



"Cross-Mediterranean Environment and Health Network (CROME)"

LIFE12 ENV/GR/001040



Report

Cross-Mediterranean Environment and Health Network

CROME-LIFE

Deliverable D.1.

Report on the Closing Conference in Athens

**LIFE ENVIRONMENT PROGRAMME
LIFE12 ENV/GR/001040**

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Report

Table of Content

Programme	4
Minutes of the CROME-LIFE Closing Conference, Athens (Greece), December 20 th , 2016.....	6
Round table	10
Pictures.....	11



Report

CROME-LIFE+ "Cross-mediterranean network for environment and health"

Closing Conference

20 December 2016, Synedriako 1 room of the Megaron - The Athens Concert Hall,
Vass. Sophias & Kokkali, PO 11521, Athens, Greece

Programme

08:30 **Registration**

09:00 **Welcome address**

Chair: Assoc. Prof. Dimosthenis Sarigiannis, Project Coordinator, Director of the Environmental Engineering Laboratory (EnvE-Lab), Aristotle University of Thessaloniki (AUTH), GREECE

Session 1 Environment and health risk: a multi-dimensional perspective

09:15 **The CROME method**

Assoc. Prof. Dimosthenis Sarigiannis, EnvE-Lab AUTH, GREECE

10:00 **Applying epidemiological methodology in prioritizing environmental interventions**

Prof. A. Linos, Director, Public Health and Hygiene Laboratory, Medical School, University of Athens, GREECE

10:30 **Endocrine Disrupters at a crossroad: a challenge for a new roadmap**

Prof. Polyxeni Nicolopoulou-Stamati, Medical School, National and Kapodistrian University of Athens, Greece

11:00 **Air pollution, heat and health in cities**

Prof. K. Katsouyanni, Medical School, University of Athens, Greece

11:30 **Coffee break**

Session 2 CROME-LIFE legacy: Synthesis of the main results obtained for the management of environmental burden and its consequences to health

12:00 **Routes of incorporation of metals and organohalogen pollutants into humans**

Prof. Joan O. Grimalt, Institute of Environmental Assessment and Water Research (IDAEA-CSIC) Barcelona, Catalonia, SPAIN

12:30 **The Northern Adriatic Cohort II in the Friuli Venezia Giulia Region: Prenatal and Childhood Exposure to Metals and Neuropsychological Maturation at 7 years**



Report

Dr. Gemma Calamandrei, Department of Cell Biology and Neuroscience, Istituto Superiore di Sanità (ISS), Rome, ITALY

13:00 **Lunch**

14:30 **Low level mercury exposure, neurodevelopment and genetic polymorphisms in birth cohort from Slovenia and Croatia**

Prof. M. Horvat, Jožef Stefan Institute, Department of Environmental Sciences, Ljubljana, SLOVENIA

15:00 **The CROME approach to estimation of cancer risk due to biomass burning in Greece**

Dr. Spyros Karakitsios, EnvE-Lab AUTH, GREECE

15:30 **Coffee break**

Session 3 CROME-LIFE policy impact: Reducing uncertainty in risk assessment of chemicals and contributing to the development of targeted public health protection measures

16:00 **Environmental chemical risk round table – the CROME policy impact**

Chairs: Assoc. Prof. Dimosthenis Sarigiannis, Project Coordinator, EnvE-Lab AUTH, GREECE, Dr. Gemma Calamandrei, Department of Cell Biology and Neuroscience, Istituto Superiore di Sanità (ISS), Rome, ITALY

Intervening:

Vasiliki Caraouli, Director of Public Health, Hellenic Ministry of Health, GREECE
Margarita Karavasili, President Citizens Inspectorate for Sustainable Development, former Special Secretary for environmental inspections, Hellenic Ministry of Environment, Energy and Climate Change, GREECE

17:00 **Concluding remarks**

Assoc. Prof. Dimosthenis Sarigiannis, EnvE-Lab AUTH, GREECE



Report

Minutes of the CROME-LIFE Closing Conference, Athens (Greece), December 20th, 2016

On 20 December, the Environmental Engineering Laboratory (EnvE-Lab) of the Aristotle University of Thessaloniki hosted the CROME-LIFE Closing Conference at the Athens Music Hall, Greece. The event garnered nearly 40 participants from the scientific, academic and policy community. At the event, international experts presented insights and novel tools for improved environmental health impact assessment and governance, making use of human biomonitoring data. Experts also outlined preventive strategies and policy measures to minimize the environmental burden of disease and protect public health.

