Cross-Mediterranean Environment and Health Network

CROME-LIFE

ANNEX 20

Deliverable D.1.7

Report on the third Interregional Workshop in Barcelona

LIFE ENVIRONMENT PROGRAMME

LIFE12 ENV/GR/001040

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Action: D.1

Report Date: 30/09/2016

http://www.crome-life.eu

Bibliographical Information

Project: Cross-Mediterranean Environment and Health Network – CROME-LIFE

Subject: Report on the second Interregional Workshop in Barcelona

LIFE ENVIRONMENT PROGRAMME
Contract No. **LIFE12 ENV/GR/001040**
Duration of Contract: 01/07/2013 - 31/12/2016
ACTION: D.1- Communication and dissemination
Editing Partner: CSIC
Other Partners: AUTH, ISS, JSI
Report Date:30/09/2016

Pages: 18 (including figures, tables, attachments)

Key Words: stakeholders engagement, networking, communication and dissemination

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Table of Content

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

Interregional Workshop, 14-16/11/2016

Parc de Recerca Biomèdica de Barcelona – PRBB. Doctor Aiguader, 88 (at ISGLOBAL), Barcelona

Workshop Agenda

Wednesday 14th of September 2016

9:00-9:20 Opening Session. Welcome and announcements
Joan Grimalt (chair organising committee and CROME organizer)
Peter van den Hazel (chair board INCHES)
Mark Nieuwenhuijsen (ISGLOBAL)

09.20-10.45 Session 1 (Auditorium) Environmental Determinants of Child Health
Chair: Stephan Böse-O'Reilly (Germany) and Mark Nieuwenhuijsen (Spain)

- Brainy approaches to children's environmental health – Philippe Grandjean (Denmark)
- Environmental Pollution and Children's Health – Phil Landrigan (USA)
- Pollution: the biggest killer on the planet. A summary of the upcoming Lancet report - Rich Fuller (USA)
- Environmental Health Issues for Spain – Joan Grimalt

10.45- 11.10 Opening Ceremony (Auditorium)
Peter van den Hazel – INCHES President
Joan Grimalt, chair Organising Committee and CROME organizer
Opening speech: Gemma Tarafa, Commissioner of Health, City Hall of Barcelona

11.10 -11.30 Break

11.30-13.00 Session 2 (Auditorium) Epidemiological longitudinal studies of child health and environment – birth cohorts- child cohorts
Chair: Ruth Etzel (USA)

- Ambient air pollution and onset of asthma in birth cohorts. The rise and fall of evidence - Achim Heinrich (Germany)
- Current findings on maternal gut microbiome and PCBs concentration in birth cohort study with omics analysis: Chiba Study of Mother and Children's Health (CMACH) - Chisato Mori (Japan)
- Preventing Exposure to Environmental Hazards -- Role of Primordial Prevention -Ruth Etzel (USA)
- Association between breastfeeding duration and cognitive development, autistic traits and ADHD symptoms: a multicenter study in Spain - Jordi Julvez (Spain)

- Maternal exposure to particulate matter and birth weight in Dutch children - Margot van de Bor (Netherlands)
- Birth Cohort Consortium of Asia (BiCCA) on Children's Environmental Health – Pau-Chung Chen (Taiwan)

11.30-13.00. Session 3 (Darwin) Child labour and other topics
Chair: Stephan Böse- O'Reilly (Germany) and Rich Fuller (USA)

- Poor education, poor job, poor health. Hanns Moshammer (Austria)
- Occupational injuries among child labourers: results from a cross-sectional study in Peru - Tobias Weinmann (Germany)
- TiPP TAPP - first steps into life – Claudia Gerken (Germany)
- Dietary Environment in Preventing Allergic Airway Diseases - H Paramesh (India)
- Childless , Workless, Worthless - Jürgen Bilger (Germany)

13.00-14.00 Lunch

13.15-14.00 Seminar/discussion session on Communicating Radiation Risks in Paediatric Imaging (Room Darwin) organised and presenterd by Maria Perez (WHO) and Donald Frush (USA)

14.00-15.30. Keynote speech: Dr. Maria Neira (WHO, Switzerland) –CEH and opportunities for action under SDG era
Session 4 (Auditorium) Developing countries and CEH: examples of action on emerging issues by WHO and partners
Chair: Marie Noel Brune Drisse (WHO, Switzerland) and Dr. Maria Neira (WHO, Switzerland)

- WHO's work on early life exposures and future health –prevention for future generation – Emiko Todaka (WHO)
- Radiation imaging communication in paediatric: situation in developing countries and focus on action - Donald Frush (USA)
- E-waste and child health WHO global initiative -Marie-Noel Bruné (WHO, Switzerland)
- Air pollution and CEH action in Brazil - Emerson da Silva (Brazil)

15.30- 15.45 Break

15.45 -16.30 Poster pitch session A (Auditorium)
Chairs: Peter van den Hazel (Netherlands) and Merce Gari (Spain)

- Prenatal exposure to environmental chemicals: associations with neurotransmitter levels in cord blood - Margot van de Bor
- Cognitive effects after low - to moderate dose exposure: study plan in a cohort of childhood cancer survivors - Elisa Pasqual
- Children exposure to phthalates and bisphenol A in LIFE PERSUADED project: preliminary results on biomonitoring and case-control studies - Cinzia La Rocca
- Mercury concentrations in commercial seafood from the western Mediterranean Sea – Rosa Maria Llull Cantallops
- A review on managing and treating mercury emissions in small artisanal gold mining – Tara Rava Zolnikov

