SEVENTH FRAMEWORK PROGRAMME

HEALS

Health and Environment-wide Associations based on Large population Surveys

FP7-ENV-2013- 603946

http://www.heals-eu.eu/

D 2.3 Report on the HEALS scientific network maintenance

WP 2 Scientific networking

Version number 1

Lead beneficiary: JSI

Date: 29.1.2016

Nature: R

Dissemination level: PU

TABLE OF CONTENTS

Document Information

Grant Agreement Number	ENV-603946	**Acronym**	HEALS
Full title	Health and Environment-wide Associations based on Large population Surveys		
Project URL	http://www.heals-eu.eu/		
EU Project Officer	Tuomo Karjalainen,- Tuomo.KARJALAINEN@ec.europa.eu		

Deliverable	**Number**	2.3	**Title**	Report on the HEALS scientific network maintenance
Work Package	**Number**	2	**Title**	Scientific network

Delivery date	**Contractual**	M18	**Actual**	31/01/2016
Status	Draft 1		Final ☐	
Nature	Demonstrator ☐	Report X	Prototype ☐	Other ☐
Dissemination level	Confidential X	Public ☐		

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Document History

Name	Date	Version	Desciption

1 Introduction

Among the objectives of HEALS is networking and synergy building with similar initiatives in Europe and outside Europe, in order to ensure better spread and exploitation of the scientific achievements of the research projects in common fields of science.

Such networking can be implemented through promoting collaboration among researchers involved in the these projects, organizing joint meetings and conferences to facilitate the exchange of experiences and information, pursuing common objective of increasing the awareness on relationship between environmental exposure and human health. Moreover HEALS benefits from a large amount of environmental (e.g., on exposure to chemicals) and health data (e.g., disease prevalence) collected in various EU and world regions by national, international and EU-funded projects and agencies. HEALS can benefit from past project, on-going projects and active participation in the preparation and participation in new projects.

Moreover, networking through active participation at international conferences, symposia and workshops are also to be exploited.

This deliverable summarizes main networking projects, organizations, partners and activities.

2 Past research projects

2.1 EU funded

ERA-ENVHEALTH, The European Environment and Health Action Plan for 2004-10 pointed to a need to strengthen networks between researchers, policy-makers and stakeholders. The FP7 ERA-ENVHEALTH project was set up to bring together European organisations planning research in the Environment and Health (E&H) arena with the objective of providing policy support. ERA-ENVHEALTH's task was to mobilise scientific research in support of European and national policies on E&H issues. The project ended in 2012, but the network still continues to collaborate striving towards better integrating environment and health research in policy. http://www.era-envhealth.eu

ENRIECO, Enrieco (Environmental Health Risks in European Birth Cohorts) is a project conducted within the European Union's 7th Framework Programme [Theme 6, Environment (Including Climate Change)]. Its overall aim is to advance our knowledge on specific environment and health causal relationships in pregnancy and birth cohorts by providing support to exploitation of the wealth of data generated by past or ongoing studies funded by the EC and national programmes. http://www.enrieco.org

DEER, (Developmental effects and reproductive disorder) The objectives of DEER are to approach the testicular dysgenesis syndrome TDS problem by investigating (1) connections between normal and abnormal foetal and neonatal reproductive development and subsequent maturation of reproductive function at puberty and adulthood systemic gene-environment interactions underlying reproductive disorders taking into account genetic susceptibility and multiple exposures and (2) connection between perinatal development and metabolic disorders in later life (obesity). www.eu-deer.net

CONTAMED (Contaminant mixtures and human reproductive health - novel strategies for health impact and risk assessment of endocrine disrupters) CONTAMED aims to explore the hypothesis that combined exposures to endocrine disrupting chemicals (EDC) in foetal life lead to adverse impacts on male human reproductive health. CONTAMED aims to inform epidemiological studies able to capture cumulative EDC exposure by developing and evaluating biomarkers for total effective internal EDC load. CONTAMED also aims to compare internal EDC exposures in humans with those resulting from controlled exposures producing clear effects in laboratory animal experiments. It is hoped that this will enhance the usefulness of animal data in making extrapolations to the human. Finally, the project intends to search for previously unrecognised EDCs in human tissues by combining analytical chemistry with in vitro EDC mode-of-action screens in bioassay-directed fractionations ('toxicity identification and evaluation', TIE) and by using metabolomic profiling to identify xenobiotic as well as endogenous biomarker metabolites. http://www.contamed.eu/

ArcRisk, (Arctic health risks: Impacts on health in the Arctic and Europe owing to climate-induced changes in contaminant cycling). Impacts on health in the Arctic and Europe owing to climate-induced changes in contaminant cycling. In this project health risks in populations in the Arctic and in selected areas of Europe due to the spreading of pollution resulting from

climate change were investigated. http://www.arcrisk.eu/

ENFIRO (Life Cycle Assessment of Environment-Compatible Flame Retardants: Prototypical Case Study) ENFIRO a European Commission-funded project offers a prototypical case study on substitution options for specific brominated flame retardants (BFRs). The project delivers a comprehensive dataset on viability of production and application, environmental safety, and a life cycle assessment of the alternative flame retardants (FRs). http://www.enfiro.eu