The conference was chaired by Assoc. Prof. Dimosthenis **Sarigiannis**, EnvE-Lab director. In particular, Assoc. Prof. Sarigiannis welcomed the participants, introduced the project consortium and kicked started the first session of the conference on "Environment and health risk: a multi-dimensional perspective". Prof. Sarigiannis explained the exposome and stressed that it is very important to keep an unbiased agnostic stance to coupling chemical exposure to health status. He also referred to the CROME Environment & Health paradigm that proposes targeted innovation steps, including: a) the operational use and demonstration of the validity of biology-based modeling tools that allow to mechanistically link environmental exposure to biomonitoring and epidemiological data; b) the operational use of an integrated approach to biomonitoring that combines the use of state-of-the-art biomarkers with reverse dosimetry and environmental data to reconstruct the effective dose human population is exposed to. The results will allow moving towards an improved environmental health risk assessment in the EU and the world; and c) the development of new and validation of existing biomarkers for environmental health risk assessment and environmental human biomonitoring.

With regard to environmental modelling, a multiscale approach is followed, accounting for the interactions across various media (air, water, sediment, soil) at different environmental scales (continental, regional and local), including major environmental processes (emissions, advection, diffusion, degradation), resulting in food web contamination.

Considering the large amount of biomonitoring data available in the scientific literature, and current discussions at WHO level to promote harmonized international and national human biological monitoring programs, it is important to take stock of these data for exposure characterization.

Thus, NOVA will contribute to the development of a framework for exposure reconstruction based on human biomonitoring data. In this context, the PBBK model will be used to identify the exposure parameters that fit best the biomonitoring data, through an iterative Bayesian optimization process.

Starting from a prior estimate of exposure that can be derived from auxiliary environmental and time-activity or dietary data, Monte Carlo sampling takes place to provide exposure information used as input to the PBBK model. The model is ran and gives estimates of the biomarker values measured in biomonitoring campaigns. Comparison of the estimated vs. the measured biomarker values will reveal the error due to the prior exposure profile used. Then, a genetic optimization algorithm is used to minimize the residual error in an iterative process. These iterations are



Report

repeated, until convergence (error minimization) is achieved among the predicted and the observed biomonitoring data.

The result is the actual exposure distribution that explains best the biomonitoring values. This methodology, is expected to derive very good results for the PBT compounds. These compounds are eliminated very slowly from human body and intra-day variability of the biomonitored values is very low. As a result, the available samples from biomonitoring campaigns will be very informative for the overall body burden and the actual target tissue distribution.

Prof. Sarigiannis went on to explain the association of biomonitoring data with health effects, saying that the project used a statistical approach based on survey-weighted logistic multivariate regression adjusted for different covariates (age, sex, socio-economic status (SES) etc.), linking internal doses with health effects and considering the interdependence of the covariates (using as metric an analogy of the "linkage disequilibrium" metric used in genome-wide association studies).

He also presented the CROME-LIFE Cross-Mediterranean study (or Common case study), a follow up study of pre-existing Children Mediterranean cohorts based on **PHIME**, involving Slovenia, Croatia, Italy, Greece, and **INMA** (Environment and Childhood), Spain. This study aims to find those gene polymorphisms that could modulate the effects of metals, particularly Hg, at low exposure in the Mediterranean cohort

Further on, he presented three additional case studies in the area of Greece and in particular the study in Asopos river, the case of the plastic recycling plant fire in Aspropyrgos and the case of biomass burning in large cities.

Finally, he presented the CROME methodology, which takes stock of biomonitoring data in the health impact assessment process, accounts for the internal dosimetry in the target tissues, setting the biological basis for understanding the interaction between environmental exposure and disease, and demonstrates in real-life environmental-health problems, what the targeted interventions should be for improving public health and protecting vulnerable groups.