- Acotinine, cadmium and pahs levels in children's urine as a result of environmental tobacco smoke exposure in two spanish locations - Helena García
- Autistic Symptoms Associated with Childhood Lead Poisoning - Wan Nedra Komaruddin
- Organohalogenated pollutants in Argentinean postpartum women living in Salta and Ushuaia - Natalia Bravo
- Considerations for policies design aimed to promote drinking water consumption in Mexican children and adolescents: Santa Fe, CDMX – Arely Vergara-Castañeda
- Prenatal early exposure to the environmental endocrine disruptors - Joaquim Rovira

15.45 -16.30 Poster pitch session B (Darwin)

Chairs: Stephan Böse-O'Reilly (Germany) and Barend van Drooge (Spain)

- School children exposure to particulate matter (coarse, fine, and quasi-ultrafine) around petrochemical complex. Respiratory tract dosimetry - Joaquim Rovira
- Noise prevention in kindergarten - Takacs Katharina Effect of diet on allergies among preschool children - Sandra Andrusaityte
- Smoking cessation consultation in pediatrics – Miguel Felipe Sánchez Sauco
- Pilot phase of TNG STUDY - Pavel Piler
- Health and safety predictors of parental attitudes towards children's school travel - Jacques Bergeron
- School environmental health: the first steps towards environmental health - Miguel Felipe Sánchez Sauco
- When parents NGOs, environmental NGOs and experts join forces to impulse actions to protect children's environmental health - Catherine Bouland
- Hazards and Risks in the Glyphosate Debate – Karl Ernst v. Mühlendahl

16.30 -18.00 Session 5 (Auditorium) Toxic Metals Intoxication

Chair: Wojciech Hanke (Poland) and Mahmood Khwaja (Pakistan)

- High Risk for Neural Tube Defects from Arsenic in Drinking Water and Rice in Asia - Yona Amitai (Israel)
- Lead intoxicated children in Kabwe/ Zambia – Stephan Böse- O'Reilly (Germany)
- Children and ASGM in West Sumbawa Regency, Indonesia - Baiq Dewi Krisnayanti (Indonesia)
- Low level arsenic exposure during pregnancy in the 3xG cohort in Flanders: less efficient detoxification is associated with higher oxidative stress – Nathalie Lambrechts (Belgium)
- Prenatal mercury exposure and fetal development and birth outcomes: results from INMA cohort – Ferran Ballester (Spain)
- Lead in soil; how can we reduce exposure to young children – Martin Eggens (Netherlands)
- Blood lead concentrations from children practicing airgun shooting - Rudolf Schierl (Germany)

16.30 -18.00 Session 6 (Darwin) Burden of disease

Chair: Peter van den Hazel (Netherlands) and Kinga Polanska (Poland)

- What is Environmental Burden of Disease? An animated video gives an answer – MyriamTobollik (Germany)
- Children's environmental burden of disease: Review of key findings - Nadine Steckling (Germany)

- Quantifying the burden of disease due to environmental risk factors in children and adolescents in Germany: the UKAGEP project - Myriam Tobollik (Germany)
- The burden of infectious diseases on congenital malformations: the case of Zika virus and microcephalia in Brazil – Roberto Ronchetti (Italy)

Tuesday 15th of September 2016

8.45 – 10.00 Session 7 (Auditorium) Pollutants at schools and homes
Chair: Achim Heinrich (Germany) and Rudolf Schierl (Germany)

- Indoor air and children's health, SINPHONIE and SEARCH projects – Eva Csobod (Hungary)
- Engaging schoolchildren in understanding the indoor environment using citizen science - Núria Castell (Norway)
- Polycyclic aromatic hydrocarbons from traffic exhausts in primary schools and cognitive development of children – Barend van Drooge (Spain)
- Multi residue and non-target screening for characterization of organic chemicals in indoor dust – Garry Codling (Czech republic)
- Assessment of Indoor Air Quality in Air - Conditioned and Naturally ventilated Schools in Delhi - Pratima Singh (India)

8.45 – 10.00 Session 8 (Darwin) Biomonitoring and Spatial Analysis
Chair: Hanns Moshammer (Austria) and Merce Gari (Spain)

- Early-life exposure to multiple environmental contaminants and birth weight: pooled analysis in four Flemish birth cohorts - Eva Govarts (Belgium)
- Spatial Pattern Analysis of Hepatitis A Cases in Children by using Geostatistical Analysis of GIS in Turkey - Ahmet Ozgur Dogru (Turkey)
- Prenatal exposure assessment approaches need to consider spatio-temporal variation of air pollution - Andrea Ranzi (Italy)
- Spatial clustering of childhood leukemia in the Region of Murcia, Spain (1998-2010) – Alberto Cárceles Álvarez (Spain)

10.00 -10.30 Poster pitch session C (Auditorium)
Chair: Ruth Etzel (USA) and Yona Amitai (Israel)