ENVIROGENOMARKERS (Genomic biomarkers of environmental health) This project was the first large-scale application of the whole range of –omics technologies in a population study aiming at (1) the discovery and validation of novel biomarkers predict increased risks of chronic diseases in which the environment may play an important role (breast cancer, non-Hodgkin's lymphoma, allergy, neurological and immune diseases, thyroid disruption) (2) the exploration of the association of such risk biomarkers with environmental exposures, including high-priority pollutants (carcinogens and immunotoxicants such as PCBs and PAHs, neurotoxicants such as cadmium, lead and ambient air pollution) and emerging exposures (such as phthalates and brominated flame retardants and (3) the discovery and validation of biomarkers of exposure to the above and other high-priority environmental exposures (e.g. water disinfection byproducts) (genomic biomarkers of environmetal health) http://www.envirogenomarkers.net

COPHES/DEMOCOPHES represents the first European human biomotoring trial on a larger scale and has its origins in the European Environment and Health Action Plan of 2004 to "develop a coherent approach on human biomonitoring (HBM) in Europe". Within this twin-project it was targeted to collect specimens from 120 mother–child-pairs in each of the 17 participating European countries. These specimens were investigated for six biomarkers (mercury in hair; creatinine, cotinine, cadmium, phthalate metabolites and bisphenol A in urine). Samples and the results are available for further exploitation. http://www.eu-hbm.info/cophes

URGENCHE (Urban Reduction of GHG Emissions in China and Europe), a team of internationally recognised scientists in the areas of health risk assessment, urban energy demand and supply scenarios, urban planning, environmental science and epidemiology – in close collaboration with city partners in both Europe and China – has developed and applied a methodological framework for the assessment of the overall risks and benefits of alternative greenhouse gas (GHG) emission reduction policies for health and well-being. http://www.urgenche.eu/project/

PHIME (Public Health Impact of long-term, low-level Mixed Element Exposure in susceptible population strata) The background was a renewed interest in toxic metals, due to a growing awareness that the exposure in the general population in Europe and elsewhere is at levels with potential to cause toxic effects in susceptible individuals. Such exposures may have a role in the etiology of common clinical diseases, as well as sub-clinical effects, which may be serious for the society. http://www.**phime.oikon**.hr/

HENVINET (Health and environment network) To protect the health of populations and individuals, policies need to integrate environmental and health issues. The aim of HENVINET is to support such informed policy making. HENVINET will review, exploit and disseminate knowledge on environmental health issues based on research and practices, for wider use by relevant stakeholders. Further, it will lead to validation of tools and results with

emphasis on the four priority health diseases of the European Environment and Health Action Plan (EHAP) 2004-2010, and will provide structured information overview that may be utilised by other actors relevant to Environment and Health Strategy. The project was build on previous research and policy initiatives such as AirNET, CLEAR, PINCHE, INTARESE and SCALE, and collected, structure and evaluate material and present it in a consistent manner, which lend itself to transparency and identification of knowledge gaps.

HEIMTSA (Health and environment integrated methodology and toolbox for scenario assessment) The aims were to (1) Develop and provide improved methods for health impact assessment (HIA) and cost benefit analysis (CBA) of environment and health issues. (2) Develop an associated set of tools, or modular integrated assessment system (IAS), for implementing the methodology Europe-wide, and (3) Apply the methods and tools to selected realistic policy scenarios at the European level. http://www.**heimtsa**.eu/

INTARESE (Integrated assessment of the health risks of environmental stressors in Europe) The project brought together a team of internationally renowned scientists in the areas of epidemiology, environmental science and biosciences to collaborate on developing and applying new, integrated approaches to the assessment of environmental health risks and consequences, in support of European policy on environmental health. The INTARESE approach was based on the principle that environmental health issues are not stand-alone issues but the result of interdependent decisions and events and can affect human health in many different interacting ways. http://www.intarese.org/

NEWGENERIS (Development and application of biomarkers of dietary exposure to genotoxic and immunotoxic chemicals and of biomarkers of early effects, using mother-child birth cohorts and biobanks). , NewGeneris is an Integrated Project conducted within the European Union's 6th Framework Programme, priority area Food Quality and Safety Its objective is to investigate the role of prenatal and early-life exposure to genotoxic chemicals present in food and the environment in the development of childhood cancer and immune disorders. http://www.newgeneris.org/

ECNIS, (Environmental Cancer Risk, Nutrition and Individual Susceptibility) was a Network of Excellence in the EU 6th Framework Programme. A major approach employed in ECNIS research is the use of biomarkers of carcinogenesis. Biomarkers of carcinogenesis are usually substances which can be measured in body fluids or tissues and provide information about a person's exposure to carcinogens or about cellular damage caused by carcinogens far earlier than the appearance of clinical disease. Furthermore, genetic polymorphisms can serve as biomarkers of individual susceptibility to carcinogenesis. ECNIS research also addresses the mechanisms by which chemicals alter cellular processes to cause cancer and the way in which food components intervene in these mechanisms. It also aims to improve cancer risk assessment, and to address important socio-ethical issues arising from the use of biomarker technology. http://www.ecnis.org/

EU BUMA (Prioritizitation of BUilding MAterialsas indoor pollution source). The BUMA project aimd to thoroughly assess the human exposure to air hazards emitted by building materials commonly used in Europe. The project gained a better understanding of the sources of hazardous compounds existing in the indoor environment and play a key role in the determination of the well-being and comfortable living of the occupants. The outputs of the BUMA project were subsequently used by policy makers, health professionals and building material producers in the enlarged European Union.

http://mech.uowm.gr/bumaproject/

CHILDRENGEnONETwORK (European network on children's susceptibility and exposure to environmental genotoxicants), This concerted action focused on essential topics in feasibility studies: Foetal exposures (placental transport), comparisons of child/adult exposures to urban air pollution, comparisons of metabolism, DNA-damage and DNA repair. Collecting, describing, evaluating and comparing available studies within Europe also compared the geotaxis effects in children versus adults. Special work packages are devoted to risk assessment and ethical considerations. A survey on available bio banks formed the basis for follow up studies in 6th framework program and beyond.

