

HEALS Newsletter

Health and Environment-wide Associations based on Large population Surveys

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



Contents

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

Welcome Note

Welcome to the first newsletter of the HEALS Project!

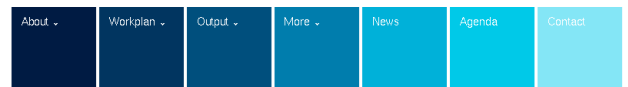
HEALS stands for Health and Environment-wide Associations based on Large population Surveys, a 60-month research project funded by the Seventh Framework Programme of the European Commission (starting in October 2013).

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

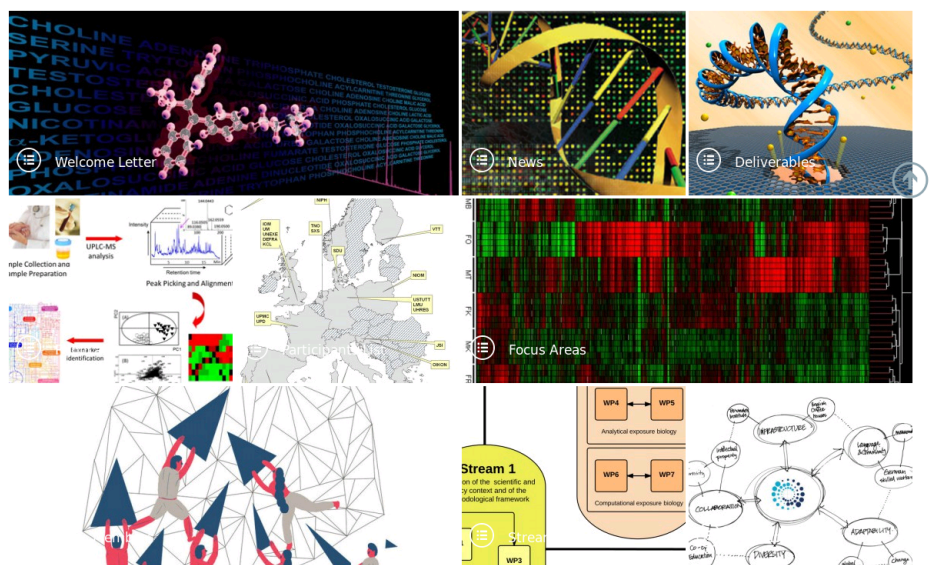


Welcome to HEALS Health and Environment-wide Associations based on Large population Surveys