- Mobile phone and other digital technology use in UK adolescents: The SCAMP Cohort – Pippa Douglas
- Quality of life of childhood brain tumor survivors: intervention, analysis and results – Alberto Cárceles Álvarez
- Transgenerational effects of treatment with antiepileptics in pregnancy: behavioural and molecular markers in a mouse study – Gemma Calamandrei
- Forests for health with the environmental midwife - Lizbeth Álvarez Gómez
- Modifiable factors related to low water intake in Mexican children and adolescents - María de los Angeles Peña Farfán
- Exposure to arsenic and mercury: associated pregnancy outcomes, and early infant developmental outcomes in gold mining areas in Tanzania - Elias Charles Nyanza

10.00 -10.30 Poster pitch session D (Darwin)

Chair: Jamie Pearce (UK) and David Bellinger (USA)

- Occupational noise exposure during pregnancy – new aspects in childs language acquisition – Soile Jungewelter
- Factors influencing breastfeeding initiation – Lizbeth Álvarez Gómez
- Neuropsychological profile of an adopted patient with Fetal Alcohol Spectrum Disorder - Esther Tobarra Sánchez
- Environmental screening on girls with early puberty disorders - Ferran Campillo i López
- Mismatch of classroom furniture and student body dimensions in schools of Delhi – Meghna Sharma
- Where physical environment is the major culprit: Mapping child health determinants against healthrelated policies and programs in an East African pastoralist community - Lioul Berhanu Alemie

10.30- 10.45 Break

10.45 -12.00 Session 9 (Auditorium) Cognitive development of children in relations to environmental exposures

Chair: Yona Amitai (Israel) and Phil Landrigan (USA)

- The impact on chemical pollution into child development from in utero to adolescence – Jordi Sunyer (Spain)
- Maternal lifestyle during pregnancy and child neurodevelopment - Kinga Polanska (Poland)
- Lifelong Exposure to Green Space and Attentional Development: A Prospective Birth Cohort Study - Payam Dadvand (Spain)
- The role of local natural space in children's social, emotional and behavioural development in Scotland: a longitudinal study - Jamie Pearce (United Kingdom)
- Prenatal exposure to outdoor airborne trace elements and cognitive and psychomotor development during childhood in four European birth cohorts - Malgorzata Joanna Lubczynska (Poland)

12.00 -13.15. S ession 10 (Auditorium) Endocrine disruptors and epigenetics

Chair: Emiko Todaka (WHO, Europe) and Chisato Mori (Japan)

- Temporal trends of organochlorine compounds and PBDEs from utero until 4 years of age in the Asturias INMA cohort - Mercè Garí (Spain)
- Early life exposure to organochlorine pesticides and behavioral development in children – Margot van de Bor (Netherlands)
- Endocrine Disrupting Chemicals (EDCs) and children's daily exposure: Physicians, scientists, NGOs and media – working together for a better policy and more protection - Johanna Hausmann (Germany)
- Persistent Organic Pollutants in women's breast milk and proximity to Municipal Waste Incinerators in the UK – Phillipa Douglas (United Kingdom)

12.00 -13.15. Session 11 (Darwin) Environmental Pediatrics for Pediatric residents

Chair: Ruth Etzel (USA) and Donald Frush (USA)

- CEH training in Brazil - Emerson Da Silva (Brazil)
- Strategies for Use of medical Imaging and Radiation Risk: What the Care Provider Should Know - Donald Frush (USA)

- Autism Spectrum Diseases, including Asperger Syndrome. Fairy Tales and Facts about Environment and Genetics - Karl Ernst von Mühlendahl (Germany)
- Environmental consulting nursing : health from the beginning - Miguel Felipe Sanchez Sauco (Spain)
- Empowering Youth and Communities to promote health and environment- The Bangalore Experience - Elizabeth Cherian Paramesh (india)

13.15-14.15 Lunch

14.15-15.30. Session 12 (Auditorium) Asthma and Respiratory Diseases
Chair: Hanns Moshammer (Austria) and Martin Eggens (Netherlands)

- An unexpected epidemic of respiratory distress - Hanns Moshammer (Austria)
- Changing kindergarten practices with localized real-time information on outdoor air: The experience of CITI-SENSE project in Oslo, Norway - Núria Castell (Norway)
- Impact of air pollution to oxidative damage in newborns and mothers – Katerina Honkova for Radim Sram (Czech republic)
- Lung function growth trajectories in children in relation to prenatal exposure to particulate matter - Cracow cohort study - Renata Majewska (Poland)
- Rapid Urbanisation and changing Prevalance of Chronic Cough in children - H. Paramesh (India)

14.15-15.30. Session 13 (Darwin) Environment and childhood cancer
Chair: Juan Antonio Ortega (Spain) and Elisa Pasqual (Spain)

- Environment and childhood cancer survivors: PLASECAP MUR - Alberto Cárceles Álvarez (Spain)
- How can the increase in childhood cancer be explained? The role of transplacental and ctransgenerational carcinogenesis– Ernesto Burgio (Italy)
- Health related quality of life of survivors of childhood extracranial neoplasms – Alberto Cárceles Álvarez (Spain)
- Descriptive analysis from a hospital based childhood cancer survivors cohort: report from the project Spain-CCSS - Elisa Pasqual (Spain)
- Secondhand tobacco smoke and survival in children with acute lymphoblastic leukemias in the region of Murcia (SPAIN) - Alberto Cárceles Álvarez (Spain)