Last but not least, he referred to the project outcomes and the selected routes for dissemination of the project best practices and knowledge transfer to the key stakeholders.

Prof. **A. Linos**, Director, Public Health and Hygiene Laboratory, Medical School, University of Athens, unfortunately did not attend the meeting.

The conference continued with the presentation of Dr. **P. Nicolopoulou-Stamati**, Scientific Director of MSc "Environment and Health. Capacity building for Decision Making" at the Medical School of National and Kapodistrian University of Athens, entitled: "Endocrine Disruptors on a cross road: A challenge for a new roadmap". Dr. P. Nicolopoulou-Stamati referred to the underlining mechanism between exposure and effects on human health and went to talk about endocrine disrupting chemicals (EDCs), the mechanism of action at a cellular level and the molecular pathway analysis. She mentioned that in our everyday lives, everybody is exposed to chemicals that exists in different sources, be it food, air, cosmetics etc. The effects of EDCs are thought to depend on both the level and timing of exposure. EDCs are suspected of being capable of acting even at very low doses, parts per trillion. Exposures are thought to have both immediate and more latent consequences, such as a heightened susceptibility to certain diseases and dysfunctions later in life. The most sensitive window of exposure to EDCs appears to be during critical periods of development (fetal development, puberty). She continued by saying that there is growing concern



Report

in the EU and worldwide about negative human health and environmental impacts possibly caused by endocrine disruptors. The EU has introduced specific legislative obligations aimed at phasing out endocrine disruptors in water, industrial chemicals, plant protection products and biocides. In REACH, endocrine disrupting chemicals are considered of similar regulatory concern as substances of very high concern. Despite the EU burden on health and money spent on science and the limited knowledge of the effects, there is still uncertainty. A wide range of chemicals commonly used for a number of everyday products – such as electronics, plastics, pesticides, cosmetics, toys, food containers, antibacterials, etc. – are suspected of having the potential to be endocrine-disrupting under certain circumstances. Some EDCs have been banned in fairly recent times but are still present in relatively large quantities in the environment. Others are naturally occurring substances and may enter the food chain.

Dr. P. Nicolopoulou-Stamati mentioned that within the EU, some Member States support a hazard-based approach and others a risk-based approach. Currently, the European Commission is working on a proposal for science-based criteria for endocrine disruptors, as required in the Plant Protection Products Regulation and the Biocidal Products Regulation. Dr. P. Nicolopoulou-Stamati also referred to the role of the NGO's and the industry in protecting humans and the environment from the harmful affects of EDCs and defining scientific criteria for better regulation.

At the event, **Klea Katsouyanni**, Professor at the Department of Hygiene, Epidemiology and Medical Statistics of the National and Kapodistrian University of Athens and King's College London, presented "Air pollution, heat and health in cities". Prof. Katsouyanni introduced the "pyramid of effects" from air pollution as well as comparative data from short-term and long-term effects from air pollution in cities on human health. The long-term effects, however, are more important in terms of health burden and more related to a biomonitoring programme. According to WHO, in 382 cities with PM10 measurements, 34 had annual means > 40 µg/m³. Five of these cities are located in Greece, while the rest are in Bulgaria, Cyprus, Israel, Italy, Spain, Bosnia, Poland, Romania, Serbia, and Turkey. Evidence is also accumulating on the effects of PM exposure on children's cognition and neurodevelopment. There are several known carcinogens incorporated in ambient particles but it is worth mentioning that, in 2012, IARC characterized diesel particles as carcinogenic.

Prof. Katsouyanni went onto talk about meteorology and climate, as human health factors. Mortality in all geographical areas displays seasonality with maxima during the winter and also acute short-term maxima during heat waves in the summer period. Morbidity displays similar or opposite seasonality depending on the cause. In conclusion, she mentioned that there is evidence that air pollution and meteorology are associated with short-term effects on health. However long-term effects of air pollution are more important in terms of total burden on disease. Long-term effects are those usually investigated within the framework of a biomonitoring programme. The association between short-term exposures and long-term effects is not well understood.

