Environmental Engineering Laboratory
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ANNUAL REPORT 2022

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Welcome message

2022 – A year of challenges and success

The Environmental Engineering Laboratory (ENVE Lab) was established at the Chemical Engineering department of the Aristotle University of Thessaloniki (AUTH) in the second half of 2011. Its objective is to act as an international center of reference for environmental engineering addressing the interactions between environment and human health and exploiting this knowledge to the design of novel processes and products serving sustainability objectives.

The main scientific foci of ENVE Lab are:

- Environment and health – development of integrated methodologies to assess the impact environmental pollution may have on human health.
- Advanced technologies for monitoring environmental pollution and waste management.
- Industrial ecology approaches to the design of industrial and urban systems with reduced ecological footprint, as well as Safe and Sustainable by Design (SSbD) chemicals, materials and processes.

Our work paradigm is based on international collaboration and scientific networking. EnvE Lab work paradigm, is graphically illustrated in Figure 1. This relies on:

- Identification of scientific challenges.
- Development of innovative methodological approaches.
- Delivery of integrated solutions that pertain to targeted and cost-efficient interventions.

Within AUTH, ENVE Lab collaborates with several analytical and biochemistry laboratories in the Schools of Engineering, Natural Sciences and Medicine. On a global scale, good collaborative links have been established with the World Health Organization, the European Center for Environment and Health, the US Environmental Protection Agency, the National Institutes for Environmental Health Science and the Schools of Public Health of the University of California at Berkeley and Los Angeles, the Johns Hopkins Bloomberg School of Public Health, and the Yale School Of Public Health, focusing on the development of operational methodologies and novel tools towards unraveling the exposome.

During 2022, the main challenges included:

(a) leading the effort on exposome and contributing to the international debate on rendering the exposome operational for precision prevention
(b) contributing to the development of the European Partnership for risk assessment of chemicals
(c) representing Greece at the Program Committee on Climate Action, Environment and Resource Efficiency of Horizon EUROPE
(d) Predicting the health risks of the Covid-19 pandemic using the in house developed model CORE.

I hope you will enjoy reading our 2022 annual report. We would be happy to work with you to roll further back the boundaries of error in our understanding of the world.

Prof. Dimosthenis Sarigiannis

Laboratory director

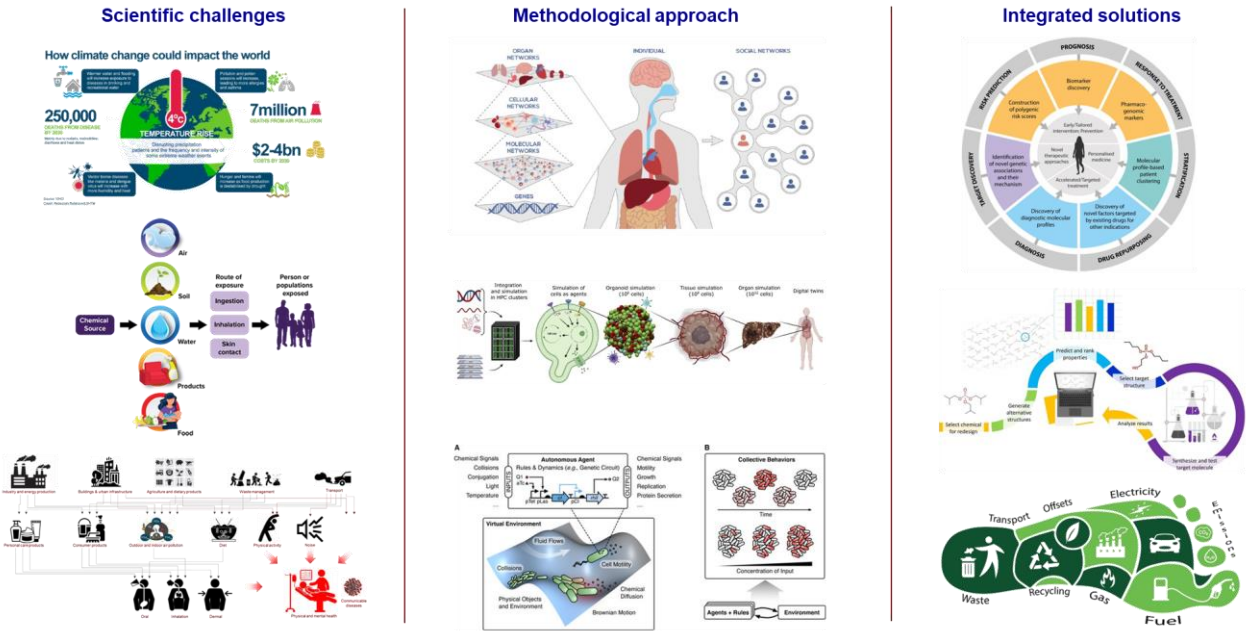


Figure 1. EnvE Lab work paradigm

Scientific Signature

EnvE Lab aims at developing integrated methodologies, knowledge management systems and technologies that can effectively shed light on the interactions between human health and the environment. Our ultimate goal is to generate the knowledge necessary to optimize interventions that protect public and consumer health cost-effectively. These include the design of technological systems that serve sustainability and respect human health.

Our concept brings together beyond-the-state-of-the-art advances in **environmental monitoring**, **human biomonitoring** and **systems biology**, **exposure monitoring** technologies and tools for **computational analyses** of the **exposure-to-health effect continuum**. The above are collated in a novel exposure biology-based methodology supported by an integrated knowledge management system at the core of the "**Connectivity approach**". Expanding the applicability domain of connectivity Approach to a wide variety of environmental stressors is a key prerogative for its scientific soundness and its impact on public policy. Various **Connectivity Approach** modules are put to test through their application in a number of population studies across different exposure settings in Europe and worldwide tackling relevant health endpoints. In addition to technical research and continuous development work, horizontal activities provide the infrastructure necessary for setting **Connectivity Approach** in its proper policy context.

Better understanding of environmental fate, exposure and toxicity mechanisms is required to ensure refined exposure and risk characterization, e.g. the precise quantification of exposure scenarios and circumstances that might set the basis for inducing potential adverse effects on humans. However, social cost increases exponentially as we approach the maximum benefit in terms of exposure reduction; it seems that there is a threshold beyond which social cost increases disproportionally to social benefit. The aim of refining the overall assessment is to identify this optimal point, so as to design cost-effective public health protection policies that foster technical and societal innovation in parallel.

The assessment process focuses on the following: (a) hazard potency of a substance; (b) its uses and mobility in the environment (affecting the amount that the population groups will come into contact); (c) the biologically effective dose of the compound reaching the target tissue; and finally (d) the response of the human body to this dose.

These attributes are influenced strongly by the interaction of the physicochemical properties of the substance(s) under study with biological and physiological characteristics. Thus, well targeted interventions at different stages of the source-to-outcome continuum ensure the optimal management of chemicals in the environment and consumer products. Our final objective is to render this analysis a *sine qua non* tool for guiding new chemical synthesis in industry (Figure 2), in accordance with the "safe and sustainable by design" principle.

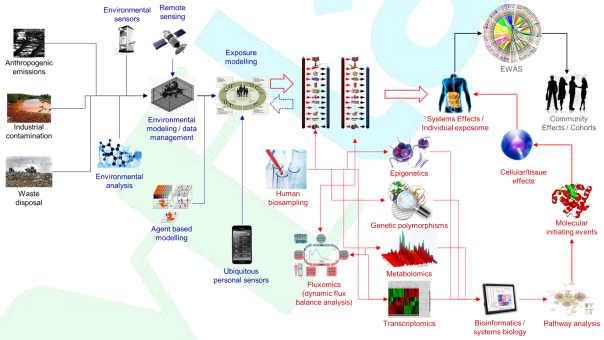


Figure 2. The Connectivity Approach

The necessity of using the **Connectivity Approach** as a novel tool for interpretation of environment and health data in order to better understand the mechanistic relationship between lifelong exposure to environmental stressors and health response has been widely recognized by the scientific, regulatory and chemical industry community; EnvE Lab's resilience in supporting this scientific signature, as well as dedication to a solid work ethics model, was rewarded by the number of different projects granted over the last years under EnvE Lab coordination, namely:

HEALS – EU FP7 project

CROME – LIFE+ project

ICARUS – EU Horizon 2020 project

NEUROSOME – EU Horizon 2020 project

URBANOME – EU Horizon Europe project

while EnvE Lab has also key contribution applying its **Connectivity Approach** in the following projects:

HBM4EU – EU Horizon 2020 project

OBERON – EU Horizon 2020 project

HERA – EU Horizon 2020 project

RAISE – EU Horizon Europe project

PARC – EU Horizon Europe project

Exposure science and chemical risk assessment

Exposome science

The exposome represents the totality of exposures from conception onwards, simultaneously identifying, characterizing and quantifying the exogenous and endogenous exposures and modifiable risk factors that predispose to and predict diseases throughout a person's life span. The methodology for assessing individual exposome proposed by EnvE Lab brings together a comprehensive array of novel technologies, data analysis and modeling tools that support efficient design and execution of exposome studies.

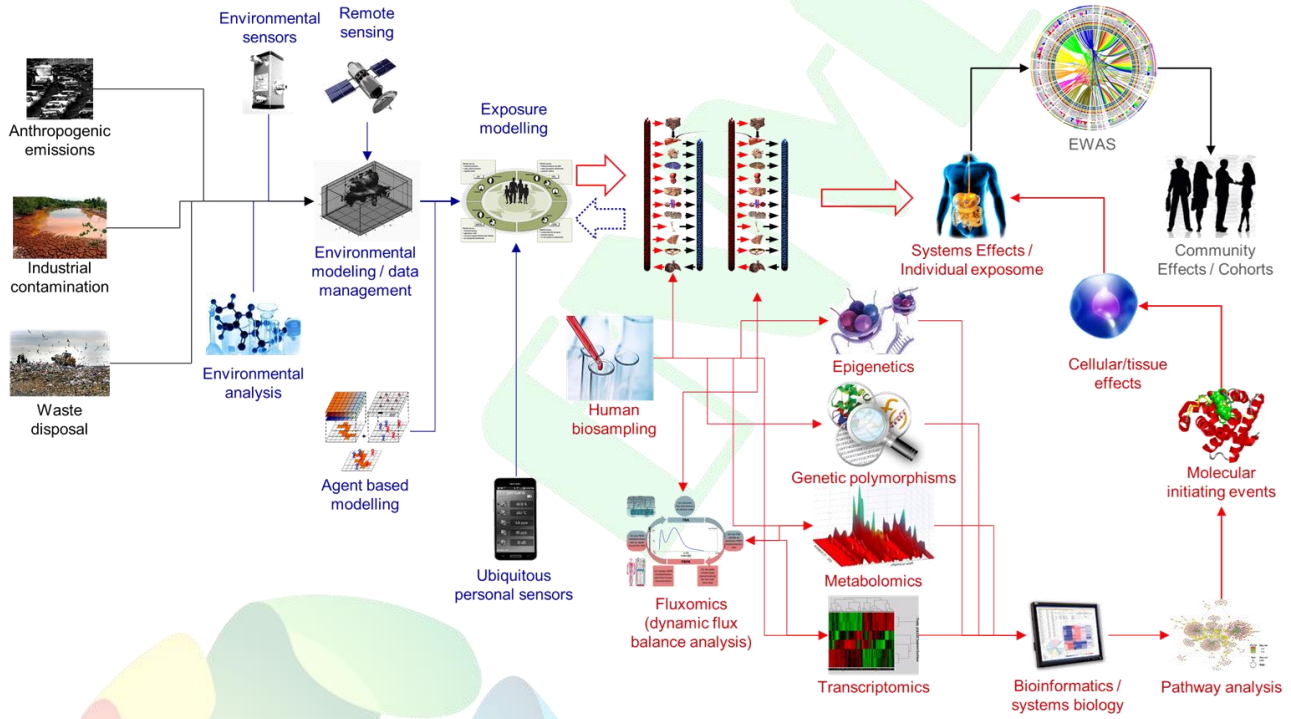


Figure 3. Conceptual representation of the technological arrays involved in the exposome assessment – the Connectivity Approach

This approach brings together and organizes environmental, socio-economic, exposure, biomarker and health effect data; in addition, it includes all the procedures and computational sequences necessary for applying advanced bioinformatics coupling advanced data mining, biological and exposure modeling so as to ensure that environmental exposure-health associations are studied comprehensively. The following are key components of the EnvE Lab paradigm towards unraveling the individual exposome:

- Human biomonitoring (HBM) and biobanking are seen as a central theme.
- Understanding of the interaction between HBM and exposure modeling (EM) or estimation is another key factor for elucidating the exposome.
- Lifestyle/behaviour patterns (such as time-activity-location, food consumption, use of consumer products, etc.) are needed to understand individual and population-based geospatial lifelines.
- Innovations in sensor technology allow us to collect environmental data at unprecedented depth and breadth.
- We propose simulating movement and interaction behaviour using agent-based models (ABM) informed by sensor technologies in order to understand the dynamics of real-world societal and environmental systems.
- Current toxicological state of the art couples estimations of biologically effective dose (BED) with early biological events to derive dose-effect models, which can be used in combination with probabilistic exposure estimates to derive biomarkers of exposure and/or effect. Combined epidemiological, clinical and genetic/epigenetic data analysis will shed light on the effect of risk modifiers such as lifestyle choices and DNA polymorphisms and methylation. Exposure assessed prospectively and tightly linked to proposed periods of vulnerability of the epigenome (e.g., periods of placental invasion or sex specification in utero) would be ideal. Observation of real clinical data and/or results of biomonitoring coupled with exposure/effect biomarker discovery systems, will produce predictive biomarkers allowing estimations of individual response to toxic insults. Metabolomics and adductomics are key to this analytical and data interpretation process. They will be functionally integrated with transcriptomics and proteomics to provide the mechanistic underpinning for establishing causality in the association between health status and exposure to environmental stressors.

European Human Biomonitoring Initiative (HBM4EU)

Aims and scope

HBM4EU is a joint effort of 30 countries, the European Environment Agency and the European Commission, co-funded under Horizon 2020.

The initiative is coordinating and advancing human biomonitoring in Europe. HBM4EU is generating evidence of the actual exposure of citizens to chemicals and the possible health effects in order to support policy making.

The HBM4EU initiative represents a novel collaboration between scientists and chemical risk assessors and risk managers, including several Commission services, EU agencies and representatives for the national level. The project has built bridges between the research and policy worlds in order to deliver benefits to society in terms of enhanced chemical safety.

HBM4EU is a five year project, that kicked off in 2017 and will run to the end of 2021.

In developing priorities for HBM4EU under the first annual work plan, the consortium conducted a prioritisation exercise in 2016 to identify those substances to be the focus of activities. A second round of prioritisation was conducted from 2017 to 2018. A third round of prioritisation is foreseen for 2020 to 2021, with the aim of feeding into a future initiative.

The overarching goal of the European Human Biomonitoring Initiative (HBM4EU) is to generate knowledge to inform the safe management of chemicals and so protect human health. We will use human biomonitoring to understand human exposure to chemicals and resulting health impacts and will communicate with policy makers to ensure that our results are exploited in the design of new chemicals policies and the evaluation of existing measures.

Key objectives include:

• Harmonizing procedures for human biomonitoring across 26 countries, to provide policy makers with comparable data on human internal exposure to chemicals and mixtures of chemicals at EU level;

• Linking data on internal exposure to chemicals to aggregate external exposure and identifying exposure pathways and upstream sources. Information on exposure pathways is critical to the design of targeted policy measures to reduce exposure;

• Generating scientific evidence on the causal links between human exposure to chemicals and negative health outcomes; and

• Adapting chemical risk assessment methodologies to use human biomonitoring data and account for the contribution of multiple external exposure pathways to the total chemical body burden.

To achieve these objectives, human biomonitoring initiatives in 26 countries were harmonised, drawing on existing expertise and building new capacities. By establishing National Hubs in each country to coordinate activities, we will create a robust Human Biomonitoring Platform at European level.

This initiative contributes directly to the improvement of health and well-being for all age groups, by investigating how exposure to chemicals affects the health of different groups, such as children, pregnant women, foetuses and workers. We will also investigate how factor such as behavior, lifestyle and socio-economic status influence internal exposure to chemicals across the EU population. This knowledge will support policy action to reduce chemical exposure and protect health.

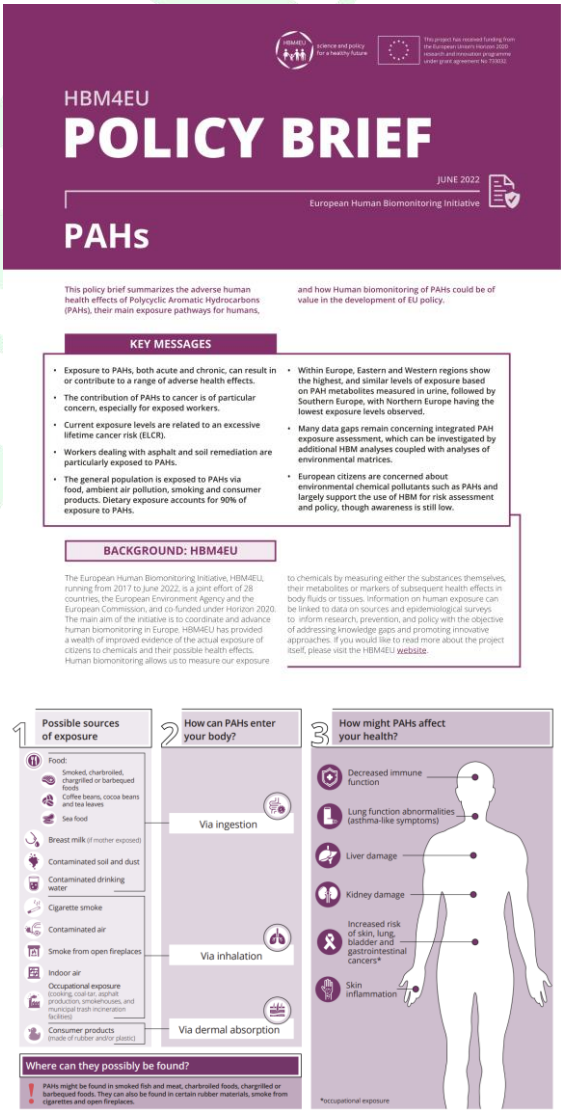


Figure 4. PAHs policy brief produced by HBM4EU

CROME study

Human biomonitoring (HBM) is a tool for health-related environmental monitoring. Human body fluids and tissues are examined for contamination with pollutants in human biomonitoring. Human biomonitoring plays an essential role in environmental health and assessing pollution levels in the population, population groups or individuals.

The HBM4EU-aligned studies focus on three age groups: children, teenagers, and adults. Participants were recruited between 2014 and 2021 in 11 to 12 primary sampling units geographically distributed across Europe. Two different matrices are collected, urine samples are collected in all age groups, and blood samples are collected in children and teenagers. In addition, participants were asked to answer extended questionnaires from where information on sociodemographics, lifestyle, health status, environment, and diet were retrieved. Biological samples from 3137 children aged 6–12 years are collected to analyse biomarkers for phthalates, HEXAMOLL® DINCH, and flame retardants. In addition, samples from 2950 teenagers aged 12–18 years are collected to analyse biomarkers for phthalates, Hexamoll® DINCH, and per- and polyfluoroalkyl substances (PFAs).

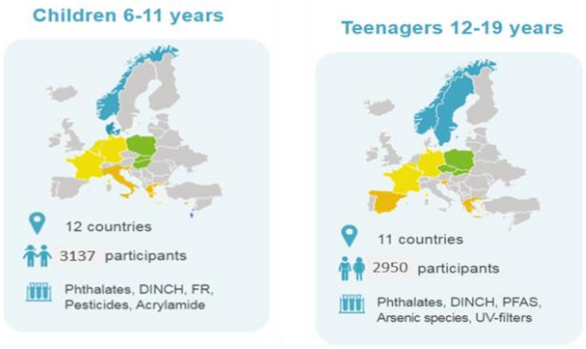


Figure 5. Geographical distribution of cohorts among Europe

There isn't any HBM program in Greece, and this is the first survey held in Greece. The CROME study (Cross-Mediterranean Environment and Health Network) collected samples in Greece (Thessaloniki) between July 2020 and March 2021. The CROME study was initiated as a parent-children cohort investigating the levels of environmental pollutants and biochemical indicators of exposure. Participants were invited through bilateral meetings and word of mouth because the covid-19 pandemic made the initial planning, i.e. to take place through the school structures, not feasible. The CROME study includes the recruitment of children and adolescents as well as their family and parents. For children, the ages are between 6-11, adolescents between 12-18 and the adults in the study are from 19-68 years. A participation rate of 50% was achieved. In total, 560 participants were recruited.

Furthermore, participants had to be included in Thessaloniki for the last 3 years. From CROME, 161 children and 150 teenagers were included in the HBM4EU-aligned studies sample. As an incentive, participants received feedback on their results. All children and teenagers provided a urine sample. In addition, a blood sample was collected for only some children (N = 55) and teenagers (N = 52). Metadata information of the study can be found in IPCHEM.

One of the groups of compounds examined was the plasticisers, phthalates metabolites and their substitute Hexamoll® DINCH. They are widely used in manufacturing plastics, to make them soft and flexible, and in personal care products. They can be found in everyday products such as soaps, suntan lotion, soft plastic toys, plastic bottles, raincoats, shoes and food packaging. However, not all countries have human biomonitoring data on phthalates investigated in the human biomonitoring DEMOCOPHES study. With only 7 countries analysing 5 phthalate metabolites (from a list of 20).

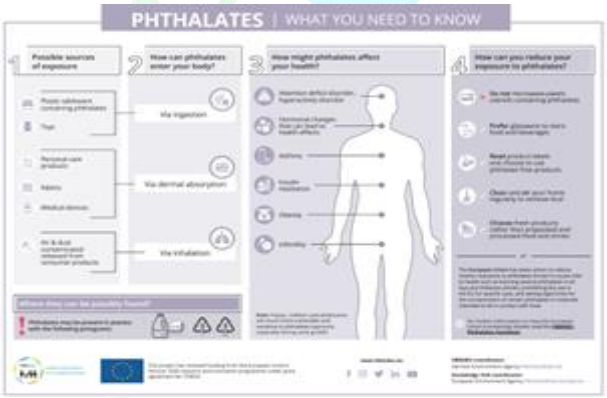


Figure 6. Factsheet from HBM4EU project on Phthalates

One of the phthalates explored in the alignment studies is DiBP. The result indicator for geographical differences provides an overview of internal exposure to DiBP in European children (6–11 years) from studies in 11

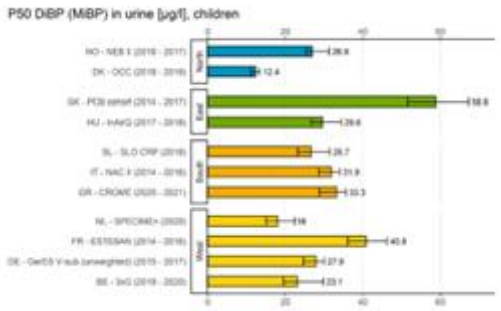


Figure 7. P50 values in DiBP exposure (MiBP in µg/L) in children (6–11 years) in the HBM4EU Aligned Studies.

European countries between 2014 and 2021 (P50 values of MiBP).

Regarding geographical differences, the exposure of children towards DiBP metabolites was highest in an eastern European study and lowest in a northern European study. The P50 values differed more between the sampling sites than between regions. The result indicator for geographical differences of DiBP metabolite concentrations in children showed that P50 values varied by a factor of almost 5 (4.7) between the sampling sites.

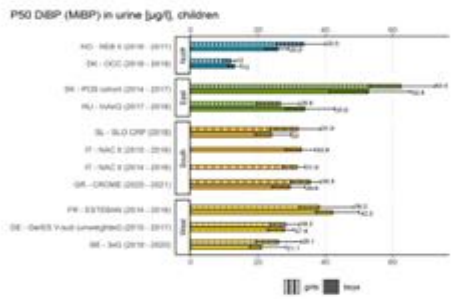


Figure 8. Result indicator regarding sex differences of P50 values of DiBP exposure (MiBP in µg/L) in children (6–11 years) in the HBM4EU Aligned Studies.

Flame retardants have been widely used since the 1970s in textiles, furnishing, plastic, and electronic equipment. Brominated flame retardants (BFRs), including polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDDs), were the primary FRs for more than thirty years

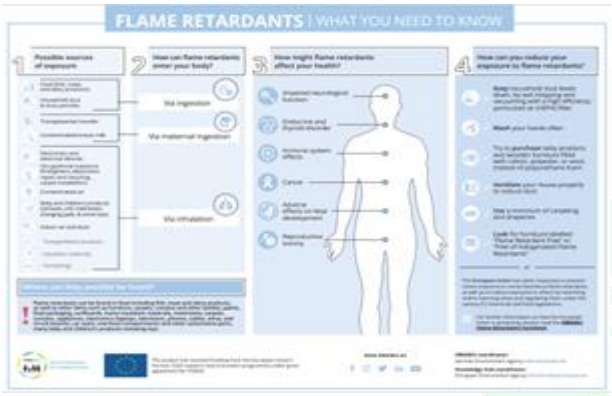


Figure 9. Factsheet from HBM4EU project on Flame Retardants

When comparing levels across three European countries, Greece had significantly lower concentrations of BDE-47 than either France or Norway (Kruskal-Wallis test, $p < 0.001$), in both the unadjusted data as well as in data adjusted for age and sex.

BDE-153 was detected in more than 40% of the blood samples from Greece and Slovenia Greece had significantly lower concentrations of BDE-153 than Slovenia ($p < 0.001$). Lipophilic compounds such as halogenated FRs are typically associated with dietary

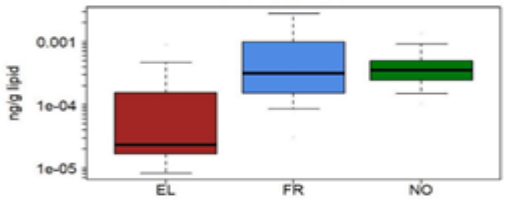


Figure 10. BDE-47 levels among three European countries

exposure and breastfeeding. Norway is one of the countries with the highest breastfeeding rate for the first six months of infancy, while Greece is known to have low exclusive breastfeeding, which could be reflected in the concentration differences of PBDEs.

Perfluoroalkyl substances (PFAS) are fluorinated chemical compounds, made by human and listed as persistent organic pollutants. They are persistent in the

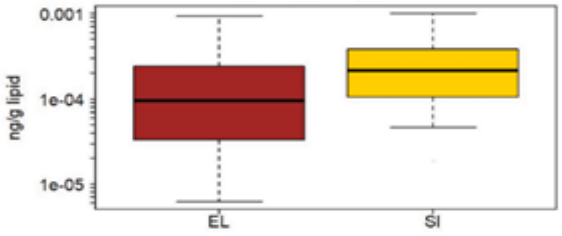


Figure 11. BDE-47 levels between Greece and Slovenia cohorts

environment, widespread and bioaccumulating in both humans and wildlife. The use of PFAS include surface coating and protectant formulations, firefighting foams, paper and cardboard packaging products, carpets, leather products, and water- and stain-proof textiles.

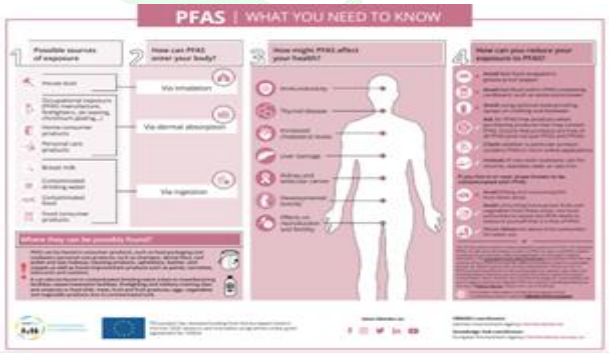


Figure 12. Factsheet from HBM4EU project on PFAS

PFOS is the most abundant PFAS compound, followed by PFOA, PFHxS and PFNA.