15.30 -15.45 Break

15.45 -16.30 Poster pitch session E (Auditorium)
Chair: Joan O. Grimalt (Spain) and Joaquim Rovira (Spain)

- Particulate matter characterisation in the schools located around petrochemical industrial complex. Infiltration of particle from outdoor to indoor air - Joaquim Rovira
- Personal exposure to PM2.5 and benzo[a]pyrene in Ostrava, Czech Republic - Katka Honkova
- AIDS orphans in Sub-Saharan Africa: A systematic review on differences between rural and urban environments - Tara Rava Zolnikov
- Training modules for paediatricians – Health effects of climate change - Colin O'Reilly
- Reality of children's new environment and future policy needs - Marija Jevtić

- Study of childhood illness for the period 2009-2011, meeting the city. Sofia & Pleven with view to effective health promotion - P. Karadzhova
- Promoting Health: Recommendations of food consumption as a tool to minimize exposure of pollutants to the children's population – Rosa Maria Llull Cantallops
- Lead and mercury exposure are associated with low resting heart rate in community children - Naixue Cui
- Potential Environmental Hazards on Child Health in a Prospective Mining Area in North Sumatra, Indonesia - Levina Khoe
- Mapping child health against health related policies and programs in East African pastoralist communities - Lioul Berhanu Alemie

15.45 -16.30 Poster pitch session F (Darwin)
Chair: Johanna Hausmann (Germnay) and Nuria Castell (Norway)

- Birth weight in relation to cord blood levels of selected elements in Slovenian mother-child pairs – Marta Jagodic
- Birth and Growth without OH: Detection and follow up from pregnancy until the end of adolescence of children at risk of neurobehavioral disorders through exposure of alcohol and illegal drugs - Maria Luisa Azurmendi
- The mercury pollution and child birth defects -Unursaikham Surenyah
- Prenatal exposure to particulate matter and the occurrence of wheezing in chest in children - Agnieszka Pac
- The role of trace elements, antioxidants and oxidative stress in very low birth weight infants - Beatrice Bocca
- The PERSIAN birth cohort; A Work in Progress – Payam Dadvand
- Psychosocial stress and obesity in Kaunas children - Regina Grazuleviciene
- Lifestyles of survivors of childhood hematologic neoplasms - Mayra Alejandra Orozco Llamas
- Air pollutants exposure and functional repair activity in placenta - Nurulshyha Md Yatim
- The role of perinatal essential fatty acids in attention deficit and hyperactivity disorder symptoms and cognitive functions - Mónica López-Vicente
- Maternal Environmental Exposure to Organochlorine Pesticides and its Effects on Birth weight – Madhu Anand

16.30 -18.00 Session 14 (Auditorium) Exposome research in children
Chair: Mark Nieuwenhuijsen (Spain) and Denis Sarigiannis (Greece)

- Human biomonitoring data analysis for metals in an Italian adolescents cohort: an exposome approach - Alberto Gotti (Italy)
- Assessing the impact of hazardous waste on children's health: the exposome paradigm -Denis Sarigiannis (Greece)
- Quantitative profiling of metabolic markers to assess dietary and microbiota related exposure factors - Zdenek Spacil (Czech Republic)
- Persistent pollutants in food items from Menorca Island - Eva Junqué (Spain)
- Prenatal exposure to perfluoroalkyl substances and cardio-metabolic risk components during early childhood – Cyntia B. Manzano-Salgado (Spain)

Session 15 (Darwin) Miscellaneous
Chair: Payam Dadvand (Spain) and Tara Zolnikov (USA)

- Health effects of consuming desalinated Sea water - implications for children - Yona Amitai (Israel)
- Maternal cell phone use during pregnancy and child behavior problems in five birth cohorts - Laura Birks (Spain)
- Determining the impact of smoking point of sale legislation among youth (Display) study: new findings from Scotland - Jamie Pearce (UK)
- Impact of prenatal exposure to environmental pollutants on autism spectrum disorder: A case report - Esther Tobarra Sánchez (Spain)
- BORN WITHOUT OH: an innovating model for preventing and managing the neurodevelopmental disorders caused by alcohol and drug prenatal exposure in a Mediterranean region - María Luisa Azurmendi Funes (Spain)

Friday 16th of September 2016

8.45-10.15 Session 16 (Auditorium) Children's environmental health policy topics
Chair: David Bellinger (USA) and Karl Ernst von Mühlendahl (Germany)

- Minamata Convention on mercury vulnerable population - Mahmood Khwaja (Pakistan) Children's environmental right - Jonas Schubert (Germany)
- Environment exposure and neuro-development in MOCEH - Mina Ha (Korea)
- Improved Relationships in Eastern Kenya From Water Interventions and Access to Water – Tara Rava Zolnikov (USA)
- Relations between the exposure of factory air polution with asthma impacted in children who live in shelter Around the district of industrial area in Jakarta, Indonesia Trial District In Jakarta Indonesia - Wan Nedra Komaruddin (Indonesia)

10.15 -10.30 Break

10.30 -12.00 Session 17 (Auditorium) Children's Health and the environment in the Mediterranean. CROME Session.
Chair: Denis Sarigiannis (Greece) and Gemma Calamandrei (Italy)