CHICOS (Developing a Child Cohort Research Strategy for Europe) is a project conducted within the European Union's 7th Framework Programme. Its overall aim is to improve child health across Europe by developing an integrated strategy for mother-child cohort research in Europe. CHICOS aims to promote an inventory of all mother-child cohorts in Europe, to evaluate existing information on outcomes and determinants from these cohorts, to identify gaps in knowledge, and to develop recommendations for research action at a European level for the next 15 years, focusing on key areas of policy concern. http:// www.chicosproject.eu/

OFFICAIR, The overall objective of the OFFICAIR project was twofold. Firstly, to establish a framework that will provide new knowledge in terms of databases, modelling tools and assessment methods towards an integrated approach in assessing the health risk from indoor air pollution, focusing on modern office buildings. Secondly, to support current EU policies, such as, the Thematic Strategy on Air Pollution and the European Environment and Health Strategy and Action Plan. http://www.officair-project.eu/

EPHECT project (Emissions, exposure patterns and health effects of consumer products in the EU), irritative and respiratory health effects were assessed in relation to acute and long-term exposure to key and emerging indoor air pollutants emitted during household use of selected consumer products. In this context, inhalation exposure assessment was carried out for six selected 'target' compounds (acrolein, formaldehyde, benzene, naphthalene, d-limonene and α-pinene). This paper presents the methodology and the outcomes from the micro-environmental modelling of the 'target' pollutants following single or multiple use of selected consumer products and the subsequent exposure assessment. The results indicate that emissions from consumer products of benzene and α-pinene were not considered to contribute significantly to the EU indoor background levels, in contrast to some cases of formaldehyde and d-limonene emissions in Eastern Europe (mainly from cleaning products). www.ephect.eu

The SINPHONIE (School indoor pollution and health: an European network observatory) project is an example of the practical implementation of the EU Environment and Health Action Plan 2004-2010; and is an example of subregional cooperation in order to implement the revised CEHAPE RPG3 (2004, 2010). With its special focus on schools and childcare facilities, the SINPHONIE project aims to define policy recommendations on remedial measures in the school environment. In order to achieve this overall objective, SINPHONIE builds on knowledge acquired in the course of earlier projects (e.g. EnVIE [http://www.envie-iaq.eu] and SEARCH [www.rec.org/SEARCH/]). It aims to expand the spectrum of available information by carrying out complex research into children's exposure to indoor air pollutants and health risks in schools. A common European database will be created using the same protocol on indoor air quality (IAQ) and other environmental parameters in schools and

related health impacts throughout Europe in order to provide evidence for use in compiling guidelines to improve air quality in schools.www.sinphonie.eu

RADPAR, The general objective of this project is to assist in reducing the significant public health burden of radon related lung cancers in EU Member States (MS). The effectiveness of the various existing radon prevention and remediation strategies in the MS will be assessed with the objective of improving them. The assessment of potential conflicts between EU energy conservation objectives in buildings and radon control technologies will be an important objective of this project. web.jrc.ec.europa.eu/radpar

MARINA stands for integrated and intelligent testing, integrated assessment, and modular interconnection of knowledge and information for validated science-based risk management methods. The approach is to shift from toxicology studies of specific individual nanomaterials towards developing tools for a more integrated systematic health and environmental safety assessment and management that can handle the overall risks for types or classes of ENM based on their physico-chemical properties. www.marina-fp7.eu/project

NANODEVICE. The main project goal is to develop innovative concepts and reliable methods for characterizing ENP in workplace air with novel, portable and easy-to-use devices suitable for workplaces. Additional research objectives are (1) identification of relevant physico-chemical properties and metrics of airborne ENP; establishment of reference materials; (2) exploring the association between physico-chemical and toxicological properties of ENP; (3) analyzing industrial processes as a source of ENP in workplace air; (4) developing methods for calibration and testing of the novel devices in real and simulated exposure situations; and (5) dissemination of the research results to promote the safe use of ENP through guidance, standards and education, implementing of safety objectives in ENP production and handling, and promotion of safety related collaboration through an internationally nanosafety platform. www.nano-device.eu

DENAMIC "Developmental Neurotoxicity Assessment of Mixtures in Children" investigates neurotoxic effects of low-concentration mixtures of pesticides and a number of common environmental pollutants in children. We focus on (subclinical) effects on learning (cognitive skills) and developmental disorders in children (e.g. ADHD, autism spectrum disorders and anxiety disorders). DENAMIC will develop tools and methods for screening of neurotoxic effects.
The developed methods and obtained results will give recommendations for risk management to the EU and WHO and will largely support the EU chemicals legislation for identifying (potential) neurotoxicants. http://www.denamic-project.eu