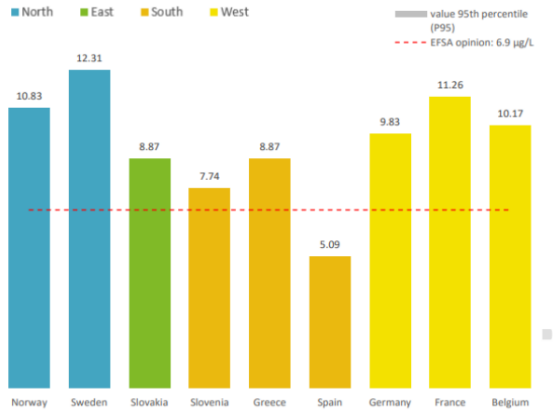


Figure 13. Levels of sum of PFOS, PFHxS, PFOA and PFNA in blood (µg/L) of 2000 teenagers in Europe – P 95 (2014-2021)

In the basic model adjusted for sex and educational level of the household, geographical region was a strongly influencing factor on the estimated exposure levels. Significantly higher levels were observed in the North and West of Europe versus the South and East for all four PFASs.

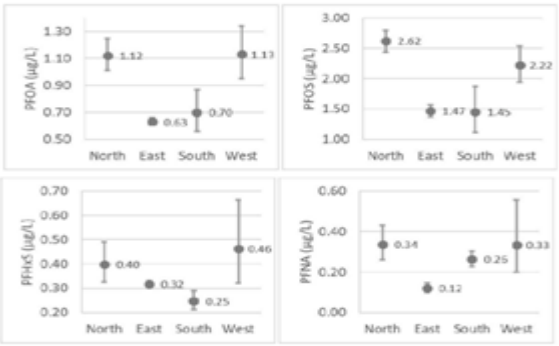


Figure 14. Plasma/serum concentrations of PFOS, PFOA, PFHxS and PFNA by European region adjusted for sex of the participant and educational level of the household.

Plasma/serum concentrations of PFOS, PFOA, PFHxS and PFNA by European region adjusted for sex of the participant and educational level of the household.

Higher PFOS levels are significantly associated with offal consumption and higher consumption of local food. Consumption of local food at least 2 times per week was associated with higher levels of PFOS.

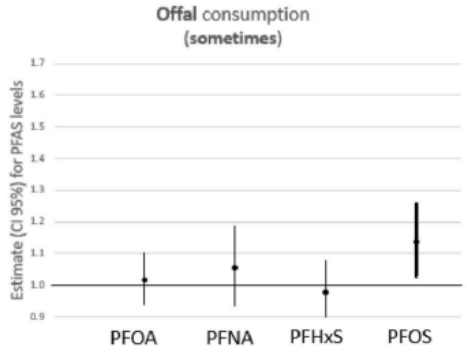


Figure 15. Associations between PFAS concentrations in teenagers and food consumption

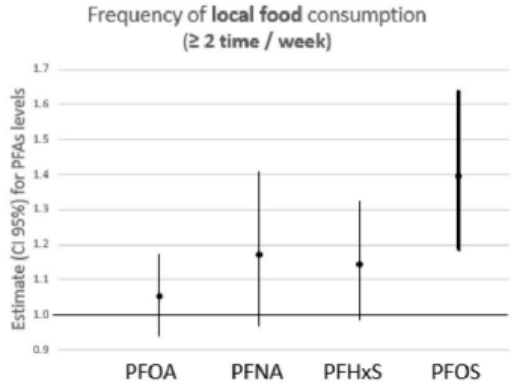


Figure 16. Associations between PFAS concentrations in teenagers and food consumption

The CROME study as it was mentioned and above includes the recruitment of children and adolescents as well as the whole family and parents. For children the ages were between 6-11, adolescents between 12-18 and the adults in the study were from 19-68 years.

The levels in human biofluids for the following exposure biomarkers have been quantified in all samples including all age levels: 15 phthalate metabolites: MEP, MBzP, MiBP, MnBP, MCHP, MnPeP, MEHP, 5OH-MEHP, 5oxo-MEHP, 5cx-MEPP, MnOP, OH-MiNP, cx-MiNP, OH-MiDP, cx-MiDP and 2 DINCH metabolites: OH-MINCH and cx-MINCH.

What is very interesting is the extreme higher level of all the phthalates in children and teenagers versus the levels in adults. Very interesting is also the fact that the participants are families meaning that the children and teenagers in this study even if they in the same house as their parents they still present higher concentrations in all phthalates measured.

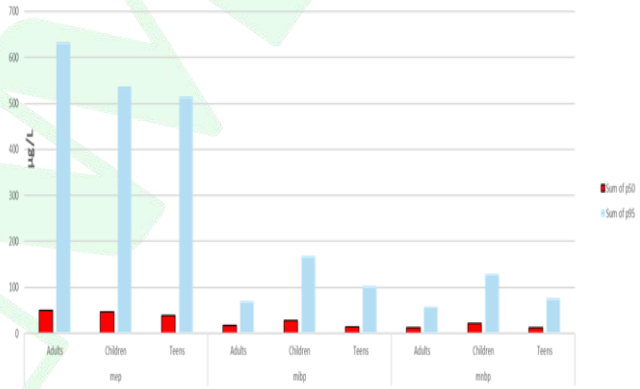


Figure 1718. Concentrations of metabolites in percentiles per age group

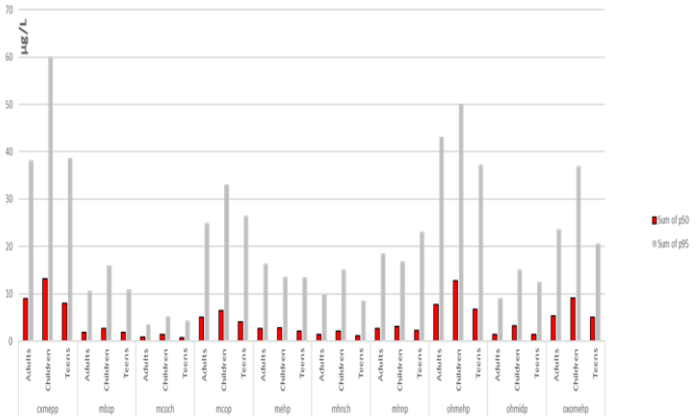


Figure 19. Concentrations of metabolites in percentiles per age group

MoM study

Mercury is a substance of high concern globally. It is biotransformed to methylmercury (MeHg), a potent developmental neurotoxicant bioaccumulating in aquatic food chains. Fish consumption during pregnancy can expose the fetus to mercury, but at the same time provides essential nutrients for optimal brain and eye development. The benefits can outweigh the risks if suitable dietary advice is followed. The harmonized European intervention study 'HBM4EU-MOM' combined fish consumption advice to pregnant women with human biomonitoring (HBM), to assess and control prenatal exposures to mercury.

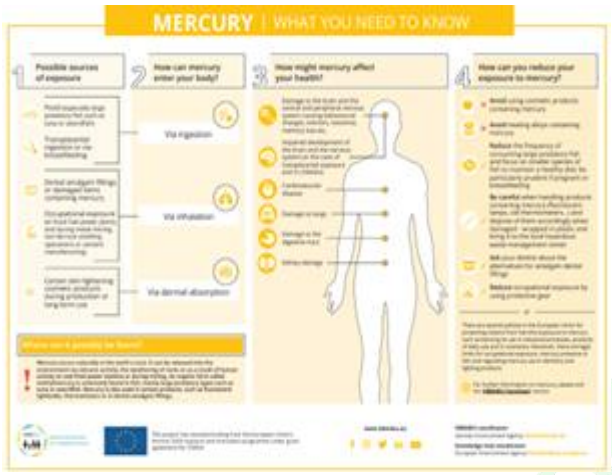


Figure 20. Factsheet from HBM4EU project on Mercury

The study was given the acronym "HBM4EU-MOM" ("Methylmercury-contrOl in expectant Mothers through suitable dietary advice for pregnancy"). Its aim was to provide new scientific evidence in support of several open policy questions on mercury, including: (a) evaluation of the effectiveness of current European policies in controlling human exposure to mercury (b) collection of new harmonised, validated, comparable information to support and evaluate policies, (c) assessment of the current geographic spread of current exposure and its determinants, (d) raising the awareness of the public and health professionals and (e) developing / providing suitable advice to vulnerable population groups.

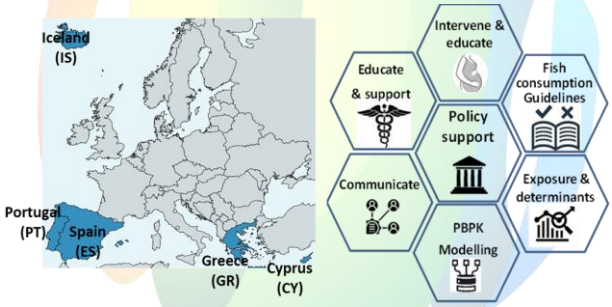


Figure 21. Map showing the EU countries participated in the HBM4EU-MOM study.

Harmonized tools for HBM and communication of dietary advice were developed and applied in five countries (Cyprus, Greece, Portugal, Spain, Iceland). 654 women, recruited during early pregnancy in 2021, provided hair samples for mercury biomonitoring and extensive information about their fish consumption practices and preferences. Targeted fish consumption advice was communicated to half of the participants of each national cohort and exposures were reassessed after ≥12 weeks.

Figure 22. Intervention Leaflet created in the frame of HBM4EU-mom study.

Mercury levels in the hair of women participating in Phases 1 and 2 of the study are presented as box and whisker plots presenting the range (vertical lines), upper and lower quartiles (box), outliers (single dots) and the 50th percentile (horizontal line in the box).

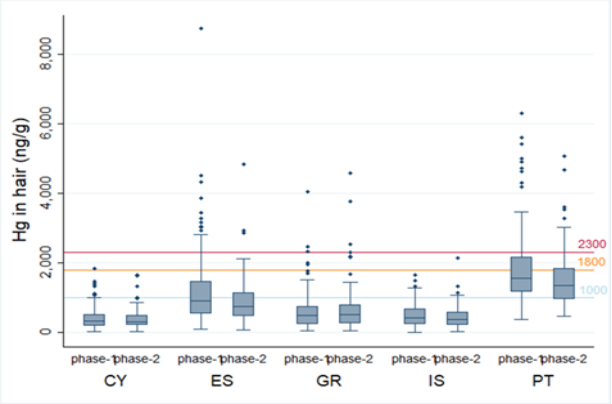


Figure 23. Distribution of Hg levels in hair (ng/g) of the study participants in Phases 1 and 2.

The levels of Hg in scalp hair of HBM4EU-MOM participants were compared with the available health-based levels that were established to protect an unborn child against neurodevelopmental toxicity.

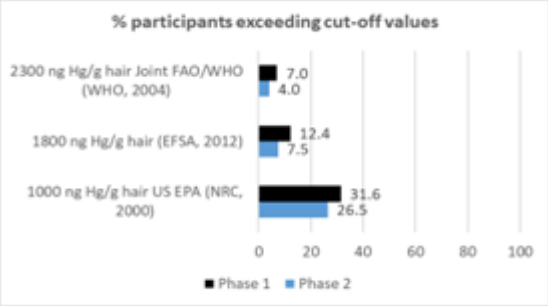


Figure 24. Percentage of participants (n Phase-1=654), who exceeding available health-based guidance values for Hg in hair

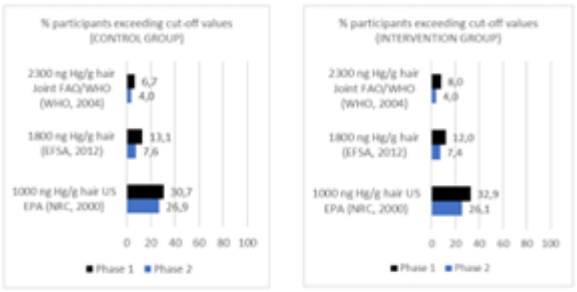


Figure 25. Percentage of participants exceeding available cut-off values for neurodevelopmental toxicity in the Control (left) and Intervention (right) groups

As hypothesized, overall fish consumption frequency was significantly associated with Hg levels in hair, both before and during pregnancy ($p<0.001$). Hair Hg was also associated with the frequency of consumption of each of the four large categories: white; small fatty; large fatty; other (in all four cases, $p<0.001$), without adjusting for possible simultaneous consumption from multiple categories.

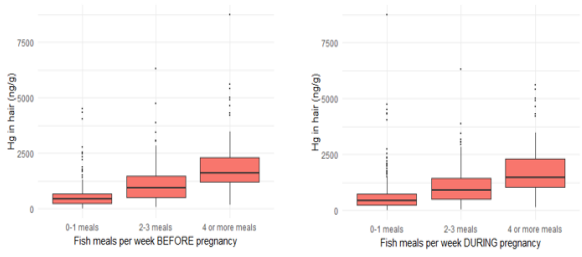


Figure 26. Hg levels in hair according to the fish consumption frequency before (left) and during (right) pregnancy (both $p<0.001$).

In the HBM4EU-MOM study, the following methodological scheme has been followed, as illustrated in 11: starting from the hair MeHg, using the PBPK model coupled with the exposure reconstruction algorithm, intake levels have been estimated. These intake levels, have been then used in the mother-foetus PBPK model (in forward mode) to estimate the internal concentration of MeHg in the developing foetus.

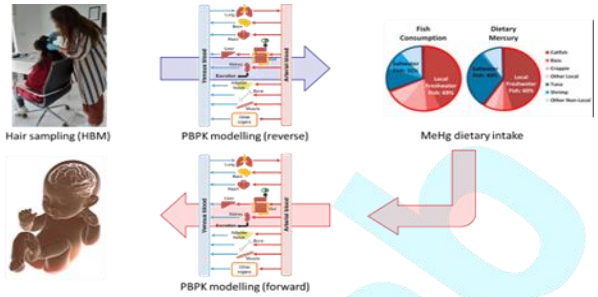


Figure 27. HBM4EU-MOM modelling methodological approach

The impact of the intervention on the potential biomarker levels (hair, urine and blood) is illustrated in Figure 22, where the computed levels of a typical individual of 0.5 µg/kg_bw/w, follows the advice and reduces her intake by 50%. From the simulation it is also evident that urine is not at all a suitable matrix for MeHg.

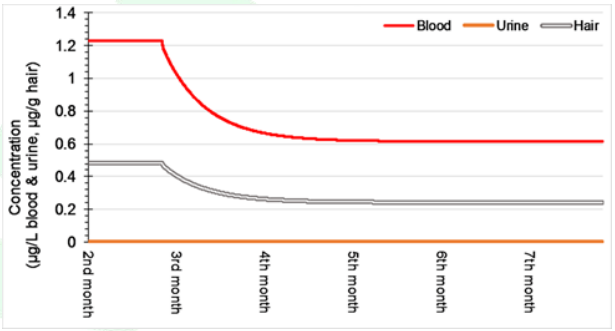


Figure 28. Reduction of MeHg concentration in hair, urine and blood following the intervention assuming a change in intake (from 0.5 to 0.25 µg/kg_bw/w).

Based on the intake levels of the mother, internal dose of MeHg in the target tissue of interest (which is the foetal brain) has been estimated. For most of the participant foetuses, internal concentration of MeHg was between 1 and 10 µg/L. At this stage it is important to mention that the reduction of maternal intake levels is reflected in reduction of internal exposure to foetus.

It has to be noted that internal concentration is an important estimate that can be used for in vitro studies investigating the impact of toxicants such as MeHg in neurons, as well as for defining the dose-response of the molecular initiating event (MIE) of adverse outcome pathways (AOPs) relevant to MeHg and neurodevelopmental disorders.

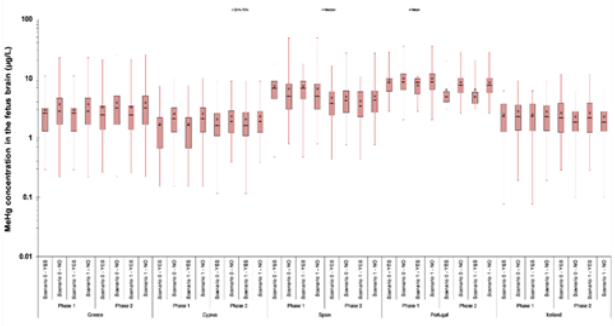


Figure 29. Internal concentration of MeHg in the brain of the developing foetus

Copper biokinetics

Copper is an essential trace element widely found and used in everyday life. Thus, it is often found in human body via several exposure routes. Copper can be found abundant in the earth's crust as it naturally occurs in rock, soil, water, plants, sediments and animals. It is an important nutrient used in cellular respiration, antioxidant defense, iron metabolism, neurotransmitter production, and connective tissue development that, in low levels is beneficial in maintaining health. The main exposure routes of copper for humans is through diet and for the general population, most exposure to copper originates from the ingestion of food. Copper mitigates to the edible end products as it is used in crops fertilizers or by using copper-containing cooking utensils.

A lot of scientific debate regarding copper is related to its biokinetic behaviour. Copper is absorbed, distributed, stored, and excreted in the body via a complex of homeostatic processes, providing a more or less constant level of this micronutrient and avoid excessive whole body amounts and toxic levels in blood and tissues. In humans, copper participates in ADME processes through a complex of homeostatic procedures, that maintain copper amounts at an almost constant level, avoiding excessive toxic quantities in tissues and blood.

By working more in depth on previous modelling efforts for copper, we concluded that they lacked a physiological basis, being able only to partially describe toxicokinetics of short-term exposure regimes, i.e. being able to describe changes that occur after a single dose for a few days, but not to describe the time course of chronic intake. For this purpose, we focused on the parameterisation of the generic PBPK model of INTEGRA. The generic PBTK model developed in INTEGRA is designed to describe in as much as possible detail the ADME processes occurring in the human body at different life stages, so as to be easily applicable to a broad variety of chemicals after proper parameterization. The model in its generic form includes the parent compound and up to three generations of potential metabolites. Major effort was on the adjustment of hepatobiliary recirculation, so that it may reflect internal excretion, in order to match better the intake-dependent intestinal absorption and internal excretion. The reabsorption term was modelled based on the data of toxicokinetics studies indicating a negligible change in blood levels. Model parameterisation was based by following the following principles:

- For an average daily intake of 1.4 mg/d for a healthy male adult of 75 kg bodyweight, a target concentration for steady state whole blood concenration was 1.35 mg/L and 12 μg/L for urine
- The feces excretion rate and the hepatobilary recirculation rate concentration had to be intake-dependent so us to maintain the blood homeostasis for a broad range of daily intake regimes (0.66 to 2.5 mg/d), following the experimental data delivered by Turnlund et al. (1998).
- Overall body burden should be kept to 110 mg, partitioned in liver, bones and muscles as described in Bost et al. (2016).

Based on the parameterisation described above, the model was able to reproduce the existing experimental data, where eleven young men were confined to a metabolic research unit for 90 d. The study was divided into three periods, where dietary copper intake was 0.66 mg/d for 24 d, 0.38 mg/d for 42 d, and 2.49 mg/d for 24 d Overall, the study identified that the amount of copper excreted was lower when dietary copper was low and increased with higher intakes of dietary copper, clearly affecting the overall amount of copper actually absorbed.The results of the measured (green points) versus the modeled (blue points) fecal excretion rate during the experimental period are presented in Figure 30. This was the result of adjusting the hepatobilary recirculation as a function of the homeostatic levels of copper in human body. In addition, the whole blood concentration (red line) and the urinary excretion (yellow line) are illustrated as well. The agreement of the model with the experimental data of this study is very important, because it reflects the capacity of the model to capture the copper homeostasis under real life intake patterns.

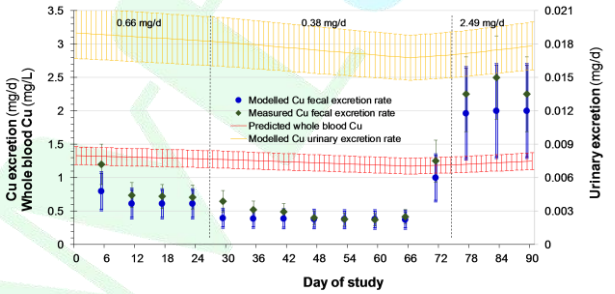


Figure 30. Measured (Turnlund et al. 1998) versus modelled feces excretion rate of copper during different intake periods, whole blood concentration and urinary excretion rate

The copper model is able to describe the lifelong exposure toxicokinentics for the general population. In the following figure, the lifecourse of the copper concentration in blood corresponds excellent with the data obtained from the available HBM studies. What is of particular interest is that the significantly lower concentration related to neonates (which is not attributed to the lower bodyweight normalized exposure for the different developmental stages) is very well captured. In addition, when the copper concentration in blood is in steady state, the amount that of copper stored in the body (~110 mg) is distributed in the tissues, while the reported equilibrium in particular tissues (28 mg in muscle, 46 mg in bones and 10 mg in liver) are explicitly captured by the model. The HBM data collected from WP10 were useful to allow us to identify the age-dependent differences of copper levels in whole blood. A summary of the modelling work is presented in Figure 31, where the lifetime course of copper in blood is described (continuous line) together with the measured data (box plots reflecting 5%, 25%, median, 75% and 95% of the measured copper levels).

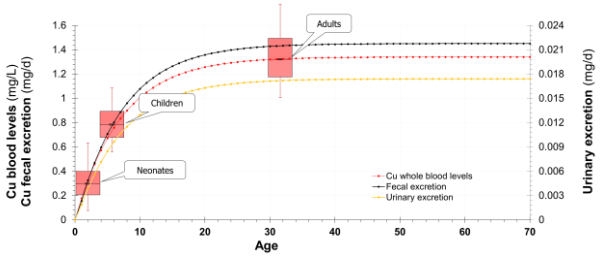


Figure 31. Lifetime course of copper in whole blood. The continuous line represents the modelled levels, while the box plots reflect the collected biomonitored levels

Risk assessment based on HBM data

This methodological work aimed at demonstrating how human biomonitoring (HBM) data can be used in conjunction with the latest reverse dosimetry tools to perform risk assessments. The intake estimates delivered herein, are based on the aggregate data available within the HBM4EU dashboard that include both the HBM4EU repository data, as well as the one from the aligned studies. A significant effort was made to provide exposure estimates for as many as possible substances, while maintaining an EU-wide coverage of exposure of different age groups. Depending on the substance and the cohort availability, populations of interest were children, pregnant women, general population and/or workers. Current available PBTK models were used together with stochastic algorithms to perform the reverse dosimetry. From the risk analysis regarding the 2nd set of priority substances, the following conclusions can be drawn:

Benzophenones: Median risk characterisation levels of the various benzophenones, are below 1 for all age groups and countries. The highest median risk characterisation ratio was observed for females, which was 0.015 compared to the males, which was 0.007.

Diisocyanates: Median risk characterisation levels of MDI depend upon the occupational activity; lowest risk ratio levels (median in the range of 0.101) were identified for spray painting workers, while the highest risk ratio levels (median in the range of 8.633) have been identified for PUR industry workers.

Aprotic solvents: With regard to aprotic solvents, median characterisation levels of NMP for Germany have been estimated in the range of 0.002 for adults, children and teenagers.

Acrylamide: Median risk characterisation levels of Acrylamide for children have been estimated in the range of 0.02 considered the toxicological reference value for tumors and 0.008 considered the toxicological reference value for other effects. Regarding adults of different European countries, the median risk characterisation ratios were 0.018 and 0.006 respectively.

Mycotoxins: Highest median risk characterisation levels of DON for adults in Italy have been estimated in the range of 3.25, followed by UK (2.93), Croatia (2.11), Germany (1.69), Sweden (0.72) and Belgium (0.54).

Pesticides: Median risk characterisation ratios of cis-permethrin and trans-permethrin for children of different European countries have been estimated in the range of 0.015 and 0.001 respectively, while highest median risk characterisation level of deltamethrin for children in Cyprus was observed in the range of 0.48. Regarding adults of different countries, the highest median risk characterisation level of cis - permethrin was observed in Belgium (0.025). The median risk level of trans – permethrin for adults of different countries was in the range of 0.0004 while the highest median risk level of adults was observed in the range of 0.06 for deltamethrin. Median risk characterisation ratios of chlorpyrifos for children and adults of different European countries have been estimated in the range of 0.09 and 0.03 respectively. Regarding Glyphosate, the median risk level for adults of Belgium and Spain was 0.0002.

Arsenic: Lowest median MOE levels of arsenic for teenagers of different countries were observed in Sweden and Spain (0.8) for toxicological reference value BMDL01 = 0.3 μg/kg_bw/day and 20.5 for toxicological reference value BMDL01 = 8 μg/kg_bw/day. Regarding adults, lower median margin of exposure values of arsenic have been estimated in Norway and Slovenia (1.6 and 2.3) for toxicological reference value BMDL01 = 0.3 μg/kg_bw/day and 43.1 and 62.2 by taking into account the toxicological reference value BMDL01 = 8 μg/kg_bw/day. However, it has to be noted, that because arsenic is genotoxic, MOE for must be 10000 in order not to signal a risk with a high need for action.

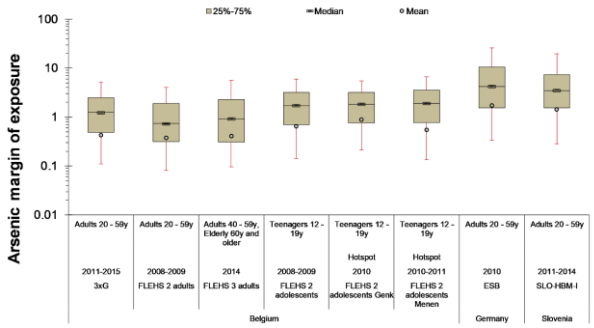


Figure 32. Margin of exposure of Arsenic (based on urine HBM) for adults, pregnant women, teenagers and workers of Belgium, Germany and Slovenia (BMDL01 = 0.3 μg/kg_bw/day). Upper end of the line: minimum value, lower end of the line: maximum value, upper end of the box: 25th percentile value, and lower end of the box: 75th percentile value

Lead: Median risk characterisation levels of lead for infants in Belgium have been estimated in the range of 0.47–1.06, followed by adults 0.21–1 and teenagers 0.14–0.37. Regarding different age groups of Czech Republic and Germany, higher median risk ratios for children were in the range of 1.1–1.4 and 0.83–1.25 respectively.

Mercury: Highest median risk ratio of methylmercury was observed for adults in Spain (0.56). The median risk characterisation level of methylmercury for different European countries was in the range of 0.11.

Overall, this important methodological work has clearly demonstrated the feasibility to perform risk assessments using HBM data and reverse dosimetry. It also emphasises how the use of these tools can provide policy makers with the information necessary to prioritise chemicals and populations for which the risk cannot be ruled out.

Exploring The Neurological Exposome (NEUROSOME)

NEUROSOME is a European integrated training network which investigates the causal associations among genetic predisposition, cumulative exposure to multiple environmental chemicals of children and neurodevelopmental disorders. The project brings together beyond- the-state-of-the-art advances in human biomonitoring and systems biology, exposure monitoring and toxicological testing technologies and advanced tools for computational analyses of the exposure-to-health effect continuum according to the exposome paradigm

Figure 33. The NEUROSOME logo

The NEUROSOME methodology will be applied in population studies across different exposure settings to neurotoxicants (metals and selected organic compounds) in Europe. This will help us understand how environmental stressors lead to or exacerbate neurodevelopmental disorders. New standards for human biomonitoring data interpretation in conjunction with environmental and exposure information will be developed for ready use in chemical mixture risk assessment. The project would rely on the evaluation and reanalysis of existing cohort biosamples (e.g. PHIME, INMA, PROBE, Taranto, CROME, HEALS, PELAGIE, MECANA) and selected re-sampling and external exposome assessment of the populations involved in the above studies.