- The NAC-II birth cohort in Friuli Venezia Giulia Region: prenatal and childhood exposure to metals and neuropsychological maturation at 7 years - Gemma Calamandrei (Italy)
- Internal dosimetry metrics for risk assessment of endocrine disruptors – the case of bisphenol A -Denis Sarigiannis (Greece)
- Urine total arsenic and arsenic species in children from Northern Italy - Beatrice Bocca (Italy)
- Neurodevelopment, low level mercury exposure and genetic polymorphisms in birth cohort from Slovenia and Croatia - Janja Snoj Tratnik (Slovenia)
- Children exposure to PAH and potential carcinogenic risk assessment from biomass burning incorporating internal dosimetry metrics - Spyros Karakitsios (Greece)
- Influence of gestational weight gain on the transfer of organochlorine pollutants into infants – Joan Grimalt (Spain)

12.00 -13.15 Session 18 (Aud) Final session
Chair: Wojtek Hanke (Poland) and Stephan Böse-O'Reilly (Germany)

- Protecting children's health from environmental harm - the perspective of WHO Regional Office for Europe - Dorota Jarosinska (WHO, Europe)

- INMA overview - Jordi Sunyer (Spain)
- Societal burden of children's exposures to neurotoxicants - David Bellinger (USA)
- Thinking of the relationship between children's health and the environment as a rights issue - The UN Committee on the Rights of the Child Day of General Discussion on Children's Rights and the Environment on 23 September 2016 - Jonas Schubert (Germany)

13.15 -13.30 Closing Ceremony:

Final part of the meeting restricted to project partners

15.30 - 17.30 This session was dedicated to plan the activities and the interaction among partners during the last phase of the CROME project

Minutes of the CROME-LIFE interregional workshop, Barcelona, September 14-16st 2016

The second CROME-LIFE interregional workshop was held in Barcelona at the premises of the Parc de Recerca Biomèdica de Barcelona (PRBB) on September 14-16st, 2016. On this occasion, the CROME meeting was merged with the International Conference on Children's Health and the Environment (INCHES). About two hundred and fifty people among researchers of academia, Ph.D. students, and government research bodies, Health Service representatives and various stakeholders participated to the workshop.

The opening ceremony was chaired by the Commissioner of Health of the City Hall of Barcelona, who gave the opening speech who welcomed the audience, acknowledging the multilevel approach of the CROME-LIFE consortium, and stressing the importance of informed and timely communication to the citizens on environmental health issues. She was accompanied by Dr. Peter van der Hazel, President of INCHES, and Joan O. Grimalt, Principal Investigator of the CROME group in Barcelona. Before that, the opening ceremony was also chaired by these two last persons together with Mark Nieuwenhuijsen from the newly formed Institute ISGlobal.

The meeting was also attended by leading representatives of the World Health Organization such as Maria Neira, Marie Noel Brune, Dorota Jarosinka and Enriko Todaka.

The meeting had a specific session devoted to the description of the results obtained in the Mediterranean populations as consequence of the CROME work. This session "Children's Health and the Environment in the Mediterranean. CROME session" was chaired by Denis Sarigiannis (Greece) and Gemma Calamandrei (Italy). In this session there were the following presentations:

The NAC-II birth cohort in Friuli Venezia Giulia Region: prenatal and childhood exposure to metals and neuropsychological maturation at 7 years - Gemma Calamandrei (Italy)

The Northern Adriatic Cohort II is a prospective mother-child cohort established in 2007 in coastal areas of Italy, Croatia and Slovenia to investigate the association between prenatal mercury exposure from maternal fish consumption and child neurodevelopment. The Italian Northern Adriatic Cohort II refers to the coastal area of the Friuli Venezia Giulia Region. At present, a biological bank collected during pregnancy and at birth from mother-child pairs is available. The data bank has collected neuropsychological outcomes measured at different developmental stages (18 months, 40 months), as well as a wide range of potential explanatory variables (socioeconomic

indicators, diet habits, child postnatal exposures, maternal lifestyle). The Cross-Mediterranean Environment and Health Network Life project has followed 200 children born within The Northern Adriatic Cohort II for follow up at 7 years. Chemical analyses consisted of measurements of the concentration of five neurotoxic metals (mercury, lead, manganese, cadmium, arsenic) in either hair or urine of each child. The neuropsychological tests included the Wechsler Intelligence Scale for Children-IV, the Developmental Neuropsychological Assessment-II, for the assessment of reading and writing skills, and the Child Behaviour Check List to identify behavioural and emotional problems in children. Ethical approval was granted by the Burlo Garofolo Child Hospital of Trieste. Results show that total mercury exposure during pregnancy and breastfeeding did not significantly affect neuropsychological performances at 18-40 months or 7 years. At 7 years the total mercury level in urine is still strongly related to the fish consumption of the mother during pregnancy and breastfeeding; there is a positive effect of fish consumption by the child on several attentional and cognitive tasks at 7 years. We found an adverse effect of manganese as measured in children's hair on the five Wechsler Intelligence Scale for Children-II score, with statistically significant decrements of the general intelligence quotient and of verbal comprehension. These results highlight the complex interaction between multiple chemical exposures, life style factors, and time of outcome assessment and support the usefulness of the integrated Cross-Mediterranean Environment and Health Network approach in risk modeling

Internal dosimetry metrics for risk assessment of endocrine disruptors – the case of bisphenol A -Denis Sarigiannis (Greece)