3 On-going projects

3.1 On-going and planned EU funded projects/programmes

The HELIX project at the Barcelona-based Centre for Research in Environmental Epidemiology will attempt to develop an early life exposome, noting that the first exposures occur during development It is build upon six existing birth cohorts across Europe and "measure the exposome" at key prenatal and early childhood time points, through the use of GIS, personal sensors, biomarkers and omics platforms. www.project**helix**.eu

EXPOsOMICs Exposomics, is a consortium based at Imperial College London. This project use smartphones that utilize GPS and environmental sensors to assess exposures. The EXPOsOMICS project aims to develop a new approach to assess environmental exposures, primarily focusing on air pollution and water contaminants. Using 'omic' techniques the collected exposure data can be linked to biochemical and molecular changes in our body. The results will help to improve our understanding on how these pollutants influence the risk of developing chronic diseases. www.**exposomics**project.eu

IFE PERSUADED: Phthalates and bisphenol A biomonitoring in Italian mother-child pairs: link between exposure and juvenile diseases (LIFE13 ENV/IT/000482) www.iss.it/lifp. The National Institute of Health in Italy and coordinator of the LIFE- PERSUADED project, that aims to assess the exposure to compounds such as bisphenol A (BPA) and di-2- ethylhexyl phthalate (DEHP) in children, aged between 4 and 14 years, and their mothers through the biomonitoring study.

HEROIC is dealing with challenges due to the increasing need for risk assessments (e.g. REACH, toxicity of mixtures), public and legislative pressure to reduce the amount of animal testing, and budget restrictions. It is clear that better coordination and exploitation of existing data is needed to optimise resource use in human and environmental risk assessment. Among the main objectives the following are relevant.: (i) Contribute to the harmonisation of tools and methods in human and environmental risk assessment by exploring how hazard characterisation and exposure assessment data can be used across disciplines; (ii) Develop a framework for integrated approaches and methodologies for human and environmental risk assessment (for all chemical classes, also including mixtures), and (iii) Facilitate better understanding and co-operation between stakeholders involved in human and environmental risk assessment, in order to improve the quality, perceived value, and acceptance of integrated risk assessment, thereby helping to improve risk management decisions. http://www.heroic-fp7.eu

EHBMI European Human Biomonitoring initiative – EHBMI is a co-fund EU programme in prepration in which several HEALS partners will contribute and from which HEALS can also benefit. The background goues to the fact that the European citizens of all ages are exposed to a wide range of chemicals through their diet, their environment and through the use of consumer products. Exposure to chemicals (including combinations of chemicals) takes place through a variety of pathways and exposure routes notably via dermal, oral or inhalative uptake (aggregated exposure).

Despite the existence of human biomonitoring (HBM) programmes at national level and the large number of research and development projects ongoing at both national and European Union (EU) level, there is a clear lack of data on aggregated exposure to single substances and to combinations of chemical substances, as well as insufficient evidence-based knowledge on the link between exposures and human health. This knowledge is essential for informing effective policy-making to protect the EU population from the impacts of chemical exposure on health. In particular, exposure to mixtures of substances is not adequately addressed, since current risk assessment procedures address the risks from substances acting in isolation. Furthermore, there is a lack of robust data on internal exposure. HBM data that represents national populations or vulnerable subgroups exist in many European countries and these data can be used to inform chemical regulations aiming to protect human health. However, a number of factors prevent the use of these data at EU level to gain a pan-European perspective. Firstly, the data were not collected according to standardised protocols and are therefore not comparable, secondly variations in the metadata characterising the datasets inhibit cross-dataset analyses, and finally available data are not representative of the European population.

In order to address these issues there is a clear need to:

i) Harmonise procedures and tools for HBM at EU level, notably with regards to sample collection, analysis and data interpretation;

ii) Provide and where missing generate internal exposure data and link this data to aggregated exposure and the related exposure pathways;

iii) Identify novel methods to accurately establish the causal links between chemical exposure and human health; and

iv) Provide policy-makers and the general public with evidence-based knowledge on the health risks associated with chemicals exposure.

The systematic evaluation of population exposure to chemicals using HBM provides a means to directly address these needs by generating robust, harmonised and comparable HBM data on chemical exposure at a European level. The protection of human health through effective and targeted chemical risk assessment and management could then be grounded in an understanding of the actual exposure of the EU population to chemicals, relevant exposure pathways and associated health impacts.

The European Human Biomonitoring Initiative (EHBMI) will establish and implement an ambitious European Joint Programme (EJP) and will provide policy makers with an EU-wide evidence base of comparable and validated exposure and health data. This will be done by integrating and building on previous EU initiatives, national HBM programmes and studies (including cohorts, epidemiological studies and health surveys).

In contrast to former projects, the proposed programme will involve national programme owners and/or the national managers of those programmes, and include policy makers at national level. This inclusive approach, combined with the aims of integrating HBM and environmental health research, will strengthen the EJP, enhance the sustainability of the initiative and amplify the impacts of the results.

In order to ensure that the knowledge we generate is targeted, timely and fit for purpose, we will establish an intense dialogue with EU policy makers responsible for assessing and managing the risks to human health from chemical exposure via the environment, diet, consumer products and occupational exposure e.g. the EU chemicals legislation under REACH (Registration, Evaluation and Authorisation of Chemicals).

HEALS will initiate and maintain these scientific networks using traditional techniques (workshops, conferences) as well as webinars and social media tools.