In the NEUROSOME study, we shall investigate:

- the effect of genetics and the signalling pathways which could modulate the detrimental effects of toxic metals (Hg and MeHg among them) and selected organic compounds (phthalates, phenols, POPs) at low exposure in Mediterranean cohorts.
- cumulative exposure of compounds relevant to neurological disorders such as toxic metals and specific organic chemicals (e.g. organophosphate pesticides), since there is a significant body of evidence showing a greater than additive effect of co-exposures to toxic metals and organic compounds.
- the interplay between genetic variability and co-exposure to environmental chemicals for extended periods of time and how this contributes to the development or exacerbation of central nervous system disorders during child development (neurodevelopmental disorders) and later in life (neurodegenerative diseases).

NEUROSOME is funded in the frame of Marie Sklodowska-Curie Actions (MSCA-ETN- ITN) with an overall budget of

3.49 million Euros from the European Commission's Framework Programme Horizon 2020 over the course of four years, starting from 01 October 2017. The project is coordinated by Prof. Denis Sarigiannis. The project consortium is made up of 9 Beneficiaries Institutions and 5 Partners Organizations among the leading and well-experienced Organisations both in Europe and USA with a huge training experience in Environment and Health.

NEUROSOME places particular emphasis on the training of young researchers providing support for 14 Early Stage Researchers (ESRs) in all. NEUROSOME seeks to train the next generation of exposome scientists able to tackle the global challenges associated with the impact on human health due to environmental exposure. Great emphasis is placed on training ESRs through collaborative exchanges and practical courses. The ultimate goal is to produce a new generation of exposome researchers, trained in academia, applied research and industry, with transdisciplinary skills (environmental end exposure modelling, human biomonitoring, -omics technologies, high dimensional bioinformatics and environmental epidemiology) and understanding of fundamental science and its direct application to environmental health challenges.

NEUROSOME aims at protecting public health against neurodevelopmental disorders using the latest advances in environmental health science, namely the exposome paradigm. Although environmental health literature is rich with knowledge on the individual steps linking environmental contamination to disease, there is a lack of established causality for developing the respective Adverse Outcome Pathways (AOPs), especially considering cumulative exposure, where different mechanisms of toxicity are involved, interacting with each other on different levels of biological organization, dynamically in time. To better describe an AOP, we need to identify all the key processes from exposure to health outcome, corresponding to different molecular signatures revealed by multiple omics technologies. Overall, this requires synthesis among different scientific disciplines, including environmental and exposure modelling, recent advances in toxicology (including in vitro, in vivo and in silico aspects) with a special focus on omics technologies and bioinformatics, as well as environmental epidemiology, taking stock of gene- and exposome-wide associations

An integrative strategy of testing systems for identification of EDs related to metabolic disorders (OBERON)

Aims and scope

Exposure to chemical substances that can produce endocrine-disrupting effects is one of the most critical public health threats. In line with the regulatory framework implemented within the European Union to reduce the levels of endocrine disruptors (EDs) for consumers, new and effective methods for ED testing are needed.

The OBERON project will build an integrated testing strategy (ITS) to detect EDs-related metabolic disorders by developing, improving and validating a battery of test systems. It will be based on an integrated approach for testing and assessment (IATA). OBERON will combine 1) experimental methods (in vitro, e.g., on 2D and 3D human-derived cells and tissues, and in vivo, i.e. in zebrafish at different stages), 2) high throughput omics technologies, 3) epidemiology and human biomonitoring studies and 4) advanced computational models (in silico and systems biology) on functional endpoints related to metabolism. Such an interdisciplinary framework will help decipher EDs based on a mechanistic understanding of toxicity by providing and making available more effective alternative test methods relevant to human health that align with regulatory needs. Data generated in OBERON will also allow the development of novel Adverse Outcome Pathways (AOPs). The assays will be pre-validated to select the test systems that will show acceptable performance in relevance for the second step of the validation process, i.e. the inter-laboratory validation as ring tests. Therefore, the OBERON project aims to support the OECD conceptual framework for testing and assessing EDs by developing specific assays not covered by the current tests and to propose an IATA approach for ED-related metabolic disorders detection, which will be submitted to the JRC and OECD community.

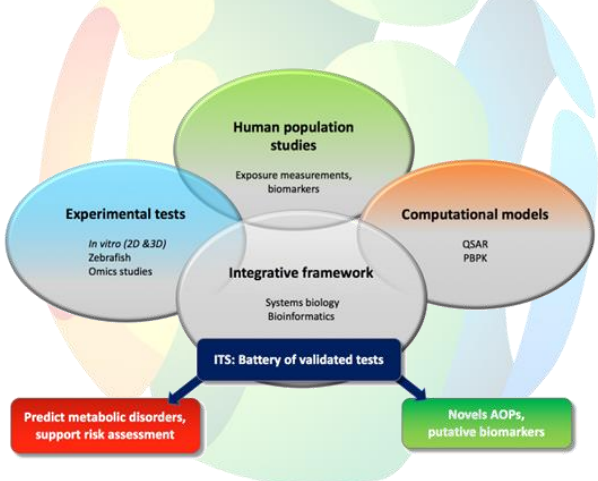


Figure 34. The OBERON platform. Data and model systems that are existing, or that will be developed within the OBERON consortium The OBERON project aims to establish an innovative IATA by providing a battery of effective and validated test systems for ED assessment of metabolic disorders.

Indeed, despite the high incidence of metabolic diseases, most available mammalian in vivo assays do not inform EDs' mechanisms of action, and metabolic disorders' specific endpoints are missing. Therefore, the developed tests should help predict ED-related metabolic diseases that are essential for industries and regulatory needs. In terms of strategy, the project will 1) involve multidisciplinary aspects (in vivo, in vitro in silico, and epidemiological studies), 2) integrate experimental and computational test systems, 3) provide effectively and validated screening tests, and 4) involve international regulatory agencies and stakeholders to meet regulatory requirements. Therefore, to reach the proposed aims, several objectives have been defined:

Objective 1: To integrate epidemiology and human biomonitoring studies with ED test systems for metabolic disorders.

Objective 2: To develop whole organism test systems to identify EDs implicated in metabolic disorders. Zebrafish studies can generate unique full-organism models based on in vivo embryo/larva models.

Objective 3: To develop human-relevant in vitro test systems to identify EDs involved in metabolic disorders and increase mechanistic knowledge by generating 2D and 3D integrated cellular models.

Objective 4: To provide computational models to help prioritise EDs based on their physicochemical properties (Quantitative Structure-Activity Relationships models: QSAR models) and to gain cellular dose information (PBPK models) that is essential for the integration of human biomarker data and meaningful extrapolation of in vitro assays results.

Objective 5: To establish an integrative testing strategy (ITS) and capture the mechanistic effects of EDs on metabolic disorders by integrating *in vivo, in vitro* and in silico test results and generate possible linkages with human exposure data from biomonitoring and cohorts. The outcomes from all integrations, including high throughput studies (omics) and the use of systems biology, will provide mechanistic knowledge such as molecular initiating events (MIEs) and key events (KEs), allowing the development of novel AOPs.

Objective 6: To propose a decisional tree based on a tiered IATA using the different validated models & tools gathered in the project. This will allow for a new substance to know which tests to be used to determine if this compound is a putative ED concerning metabolic disorders.

Objective 7: Cooperation with regulatory agencies and international organizations.

Multi-omics analysis

The multi-omics analysis is a powerful approach enabling the interpretation of omics data at a higher level than individual biomarkers, thus providing mechanistic insight into metabolic pathways dysregulation, which is causative or indicative of metabolic disorders.

In the OBERON project *in vivo* and *in vitro* samples were exposed to 10 compounds related to ED metabolic disorders. Two of the compounds presented here are Amiodarone, which was used as a positive control, and the common phthalate compound DEHP. In the case of *in vivo* samples, omics data optioned by the zebrafish larva five days post fertilization (5dpf) after exposure to DEHP and Amiodarone. In the case of the *in vitro* samples, expressed genes and metabolites resulted from the 3D HepaRG transcriptomics and metabolomics analysis, respectively. The INTEGRA computational platform was used to calculate the concentrations of the chemicals through the extrapolation from human biomonitoring data.

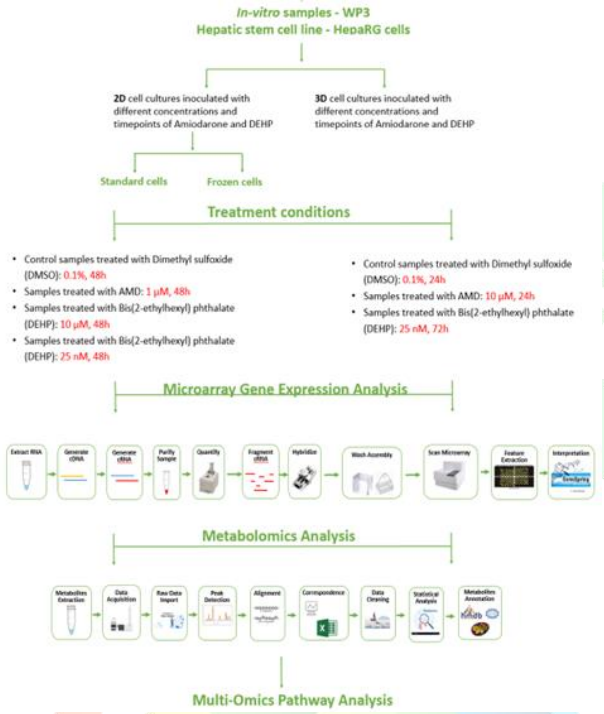


Figure 35. Transcriptomics, and metabolomics analysis workflow. Regarding metabolomics, untargeted metabolomics analysis was performed, using an Agilent 6540 QTOF instrument, two different analytical columns (C18 - RP and HILIC), and two different ionization modes

Two methods were used for the integrated analysis of transcriptomic and metabolomic data that exploits the fact that genes and metabolites are linked through biochemical reactions; the over-representation analysis (ORA) and the enrichment analysis (EA). ORA is a widely used method to determine whether known biological functions or processes are enriched in experimentally-derived biomarkers lists. The disadvantage of ORA is that once a biomarker passes the statistically significant threshold and is included in the import list, will be treated with identical weight to all the other items in the list. To overcome this, a multiple-testing correction was applied during the statistical analysis to minimise the false positives in the transcriptomics and metabolomics list.

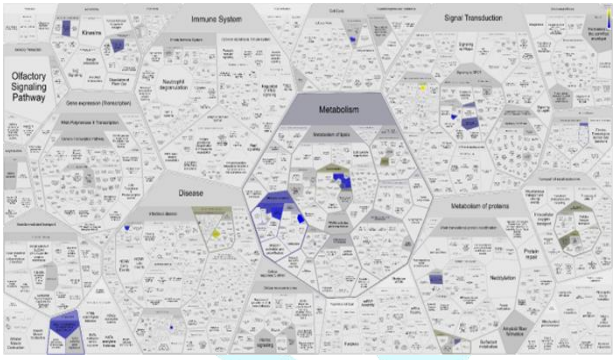


Figure 36. Overview of the dysregulated pathways based on the differentially expressed genes.

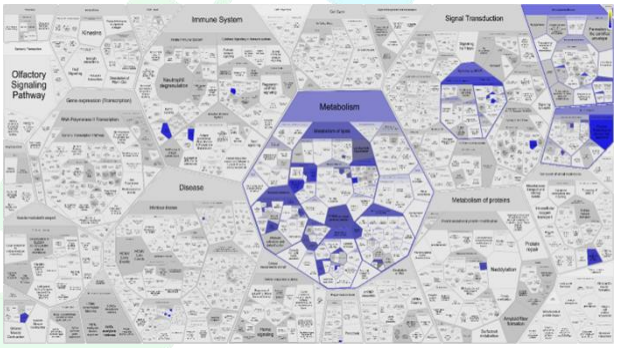


Figure 37. Overview of the dysregulated pathways based on the differentially expressed metabolites.

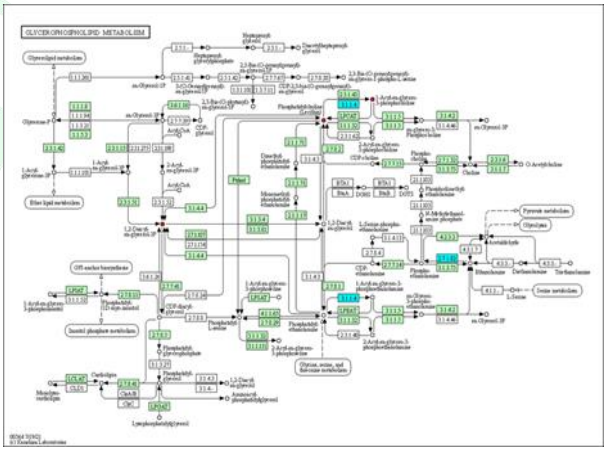


Figure 38. Glycerophospholipids metabolism, a subpathway of lipids metabolism, found to be significantly dysregulated, due to the differentially expressed values of the following genes and metabolites: phospholipase A2 group IIE (PLA2G2E), ethanolamine kinase 2 (PLA2G2E), phosphatidylcholine (C00157), phosphatidate (C00416), 1-acyl-sn-glycero-3-phosphocholine (C04230).

Systems biology models

Our approach to the development of systems biology mathematical models includes a purely computational method, where it is carried out by importing the results of pathways analysis which has as input coming from the multi omics produced in the framework of OBERON pro. More specifically, taking all the pathways that have been found and by referring them to KEGG database and with use of Bioconductor, are being imported into the R programming environment, in KGML format, a structured text format that has a lot in common with SBML. This type of methodology could be generalized if, instead of using pathway analysis data as input, KEGG pathway id is being imported directly. Some preliminary results of the mathematical network of endogenous metabolites are illustrated below (Figure 39).

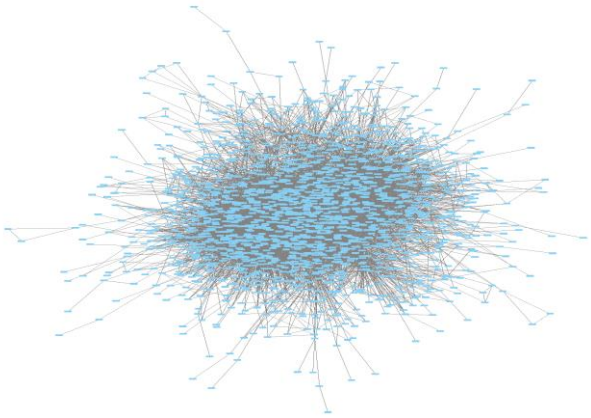


Figure 39. Systems Biology Network

Our analysis includes the total number of nodes and edges that are involved in every metabolic pathway. In this way, many pathways with several hundreds of endogenous metabolites as well as interactions between them are collected in a format that is machine readable. At this point using MINER, a text mining toolbox, which we developed here in Thessaloniki, the .KGML files are converted into a large-scale system of differential equations, by combining information that contained in data obtained from the KEGG database. A graphical abstract of our methodology is shown at Figure 40.

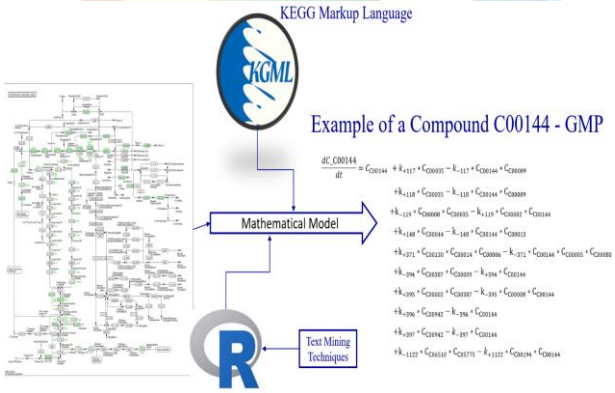


Figure 40. Graphical Abstract of transformation between KGML format to systems biology mathematical model

As can be seen, for each endogenous metabolite there is a differential kinetic equation that describes it. A graphical summary of this methodology is lied below. The next step regards with the parameterization of the mathematical model that has been constructed, and more specifically the determination of the kinetic parameters that enter into the differential equations. To achieve this, a combined set that originated from the BRENDA, SABIO and UNIPROT databases with information related to: (a) Turnover Number of wild enzymes; (b) Sequence Information concerning wild enzymes; (c) Endogenous metabolites (substrates and products) structure information; (d) .mol files of every endogenous metabolite is being constructed.

By constructing the datasets, three different Deep Learning models were implemented by using the following well known algorithms: (a) xgBoost; (b) TensorFlow and Keras; (c) R – Neuralnet.

Three different algorithms were tested aiming at which one fits better the data as well as for possible deviations during the evaluation tests. An important point of view that requires a lot of time and effort concerns the selection of parameters regarding the models that were tested. For that reason, we have spent a lot of time testing different sets of optimization parameters to find the appropriate one that returns the highest performance for the constructed model.

Next step of this methodology is the development of AOPs. Given that, it is possible to know all the nodes with which an endogenous metabolite is connected/interacts, as well as the differential kinetic equation that describes this part of the process by using MINER. As result of that, hundreds of endogenous metabolites are used for the construction of those models. Consequently, with a perturbation signal on a node it is directly known, which other nodes will be quantitatively affected and to what extent and potentially the deregulation of the system if it is not turn back to its normal condition.

Given a known outcome, as the ones that can be seen below and were investigated during OBERON project: (a) obesity; (b) diabetes; (c) chronic liver diseases or (d) metabolic syndrome; (e) steatohepatosis, and by adopting a bottom-up approach by looking at databases like DisGeNET, it is known which genes are the ones that associated with which diseases and in this way, building AOPs and branches of them can be initiated, ending up on the other side of the chain where there will already be existed pieces of information about every chemical that has been studied in the framework of OBERON project. In this way, it is possible to know all the KERs (Key Events Relationships) as well as all the key events that lead to the occurrence of an AOP and sum up them to a systems biology model. In addition, can be constructed very comprehensive AOP networks based on a chemical and an outcome. This procedure will give to a third person a clear view for the rest of components of an in silico AOP.

Simultaneously, this specific approach allows the construction of particularly comprehensive kinetic qAOPs, which is one of the main goals of the present project, since every kinetic node is already known from the systems biology model that has been developed. As can be seen, all key points and paths leading to an AOP are already quantified (qKE, qKER). Given that, Integrative testing strategy can be fed with very helpful data and directly use these models.

Computational tools towards IATA

Text Mining Tools

Tools based on artificial intelligence that can be used to systematically explore available toxicological data (and not only) that can be parsed in the scientific literature. Two different tools were developed in the framework of the OBERON project:

- AOP-helpFinder developed by INSERM
- Miner· A Text Mining Toolbox developed by AUTH

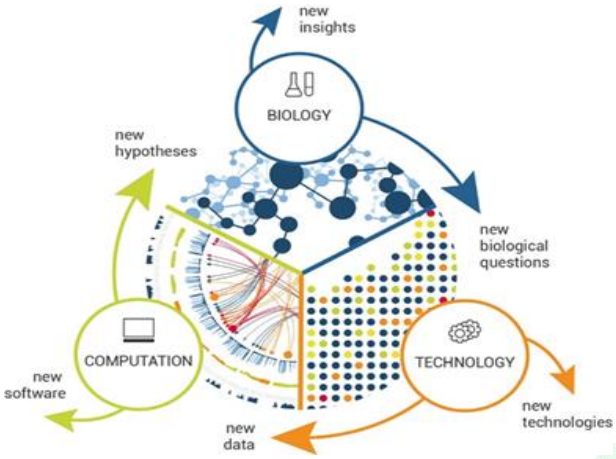


Figure 41. Systems Biology Approach

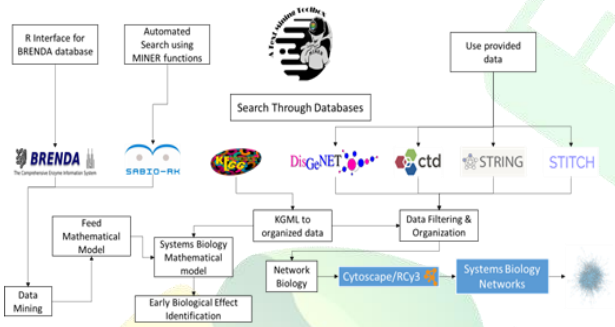


Figure 42. Applications of MINER

The OBERON Database

The development of the OBERON database hosting by AUTH IT Center for the storing and sharing of the different types of data involved in the project, revolves around the Dataverse Software. The Dataverse software offers a variety of features:

- Support for FAIR Data Principles
- Data citation for datasets and files
- APIs for interoperability and custom integrations
- Versioning
- File hierarchy and file previews
- Various Integrations (Dropbox, Github)
- File download in R and TSV format

The system will be prepared to accommodate future adapters either for locally stored or remotely stored datasets and integrate them in the Integrated Data Management system.

Molecular biology/biochemistry and clinical data will be retrieved from the existing databases and/or performed experiments, and accessed through hyperlinks and query scripts.

Additionally, another goal is to create a tool/library with a user-friendly interface based on the R codes developed for the bioinformatics analysis of the transcriptomics, and metabolomics analysis.

Integrative testing strategy

The main objective is to make the most efficient use of all available data and converge toward an integrated testing strategy (ITS) that couples advanced bioinformatics and computational analysis of toxicological and biomonitoring data to targeted testing assays.

We will combine and leverage two approaches 1) identifying the relevant mechanism as AOP and 2) composing the IATA to reflect its key events or by data mining via machine learning, e.g. Bayesian networks, to optimize the strategic data integration.

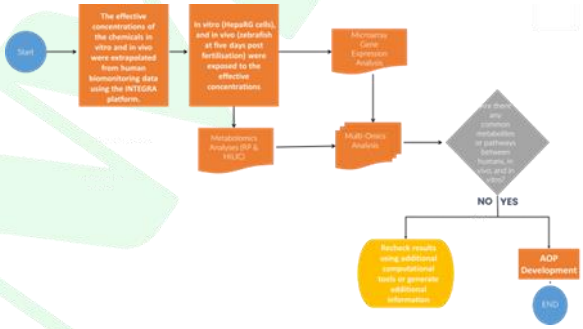


Figure 43. Integrative testing strategy workflow

Database with omics biomarkers

Creation of a database with the omics biomarkers based on the transcriptomics & metabolomics analysis of human, *in vivo, & in vitro* samples. The integration of multi-omics data will increase our knowledge of the effects of EDCs exposure to metabolic disorders and will lead to the identification of valuable biomarkers.

Partnership for the Assessment of Risks from Chemicals (PARC)

Aims and scope

PARC is a 7 years public-public partnership under Horizon Europe with a 400 millions euros co-funded budget. PARC started as an initiative where the European Union, prepared with early involvement of Member States and Associated Countries, together with public partners (EU and National Risk Agencies, Universities, Public Research Organisations), commit to jointly support the development and implementation of a programme of research and innovation activities in relation with the assessment of risk of chemicals. PARC is an EU-wide research and innovation partnership programme to support EU and national chemical risk assessment and risk management bodies with new data, knowledge, methods, networks and skills to address current, emerging and novel chemical safety challenges.

Figure 44. PARC participating countries

PARC will facilitate the transition to next generation risk assessment to better protect human health and the environment, in line with the Green Deal?s zero-pollution ambition for a toxic free environment and will be an enabler for the future EU Chemicals Strategy for Sustainability?. It builds in part on the work undertaken and experience acquired in past and on-going research and innovation actions, but goes beyond by its vocation to establish an EU-wide risk assessment hub of excellence. To contribute to several expected impacts of destination 2 “Living and working in a health-promoting environment”, PARC will organise the activities to reach three specific objectives: - An EU-wide sustainable cross-disciplinary network to identify and agree on research and innovation needs and to support research uptake into regulatory chemical risk assessment. - Joint EU research and innovation activities responding to identified priorities in support of current regulatory risk assessment processes for chemical substances and to emerging challenges. – Strengthening existing capacities and building new transdisciplinary platforms to support chemical risk assessment. The Partnership brings together Ministries and national public health and risk assessment agencies, as well as research organisations and academia from almost all of EU Member States. Representatives of Directorates-General of the EC and EU agencies involved in the monitoring of chemicals and the assessment of risks are also participating. PARC will meet the needs of risk assessment agencies to better anticipate emerging risks and respond to the challenges and priorities of the new European policies.

PARC’s general objective is to consolidate and strengthen the EU's R&I capacity for chemical RA to protect human health and the environment. Linked to this are three specific objectives (SO) around which the 9 Work Packages (WP) of PARC are structured and for which 13 realistic, measurable, achievable and verifiable operational objectives (OO) are developed.

- PARC’s first SO1 is that EU and national risk assessors and regulatory entities come together with the scientific community in a cross-disciplinary network to set priorities for R&I in chemical RA.
- Specific objective 2 (SO2) is that European and national RA entities and their scientific networks carry out a joint R&I programme to respond to the agreed priorities in chemicals RA
- Specific objective 3 (SO3) is that European risk assessors, their scientific network and the wider stakeholder community have access to the R&I capacities required to implement innovative chemical RA.

EnvE Lab has a particular contribution to PARC, with an overall budget of ~ 9 M€, involved in various activities of NAMs, while also co-leading the work on lifelong exposure biokinetics, as well as the WP8.

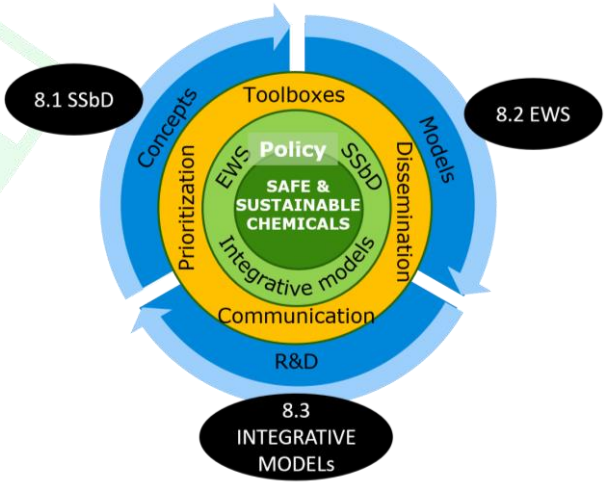


Figure 45. Concepts and toolboxes positioning within PARC

This WP aims to support the development and consolidation of new concepts and approaches as Safe and Sustainable by Design, trans-regulatory approaches for early warning systems, identification of information needs and integrative models approaches for chemical exposure, hazard and risk assessment. This requires an agreement of a joint understanding in the stakeholder community and the identification of tools and methods to support their practical use. Based on the concepts, tools and methods to support their practical use will be identified or developed, and made interoperable in an integrative modelling network.

Safe and Sustainable by Design (SSbD)

For sustainable chemical innovation, the other key pillar of the CSS is the transition to chemicals that are Safe and Sustainable-by-Design. The SSbD concept is defined as a process to accelerate widespread market uptake of new and alternative chemical products and technologies that deliver greater consumer confidence in their safety, environmental and societal benefits and advance the transition towards a circular economy and climate-neutral society. Currently SSbD is at the core of institutional, process and technological systems innovation in the chemical industry and in chemical engineering in Europe and it has been integrated in the national research and innovation agenda in Greece.

In this study we presented an innovative tool for integrated health risk assessment of plastic products and of plastic-containing goods during their whole life cycle until their final disposal as waste. The INTEGRA LCA software couples the integrated external and internal exposure assessment capabilities of the INTEGRA computational platform with life cycle impact assessment.