The second session of the conference was dedicated to the CROME-LIFE legacy: "Synthesis of the main results obtained for the management of environmental burden and its consequences to health". At this session, the project team showcased the project final findings regarding the impact of exposure to environmental chemicals on health across the Mediterranean basin.



Report

In particular, Prof. Joan O. **Grimalt**, Institute of Environmental Assessment and Water Research (IDAEA-CSIC) Barcelona, Catalonia, presented "Ascertainment of ways of incorporation of metals and organochlorine compounds into humans". He introduced the Spain case study, which focused on detection of mercury in hair of the infant population of Minorca and València. Studies showed that fish and seafood was the main source of incorporation of mercury, but after detailed analysis it was found that other Mediterranean fish species are also a source of mercury (above EU recommendations) relevant for the cohorts of Minorca and València. The role of fish and local food as a source and way of exposure to mercury has drawn the attention of the local stakeholders. J. Grimalt, also presented the analyses of the organochlorine compounds in the air, a study conducted in the area of Flix, Spain.

Next, Dr. Gemma **Calamandrei**, Department of Cell Biology and Neuroscience, Istituto Superiore di Sanità (ISS), Rome, presented "The NAC-II birth cohort in Friuli Venezia Giulia Region: prenatal and childhood exposure to metals and neuropsychological maturation at 7 years". In specific, she presented the CROME-LIFE Cross-Mediterranean study, which is a follow up study of pre-existing Children Mediterranean cohorts of the PHIME and INMA projects. The aim of the study is to assess the long-term effects of metals' exposure on neuropsychological functions at 6-7 years considering the modulatory role of life style factors, as well as to find those gene polymorphisms that could modulate the effects of metals, particularly Hg, at low exposure in the Mediterranean cohort. She also referred to the metals and metalloids with known neurotoxic activity. These are: mercury, lead, manganese, arsenic, cadmium, copper, zinc and selenium. The neurodevelopmental disorders that these elements may cause are disabilities in brain functioning that affect a child's behaviour, social competencies, memory, or ability to learn. They include a range of clinical and sub-clinical conditions: mental retardation, learning disabilities, ADHD, autism spectrum disorders (ASDs), speech and language disorders, dyscalculia, dyslexia and others. Neurodevelopmental disorders are also caused by environmental factors such as environmental chemicals, drugs in pregnancy, obstetric complications and maternal infection, as well as gene factors, SNPs, epigenetics, copy number variants etc. Variations in genes involved in synapse development predispose to vulnerability to environmental stressors increasing the risk of developmental delay in several behavioural domains. Dr Calamandrei concluded with the strengths of the CROME common study and its usefulness for future application.

Prof. M. **Horvat**, Jožef Stefan Institute, Department of Environmental Sciences, Ljubljana, presented "Low level mercury exposure, neurodevelopment and genetic polymorphisms in birth cohort from Slovenia and Croatia". Prof. M. Horvat mentioned that it is generally accepted that the formation and bioaccumulation of MeHg is the most critical point of environmental quality in mercury pollution. The reduction of MeHg in food can therefore be defined as the priority objective with regard to the mercury contamination problem. She then went on to introduce the Mediterranean study, a Longitudinal cohort study of prenatal exposure to mercury (Hg) in the Mediterranean region. Overall, the study aimed to assess association between exposure to low-to-moderate levels of Hg and neurodevelopment of prenatally exposed children, while in particular to investigate gene polymorphisms that could modulate the association between Hg and neurodevelopment. Epidemiological studies have demonstrated that the developmental



Report

neurotoxicity is associated with prenatal methyl mercury (MeHg) exposure (Grandjean and Landrigan 2006), while Susceptibility to mercury may be modified by genetic factors.

Finally, Dr. Spyros **Karakitsios**, EnvE-Lab AUTH, presented "The CROME approach to estimation of cancer risk due to biomass burning in Greece". An extensive campaign was carried out from January to April 2013 at two locations in the urban area of Thessaloniki to determine the chemical composition of urban aerosols and to correlate their toxicity with biomass combustion as a way of residential heating. PM₁, PM_{2.5} and PM₁₀ particles were collected in Teflon filters using low flow air samplers in two air pollution monitoring stations, representative of urban/residential and traffic influenced pollution respectively. The results showed that PM (PM₁, PM_{2.5}, PM₁₀) and PAHs concentrations, during the cold period, were higher in the urban background monitoring station than in the traffic station. This pattern was attributed to biomass combustion, which can be considered as the primary source of PAHs in the populated areas of Thessaloniki during winters time.