Bisphenol A (BPA) remains one of the most controversial industrial chemicals with respect to early developmental stage exposure and effects. The current study aims at a comprehensive exposure analysis of BPA, using an integrated exposure modelling framework that comprises far field and near field exposure modelling coupled to a dynamic lifetime physiologically based pharmacokinetic model. Exposure analysis was applied in European data, largely based on literature review of BPA food residues, as well as exposure reconstruction of human biomonitoring data. The latter were further assimilated through an advanced exposure reconstruction modelling framework. Special attention was paid to the assessment of BPA internal exposure through critical developmental stages such as gestation, by modelling the mother-fetus toxicokinetic interaction. The analysis indicated that current exposure levels in Europe are below the temporary tolerable daily intake of 4 μg/kg body weight/day proposed by the European Food Safety Authority. For chemicals with widespread consumer applications such as BPA, environmental pathways contribute insignificantly to BPA intake, while overall exposure is dominated by specific consumer behaviors. For BPA these pertain to consumption of canned food and beverages and the use of medical products found in neonatal intensive care units, such as bags containing intravenous fluids and total parenteral nutrition and tubing associated with their administration. Premature neonates hosted in intensive care units have also been also identified as the only population group that potentially faces some risk related to BPA exposure, especially when accounting for the immaturity of the detoxification pathway. In principle, health risks might be underestimated for specific population groups (e.g. neonates and infants) if the assessment does not take into account the variability in internal exposure due to genetic, physiological and developmental factors. In utero exposure was found to be highly associated to maternal exposure; actual fetal exposure was higher than maternal exposure by almost 20% due to the presence of β–glucuronidase in the placenta. Nevertheless, at the current levels of maternal exposure to BPA, in utero exposure is also very low, and significantly below the respective biologically effective dose derived from the European Food Safety Authority temporary tolerable daily intake. Exposure reconstruction of literature available on human biomonitoring data resulted in very low intake estimates, similar to the ones estimated from the

exposure models. Using biological pathway altering dose derived from in vitro BPA toxicity assessment as the internal exposure reference value, the maximum derived internal exposure values of the worst-case exposure scenarios (premature neonates) are 10 times lower to the lower 99th percentile of the Biological Pathway Activating dose, indicating that there is no reason for concern for individual or aggregate scenarios of BPA exposure. In addition, the use of the internal dosimetry module allowed the translation of the European Food Safety Authority temporary tolerable daily intake into a biomonitoring equivalent urinary BPA-Glu concentration of320 μg/L. Comparison of this value to the collected biomonitoring data shows that the current existing levels of BPA in EU are 2 orders of magnitude below the European Food Safety Authority temporary tolerable daily intake; this margin of safety is in the same magnitude of order to the one estimated when daily intake is estimated from human biomonitoring data.

Urine total arsenic and arsenic species in children from Northern Italy - Beatrice Bocca (Italy)

Arsenic (As) exposure during childhood has been associated with neurobehavioral effects in population-based cohort studies. In addition, variations in As on children health outcomes may be, to some extent, related to exposure to different As species. Within the Cross-Mediterranean Environment and Health Network-Life project, aimed at assessing the health risk due to exposure to neurotoxic chemicals, a cohort of 200 children at 7 years (the Northern Adriatic Cohort II Public Health Impact of Long-term, Low-level Mixed Element Exposure in Susceptible Population Strata cohort) from the coastal area of Friuli Venezia Giulia Region (Italy) was analyzed for As exposure. Total As concentration was determined in children's urine by high resolution inductively coupled plasma mass spectroscopy. Then, the concentrations and distributions of urinary As species, including inorganic arsenic (iAs) [arsenite (iAsIII) and arsenate (iAsV)], monomethylarsonic acid (MMA), dimethylarsinic acid (DMA), arsenobetaine (AsBet) and arsenocholine (AsChol), were determined by high-performance liquid chromatography combined with inductively coupled plasma mass spectrometry. Ethical approval was granted by the Cross-Mediterranean Environment and Health Network-Life. Results indicated a good agreement between the values obtained for total As (median, 10.6 μg/L) and the sum of species. The order of As species excretion in urine of children was: AsBet > DMA > MMA ≅ iAsIII > iAsV (AsChol was at trace levels); moreover, the second methylation step was more active than the first one (DMA > MMA). In conclusion, in children, inorganic arsenics (AsIII and AsV) were metabolized to the less toxic forms as DMA and MMA through the methylation process. In addition, a very high percentage of urine As was present as AsBet which is essentially harmless and suggestive of dietary As. Due to the different toxicity of As compounds, speciation of As in urine was confirmed to be more convenient for health risk assessment than measuring total As concentration and it can give valuable information about the metabolism of As species within children's bodies.