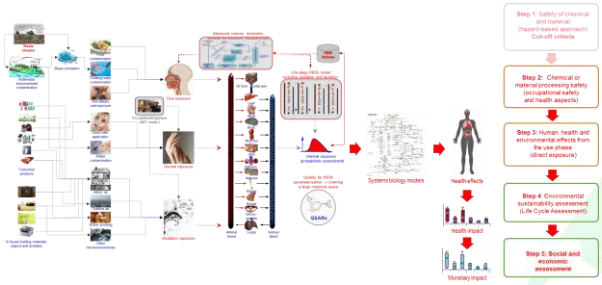


Figure 46. The INTEGRA LCA conceptual framework

The integrated software platform allowed us to perform a first-of-its-kind analysis of adverse health outcomes attributable to chronic exposure to persistent organic pollutants associated with plastic material use and disposal. A comprehensive review of up-to-date information on plastic products and plasticizers used by the urban population was performed to build up the application-specific release/emissions inventory. This review included both plastic products and plasticizers used in food packaging.

Compounds of interest in this regard include bisphenol A, phthalates such as DEHP and its metabolites, DINCH, di-(2- ethylhexyl)adipate. Integration of all human exposure routes and pathways to the toxic compounds contained in plastic was done at the level of systemic internal dose, that was linked with adverse health outcomes reported in the literature to quantitatively assess the related health risk. Our analysis highlights that landfilling is the worst waste management strategy on a global scale. At the same time, the investigated options for waste treatment coupled with energy and material recovery would result in very important benefits in terms of greenhouse gas emission reduction. However, not all options are equally benign to the local environment and to the health of the local population, since both the former and the latter are still affected by non-negligible local emissions.

Regarding public health impacts, adverse effects on the endocrine system with cascade impacts on human reproduction, metabolic syndrome and, even, neurotoxicity after chronic exposure to the persistent organic chemicals found in plastic products and waste were estimated. The coupled integrated exposure and life cycle assessment methodology developed herein and translated into the INTEGRA LCA platform is a significant step towards the direction of comprehensive, precise and transparent estimation potential health risks associated with use, management and disposal of plastics in urban settings and for the implementation of the SSbD concept in the design, manufacturing and end-of-life management of plastic products or of plastic-containing consumer goods. The incorporation of life cycle analysis produces different conclusions than a simple environmental impact assessment based only on estimated or measured emissions. Taking into account the overall life cycle of both the waste streams and of the technological systems and facilities envisaged under the plausible scenarios analyzed herein, alters the relative attractiveness of the solutions considered and enhances the robustness of the health impact assessment.

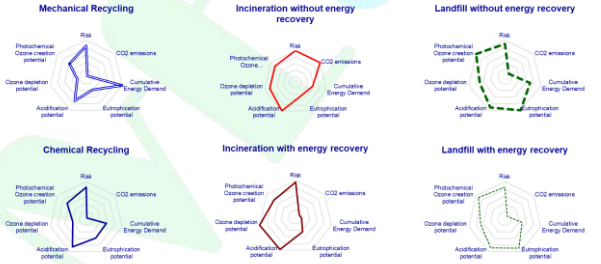


Figure 47. Normalised risks and environmental impacts for the investigated plastic waste management options

INTEGRA LCA is empowered through the use of quantitative structure-activity relationship models for property prediction supported by a machine learning-based search engine that explores the relevant chemical space for alternative molecules that would eventually minimize the environmental and human health hazards associated with their use in consumer products. Thus an integrated framework for selection of chemicals for product redesign has been coined; the computer-aided workflow we present supports the redesigning of these chemicals to achieve the sought of environmental and human health objectives using in silico generated structure suggestions. The overall concept is further evolved, so tools of different complexity and data requirements will assess the SSbD criteria at various stages of innovation.

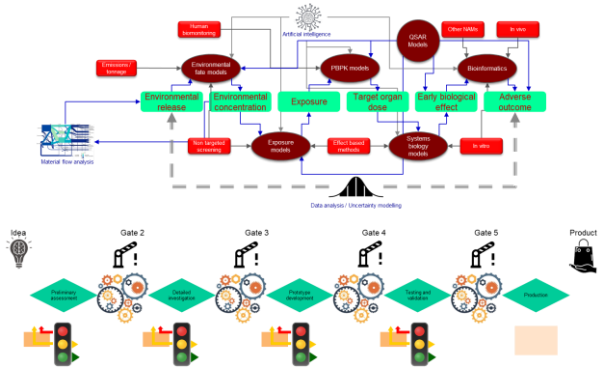


Figure 48. Safe gate assessment – innovation stage

Early Warning System (EWS)

Establishment of an early warning system (EWS) for identification of new and existing potentially hazardous substances is a key component in PARC. An EWS consists of early warning monitoring tool components to identify chemical hazards in humans and environmental matrices that may be associated to an unacceptable risk. For prioritization of new chemicals, various tools can be used in combination or independently such as time trend analysis in combination with advanced statistical and machine learning tools in humans and wildlife, exposure assessment by linking human exposure to food, drinking water, indoor environment and their sources, and combination of chemical and toxicity tools in humans and in the environmental samples to prioritize new drivers of toxicity. A key component is to communicate risks, facilitate awareness of risks and disseminate warnings to inform risk assessors and risk managers at an early stage of future challenges or emerging risks. The activities will involve methodological development of early warning monitoring tools and prioritization framework to identify emerging chemical threats. The developed computational, chemical and toxicology methods will be integrated to create a prioritization framework to identify new prioritized substances and their sources in society which will provide assistance in the identification and dissemination of information on emerging issues and identified emerging risks.

In PARC, a review of existing early warning systems has been carried out, main sources of information, ways to organise the data as well as key steps that have to be implemented in the EWS have been identified.

- The first step, picking up signals, involves searching and tracing information on new or emerging chemical risks and their possible related effects, using various sources (e.g., scientific literature, news sites, websites, electronic databases and stakeholder networks). For risks to humans (workers or consumers), epidemiological research and case reports are also valuable sources of information. While clear criteria help the process of filtering out relevant signals, initial expert assessment is an essential factor in the signal evaluation process.
- The next step is to check if the signal has been identified previously and, if so, whether actions or regulatory measures have already been implemented. This could lead to an immediate follow-up action, such as informing enforcement or inspection authorities, depending on the kind of signal. If the identified concern is already sufficiently covered and there is no need for further enforcement actions, additional information collection and prioritisation is considered unnecessary.
- During the next step, 'signal strengthening', additional evidence should be obtained, in order to assess the causality between the chemical exposure and the harmful effect.
- A 'prioritisation of risks' then follows, in which an indication of the severity of the risk will be provided based on the information obtained during the 'strengthening of signals'. The prioritisation step will result in a list of potential NERCs requiring a follow-up procedure.
- Finally, follow-up measures are defined, including derivation of a safety limit and actions to be taken.

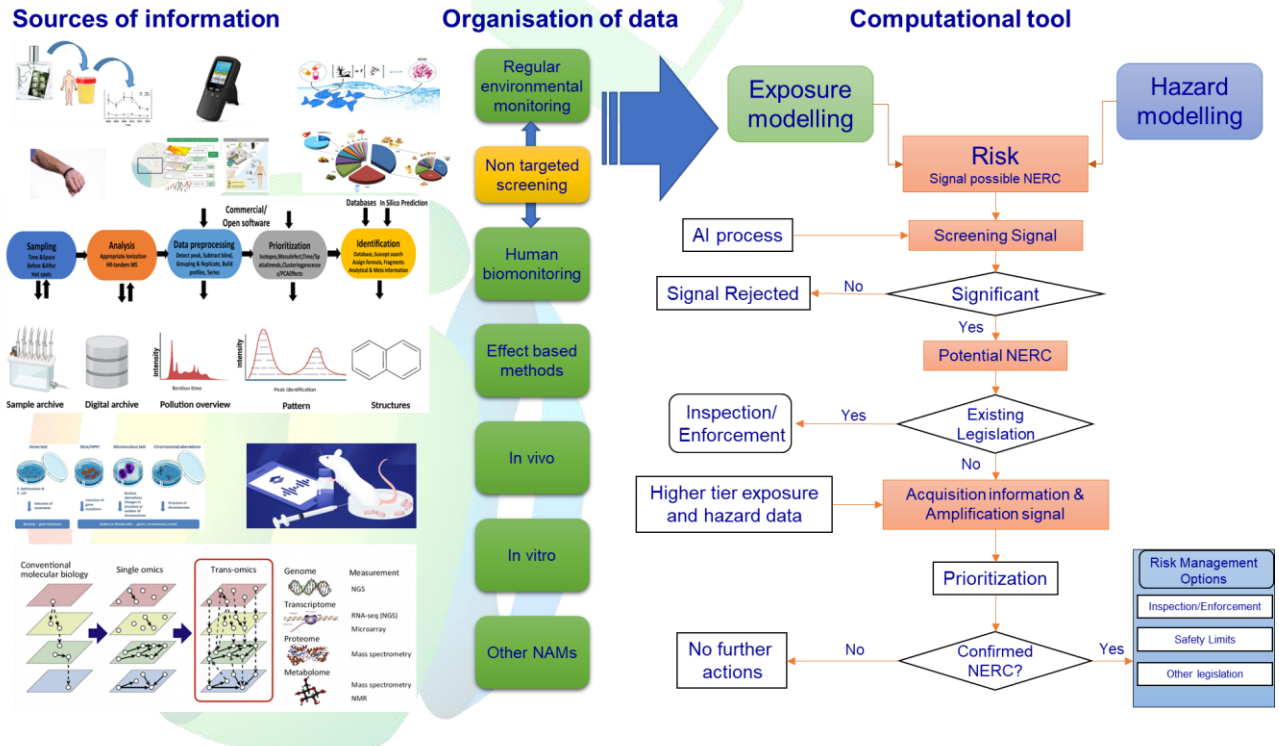


Figure 49. Concept of the EWS developed in PARC

Integrative models

Another key component of the Integrative exposure, hazard and risk modelling: This task will develop an overarching integrative model that places all modelling approaches carried out in the Partnership in a harmonised perspective. This overarching concept will be implemented in a network of tools forming a federated cloud infrastructure that addresses the modelling needs identified within the Partnership. Particular emphasis is placed on the technical and developmental part and on adopting the FAIR principles and promoting these to the models of the cloud infrastructure. The procedures associated with these objectives will be put in place in this task and the corresponding software development including development and integration of models and the corresponding user interfaces and overall system architecture will be coined herein.

As a starting point, the work in integrative modelling will focus on human health risk assessment, and in particular on the use of dietary and non-dietary exposure models, new approach methodologies (NAMs) for toxicological testing, in-vitro in-vivo extrapolation (IVIVE) and validation with human biomonitoring (HBM) data. We will use the inventory of requirements to design conceptually elements in the PARC model network that are needed to address the modelling needs.

To better respond to contemporary risk assessment needs and foster the transition towards next generation risk assessment, initial work of the integrative modelling will try to fill the gaps of comprehensive methodological workflows for evaluating multiple lines of evidence associated with both exposure related (dietary, environmental, personal activity and exposure, HBM) and hazard (NAMs, in vitro testing) related data. The integrative modelling tool network to be developed will allow the quantitative association among the heterogenous data that are available and will be generated in the field of risk assessment. Aiming at a successful design of the model network, we will track the needs of data processing and modelled data generation, following the exemplified case study on risk assessment of bisphenols (BPA, BPS, BPF). For this group of compounds, the project needs several types of data, and it will rely on external collaborations to retrieve and/or generate these data. In this project an ontology will be defined using the example data as inspiration. An overview of models that are available or needed will be defined, and available tools will be matched to this overview. Daily intake and exposure estimates will be accounted for several population groups, including the most susceptible ones (fetus, neonates, children), as well as occupationally exposed and high-end consumer population groups. Exposure will be estimated by combining bottom up (by aggregating multisource, multipathway, multiroute exposure), and top down (reconstruction of available HBM data), accounting for the best data available. The aim is to identify the needs for aggregate (multi-source, multi-pathway and multi-route exposure) modelling, including multimedia environmental emission and fate modelling, food contact materials migration, as well as percutaneous and inhalation exposure for consumer and occupational settings. Toxicokinetics of bisphenols and especially during the prenatal and perinatal period play a particular role. A framework for assimilating HBM data, and translating them into external, intake-level amd internal exposure estimates (exposure reconstruction) will be defined. Quantitative AOPs (qAOPs) will be constructed to describe the toxicodynamics after triggering of MIEs and downstream key events. Relevant key events will be assessed combining relevant cell-based system and holistic approaches, including toxicogenomics and co-expression analysis. NAM toxicity assessment metrics and approaches will be used for delivering risk characterisation estimates. Internal dosimetry models will hold a key role, serving the need for translating external exposure estimates into internal dosimetry metrics, for quantitative in-vitro in-vivo extrapolation (QIVIVE), while it is also a key component of the models for exposure reconstruction starting from HBM data. Moreover, the impact of co-exposure to the three bisphenols in the biologically effective dose and the way this impacts the QIVIVE extrapolation will also be examined. Aiming at addressing these questions, precise needs for the various models and modules, will be mapped and translated to model network needs. Towards this aim, the work carried out so far regarding bisphenol A, has resulted in the precise identification of age, route and genetics related bioavailability differences. The effect of age is related to differences in (a) physiological parameters such as tissue composition, blood flows, cardiac and respiratory rate and (b) the maturity of the conjugation activity. Taking into account the physiologically-based approach for scaling to children and the most recent findings regarding the ontogeny of enzymes involved in BPA detoxification an age-dependent bioavailability difference factor of 2 to 3.5 is considered between infants and adults. Similarly, significant bioavailability differences occur based on the route of exposure; In the case of inhalation, BPA enters directly in the blood stream from the alveoli and the lack of first pass metabolism results in bioavailability differences up to 6 times compared to a similar dose administrated orally. In the case of dermal exposure, the lack of first pass metabolism is somehow decompensated by slower absorption. Finally, a major factor that differentiates BED within a population is the presence of genetic variants of key enzymes involved in BPA conjugation; in vitro kinetic studies have identified that D85Y substitution in UGT2B15 decreases enzymatic function and that the polymorphic alleles of UGT2B15 are translated in variations in the metabolism of BPA. The effect of all the described above parameters is summarized in Figure 5, where for the same bodyweight normalized dose, free plasma BPA is estimated accounting for differences in age, route of exposure and genetics presented in Figure 50.

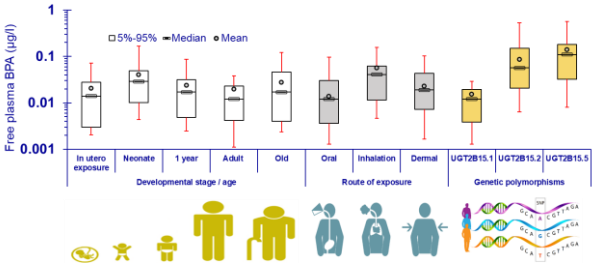


Figure 50. Key parameters inducing bioavailability differences in BPA

Chemical safety in industrial settings

The purpose of this study was the development of a methodology for dynamic optimization of the spatial configuration of the building infrastructure in oil refineries applying quantitative risk assessment (QRA) principles. The method developed focuses on fatal effects from possible accidents in production and storage units according to API 752. In brief, QRA is used as a bridge to quantify the risk and apply API 752 standards as guide towards plant design optimization when retrofitting is at hand.

The assessment methodology includes the classification of the buildings of interest according to API 752, the identification of accident scenarios that may affect these buildings, the identification of the relevant equipment, the consequences and risk assessment of the selected scenarios, the individual and social risk assessment within the buildings, the selection of the appropriate assumptions for the risk assessment and the identification of security enhancement measures. This enhancement is one of the most important tasks due to its affection on measures budget.

We have applied this integrative approach to study the possibilities for safety optimization in a typical large-scale European refinery by re-designing the spatial configuration of the administrative and worker buildings on site. In our application, the buildings included were 64. The building cohort consists of (a) 5 buildings constructed by reinforced concrete; (b) 28 buildings constructed by reinforced concrete frame and brickwork masonry; (c) 17 are constructed by steel and metal frame; (d) 14 ISOBOX buildings.

Modeled accidents comprised BLEVE-fireballs, jet fire, pool fire, flash fire, and UVCEs. The selection of the mathematical models to describe each accident was based on assiduous check of model' attributes and the related recommendations of industrial and health and safety standard organizations, such as TNO, UK Health and Safety Executive, and DNV GL. Weather conditions selection played a key role in the results as the appropriate parameter selection (e.g., the distance in which ignition surface will be found or the height of interest, etc.). We performed the simulations using Phast/Safeti v.8.22 (DNV-GL) and updated it with in-house models of key processes including specific measures designed to optimize the safety performance of the plant. Event tree identification, equipment failure frequencies, and ignition probabilities determination were based on the BEVI manual by the Dutch Ministry of the Environment, while data from the European Gas Pipeline Incident Data Group (EGIG) were used for the underground gas pipeline. The mortality criteria inside buildings were determined in the technical specifications of the study based on literature and computational research.

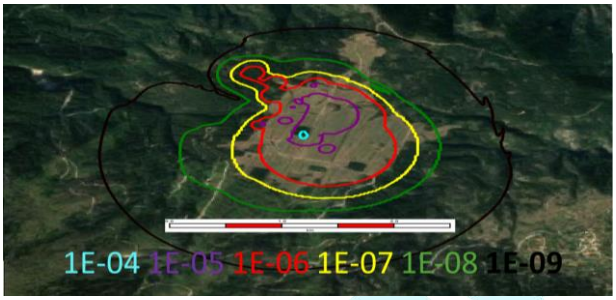


Figure 51. Location Specific Risk (Fatal Probability)

According to the results regarding location specific risk (LSR), Figure 51, there was a need to take measures in the buildings where the probability of loss of life is bigger than the fatality risk limit adopted as acceptable according to the technical specifications of the study (1E-05). Indicatively, one of the measures mentioned is the movement of some mobile buildings in new locations. In addition, Societal Risk calculation proved that the refinery was operating above the limits set by RIVM in the EU (RIVM guidelines were adopted in the technical specifications). In order to evaluate the possible measures and the normal operation of the refinery according to API 752 we carried out a horde of parametric studies.

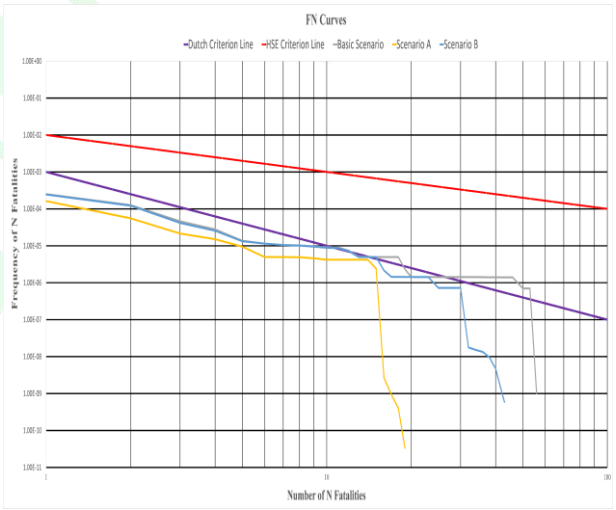


Figure 52. FN Curve per tested scenario

Recommendations included the shielding of selected buildings against thermal radiation using external thermal insulation, the use of high-strength exterior windows against high temperatures, and the appropriate change of orientation of external openings of the buildings.

Overall, our dynamic optimization methodology for plant and process safety by design has been demonstrably attractive as a means to ensure inherent safety in plant retrofits or new designs by integrating traditional quantitative risk assessment at the process level with optimization algorithms fed with acceptable risk criteria and spatial optimization of buildings in complex plant configurations such as large-scale oil refineries.

Detection of Indoor Airborne Chemical & Biological Agents Thematic Group

Aims and scope

The European Reference Network for Critical Infrastructure Protection (ERNCIP) will provide a framework within which experimental facilities and laboratories will share knowledge and expertise in order to harmonize test protocols throughout Europe leading to better protection of critical infrastructure against all types of threats and hazards and to the creation of a Single Market for security solutions. The ERNCIP Detection of Indoor Airborne Chemical & Biological Agents Thematic Group which is led by EnvE Lab, will define scenarios for indoor, airborne contamination (threat, contamination area, topology, conditions of use for the equipment, etc.), which are realistic/are considered important in the EU or have been used in other projects. This activity will be supported by the use of the state-of-the-art on flow and dispersion 3D modelling/simulation and source term evaluation from detector network measurements.

Figure 53. ERNCIP Detection of Indoor Airborne Chemical & Biological Agents Thematic Group logo

The overall aim of this thematic group is to investigate issues that can be addressed on the EU level regarding Detection, Identification and Monitoring (DIM) of airborne, chemical and biological threats in enclosed spaces. Towards this aim, three main activities have been foreseen during the next months for accomplishing the TG objectives. In order to evaluate the applicability of the current sensor technologies and what has to be done, it is critical to evaluate what are the actual needs that have to be addressed i.e. what we expect from the sensors against CB threats in enclosed spaces. Thus, a critical starting point of the overall approach will be the definition of relevant scenarios of indoor airborne threats (chemical and biological) in critical infrastructures. The needs that have to be addressed will define the criteria for performing a critical review on the existing sensors available in the EU and used either for chemical or for biological agents. Computational simulations will provide the spatial and temporal gradients of contamination within indoor critical infrastructures. Finally, evaluation of capabilities of existing sensors based on their capability to give early warning will allow us to identify gaps and define requirements for next generation detectors in the EU.

Results

More in detail, specific questions have to be answered, such as:

- Define the criteria and usage scenarios, suitable for chemical and biological DIM of contamination by airborne substances in enclosed spaces.
- Gather information from the relevant stakeholders and from the literature on the potential chemical and biological threats.
- Define typical threat scenarios, as most relevant
- Perform a critical review on the existing sensors available in the EU, based on the criteria and usage scenarios identified in Task 1. This will allow us to evaluate the suitability of the existing technologies for early and accurate identification of indoor airborne chemical and biological threats. Parameters to be examined, include whether to add a commercial off-the-shelf product or not, products under development/close to release or prototype - Technology Readiness Levels (TRL) level should be taken into account.
- To challenge the existing technologies against quantitative results, to identify gaps, future areas and emerging technologies. Specific considerations include:

The main scope of sensor use, is the (as possible as early) detection, identification and monitoring of the contamination with a toxic agent within an enclosed indoor location. The capability of a sensor to (a) early detect and (b) to identify a threat is of major importance. The importance of these capabilities are graphically illustrated in Figure 1, where the difference in the capability of detection (detector 1 and detector 2, with different detection limits) and eventually the identification of a hypothetical threat agent X, results in significant differences in actual exposure and internal dose, defined as the Area Under the Curve (AUC), that represents the integral of internal dose in time. These differences in actual dose will result in completely different casualty patterns. This comprehensive exposure and toxicokinetics and toxicity framework provides a robust analysis to be used for the assessment of the suitability of sensors and sensoring systems.

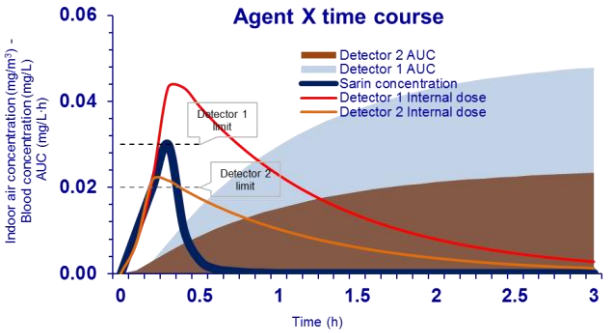


Figure 54. Agent X environmental and toxicokinetic time dynamics following a hypothetical attack under two different detection capabilities scenarios

Climate change, air pollution and human health

Integrated Climate forcing and Air pollution Reduction in Urban Systems (ICARUS)

Aims and scope

The ICARUS main objective is to develop integrated tools and strategies for urban impact assessment in support of air quality and climate change governance in EU Member States leading to the design and implementation of appropriate abatement strategies to improve the air quality and reduce the carbon footprint in European cities. We will develop detailed policies and measures for air pollution and climate control for the short and medium term (until ca. 2030). For the long term perspective (2050 and beyond) we will develop visions of green cities and explore pathways on how to start realizing these visions. The specific project objectives are to:

- quantitatively assess the impact of current and alternative national and local policies on reducing greenhouse gas (GHG) emissions and improving air quality through a full chain approach and evaluate the future public health and well-being impacts of these policies in European cities.
- evaluate (using source apportionment and atmospheric modelling) the current contributions of the different pollution sources linked to urban activities including heat and power use in the urban building stock, urban traffic and transportation needs, energy production, industrial activities including energy production, agriculture and trans-boundary pollution with respect to GHG-emissions, air quality loading, public health and well-being of the population.
- propose measures of technological (i.e. measures that will lead to a reduction of emissions at the source) and non-technological (i.e. measures that induce behavioural changes) nature to reduce both carbon footprint and air quality burden (win-win solutions). Techno-economic analysis of possible scenarios for the introduction of such measures will result in the definition of cost-effective environmental and climate protection and air quality management plans adapted to the specific needs of different EU cities and regions. The effect of these measures will be evaluated jointly taking into account the socioeconomic drivers related to the existing and projected scenarios.
- develop visions of green cities with clean air, close to zero or negative carbon footprint and maximal wellbeing
- develop a pathway for the realization of these visions in the next 50 years and propose first steps down that road in the form of a concrete plan towards achieving these visions in the participating cities.
- raise awareness of the citizens about the impacts on public health and climate change caused by their activities or with changes in their activities.

The policy analyses results mwill allow us to determine the most sustainable GHG mitigation and air quality (AQ) improvement strategies. The latter will be proposed to the authorities competent for atmospheric pollution and climate protection management and to the main industrial end-users as guidance for decision making that would lead towards maximizing the net public health and wellbeing benefits while taking into consideration the costs associated with air pollution and climate change in the EU.

We will employ state-of-the-art technologies for fusing the necessary environmental and ancillary information to allow for cost-effective air pollution monitoring and assessment. The tools developed will allow the analytical accounting of the main industrial and area emission sources in the area and the creation of precise and updated emission inventories. An **integrated approach** will be used for air pollution monitoring combining ground-based measurements, atmospheric transport and chemical transformation modelling and air pollution indicators derived from satellite, airborne and personal remote sensing. Thus, air quality will be readily assessed across different spatial scales in the participating cities. Based on the advanced monitoring activities outlined above, a **cloud-based solution** will be developed to inform citizens of environmental friendly alternatives that may have a positive impact on their health, motivate them to adopt these alternative behaviours by offering them refundable coupons and controlling them either instantly or over a period of time for the application of the alternative actions. Citizens would use web or smartphone/tablet-based applications to be informed about actions, collect and redeem coupons from the participating organisations. Our findings will be translated into a **web-based guidebook** that will provide an estimate of the effects of a number of policies in every participating city and will also give guidance to other European cities.

ICARUS will develop a vision of a future green city: a visionary model that will seek to minimize environmental, climate and health impacts in the participating cities. To this aim we will develop a **transition pathway**, which will demonstrate how current cities in Europe could be transformed towards green cities within the next 50 years. To raise citizen awareness regarding the impacts of their activities on air pollution and climate forcing and increase societal acceptance of emission reduction policies, a **web- and smartphone/tablet-based tool** will be developed to inform citizens in participating cities about how their life style affects their carbon footprint and the health impacts of their actions/consumer choices.

Personal exposure assessment using portable sensors data and Agent Based Modelling (ABM).

As already mentioned, innovations in sensor technology create possibilities to collect environmental data at unprecedented depth and breadth. Measuring, though,

personal exposure directly requires a large number of people and therefore is often not feasible due to time and financial constraints. Considering the substantial hurdles involved in collecting personal exposure data for whole populations, a decision has been made to simulate human movement and interaction behaviour using Agent Based Modelling (ABM), a simulation technique that enables a better understanding of the behaviour of individuals and populations in social and evolutionary settings. This approach can produce data that could fill in gaps that exist in traditional datasets, taking into account different activity patterns and Socioeconomic Status (SES) data.

A spatially explicit ABM platform was established, modelling the city of Thessaloniki. The model can feed into a population-based exposure assessment without imposing prior bias, but rather basing its estimations onto emerging properties of the behaviour of the computerised autonomous decision makers (agents) that compose the modelled system (city). City's population data, vehicles fleet information, road and buildings networks were transformed into human, vehicle, road and building agents respectively. Particular emphasis is being given in the case of in-model incorporation of SES data. Time – use survey outputs with data on lifestyle/behavioural patterns were associated with human agent behavioural rules, aiming to model representative to real world conditions.