Development of a networking plan to expand and maintain scientific networks during the course of the project. We will use traditional techniques (workshops, face-to-face meetings, conference presentations) as well as webinars and social media tools.

The concrete examples already included in the DoW include the following:

WP 12 thematic linkages: ToxHub database of the HEROIC project supports European data integration. The database has been designed to accommodate both geo-referenced and non-spatial data. Geo-referenced data (i.e. environmental, exposure, population, satellite and GPS sensor-based data) will be included to capture spatial variability of exposure information and support spatial analysis thereof using a Geographical Information System (GIS). Spatially differentiated analysis may support the development of more refined exposure and risk assessment and thus contribute to the development of more refined risk management measures. This is particularly important when policy-relevant conclusions need to be drawn. Non-spatial datasets has also been also included through linkage to a number of publicly available databases to retrieve molecular biology/biochemistry and clinical data that already exist or that are produced during the project as needed to perform EWAS to the population surveys addressed in Stream 5 of the HEALS project.

First steps include: (a) the definition of the Database functionalities; (b) the identification of the main information sources and (c) the incorporation of the datasets the GeoDatabase platform will include towards the implementation of the HEALS approach. The results of this process will be analysed and discussed within the HEALS consortium during technical meetings in close collaboration with all the other Streams. Based on these deliberations the technical team of WP12 will define the HEALS platform functional specifications which will guide the development of the overall HEALS database design. Special care will be paid to compatibility with ToxHub (HEROIC), and IPCHeM (JRC). A key functionality is the possibility to readily deliver relevant HEALS data to the IPCheM database.

IPChem the Information Platform for Chemical Monitoring is a single access point for discovering chemical monitoring data collections managed and available to European Commission bodies, Member States, international and national organisations and researchers. The Platform aims to support a more coordinated approach for collecting, storing, accessing and assessing data related to the occurrence of chemicals and chemical mixtures, in relation to humans and the environment. https://ipchem.jrc.ec.europa.eu

In WP 15 additional inputs that helps also in the implementation of work is based on the result from the European commission-funded project DENAMIC "Developmental Neurotoxicity Assessment of Mixtures in Children" that is investigating neurotoxic effects of low-concentration mixtures of pesticides and a number of common environmental pollutants in children on (subclinical) effects on learning (cognitive skills) and developmental disorders in children (e.g. ADHD, autism spectrum disorders and anxiety disorders). Of interest for HEALS will be the results of two distinct DENAMIC pillars: (i) The first pillar involves hazard characterisation for neurotoxic chemicals and (environmentally relevant) mixtures thereof. Novel tools, testing methods and procedures for screening (mixtures of) chemicals for neurotoxicity are developed, together with improved assessment methods for exposure and effects. In the second pillar (exposure/epidemiology), perinatal and early-childhood exposure

will be studied in maternal urine and cord blood, as well as breast milk and urine of the child. In the epidemiological part these developed integrated tools are tested in a tailor made cohort of mother/child pairs focusing on learning and developmental disorders, including the onset of ADHD. In both the experimental and epidemiological part of DENAMIC, biomarkers for developmental neurotoxicity will be developed and/or validated by using innovative biotechnology tools. (ii)An important aspect of DENAMIC that will be of utility in HEALS is the development of biomarkers for (developmental) neurotoxicity in animal models using (epi-)genomics, proteomics and metabolomics as HEALS is not going to conduct ex vivo and in vivo studies in mouse and zebra-fishes. The links with DENAMIC will be established through collaborations, exchanges, publications and other initiatives including common initiatives like a workshop. The fact that two of HEALS partners are also DENAMIC partners will help in liaising. In HEALS, the neurodevelopmental toxicity of metals/metalloids, pesticides and organic compounds with EDC activity will be studied on mother-child cohorts where both exposure (fetal and/or neonatal) and neuropsychological outcomes have been measured. They include the EDEN cohort (France, n= 1,200), the ReproPL cohort (Poland, n = 400), the PHIME cohort (Slovenia and Croatia, n = 675), and the JSI cohort (Slovenia, n = 600) for a total of 2,875 children in whom exposure assessments have been or will be performed.

WP 16 linkages: The thematic linkages in WP 16 is based on integration of information from national studies. The work includes information from re-existing twins data come from: twins registries of Denmark, Finland, Italy, Netherlands, Norway, Sweden, UK as well as from Australia. Population-based data derive from national studies:

- *Italy* (a. about 3,000 subjects of a general sample living in Pisa (national founds); b. about 2,000 schoolchildren of the Italian CCM study founded by Italian Ministry of Health; c. about 500 adolescents in Sicily– RESPIRA projects founded by EU).
- *France* (a. 1,200 mother-baby pairs from the EDEN study; b. 1,000 adults subjects from the OQAI study; c. 470 from FERMA study; d. 7,242 schoolchildren from the 6 Cities Study; e. 2,100 elderly from the 3C study); f. 600 elderly from the DG-SANCO funded GERIE Study);
- *UK* (1,185 children from MAAS Study recruited prenatally between 1995-1997 followed up until age 11);
- *Portugal* (a. 2,943 adolescents from EPITeen study; b. about 7,000 mother-baby from Geração 21);
- *Poland* (1,700 mother-child from REPRO_PL);
- *Spain* (920 adults from CHIS2000).