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

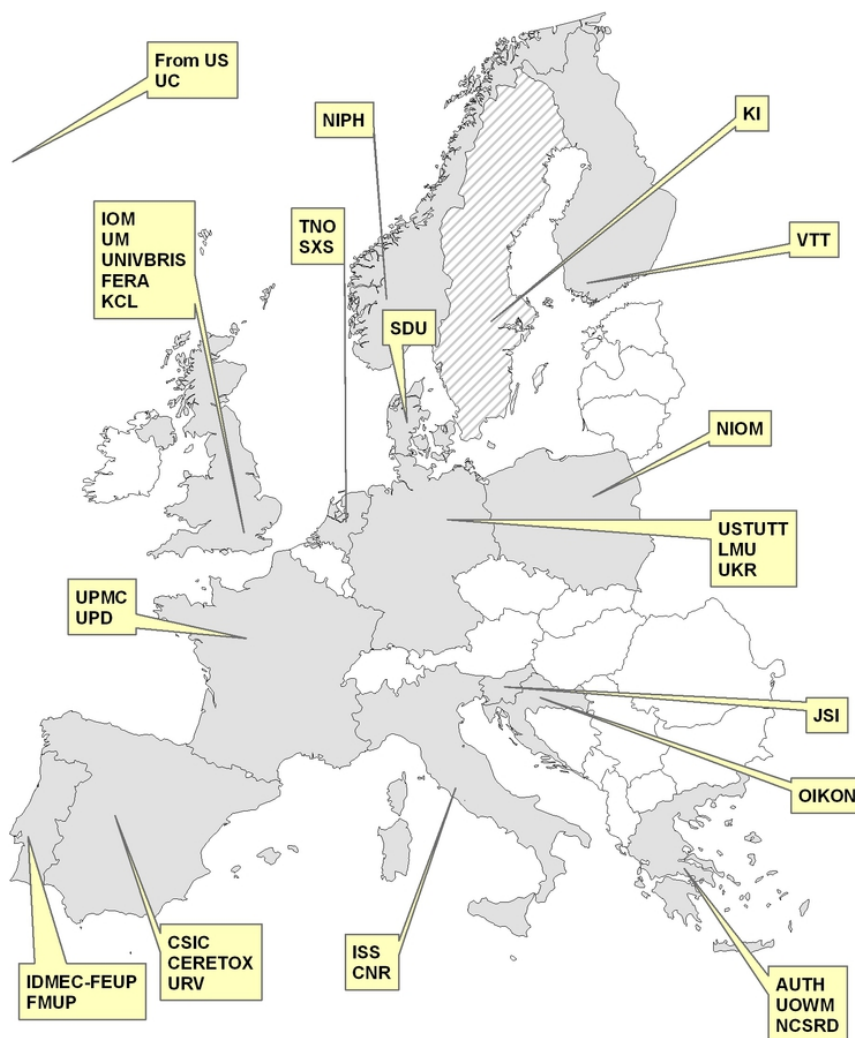
Introducing HEALS

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

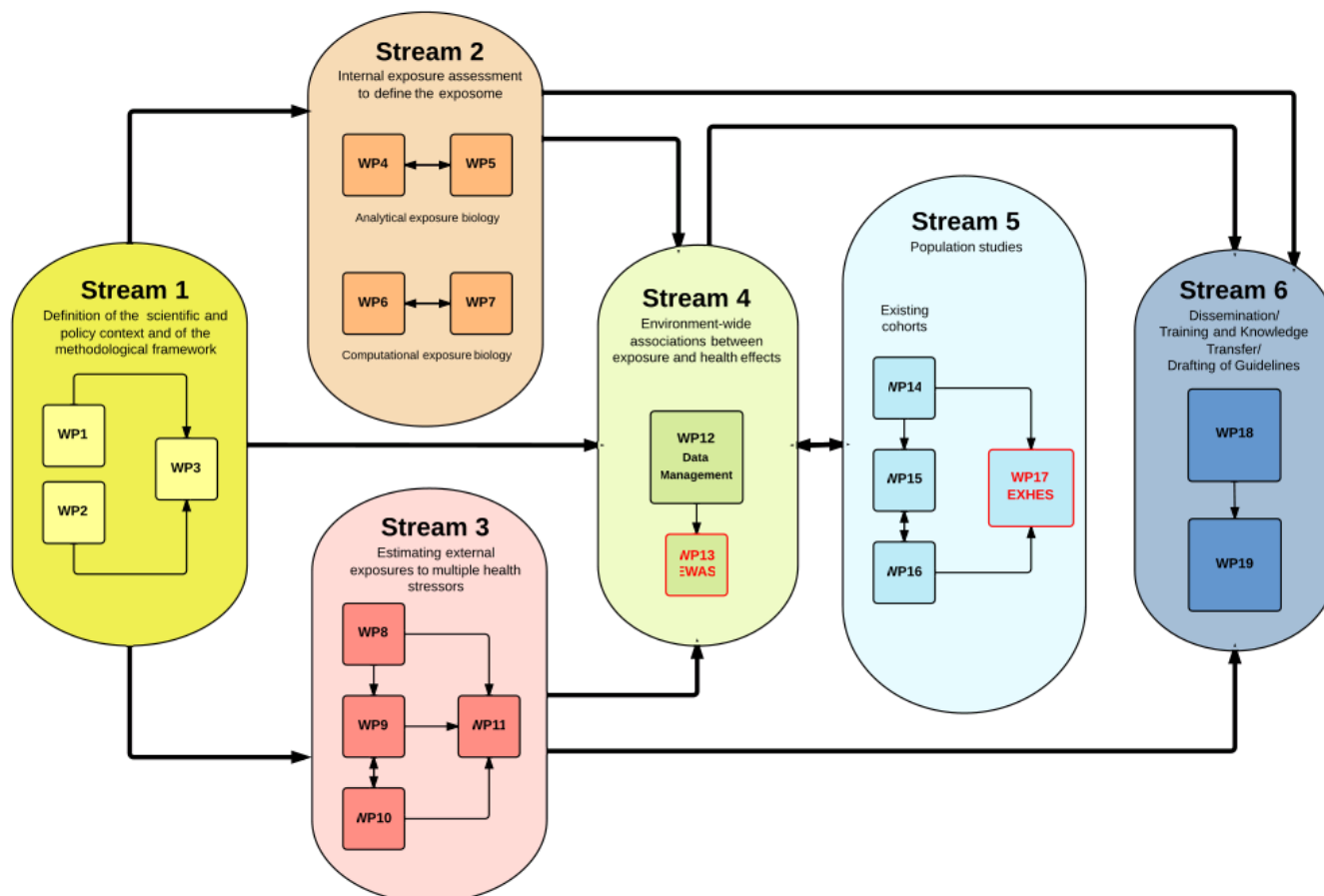
1. Université Pierre et Marie Curie - Paris 6 (UPMC, France)
2. Aristotle University of Thessaloniki (AUTH, Greece)
3. Institute of Occupational Medicine (IOM, United Kingdom)
4. Universität Stuttgart (USTUTT, Germany)
5. Institut Jožef Stefan (JSI, Slovenia)
6. Université Paris Descartes (UPD, France)
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) Aristotile University of Thessaloniki (AUTH)
 Paris, France 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.