At the end of a model run, activity patterns can be determined for every human agent, as an outcome of the prevalence of specific preferences and decision-making throughout the simulated time of experiment. Different human agents based on different characteristics (age, gender, SES indicators) will express different behaviours and this could lead to a different exposure profile. It is then possible to extract human agents' trajectories on a GIS format together with a database that contains their coordinates and activities in time through different locations/microenvironments. The GIS layer can then be superposed onto Air Quality maps. In this model, individual exposure to PM concentration is deduced via superimposing the human agent's trajectory on daily average PM10 concentration maps, modelled for urban Thessaloniki. These maps are the outcome of data fusion from ground observations, pollutants dispersion modelling and satellite images. The high spatial resolution map allows us to calculate exposure at the level of building block. For the cases where human agents are located indoors, indoor concentration is estimated using the INTERA computational platform. Personal exposure, expressed as inhalation-adjusted exposure to air pollutants is then evaluated by assigning pollutant concentrations to an agent based on his/her coordinates, activities and the corresponding inhalation rate.

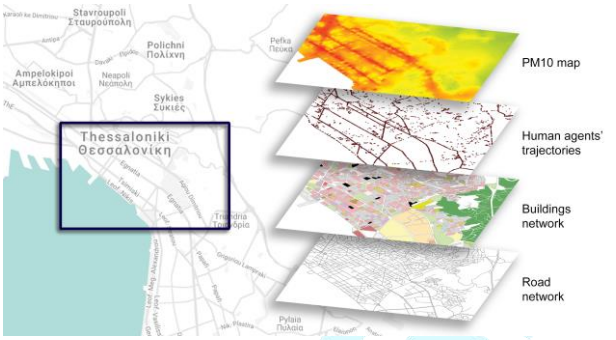


Figure 55. Personal exposure assessment using Agent Based Modelling (ABM).

The ABM model can be validated against real "time-geography" of exposure data, retrieved by exposure assessment campaigns, like the Thessaloniki sensors campaign (*mentioned in a previous chapter)*. Virtual time-activity data and exposure profiles of human agents can be compared to and be validated against the real data of campaign participants with a similar sociodemographic background.

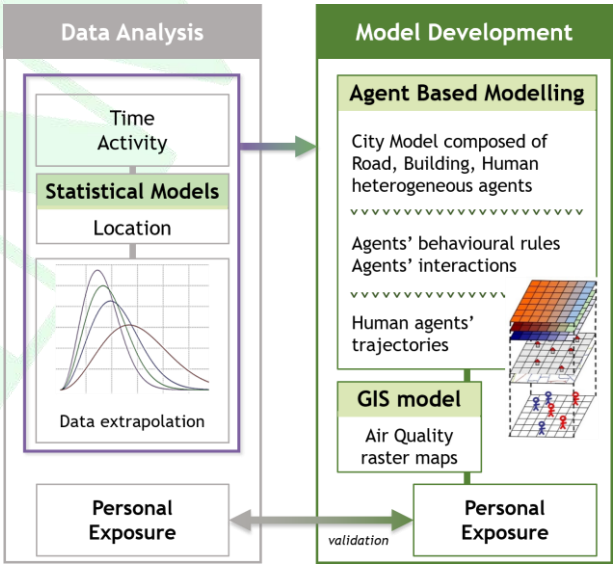


Figure 56. From sensors data to a personal exposure model.

An example of the ABM derived exposure profiles is showcased below. This study goes beyond the approach of classic epidemiology where outdoor PM concentration is the main proxy for assessing exposure. Here, exposure timeseries are based on outdoor (*red line*) as well as indoor (*green line*) concentrations that were estimated based on personal trajectories. Then exposure to PM_{10} (*black line*) as well as inhalation adjusted exposure (*blue line*) were also calculated. Furthermore, exposure assessment was extended to the calculation of intake dose, taking into account a representative body weight and breathing rate, based on the agent's age and gender.

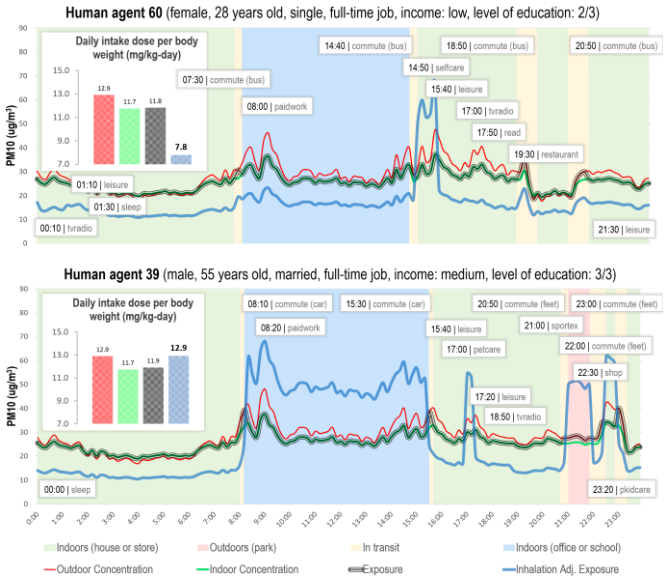


Figure 57. Exposure to PM10 and daily intake dose of two human agents. Personal exposure *in black*; inhalation adjusted exposure *in blue.*

Figure 18 illustrates an example where the effect of sociodemographic characteristics in exposure refinement can be clearly observed, since for two human agents that are phenomenally exposed to similar outdoor PM10 levels (12.9 μg/m^3), the actual exposure in terms of daily intake is differentiated by 65% (7.8 and 12.9 μg/m^3 respectively), due to the prevalence of different behaviours.

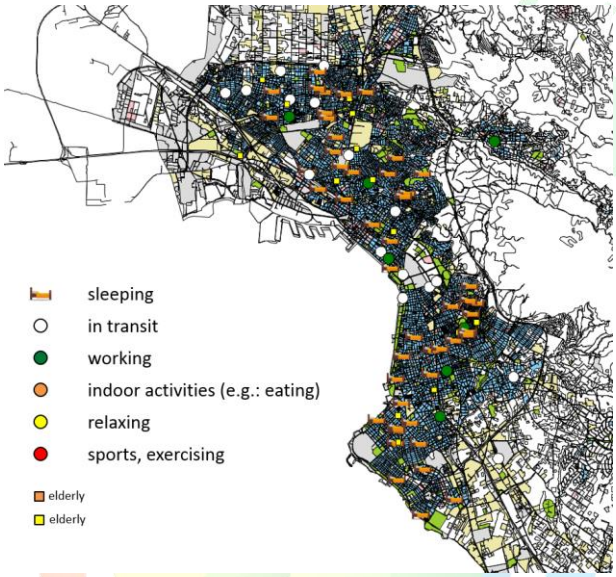


Figure 58. Moving human agents on a representative day in the city of Thessaloniki - running example of the ABM platform.

On average, personal exposure results were between 10 and 20% more accurate than the equivalent estimate using outdoor PM concentration as exposure proxy. The identification of exposure peaks and troughs throughout the day leads to useful conclusions regarding capping exposure to high pollution levels.

Overall:

- The ABM approach brings a new way to study the complex systems, allowing to take into account the heterogeneity of the entities composing a system.
- This approach permits the **cost-effective construction of refined time-activity diaries and diurnal exposure profiles.** The refined exposure assessment model can address effectively vulnerable population sub-groups, integrating socio-economic status indicators.
- Utility functions are provided that can shape human agents' preferences based on individual characteristics. **Different SES groups will follow different behaviours and this will be reflected in different decisions regarding mode of transport, consumer products or even diet patterns**. Eventually this will result to a more accurate exposure assessment.
- Changes in exposure levels can be calculated for individuals and specific subgroups of population based on different spatio-temporal behaviours.
- This approach can also be established for different cities, without changing the basic programming architecture.
- ABM-generated distributions of human agents' behavioural patterns can also work as an input into a probabilistic exposure assessment model.
- This study represents the first step towards improving the calculation process of population exposure to environmental substances so that we would be able to draw better conclusions on the association between environment and health.
- Such a model could be further used in order to study the effect of different measures/policies to reduce pollution levels in cities/countries. It can be used as a means for estimating and comparing the probable effects of different public health strategies prior to implementation. These simulations can lead to better initial choices and reduce the time and expense required to identify effective strategies.

Urban Observatory for Multi-participatory Enhancement of Health and Wellbeing (URBANOME)

Aims and scope

URBANOME aims at building a common EU Framework for evaluating comprehensively multi-sector policies in urban settings supporting the "Health in all Policies" approach of WHO. In this light the overall objective of URBANOME is to promote urban health, wellbeing and liveability, through systematically integrating health concerns in urban policies and the activities of urban citizens, on the basis of detailed and comprehensive evidence on environmental health determinants, the spatial distribution of these in the city, and the social distribution of their impact among different population groups, accounting for different life styles and behaviours. Integration of health concerns, environmental stressors and social equality in public and private activities help alleviate a wide range of contemporary urban challenges, specifically social cohesion and health inequality, and promote the transition of European cities to sustainable, climate proof, smart and inclusive urban economies.

URBANOME brings together the complete set of environmental, social, and functional features of a city in an integrative analytical framework that would facilitate the identification of the main determinants of urban health and wellbeing and support co-creation and testing of policies and precision interventions designed to improve urban health and wellbeing through Urban Living Labs.

The URBANOME approach will be applied through pilots built by the Urban Living Labs in Aarhus, Athens, Aberdeen, Madrid, Milan, Ljubljana, Stuttgart, Paris and Thessaloniki tackling various levels of environmental exposures, age-dependent susceptibility windows, inter-individual variability, gender differentiation of exposure, and socio-economic disparities. These will allow us to draw conclusions regarding the determinants of urban health and wellbeing that will be translated into evidence–based policy recommendations considering socio-economic and environmental factors leading to urban health inequalities.

URBANOME is part of the European Cluster on Urban Health which includes other research projects funded in the frame of the same call.

To achieve this overall objective, URBANOME has the following specific objectives and will:

- SO1 Develop an integrated methodological framework and a big data computational ecosystem and decision support system accounting for the physical, mental, socio-economic, operational and structural characteristics of a city which affect human health.
- SO2 Provide an accurate spatial and temporal resolution of environmental exposures in a personalized manner and identify the patterns of socio-spatial environmental inequalities finally leading to social cohesion improvement.
- SO3 Investigate the impact of environmental stressors on mental, cognitive, social and physical wellbeing particularly on vulnerable population groups, including hard-to reach citizens, and considering gender differences.
- SO4 Raise public awareness regarding urban health and wellbeing and engage urban citizens through Urban Living Labs (ULLs), including big data collection and citizen science-led participatory governance.
- SO5 Alleviate environmental health injustice in cities.
- SO6 Build solid partnerships with other relevant parties in urban health, including policy makers, experts, local authorities, business and local communities to better connect research to practical needs and user demands.
- SO7 Develop and promote effective, innovative and inclusive governance and planning adapted to local urban contexts which foster long-term health and wellbeing in cities.
- SO8 Provide prognostic markers regarding the effect of environmental stressors in the main non-communicable diseases (NCDs).
- SO9 Establish an evaluation framework to assess cost-effectiveness as well as barriers and facilitators to the implementation of identified policy actions aiming to support urban development and city planning towards improved urban health and wellbeing as well as social cohesion.
- SO10 Creation of new business opportunities (in mobility, entertainment, culture, etc.) aimed at enhancing urban health and wellbeing through co-creation and co-maintenance of sustainable, egalitarian and healthy cities.

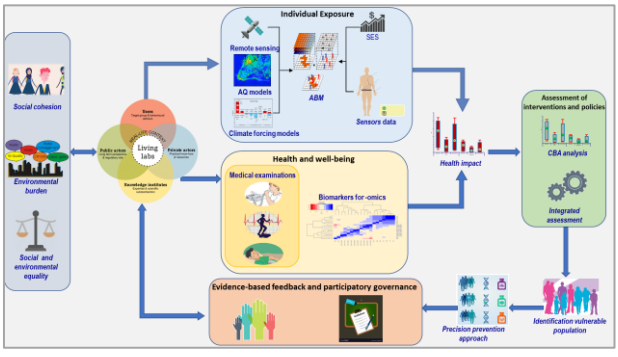


Figure 59. Flowchart depicting the interconnections between the main components of the URBANOME paradigm

Integrating Environment and Health Research: a Vision for the EU (HERA)

Aims and scope

Citizens across the EU and the world are extremely concerned by the deterioration of their environment and its effects on both human and ecosystem health. It is recognized that environmental degradation and pollution, climate change, exposure to harmful chemicals and other stressors, diet quality and behaviour, and the destabilization of the ecosystem biodiversity and functioning, damage health and quality of life, and disproportionately affect socially disadvantaged and vulnerable population groups. Emerging and Re-emerging infectious diseases and the dramatic increase in certain chronic non-communicable diseases are recognized threats for European and international public health. Increasing knowledge stresses that various threats to human population such as malnutrition, illnesses, increases of zoonoses, etc., are dependent on ecosystem deterioration. In addition, it is believed that the socio-economic costs of such deterioration are very significant and there are strong expectations that public policies could develop preventive and protective actions. Conversely, these negative outcomes should be balanced by the positive effects that healthy environments, can have on human and ecosystem health.

The overall aim of HERA is to set the priorities for an environment and health research agenda in the EU by adopting a holistic, systemic and inclusive approach in the face of global environmental changes. Research is expected to support decision-making and to help attaining the ultimate goals of protecting and improving ecosystem quality and human health. The HERA strategy will be based on a shared vision of the best knowledge on environment and health (EH) interactions that we wish to have by 2030, the most efficient and realistic way to achieve such knowledge and to translate it for the benefits of the EU citizens. Better knowledge and evidence are needed on ecosystem-health interactions, prevention and resilience mechanisms and, the best methods and tools to implement and monitor policies and decisions. The shared HERA vision will aim to identify both the environmental opportunities for health improvements and the major environmental problems and challenges that need to be addressed. This requires a close and continuous interactions with the numerous and diverse stakeholders that are particularly concerned by these issues. The following primary aims will be pursued:

Aim n°1 - to proactively identify key sectors and policy areas in the field of environment and health that will benefit from additional scientific evidence in the next decade;

Expected outcomes: 1) more proactive Environmental Health (EH) community and more policy-relevant EH research; 2) more attention paid to EH in all policies; 3) better knowledge exchange between countries; 4) closer dialogue between the scientific and the policy communities on EH-related matters

Aim n°2 - to develop a European medium-term research and innovation strategy and agenda covering key strategic research and policy aspects;

Expected outcomes: 1) stronger support for the development of more creative and innovative research in line with policy issues; 2) improved association between socio-economic impact determination and environment and health research; 3) development of a research and innovation agenda for the environment, climate and health nexus as input to the next framework programme focusing on providing scientific evidence for preventive and precautionary actions.

Aim n°3 - To propose strategies and tools to respond to the new and continuing challenges in environment and health nexus in the next decade, by ensuring the engagement of all stakeholders, increasing coordination and cross-fertilisation of ideas, and contributing to the European environment and health process and policy activities.

Expected outcomes: 1) increased multidisciplinary and transectoral coordination between environment, ecosystem quality climate and health projects supported across sectors; 2) development of a cross-cutting stakeholder community; 3) efficient contribution to the European WHO environment and health process and the implementation plan resulting from the Ostrava Ministerial Declaration.

The specific objectives and challenges through the HERA workplan.

Objective 1: to establish a research agenda for the next decade addressing identified gaps, policy needs and integrating environment, ecosystem quality and health research.

Objective 2: to establish efficient coordination with major stakeholders including national, EU as well as relevant international actors.

Objective 3: to identify policy needs for the next decade. This objective will build on previous activities such as ERA-ENVHEALTH.

Objective 4: to identify scientific, technical as well as social, economic, and organisational hurdles to meet policy needs for the next decade.

Objective 5: to develop resources such as technical guidelines reflecting state of the art in health, social and economic impact assessment in different sectors.

Objective 6: to disseminate our work and contribute to education with emphasis on countries with less developed EH research.

Unraveling the blood transcriptome after "real-life" exposure of Wistar-rats to PM2.5, PM1 and ambient air, and association to water-soluble metal fraction in a sub-urban environmental monitoring station (ESPA)

Aims and scope

Particulate matter (PM) is one of the most important environmental issues in Europe with major health impact. Various sizes of PM are suspended in the atmosphere and contributes to ambient air pollution. The current study aimed to explore the differential gene expression in blood, and the effect on the respective biological signaling pathways in Wistar rats, after exposure to $PM_{2.5}$ and PM_1 ambient air particles for an eight-week period. A control group was included with animals breathing non-filtered atmospheric air. In parallel, filtered $PM_{2.5}$ and PM_1 was collected in separate samplers. In order to understand the biological mechanisms triggered on the gene expression level by $PM_{2.5}$ and PM_1 exposure and lead to airway inflammation, in this study, we aimed to evaluate the following hypotheses: (1) How the natural exposure to $PM_{2.5}$ and PM_1 in Wistar rats can alter the gene expression in blood after whole genome analysis using microarray probes in comparison to the control group; (2) Which biochemical pathways are differentially regulated after exposure to different air particulate matter and what is the type of immune response triggered after exposure to $PM_{2.5}$ and PM_1; and (3) How altered gene expression in rats after exposure to $PM_{2.5}$ and PM_1 from a traffic-related area would correlate with the concentrations of other measured components such as heavy metals.

PM-component analysis showed high concentrations of Fe, Pb, Mn and Zn for both particle size analysis and high concentration of Cu was observed in $PM_{2.5}$ filters. The water-soluble fractions identified in the atmosphere of Kalamaria site were found to represent 0.36% and 0.52% of the total mass of PM_1 and $PM_{2.5}$, respectively.

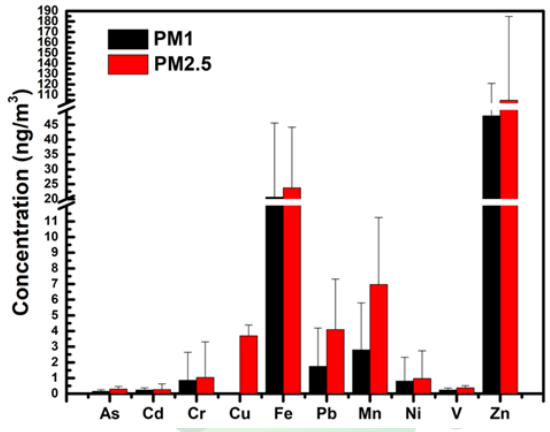


Figure 60. Comparison between water-soluble concentrations in PM1 and PM2.5 samples from Kalamaria environmental monitoring station.

To investigate the alterations in blood gene expression depending on the different air particle size inhaled by Wistar rats, a gene expression profiling analysis on blood samples was performed applying microarray probes. Two different groups of animals were exposed to $PM_{2.5}$ and PM_1 filtered air and a third one, which was designated as control group was exposed to natural atmospheric air. After the background correction, 45738 detected probes in all samples were subjected in statistical analysis on Genespring and different pathway analysis. The Venn diagram shows the different and common probes that were expressed in each different group. Thirty-two probes were expressed only at the control and $PM_{2.5}$ group and 11 probes were expressed only at the PM_1 and $PM_{2.5}$ groups, whereas 45695 probes were expressed in all the study groups. In addition, after data normalization and coefficient of variation filtering 18836 probes were analyzed in pairwise conditions. Probe distribution after normality in comparison between groups is shown at the normality scatter plot.

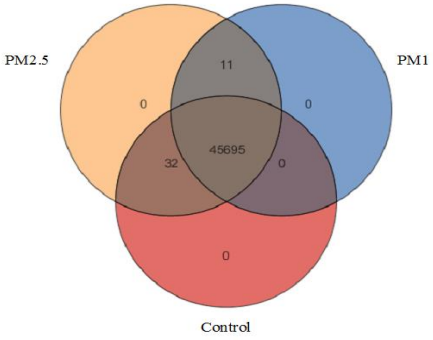


Figure 61. Venn diagram showing the expression of the different microarray probes. Out of 45738 probes only 11, probes were expressed in $PM_{2.5}$ and PM_1 group and 32 probes were expressed in Control and $PM_{2.5}$ group

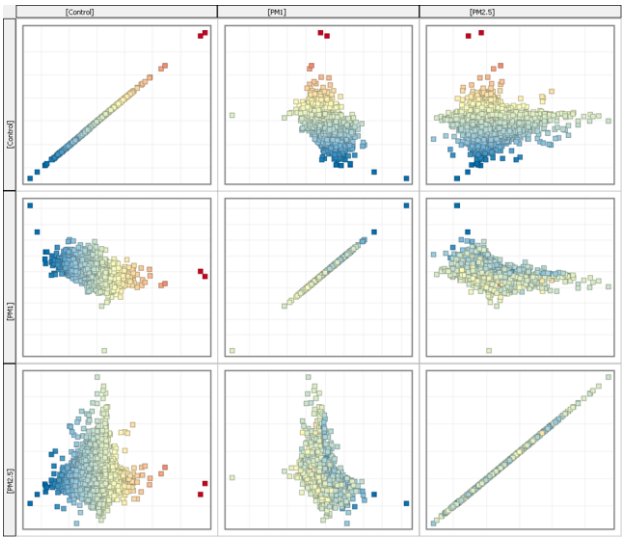


Figure 62. Scatter plot showing distribution of expressed probes after normalization

Moreover, a general gene clustering analysis is shown in Figure 63. Pairwise comparison of the control group

compared to the $PM_{2.5}$ group showed 23 differentially expressed genes (DEGs), from which 4 were significantly up-regulated and 19 were down-regulated. The most important gene targets for further pathway analysis to study their possible biochemical role were the Rasgrf1 (FC: 7.89), the Plekhb1 (FC: 3.78), Trim33 (FC: -2.52), Trim65 (FC: -12.92), Car4 (FC: -3.92), S100a8 (FC: -3.52), S100a9 (FC: -2.72), Alpl (FC: -2.95), Np4 (FC: -6.97 and -11.39) and the Prok2 (FC: -16.49, and -6.97). In pairwise analysis of the $PM_{2.5}$ and PM_1 group, 10 significantly up-regulated genes (12 probes) for $PM_{2.5}$ group were identified and no down-regulation was displayed. The identified target genes are the Np4 (FC: 1.89 and 2.12), the Trim65 (FC: 4.61), Alpl (FC: 3.45 and 2.41), Serpinb1a (FC: 2.22), and the Serpinb11 (FC: 4.07). Comparison of the control group to PM_1 group showed 5635 differentially regulated probes and more specifically 3069 up-regulated and 2566 down-regulated probes.

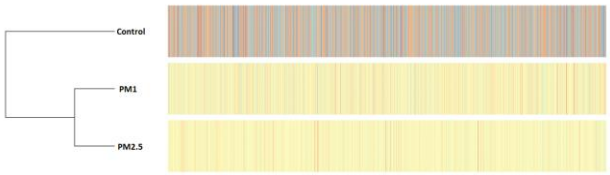


Figure 63. Heatmap of gene expression clustering between control (non-filtered air) group and PM_1 and $PM_{2.5}$ group

Due to the fact that the results produced a large amount of data, in order to connect the outcome to the results from previous comparisons we sought to perform a Gene Set Enrichment Analysis (GSEA) and link our results with KEGG and WikiPathways database. A gene set enrichment analysis was performed to identify the biochemical pathways in which the significantly differentially regulated genes at the control-PM1 pairwise comparison participate. Our results showed severe activation of the interleukin cascade of events between control and PM1 group and the respective pathways displayed many differentially expressed genes in IL-4 (8 genes), IL-1 (9 genes), IL-7 (11 genes), IL-5 (15 genes), IL-9 (8 genes), IL-6 (20 genes), and IL-2 interleukins (20 genes). Our results correlate also with the activation of p53 (15 genes), TNF-a (36 genes) and in addition strong activation was shown in T-cell (32 genes), B-cell (41 genes), and Toll-like (19 genes) receptor pathways.

One of the genes that were significantly up-regulated at the control group inhaling non-filtered air compared to the other two groups is the RASGRF1 gene (FC: 7.9). The latter gene is a guanine nucleotide exchange factor, which promotes the release of GDP from inactive Ras and stabilizes the apoprotein, and the hypermethylated status was found to be a potential risk factor for colorectal cancer, in experiments performed in rats

TRIM65 (FC: -12.92) is an important gene that was significantly down-regulated in the control group. The latter gene has been shown that act as a negative regulator of miRNA activity, regulating miRNA-driven suppression of mRNA translation by targeting TNRC6 (trinucleotide repeat containing six) proteins for ubiquitination and degradation. At this point, it should be noted that in pairwise comparison of PM2.5 to PM_1 group showed up-regulation of TRIM65 gene (FC: 4.61) at $PM_{2.5}$ group. The latter result indicates that it would interest to research further the role of fine particles between 2.5 and 1 μm on TRIM65 regulation and the factors that contribute and alter the expression.

An important result is the up-regulation of ALPL gene (FC: -2.95 in control group). Epidemiological evidence has shown that mutations of the latter gene are linked to hypophosphatasia, which is a rare genetic disorder characterized by abnormal development of bones and teeth.

Finally, one of the most significant findings in this study is the statistically significant down-regulation of the PROK2 (prokinetisin-2) gene. The latter is a member of prokineticins gene family and the respective signaling pathways have been implicated in several important physiological functions, including gastrointestinal smooth muscle contraction, circadian rhythm regulation, neurogenesis, angiogenesis, pain perception, mood regulation, and reproduction.

In summary, “real-life” exposure of Wistar rats showed significant alterations in gene expression after whole genome microarray analysis, that is possible to be related with high concentrations of heavy metals present in particle mixtures. Furthermore, we can conclude the following: 1) the smaller the size of the inhaled particles, the more gene alterations are triggered, as in our results differentially regulated genes between control-PM1 comparison were 200 times more, compared to control-PM2.5 comparison; 2) specific target-genes were selected as candidate biomarkers of effect after exposure to filtered or non-filtered atmospheric air for further research in order to develop novel AOPs leading to carcinogenicity and other pathogenic conditions; 3) in this study it was clearly indicated that perturbations in inflammatory pathways are significantly enhanced in smaller particles (<1 μm) and further research needs to elucidate the mechanistic interaction of the altered genes in relation to respiratory pathogens and allergies; and 4) a “real-life” exposure model using Wistar-rats was evaluated and it could be used from the scientific community in future research.

This work was supported by the Operation Programme (ESPA) in Human Resources Development, Education and Learning Co-funded by Greece and the European Union. Number of Scholarship: 95382.

Development of "green" tile (KERAMI)

Aims and scope

Due to the continuous increase of atmospheric pollutants and their adverse effects on human and environmental health, the need for the development of a new bioclimatic product which could improve our living environment is crucial. The main adverse outcomes to human health, associated with exposure to NO_2, are shortness of breath, cough and increased risk of respiratory diseases. NO_2 is associated with various respiratory adverse effects on human health while at high levels, NO_2 causes inflammation in the airways.

The KERAMI Project is being conducted in collaboration with "KEBE S.A.–Northern Greece Ceramics", aiming to develop a novel "green" tile which will have photoreflective and photocatalytic properties for use in cool roofs. The research is based on the need for products that are non-hazardous to the environment and able to improve living conditions.

This comprises a clay roofing tile with a coating of nanomaterials on its surface. Due to its well-known photoreflective and high photocatalytic properties under ultraviolet radiation, titanium dioxide (TiO_2) is chosen as a raw material for coating cooling roof tiles. TiO_2 is known for its photocatalysis, its zero toxicity, and its ability to degrade organic pollutants. It is also widely available, low cost and can be stimulated directly by ultraviolet radiation.