Round table

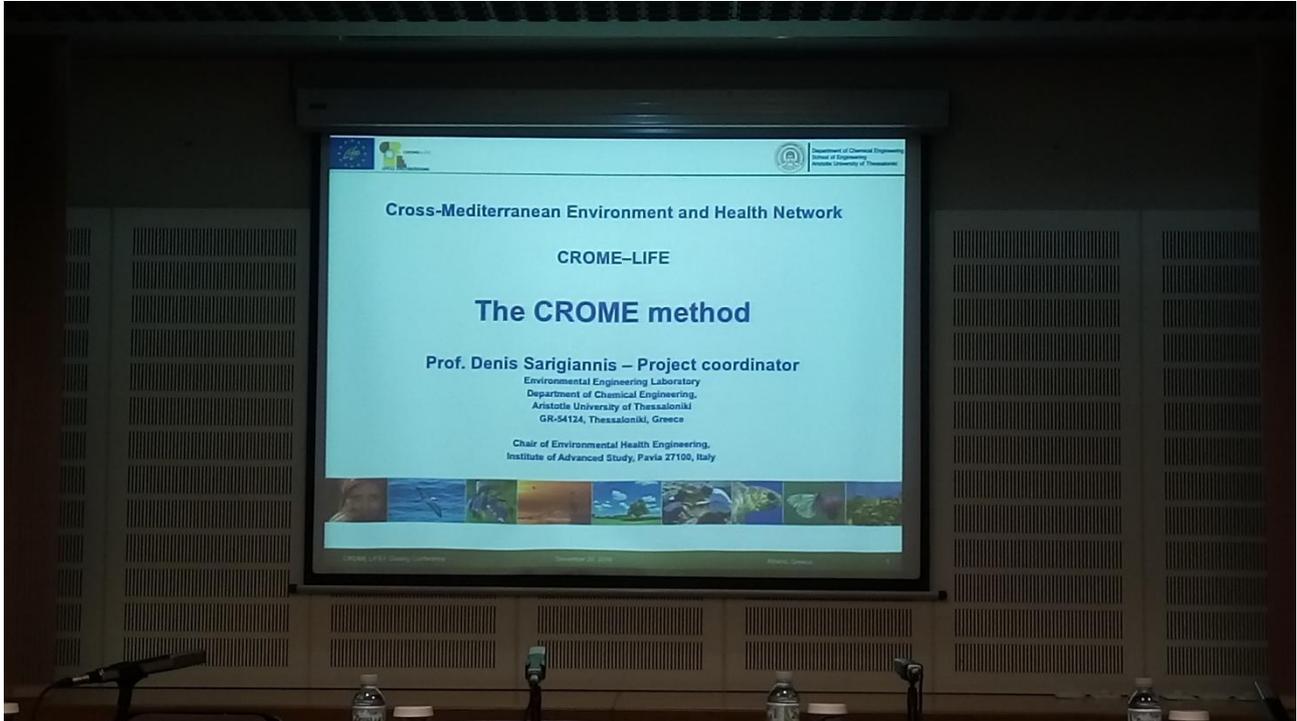
Session 3 was on CROME-LIFE policy impact: "Reducing uncertainty in risk assessment of chemicals and contributing to the development of targeted public health protection measures" and included a round table on environmental chemical risk. The session was chaired by Assoc. Prof. Dimosthenis Sarigiannis, with the contribution of Dr. Gemma Calamandrei, Dr. Alessandro Alimonti and Ms. Vasiliki Caraouli, Director of Public Health, Hellenic Ministry of Health, Greece. The discussion focused on the need for the development of targeted measures for the protection of public health and reduction of uncertainty in risk assessment of chemicals.

All conference presentations can be downloaded from the CROME-LIFE website at: <http://www.crome-life.eu/index.php/crome-closing-event-presentations/>



Report

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Report





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Report