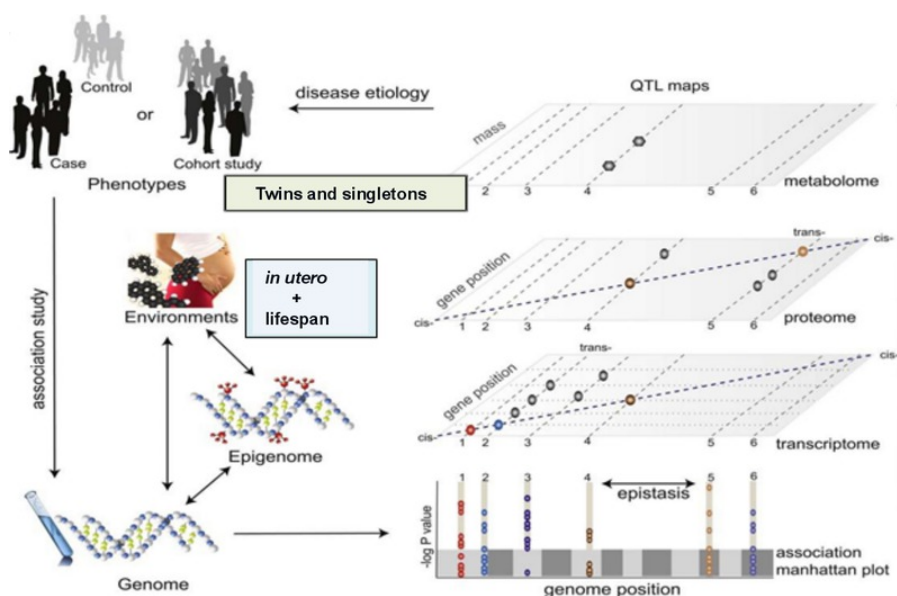
It is the prospective cohort study design through the new cohorts of singletons and twins that will be recruited since *in utero* life and followed-up for 3 years and of their parents (the Exposure and Health Examination Survey (EXHES)) that best suits the "expo-

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 Universität München (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 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 breakout 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) 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 Madrydn,*

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, Biotecnología al día, 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/observatori/observatori-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 interface. At the top, there are navigation links for 'MY TNO' (Log in | Register), 'LANGUAGE' (Nederlands | English), and 'CONTACT' (Contact information). Below this is a main navigation bar with 'HOME', 'FEATURED', 'THEMES', 'EXPERTISE', 'ABOUT US', 'DIRECTLY TO', and 'WORKING AT TNO'. The main content area features a 'PRESS' sidebar with links to 'Archive', 'News', 'Agenda', 'TNO TIME', 'Press Office', and 'Dossiers'. The main article is dated October 28, 2013, and includes a contact box for Dr R.H. (Rob) Stierum with his phone number and a 'Contact me' link. The article title is 'TNO PARTICIPATES IN HEALS, THE LARGEST EUROPEAN UNION PROJECT TO STUDY HEALTH IN RELATION TO THE ENVIRONMENT'.

© 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 interface. At the top, there are logos for 'GOBIERNO DE ESPAÑA', 'MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD', and 'CSIC'. Below this is a navigation bar with 'inicio', 'quiénes somos', 'centres in Catalonia', 'servicios en la delegación', 'noticias', 'divulgación', 'agenda', and 'enlaces'. The main content area features a 'ARCHIVO DE NOTICIAS' sidebar with a list of years from 2014 to 2011. The main article is dated January 29, 2014, and includes a search bar and a 'Contacto' box with contact information for Mercè Fernández. The article title is 'HEALS, a European project for identifying lifetime exposure to contaminants'. The article text describes the objective of the HEALS project and lists the consortium members.

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 Tromso (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
- 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

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 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>
- 14avas 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>
- Biometals 2014: *A conference exploring metals in biology, medicine and the environment***
 13–18 July 2014, Durham (NC, USA)
<http://biometals2014.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>

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

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