Titanium dioxide (TiO_2) is a well-known photocatalytic material, non-hazardous to human health and environment. The addition of a thin film coating of titanium dioxide nanoparticles onto the surface of ceramic roof tiles improves the properties of natural ceramic roof tiles as it can photo catalytically degrade air pollutants and improve thermal conditions of a building during summer days.

Novel TiO_2 nanoparticles were developed along with the addition of polyethylene glycol (PEG), which was added as a surface active material, to increase the catalytic surface of the nanoparticles. For this reason, deionized water was mixed with 2.5 % w/v of one of each of the three types of TiO_2 and 0.208 mass % of PEG (MW: 600), while inserted into an ultrasonic bath (50 min). For the characterization of the nanoparticles, all prepared samples were subsequently dried at 100°C and 290°C. At 290°C, PEG degrades and leaves a mesoporous photocatalytic structure. TiO_2 nanoparticles without PEG have also been developed as control samples, following the same procedure. In total, 12 samples with and without PEG have been developed. For the preparation of the final "green" clay roofing tiles, aqueous suspensions of all nanoparticles were sprayed onto the surface of the roof tiles and formed a coating with photocatalytic and photoreflective properties.

Characterization techniques including Scanning Electron Microscopy (SEM) and BET Method (Brunauer-Emmett-Teller) were used for the examination of the distribution of nanoparticles onto the surface of the tiles and for the estimation of their specific surface areas, respectively. Additionally, XRD analysis was performed for the determination of the phase compositions of the purchased nanoparticles. The particle size distribution of the nanoparticles was estimated by a laser diffraction technique using a Malvern Instruments, zeta-nano series, Nano ZS.

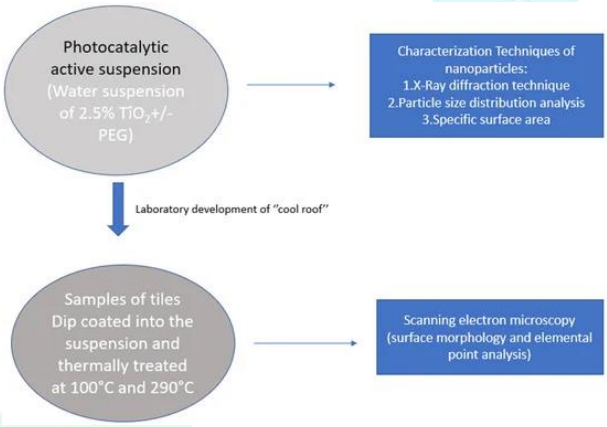


Figure 64. Representation of the experimental methodology

The photoreflectance of the novel nanoparticles was measured by a spectrometer IFS-113V made from Bruker Physik AG, Silberstreifen, 7512 Karlsruhe-Rheinstettent/B.R. Deutschland.

The photocatalytic activity of the samples was evaluated by monitoring the decomposition of NO gas with the use of an experimental set-up that was developed by the research team and consisted by the reactor, a UV source, a nitric oxide (NO) supply and flow rate valves.

Results

Based on the results obtained from the particle size distribution analysis, it was exhibited that the sizes of all the newly developed nanoparticles ranged within the fraction of 70 to 110 nm. SEM images of all types of samples exhibited uniform dispersion of the nanoparticles onto the surface of the tiles, with the majority of them forming spherical shaped particles (Figure 65).

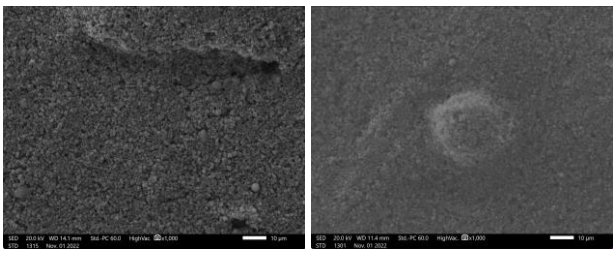


Figure 65. (A) SEM image of TiO_2/PEG nanoparticles dried; (B) SEM image of TiO_2/PEG nanoparticles

Based on the results obtained by XRD analysis, the diffraction patterns exhibited strong diffraction peaks corresponding to anatase and rutile phases.

For the estimation of the specific surface area of the newly developed nanoparticles, TiO_2 samples of all crystalline

phases with PEG were dried at 290°C and the ones with Pluronic F-127 were dried at 350°C. These temperatures were selected as they are the temperatures in which the two polymers degrade and leave a mesoporous photocatalytic structure, which enhances the photocatalytic activity of the samples. According to the results obtained by the BET analysis, the addition of the polymers changed the specific surface area of the samples. More specifically, TiO_2/PEG nanoparticles exhibited greater surface areas (91.5 m^2 /g) than the TiO_2 nanoparticles without PEG (77.7 m^2 /g). For the mixture of rutile and anatase TiO_2/PEG nanoparticles, the specific surface area was 58.9 m^2 /g, while for the same type of nanoparticles without PEG, the respective surface area was 49.9 m^2 /g. For this reason, these nanoparticles were selected for further examination of their photoreflective and photocatalytic activity.

Reflectance measurements of the selected TiO_2/PEG nanoparticles demonstrated great results with the reported total solar reflectance (UV, Vis and NIR spectra) exceeding 80% (Figure 66).

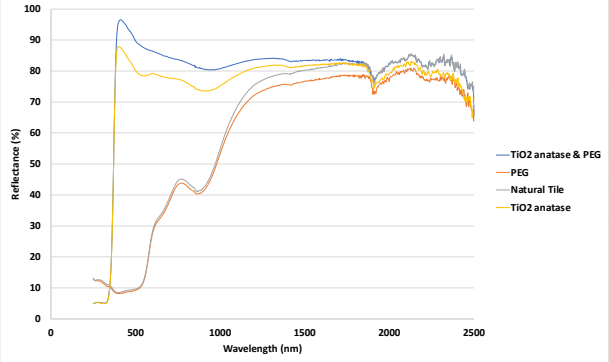


Figure 66. Reflectance of the examined samples.

Table 1: Reflectance measurements of the examined tiles

Sample	Reflectance charachteristics of the considered tiles (ASTM G173)			
	TSR (250 - 2500 nm)	NIR (700 - 2200 nm)	UV (280 - 400 nm)	Vis (380 - 780 nm)
Natural Tile	0,39	0,58	0,1	0,23
TiO_2	0,76	0,77	0,45	0,79
TiO_2+PEG	0,81	0,8	0,46	0,85
PEG	0,38	0,56	0,09	0,23

According to Figure 66 and Table 1, the tile sprayed with TiO_2 anatase/PEG nanoparticles exhibited enhanced photoreflective activity which reached up to 81% of the total spectrum (250-2500nm), as also in UV, Vis and NIR regions. The increase of the TSR with the addition of TiO_2 anatase/PEG nanoparticles was more than 100%. The tile coated with PEG showed the same photoreflective capability with the control sample (natural tile).

The results of the photocatalytic performance of the TiO_2/PEG samples are depicted in Figure 67. The photocatalytic oxidation experiments were carried out using initial NO concentrations of approximately 0.9 ppm.

Results showed that the photocatalytic oxidation reaction takes place immediately when the sample is exposed to the visible light and NO_2 concentration increases and reaches a stable condition quickly. This phenomenon also indicates that no photocatalytic oxidation reaction takes place in dark.

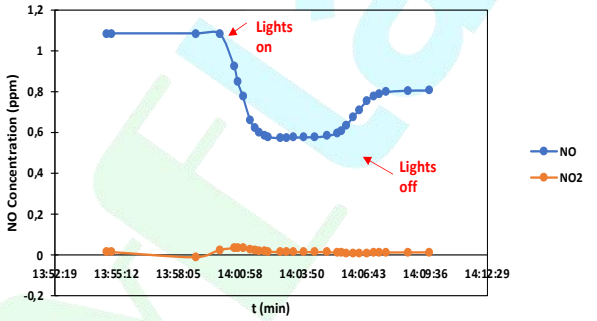


Figure 67. Photocatalytic performance of the TiO_2/PEG nanoparticles.

The results reported in this study indicate that the novel TiO_2 nanoparticles, used as a photocatalytic and reflective coating onto the surface of roof tiles, exhibit high reflectivity and great photocatalytic activity.

"Green" roof tiles prove to be ideal for the enhancement of environmental protection and reduction of air pollution by decomposing pollutants, while also promoting the decrease of energy consumption, due to reduced use of air conditioning systems, maintaining cool temperatures in the interior of buildings occupants and reducing the urban-heat island phenomena.

Titanium dioxide has many polymorphs, the two most significant of which are the stable rutile and the metastable anatase. These polymorphs exhibit different properties and consequently different photocatalytic performances. Anatase has high photoreactivity and can reflect long wave ultraviolet (UVA) and visible light.

Based on the results obtained from this study, it is indicated that the newly developed nanoparticles show good promise for the industrial development of depolluting ceramic tiles.

This research study was funded by the Operational Programme Competitiveness, Entrepreneurship and Innovation 2014-2020 (EPAnEK) of the Ministry of Economy and Development, aiming to develop a novel "green" tile which will have photoreflective and photocatalytic properties for use in cool roofs.

Determination of Particulate Matter in Dental Clinics: The effectiveness of different air purifiers and the central ventilation system

Aims and scope

The purpose of this study was to measure the number and concentration of airborne particulates occurring within a dental clinic while performing different dental procedures that produce aerosols, with and without the simultaneous use of air purifier systems and a central ventilation system. The results showed a reduction in airborne particulates and hence a potential reduction in SARS-CoV-2 virus transmission risk. The aerosols generated by standard dental procedures can cause transmission of the virus to both staff and others present within the treatment area. As with all infections, although it is impossible to completely eliminate the risk of transmission, it is crucial that appropriate air purifying systems are applied to minimize risk of transmission as much as possible. A Mini Laser Aerosol Spectrometer - IAQ-11R (by GRIMM Aerosol) automatic data recorder was used to determine particulate matter in real time. The Mini Laser captures airborne particulates with diameters of 0.25-32.0 μm and classifies them into 31 size channels. Two cycles of measurements were performed as described below. In the first cycle, the dental clinic was not open to the public and experiments were carried out on the effectiveness of different air purifier systems. In the second cycle, the central ventilation system was switched on, and then measurements were taken during real-time dental procedures on patients.

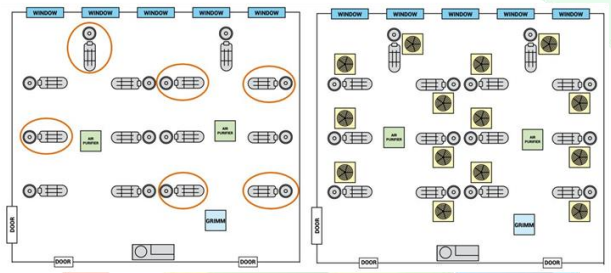


Figure 68. Sketch of the dental clinic indicating the position of the air purifiers and the measurement instrumentation. The orange circles indicate the position of the patients.

Results

The initial concentrations of airborne particulates recorded during dental procedures without the use of air purifier systems and with closed windows reduced by 68% for PM_{10}, 77% for $PM_{2.5}$ and 81% for PM_1 when the same procedures were carried out with the simultaneous use of air purifying systems. Reduced concentrations were also recorded when clinic windows were kept open during tooth grinding work and when air purifying systems were used. In this case, concentrations of airborne particles reduced by 78% for PM_{10}, 83% for $PM_{2.5}$ and 76% for PM_1 (Figure 69). The majority of the particulates captured had diameters of 0.25 to 0.50 μm and 1.0 to 5.0 μm (Figure 70). In experiments where dental procedures were performed with high-speed handpiece and without air purifiers and with closed windows, concentrations appear to be high while when grinding was performed in combination with VacStation and closed windows, the concentrations reduced 27% for PM_{10}, 21% for $PM_{2.5}$ and 19% for PM_1 and when grinding was carried out with the simultaneous use of Winix, and with open clinic windows, particle concentrations reduced by 73% for PM_{10}, 73% for $PM_{2.5}$ and 65% for PM_1 (Figure 71). During grinding with low-speed rotating instruments and with the use of Winix and VacStation, and with closed clinic windows, the concentrations of PM were lower than grinding with the use of only Winix and without VacStation. The reduction in particle concentrations observed when using both Winix and VacStation was 63% for PM_{10}, 37% for $PM_{2.5}$, and 18% for PM_1 (Figure 72).

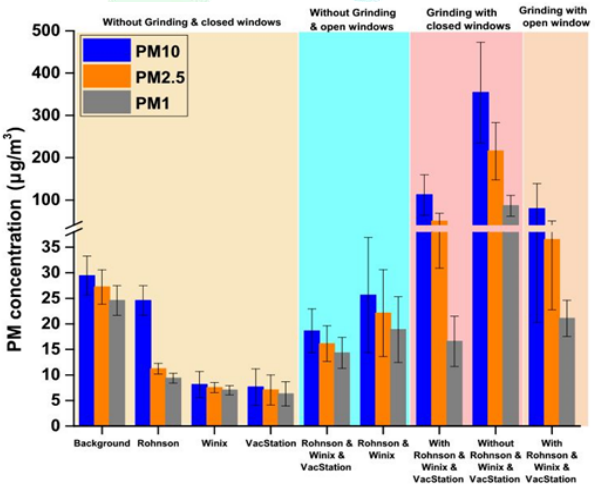


Figure 69. Mean concentrations of particulate matter under different conditions. RWV = Rohnson & Winix & VacStation

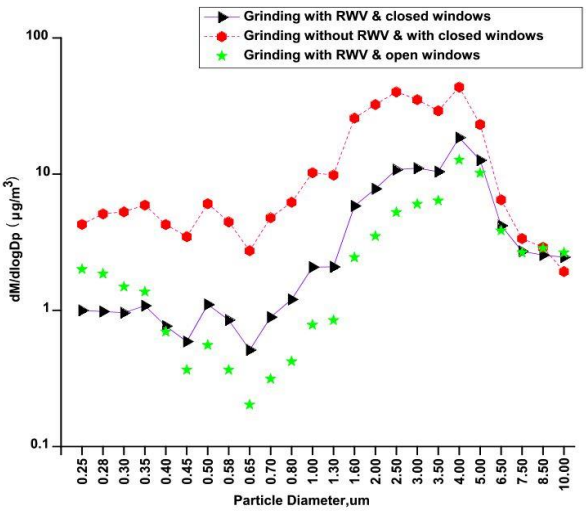


Figure 70. Mass size distribution of particles during dental procedures

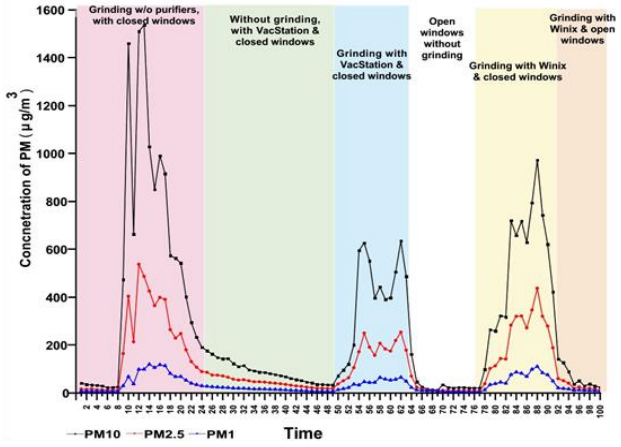


Figure 71. Grinding procedures using high-speed handpiece

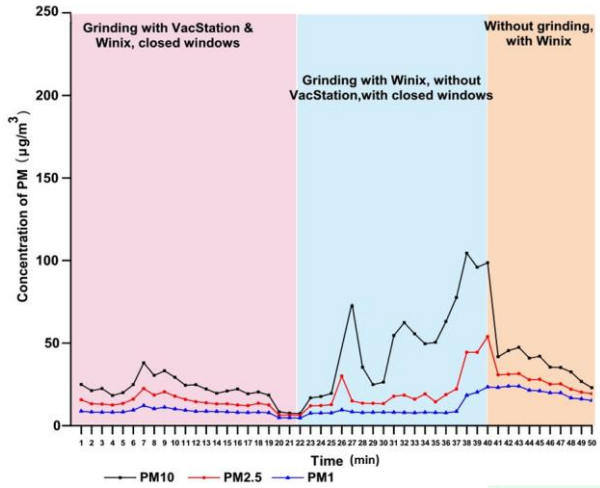


Figure 72. Grinding procedures using low-speed handpiece

The measurements of airborne particles taken in a dental clinic with the simultaneous operation of a central ventilation system are described below. presents the mean concentrations of particulate matter PM_1, $PM_{2.5}$ and PM_{10} recorded in different conditions. The concentration of particles recorded with the simultaneous operation of both ventilation system and air purifiers, fell by 30% for PM_{10} compared to concentrations recorded when only the central ventilation was switched on. However, the combination of ventilation and Airocide reduced concentrations of PM_{10} by 15%, $PM_{2.5}$ by 26%, and PM_1 by 27%. The simultaneous use of ventilation and Winix reduced PM_{10} concentrations by 15% while concentrations of $PM_{2.5}$ and PM_1 remained constant. Figure 73 also shows that the mean concentrations of PM_1 recorded during dental procedures carried out with ventilation and Airocide, remained lower than those recorded when using ventilation alone. Significant differences in particle matter concentrations were not observed with the simultaneous operation of the central ventilation system and the different air purifiers.

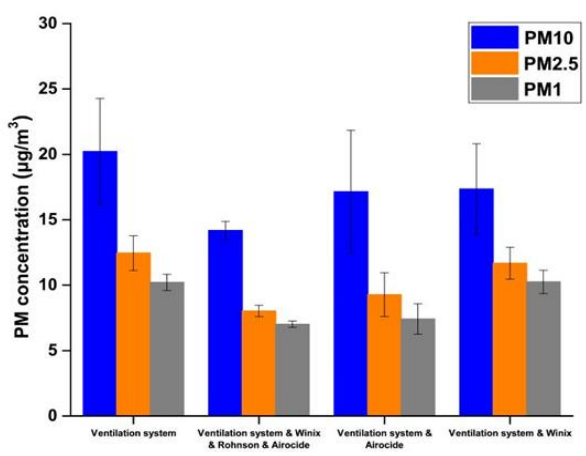


Figure 73. PM recorded during dental procedures with the simultaneous operation of central ventilation system and air purifiers

Figure 74 shows that the majority of the particulates captured had diameters of 0.25-0.30 μm, 0.5 μm and >0.8 μm. A 51% reduction in 0.25 μm particles was achieved when using ventilation with the Airocide purifier.

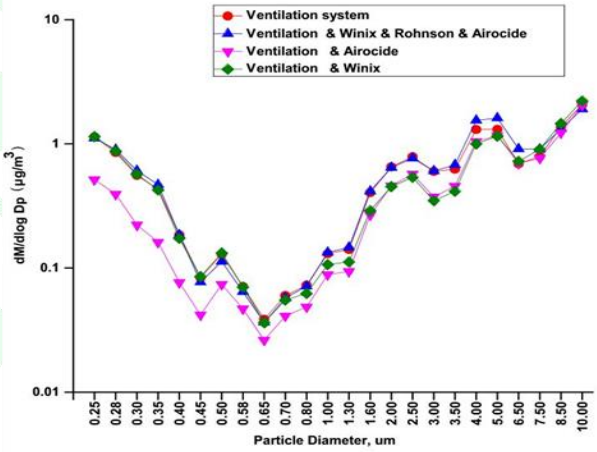


Figure 74. Mass size distribution of particles during dental procedure

The results showed a statistically significant difference between the concentrations of particulate matter generated by dental procedures under different conditions. These results show that the use of a central ventilation system may be useful for any dental clinic and indeed for any busy indoor spaces, especially health care facilities. Additionally, air purifier systems operated in combination with a central ventilation system contribute to the further reduction of potentially hazardous aerosols. As the cost of installing a central ventilation system in the premises of a small, private, dental clinic is often prohibitive, it is crucial that air purifiers should be used during treatment procedures.

Industrial contamination, waste and human health

Waste and health

Athens, the capital of Greece, is populated with around 5 million inhabitants. The average amount of municipal solid waste is equal to 6 ktn/d (Hellenic Statistical Authority 2008). The average composition of the waste in Attica (Figure 75) includes organics (42%), paper (29%), plastic (14%), metal (3%), and other material (6%).

Figure 75. The main waste management site in the area of Athens (landfill in Fili) and the respective waste composition

The average transportation distance of the MSW is 19 km. Two of the main MSW facilities in Athens are the landfill in Fili. The HERACLES (Waste Management) Greek cohort, is a study aiming at assessing the contribution of environmental contamination due to waste management practices in the urban and periurban environment associated to children neurodevelopment. The study has been established in 2012.

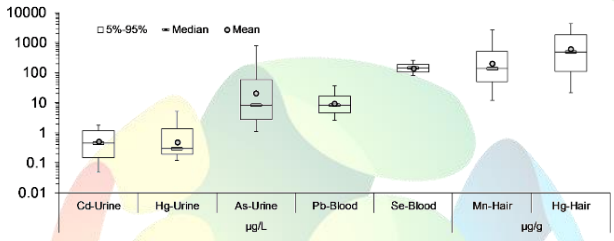


Figure 76. Levels of heavy metals in the various human biospeciments

Around 350 children aged 3 to 8 living in the proximity between 0.5 to 12 km were enrolled. For the association, several exposure factors have been investigated, including exposure to heavy metals, such as Cd, Hg and As in urine, Pb in blood, Mn and Hg in hair (Figure 76), exposure proxies, such as distance from the contaminated sites, concentration of heavy metals in the soil of the child address, additional factors considered as exposure and effects modifiers such as sociodemographic parameters (socioeconomic status, mother education, father education, stress events) as well as child anthropometric parameters and post-delivery factors (child body mass index, child gender, breastfeeding, presence of micronutrients, minerals and vitamins, Se in the mother plasma during pregnancy, delivery and in cord blood). Finally, detailed dietary habits, such as consumption of meat products (pork meat, beef, lamb, sausages), fish, sea food, poultry (eggs, chicken), dairy products (milk, yogurt), nuts, fruits, vegetables and snacks (biscuits, chocolates) were also recorded. Neurodevelopmental progress in children was estimated with (a) the Child Behavior Checklist, also called the Achenbach System of Empirically Based Assessment, is a report form to screen for emotional, behavioral, and social problems and (b) Wechsler Intelligence Scale for children – Fourth Edition (Wechsler, 2003), which is an individually administered measure of intelligence intended for children. WISC-IV yields measure of general intelligence as reflected in both verbal and nonverbal (performance) abilities and specific indices including verbal comprehension, perceptual reasoning, working memory and processing speed. Auto-correlations of the various parameters, are illustrated in the correlation globe (Figure 77).

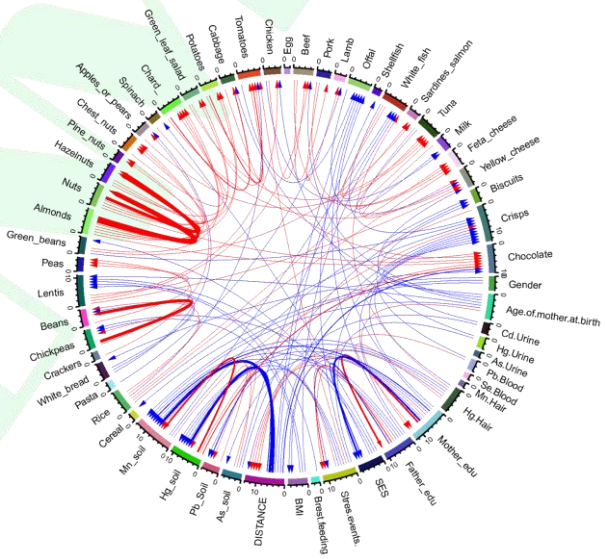


Figure 77. Correlation globe of environmental, dietary and exposure factors in the HERACLES study

EWAS analysis results relevant to the Child Behavioral CheckList (CBCL) test battery results show that socio-cultural factors are strongly associated with children behavior. More specifically the mother school title and the age of the mothers at birth show both a robust statistical association (p-value<0.05 and in some cases p-value <0.01) with most of the CBCL indices considered. Looking at the volcano plots both parameters show a negative association with the CBCL scores indicating that lower educational level of the mothers as well as a lower age of the mother at the children birth may have negative impact on the children behavior. The stress index was derived by merging the total number of stressful events detected by the mother and their average intensity is also playing an important role on the children behavior (p-value<0.05 and in some cases p-value<0.01) showing a negative effect on both internalizing and externalizing problems indices such

as anxiety and depression, withdrawal and depression and somatic complaints, aggressive and rule-breaking behavior. The concentration of lead in blood shows a strong statistical significance (p-value <0.05) with most of the CBCL indices analyzed. In this case the association shows a positive direction revealing a negative impact of higher blood concentration of lead on the on cognitive functions in children. Of opposite sign but still with robust statistical significance is the association of the concentration of selenium in blood which appears to beneficially, especially with regard to Internalizing Problems and ADHD as measured by CBCL battery indices. These results confirm the antioxidant properties of selenium which is a well-known regulator of brain function.

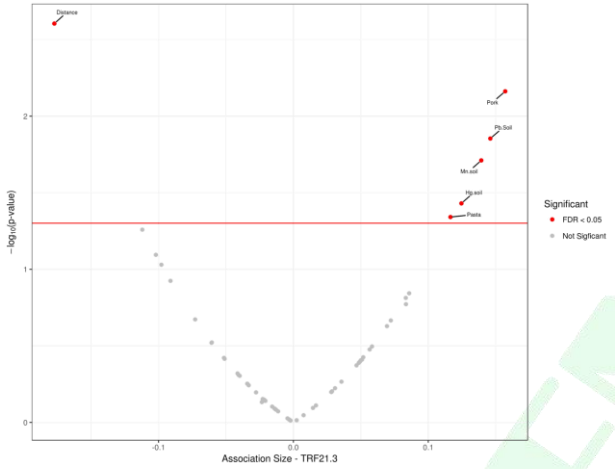


Figure 78. Associations of attention deficit / hyperactivity problems (from the CBCL test battery) with the environmental, dietary and exposure factors

Distance of the residence address from the waste management site was found also to be a key factor associated with almost all the indices of the WISC IV test. More specifically, this variable showed a robust statistical association (p-value <0.001) with the Intelligence Quotient (IQ), Verbal Comprehension index, Perceptual Reasoning index, Working Memory index. Analysis of the results shows a positive association with the WISC IV scores indicating that living far from the waste management site has a positive impact on the children cognitive functions. Interesting conclusions can be drawn from the analysis of food consumption patterns. Tomato consumption appears to be statistically (p-value <0.05) associated with intelligence quotient (Figure 79), Verbal Comprehension index and Working Memory index while cereal consumption reveals a strong association (p-value < 0.01) with the Perceptual Reasoning index. Both food items are positively associated with cognition indices meaning that their consumption has potential positive effects on the cognitive functions of the children. Epidemiological evidence suggests that consumption of lycopene, a natural antioxidant present in tomatoes, is able to reduce the risk of chronic diseases such as cancer, cardiovascular diseases as well as psychiatric syndromes.

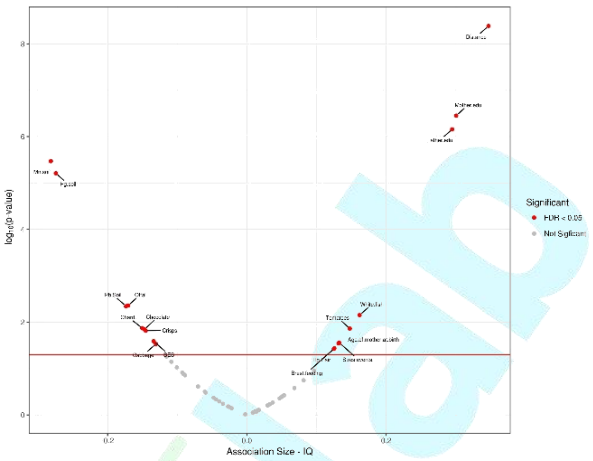


Figure 79. Association of intelligence quotient (from the WISC-IV test battery) with environmental, dietary and exposure factors

Consumption of fish showed a hybrid behavior depending on the type of fish and the neurodevelopmental indicator considered: higher consumption of white fish appears to have positive effects on the IQ and Verbal Comprehension index (p-value <0.001) while higher consumption of white fish reveals a negative effect (p-value <0.01) on Perceptual Reasoning index and Working Memory index.