European SINPHONIE (n=5,000 schoolchildren and n=1,000 teachers), the HESE European study (n=500 schoolchildren) and GERIE Studies (n=500).
In this work, results from the EU-funded OBELIX project will be taken into account. The "OBesogenic Endocrine disrupting chemicals: LInking prenatal eXposure to the development of obesity later in life" has provided useful data on whether prenatalexposure to endocrine disrupting compounds in food plays a role in the development of obesity and related disorders later in life through a multidisciplinary approach that combined epidemiology, neonatology, endocrinology, toxicology, analytical chemistry and risk that will be of integrated in the HEALS approach. The links with OBELIX is established through collaborations, exchanges, publications and other initiatives including common initiatives like a workshop.

European countries (DEMOCOPHES, n=1,000), Slovenia (PHIME and DEMOCOPHES,

n=600), France (EDEN, n=1,200), Spain (INMA and CHIS2000, n=1,820), Croatia (PHIME, n=285) and Poland (RePRO_PL, n=1,700), exposed to phthalates, Bisphenol A and/or monitored for hormone activity in blood by the Calux assay, and Portugal (EPITeen, n=2160) for a total of almost 8,500 individuals. In addition, twin registries and cohorts in Europe and Australia will also contribute to these WPs for a total of almost 150,000 individuals with information on BMI and diabetes.

3.2 On-going projects and activities outside Europe

3.2.1 USA

In the US, the National Academy of Sciences hosted a meeting in December 2011 entitled "Emerging Technologies for Measuring Individual Exposomes." A Centers for Disease Control and Prevention overview "Exposome and Exposomics" outlines the three priority areas for researching the occupational exposome as identified by the National Institute for Occupational Safety and Health.[10] The National Institutes of Health (NIH) has made investments in technologies that support exposome-related research, including biosensors, and supports research on gene-environment interactions. In May, 2013, the National Institute of Environmental Health Sciences (NIEHS) awarded a Core Center Grant to Emory University that is focused on the exposome.

NIOSH's- USA focus in the exposome lies in its efforts to improve our understanding of occupational exposures and resulting work-related diseases. The Institute's ongoing contributions to occupational epidemiology, the development of sensitive analytical methods, characterization and validation of biomarkers, improving sampling strategies and development of exposure databases will advance the field of occupational exposomics. As occupational exposures and their relationship to diseases are elucidated, these contributions will lead to improved occupational health. The exposome provides an opportunity to understand occupational diseases and how to prevent them.

In 2012, NIEHS (National Institute of Environmental Health Studies) implemented a new Strategic Plan, which includes a major goal to promote exposome research and create a blueprint for incorporating exposure science into human health studies. The Institute is working to transform exposure science by improving the characterization of environmental exposures, defining and disseminating the concept of the exposome, and creating the necessary tools, technologies, and research capacity. In 2013, **NIEHS funded the HERCULES Center at Emory University, which is conducting exposome-focused research** and also developing new tools and technology for assessing the exposome. As a leader in environmental health sciences, NIEHS has been at the forefront of the exposome efforts and is continually committed to engaging the scientific community in the endeavor to clearly define the exposome and creating research opportunities to explore it.

In 2015, NIEHS is soliciting the Children's Health Exposure Analysis Resource (CHEAR), a major new infrastructure to provide access to laboratory analyses of biological samples from NIH-funded studies on children's health and a suite of associated data science tools, including an exposure data repository. There is also a companion program being led by the National Institute for Biomedical Imaging and Bioengineering to establish capabilities for characterizing the external environment in pediatric studies. Together, these two programs will enable the most comprehensive analyses of the exposome for studies of children's health to date.

3.2.2 Canada

The Canadian Epigenetics, Environment and Health Research Consortium (CEEHRC) supports leading edge research on the role of DNA and environment interactions in human health and disease. This initiative will ensure that Canada plays a leadership role in the field of epigenetics by putting research discoveries into practice.
CEEHRC is in partnership with most of CIHR's Institutes and is co-led by the following Institutes:

- Neurosciences, Mental Health and Addiction
- Genetics
- Cancer Research

External partners include Genome BC, Genome Quebec, Genome Canada, and Fonds de recherche Santé (FRQS), among others. CEEHRC is currently identifying and developing collaborations with funding organizations and stakeholders to enhance health research in this area. http://www.cihr-irsc.gc.ca

3.2.3 South Korea

In Korea the Ministry of the environment has programme on Human health and chemicals addressing in particular he following classes: Asbestos, Chemical Terrorism and Accidents, Dioxin, Endocrine Disruptors, Hazardous Chemicals Control, Health Impact Assessment System, Nano Materials, POPs (Persistent Organic Pollutants), Polychlorinated biphenyls (PCBs), Response to REACH, Restricted or Prohibited Chemicals Designation System, Risk Assessment, Toxics Release Inventory(TRI).