Neurodevelopment, low level mercury exposure and genetic polymorphisms in birth cohort from Slovenia and Croatia - Janja Snoj Tratnik (Slovenia)

The aim of the present study was to evaluate association between prenatal exposure to mercury and the neurodevelopment of children, taking into account relevant confounders and some relevant genetic polymorphisms. We examined apolipoprotein E (Apoe) and glutathione transferase (GSTM1 and GSTT1), the genes that are hypothetically involved in elimination of mercury from the body, and Apoe in neurodevelopment. The study population was comprised of 601 mother-child pairs recruited from the central Slovenia region and 243 from Rijeka, on the Croatian coast of the northern Adriatic. Determination of total mercury in cord blood, neurodevelopment assessment using Bayley Scales of Infant and Toddler Development, Third Edition (Bayley III) at 18 months of

age and genotyping was done in 361 children; 237 of them were from Slovenia and 124 from Croatia. The National Ethics Committees of Slovenia and Croatia approved this study. The results showed a negative association between low-to-moderate mercury exposure levels and cognitive outcomes and with fine motor scores at 18 months of age. The observed decrease in cognitive function was significant only in children carrying at least one Apoe ε4, while the decrease in fine motor score was independent of the Apoe genotype. Adjusting for selenium and lead revealed positive association between selenium and language and negative between lead and motor function, but only in the subgroup of children not carrying the ε4 allele. The GSTT1 genotype revealed positive association between cord blood selenium and cognition in children without gene deletion (β=11.8, p=0.008), but not in children with GSTT1 deletion (β=-15.1, p=0.128). The present study indicates that even low-to-moderate mercury exposure in children with normal neurodevelopmental outcome can be associated with lower cognitive and fine motor Bayley III scores and that stratifying for specific genotypes and accounting for beneficial and other potentially neurotoxic substances is crucial in assessing such associations. The present study indicates that even low-to-moderate mercury exposure in children with normal neurodevelopmental outcome can be associated with lower cognitive and fine motor Bayley III scores and that stratifying for specific genotypes and accounting for beneficial and other potentially neurotoxic substances is crucial in assessing such associations.

Children exposure to PAH and potential carcinogenic risk assessment from biomass burning incorporating internal dosimetry metrics - Spyros Karakitsios (Greece)

The current study deals with the assessment of the children's cancer risk attributable to exposure to polycyclic aromatic hydrocarbons (PAHs), under an increased use of biomass for space heating in Greece since the winter of 2012-2013. The study incorporated ambient air particulate matter (PM) sampling in several sites, as well as chemical analysis of PAHs and levoglucosan, as the most specific tracer of biomass combustion. External exposure was estimated accounting for PAHs concentration variability among the various locations and the use of personal sensors providing information on location, temperature and intensity of activity. Internal exposure to PAHs was estimated taking into account the deposition of the respective PM fractions across the human respiratory tract and the respective PAHs concentration of the respective PM fractions. Deposition at different regions of the human respiratory tract was estimated using the Multiple-Path Particle Dosimetry model. Potential cancer risk due to exposure to the mixture of urban ambient air PAHs was calculated using the toxicity equivalence factor approach using as basis the benzo(a)pyrene cancer potency. Cancer risk was estimated from the integral of the toxic equivalent quotient of the different size of PM deposited daily across different human respiratory tract regions, by a slope-factor equal to 0.25·10-6 ng/kg body weight/day) function, initially derived by the benzo(a)pyrene Inhalation Unit Risk (equal to 0.88·10-6 (ng/m3)-1). This refined exposure and risk characterization methodology allowed us to identify significant differences experienced by the different age group, as well as people living in different areas within an urban agglomeration. The human respiratory tract deposition results indicated that the lower respiratory tract of infants and children (up to 14 years old) can retain up to 74% higher mass fraction of PM1 particles than that of adults. The maximum difference in the thoracic deposition between adults and children (referring to children between 3 and 8 years old) is that of 68% and 230% for the PM2.5-1 and PM10-2.5 fractions respectively. Thus, the PM2.5 and PM1 fractions rather than PM10 contribute to a greater extent to the absorption of PAHs by the respiratory tract in younger individuals compared to adults. The estimated lung cancer risk was above 10-6 for the areas affected by biomass combustion. Age dependent differences in the estimated risk were mainly attributed to the respiratory physiology differences and the increased intensity of activity characterizing children, favoring the deposition of

smaller (and more toxic particles) in children. In addition, biomass emitted particles were found to be more toxic (in terms of PAHs content) than the ones emitted from traffic sources. Age dependent differences in human physiology, combined with the increased intensity of activity characterizing children, resulted in 2-3 times higher risk estimates from exposure to PAHs compared to adults.

Influence of gestational weight gain on the transfer of organochlorine pollutants into infants. Joan Grimalt (Spain)

Transplacental transfer and breastfeeding are the main transport routes of organic pollutants to children at the beginning of life. These transmission mechanisms primarily depend on the maternal pollution burden, but its impact may be modulated by physiological effects. We found that gestational weight gain (GWG) exerts a considerable influence on the content of hydrophilic and low volatile pollutants in cord blood and breast milk. We measured levels of 14 organochlorine pesticides, 7 polychlorobiphenyls and 14 polybromodiphenyl ethers (PBDEs). Persistent organic pollutant neonatal concentrations were inversely associated with GWG after adjustment for age, pre-pregnancy body mass index, educational level, and fish consumption. On average, neonates of women with high or recommended GWG as defined by the Institute of Medicine had lower persistent organic pollutant concentrations than neonates of mothers with low GWG. This study was approved by the ethics committees of the Clinical Research Ethical Committee of the Municipal Institute of Health Care, the Ethics Committee of the Donostia Hospital and San Agustin Hospital, and informed consent was provided by every participant. Colostrum from mothers with low GWG also had significantly higher concentrations of polychlorobiphenyls and 4,4'-dichlorodiphenyldichloroethylene than colostrum from mothers who gained weight within Institute of Medicine recommendations or in those who exceeded this threshold. Statistically significant differences were also found in the colostrum: maternal serum ratios of these compounds. Women with low GWG retained higher pollutant amounts in colostrum. The higher mobilization of stored organic pollutants observed in pregnant women with low GWG plays a role for in utero pollutant exposure and during breastfeeding. The present findings suggest an association between infant exposure to persistent organic pollutants and inadequate GWG, encouraging pregnant women to meet the recommended Institute of Medicine guidelines to reduce the accumulation of these pollutants in newborns and during breastfeeding.