A key finding of the study is that concurrent evaluation of environmental, societal and nutrition factors, allowed the identification of the most critical parameters. Distance of the family residence from the landfill was identified as the most important parameter, highlighting the contribution of the area contamination to child neurodevelopment. However, the beneficial effect of parental education and of children/family socio-economic status need to be underlined. Additional beneficial effects arise from specific dietary patterns such as consumption of white fish and tomatoes, while the same occurs for breast feeding. White fish is rich in omega 3 fatty acids. Direct actions of omega-3 polyunsaturated fatty acids on neuronal composition, neurochemical signalling and cognitive function constitute a multidisciplinary rationale for classification of dietary lipids as "brain foods." The validity of this conclusion rests upon accumulated mechanistic evidence that omega-3 fatty acids actually regulate neurotransmission in the normal nervous system, principally by modulating membrane biophysical properties and presynaptic vesicular release of classical amino acid and amine neurotransmitters. On the other hand, tomatoes are considered as strong antioxidants, providing protection against the reactive oxygen species (generated by heavy metals) that affect neuronal mitochondria and eventually children neurodevelopment.

Quantification and characterization of microplastics in the Thermaic Gulf

Rationale

The abundance and distribution of microplastics has largely increased during last years and the respective implications on the environment and human health is an emerging field in research. In addition, recent studies in the closed Mediterranean Sea in Spain and Italy have shown an extended occurrence of microplastics (MPs) in different environmental samples. This study is focused on the quantification and the characterization of microplastics in the Thermaic Gulf in northern Greece. The marine biota of the gulf is strongly affected by human activities such as the urban activity of Thessaloniki, discharge from primary and secondary wastewater treatment units, and the industrial area of Sindos on the western side of the city. Other human activities, such as aquaculture and shipping, also occur within the gulf itself and are directly related to marine pollution. Sediment samples were collected from five beaches located on the eastern side of the gulf. Surface water samples were taken at three different locations from the shoreline, and the gastrointestinal tracts of different fish species were analyzed for microplastic contents. The microplastics of each sample were quantified and the polymer type of each was identified. This is the first study to provide novel data regarding microplastics in Thermaic Gulf, as part of a broader research on microplastics within the Mediterranean.

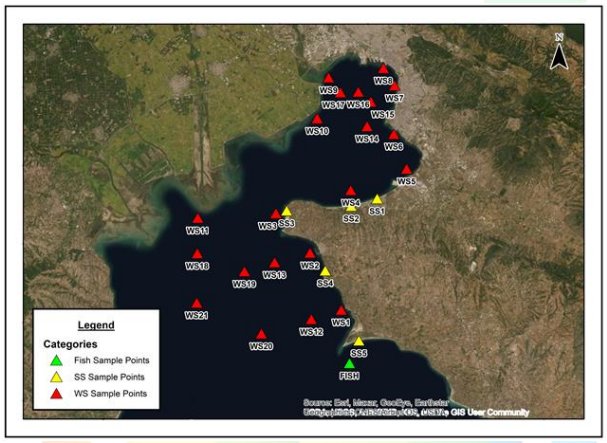


Figure 80. Locations of sampling sites in the study area of Thermaic Gulf.

Briefly, samples from different sediments origin such as seawater, local beaches and seven commercially available fish species were collected and analyzed. Microplastics particles were extracted and classified by size, shape, colour and polymer type. This is the first detailed investigation of MPs in Thermaic Gulf, which raises concerns on their potential negative effects.

Surface water

A total of 28,523 microplastic particles were recorded in the surface water samples, with their numbers ranging from 189 to 7,714 particles per sample. The mean concentration of MPs recorded on the surface water was 1.9 ± 2 items/m^3 or 750,846 ± 838,029 items/km^2. All the surface water samples contained microplastic particles (MPs) and this shows that the study area is heavily polluted. Most of the particles were white in colour (45%), and the most abundant shape was fragments accounted for 67% of the MPs.

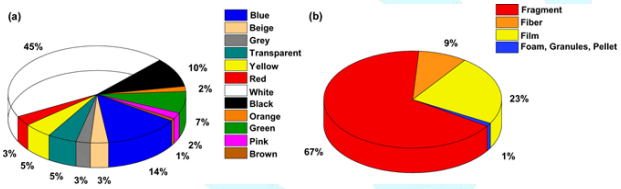


Figure 81. (a) The proportion of microplastic colour and (b) shape in the water samples from the coast area of Thermaic Gulf

The highest concentrations of MPs were found at distances of 10 km from the shoreline and the lowest at distances of 5 km. The highest concentration was observed in Epanomi, which can be attributed to the presence of intense tourism in this area in the summer. Despite the area of Sindos being heavily influenced by local industrial activities, it showed similar MP concentrations to those in the area of Thessaloniki.

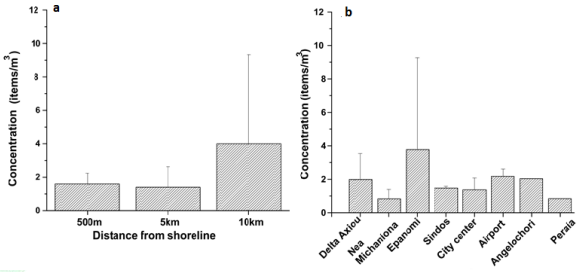


Figure 82.(a) the average concentration of MPs at distances of 500m, 5km and 10km from the shoreline, (b) concentration of MPs per sampling site

Fish

Two hundred and forty-four (244) microplastic particles were extracted from the 72 fish samples taken from the gulf. Of these, 86 particles were found in the gills and 158 were found in the gastrointestinal organs of the fish. Concerning fish deposition, microplastics were detected in intestines and mean concentrations per species ranged from 1.3 ± 0.6 to 15.0 ± 1.5 items/individual. The differences in microplastic concentrations between species were statistically significant ($p < 0.05$) and showed that mesopelagic fish contained the highest concentrations, followed by epipelagic species. The majority of the MP particles extracted from the fish samples were white in colour (45%). Concerning the shape parameter, most of the MPs extracted from the fish samples were fibrous (60%), followed by fragments (29%), and film (10%).

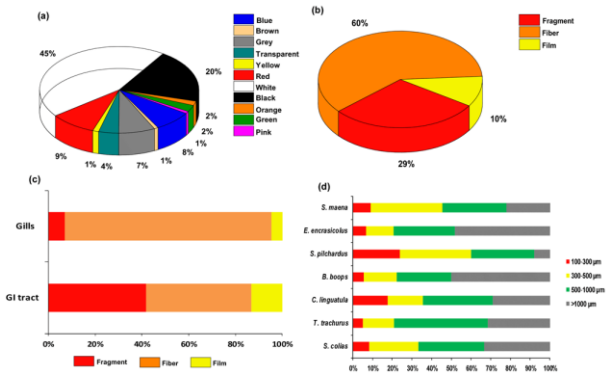


Figure 83. (a) The proportion of microplastic colour in fish samples, (b) the proportion of microplastic shape in fish samples, (c) and in gills and gastrointestinal organs, (d) microplastic size distribution in fish samples

Sediment

Sediment sample analysis revealed 14,790 microplastic particles, of which 1,825 were large microplastics (LMPs, 1-5mm) and 12,965 were small microplastics (SMPs, <1mm). Furthermore, sediment samples showed a mean concentration of 733 ± 136 items/m^2, with the concentration of LMPs being 90 ± 12 items/m^2 and the concentration of SMPs being 643 ± 132 items/m^2. The majority of MPs in the sediment samples was white (33%). These results are in agreement with those of the water samples taken from the same three sampling sites. The predominant shape of the MPs extracted from the sediment samples was identified as fragments that accounted for 83% of the total MPs.

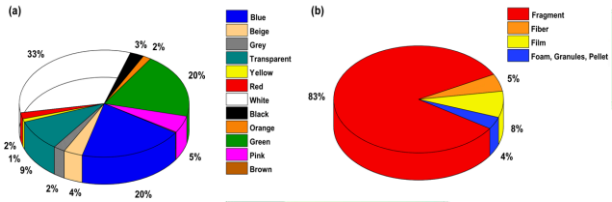


Figure 84. (a) The proportion of microplastic (a) colour and (b) shape in sediment samples.

In this study, samples were taken at distances of 5, 10 and 15 m from the shoreline and the results showed clearly that upper sections of the beaches contained higher numbers of MPs. This is due to the action of waves and wind that thrust the MP particles onto the upper areas of the beaches.

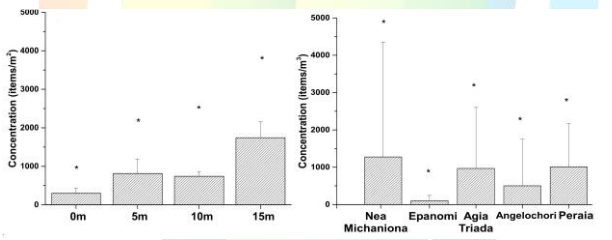


Figure 85. (a) concentration of MPs per sampling site, (b) the average concentration of MPs at distances of 0 m, 5 m, 10 m and 15 m from the shoreline (*means that there is significant difference between the samples ($p<0.05$))

Raman spectroscopy was also applied to randomly selected MPs extracted from sediment samples and five types of polymer were identified (Figure 86). The commonest polymer in the sediment samples was found to be polypropylene (PP) with 42%. This was followed by polyethylene polymers of different densities, the most frequent being high-density polyethylene (HDPE) with 33%, and the least frequent being low-density polyethylene (LDPE) with 13%. A significant quantity of polystyrene (PS) (10%) was also recorded together with a small quantity (2%) of polyvinyl chloride (PVC). This low percentage of PVC was expected because the density of this material is usually higher than that of the saline solution used in the density separation process, therefore, it cannot float on the surface of the saline solution or be separated with the supernatant during filtration.

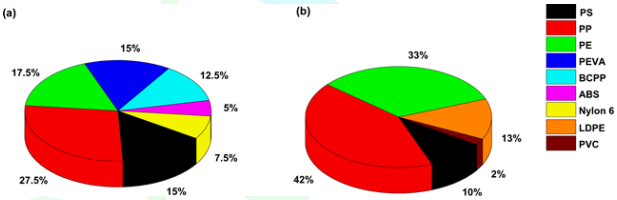


Figure 86. Polymer types of the microplastic particles extracted from (a) surface water samples and (b) from sediment samples taken from Thermaic Gulf

Microplastics were recorded in surface seawater, sediment, and fish samples of Thermaic Gulf. The results indicate a relation between the three different parts of the marine ecosystem. Inadequate solid waste treatment and the excessive use of plastics have led to the accumulation of plastic debris on beaches and in seawater. These microplastics have been consumed by local fish populations and may be a threat to human health, especially considering that the species sampled are commercially available. The highest concentrations of microplastics in surface seawater were recorded 5 to 10 km from the coastline and this may be attributed to the study area's prevailing water currents. Significant concentrations of microplastics were observed on isolated beaches in the gulf, which indicates that pollution by microplastics can also occur in areas not directly affected by anthropogenic activity, as particles are carried by air and water currents. Strict regulations are required to prevent the dispersion of microplastics into the environment by reducing their use at the source. However, even if the use of microplastics is banned, larger plastic items already present in the environment can be degraded into microplastics. The industrial use of biodegradable materials is considered essential in order to minimize the usage of plastics, especially during the present COVID-19 pandemic.

Life cycle analysis of municipal waste management - Industrial symbiosis options for reduced ecological footprint

Municipal solid waste (MSW) management is nowadays one of the biggest problems in both developed and developing countries. Prevention, recycling, treatment and final disposal of MSW are regulated through a number of general policy principles and international directives. It is imperative therefore to create awareness among local authorities, manufacturers, companies and generally society of the available varied technological solutions.

Integrated waste management solutions using the concept of industrial symbiosis (IS) have been developed and evaluated taking into account the European and national waste management legislation. IS, as part of the emerging field of industrial ecology focuses on the flow of materials and energy through local and regional economies. IS engages traditionally separate industries in a collective approach to drawing competitive advantage involving physical exchange of materials, energy, water, and/or by-products. The keys to IS are collaboration and potential synergies offered by geographical proximity and industrial function. Life Cycle Assessment (LCA) provides the methodological framework. LCA is conducted according to ISO 14040 Moreover, LCA used to describe the environmental impacts of products and processes while assessing the material and energy flows throughout their lifetime.

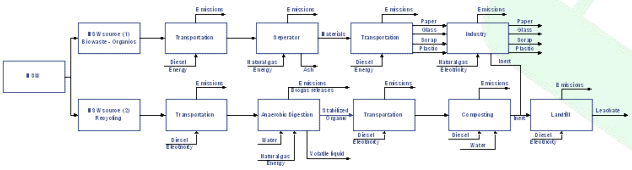


Figure 87. Waste management scenario: Waste is pre-treated and pre-sorted into biodegradable and non-biodegradable material for further anaerobic digestion and composting. Residues end in landfill. Plastic, paper and ferrous material are recycled.

Indicators of efficiency, effectiveness, and environmental and public health impacts are used to facilitate the comparative evaluation of the different MSW management scenario. Hence, material flow accounting, gross energy requirement, exergy and emergy intensity, local, regional and global emission and release intensity and morbidity or mortality indicators are used to support the comparative assessment.

This integrated framework was applied in the case of MSW management in the two larger cities in Greece, Athens and Thessaloniki, with a special focus on energy and material balance, including potential global and local scale airborne emissions as well as groundwater and soil releases. Public health impacts were assessed based on adverse effects on respiratory health, congenital malformations, low birth weight and cancer incidence.

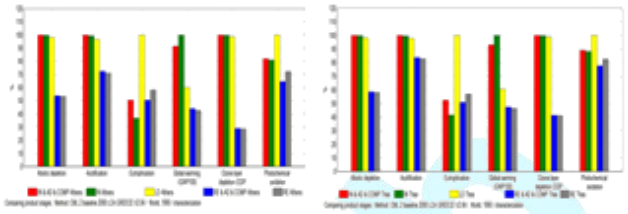


Figure 88. Impact categories of life cycle assessment for Athens and for Thessaloniki

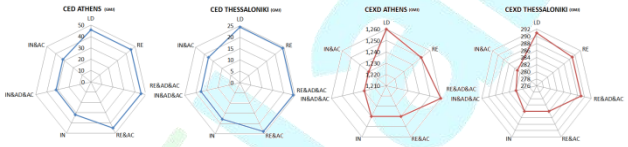


Figure 89. Cumulative Energy and Exergy Demand for Athens and for Thessaloniki

A significant and non-intuitive result is the fact that integrated framework analysis produces different conclusions than a simple environmental impact assessment based only on estimated or measured emissions. Taking into account the overall life cycle of both the waste streams and the technological systems and facilities envisaged under the plausible scenarios analyzed herein, modifies the relative attractiveness of the solutions considered. The results of the assessment based on selected impact indicators lead to the following conclusions: biological methods have the smallest abiotic matter, acidification potential, greenhouse gas effect, ozone depletion and photochemical oxidation among the waste management systems considered.

However, not all options are benign on the local environment and on the local population health, since both can be influenced by non-negligible local emissions.

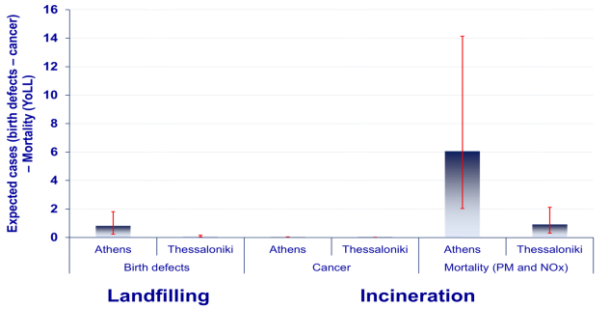


Figure 90. Health impact assessment among the various waste management options

As far as public health is concerned, adverse effects on respiratory health, congenital malformations, low birth weight and cancer incidences are still observed especially from incineration and landfilling.

Innovative waste management and energy recovery systems

Waste-to-energy systems and algae photo-bioreactors

Valorization of zero or negative value raw materials has become the hot spot of the 21st century with the biological methods leading the way. From composting to the fourth generation bio-refinery, microorganisms are utilized thanks to their abilities to bio-convert different organic macromolecules into valuable materials and renewable energy resources. Throughout this quest for identification of renewable resources, great attention has been paid into the evolution of the anaerobic digestion into a robust process able to treat a plethora of mixed substrates. While microorganisms are able to valorize different waste streams, they have a number of inherent limitations which through appropriate management can be bypassed or ever used in advantage of another biological process in a win-win process scheme. One of these limitations is the inefficiency of anaerobic microorganisms to convert a number of natural macromolecules into biogas mainly due to slow hydrolysis.

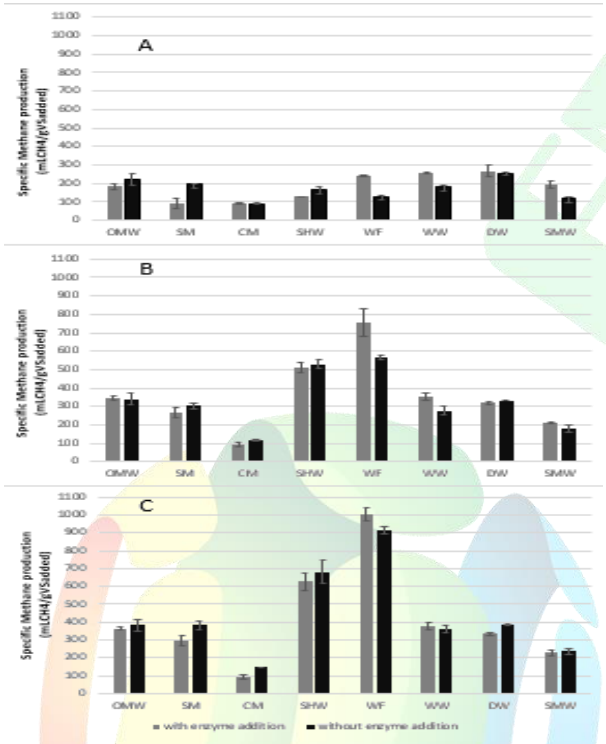


Figure 91. Specific methane production (mL/gVS_{added}) on days 5, 12 and 30 for the enzymatically pretreated and not pretreated substrates (Olive Mill Waste, Sterilized Mass, Cattle Manure, Slaughterhouse Wastes, White Fat, Winery Wastes, Distillery Wastes, Slaughterhouse, Solid Mill Wastes)

In order to improve the efficiency of the process toward these macromolecules, in the last couple of years a number of small scale digestion experiments took place in our laboratory where we assessed the effectiveness of initial enzymatic pretreatment enhanced by the addition of commercially available enzymes. Based on the generated data, the effect that the examined enzymes have on the anaerobic digestion of the mixed substrates can be divided into three categories:

A) No or negligible effect, as is the case of olive mill and distillery waste.

B) Positive effect on the process with the methane production taking place faster and the organic matter exhausts more rapidly. This category includes white fat and olive mill solid waste.

C) Negative effect with the methane production taking place slower and the cumulative methane production being lower when compared to the methane generated by the batches that no external enzymes added. This category includes cattle manure and sterilized mass.

Photo bioreactors

Another inherent limitation of anaerobic digestion is the generation of carbon dioxide during anaerobic respiration. This in some cases can be volumetrically equal to the generated methane. The presence of carbon dioxide in the biogas is undesirable as it is reducing the heating value of the gas while increasing storage and management costs. In order to reduce the concentrations of carbon dioxide from the biogas, we designed and constructed a bench-scale anaerobic digestion system coupled to photo-bioreactors where algae are employed for the valorization of the carbon dioxide, hydrogen sulfide and ammonia available in the biogas.

Figure 92. The photo-bioreactors within the temperature controlled cabinet

After harvesting algal biomass will be used for the recovery of high value added products, raw material for fuel manufacturing and industrial product development. Algae are a group of photosynthetic microorganisms that can fix carbon dioxide from different sources into biomass. During the last years this ability of algae has been explored in order to identify pathways through which the application of these species can reduce the environmental burden of human activities. Algae are an important carbon sink and their cells can contain more than 50% of fats and oils, sometimes rich in ω-3, from where pharmaceuticals or raw material for biodiesel production can be extracted. It noteworthy that for every kg of algal biomass, 1.65-1.83 kg of CO_2 must be consumed. The spent algae cells can be further valorised as activated carbon building blocks or substrate to anaerobic digesters.

Biomethanation of cellulose rich agro-waste

Cereal farming is the main agricultural activity worldwide generating 1-3 tons of cellulose rich waste per ton of grain product. The main wastes of this process are the two straw types as well as the husk in the case of rice. While a small proportion of the agrowastes are used as feed for ruminants, a significant volume is burned on the fields prior to the new agronomic year. Recently, the exploitation of cellulose-rich waste has started to gain momentum as a possible substrate in biorefineries. Toward this target, the wheat and rice straws as well as the rice husk were selected and assessed as substrates to anaerobic digestion process. The substates underwent milling in a hammermill and three fractions were generated, these were the 2 cm, 1 cm in length as well as in a powder form. In addition, the enzymes cellulase and xylanase were added into the substrates in order to evaluate the effect of the biological pretreatment methods. The enzymatic coctails evaluated were these composted by 10, 50 and 100 mg /gVS_{added} per enzyme. The mechanical and biological pretreatment of the substrates was investigated in batch as well as continuous CSTR type reactors.

Figure 93. Batch and CSTR reactors

According to the results, the highest methane production 370 $mLCH_4$/ gVS_{added} offered by the wheat straw when it was pretreated through milling into 1 cm fractions with the addition of 10mg/gVS_{added} of cellulase and xylanase.

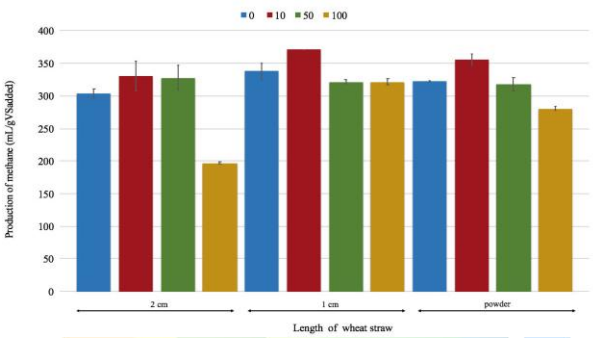


Figure 94. Methane production

It was found that the mechanical or biological pre-treatments in a number of cases inhibited the process. It seems that the type of pretreatment and required enzyme is a substrate specific method and significant pretreatment experimentation should be used before a pretreatment method becomes standardized within a biogas production facility.

Microalgae cultivation for biofuel production

Microalgae cultivation for biofuel production is a promising economic activity toward sustainable development. Biofuels derived from algae biomass offer several advantages compared to the biofuels generated at the first and second generation biorefineries. An advantage of microalgae is their ability to utilize carbon in closed systems. Although, algae cultivation it seems as an easy and first class solution to a number of environmental and economic issues, the availability of sustainable carbon dioxide sources is limited.

During the experimentation period batch photoreactors were used and different concentrations of biogas was added into the systems. The aim was to evaluate the effect of pH and to assess the growth potential of the microalgae *Chlorella vulgaris* with biogas as substrate. In order to evaluate acceptance and growth rate of the algae the batches were fed with 1.1, 2.3 και 3.4 g CO_2/L·d. Furthermore, the biomethanation of the generated biomass was also studied. For the biomethane potential tests a similar biogas test was used with organic loadings ranging between 6.25 and 18.75 gVS/L.

Figure 95. Biomass concentration based on cultivation cycle

According to the results the highest biomass concentration of 2.3 g/L, in a 10-day cultivation circle, achieved for the feeding rate of 2.3 g CO_2/L·d while the highest bioconversion efficiency of CO_2 offered by the 1.1 g CO_2/L·d with approximately 26%. Moreover, the highest methane production was offered by the anaerobic digestion of microalgal lipids and measured at 669 mL CH_4/gVS. Growth of *Chlorella vulgaris* on biogas is a possible and sustainable method for biogas polishing. The results of anaerobic digestion suggest that microalgae biomass offers a high quality substrate that can be used for biomethane production.

EnvE Lab international profile

International collaborators network

EnvE Lab has a broad network of collaborators in each thematic area. In total, EnvE Lab collaborates with 56 research and academic institutions covering 28 different countries across the world in the frame of the six projects running in 2022.

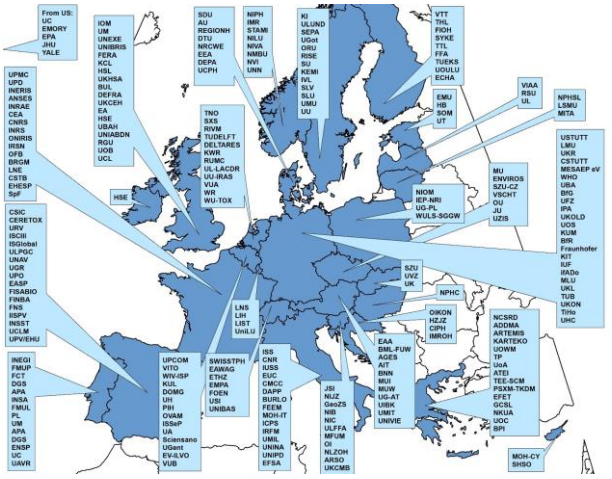


Figure 96. EnvE Lab collaborator network

In 2022 these collaborations gave rise to 55 presentations given in international fora. During the same period ten joint papers were published in international peer-reviewed journals and two book chapters were prepared.

World Health Organization (WHO)

Over the last ten years EnvE Lab has established a close collaboration with the WHO European Centre for Environment and Health, which includes:

- The development of **integrated methodologies for health impact assessment**,
- The assessment of **combined or multiple exposure to health stressors in indoor built environments**.
- Analysis of **Environmental Health Economics** to quantify the socioeconomic dimension of environmental pollution.
- Assessment of current state of play in **human biomonitoring**.
- Overview of **human exposure to endocrine disruptors** in Europe.
- **Waste and human health**;

European Food Safety Authority (EFSA)

EnvE Lab has also initiated a collaboration with EFSA on the development of effect biomarkers based on NAMs approaches. The proposed methodology relies on the integrated pathway-level analysis of transcriptomics, proteomics and metabolomics data from both *in vitro* and in vivo studies. The methodology has been showcased in relation to EDCs exposure; co-exposure to common EDCs disturb biochemical processes related to mitochondrial respiration during critical developmental stages that are clinically linked to metabolic outcomes. Thus, omics-informed NAMs allow for the identification of early biological effect markers and could support mechanistic understanding of toxicity, including AOPs and AONs. The above case study highlighted the need for integration and for tools that link complex environmental and human exposure dynamics with biological perturbations over time, identified by omics-based effect biomarkers.