3.2.4 Japan

The Japan Environment and Children's Study (JECS), a birth cohort study involving 100,000 parent-child pairs, was launched in 2011 in order to evaluate the impact of various environmental factors on children's health and development. The concept plan of JECS was published in March 2010 after three years of development within expert groups and public discussions about the research hypotheses and aims. Pilot studies started in 2008 in four universities, and samples from two preceding cohorts (Hokkaido and Tohoku) are also used for establishing exposure measurement protocols. The recruitment of hundred thousand pregnant women was achieved in March 2014. Health outcomes and exposure measurements will continue until the participating children become 13 years old. http://www.env.go.jp/en/chemi/hs/jecs/

3.2.5 China

China Environment and Health Initiative: Generating new research on the connection between health, environment, and development in China. China's rapid industrialization and urbanization have given rise to a range of environmentally-related threats to human health. While the health effects are becoming clear, the drivers of these problems, and the challenges they raise for governance have yet to be adequately explored. The SSRC's China, Environment and Health Initiative seeks to foster collaboration among researchers from the social, medical and environmental sciences, and to promote the generation and dissemination of new, social science-based research on environment and health. CEHI works in close collaboration with Chinese partner institutions through the Forum On Health Environment and Development (FORHEAD). http://www.ssrc.org/programs/china-environment-and-health/

3.3 On-going national projects

There are numerous national environment and health studies within countries participating in HEALS and outside. These projects are already integrated in the programme of the HEALS respective work packages.

The following national HBM programmes are to be mentioned and collaboration to be established:

Country	**National HBM programe**
Belgium	FLEHS 2, reference HBM, 2007-2011
Czech republic	HBM, launched in 1994
Finland	occupationally exposed, latest 2011
Italy	ABC program: Cross-sectional survey on health, life-style, and exposure biomarkers of the population living in the area of Civitavecchia, 2013.2015
	SPOTT. Longitudinal Study, short term effects and epidemiological health survey. 2013-2018
	Neurocognitive functions and interactions between metals and health outcomes, 2014-2016
	PROBE, 2008-2010
	PROBE-Adolescent, 2009
Slovenia	National HBM 2007-2015
Spain	BIOAMBIENT.ES: cross-sectional human biomonitoring survey in Spain, launched in 2007

4 International Agencies and programmes

4.1.1 WHO

Environmental health addresses all the physical, chemical, and biological factors external to a person, and all the related factors impacting behaviors. It encompasses the assessment and control of those environmental factors that can potentially affect health. It is targeted towards preventing disease and creating health-supportive environments. This definition excludes behavior not related to environment, as well as behavior related to the social and cultural environment, and genetics. In resolution WHA68.8 (2015) the Director General requested, inter alia, to propose to the Sixty ninth World Health Assembly a road map for an enhanced global response to the adverse health effects of air pollution. In response to this request, a draft road map has been developed and presented at the GA meeting in January 2016. who.int/gb/ebwha

4.1.2 EU Agencies and bodies (http://ec.europa.eu/health/)

The section on health in the EU has been created as a trustworthy gateway to a wide range of information and data on health-related issues and activities at both European, national and international level. The content is produced by the European Commission, the Member States of the EU and the European Economic Area (EEA), plus EU candidate countries; by international organisations; and by pan-European non-governmental organisations in the area of public health.

Health and the Environment policy:

Public health is affected by a whole range of environmental factors:

- airborne pollutants – cause or exacerbate respiratory diseases, allergies, poisoning and cancer.
- unsafe environments – can be responsible for accidents, injuries and reluctance to be physically active
- other factors - chemicals, food contamination and allergies, soil pollution, housing quality, planning decisions, noise, water, sanitation, etc.

Health and Climate change

The Commission's 2009 working paper on impact of climate change on human, animal and plant health explains:

- how climate change will affect human, animal and plant health
- what action the EU and its member countries must take in response to these changes
- what tools and financing are already available to tackle the challenges that will arise..

Scientific Committee on Health and Environmental Risks (SCHER). The Committee provides opinions on health and environmental risks related to pollutants in the environmental media and other biological and physical factors or changing physical conditions which may have a negative impact on health and the environment (e.g. in relation to air quality, waters, waste and soils). It also provides opinions on life cycle environmental assessment. It shall also address health and safety issues related to the toxicity and eco-toxicity of biocides.

5 Collaboration with relevant NGOs

HEAL: The Health and Environment Alliance (HEAL) is a leading European not-for-profit organisation addressing how the environment affects health in the European Union (EU). They demonstrate how policy changes can help protect health and enhance people's quality of life. With the support of more than 70 member organisations, HEAL brings independent expertise and evidence from the health community to different decision-making processes. Our broad alliance represents health professionals, not-for-profit health insurers, doctors, nurses, cancer and asthma groups, citizens, women's groups, youth groups, environmental NGOs, scientists and public health institutes Members include international and Europe-wide organisations as well as national and local groups in 25 countries both within EU member states and the wider European region, as defined by the World Health Organisation (WHO). http://www.env-health.org

EPHA is a change agent – Europe's leading NGO advocating for better health. It is a dynamic member-led organisation, made up of public health NGOs, patient groups, health professionals, and disease groups working together to improve health and strengthen the voice of public health in Europe. EPHA is a member of, among others, the Social Platform, the Health and Environment Alliance (HEAL), and the EU Civil Society Contact Group. Its mission is to bring together the public health community to provide thought leadership and facilitate change; to build public health capacity to deliver equitable solutions to European public health challenges, to improve health and reduce health inequalities**.** Its vision is of a Europe with universal good health and well-being, where all have access to a sustainable and high quality health system: A Europe whose policies and practices contribute to health, both within and beyond its borders. http://www.epha.org

