtgs\\_cur.htm](http://www.isesweb.org/Meetings/mtgs_cur.htm)
- **ICCE 2015. 15 EuCheMS International Conference on Chemistry and the Environment.**  
20–25 September 2015, Leipzig (Germany)  
<http://www.icce2015.org/>
- **ERS International Congress 2015. European Respiratory Society**  
26–30 September 2015, Amsterdam (Netherlands)  
<http://www.erscongress.org/>

### Editorial Board

Prof. Joan O. Grimalt   Dr. Mercè Garí



### Editorial Information

If you wish to contribute to the *Newsletter* or share information for publication, please contact Mercè Garí:

[merce.gari@idaea.csic.es](mailto:merce.gari@idaea.csic.es)

This project has received funding from the European Union's Seventh Programme for research, technological development and demonstration under grant agreement No 603946