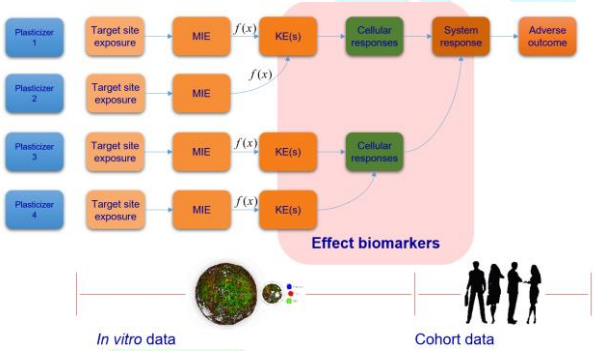


Figure 97. Pathway based approach towards AONs, assimilating omics data coming from both *in vitro* and human cohorts

The White Tower Forum on Urban Health and Sustainability

The 1st International Conference on Urban Health and Sustainability, under the title 'The White Tower Forum on Urban Health and Sustainability' was held hybrid (in person and online), on June 29 and 30 at Thessaloniki. The main host and organizer of the event was the URBANOME Coordinator & EnvE-Lab Director, Professor Dimosthenis Sarigiannis. The two-day event, entitled "The post-COVID 19 era. Healthy, Sustainable Cities: Challenges, Opportunities and Prospects", was organized by the Department of Environmental Engineering (EnvE-Lab) AUTH, the HERACLES Research Lab for Health and Exposure, the URBANOME Project, and the Urban Health Cluster. Special sessions were held with invited speakers that highlighted the importance of adopting urban sustainability in our societies, while interesting panel discussions approached and captured the new post-covid reality, providing the means for a fruitful dialogue between the scientific community and the social and public institutions. Professor Sarigiannis set the pace for intriguing conversations regarding Environment, Climate Change & Health, while commenting that the event's goal was to highlight those concepts that foster the transformation of our cities so that they can promote public health and wellbeing, while they adopt the urban sustainability in their core both in Greece and across Europe.

Figure 98. EnvE Lab organizing committee of the 1st International Conference on Urban Health and Sustainability

EnvE Lab response to societal needs

COVID-19

Aiming at the efficient management of the COVID-19 pandemic, we developed a multi-modal computational tool for the evaluation of the public health risk from the COVID-19 epidemic in Greece, Italy and USA and we have evaluated the effectiveness of different pharmaceutical and non-pharmacological intervention scenarios for public health risk management. Graphical abstract of our model is presented very brief in Figure 99.

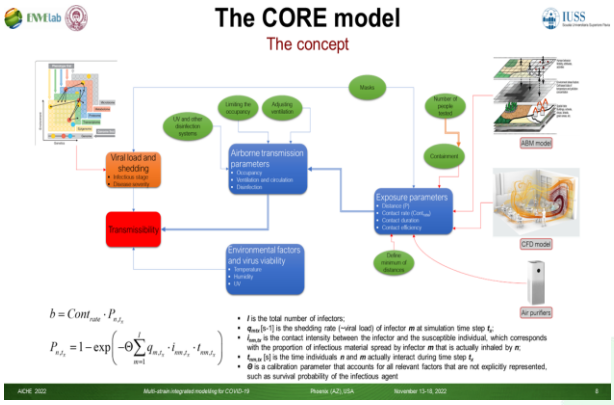


Figure 99. Graphical abstract of the CORE model

The mathematical model is based at the following flowchart (Figure 100).

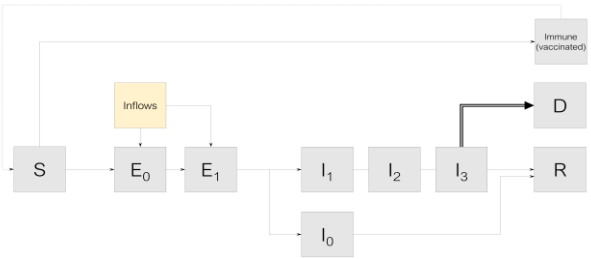


Figure 100. System configuration of the CORE model for COVID-19 risk management

Contact rates for the different population groups within the CORE model, are estimated using Agent-Based Modelling (ABM). ABM results are illustrated in Figure 101 for the different age groups in case that the schools will be opened or closed, in a scenario that was widely discussed during COVID-19 pandemics. With regard to our scenario analysis results, it was found that both the extent of population vaccination, as well as the daily number of testing (including self-tests) are critical to reducing the contagion spread which was something that fully confirmed during the pandemics. It has also been shown through many different scenarios that self-tests are the most precious ally in combating pandemic. A very important observation was that the lockdown transposed the time when the pandemic wave reached its peak, and only offer some more time to health workers prepare themselves.

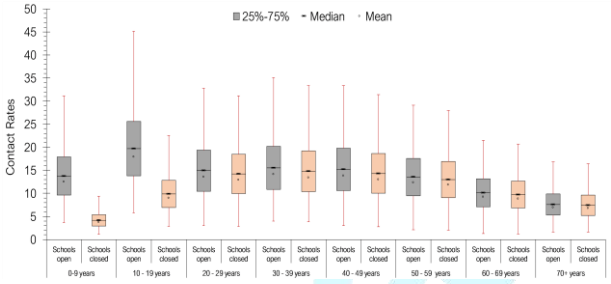


Figure 101. Estimated contact rates per age groups in the case all educational activities are carried out online

Epidemiological surveillance continues even if the pandemic has turned into an endemic disease. Based on the weekly announcements of the National Public Health Organization, predictions are updated, and simultaneously are enriched with data of the most recent mutations that are circulating in the community. The figures below describe COVID-19 pandemics in Greece since its beginning.

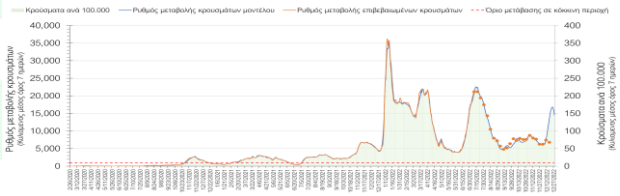


Figure 102. Epidemiological situation in Greece, related to cases

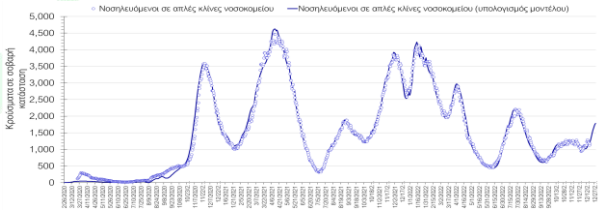


Figure 103. Epidemiological situation in Greece, related to cases in serious condition (hospitalized)

Figure 104. Epidemiological situation in Greece, related to cases in critical condition (intubated in ICU)

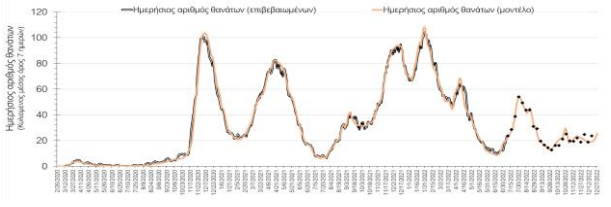


Figure 105. Epidemiological situation in Greece, related to deaths

EnvE Lab in the news – TV interviews (selected)

Figure 106. An interview at OPEN TV Channel with Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about the outbreak and peak of covid cases. **Watch the video at:**

https://www.ethnos.gr/embed/100038

Figure 107. An interview at CRETA TV Channel with Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about fears of the emergence of new mutations and for the gradual relaxation of measures and return to normality for the Easter period. **Watch the video at:**

https://www.facebook.com/TVCretaOfficial/videos/981454345806497

Figure 108. An interview at OPEN TV Channel with Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about summer migrations and new strains of omicron and what we need to do to protect ourselves from the lifting of summer measures. **Watch the video at:**

https://www.youtube.com/watch?v=Fc95gKWaEHE

Figure 109. An interview at VERGINA TV Channel with Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about the need for disinfection devices in schools for air quality in classrooms. **Watch the video at:**

https://www.youtube.com/watch?v=YVzq28CzEfU

Figure 110. An interview at EGANTIA TV Channel with Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about the dynamic transmissions of coronavirus and the spread of a new wave in view of winter and the importance of vaccination. **Watch the video at:**

https://www.youtube.com/watch?v=3SqH6-QtOFc

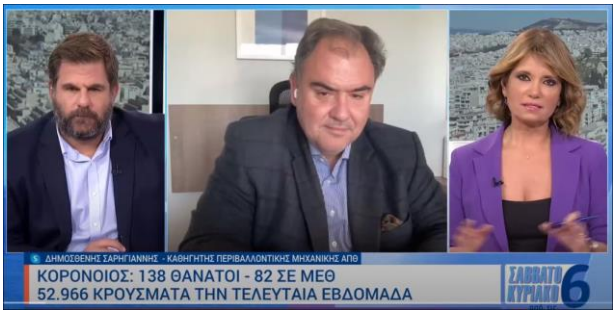


Figure 111. An interview at ERT TV Channel with Professor Dimosthenis Sarigiannis, EnvE Lab director, talking about the appearance of sub-variants and the necessity of vaccination for the spread of covid. **Watch the video at:**

https://www.youtube.com/watch?v=wKumT8GFZsw

Publications & Conferences

Journal Publications

Anesti O., Papaioannou N., Gabriel C., Karakoltzidis A., Dzhedzheia V., Petridis I., Stratidakis A., Dickinson M., Horvat M., Snoj Tratnik J., Tsatsakis A., Karakitsios S., Sarigiannis A. ***An exposome connectivity paradigm for the mechanistic assessment of the effects of prenatal and early life exposure to metals on neurodevelopment***. Frontiers in Public Health (2022), *in press*.

Sy, M., Eleftheriadou, D., Jung, C., Lindtner, O., Karakitsios, S., Sarigiannis, D., Greiner, M. ***Assessment of the long-term exposure to lead in four European countries using PBPK modeling***. Exposure and Health (2022), *in press*.

D. Richterová, E. Govarts, L. Fábelová, C. Gabriel, D. Sarigiannis, ……. M.Esteban López, T. Göen, Ľ. Palkovičová Murínová, ***PFAS levels and determinants of variability in exposure in European teenagers – Results from the HBM4EU aligned studies (2014–2021).*** International Journal of Hygiene and Environmental Health, (2023), 247, 114057.

Tessa Schillemans, Nina Iszatt, Sylvie Remy, Greet Schoeters, Catherine Gabriel, Denis Sarigiannis, …….Nina Vogel, Maria Uhl, EvaGovarts, Agneta Åkesson, ***Cross-sectional associations between exposure to per- and polyfluoroalkyl substances and body mass index among European teenagers in the HBM4EU aligned studies.*** Environmental Pollution, (2023), 316, 120566.

Veronica van der Schyff, Jiri Kalina, Eva Govarts, Liese Gilles, Catherine Gabriel, Dimosthenis A. Sarigiannis, ……Lisa Melymuk, ***Exposure to flame retardants in European children — Results from the HBM4EU aligned studies.*** International Journal of Hygiene and Environmental Health, 247 (2023) 114070.

W. Bil, E. Govarts, C. Gabriel, D. Sarigiannis, …… M. Uhl, G. Schoeters, ***Approaches to mixture risk assessment of PFASs in the European population based on human hazard and biomonitoring data.*** International Journal of Hygiene and Environmental Health, 247 (2023) 114071.

Marx-Stoelting, P., Rivière, G., Luijten, M., Sarigiannis, D., Karakitsios, S., …..Rousselle, C., Sanders, P. ***A Walk in the PARC – Developing and Implementing 21st Century Chemical Risk Assessment in Europe***. Archives of Toxicology (2022), *in press*.

Gerofke, A., David, M., Schmidt, P., Vicente, J.L., Buekers, J., Gilles, L., Colles, A., Karakitsios, S., Sarigiannis, D., … ***From science to policy: How European HBM indicators help to answer policy questions related to phthalates and DINCH exposure***. International Journal of Hygiene and Environmental Health 247 (2022), 114073.

Bajard, L., Adamovsky, O., Audouze, K., Baken, K., Barouki, R., Beltman, J.P., Karakitsios, S., Sarigiannis, D…. ***Application of AOPs to assist regulatory assessment of chemical risks - Case studies, needs and recommendations***. Environmental Research (2022), 114650, 2022.

Lange, R., Vogel, N., Schmidt, P., Gerofke, A., Luijten, M., Bil, W., Santonen, T., Karakitsios, S., Sarigiannis, D…. ***Cumulative risk assessment of five phthalates in European children and adolescents***. International Journal of Hygiene and Environmental Health (2022) 246, 114052.

Persico, M.G., Gotti, A., Bugnoni, F., Visave, J., Karakitsios, S., Sakellaris, I., Sarigiannis, D. ***Air pollution health impact assessment and cost-benefit analysis of win-win policy solutions at the urban scale in the city of Milan***. Fresenius Environmental Bulletin (2022) 31:8A, 8315-8320.

Visave, J., Persico, M.G., Gotti,A., Bugnoni, F., Karakitsios, S., Sakellaris, I., Sarigiannis, D. ***Measuring personal exposure - a Milan case study***. J Fresenius Environmental Bulletin 31 (8 A), 8309-8314.

Papadaki, K., Karakitsios, S., Sarigiannis, D. ***Modeling of the total elimination half-life for environmental chemicals***. Environmental Research (2022), in press.

Domínguez-Romero, E., Komprdová, K., Kalina, J., Bessems, J., Karakitsios, S., Sarigiannis, D. A., &

Scheringer, M. ***Time-trends in human urinary concentrations of phthalates and substitutes DEHT and DINCH in Asian and North American countries (2009–2019)***. Journal of exposure science & environmental epidemiology (2022) https://doi.org/10.1038/s41370-022-00441-w

Gilles, L., Govarts, E., Rodriguez Martin, L., Andersson, A.-M., Appenzeller, B. M. R., Barbone, F., Castaño, A., Coertjens, D., Den Hond, E., Dzhedzheia, V., Eržen, I., López, M. E., Fábelová, L., Fillol, C., Franken, C., Frederiksen, H., Gabriel, C., Haug, L. S., Horvat, M., Schoeters, G. ***Harmonization of Human Biomonitoring Studies in Europe: Characteristics of the HBM4EU-Aligned Studies Participants***. International Journal of Environmental Research and Public Health (2022) 19(11), 6787.

Huuskonen, P., Karakitsios, S., Scholten, B., Westerhout, J., Sarigiannis, D. A., & Santonen, T. ***Health Risk Assessment of Ortho-Toluidine Utilising Human Biomonitoring Data of Workers and the General Population***. Toxics (2022) 10(5), 217.

Sakellaris, I. A., Bartzis, J. G., Neuhäuser, J., Friedrich, R., Gotti, A., & Sarigiannis, D. A. ***A novel approach for air quality trend studies and its application to european urban environments: The ICARUS project***. Atmospheric Environment (2022), 273, 118973.

Conference presentations (selected)

1. Frydas, D. Schultz, S. Karakitsios, D. Sarigiannis. **Whole Genome Microarray Analysis Reveals Possible Effect Of Di-2-Ethylhexyl Phthalate (DEHP) On Galactose Metabolism: Identification Of Ortholog Genes In Zebrafish And Human Cell Lines**. SAAOP 2022, VIRTUAL, 22/02/2022.
2. D.A. Sarigiannis, S. Karakitsios. **EU Chemical Strategy For Sustainability: Introducing Safe And Sustainable By Design Chemicals, Materials And Products**. 13rd Panhellenic Scientific Conference in Chemical Engineering, Patras, Greece, 2-4/06/2022.
3. N. Papaioannou, C. Gabriel, M. Dickinson, I. Petridis, J. Rovira, V. Kumar, M. Schuhmacher, S. Karakitsios, D. Sarigiannis. **EXHES study reveals the impact of prenatal exposure to metals, PFAS, organophosphates, and organochlorines on early child development**. 13rd Panhellenic Scientific Conference in Chemical Engineering, Patras, Greece, 2-4/06/2022.
4. D.A. Sarigiannis. **The EU Green Deal and climate action in Europe**. CEMEPE and SECOTOX Conference 2022, Mykonos, Greece, 5-9/06/2022.
5. D.A. Sarigiannis, M. Kermenidou, S. Karakitsios. **Refining PM exposure using low-cost portable sensor data and human respiratory tract deposition modelling**. CEMEPE and SECOTOX Conference 2022, Mykonos, Greece, 5-9/6/2022.
6. D.A. Sarigiannis, V. Kokkaraki, S. Karakitsios. **Toxicokinetic interactions of industrial chemical mixtures as internal exposure modifiers**. CEMEPE SECOTOX Conference 2022, Mykonos, Greece, 5-9/6/2022.
7. D.A. Sarigiannis, A. Gypakis, S. Karakitsios. **Towards The Development Of Safe And Sustainable By Design Chemicals, Materials And Products**. SuST 2022, Nisyros, Greece, 14-17/09/2022.
8. D.A. Sarigiannis, A. Gypakis, A. Gotti, S. Karakitsios. **The climate exposome**. SuST 2022, Nisyros, Greece, 14-17/09/2022.
9. D.A. Sarigiannis, A. Gotti, S. Karakitsios. **Life cycle-based health risk assessment of plastic waste**. SuST 2022, Nisyros, Greece, 14-17/09/2022.
10. D.A. Sarigiannis. Towards **COVID-19 Risk Emergency toolbox - an integrated system for reliable early alert and effective public health risk management**. CEMEPE and SECOTOX Conference 2022, Mykonos, Greece, 5-9/06/2022.
11. D.A. Sarigiannis. **The climate exposome: a new tool for addressing the health impacts of climate change**. CEMEPE and SECOTOX Conference 2022, Mykonos, Greece, 5-9/06/2022.
12. D.A. Sarigiannis, A. Gypakis, S. Karakitsios. **Towards Towards the development of safe and sustainable by design chemicals, materials and products**. 8th European Bioremediation Conference, Creta, Greece, 12-17/06/2022.
13. D.A. Sarigiannis. **A Computational and Testing Toolbox Towards Safe and Sustainable by Design Chemicals**. 9th IUPAC International Conference on Green Chemistry, Athens, Greece, 5-9/9/2022
14. C. Frantzidis, D. Mantziari, C. Plomariti, D.A. Sarigiannis, P. Bamidis. **Assessing the impact of environmental stressors on physical and mental health: A multi-modal big data perspective of the URBANOME approach**. ISES 2022, Lisbon, Portugal, 25-29/9/2022.
15. S. karakitsios, A. Karakoltzidis, D.A. Sarigiannis. **Urban dynamics and COVID-19 transmission**. ISES 2022, Lisbon, Portugal, 25-29/9/2022.
16. D.A. Sarigiannis, S. karakitsios. **Computational exposure modelling to support integrative health risk assessment**. ISES 2022, Lisbon, Portugal, 25-29/9/2022.
17. D.A. Sarigiannis, S. Karakitsios, A. Gypakis. **A Toolbox to Support the Development of Safe and Sustainable By Design Chemicals, Materials and Products**. 2022 AIChE Annual Meeting, Phoenix, 13-18/11/2022.
18. D.A. Sarigiannis, A. Karakoltzidis, S. Karakitsios. **Multi-Strain Integrated Modelling for COVID-19**. 2022 AIChE Annual Meeting, Phoenix, 13-18/11/2022.
19. D. Schultz, N. Papaioannou, T. Papageorgiou, C. Gabriel, I. Frydas, S. Karakitsios, D.A. Sarigiannis. **Investigating the neurodevelopmental exposome: a proposed transcriptomic and metabolomic analysis of mother-child cohort pairs in Portugal**. 2022 AIChE Annual Meeting, Phoenix, 13-18/11/2022.
20. D. Schultz, I. Frydas, N. Papaioannou, S. Karakitsios, D.A. Sarigiannis. **A comparison of three statistical methods for transcriptomic microarray analysis**. 2022 AIChE Annual Meeting, Phoenix, 13-18/11/2022.
21. N. Papaioannou, C. Gabriel, S. Karakitsios, D.A. Sarigiannis. **High-Performance bioinformatics workflow incorporating metabolomics data analysis, processing, and integration within the exposome concept**. 2022 AIChE Annual Meeting, Phoenix, 13-18/11/2022.
22. D.A. Sarigiannis, S. Karakitsios, A. Gotti. **Health impact assessment of climate change mitigation and adaptation policies**. ISEE 2022, Athens, Greece, 18-21/11/2022.
23. D.A. Sarigiannis, A. Gypakis, A. Stratidakis, F. Nikiforou, E. Renieri, S. Karakitsios. **INTEGRA LCA: A computational toolbox for safe and sustainable by design chemicals and materials**. ICT 2022, Maastricht, NL, 18-21/11/2022.
24. N. Papaioannou, C. Gabriel, O. Anesti2, S. Karakitsios, K. Polanska, W. Hanke, M. Horvat, D.A. Sarigiannis. **Adverse Outcome Pathway Network connecting glutamate metabolism, the TCA cycle, and amino acid metabolism with adverse neurodevelopmental outcomes in humans associated with exposure to metals**. ICT 2022, Maastricht, NL, 18-21/11/2022.

Invited talks (selected)

HELLENIC REPUBLIC
MINISTRY OF DEVELOPMENT AND INVESTMENTS

Invited talk at the Sectoral Scientific Council Of Engineering Sciences, organised by the Greek Republic, Ministry of Development and Investments, National Research, Technology & Innovation Council, held in Athens, Greece, February 8. Lecture titled "**Chemical-Biochemical-Biomedical Engineering**".

SABYDOMA

Invited talk at the workshop A Stakeholder's Perspective of Safe-and-Sustainable-by-Design (SSbD), organised by the SABYDOMA consortium, held virtyally, February 18. Lecture titled "**Safe and Sustainable-by-Design in the PARC project**".

Yale SCHOOL OF PUBLIC HEALTH

Invited talk at the Public Health Toxicology Lectures, held virtually, organised by the Yale school of public health, New Heaven, USA, March 10. Lecture titled "**Exposome Science**".

13 Πανελλήνιο Επιστημονικό Συνέδριο Χημικής Μηχανικής

Invited talk at the 13th Panhellenic Scientific Conference of Chemical Engineering, held in Patra, Greece, June 3. Lecture titled "**Systems biology modelling and COVID-19 pandemic dynamics**".

ERFC

Invited talk at the Training workshop on Air Quality and Health Organized by ERFC, held in Thessaloniki, Greece, July 19. Lecture titled "**Air Quality & Health Index, Post-pandemic era**".

KIT
Karlsruher Institut für Technologie

Invited talk at the webinar "Sensors for Air Quality Monitoring", held virtually, organised by the Karlsruhe Institute of Technology, held in Garmisch-Partenkirchen, Germany, July 20. Lecture titled "**Refined PM personal exposure monitoring using wearable sensors**".

Yale SCHOOL OF PUBLIC HEALTH

Invited talk at the Summer Research Experience in Environmental Health Sciences, held virtually, organised by the Yale school of public health, New Heaven, USA, July 25. Lecture titled "**Bootcamp 5: Urban Health**".

Yale SCHOOL OF PUBLIC HEALTH

Invited talk at the Summer Research Experience in Environmental Health Sciences, held virtually, organised by the Yale school of public health, New Heaven, USA, July 27. Lecture titled "**A biological systems connectivity framework for identification of effect biomarkers for endocrine disruptors using cross-omics data and systems biology modelling**".

IUPAC
INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

Invited talk at the 9th IUPAC International Conference on Green Chemistry, held in Athens, Greece, September 9. Lecture titled "**A Computational and Testing Toolbox Towards Safe and Sustainable by Design Chemicals**".

efsa
European Food Safety Authority

Invited talk at the Thematic Workshop on Biomarkers of Effect, organised by EFSA, held in Parma, Italy, September 22. Lecture titled "**A biological systems connectivity framework for identification of effect biomarkers for endocrine disruptors using cross-omics data and systems biology modelling**"

ΠΕΡΙΦΕΡΕΙΑΚΟΣ ΣΥΝΔΕΣΜΟΣ ΦΟΡΕΩΝ ΔΙΑΧΕΙΡΙΣΗΣ ΣΤΕΡΕΩΝ ΑΠΟΒΛΗΤΩΝ
ΦΟΔΣΑ
ΚΕΝΤΡΙΚΗΣ ΜΑΚΕΔΟΝΙΑΣ

Invited talk at the Evaluation Symposium for the existing Plan of the Region of Central Macedonia for Adaptation to Climate Change, held in Thessaloniki, Greece, November 5. Lecture titled "**Readiness of organizations and citizens for Adaptation to Climate Change – Forecasts of the Central Macedonia PESKPA**".

Laboratory Personnel

Dimosthenis A. Sarigiannis, Director

M.Sc., PhD (University of California, Berkeley, USA) is Professor specialising on environment and health engineering at the Department of Chemical Engineering of the Aristotle University of Thessaloniki and the institute for Advanced study of Pavia. He is also senior scientist at the Chemical Assessment and Testing unit of the Institute for Health and Consumer Protection at the European Commission's Joint Research Centre (currently on leave). At the European Commission he has served as Scientific Coordinator of the IHCP, Action Leader for Consumer Product Safety and Quality and Community Reference Laboratory for Food Contact Materials, Action Leader for Human Exposure to Environmental Stressors and Health Effects and for Assessment of Chemicals at the European Chemicals Bureau, Scientific Assistant to the JRC Director General, Strategy Manager of the IHCP and as science advisor to the Greek Minister of the Environment. He was a principal contributor to the REACH Regulation and to the Environment and Health Action Plan and is currently member of the Health and Environment Working Party and of the Health Security Committee. He has been pioneering efforts to coupling biology-based modelling with toxicogenomics discovery systems for developing a mechanistically based understanding of the health risk of environmental chemical mixtures.

Dr. Spyros Karakitsios is an environmental health scientist, with studies in physics (B.Sc.), chemistry (M.Sc.) and biology (PhD) with expertise in exposure biology.

Dr. A Gotti is a Physicist of the University of Milan with over 25 years of experience in health impact assessment, data analysis, exposure and PBPK modelling.

Dr. Ioannis Zarkadas is an Environmental Engineer from the University of Leeds (UK), his research activities focus on waste management, anaerobic digestion, LCA.

Dr. Catherine Gabriel is a Chemical Engineer, with studies in Advanced Chemical Engineering (M.Sc.) and Inorganic Chemistry (PhD), with expertise in analytic chemistry.

Dr. Ilias Frydas is a Molecular Virologist and holds a PhD from the Veterinary Medicine School of the Ghent University in Belgium with expertise in NAMs.

Dr. Marianthi Kermenidou (Post-Doc Researcher) is Environmental Engineer, with a MSc degree, with expertise in environmental monitoring and analysis.

Dr. Anthoula Chatzimpaloglou is a chemist with a focus on human biomonitoring and development of analytical methods in biological or environmental samples.

Dr Anastasia Georgiou is a molecular biologist with expertise in reproductive and developmental biology, cell biology and gene expression analysis.

Dr. Elisavet Renieri, is a biologist and holds a PhD in Toxicology related to human health risk assessment for cumulative exposure to chemicals. She is also European Registered Toxicologist (ERT).

Nafsika Papaioannou is a Chemical Engineer. Her expertise lies in analysing complex omics data into biological pathway/network, with a particular focus on EDCs.

Achilleas Karakoltzidis is a Chemical Engineer. His research interests are mainly focus on Systems Biology modeling combining AI, and Process Safety.

Maria Kouroutzi is a Materials Engineer, focusing on the development of Safe and Sustainable building materials.

Fotini Nikiforou in Chemical Engineer. Her research activities focus on risk, exposure, and sustainability assessment with experience in omics data analysis.

Thanasis Papageorgiou is a PhD Student Researcher, with studies in Chemistry (B.Sc.) and in Toxicology (M.Sc.) from UoTh, focusing on omics analysis.

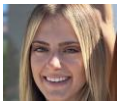
Alkistis Kevrekidou is a Chemical Engineer with studies in biomolecular engineering (M.Sc.), focusing on risk assessment and on circular economy.

Dayna Schultz is a molecular and analytical toxicology (MSc). Her research focuses on human toxicology, omics analysis, computational toxicology, and bioinformatics.

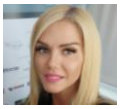
George Sarigiannis is an informatics scientist with particular expertise on data management, data security and GDPR implementation.

Antonis Stratidakis is Materials Engineer, with expertise in Toxicology, and neurodevelopmental disorders adverse outcome pathways development.

Ioanna Kantara is a Psychologist from the Aristotle University of Thessaloniki and she holds a Master in Public Health.



Maria Dolapsaki is a MSc Student in Public Health Nutrition at Medical School, and she has a diploma in Nutritional Sciences and Dietetics of International Hellenic University.



Niki Mistou is an administrative assistant with more than 20 years of working experience in administrative and financial management in SMEs and academy.