Impact into the media

The CROME work reported in this Conference had high impact in the media who showed interest in relation to:

a) Problems related with mercury in the Mediterranean Sea:

Newspapers: La Vanguardia (2 times), ABC, 20 Minutos, Diario de Ferrol, El Ideal Gallego, El Progreso, El Punt Avui, Diario de Arousa, El Periodico (2 times), Mediterraneo, and others

TV: In the news of TV3.

b) Problems related with atmospheric pollution:

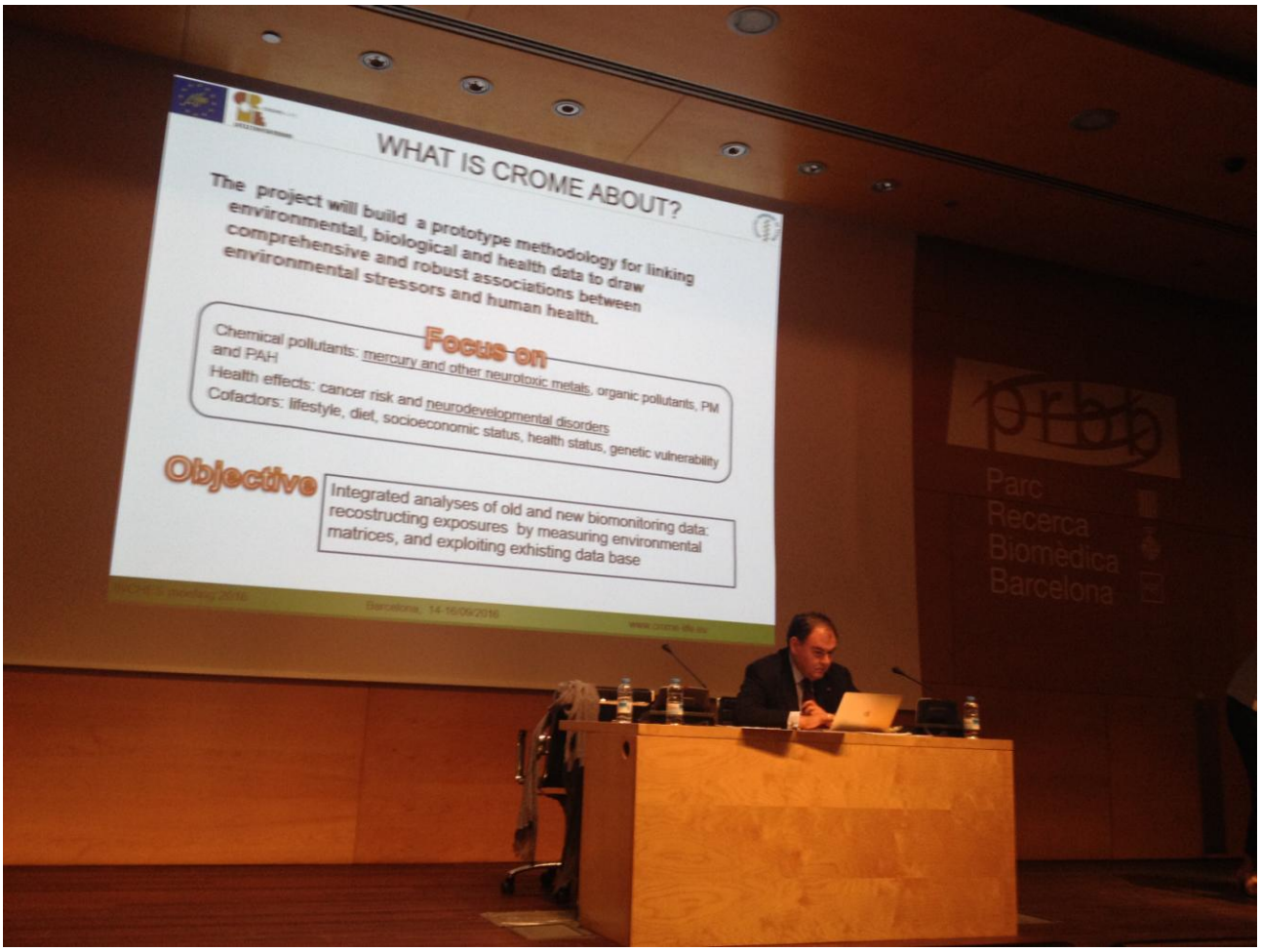
Radio 5

Scientific impact after the meeting

The abstracts of the meeting have been published in the **Journal of Health and Pollution Dec 2016, Vol. 6, No. 12 (December 2016) pp. S1-S154.**

A special issue of **Environmental Research** is prepared with the presentations at this Barcelona Meeting. Twenty-nine papers were submitted for publication to this issue. Five have been rejected and the rest (24) are still into the review process.

Images

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