The European Environmental Bureau (EEB), set up in 1974, is Europe's largest coalition of grassroots environmental organizations**.** What makes us stand out is our expert insight on a vast amount of environmental issues; ranging from biodiversity, to waste, nanotechnology, chemicals, ecolabel, and climate change and many others. It meets the members regularly in working groups which focus on important environmental issues, and we then work to promote their demands at European and global level**.** Their policy officers are in almost constant dialogue with the European institutions (Commission, Parliament and Council) and relevant departments of the United Nations (UNDESA, UNEP) and OECD and strive to improve or protect environment laws in Europe and beyond. http://www.eeb.org

GLOBAL 2000 is an independent Austrian environmental organization. GLOBAL 2000 is a member of Friends of the Earth, the largest international network of environmental organizations. Since 1982, GLOBAL 2000 has been working on controversial social themes to uncover potential hazards for humans and the environment. GLOBAL 2000 closely monitors the development of environmental policy in Austria and is committed to ecological fairness and a future worth living both locally and around the globe. Helping victims of ecological disasters is part of our work. GLOBAL 2000 is a member of Friends of the Earth, the largest international network of environmental organizations. To reach our goals, we cooperate with other environmental organizations, citizens' initiatives, independent action groups and selected corporate entities. https://www.global2000.at

ChemSec, the International Chemical Secretariat, is a non-profit organisation founded in 2002 by four environmental organisations. Thier vision is a world free of hazardous chemicals. To achieve this, we strive to reach broad acceptance in society of the key principles of Precaution, Substitution, Polluter Pays and Right to Know. Their approach involves highlighting the health and environmental risks of hazardous substances and the urgent need to phase them out. Making accurate, science-based information available and acting as a catalyst for open dialogue between business, authorities and NGOs. Developing concrete tools for effective action and monitoring the progress of legislative processes. All our work aims to stimulate public debate and action on the necessary steps towards a world free of hazardous chemicals. http://chemsec.org

6 Conferences, symposia, workshops

Development of a web-based overview of existing 'exposome relevant' networks/programs in EU and globally. In this context, we shall be proactive in setting up exposome- speficic symposia and scientific sessions in international conference series including the ones listed below.

ISES: **The International Society of Exposure Science (ISES)** is committed to creating a safer and healthier world by advancing exposure science and promoting the use of exposure science in the fields of public, occupational, and environmental health. The ISES understands that there is a need for relevant exposure information and the tools to develop exposure information in a timely fashion. Exposure scientists -- a community known for its interdisciplinary, creative, and pragmatic approach to problem solving -- are leaders in improving and expanding exposure information.

Events in 2016:

- ISES 2016: 26th ISES Annual Meeting, Interdisciplinary Approaches to Health and the Environment, Utrecht, The Netherland, October 9-13, 2016; (2) ISEE-ISES AC2016
- Conference of International Society for Environmental Epidemiology and International Society of Exposure Science – Asia Chapter 2016 , Sapporo, Japan, June 26-29, 2016;
- 2nd International Conference on Human Biomonitoring 2016, Science and policy for a healthy future Langenbeck-Virchow-Haus , Berlin, Germany, April 17-19, 2016

ISEE: The International Society for Environmental Epidemiology (ISEE) provides a forum for the discussion of problems unique to the study of health and the environment. With membership open to environmental epidemiologists and other scientists worldwide, ISEE provides a variety of forums for discussions, critical reviews, collaborations and education on issues of environmental exposures and their human health effects. Annual conference 2016, ISEE 2016 Rome, Italy, September 1-4, 2016.

SETAC Europe is a geographic unit (GU) of the Society of Environmental Toxicology and Chemistry (SETAC), established to promote and undertake activities of SETAC in Europe, and to support activities of SETAC in the Middle East and in Africa, SETAC's newest GU. SETAC Europe (SE) adheres to the mission and goals of the global Society of Environmental Toxicology and Chemistry and is dedicated to support the development of principles and practices for protection, enhancement and management of sustainable environmental quality and ecosystem integrity. The Annual meeting in 1016 will be organized in Nantes, 22-26 May 2016.

SOT Society of toxicology. The SOT Annual Meetings are the largest meeting of its kind. This annual event features a broad range of scientific sessions and a thematic program that provides participants with a unique opportunity to deepen their knowledge in topical areas and interact with leaders in their respective disciplines. Annual meeting in 2016 will be organized in March in New Orleans, Louisiana, USA.

EUROTOX **EUROTOX** aims to foster toxicology, both scientifically and educationally, in all countries of Europe. To this, EUROTOX organises an *annual scientific congress, workshops, and postgraduate training courses*. the 52nd Congress of the European Societies of Toxicology to be held in Istanbul **from the 4th to the 7th of September, 2016. In Istanbul.**

EEMS The European Environmental Mutagensis Society is a scientific society that encourages the study of mutagens and substances of related biological activity in the human environment, particularly as these mutagens may be of concern to public health, and to engage in and sponsor research, study and dissemination of information relating to the foregoing." The EEMS is a scientific society that encourages the study of mutagens and substances of related biological activity in the human environment, particularly as these mutagens may be of concern to public health, and to engage in and sponsor research, study and dissemination of information relating to the foregoing."

ICHMET The International Conference on Heavy Metals in the Environment (ICHMET) is a unique event in the calendar of the environmental science congress. It focuses neither on a specific metal, nor on a specific environmental medium, but instead aims to provide a unique platform for discussion and presentation of state-of-the-art research activities to a broad international scientific community. In 2016 the conference will take place in Gent, Belgium, 12 – 15 September